REDUCING INTER-OBSERVER VARIABILITY IN DCE-MRI USING SEMI-AUTOMATIC LESION SEGMENTATION AND HISTOGRAM ANALYSIS - COMPARISON TO MANUAL REGION OF INTEREST PLACEMENT.

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Background: Inter-observer variability is of particular importance in the setting of multi-center clinical trials, because of its potential to decrease the achievable reproducibility among studies. In clinical trials, every effort is made to control all potential sources of variation, but a high likelihood remains that measurements will be performed by different observers, causing additional variability. In this context, DCE-MRI would benefit from approaches that guide observer measurements and thereby improve inter-observer and potentially intra-observer reproducibility.

Purpose: To investigate the inter-observer variability of software-assisted, semi-automatic lesion segmentation and histogram analysis in comparison to manual ROI placement in a multi-observer setting on DCE-MRI data.

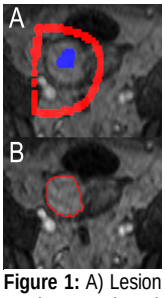

Figure 1: A) Lesion tagging and B) resulting semi-automatic segmentation.

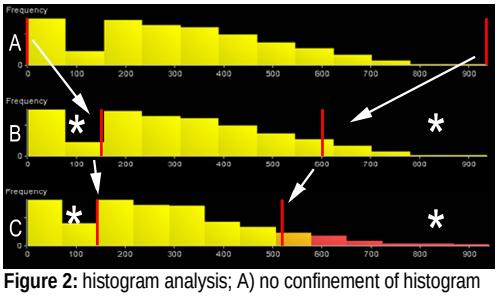

Figure 2: histogram analysis; A) no confinement of histogram data, B) user defined "peak" and C) combination of user-defined "peak" and a 10-90% threshold (marked red). * indicates excluded histogram data.

Table 1: Mean ± standard deviation (min/max) of within subject variation between observers by each measurement method for manual ROI placement and semi-automatic lesion segmentation.

measurement method	manual ROI placement	semi-automatic lesion segmentation	absolute difference in inter-observer variability
Ia) auto seg. vs. IIa) 3/4 ROI	20.1±4.3% (13.7-26.6%)	10.8±2.6% (6.8-14.7%)	-9.2%
Ib) auto+histo seg. vs. IIb) user-defined ROI	35.8±7.8% (24.0-47.2%)	20.2%±6.3% (10.0-28.5%)	-15.6%
Ic) auto+histo seg. +thresh vs. IIc) targeted ROI	29.6±7.8% (13.4-39.8%)	18.1±4.7% (10.6-25%)	-11.5%
overall	28.5±9.3% (13.4-47.2%)	16.4%±6.2% (6.8-28.5%)	-12.1%

Material and Methods: Uterine fibroids were considered as perfusion model because lesions are well delineated and reside in a low motion environment. 15 uterine fibroid lesions in 15 female patients (mean age 44 years, range 28-60) were retrieved from PACS and defined as the study group. All DCE-MRI studies were performed at 1.5T (Avanto, Siemens, Erlangen, Germany), using variable flip angle T1 mapping (flip angles: 2, 8, and 20 degrees) and a 4D, time resolved MR angiography sequence with interleaved stochastic trajectories (TWIST) after the injection of 0.1 mmol/kg gadobenate dimeglumine (Bracco Diagnostics, Princeton, NJ). All DCE-MRI studies were processed on a dedicated DCE-MRI post-processing platform, Tissue4D™ (Siemens Healthcare, Erlangen, Germany) with Tofts model implementation. Parametric maps of the pharmacokinetic parameter K^{trans} were saved for each case and transferred to a semi-automatic DCE-MRI analysis software (MR ONCO-TREAT, Siemens Healthcare, Erlangen, Germany). Five observers (MD, JH, SF, SB, TH) performed three different methods of semi-automatic lesion segmentation and manual ROI placement per study on a single previously selected uterine fibroid which was identified by slice position. Measurement was done in random order and repeated 3 times for each study. The guided measurement methods consisted of semi-automatic lesion segmentation (Figure 1) and (Ia) no confinement of histogram data ("auto seg."; Figure 1+Figure 2A); (Ib) segmentation of the histogram by observers based on "peak" identification and exclusion of baseline "noise" ("auto + histo seg."; Figure 1+Figure 2B); (Ic) further refinement of the previous segmentation after applying a relative threshold only including 10-90% of histogram data ("auto + histo seg + thresh."; Figure 1+Figure 2C). Manual ROI placement methods were: (IIa) a large ROI encompassing at least 3/4 of the uterine fibroid on the largest axial section ("3/4 ROI"); (IIb) a "user-defined ROI" aimed at the most enhancing component of the uterine fibroid; (IIc) a "targeted ROI" directed at a specific location by slice position and description. The measurement methods applied for semi-automatic lesion segmentation and manual ROI placement were compared since the principles of lesion segmentation were similar. Between each category the user impact varied, from plainly selecting the whole lesion (Ia vs. IIa) to very specific instructions (Ic vs. IIc). The root mean square coefficient of variation (rmsCoV) was calculated to estimate the within subject variation between observers (inter-observer variability).

Results: Table 1 demonstrates the within subject variation between observers for each measurement method. Semi-automatic lesion segmentation reduced the inter-observer variability significantly ($p<0.01$) which is additionally expressed by smaller standard deviations compared to manually placed ROIs. The overall reduction in inter-observer variability by semi-automatic lesion segmentation was 12.1%. Reduction of inter-observer variability and standard deviation is graphically demonstrated by Figure 3 for different measurement methods and by Figure 4 for each pair wise observer comparison.

Conclusion: Semi-automatic lesion segmentation is able to significantly reduce variability in a multi-observer setting compared to a conventional manual ROI placement. By means of semi-automatic lesion segmentation and advanced histogram analysis the impact of the observer is more controlled but not completely removed to allow for observer input and inspection of the results. Semi-automatic lesion segmentation may be a tool to address the issue of inter-observer variability in multi-center clinical trials, therefore improving the overall reproducibility of DCE-MRI.

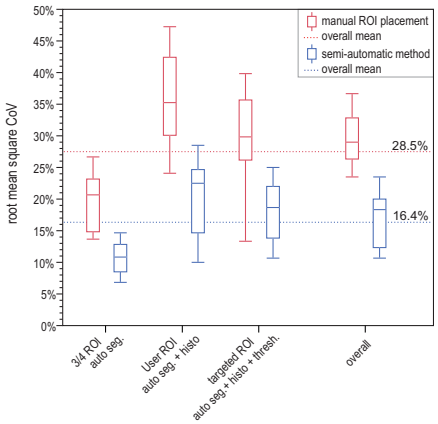

Figure 3: Within subject variation between observers for each category of comparable measurement methods is demonstrated. Overall mean for semi-automatic lesion segmentation and manual ROI placement is represented by reference lines.

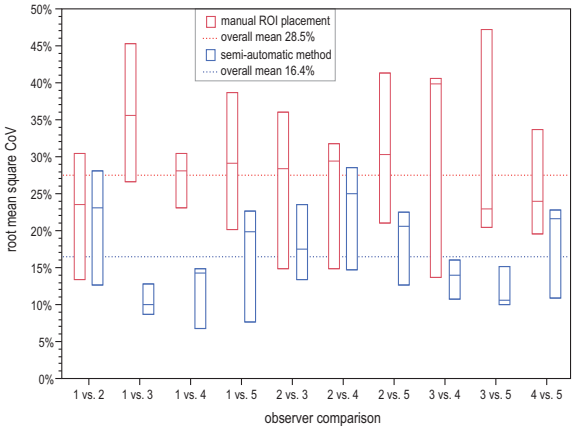

Figure 4: Within subject variation between each pair wise observer comparison is displayed. Overall mean for semi-automatic lesion segmentation and manual ROI placement is represented by reference lines.