# REPRODUCIBILITY OF DYNAMIC CONTRAST-ENHANCED MRI PERFUSION PARAMETERS ON VARIOUS COMPUTER AIDED DIAGNOSIS WORKSTATIONS: TAKING A PEEK INTO THE BLACK BOX.

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**Background:** Assessment of tissue perfusion by means of model-based dynamic contrast-enhanced MRI (DCE-MRI) with derivation of quantitative ($K^{trans}$, $k_{ep}$, $v_e$) and semi-quantitative (iAUGC) pharmacokinetic (pk) parameters was introduced 20 years ago[1]. Since then, the potential of this concept to serve as a non-invasive biomarker has been shown by various preclinical and clinical studies[2-4]. Many efforts are currently underway to establish the accuracy and precision of this approach to enable comparison of pk parameters across imaging platforms, clinical sites and time[5]. Although many factors contributing to overall measurement error have been identified, the effect of commercially available DCE-MRI post-processing solutions on pk measurement derivation has yet to be defined.

**Purpose**: To test the reproducibility of model-derived quantitative and semi-quantitative pk parameters between various commercially available post-processing solutions for DCE-MRI.

**Material and Methods:** Uterine fibroids were considered as perfusion model because lesions are well delineated and reside in a low motion environment. The 15 largest uterine fibroids in 15 randomly selected female patients (mean age 44 years, range 28-60 years) were 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). DCE-MRI studies were post-processed on four unique commercially available workstations using a Tofts model paradigm: Tissue4D™ (Siemens, Erlangen, Germany), DynaCAD™ (Invivo, Gainesville, Florida, USA), Aegis™ (Sentinelle Medical, Toronto, Ontario, Canada) and CADvue™ (iCAD, Inc. Nashua, NH, USA). Subject-related settings for DCE-MRI post-processing (e.g., weight, contrast type & volume, T1 mapping, contrast arrival time, arterial input function [AIF]) were specified if requested by the software. If T1 mapping was not an available parameter (DynaCAD ™, Aegis ™) an average T1 time of 1043 ms was used based on T1 map calculations from all datasets. Five readers prospectively measured $K^{trans}$, $k_{ep}$, $v_e$, and iAUGC by placing two unique regions of interest ([ROI], user defined vs. targeted placement) within a single previously selected uterine fibroid. Measurement was done on each workstation in random order and repeated 3 times for each study, resulting in 7200 data points. Mean comparison (ANOVA), intraclass-correlation coefficient (ICC), root mean square coefficient of variation (RMSCoV) to estimate within subject coefficient of variation (wCV) and Bland-Altman limits of agreement were calculated.

**Table 1:** Workstation combinations producing no significant difference in output by pk parameter

| pk parameter | workstation combination |
|---|---|
| $K^{trans}$ | *Aegis ™ - DynaCAD ™*<br>*CADvue ™- Tissue4D ™* |
| $k_{ep}$ | *Tissue4D ™- DynaCAD ™*<br>*Aegis ™- CADvue ™* |
| $v_e$ | *DynaCAD ™- CADvue ™* |
| iAUGC | *DynaCAD ™- CADvue ™* |

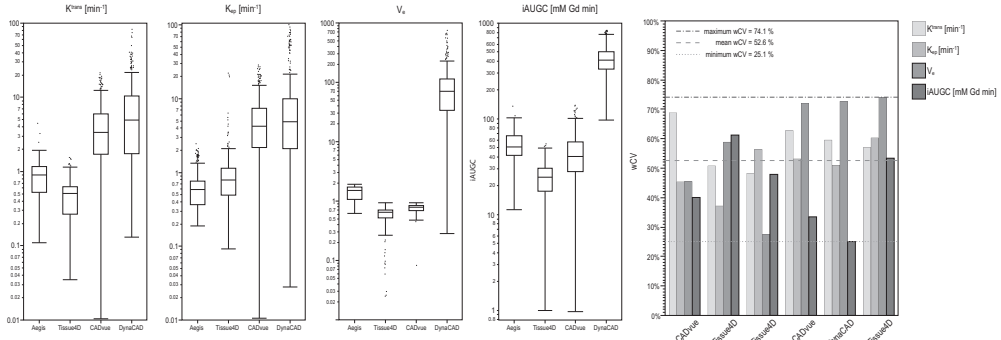


**Figure 1:** Median comparison of raw pk ouput by workstation

**Figure 2:** wCV for each workstation combination by pk parameter

**Results:** Initial median comparison (Figure 1) revealed a difference of pk data output from two workstations by a magnitude of 10 (*CADvue ™: $K^{trans}$, $K_{ep}$; DynaCAD ™: $K^{trans}$, $K_{ep}$, $V_e$* ) or 100 (*DynaCAD ™: $V_e$*) compared to the other. Figure 2 demonstrates the wCV for each workstation comparison by pk parameter (range: 25.1 to 74.1%, calculated by RMSCoV). Figure 3 demonstrates Bland-Altman limits of agreement for each workstation comparison by pk output following rescaling to account for magnitude differences in pk expression between workstations. Table 1 illustrates between which workstation combinations there was no significant difference for each rescaled pk parameter. ICCs showed a strong correlation between readers significantly >0.9 ($p<0.05$; range 0.95-0.98). Pharmacokinetic measurements were not significantly different between the two ROI methods ($p>0.05$; mean ICC 0.85; range 0.58-0.95). The range of ICCs for each workstation comparison by pk parameter were: $K^{trans}$ 0.33-0.68, $k_{ep}$ 0.02-0.81, $v_e$ -0.03-0.72, and iAUGC 0.47-0.78.

**Conclusion:** There is substantial variability for DCE-MRI pharmacokinetic parameters ($K^{trans}$, $k_{ep}$, $v_e$, iAUGC) across different commercially available DCE-MRI post-processing solutions. Although the Tofts and Kermode model is fairly standardized[6], there are many parameters (T1 map, AIF type, subject specific data, model goodness of fit)[7] that can affect the pk output. If DCE-MRI is to succeed as a widely incorporated biomarker, the industry must agree on a post-processing standard.

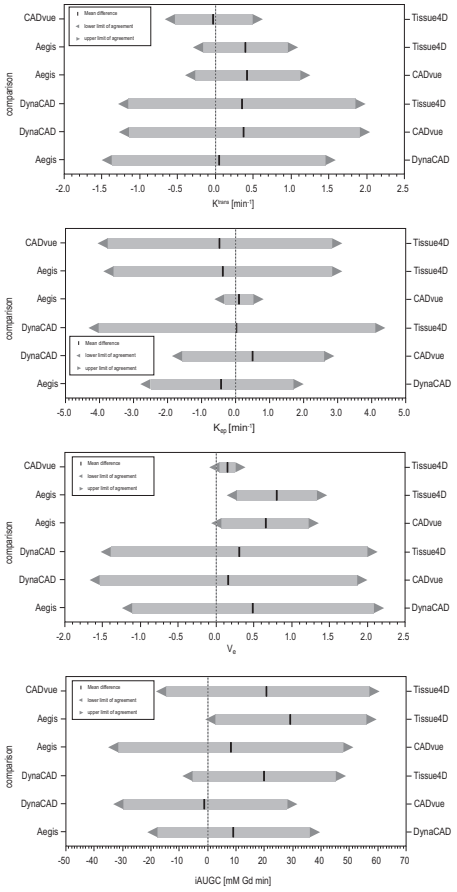


**Figure 3**: Bland-Altman mean difference and limits of agreement for each workstation comparison by pk output

**References:**

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