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

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 BRAIN TUMORS – PREVALENCE AND INCIDENCES

- 18,600 brain tumor deaths/year in the US.
- GBM most aggressive. Median survival of 12 months (2.3 years of life lost).
- Current treatment: maximal surgical resection, radiotherapy, and concomitant and adjuvant chemotherapy with temozolomide.
- Poorly understood complex microenvironment (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?
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, quantifying 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
  - Haralick features
  - Laws Energy
  - Gabor features
Can we distinguish radiation effects from tumor recurrences?

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

Texture descriptors for necrosis versus tumor recurrence

0.60 ≤ Accuracy ≤ 0.65

Sub-visual texture feature - COLLAGE

*patented
Can we distinguish radiation effects from tumor recurrences?

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

<table>
<thead>
<tr>
<th>Method</th>
<th>Primary (RN vs. rBT)</th>
<th>MET (RN vs. rBT)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Haralick</td>
<td>55.6 ± 1.2</td>
<td>58.3 ± 1.5</td>
</tr>
<tr>
<td>LBP</td>
<td>56.8 ± 1.1</td>
<td>59.2 ± 1.3</td>
</tr>
<tr>
<td>HoG</td>
<td>57.1 ± 1.2</td>
<td>59.5 ± 1.4</td>
</tr>
<tr>
<td>Gabor</td>
<td>57.4 ± 1.3</td>
<td>59.8 ± 1.5</td>
</tr>
<tr>
<td>CollAGE</td>
<td>58.0 ± 1.4</td>
<td>60.2 ± 1.6</td>
</tr>
</tbody>
</table>

Can we distinguish radiation effects from tumor recurrences?
Quantifying grades of cerebral radiation necrosis vs. Tumor

CollAGE discriminate necrosis from recurrent cancer

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

Human-machine comparison for radiation necrosis vs. recurrent tumors

Prasanna et al. ISMRM (2015)
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

- 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 semantic 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

540 features extracted. e.g., Law, Haralick, Gabor
PCA Analysis
T2, Edema:
Sensitivity of 88.2%
(PPV = 0.83, NPV = 0.90)
N = 78 patients
Beig et al., SNO 2016.

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

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.
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