Technical Overview of Diffusion-Related MRI in Rectal Cancer

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Disclosure: TLC is co-inventor of DWI-related IP assigned to and managed by the University of Michigan

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Diffusion-related Technologies
Applicable to Rectal Cancer Clinical Trials

Subjective:
• DWI (ADC)

Quantitative:
• ADC
• IVIM
• DKI ("non-gaussian" diffusion models)
Routine UM Rectal CA MRI Protocol For (Re)Staging

Key sequences - preferred @3T:

• T2WT FSE hi-res (0.4 x 0.7 x 3mm)
  - Sag / Ax-Oblique / Cor-Obl

• Ax oblique DWI (2 x 2 x 3mm)
  - b-values = 0, 100, 800, 1600 s/mm²

• No IV-contrast
Staging (template) - DisTANCE*

- Distance(s)
  - Including from anal verge
    - Low: 0-5 cm
    - Mid: 5-10 cm
    - High: 10-15 cm

- Craniocaudal extent of tumor

- Circumferential extent of tumor

Recommendations - Role of DWI in Rectal CA

European Society of Gastrointestinal and Abdominal Radiology (ESGAR):

- Protocol should include 2D T2-wt in 3 planes and a DWI with high b-value of ≥ 800
- DWI and ADC maps should be assessed visually
- Quantitative ADC measurements are not routinely advised in daily practice due to a lack of standardized protocols and validated thresholds
- DWI is recommended for restaging of the yT-stage
- DWI alone may not reliably identify patients with complete response


Recommendations - Role of DWI in Rectal CA

American College of Radiology (ACR):

- MRI accuracy is dependent on obtaining high-resolution T2-wt images (0.5-0.6 mm in-plane voxel size) that are perpendicular to the plane of the tumor.
- Addition of qualitative DWI to conventional high-resolution T2-wt improves the diagnostic performance of MRI in the evaluation of pathologic complete response.
- Only moderate diagnostic accuracy improvement going from 1.5 T to 3 T.
- Reduced-FOV DWI may demonstrate better image quality than full-FOV DWI.

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Quantitative ADC in ChemoRad Tx Response Assessment

Studies show higher mean post-Tx ADC values in complete responders compared to patients with residual disease.

Quantitative ADC in ChemoRad Tx Response Assessment

While post-Tx higher ADC values were seen in complete responders, fibrosis after CRTx may also show as a hypointensity on ADC & may be misinterpreted as a viable tumor.

Technical Improvement by Reduced FOV (rFOV) DWI

- rFOV DWI provided significantly better IQ & lesion conspicuity than full FOV DWI
- DWI (ADC) can be used in evaluation of histological T staging of rectal cancer
- rFOV had no significant impact on ADC values

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**Beyond ADC: Non mono-exponential diffusion biomarkers**

- Intra Voxel Incoherent Motion (IVIM)

\[
\frac{S(b)}{S_0} = f_p \cdot e^{-b \cdot D^*} + (1 - f_p) \cdot e^{-b \cdot D_{tiss}}
\]

- perfusion fraction \( f_p \)
- blood pseudo-diffusion \( D^* \)
- tissue diffusion \( D_{tiss} \)
**Beyond ADC: Non mono-exponential diffusion biomarkers**

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- **Kurtosis**
  \[
  \frac{S(b)}{S_0} = e^{[-b \cdot D_k + \frac{K}{6} (b \cdot D_k)^2]}
  \]

- **Stretched Exponential**
  \[
  \frac{S(b)}{S_0} = e^{-(b \cdot DDC_\alpha)^\alpha}
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Beyond ADC: Non mono-exponential diffusion biomarkers

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- **IVIM & Kurtosis**
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  \]

Be wary of false apparent kurtosis due to noise floor effects.
IVIM of Rectal CA


- High b-sampling of perfusion regime for fair assessment of $D^*$ & $f_p$ metrics
- $D_{tiss}$ & ADC increased post-CRTx ($N=31$, $p<0.01$)
- $D_{tiss}$ & ADC higher in good vs poor resp ($p<0.02$)
- No improvement in $D_{tiss}$ & ADC histogram metrics
- $D^*$ & $f_p$ did not change post-CRTx
- $D^*$ & $f_p$ not useful in assessing response

- DKI & ADC of untreated patients (N = 56) with histopathology grading (WHO & PDCs)
- ADC and $D_K$ (diffusivity) negatively correlated w/ histopathologic grade
- Kurtosis positively correlated w/ histopath grade
- Kurtosis outperformed ADC & $D_K$ in separating high- & low-grade & high-grade rectal adenocarcinoma
Summary - Inclusion of Diffusion MRI in Future Clinical Trials?

Usual Considerations and Challenges:

- Evidence of potential value-added by DWI? ✓ Yes
- Require additional DWI acquisition beyond SOC? ✓ No
- Consensus on DWI acquisition & parameters? ~ Reasonable agreement
- Require vendor involvement for new DWI methods or standardization? ✓ No
- Is target anatomy prone to DWI artifact due to:
  - Poor fat-suppression? ✓ No
  - Patient motion? ✓ No
  - Geometric distortion / eddy currents / shim? ✓ No
  - Gradient nonlinearity? ✓ No
- Issues with lesion segmentation? X Yes, as always
- Choice of DWI-related metrics?
  - DWI ✓ Yes
  - ADC ✓ Yes
  - IVIM (perfusion, $f_p$ and $D^*$) X Not compelling & is costly
  - DKI promising w/ only requirement $b \approx 1600$ ~ Worth it to include $b \approx 1600$
- Practical: site qualif, phantoms, analysis SW ... ? ✓ Phantoms & SOP exist, ~ SW
Thank You!

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