

# NdH/dT: A new quantitative measure for Diffusion Weighted Imaging based evaluation of abdominal tumor response to therapy

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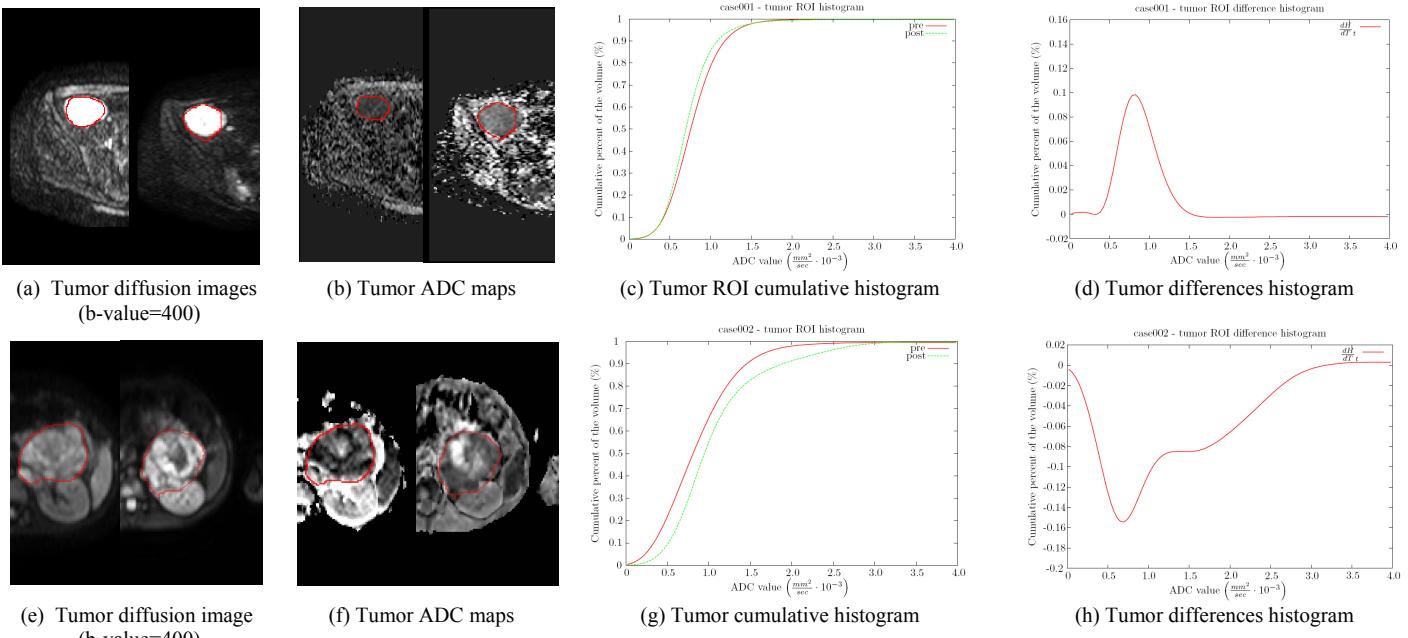
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**Introduction:** Quantitative evaluation of tumor response to therapy is playing an important role in management of patients with abdominal tumors. In the recent years, Diffusion Weighted Imaging (DWI), was proposed as an imaging-based bio-marker that can quantify the diffusivity of the water molecules inside the body. The derived Apparent Diffusion Coefficient (ADC) map is used to measure the actual diffusivity of the tissue. Changes in the ADC values are inversely correlated with tumor's cellularity and used to evaluate the tumor's response to therapy. Current techniques use the mean or median ADC value of the tumor Region Of Interest (ROI) to quantify the tumor response. However, the response of ADC to therapy in the clinical setting was found to be more complex to quantify, due to inherent pre-treatment and post-treatment heterogeneity observed within human tumors and due to global changes in the body diffusivity during the therapy. Thus, advanced measurements to quantify the tumor response more accurately should be developed [1]. Voxel-based approaches like the FDM map [2], require complex post-processing, including non-rigid registration of the abdominal images which might introduce the registration error into the ADC computation.

We have developed a new approach to quantify the tumor's response to therapy based on entire cumulative histogram analysis. Our approach provides a single number that encapsulates the overall tumor diffusivity changes over time. It is not sensitive to the global body diffusivity changes, to the histogram binning effects, and do not require any complex pre-processing steps.

**Materials and Methods:** Datasets of three representative patients with abdominal tumors with various response types were selected from the hospital archive. Each dataset was consisting of structural and diffusion imaging, before and after the therapy. Each diffusion imaging was consisting of three diffusion images that were acquired with b-values of 0,400,800 sec/mm<sup>2</sup>. ADC maps were calculated by fitting a decaying exponential function to the b-value images using custom software written in C++. Tumors and healthy organs ROIs were segmented manually based on both structural and diffusion (b-value=400sec/mm<sup>2</sup>) images using the ITK-SNAP segmentation tool (Fig. 1a-b,e-f). The response to therapy was quantified using the following steps: For each patient, ROI and time-point, the ADC normalized cumulative histogram was computed (Fig. 1c,g). Next, the difference between the histograms over time were computed (Fig. 1d,h) for both the tumor (dH/dT<sub>t</sub>) and healthy (dH/dT<sub>h</sub>) ROIs (Fig. 1d,h). Finally the Area Under the Curve (AUC) was computed for each difference histogram, where the tumor's histogram AUC was normalized by the healthy organ's histogram AUC (NdH/dT=(dH/dT<sub>t</sub>)/(dH/dT<sub>h</sub>)) to alleviate the global changes in the body diffusivity. The resulting measurement provides a single number that encapsulates the entire changes in the ADC. The sign of the number represents the overall tumor response to therapy with respect to normal organ changes. Positive value means an overall ADC change in similar direction to the ADC change in the normal organ while negative value represents a change in opposite direction. The measure magnitude represents the overall change in percents of the overall ROI volume normalized by the normal percent of change. Absolute values larger than 1 represent an overall change of the ADC which is more than the normal diffusivity change.

**Results:** The proposed measurement was calculated for each patient, and compared to tumor response as defined by an expert. The cumulative histograms, the differences histograms for two representative patients are presented in Fig. 1. Fig. 1a-d presents the measurements for a patient with homogenous in which the tumor did not respond to the therapy, and Fig. 1e-h presents the same measurements for a patient with heterogeneous tumor in which the cellularity of the tumor reduced due to the therapy. Different histogram bin sizes were compared to confirm that our method is not sensitive to histogram binning effects. The NdH/dT values for the 3 cases were: 0.37, 6.02, and 2.97. These values are corresponding to the qualitative evaluation of the responses as evaluated by an expert: no response, higher diffusivity, and higher diffusivity, respectively.



**Figure 1.** Images and histograms of two patients. (a,e) DWI images (b-value=400) before (left) and after (right) therapy, (b,f) ADC maps before (left) and after (right) therapy. The tumors are encircled in red. (c,g) Cumulative histograms of the ADC values, before (red) and after (green) therapy. (d,h) The differences between time-points histograms.

**Discussion:** The analysis of the results confirmed that our measurement provides a quantification of tumor's response to therapy based on diffusion imaging which is comparable to an expert qualitative evaluation. The NdH/dT measure is simple and intuitive to interpret, unlike existing methods that use the difference between the tumor ROI median/mean values solely. The NdH/dT measure encapsulates the entire tumor response, including the tumor heterogeneity, without prior image non-rigid registration which is susceptible to the inherit registration error.

## Bibliography:

[1] Padhani AR, et al. Diffusion-weighted magnetic resonance imaging as a cancer biomarker: consensus and recommendations. *Neoplasia*. 2009;11(2):102-25.  
 [2] Moffat BA, et al. The functional diffusion map: an imaging biomarker for the early prediction of cancer treatment outcome. *Neoplasia*. 2006;8(4):259-267.