MRI quantification of tumor heterogeneity for diagnosis and response assessment of bladder cancer

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Bladder Cancer Research

• Collaboration efforts between
  – Wright Center of Innovation in Biomedical Imaging
  – Urologists and Medical Oncologists at OSU

• Goals
  – To develop an advanced MRI protocol with data analytical tools to improve
    • Localization/detection
    • Tumor and node staging
    • Early assessment of neoadjuvant chemotherapeutic response
Morphologic MRI

Anatomical imaging: high soft tissue contrast and spatial resolution
Quantitative MRI

- **Dynamic contrast-enhanced MRI (DCE-MRI):**
  - To quantify microcirculation (micro-vascularity and permeability)

- **Diffusion-weighted MRI (DWI):**
  - To quantify water diffusion (micro-cellularity)

- **Amide proton transfer MRI (APT-MRI):**
  - To quantify the mobile protein level
Quantitative DCE-MRI

- Passage of a Gd-based contrast agent (CA) into tumor micro-vessels results in quantifiable signal enhancement.

60 dynamic scans
Single dose (0.1 mmol/kg body weight)
at 0.5 ml/s IV rate
Quantitative DCE-MRI

- Model-based pharmacokinetic parameters
  - $Amp$: amplitude of signal enhancement
  - $k_{ep}$: exchange rate of CA from the EES to plasma
DCE-MRI with k-means clustering

• To assess heterogeneity in microcirculation characteristics
  – Heterogeneous distribution of micro-vasculature ($Amp$) and permeability ($k_{ep}$)

• To identify a biomarker for cancer diagnosis
k-means clustering of Amp and $k_{ep}$

- A tumor is segmented in 3 clusters

**T2W-MRI**

**T1W DCE-MRI**

Cluster 1: Low Amp, low $k_{ep}$

Cluster 2: High Amp, low $k_{ep}$

Cluster 3: Low Amp, high $k_{ep}$
Characterization of heterogeneity

T1W DCE-MRI

- Quantitative measurements:
  - Cluster 1 volume fraction (VF)
  - Cluster 2 VF
  - Cluster 3 VF
Results: response assessment

At mid-treatment point, responders and non-responders showed the opposite changes in microcirculation characteristics.

Responder

Non-responder

J. Magn Reson Imaging 2014, Nguyen et. al
Cluster VF as a classifier of response

- At mid-treatment point, all the changes in 3 cluster VFs were statistically significant (P ≤ 0.005)
- Cluster 2 VF was the best classifier
Results: tumor staging

- Tumor stages were found to be correlated with 3 cluster VFs

Stage T1

Stage T2

Stage T3

Stage T4
Summary

• DCE-MRI with k-means clustering
  – To characterize the heterogeneity of tumor microcirculation
  – Cluster VF can be used as a quantitative read-out
  – Potential biomarkers for response assessment and tumor staging
Future directions

- DCE-MRI with k-means clustering
  - Patient accrual to validate/identify a biomarker(s)
  - Apply the methodology to differentiate malignant from benign tissues

- Other applications
  - Data analysis tools: Histogram analysis
  - MRI futures: micro-cellularity (DWI), mobile protein levels (APT-MRI)
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