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)

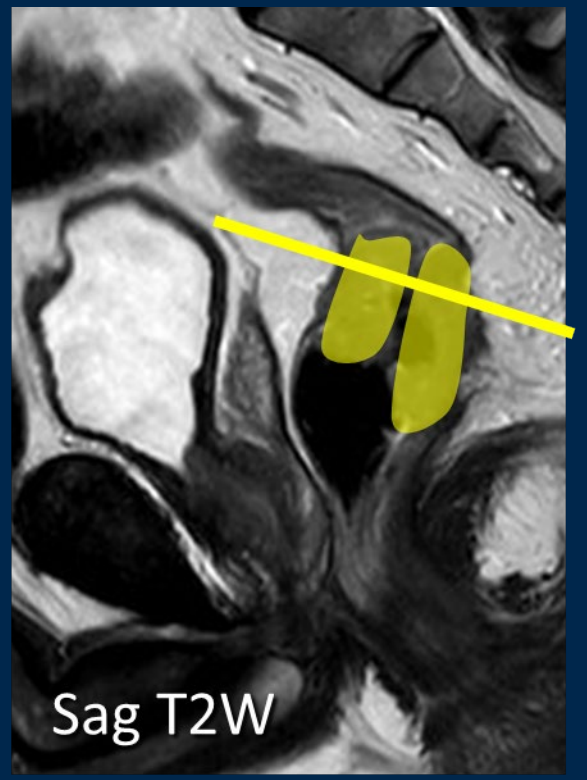
Quantitative:

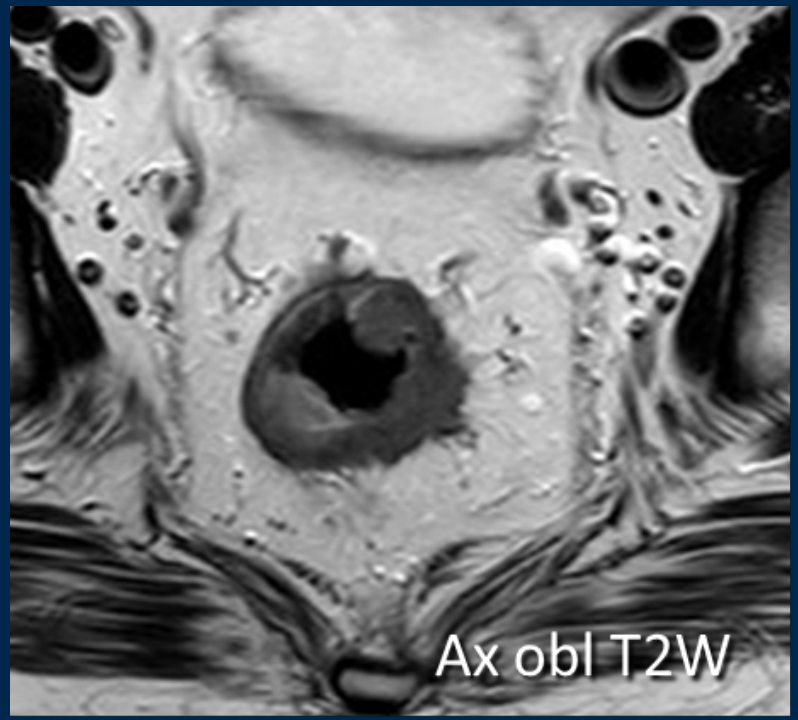
- ADC
- IVIM
- DKI (“non-gaussian” diffusion models)

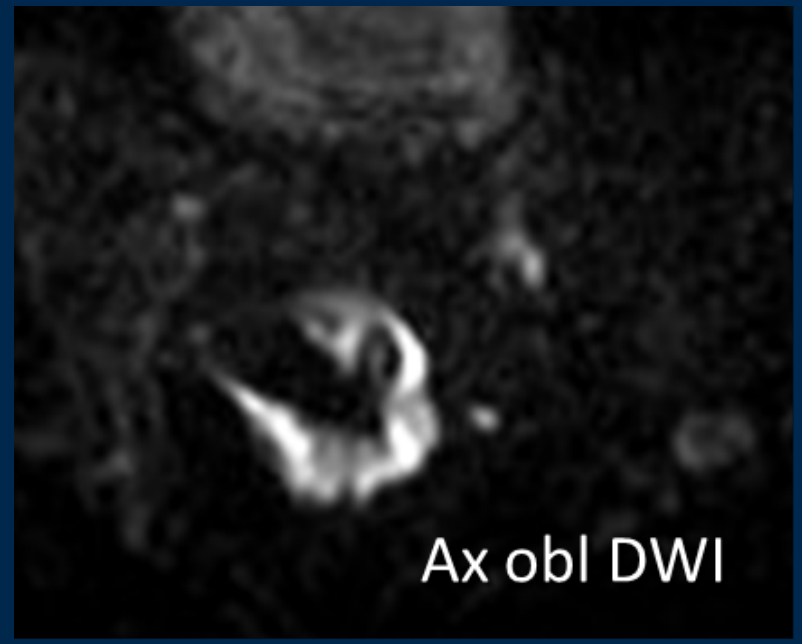
Routine UM Rectal CA MRI Protocol For (Re)Staging

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/mm^2
- No IV-contrast



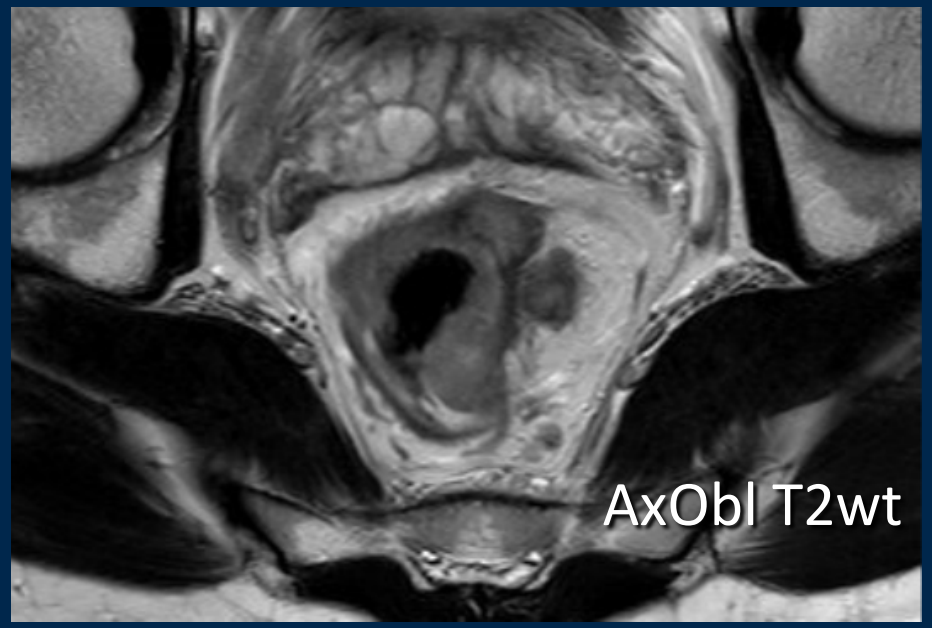


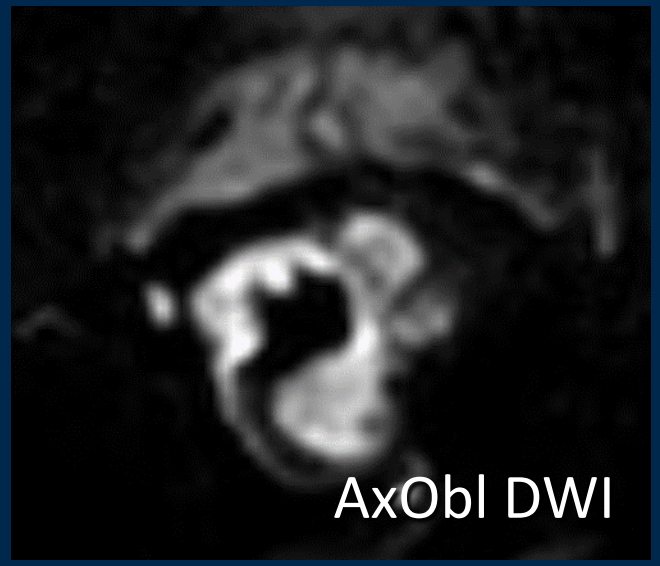


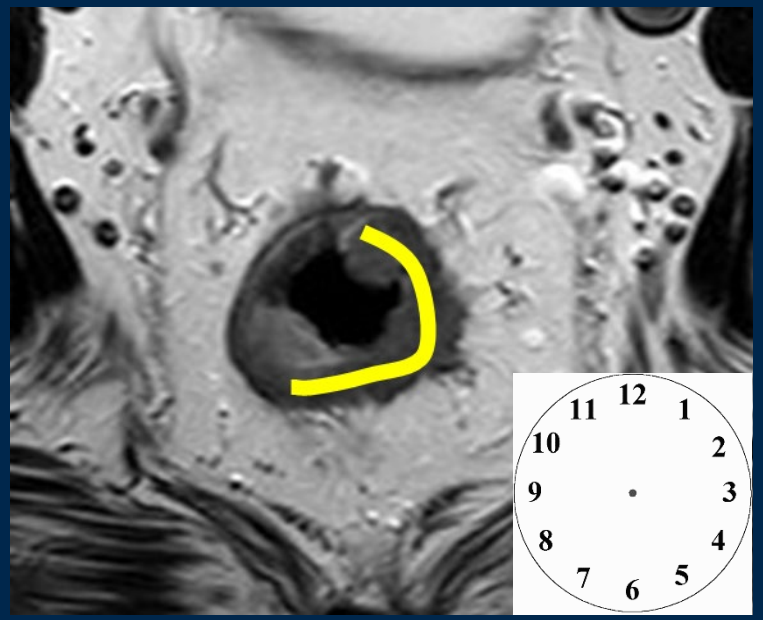
Staging (template) – DisTANCE*

- 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

* Nougaret, S., et al., *The use of MR imaging in treatment planning for patients with rectal carcinoma: have you checked the "DISTANCE"?* Radiology, 2013. **268**(2): p. 330-44.







Recommendations – Role of DWI in Rectal CA

European Society of Gastrointestinal and Abdominal Radiology (ESGAR):

Beets-Tan, R.G., et al., Magnetic resonance imaging for the clinical management of rectal cancer patients: recommendations from the 2012 European Society of Gastrointestinal and Abdominal Radiology (ESGAR) consensus meeting. Eur Radiol, 2013. 23(9): p. 2522-31.

Beets-Tan, R.G.H., et al., Magnetic resonance imaging for clinical management of rectal cancer: Updated recommendations from the 2016 European Society of Gastrointestinal and Abdominal Radiology (ESGAR) consensus meeting. Eur Radiol, 2018. 28(4): p. 1465-1475.

- 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):

Expert Panel on Gastrointestinal, I., et al., ACR Appropriateness Criteria(R) Staging of Colorectal Cancer: 2021 Update. J Am Coll Radiol, 2022. 19(5S): p. S208-S222.

- 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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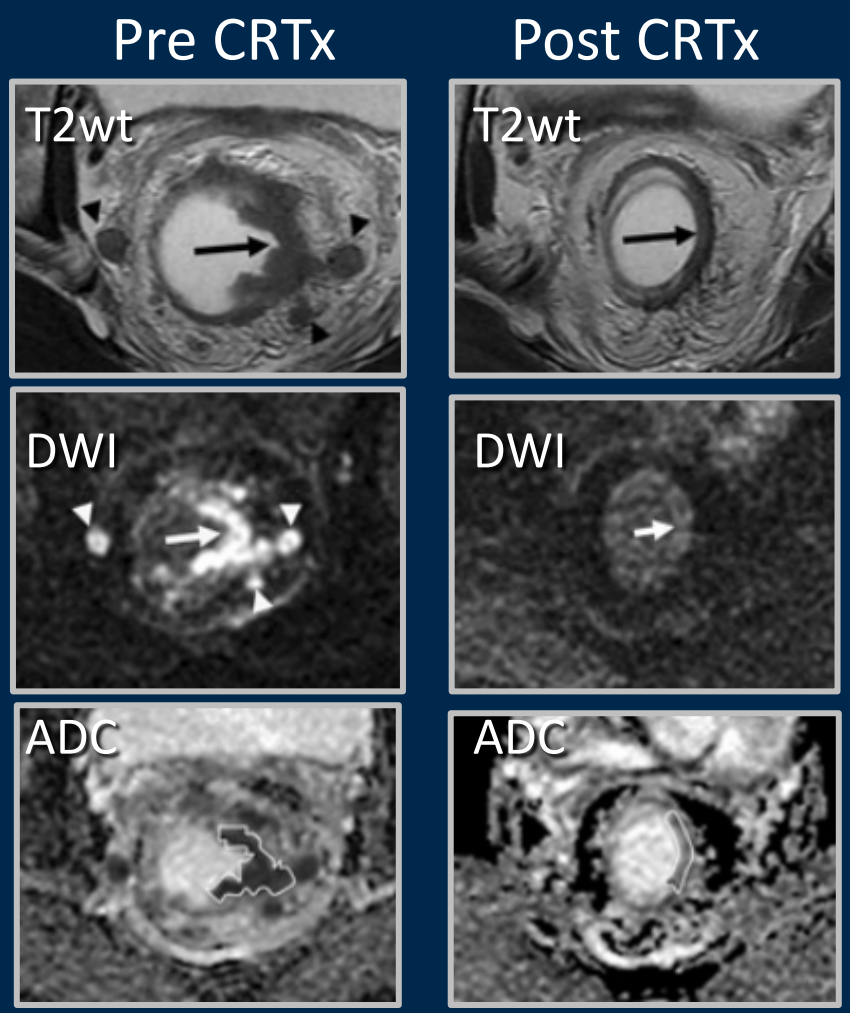
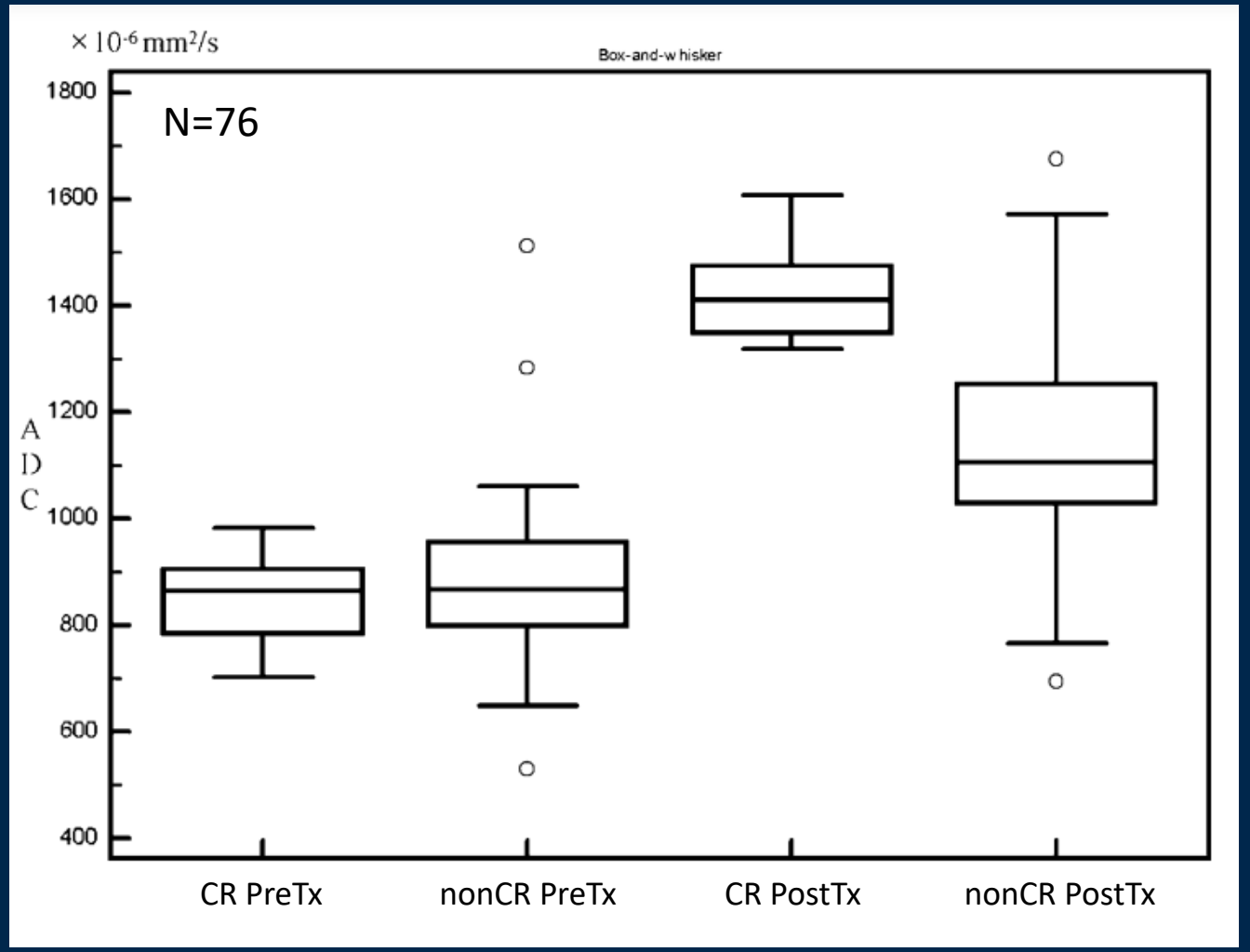
Quantitative ADC in ChemoRad Tx Response Assessment

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

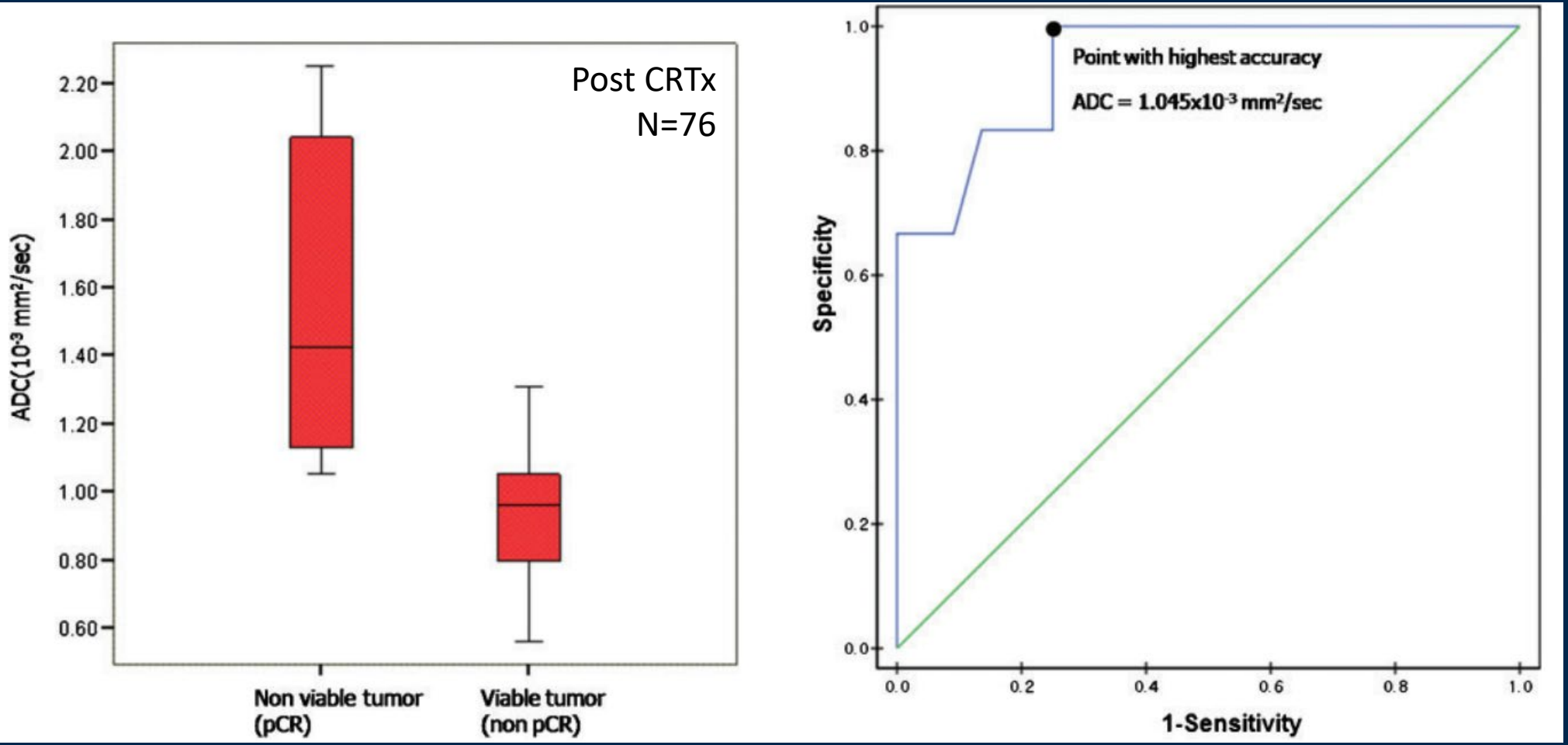




Kim, S.H., et al., Apparent diffusion coefficient for evaluating tumour response to neoadjuvant chemoradiation therapy for locally advanced rectal cancer. Eur Radiol, 2011. 21(5): p. 987-95.

Quantitative ADC in ChemoRad Tx Response Assessment

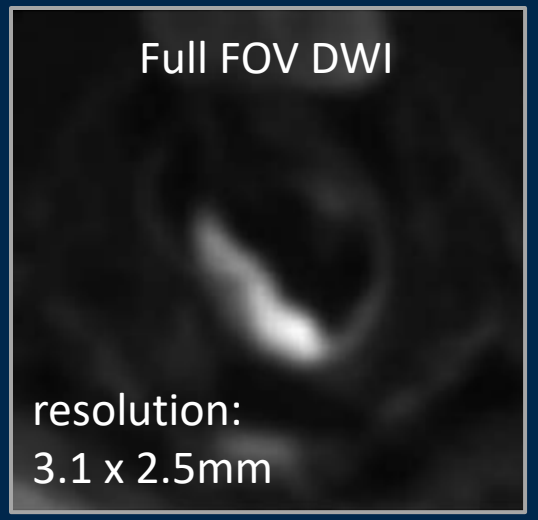
While post-Tx higher ADC values were seen in complete responders, fibrosis after CRTx may also show as a hypointensity on ADC & may be misinterpreted as a viable tumor

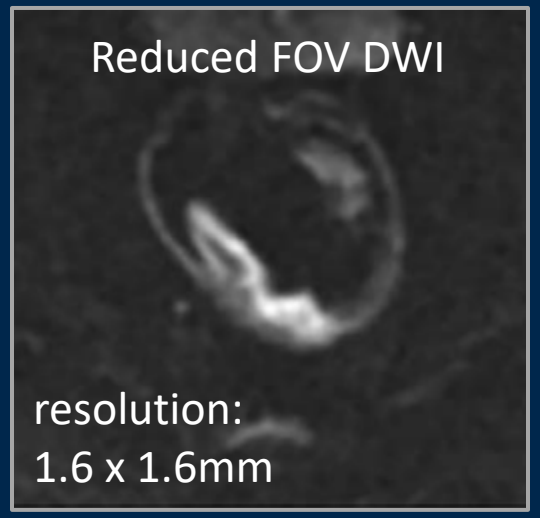


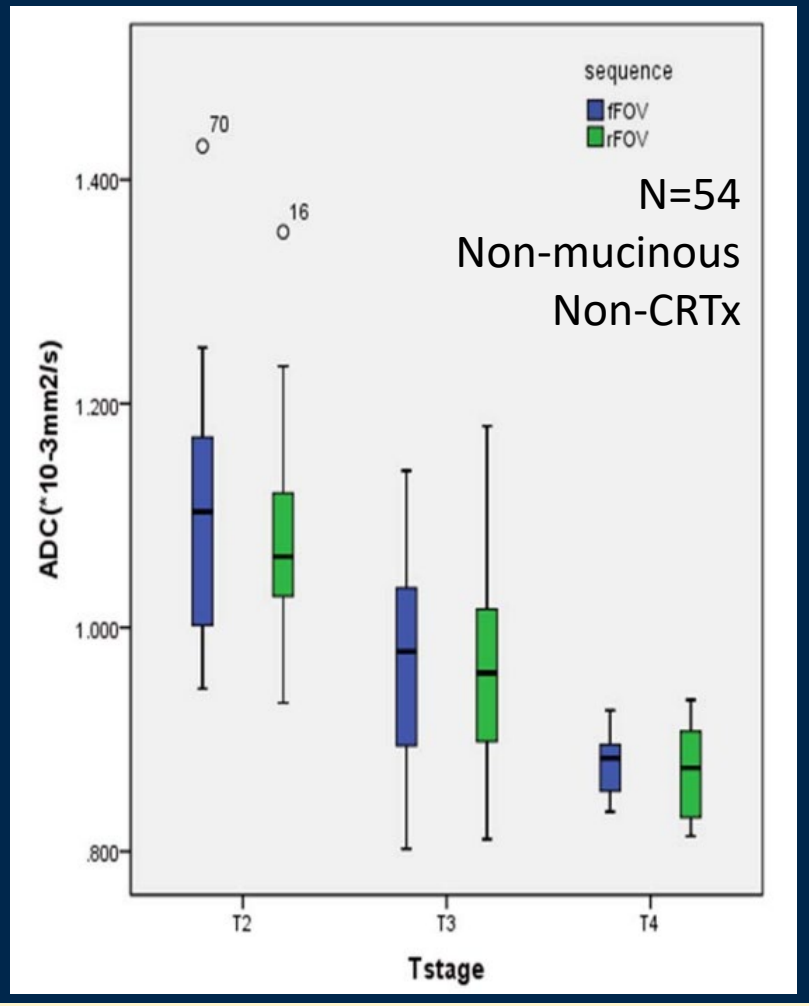
Song, I., et al., Value of diffusion-weighted imaging in the detection of viable tumour after neoadjuvant chemoradiation therapy in patients with locally advanced rectal cancer: comparison with T2 weighted and PET/CT imaging. Br J Radiol, 2012. 85(1013): p. 577-86.

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







Peng, Y., et al., Comparison of reduced field-of-view diffusion-weighted imaging (DWI) and conventional DWI techniques in the assessment of rectal carcinoma at 3.0T: Image quality and histological T staging. J Magn Reson Imaging, 2018. 47(4): p. 967-975.

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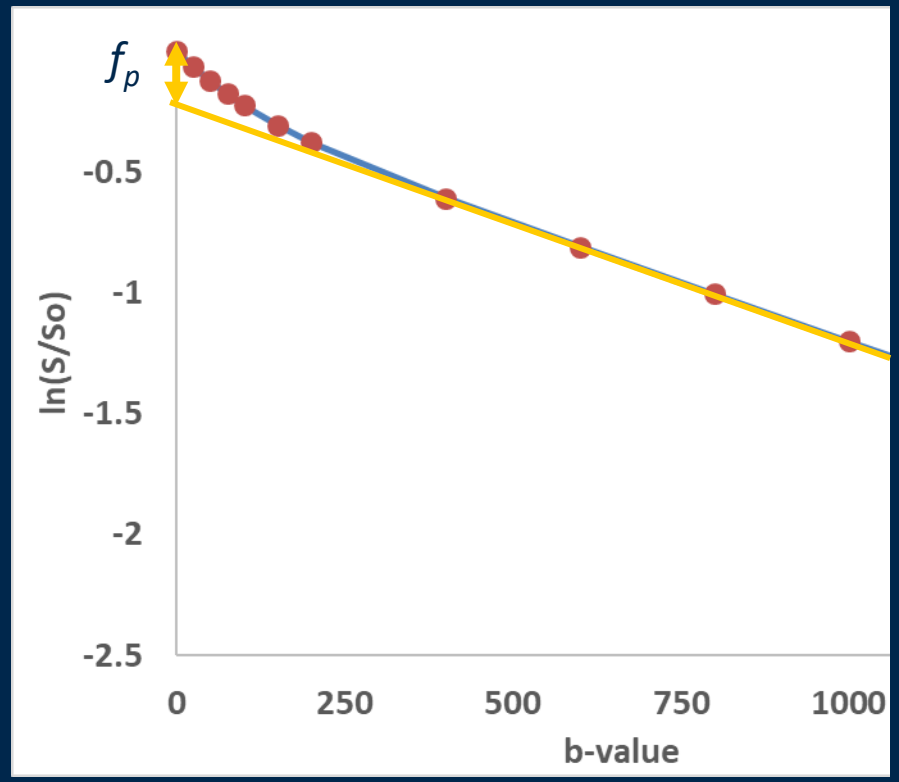
Beyond ADC: Non mono-exponential diffusion biomarkers

- Intra Voxel Incoherent Motion (IVIM)

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

  - perfusion fraction f_p
  - blood pseudo-diffusion D^*
  - tissue diffusion D_{tiss}



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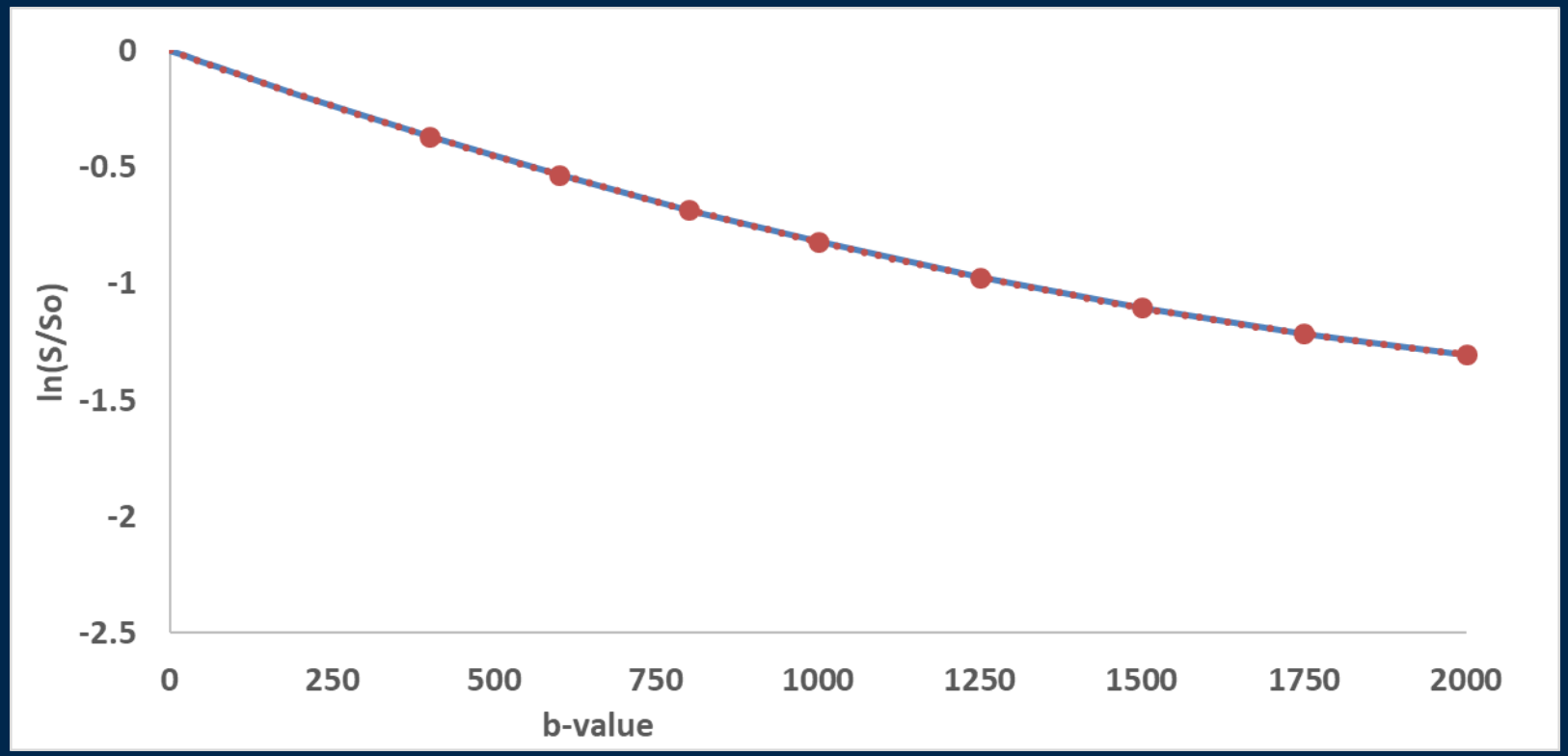
- Kurtosis

$$\frac{S(b)}{S_o} = e^{\left[-b \cdot D_k + \frac{K}{6}(b \cdot D_k)^2\right]}$$

- Stretched Exponential

$$\frac{S(b)}{S_o} = e^{-(b \cdot DDC_\alpha)^\alpha}$$



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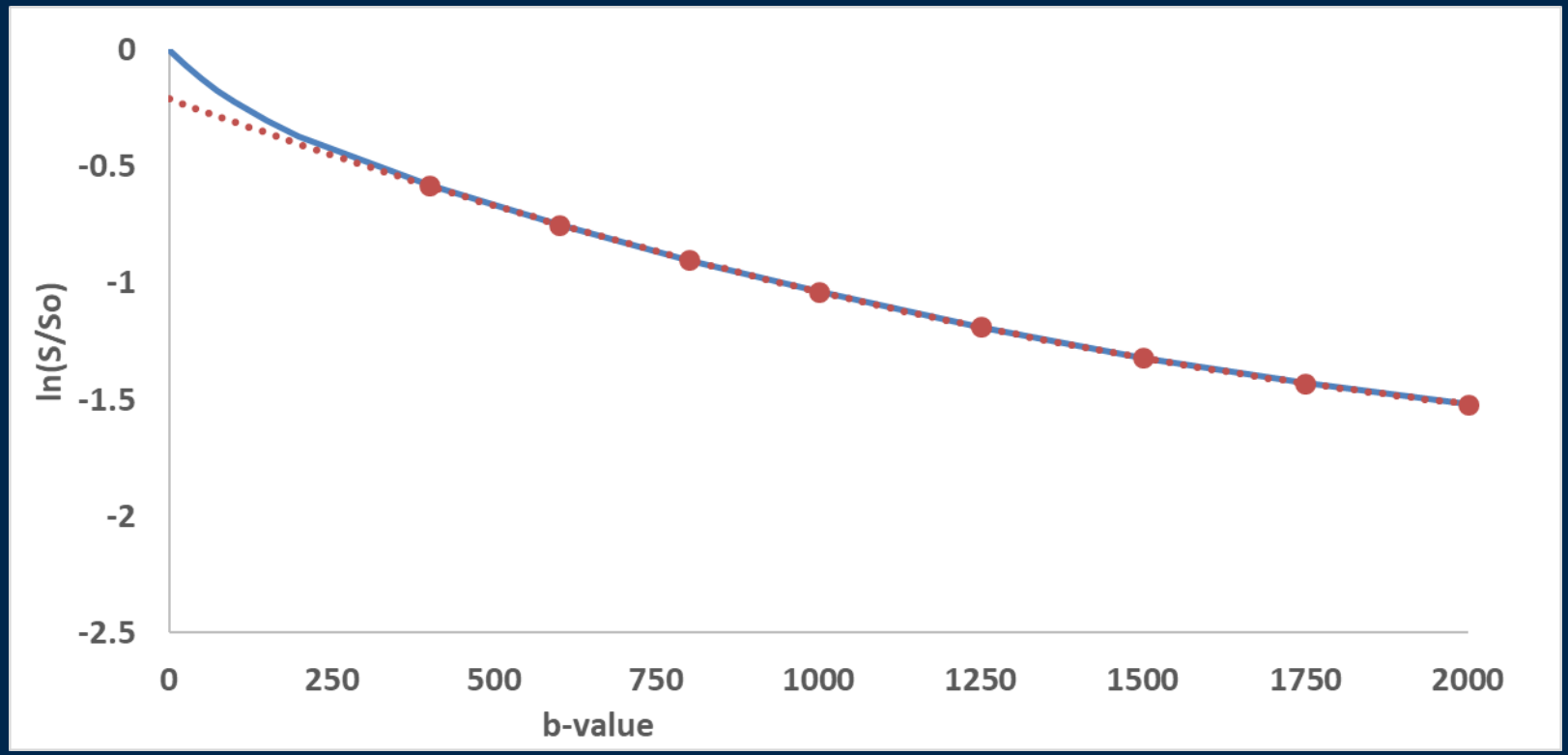

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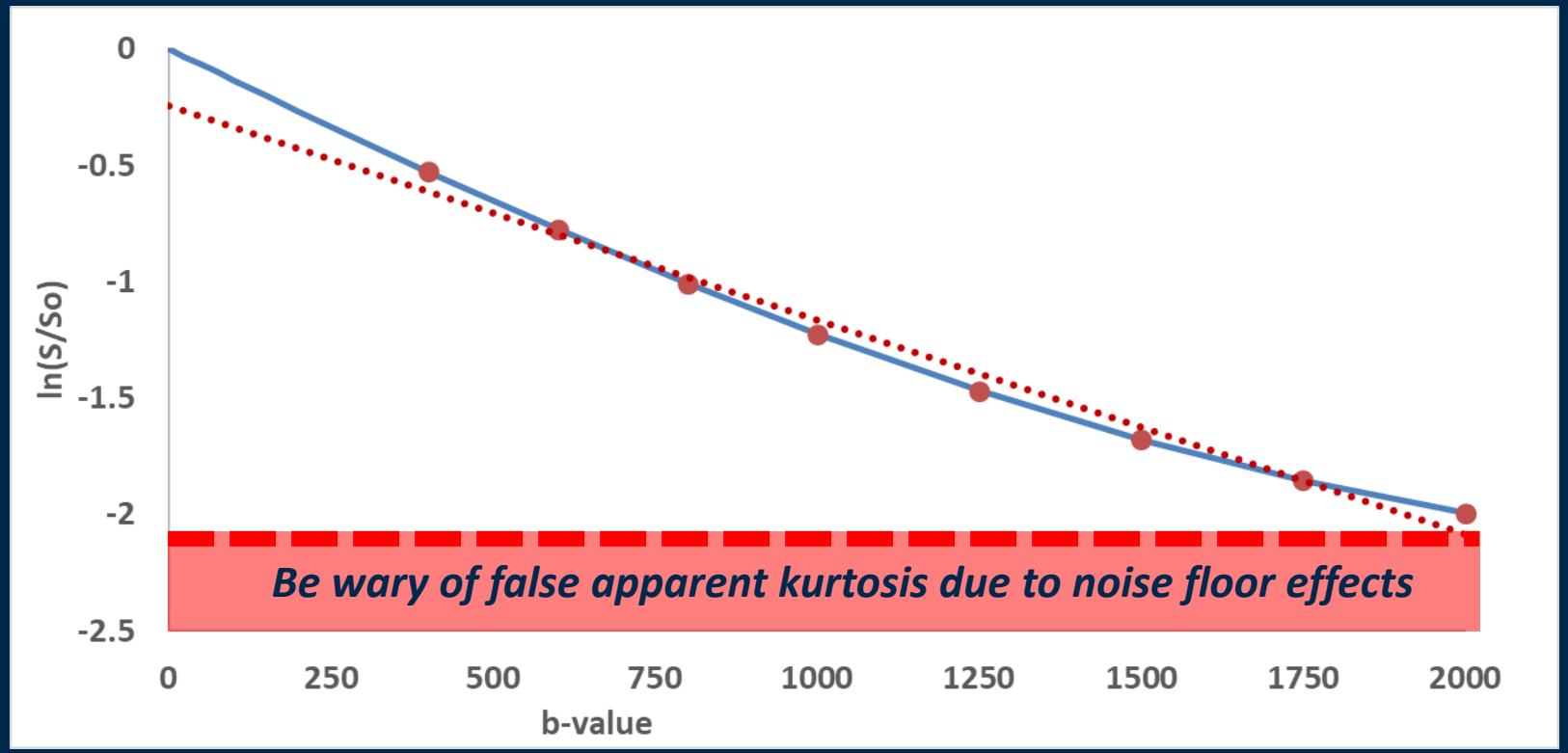
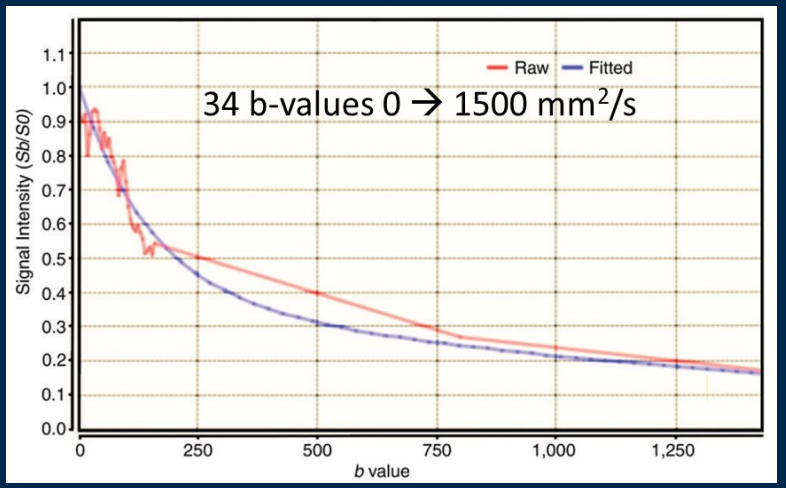
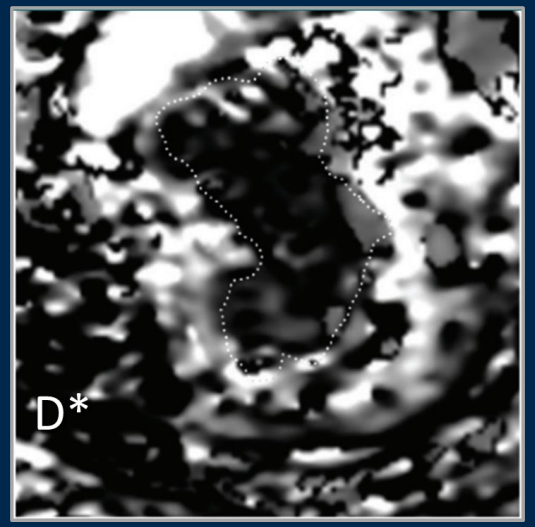


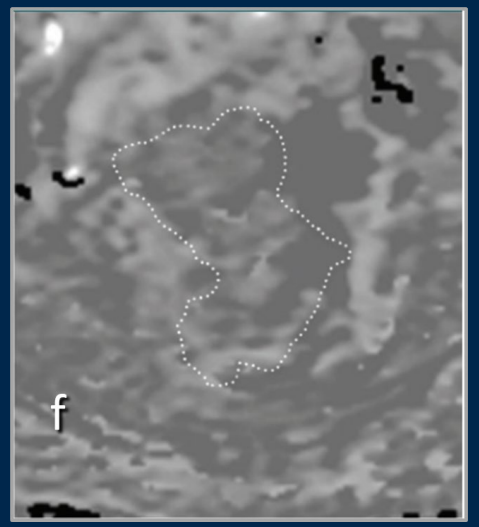
IVIM of Rectal CA

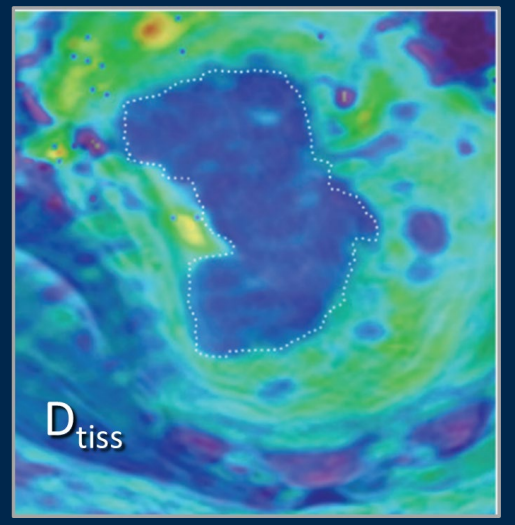
Nougaret, S., et al., Intravoxel Incoherent Motion-derived Histogram Metrics for Assessment of Response after Combined Chemotherapy and Radiation Therapy in Rectal Cancer: Initial Experience and Comparison between Single-Section and Volumetric Analyses. Radiology, 2016. 280(2): p. 446-54.

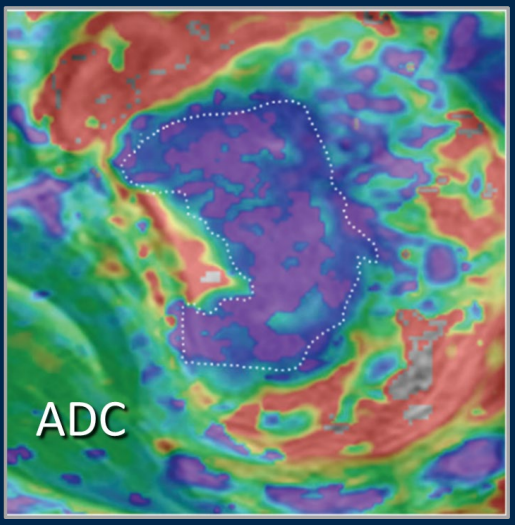
- High b-sampling of perfusion regime for fair assessment of D* & f_p metrics
- D_{tiss} & ADC increased post-CRTx (N=31, p<0.01)
- D_{tiss} & ADC higher in good vs poor resp (p<0.02)
- No improvement in D_{tiss} & ADC histogram metrics
- D* & f_p did not change post-CRTx
- D* & f_p not useful in assessing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











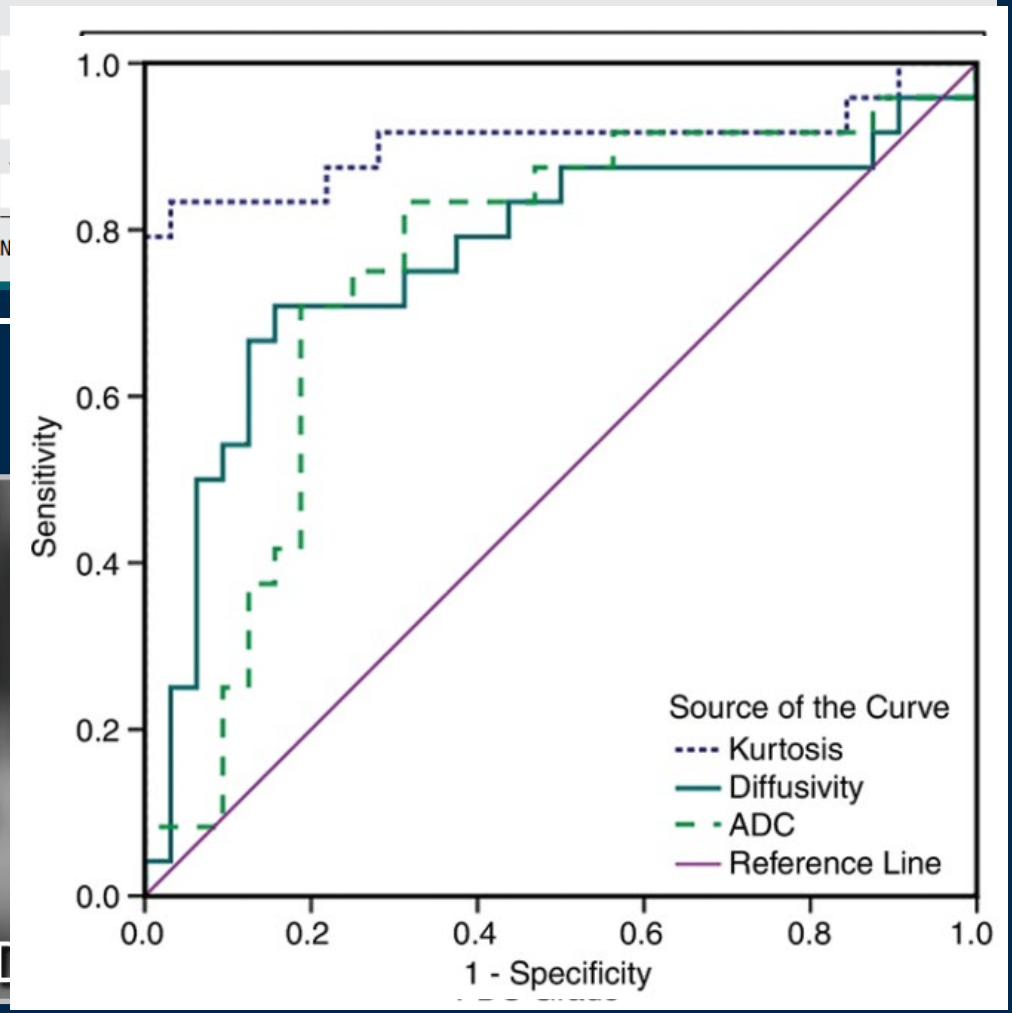
Diffusion Kurtosis Imaging of Rectal CA

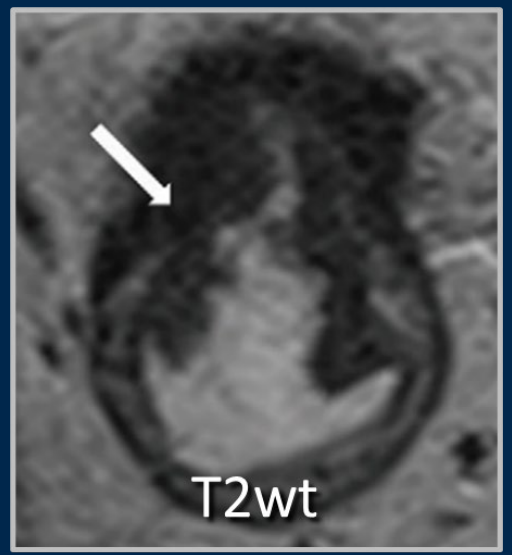
Zhu, L., et al., Diffusion Kurtosis Imaging Study of Rectal Adenocarcinoma Associated with Histopathologic Prognostic Factors: Preliminary Findings. Radiology, 2017. 284(1): p. 66-76.

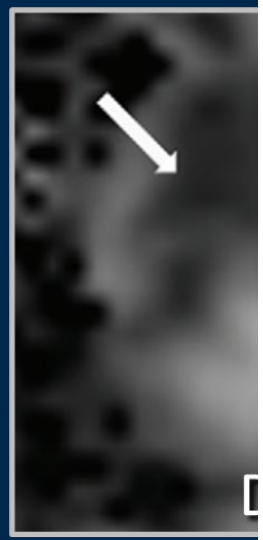
- DKI & ADC of untreated patients (N = 56) with histopathology grading (WHO & PDCs)
- ADC and D_K (diffusivity) negatively correlated w/ histopathologic grade
- Kurtosis positively correlated w/ histopath grade
- Kurtosis outperformed ADC & D_K in separating high- & low-grade & high-grade rectal adenocarcinoma

Correlation Coefficients between Kurtosis, Diffusivity, and ADC and Both Grading Systems

Parameter	WHO Grade	PDC Grade





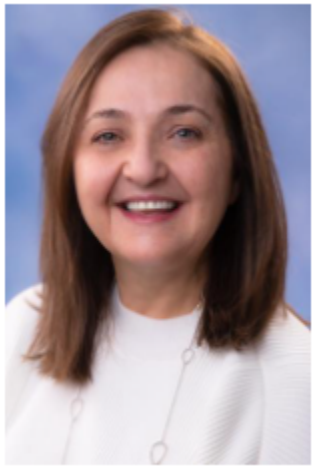


Summary - *Inclusion of Diffusion MRI in Future Clinical Trials?*

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: ✓ *No*
  - Poor fat-suppression?
  - Patient motion?
  - Geometric distortion / eddy currents / shim?
  - Gradient nonlinearity?
- Issues with lesion segmentation? ✗ *Yes, as always*
- Choice of DWI-related metrics?
  - DWI ✓ *Yes*
  - ADC ✓ *Yes*
  - IVIM (perfusion, f_p and D*) ✗ *Not compelling & is costly*
  - DKI promising w/ only requirement b≈1600 *~ Worth it to include b≈1600*
- Practical: site qualif, phantoms, analysis SW … ? ✓ *Phantoms & SOP exist, ~ SW*

Thank You!



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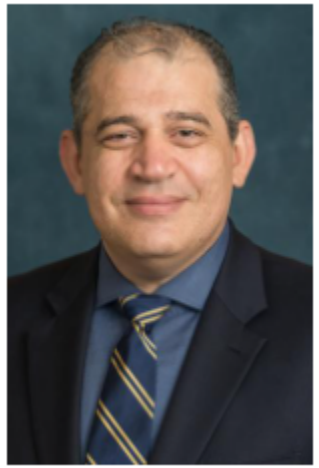

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