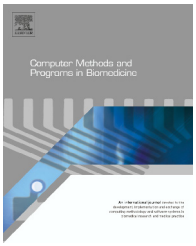
COMPUTER METHODS AND PROGRAMS IN BIOMEDICINE 111 (2013) 480–487

journal homepage: www.intl.elsevierhealth.com/journals/cmpb



Validation study of a fast, accurate, and precise brain tumor volume measurement

Mong Dang[a,*], *Jayesh Modi*[a], *Mike Roberts*[b], *Christopher Chan*[c], *J. Ross Mitchell*[d]

[a] *Imaging Informatics Lab, 2500 University Drive NW, Calgary, AB T2N 1N4, Canada*
[b] *School of Engineering and Applied Sciences, 29 Oxford Street, Cambridge, MA, USA*
[c] *Diagnostic Imaging, 2500 University Drive NW, Calgary, AB T2N 1N4, Canada*
[d] *Mayo Clinic, 13400 E Shea Boulevard Scottsdale, AZ 85259, USA*

ARTICLE INFO

Article history:
Received 15 January 2013
Received in revised form
13 March 2013
Accepted 17 April 2013

Keywords:
Volume
Segmentation
Image processing
Brain tumor
Magnetic resonance imaging

ABSTRACT

Precision and accuracy are sometimes sacrificed to ensure that medical image processing is rapid. To address this, our lab had developed a novel level set segmentation algorithm that is 16× faster and >96% accurate on realistic brain phantoms.

Methods: This study reports speed, precision and estimated accuracy of our algorithm when measuring MRIs of meningioma brain tumors and compares it to manual tracing and modified MacDonald (MM) ellipsoid criteria. A repeated-measures study allowed us to determine measurement precisions (MPs) – clinically relevant thresholds for statistically significant change.

Results: Speed: the level set, MM, and trace methods required 1:20, 1:35, and 9:35 (mm:ss) respectively on average to complete a volume measurement ($p < 0.05$). Accuracy: the level set was not statistically different to the estimated true lesion volumes ($p > 0.05$). Precision: the MM's within-operator and between-operator MPs were significantly higher (worse) than the other methods ($p < 0.05$). The observed difference in MP between the level set and trace methods did not reach statistical significance ($p > 0.05$).

Conclusion: Our level set is faster on average than MM, yet has accuracy and precision comparable to manual tracing.

1. Introduction

Brain tumor volume measurement in MRI (magnetic resonance imaging) and CT (computed tomography) volumes is often used to aid treatment [1–3]. Volume measurement techniques have three important features that impact their clinical utility: speed (the total time required to make a measurement); accuracy (the ability to correctly identify the specific image voxels in the lesion); and, precision (the ability to obtain similar repeated measurements). However, one or more of these properties are often sacrificed during clinical application. For example, methods requiring an operator to visually inspect change in tumor size are fast, but have large inter-observer variability (and thus, poor precision) [4]. Conversely, methods that require manual outlining, slice-by-slice, are more accurate and precise, but more time-consuming [4].

A common clinical practice is to use the modified MacDonald (MM) Criteria for volume measurement [5]. With this method, the operator must specify: (1) the number of image slices in which the tumor is visible; and (2) the maximum cross-sectional and orthogonal diameters of the tumor. By assuming that the tumor is a perfect axis-aligned ellipsoid, the MM Criteria can estimate the tumor's volume from these measurements. Although this method is fast, it suffers from low accuracy and reliability [6] since tumors are rarely

* *Corresponding author*. Tel.: +1 403 400 6446.
E-mail address: mdang@ucalgary.ca (M. Dang).
0169-2607/$ – see front matter © 2013 Elsevier Ireland Ltd. All rights reserved.
http://dx.doi.org/10.1016/j.cmpb.2013.04.011

axis-aligned ellipsoids. Also, it requires the operator to estimate the cross-sectional major and minor axes of the tumor by visual inspection, and this process can be error-prone.

Consequently, there is significant interest in new computer-assisted measurement methods that are accurate and precise, yet fast enough for clinical use [4,7–12]. A promising family of computer-assisted techniques use level sets [13,14]. These algorithms generally require placement of a *seed* region-of-interest (ROI) in the image. The seed is typically a small sphere, and can be placed with a single mouse click. Level set algorithms iteratively deform the seed surface to envelop an ROI. The rate of surface growth and contraction is controlled by local image properties, and surface curvature [15]. This curvature-dependent growth encourages a smooth surface, and "prevents the surface from leaking into undesired areas across weak, incidental connections at ROI boundaries" [16]. Moreover, level set algorithms allow one to vary the surface curvature to control growth. These properties make level set algorithms robust and flexible during challenging volume measurement tasks [17].

However, level set segmentation has been too computationally intensive, and time consuming, for widespread clinical use. Therefore, we developed a novel massively parallel level set algorithm that runs on commodity graphical processing units (GPUs). Our algorithm is 16× faster than the previous fastest algorithm, and several hundred times faster than non-GPU algorithms [16]. Our new algorithm improves performance without reducing accuracy [16] when measuring known tissue volumes in a realistic brain phantom. However, its speed, accuracy and reliability are not known for measuring lesions in patient exams.

A study performed by Cates et al. demonstrated that level set algorithms have measurement accuracies similar to hand tracing methods [17]. They had students and staff work with 9 cases. But limited resources prevented intra-subject comparisons [17].

Here we report on a repeated-measurement study involving two radiologists and a biomedical engineering masters student. These operators made 450 measurements of meningioma brain tumors in 25 preoperative patient MR exams using our new tool, manual outlining, and the MM "ellipsoid" method. These data allowed us to compare the speed and estimated accuracy of the three volume estimation techniques. Importantly, it also allowed us to calculate and compare between- and within-operator measurement precision (MP) [18]. Changes in lesion volume less than MP values can be explained entirely by variability in the measurement process. Consequently, MPs are important parameters that allow clinicians to determine when statistically significant changes in volume have occurred. Both accuracy and precision are important characteristics of volume measurement methods. Our primary contribution here is a detailed analysis of the MP of three volume segmentation algorithms.

2. Patients and methods

This study received institutional review board approval. Three hundred brain tumor patients were selected randomly from a neurosurgical image database. The inclusion criteria were: a preoperative meningioma tumor; good quality MRI scans performed on a 1.5T Siemens Magnetom MR scanner (Siemens Healthcare, Germany); and tumors that were homogeneously enhancing. Thirty-one cases met all inclusion criteria. The MR acquisition parameters are provided in Table 1. Six of the 31 cases were used for training and 25 for analysis. The MR images were anonymized to remove all patient identifiers using DICOM Anonymizer Pro [19,20]. All cases were then loaded into OsiriX (Pixmeo, Geneva, Switzerland), for the MM and trace measurements. Both OsiriX and DICOM Anonymizer Pro were run on an iMac 3.2 GHz Intel Core i7, Mac OS X Snow Leopard (Apple, Cupertino, CA). Our level set method was performed on an Intel 2.5 GHz Xeon Processor with 4 GB of memory running Microsoft Windows 7 Professional (Microsoft, Redmond, Washington) and an NVIDIA GTX 480 GPU with 1.5 GB of video ram (Nvidia, Santa Clara, CA) [16].

Table 1 – Imaging parameters of the T1-weighted scans.

Magnet	1.5 Tesla (Siemens Healthcare, Germany)
Image type	T1-weighted RAGE, post-gadolinium
Image plane	Axial
Field of view	256 mm
TR	1900 ms
TE	3.37 ms
Slice thickness	1 mm
Slice gap	0 mm
NEX	1
Bandwidth	130 Hz/Px
Scan time	5.21 min

2.1. *Tumor volume measurements*

Three operators: JM, a neuroradiology fellow; CC, a radiology resident; and MD, a biomedical engineering master's student; collected measurements for this study. A non-radiologist was included since many centers have technologists perform tumor volume measurements. The study proceeded in two phases. In the *training phase*, operators gained experience with the tools, and reached consensus on specific methods (i.e. data loading and measurement sequence) and operator-adjustable parameters (i.e. seed region's window, level, and curvature influence). In the *measurement phase*, operators performed repeated measurements of tumor volumes.

2.1.1. *Training phase*

Operators practiced the MM, trace and level set methods on six training cases, selected at random from the 31 in our study. There were two days between practice sessions for each operator and method.

2.1.2. *Measurement phase*

Fig. 1 describes the measurement phase for all three methods. We were concerned that operators might consider segmentations by the highly automated level set tool to be more accurate. Therefore, operators completed measurements in the order AABBCC, where A was the MM method, B was the trace method, and C was the level set method. To reduce learning effects, a gap of one week was enforced between repeated measurements, and methods. The 25 non-training cases were each measured twice, by 3 operators, using each method, for a total of 450 measurements (25 cases × 2