Quantitative CT for Volumetric Analysis of Medical Images: Initial Results for Liver Tumors

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ABSTRACT

Quantitative CT for volumetric analysis of medical images is increasingly being proposed for monitoring patient response during chemotherapy trials. An integrated MATLAB GUI has been developed for an oncology trial at Georgetown University Hospital. This GUI allows for the calculation and visualization of the volume of a lesion. The GUI provides an estimate of the volume of the tumor using a semi-automatic segmentation technique. This software package features a fixed parameter adaptive filter from the ITK toolkit and a tumor segmentation algorithm to reduce inter-user variability and to facilitate rapid volume measurements. The system also displays a 3D rendering of the segmented tumor, allowing the end user to have not only a quantitative measure of the tumor volume, but a qualitative view as well. As an initial validation test, several clinical cases were hand-segmented, and then compared against the results from the tool, showing good agreement.

Keywords: volumetric analysis, disease progression, computed tomography (CT), software

1. INTRODUCTION

This paper focuses primarily on metastatic liver cancer. In diagnosing cancer and planning for treatment, radiologists have several non-invasive imaging procedures available such as computed tomography (CT), Magnetic Resonance (MR), and positron emission tomography (PET). For solid tumors, CT is often used to estimate the volume of tumor, both for initial diagnosis and for determining the response to treatment.

Currently, the standard metric by which disease progression is measured is "Response Evaluation Criteria in Solid Tumors", or RECIST [1]. However, RECIST has several shortcomings [1], [2]. It uses only a single 2D slice plane, ignoring the fact that tumors are non-homogenous and are 3D structures [1], [2]. Therefore, it has been proposed that a volumetric method could better evaluate the tumor progression [2].

Computer segmentation algorithms can be used on each CT slice to determine the extent of the tumor. The image slices can then be stacked on top of one another, creating a volume. Using physical spacing information inherent in the image slices, it is possible to reconstruct the tumor from the segmented data as well as estimate the tumor volume.

A MATLAB GUI for semi-automatic segmentation of liver tumors is presented here. The tomographic images from CT contrast studies are pre-processed using an adaptive filter. The slices then undergo tumor segmentation using a semi-automatic threshold based region growing algorithm. Finally, the volume of the tumor is calculated and a 3D visualization of the tumor is shown. As an initial validation, the results of the tool are compared to the results of manual segmentation.

2. METHODOLOGY

2.1 Test Dataset
For a clinical trial focused on liver metastatic disease, a quantitative method of evaluating a patient's CT images is being developed. As an initial step, a de-identified database of CT images was created under an approved Institutional Review Board protocol. This database provides a sufficient number of CT images with liver metastases for our initial testing.

2.2 Program Flow
The tumor was segmented as illustrated in Figure 1:

1) Filter the images with an adaptive filtering scheme, namely the "Curvature Anisotropic Diffusion Filter" [3].
2) The user places a seed point within the tumor. A threshold based region growing algorithm is then used to segment tumor from non-tumor. The results can then be evaluated, and additional seed points can be used to refine the segmentation if needed.
3) The segmented tumor voxels from each slice are then placed together in one 3D volume. The overall tumor volume is then calculated from the total volume of the component voxels.

These steps are carried out using the MATLAB GUI shown in Figure 3 on the next page.
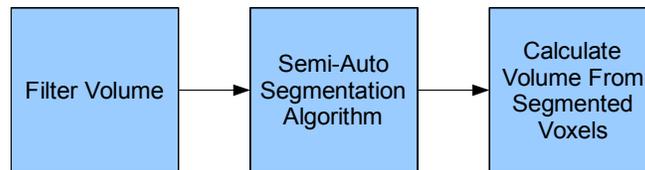

Figure 1: Program Flow Concept

2.3 Filtering Schema
The Curvature Anisotropic Diffusion Filter was implemented using ITK calls via MATITK [4]. This filter was selected because it smoothed the image while preserving the boundaries between regions. Other filters were investigated, but the CADF was used as it gave the most consistent results during segmentation testing. Also, to help reduce the parameter selection variations among users, the filter parameters are fixed with a time step of 0.0625, 5 iterations, and a conductance of 5.These parameters were selected by trial and error to see which best suited the segmentation algorithm. Figure 2 highlights the strong denoising characteristics of the filter along with its edge preservation (as compared to a median filter).
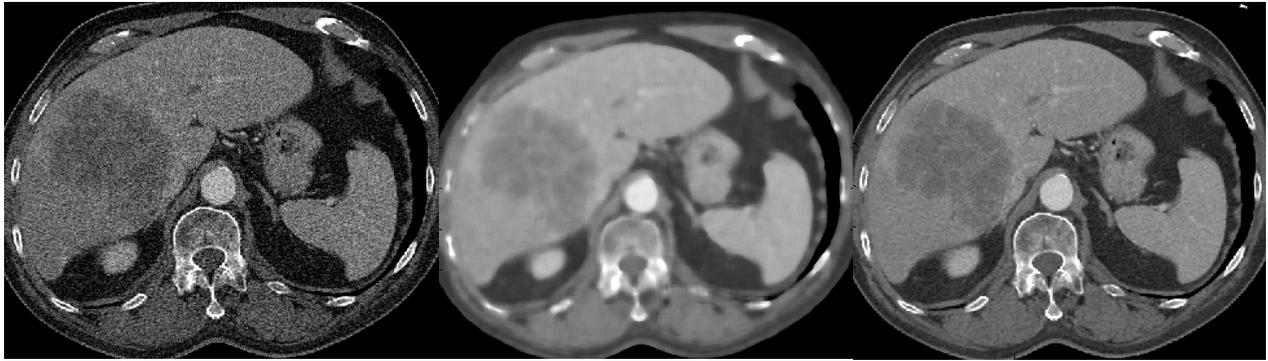
(a)   (b)   (c)

Figure 2: (a) Original Image (b) Median Filtered 10 x 10 (c) Filtered with Curvature Anisotropic Diffusion
Filter (time step: 0.0625, iterations: 5, conductance: 5)
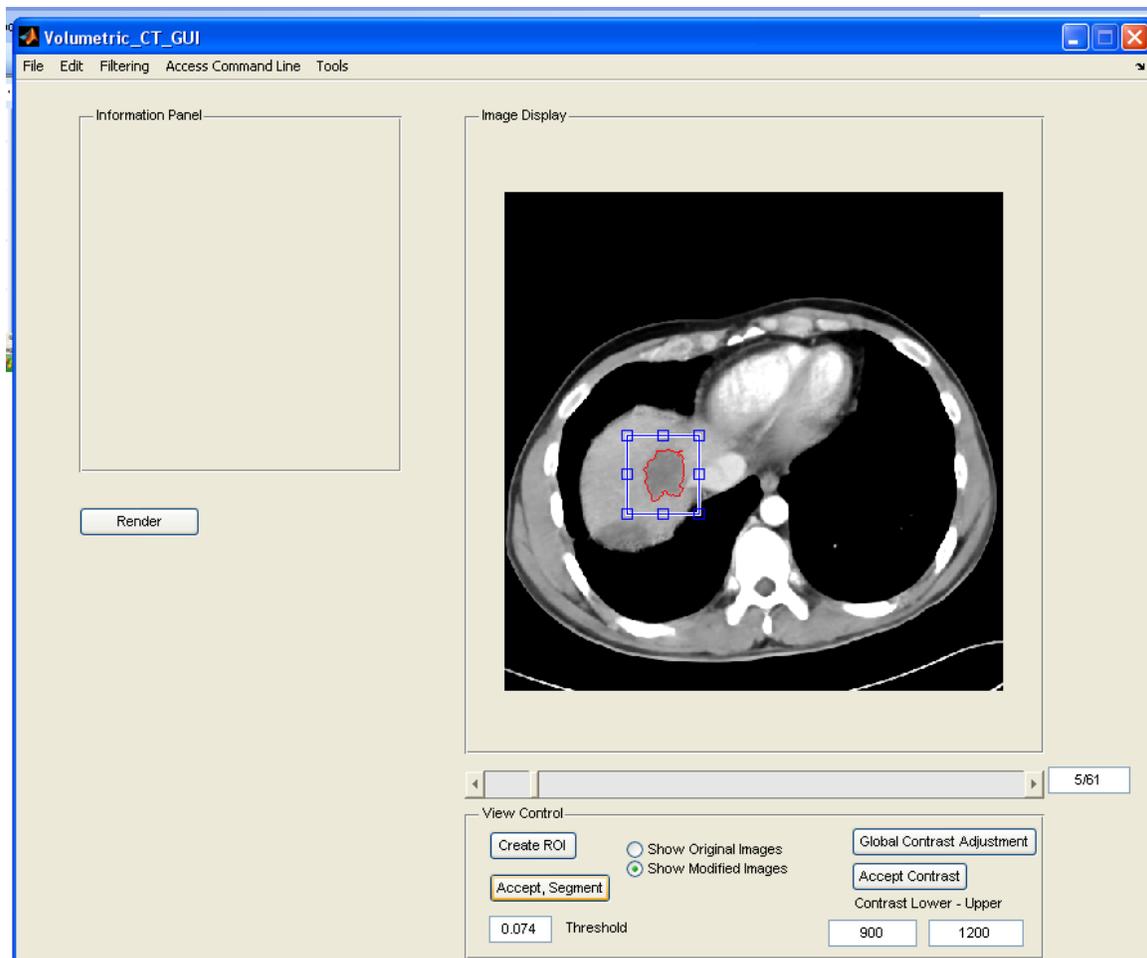

Figure 3: The MATLAB GUI with a segmented tumor slice. The region of interest is depicted in blue, and the
segmentation bounds are depicted in red.

2.4 Segmentation Algorithm

The region growing algorithm was based on an average-intensity threshold decision rule. The difference between the average intensity (in Hounsfield units) of the voxels in the region was compared with the intensity value of the voxel in question. If the difference was below a certain threshold, the voxel would be considered part of the tumor (see Equation 1 below). To allow the user to compensate for the variance in Hounsfield units among different lesion types, an adjustable threshold was implemented. The segmented tumor from each slice was then reconstructed into a volume. The physical volume was then found via voxel counting (see Equation 2 below).

$$\text{Mean}_{\text{region}} - \text{Voxel}_{i,j} < \text{Threshold} \qquad , 1$$
$$\text{Else} \qquad\qquad , 0$$

Equation. 1: Region growing algorithm's threshold based logical inclusion function

$$\hat{V} = voxelPhysicalVolume \times \sum_{x} \sum_{y} \sum_{z} voxel_{x,y,z}$$

Equation. 2: Formula for estimate of total volume of tumor

The results of the segmentation algorithm are outlined in red to allow the user to validate the results of the semi-automatic segmentation. The user may either opt to re-segment or perform a manual segmentation if the results are not to specifications. An example of this functionality is shown in the MATLAB GUI in Figure 3.

3. RESULTS AND DISCUSSION

The program was evaluated by comparing its semi-automatic segmentations with manual segmentations. A medical student segmented five clinical cases from the ISIS center de-identified database by hand via ITK-SNAP [5] (two segmentations per case). The same student then used the semi-automatic segmentation with the MATLAB GUI to segment the same five cases. These five cases consisted of small to large liver tumors, with some having one tumor and others having multiple tumors.

Case/ Test Run Number	Manual Segmentation Volume (mm³)	Semi-Automatic Segmentation Volume (mm³)	Volume Difference (mm³)	Volume Difference (%)	Time Manual Segmentation (MM:SS)	Time Semi-Automatic Segmentation (MM:SS)	Time Difference (MM:SS)
1/1	583,049	567,720	15,329	3	40:46	11:51	28:55
1/2	580,401	566,631	13,770	2	35:00	14:30	20:30
2/1	2,501	2,972	471	19	04:57	01:53	03:04
2/2	2,591	2,620	29	1	04:30	02:14	02:16
3/1	3,840	3,913	73	2	05:05	01:35	03:30
3/2	3,499	3,307	192	5	03:33	03:30	00:03
4/1	49,083	43,159	5,924	12	24:45	12:02	12:43
4/2	46,687	41,128	5,559	12	16:48	13:20	03:28
5/1	27,614	29,916	2,302	8	14:18	03:30	10:48
5/2	27,867	30,238	2,371	9	11:48	05:30	06:18
			Average	**7**			

Figure 4: Volume and time results for manual versus semi-automated segmentation

Figure 4 presents the results. With the assumption that the medical student represents ground truth, the program obtained close results. The average volume percent difference was 7%. In case 2, run 2, there was only a difference of 29 mm³, which resulted in a percent difference of 1%. The worst case (in terms of percent difference) was case 2, run 1, which had a difference of 471 mm³, resulting in a percent difference of 19%. It

was noted that the program matched up very well with manual results on the cases that had medium to large tumors. Smaller tumors tended to have less well defined regions, and as such a difference between the algorithm's computation and the medical student's perception became more pronounced.

Figure 4 also demonstrates the time savings afforded to the end user by the program. Medium sized to larger sized tumors tended to have the greatest time savings, especially if multiple lesions were present (case 1 and case 4), saving the end user as much as a half-hour. This is because the larger tumors had many slices over which the tumor was distributed. Smaller lesions tended to have lesser time savings, as they are over few slices, and can be quickly delineated by hand.

Figure 5 on the next page demonstrates partial results (for brevity, only one lesion is shown segmented) from case #1 in the GUI environment. The final window shows the rendered volume, giving the physician a qualitative view of the spatial structure of the tumor. The calculated volume is also displayed within the rendered window.
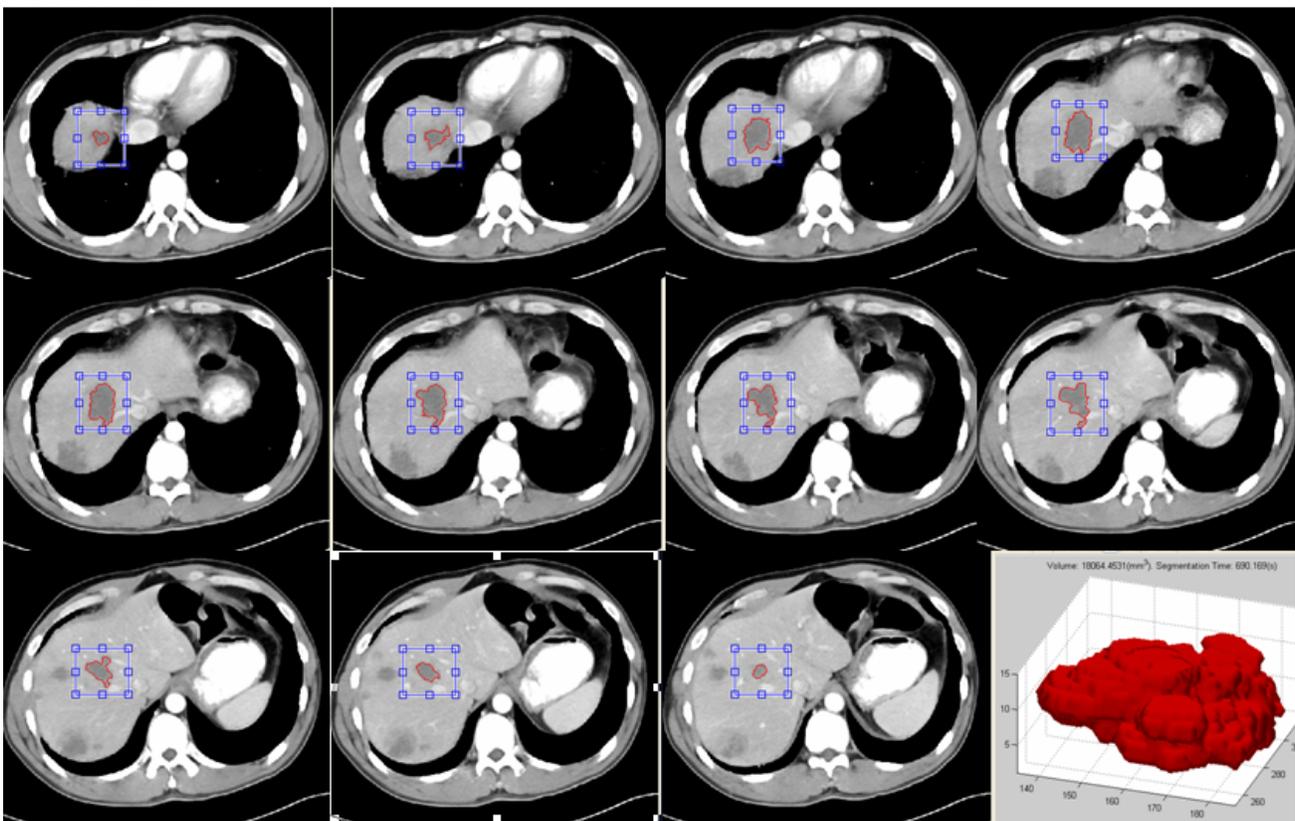

Figure 5: Liver tumor from Case 1 showing semi-automatic segmentation across 11 slices. Blue box is region of interest; red outline is segmented result. Segmentation results are rendered as a volume in the last frame.

4. CONCLUSIONS

This paper describes a MATLAB GUI for providing physicians with volumetric data about liver tumors. An adaptive filtering system and a region growing segmentation algorithm have been implemented to allow for segmenting tumor from healthy liver tissue. The program computes the tumor volume based on segmented CT slices and also renders the segmented tumor to allow the physician to visualize the tumor. Preliminary testing has shown that the program is in good agreement with manual segmentation, and can significantly

improve the speed of segmentation, realistically allowing for its use in a clinical setting. In summary, this work is a novel integrated platform for liver tumor volumetric analysis applicable to a clinical setting. This work is timely in that quantitative imaging for disease progression analysis is a topic of great clinical interest.

Acknowledgements

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