Technical Report

Automated Tumor Volumetry Using Computer-Aided Image Segmentation

Bilwaj Gaonkar, MS, Luke Macyszyn, MA, MD, Michel Bilello, MD, PhD, Mohammed Salehi Sadaghiani, MD, Hamed Akbari, MD, PhD, Mark A. Atthiah, MD, Zarina S. Ali, MD, Xiao Da, MS, Yiqang Zhan, PhD, Donald O' Rourke, MD, Sean M. Grady, MD, Christos Davatzikos, PhD

Rationale and Objectives: Accurate segmentation of brain tumors, and quantification of tumor volume, is important for diagnosis, monitoring, and planning therapeutic intervention. Manual segmentation is not widely used because of time constraints. Previous efforts have mainly produced methods that are tailored to a particular type of tumor or acquisition protocol and have mostly failed to produce a method that functions on different tumor types and is robust to changes in scanning parameters, resolution, and image quality, thereby limiting their clinical value. Herein, we present a semiautomatic method for tumor segmentation that is fast, accurate, and robust to a wide variation in image quality and resolution.

Materials and Methods: A semiautomatic segmentation method based on the geodesic distance transform was developed and validated by using it to segment 54 brain tumors. Glioblastomas, meningiomas, and brain metastases were segmented. Qualitative validation was based on physician ratings provided by three clinical experts. Quantitative validation was based on comparing semiautomatic and manual segmentations.

Results: Tumor segmentations obtained using manual and automatic methods were compared quantitatively using the Dice measure of overlap. Subjective evaluation was performed by having human experts rate the computerized segmentations on a 0–5 rating scale where 5 indicated perfect segmentation.

Conclusions: The proposed method addresses a significant, unmet need in the field of neuro-oncology. Specifically, this method enables clinicians to obtain accurate and reproducible tumor volumes without the need for manual segmentation.

Key Words: Tumor segmentation; volumetric analysis; geodesic distance.

Quantification of tumor volume has become increasingly important for diagnosis, staging, assessment of therapy response, and more recently determination of eligibility for clinical trial enrollment (1–3). Currently, assessment of tumor volume is based on two-dimensional (2D) measurements, using standards such as the MacDonald criteria (4) for gliomas, Herscovici criteria (5) for meningiomas, or the RECIST standards for general oncology (6).

These criteria allow clinicians to obtain a rough estimate of tumor volume by sacrificing accuracy for speed. An accurate measurement of tumor volume, however, requires a complete segmentation of the tumor. This type of segmentation, which can currently be performed manually, requires a tremendous amount of time and hence is not widely used. Thus, automation of tumor segmentation represents an important clinical need that would be invaluable for treating and monitoring patients with brain tumors. Furthermore, such automatic segmentations are likely to be more reproducible and therefore preferable over manual segmentations because of their consistency, which is especially important for longitudinal tumor monitoring.

The neuroimaging community has attempted to address the need for automatic tumor segmentation over the past two decades. The earliest methods included the use of fuzzy clustering-based approaches (7,8). Direct application of such methods leads to a large number of false-positive voxels labeled as tumors. Later methods based on level sets and active contours (9,10) often fail in the context of aggressive tumors harboring significant structural complexity. Machine-learning–based methods have been fairly successful at the

Acad Radiol 2015; ■:1–9

From the Department of Radiology, University of Pennsylvania, 3600 Market St, Suite 380, Philadelphia, Pennsylvania, 19104 (B.G., M.B., M.S.S., H.A., X.D., C.D.); Center for Biomedical Image Computing and Analytics (B.G., L.M., M.B., H.A., X.D., C.D.) and Department of Neurosurgery (L.M., M.A.A., Z.S.A., D.O.R., S.M.G.), University of Pennsylvania, Philadelphia, Pennsylvania; and Siemens Medical Solutions, Malvern, Pennsylvania (Y.Z.). Received August 26, 2014; accepted January 8, 2015. B.G. and L.M. contributed equally to the study. Conflicts of Interest: None. Funding Sources: This work was supported in part by grants R01NS042645 from National Institutes of Health (PI: Davatzikos). **Address correspondence to:** B.G. e-mail: bilwaj@gmail.com

http://dx.doi.org/10.1016/j.acra.2015.01.005

task of tumor segmentation (11–21). However, these methods are often tumor type specific and very sensitive to changes in noise and acquisition protocol. Additionally, there is a constant need for retraining with most learning-based methods when there is a slight change in the imaging protocol or if the scanning site changes. Furthermore, many of these methods are based on complex algorithms that are expensive to reimplement and difficult to integrate into existing clinical workflows. Finally, most of these methods have been validated in a narrow and limited research setting and not necessarily in a clinical setting. In general, the narrow focus of previously described techniques has prevented their widespread utilization in the clinical arena.

In this work, we present a novel tumor segmentation technique that is semiautomatic, fast, and based on a relatively simple learning-free algorithm. We have validated our method on three different tumor types acquired under a diverse set of image acquisition protocols and resolutions and drawn from studies using different preprocessing steps. Qualitative and quantitative results present the efficacy of the proposed method in the presence of substantial noise, scanner variation, processing variation, and tissue (tumor) heterogeneity.

MATERIALS AND METHODS

Institutional review board approval was obtained for this study with waiver of informed consent for retrospective review of medical records. All imaging data came from patients treated at the Hospital of the University of Pennsylvania. In general, these imaging studies contained differences between cases in terms of resolution, noise level, and pixel spacing. Overall, our data set contained images of 24 glioblastomas, 15 meningiomas, and 15 metastatic brain tumors. T1 contrast-enhanced images were available for all tumors and were used for automatic and manual segmentations.

The data used in this project varied across cases in terms of acquisition protocol, resolution, and pixel spacing. It was sequentially chosen. Some of the data came from a 3.0-T magnetic resonance (MR) imaging scanner systems (Siemens and GE Healthcare) and some of it came from a 1.5-T systems. Similarly, the pixel spacing varied from 0.42×0.42 to 0.97×0.97, and image dimensions varied between 256×256 to 512×512. Slice thicknesses during acquisitions varied between 1 and 5 mm. The echo times and repetition times involved in computing the T1 images also varied. This was a retrospective study, and we used a random sample of cases available on the internal University of Pennsylvania Picture Archiving and Communication System.

Thus, there was tremendous variation between cases with respect to noise and inhomogeneity. The segmentation results presented here are testimony to that the proposed method is able to successfully segment these brain tumors in spite of the considerable variation in the underlying data.

We use the adaptive geodesic algorithm described by Gaonkar and Shu (22) to segment brain tumors. This is a semiautomatic method that was originally devised to segment the vertebral column on computed tomographic images using the adaptive geodesic distance (23,24). The method is fast, easy to use, and robust to noise and bias. A seed region is placed by the clinician inside a tumor, and the segmentation algorithm is initiated. The "adaptive geodesic distance" is a mathematical measure that may be computed at any voxel within the image. At a given voxel, this measure provides a joint quantification of 1) the spatial distance of the voxel from the seed region and 2) the variation of the image intensity profile between the voxel and the seed, both of which are important clues for tumor segmentation The algorithm computes the adaptive geodesic distance at every voxel in the image to yield an "adaptive geodesic distance transform image." This transformed image appears as a geodesic distance–weighted inverse of the original MR image (Fig 1b) and thresholding of this image generates the final segmentation mask. Because of the computational efficiency of this approach, the "adaptive geodesic transform image" can be performed in a matter of seconds. A detailed explanation of the algorithm and the associated intuition is provided in the following.

Geodesics are the generalization of straight lines to curved spaces. The pedagogic example of a geodesic is given in relation to the earth's surface. If one were to travel along a straight line from the North Pole to the South Pole, one would have to burrow through the earth's core to travel. It is much easier to make this journey over the surface of the earth. In this case, the distance traveled along the earth's surface is the geodesic distance which is considerably larger than the straight line distance between the poles.

To apply the concept of geodesic distances to image segmentation, we can imagine the intensity profile of a 2D image to define a surface in 3D space. The geodesic distance between two points is the shortest path between the two points as measured while moving along the surface.

Given an initial voxel (or set of voxels) inside the tumor, we can compute the geodesic distance to this point (or set of points) from every other voxel in the image. This allows for the construction of a geodesically transformed image whose voxel intensities are the geodesic distances from the initially picked voxel. Geodesic segmentation then involves segmentation of the geodesically transformed image by thresholding.

For nonheterogeneous solid tumors such as meningiomas, direct application of the aforementioned geodesic segmentation technique is sufficient. The geodesic distance described by Criminisi (23) is still based on a metric that is locally dependent on image gradients alone. To adapt the technique to segment more complex and heterogeneous tumors such as glioblastomas, we need to locally vary the metric on the basis of prior knowledge. This leads to the adaptive geodesic distance which we used to segment all tumors in the paper.

The naive computation of the geodesic distance transform would entail visiting every voxel and computing the geodesic distance using a discretized form of the Euler–Lagrange equations. Mathematically, this involves solving the minimization: