ASSESSMENT OF HEPATOCELLULAR CARCINOMA IN FRESH LIVER EXPLANTS USING A NON-GAUSSIAN DIFFUSION KURTOSIS MODEL.
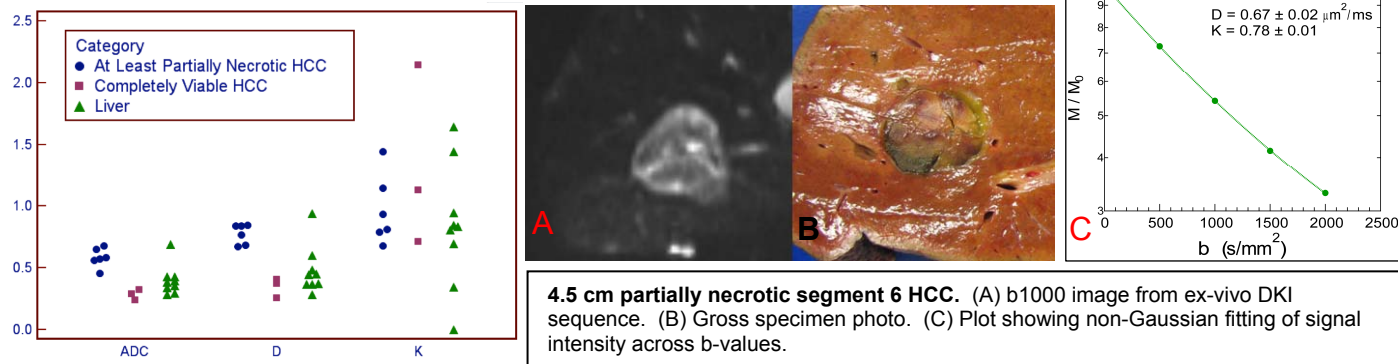
A. B. Rosenkrantz[1], E. E. Sigmund[1], B. E. Niver[1], G. R. Morgan[2], B. Spieler[1], A. G. Gilet[1], and C. H. Hajdu[3]

[1]Radiology, NYU Langone Medical Center, New York, New York, United States, [2]Transplant Surgery, NYU Langone Medical Center, New York, New York, United States, [3]Pathology, NYU Langone Medical Center, New York, NY, United States

Introduction: Diffusion-weighted imaging (DWI), including evaluation of quantitative apparent diffusion coefficient (ADC) values, has shown potential for assessment of hepatocellular carcinoma (HCC)[1], including lesion detection, characterization, and monitoring of treatment response. In a clinical setting, ADC values are generally obtained using a Gaussian diffusion model and corresponding mono-exponential signal decay versus encoding factor (b-value). However, water diffusion within tissues is often non-Gaussian in character. The higher order diffusional kurtosis analysis quantifies non-Gaussianity and may show greater sensitivity to structural heterogeneity among biologic tissues[2]. This approach, which requires a larger maximal b-value than typical clinical protocols, yields both a corrected ADC value and a mean kurtosis of the tissue; the latter dimensionless parameter reflects the extent of non-Gaussian diffusion and increases with greater tissue microstructural complexity. Diffusion kurtosis imaging has been applied for brain gliomas and head and neck squamous cell carcinomas[3,4]. However, this model is technically more challenging in the liver given that low liver T2 relaxation time and respiratory motion limit the ability to obtain sufficient liver SNR at high b-values. Use of an ex-vivo model may facilitate obtaining sufficient SNR for this purpose. Therefore, our aim in this study was to assess the feasibility and potential utility of diffusion kurtosis imaging (DKI) for evaluation of HCC using fresh liver explants.

Methods: Eight patients (6M;2F; age 55±14y) with HCC who underwent liver transplantation were included in this prospective study after providing written informed consent. Seven of these patients had previously undergone trans-arterial chemo-embolization (TACE). The fresh explanted liver underwent MRI on a 1.5T system (Siemens Avanto) within 24 hours following surgery, prior to tissue fixation. The MRI included a DKI sequence using a single-shot EPI technique with tri-directional diffusion-sensitizing gradients and the following parameters: TR/TE 4900/100ms, FOV 330*248 mm, matrix 226*226, rBW 1580 Hz/pixel, 20 slices, slice thickness 8 mm, no gap, GRAPPA 2, b-values of 0, 500, 1000, 1500, and 2000 s/mm^2, 19 averages, total acquisition time 20:27min. A hepatopathologist and radiologist reviewed pathology data and MR images jointly to identify HCC suitable for assessment with the DKI sequence. The pathologist independently evaluated each HCC for necrosis. Two radiologists in consensus placed an ROI on each slice through the HCC for each b-value of the DKI sequence. The resulting signal intensity measurements were used to compute diffusivities using both a mono-exponential and non-Gaussian fit (ADC and D, respectively), as well as the mean kurtosis (K). A weighted average, based upon cross-sectional area for each slice on which the HCC was visible, was obtained for each of these metrics for each lesion. These metrics were also calculated for the background liver using a single ROI within the right lobe. Comparisons were performed between HCC and liver, as well as between completely viable and at least partially necrotic HCC.

4.5 cm partially necrotic segment 6 HCC. (A) b1000 image from ex-vivo DKI sequence. (B) Gross specimen photo. (C) Plot showing non-Gaussian fitting of signal intensity across b-values.

Results: 9 HCC (mean size 2.5±1.4cm) were included, of which 3 were entirely viable and 6 were at least partially necrotic. ADC and D were strongly correlated for both liver (r=0.967, p=0.006) and for HCC (r=0.950, p=0.007). However, there was no significant correlation between either ADC or D with K for either liver or HCC. Relative contrast between liver and HCC was greater for K (0.314) than for ADC (0.203) or D (0.222), although these differences did not reach statistical significance. The 3 entirely viable HCC exhibited the lowest values of both ADC and D among the 9 HCC in the sample. Among the 6 remaining HCC that were at least partially necrotic, 5 exhibited an ADC and D that was greater than that of the liver. K varied from 0.00 to 1.64 (mean 0.84) for liver and from 0.68 to 2.15 (mean 1.09) for HCC. No significant difference in K was evident between the 3 viable and 6 at least partially necrotic HCC.

Conclusions: We used an explant model to demonstrate the feasibility of HCC assessment using DKI, a diffusion model incorporating an extended b-value range and non-Gaussian fitting of observed signal intensities. This approach yielded an additional parameter K that (1) did not correlate with either ADC or D, implying non-redundant structural sensitivity; (2) exhibited greater separation of HCC and surrounding liver; and (3) did not appear sensitive to HCC necrosis following TACE. ADC metrics from the kurtosis model continued to distinguish necrotic HCC, as has been observed with simpler diffusion models. Limitations of this study include the small sample size, an absent model for the structural sensitivity of apparent kurtosis specific to normal hepatic parenchyma vs. HCC, and confounding effects from post-mortem tissue matrix modifications. In addition, while DKI was applied in an explant model, this approach may be difficult to apply in-vivo due to limited liver SNR when using the requisite high b-values. Alternate diffusion sequences/protocols with greater SNR or lower distortion may have potential for performing DKI of HCC following TACE in a clinical setting.

References: [1] Kamel IR et al. Radiology 2009. [2] Jensen JH et al. MRM 2005. [3] Raab P et al. Radiology 2010. [4] Jansen JFA et al. AJNR 2010.