Methodology for visualization and perfusion analysis of 4D dynamic contrast-enhanced CT imaging

W Wee[1, 2], B Driscoll[2] and C Coolens[2, 3]

1 Clinical Engineering, University of Toronto, Toronto

2 Radiation Medicine Program, Princess Margaret Hospital, Toronto

3 Department of Radiation Oncology, University of Toronto, Toronto

Abstract

The use of quantitative functional imaging methods is become more prominent in radiotherapy in the role of target definition and early response detection of treatment efficacy. The development of 4D perfusion CT (4D pCT) requires more sophisticated methods of acquiring 3D functional parameters maps. This paper proposes a novel method for (a) segmenting vasculature and perfused tissue from 4D dynamic contrast-enhanced (DCE) CT scans containing other anatomical structures, and (b) subsequently creating 3D functional parameter maps of perfused tissue for tracer kinetic analysis. The methodology was tested on 4D DCE CT scans of phantom as well as liver and brain patient data. Preliminary quantitative and qualitative results have shown the effectiveness of the proposed methodology for automatically and accurately segmenting contrast-enhanced tissue as well as analysis of perfusion characteristics. This is a first step to achieving a volumetric, quantitative functional imaging method.

Keywords

ICCR, radiation therapy, computer, segmentation, 4D perfusion CT

Introduction

Advancements in volumetric CT have resulted in improved acquisition times with larger 3D volumes [1]. This has enabled the development of 4D perfusion CT (4D pCT). This is the process of injecting contrast and acquiring dynamic 3D volumes over time (DCE-CT) for subsequent tracer kinetics modeling [2]. Within radiation oncology, the main applications of perfusion CT imaging are for target definition and evaluation of early treatment response by quantitative measurement of changes in tumor neo-vascularisation, characterized by parameters such as vascular density, perfusion (i.e. blood flow) and vessel permeability [2]. The inherent 3D nature of these dynamic volume acquisitions theoretically allows for volumetric functionality maps. Instead of traditional 2D region-of-interest (ROI) based analysis it is possible to investigate a voxel-based correlation to the 3D treatment dose distribution. In order to achieve this level of perfusion modeling on a voxel-by-voxel basis, 4D visualization and segmentation of the vascular anatomy and perfused tissue becomes crucial.

Conventional methods for automatically segmenting anatomical structures utilize a single 3D volume and intensity thresholding. These methodologies may be prone to image noise, partial volume effects and applying them proves difficult to segment/analyze vessels and perfused tissue [2]. However, by observing the intensity change over time for a given voxel within the 4D pCT data set, it may be possible to reduce or mitigate these problems. Therefore this paper proposes a novel method for segmenting vasculature and perfused tissue from 4D pCT scans containing other anatomical structures and subsequently creating 3D functional parameter maps of perfused tissue. Moreover this is a first step to achieving a volumetric quantitative functional imaging method.

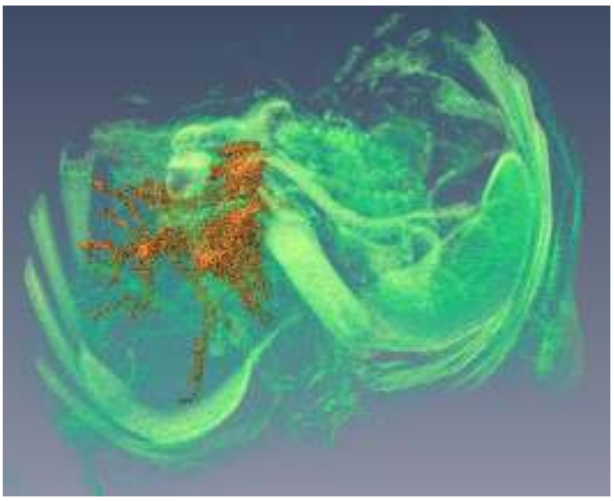

Figure 1: Segmented liver vessels superimposed on a 3D volumetric CT mask file

Material and Methods

Experimental Setup

The proposed 3D segmentation methodology was tested on three different DCE CT scans (i.e. brain, liver, tubes), to evaluate its effectiveness in segmenting different

tissues and materials under differing scanning protocols. The 4D DCE data was acquired on a 320-slice CT scanner (Toshiba, AquilionONE). The scan parameters for the 4D DCE CT scans are listed in Table 1:

Experiment	Tube Current [mA]	Tube Voltage [kV]	Voxel Dimensions [mm]
Brain	100	120	0.468 x 0.468 x 0.5
Liver	100	120	0.781 x 0.781 x 0.5
Tubes	350	120	0.625 x 0.625 x 0.5

Table 1: CT Experimental Protocol

The clinical scans (i.e. brain and liver) were segmented to allow for visual validation of the methodology's ability to segment vessels and perfused tissue. The tubes, used as controls, were submerged in a water phantom and connected to a flow pump, which injected contrast agent into the tubes. It was assumed contrast was well mixed inside the tubes. This formed a control used to test the methodology's ability to accurately segment and calculate the volumes of the tubes.

Methodology

The sequence of stages used to create a 3D segmentation of vessels and perfused tissue is listed below, with a detailed description following.

1. *Preprocessing*
   a) Obtain intensity vs. time curves for all voxels on a given slice.
   b) Compare time curves and identify key characteristics that differentiate vessel and perfused tissue voxels from other anatomical structures.
   c) Change the thresholds of the filters to accommodate these characteristics. Filters integrated into the system include:
      - Characterization of voxels
      - Best of fit comparison
      - Difference between absolute maximum and minimum intensities

2. *3D Volume Analysis (Running the Algorithm)*
   a) Eliminate time points where significant motion artifacts occur.
   b) Create an initial 3D volume and subsequently analyze each of the volume's slices:
      i. Remove voxels outside the field of view (FOV) or are not vessels or perfused tissue.
      ii. Evaluate each voxel's intensity over time and filter voxels that do not meet the chosen thresholds.
   c) Output the analyzed results as 3D mask files.

3. *Post-Processing*
   a) Use a segmentation tool to create the final segmentation mask file.

1. Preprocessing

The preprocessing stage sets up the algorithm's filter thresholds in order to discriminate between different tissue types, based on their intensity over time. The flexibility to adjust the thresholds, different tissue types can be analyzed, since the intensity values vary depending on the vessels and tissue of interest, the amount of contrast injected into the patient or system and the scanning protocols.

Initial analysis of the DCE-CT scans has revealed a number of characteristics that can be used to distinguish different tissue types. These characteristics include:

- Base line voxel intensity before the contrast is injected into the patient or tubes.
- Magnitude of difference between the absolute maximum and minimum intensities.
- Shape of the intensity-time curve based on *a priori* knowledge tissue contrast uptake.

The assumption for these characteristics is that noise observed in the scans is uniform, having a mean of 0 HU with relatively small magnitude, thus having minimal impact on the signal to noise ratio.

Acquiring these thresholds was done as follows:

1. Obtain and compare intensity-time curves for all voxels on a given volume slice. This creates a 512 x 512 voxel intensity-time curve array.
2. Select voxels from different tissue types (e.g. arteries, veins, perfused tissue, bone, air).
3. Determine what thresholds, for the characteristics, are required to distinguish the different tissue types.

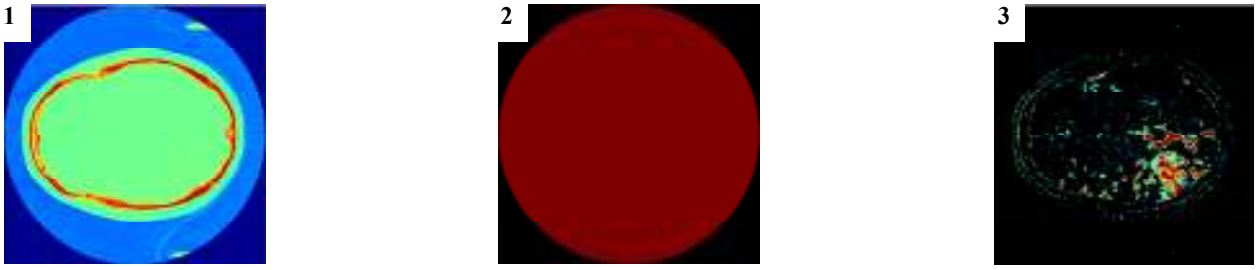

Figure 2: '3D Volume Analysis' on a given slice. (1) Original raw slice from a brain CT scan. (2) Initial filtering of voxels outside the FOV. (3) Algorithm's output: Difference between maximum and minimum intensities algorithm. Red voxels indicate greatest difference in intensities.

2. *3D Volume Analysis*

The core of the proposed methodology is the 3D segmentation algorithm. The algorithm begins by reducing artifacts introduced by motion. This is useful when analyzing 4D pCT scans of the liver or lungs, because of breathing artifacts. The elimination of these time points is accomplished by detecting time points where a significant number of voxels change in intensity more than the possible amount due to contrast uptake, between any two time points. Although this is not the optimal method for dealing with motion artifacts, the benefits from removing time points are two fold. Firstly, it reduces computational time. Secondly it decreases the possibility of introducing blurring of vessel and perfused tissue edges by restricting the analysis of voxels to the initial location of the tissue of interest. The ideal technique to deal with motion artifacts is to use non-rigid deformable registration. This would allow the algorithm to analyze the full series of DCE-CT scans.

The next step of the algorithm is to create a matrix of valid voxels on the current slice being analyzed. This is accomplished in two stages:

1. Remove voxels outside the FOV. These are voxels that do not change in intensity over time.
2. Eliminate voxels from non-perfused tissue (e.g. bone and air). The justification for removing bone and air voxels is that the perfusion of contrast only occurs in vessels and perfused tissue, defined to have a CT number between 0 and 300 HU.

The final step is the analysis of each voxel and filtering out of unwanted voxels. The overall '3D Volume Analysis' process is illustrated in figure 2. The motivation for this step is also to reduce computation time and minimize blurring. In addition, this step is novel from other segmentation procedures because it does not require the manual segmentation of unwanted anatomical structures like bone.

3. *Post-Processing*

The algorithm outputs three 4D mask files (3D volumes with color maps that indicate magnitude). These mask files contain the following results:

- Best of fit of the intensity-time curves
- Difference between the maximum and minimum intensities
- Time to reach the maximum intensity

These mask files were subsequently visualized and segmented using Amira (Visage Imaging, 4.1.1). An example of the algorithm's mask file output and the 3D segmented volume is illustrated in figure 3.

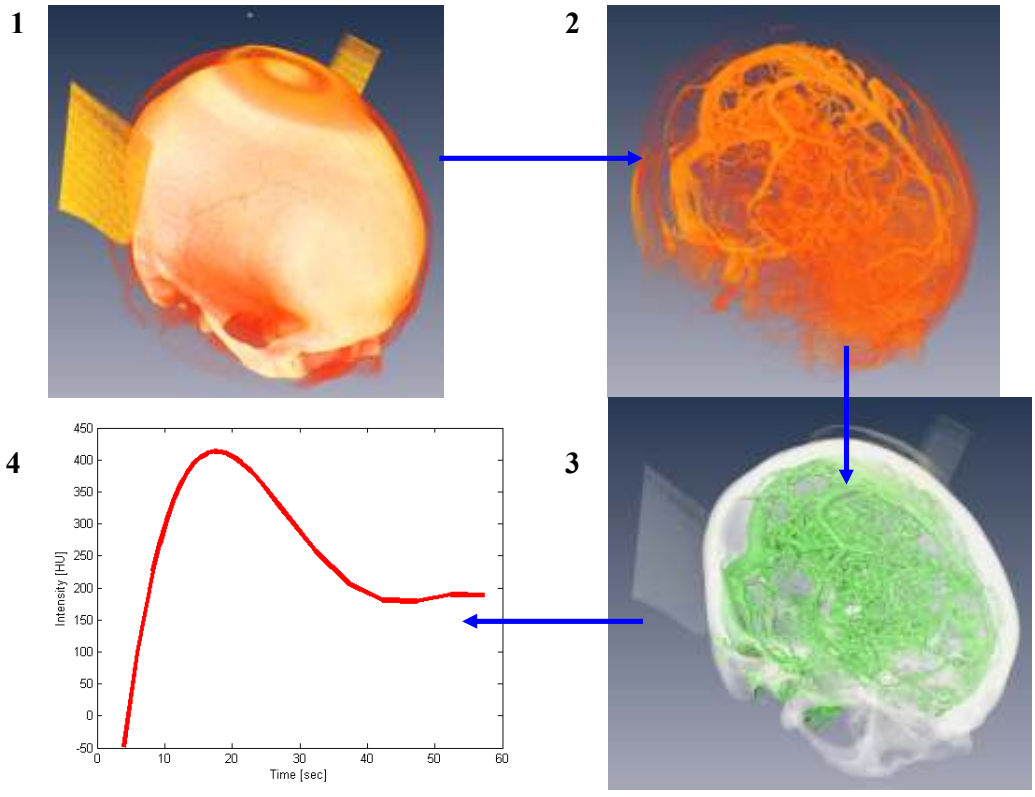

Figure 3: 3D Volume Segmentation Process. (1) Original CT brain scan. (2) Algorithm output: Maximum minus minimum intensities. (3) Segmented vessels and perfused tissue superimposed on CT scan. (4) Post-analysis of a vessel voxel.

Results and discussion

Preliminary tests were performed to check the methodology's ability to accurately determine the volume for different sizes of tubing. The tube dimensions and results are shown in tables 2, 3. The segmented coiled tube is shown in figure 4.

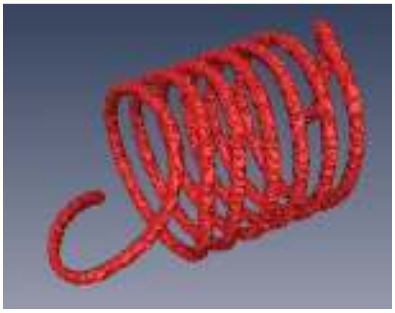

Figure 4: Segmented Coil

	Radius [mm]	Length [mm]
Coiled Tube	1.5875	1000.0
Tube 1	3.175	2.5
Tube 2	3.175	8.0

Table 2: Tubing Dimensions

	Volume Actual [mm^3]	Volume Segmentation Model [mm^3]	Error [%]
Coiled Tube	7917.3	7881.4	0.045
Tube 1	80.7	79.2	1.9
Tube 2	253.4	267.2	5.4

Table 3: Comparison of volumes between the physical tube and segmented region.

These preliminary results indicate that the proposed methodology for segmenting 3D volumes using DCE-CT scans is not only feasible but also highly accurate.

In addition when applied to clinical 4D DCE CT scans such as the liver (Figure 1) and the brain (Figure 4), the algorithm correctly extracted the vessels and perfused tissue, as validated by a clinician.
An example volumetric parameter map of time to peak enhancement is shown in Figure 5.
Although the results are sensitive to partial volume effects and thresholds (because they determine the extent of tube sidewall included in the segmentation and volume calculation) this is similar to conventional methods.

Future work for the proposed methodology includes

- Incorporating non-rigid deformable registration
- Automating pre-processing stage
- Further reducing computational time
- Incorporation into clinical 4D pCT

Conclusions

A novel method was presented for segmenting 4D DCE CT scans and automatically creating 3D functional parameter maps (such as the maximum minus minimum intensities shown in figure 3) of perfused tissue. Preliminary results of volume definition in tubes showed a high level of segmentation accuracy. In addition, evaluation of clinical data suggests this method is an excellent alternative to manually segmenting perfusion tissue. Moreover with the ongoing development of 4D pCT, this segmentation methodology provides the foundation for further analysis of perfusion parameters, setting the stage for more sophisticated methods of analyzing tumor neo-vasculature.

References

[1] Coolens C *et al.*, 2009 Implementation and characterization of a 320-slice volumetric CT scanner for simulation in radiation oncology *Medical Physics* **36** 5120-5127
[2] Miles K A and Griffiths M R 2003 Perfusion CT: a worthwhile enhancement? *The British Journal of Radiology* **76** 220-231

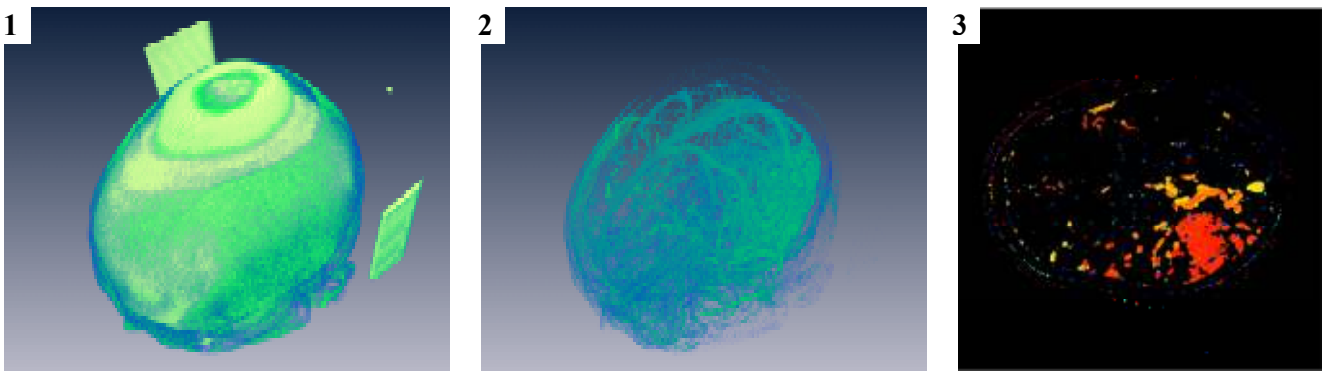

Figure 5: (1) Original CT scan. (2) Time to peak intensity output. Brighter colors signify voxels that reached their maximum intensity earlier. (3) Time to peak intensity on a slice. Redder hues signify voxels that reached their maximum intensities earlier.