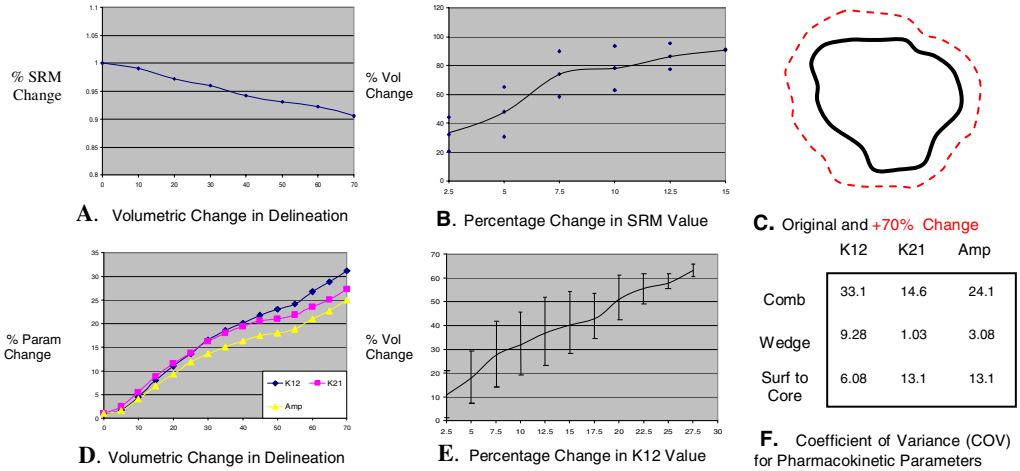
Sensitivity of DCE-MRI to Fractional Volumetric Changes in Tumor Delineation: A Semi-Automated Study

D. H. Wu[1], R. Alam[2], and N. Mayr[3]

[1]Radiological Sciences, Oklahoma University Health Science Center, Oklahoma City, Oklahoma, United States, [2]Computer Science, University of Oklahoma, Norman, Oklahoma, [3]Ohio State University Medical Center, Columbus, Ohio, United States

Purpose: Tumor delineation plays an integral role in the evaluation and monitoring of cancer progression. Clinically, delineation of tumor size and location are known to vary among physician evaluators, regardless of subspecialty[1]. Tumor delineation has been shown to vary within and between different clinicians over time[2]. Dynamic Contrast Enhanced MRI (DCE-MRI) has shown promise for serial assessment of tumor responsiveness[3]. Imaging analysis tools such as DCE-MRI have become increasingly sophisticated and consequently are developing to be more quantitatively precise.. However, a recent report showed in a head-to-head comparison between two individuals with breast DCE-MRI that there are significant differences[4]. This report illustrated mean differences of 16-17% for K_{trans}, v_e, and k_{ep}. These and other studies demonstrate that it is critically important to better understand DCE-MRI stability in the presence of variation in tumor delineation. In this work, we describe and evaluate a semi-automated means to evaluate the impact of fractional changes in spatial size of delineation and its impact on DCE-MRI pharmacokinetics and standard ratio metrics (SRM).



A. Volumetric Change in Delineation

B. Percentage Change in SRM Value

C. Original and +70% Change

D. Volumetric Change in Delineation

E. Percentage Change in K12 Value

	K12	K21	Amp
Comb	33.1	14.6	24.1
Wedge	9.28	1.03	3.08
Surf to Core	6.08	13.1	13.1

F. Coefficient of Variance (COV) for Pharmacokinetic Parameters

Figure 1: A) Sample volumetric percentage change against plotted vs. SRM in one patient case, B) Statistical distribution over 66 studies for % change in SRM vs volumetric change, C) Illustration of 70% change in volume around a manual tumor delineation, D) A pt. case showing pharmacokinetic parameter change as a function of volume change, and E) Statistical distribution over 14 pharmacokinetic patients of the K_{12} parameter, F) Table of results with COV for Pharmacokinetic parameters (K12,K21 and fitted amplitude) for 32 combination segment, eight wedges segments and four surface-to-core segments.

Methods: DCE-MRI data was assessed from 66 cervical cancer patient studies that were obtained over the course of a decade. Each patient was imaged at one pre- and two post-radiotherapy time points. The DCE-MRI protocols used for these studies differed over this period, but were consistent with the contemporary protocol standards during that time. For all studies, we produced standard ratio measures (this measure was capable of being produced across all studies). For pharmacokinetics analysis we selected a fixed pool of 14 pre-therapy cases that had Arterial Input Function (AIF) evaluated on a patient-by-patient basis. Variation in tumor delineation analysis was performed as follows: initial comparison was derived from manually drawn regions of interest (ROIs) by an expert. Delineation was defined on T2 images (our standard protocol) so as to reduce potential bias when computing functional maps . Variation in tumor size was evaluated from 50% of the original volume up to 200% of the size in 5% increments. Sequential increases were achieved using morphological dilation $A \oplus B = \{x \mid [(\hat{B})_x \cap A] \subseteq A\}$ and sequential decreases were achieved by erosion $A \otimes B = \{x \mid (B)_x \subseteq A\}$ where B is a structuring object (3x3x3 square in cases of 3D series and 3x3 for 2D series). For example, in the increasing cases, we morphologically dilated the delineation and then further compared the number of added pixels against the number of pixels that were additionally needed to reach the next fractional interval. The morphological operation was continued iteratively until the desired number of pixels was exceeded. After that a priority score was given to pixels based on Euclidean distance and measure of adjacency to previous fractional change in delineation so that pixels were removed based on a this score.

Results: Pharmacokinetics typically varied less than 30% for K_{12} (similar results were seen on other pharmacokinetic parameters: K_{21} and amplitude) with respect to normalized measure values . The standard ratio measures varied over the 66 patients to less than 15% over an increase in tumor volume of up to 70%. Variation was greatest in the pharmacokinetics cases; where a 10% change in signal was produced on average by a delineation change of 32%+/-10%. RSI measures that produced the equivalent change in standard measures of 10% were demonstrated on average by an increase of 80% +/- 20% of the volume.

Discussion: There is a need to establish spatial threshold tolerance levels in tumor delineation accuracy for DCE-MRI, although this is not always practical when it requires multiple delineators over large amounts of tumor data. We have provided a new methodology and report results from our evaluation of the sensitivity of tumor volume in both SRM and pharmacokinetic methods. Both metrics seem to perform well under even large changes in volume. However, standard measures seem to tolerate a larger change 80% in tumor delineation volume to only 32% for pharmacokinetic parameters. Additional complexity in the pharmacokinetics may provide the increased sensitivity to volumetric changes. In this work, we have created a method that evaluates variation in functional measure compared to delineation size without significant burden to clinical personnel. This semi-automated evaluation permits a finer granularity in the evaluation of DCE-MRI based on size variation and may provide additional guidelines for the level of error tolerance in tumor delineation when used for DCE-MRI assessment.

References:

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