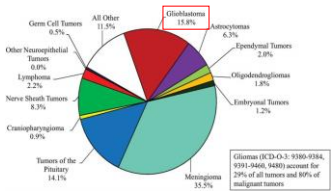
RADIOMICS, RADIO-GENOMICS, RADIO-PATHOMICS: CONNECTING THE DOTS TOWARDS PERSONALIZED MEDICINE IN BRAIN TUMORS

Pallavi Tiwari, Ph.D.
Assistant Professor, Biomedical Engineering
Director, Brain Image Computing Laboratory
Case Western Reserve University

Brain Tumors– Prevalence and Incidences



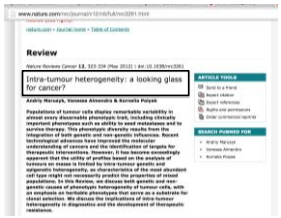
- 18,600 brain tumor deaths/year in the US.
- GBM most aggressive. Median survival of 12 months [21.3 years of life lost].
- Current treatment: maximal surgical resection, radiotherapy, and concomitant and adjuvant chemotherapy with temozolomide.
- Poorly understood complex micro-enviornmnent (hanahan and Weinberg 2000).

Precision Medicine

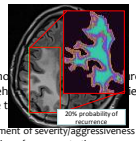
An emerging approach for disease treatment and prevention that takes into account individual variability in genes, environment, and lifestyle for each person.

FUNDAMENTAL QUESTIONS

- WHO TO TREAT?
- HOW TO TREAT?
- WILL THE TREATMENT WORK?

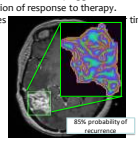

Review

Intra-tumour heterogeneity: a looking glass for cancer?



Intra-tumo res
tumor beh ent's
response t

- Assessment of severity/aggressiveness
- Prediction of response to therapy.
- Changes time.

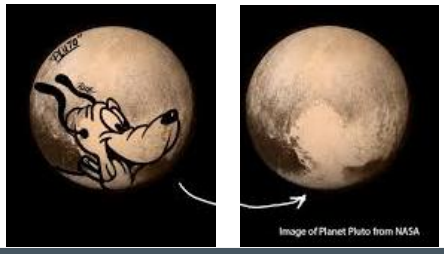


6

Radiomics: Study of capturing subtle differences in imaging that are not visually appreciable

- Local Texture-based Radiomics Features
- Global Structural Radiomics Features

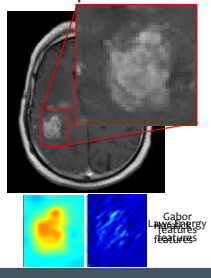
Apophenia: Tendency to "unlock" hidden meaningful patterns



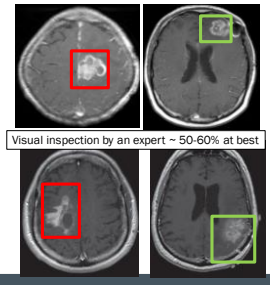
Radiomics: Local Image Feature Representations

- What is texture?
  - Capturing local intensity statistics within small neighborhoods, quantify smoothness, heterogeneous appearance etc.
- Feature types:
  - 1st order Statistical: Mean, range
  - 2nd order Statistical: Statistics based on co-occurring intensities
  - Laws features: characterize edges, waves, ripples
  - Gabor: Multi-scale, multi-orientation filter responses

J.C. Russ. The Image Processing Handbook. CRC Press, 5th edition, 2007.

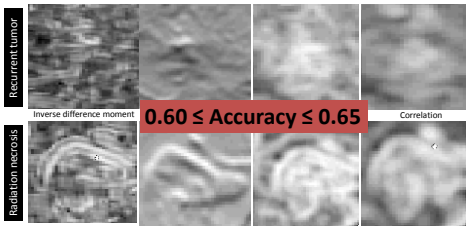


Can we distinguish radiation effects from tumor recurrences?



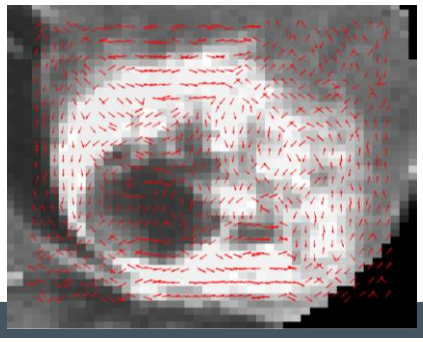
Visual inspection by an expert ~ 50-60% at best

Texture descriptors for necrosis versus tumor recurrence



Tiwari et al, SNO (2013), SPIE 2014

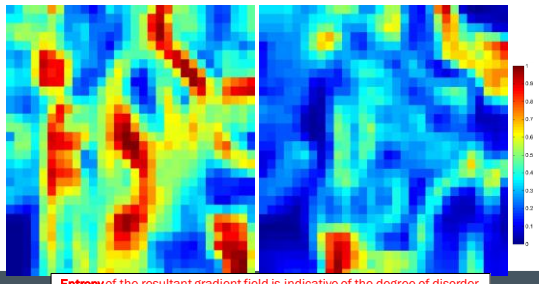
Sub-visual texture feature - COLLAGE



*patented

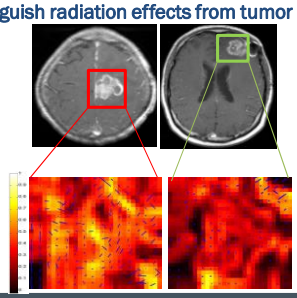
COLLAGE: entropy of localized gradient orientations

*Patented

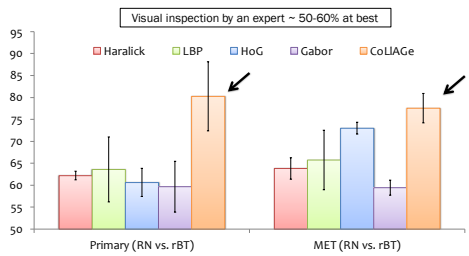


Entropy of the resultant gradient field is indicative of the degree of disorder in the pathology

Can we distinguish radiation effects from tumor recurrences?

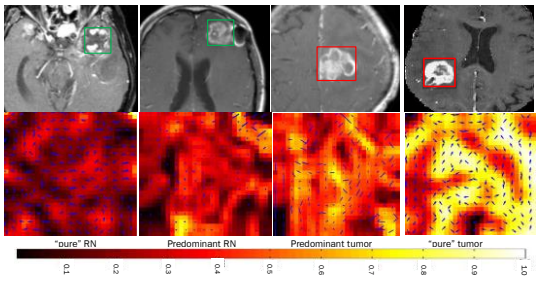


Can we distinguish radiation effects from tumor recurrences?



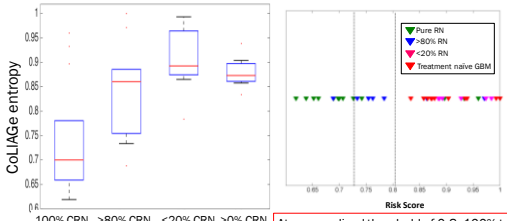
Prasanna, Tiwari et al, MICCAI (2014)
Nature Sci Reports (under review)

Quantifying grades of cerebral radiation necrosis vs. Tumor



Prasanna et al. ISMRM, SNO (2015)

COLLAGE discriminate necrosis from recurrent cancer

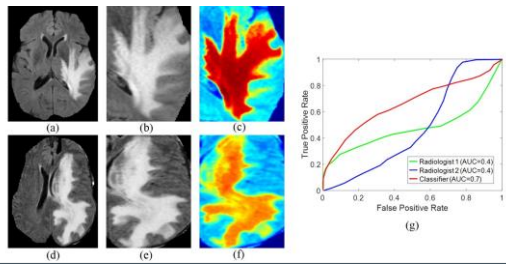


Pathology	CoLIAGe entropy
'pure' CRN	0.74 +/- 0.11
'predominant' CRN	0.84 +/- 0.10
'predominant' tumor	0.91 +/- 0.06
Treatment-naïve GBM	0.88 +/- 0.03

At a normalized threshold of 0.8, 100% tumor patients and 67% CRN patients were correctly identified using CoLIAGe values

Prasanna et al. ISMRM (2015)

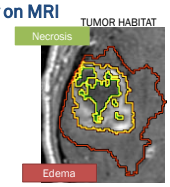
Human-machine comparison for radiation necrosis vs. recurrent tumors



Prasanna et al. RSNA (2016)

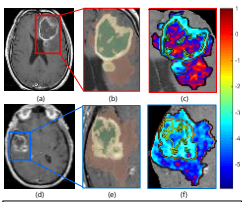
Lesion "habitats": mapping disease heterogeneity on MRI

- Current methods employ a global volumetric measure (McDonald criteria).
- 10% cells outside solid tumors are tumor. Complex micro-environment.
- Habitat is defined as different sub-compartments within and around the lesion

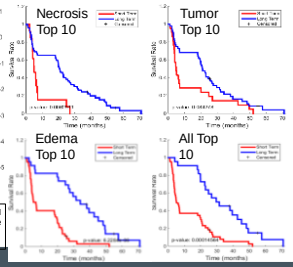


Hypothesis: These sub-compartments together in conjunction create a "**microcosm**" for tumor growth and contribute in survival.

GBM: Radiomic Markers Across Tumor Habitat on Treatment-Naïve MRI can Predict Survival in GBM Patients

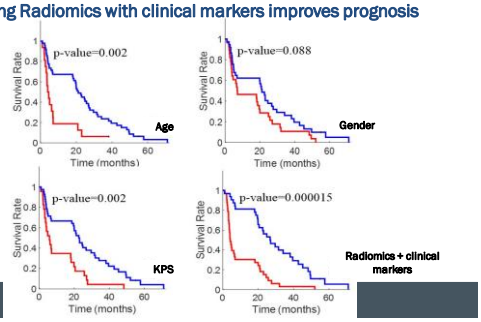


Gd-T1 MRI for STS (a) and LTS (d). Compartmental segmentations for necrosis, tumor, edema (b, e). Qualitative representation of Haralick Entropy feature (c, f).



Tiwari et al., RSNA (2015)

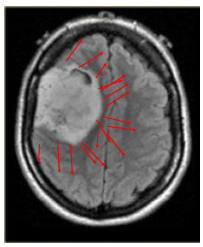
Combining Radiomics with clinical markers improves prognosis

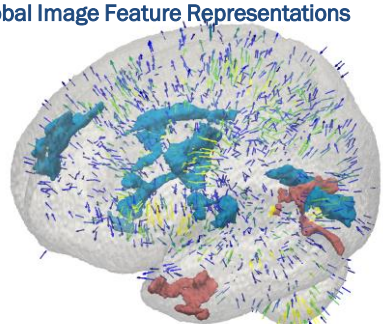


Radiomics: Study of capturing subtle differences in imaging that are not visually appreciable

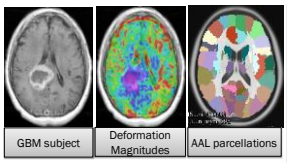
- Local Texture-based Radiomics Features
- Global Structural Radiomics Features

Radiomics: Global Image Feature Representations





Deformation due to GBM mass-effect prognostic of overall survival



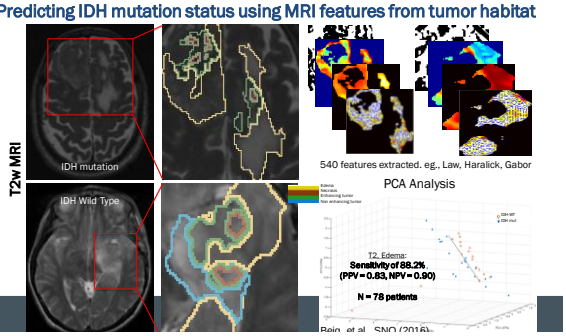
- Correlate deformation distribution within each AAL cortical/subcortical regions with survival (days).
- N=30 left-hemispheric tumors, n=24 right-hemispheric tumors.
- Left-hemispheric (14 short-term, 12 long-term), Right-hemispheric (12 short-term, 12 long-term)

Deformation in somato-sensory, visual and sematic processing areas, primary auditory cortices and memory areas due to right-hemispheric tumor mass-effects may be prognostic of overall survival.

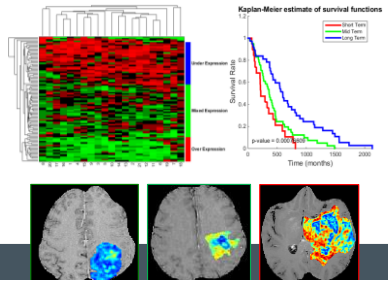
Mitra et al., SNO (2016)

Radio-genomics: Predicting mutational status, molecular subtype, genetic pathways

Predicting IDH mutation status using MRI features from tumor habitat



Radio-genomic analysis of hypoxia pathway reveals MRI features predictive of overall survival in glioblastoma



Radio-pathomics: Understanding the biological underpinning of tumor on imaging

Radio-pathomics for radiation necrosis vs. recurrent tumors – Correlating COLLAGE to known pathological processes

Pathologic feature number	Feature type
P1	Vessel-wall thickening
P2	Zonal necrosis
P3	Demyelination

CETD number	Feature type
R1	Entropy
R2	Energy
R3	Inertia
R4	Inv. Diff. Moment
R5	Correlation
R6	Meas Of Corr 1
R7	Meas Of Corr 2
R8	Sum Average
R9	Sum Variance
R10	Sum Entropy
R11	Difference Average
R12	Difference variance
R13	Difference entropy

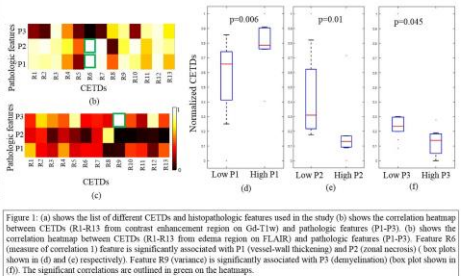


Figure 1: (a) shows the list of different CETDs and histopathologic features used in the study (b) shows the correlation heatmap between CETDs (R1-R13 from contrast enhancement region on Gd-T1w) and pathologic features (P1-P3). (b) shows the correlation heatmap between CETDs (R1-R13 from edema region on FLAIR) and pathologic features (P1-P3). Feature R6 (measure of correlation 1) feature is significantly associated with P1 (vessel-wall thickening) and P2 (zonal necrosis) (box plots shown in (d) and (e) respectively). Feature R9 (variance) is significantly associated with P3 (demyelination) (box plot shown in (f)). The significant correlations are outlined in green on the heatmaps.

CONCLUDING REMARKS

- Radiomics have the potential to complement personalized prognosis, and treatment evaluation to address questions such as:
  - Who to treat?
  - How to treat?
  - When to treat?
  - Did the treatment work?
- Radio-genomics, radio-pathomics allow interactions across length scales and provide mechanisms to identify “image biomarkers” for prognosis and treatment evaluation.
- Radiomic techniques not only allow for bench-to-bedside personalized medicine solutions, but also provide reliable and reproducible tools for feature discovery.

Acknowledgements

Collaborators:

- Dr. Anant Madabhushi (Director, CCIPD)
- Dr. Lisa Rogers (UH)
- Dr. Leo Wolansky (UH)
- Dr. Mark Cohen (UH)
- Dr. Marta Couce (UH)
- Dr. Andrew Sloan (UH)
- Dr. Shabbar Danish (UMDNJ, Rutgers)
- Dr. Raymond Huang (BWH, Boston)
- Dr. Marco Pinho (UT Southwestern)
- Dr. T.C. Lam (Tuen Mun Hospital, China)
- Dr. Susann Brady-Kalnay (CWRU)

Funding:

- Case Comprehensive Cancer Center
- Coulter Translational Phase I, II, III Award
- Ohio Third Frontier
- NSF i-corps

http://bric-lab.com
http://ccipd.case.edu

THANK YOU FOR YOUR ATTENTION