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Segmentation of solid subregion of high grade gliomas in MRI images based on active contour model (ACM)

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Abstract. Gliomas are tumours arising from the interstitial tissue of the brain which are heterogeneous, infiltrative and possess ill-defined borders. Tumour subregions (e.g. solid enhancing part, edema and necrosis) are often used for tumour characterisation. Tumour demarcation into substructures facilitates glioma staging and provides essential information. Manual segmentation had several drawbacks that include laborious, time consuming, subjected to intra and inter-rater variability and hindered by diversity in the appearance of tumour tissues. In this work, active contour model (ACM) was used to segment the solid enhancing subregion of the tumour. 2D brain image acquisition data using 3T MRI fast spoiled gradient echo sequence in post gadolinium of four histologically proven high-grade glioma patients were obtained. Pre-processing of the images which includes subtraction and skull stripping were performed and then followed by ACM segmentation. The results of the automatic segmentation method were compared against the manual delineation of the tumour by a trainee radiologist. Both results were further validated by an experienced neuroradiologist and a brief quantitative evaluations (pixel area and difference ratio) were performed. Preliminary results of the clinical data showed the potential of ACM model in the application of fast and large scale tumour segmentation in medical imaging.

1. Introduction

Glioma is a type of tumour that initiates from the interstitial tissue of the brain. Astrocytic tumour can be grouped to diffuse astrocytoma, anaplastic astrocytomas or malignant glioblastoma multiforme (GBM) respectively labelled by grade II, III or IV according to the World Health Organization (WHO) guidelines [1], where high grade gliomas are grade III and IV. Glioma grading facilitates the management of the disease and establishes the prognosis of the patient. Glioma is characterised by heterogeneous neoplasms consisted of several subregions that include the solid part, cystic (necrotic) part, varying degrees of tumour infiltration in normal tissue as well as microvascular cellular proliferation and edema [2]. The enhancing solid subregion is the wanted part identified by the clinicians because it is the part where biopsy sites were taken as it is considered to resemble the histopathology of the brain tumour most closely. The growth of the solid subregion primarily comes from cellular proliferation [3]. Magnetic Resonance Imaging (MRI) is commonly used for biopsy management and



characterisation of gliomas. A combination of selected MRI sequences (pre- and post-contrast T1-weighted (T1W), T2-weighted (T2W) and T1 Fluid-Attenuated Inversion Recovery (FLAIR)) is often employed for tumour subregions delineation [4]. Manual delineation of gliomas is not only time-consuming but also subjected to intra- and inter-observer variability which potentially leads to substantial inconsistency in the delineation of the region of interest (ROI). Furthermore, similar results are not reproducible even though for the same observer. These problems can be addressed by engaging automatic segmentation methods. Accurate segmentation is challenging due to high diversities of tumour properties and characteristics even within the same tumour grade, occurrence of heterogeneity within the tumour, unpredictable growth of the tumourous cells and vague boundaries. To date, there are many segmentation methods available for brain tumour and active contour model (ACM) is one of the most robust techniques [5].

2. Methodology

2.1. MRI data retrieval and pre-processing

The brain MRI data for pre- and post-gadolinium T1W, T2W and FLAIR sequences of four histologically proven high-grade gliomas (n=1 for grade III & n=3 for grade IV) were retrieved from the database after ethical approval was obtained. These glioma patients were scanned on a 3T MRI (Signa HDx, General Electric, USA). The pre- and post-contrast T1W MRI images were used for ACM segmentation where all the slices were gone through to obtain a single slice image with the largest region of the solid subregion while the T2W and FLAIR MRI images were used to assist the manual delineation. The solid subregion was determined as the portion of the tumour that exhibits isointense signal on T1W images and iso- to hyperintense signal on T2W images, with presence of tumour enhancement. The MRI images were pre-processed prior to segmentation by employing image subtraction followed by skull-stripping to remove the non-cerebral tissue region such as skull, scalp, and meninges.

2.2. Active contour model segmentation

Local region based ACM is preferable for medical image segmentation due to robustness to initialization and noise [6]. ACM for objects detection in an image is based on techniques of curve evolution and the level set method. The basic idea of ACM or snakes is to evolve a curve in a given image until it is guided to stop at the boundary of the desired object. Region based models exploit global region information by employing features such as intensity, colour, and texture. ACM is advantageous because it is able to detect objects whose boundaries are not necessarily defined by the gradient. The general formalism of the ACM model is based on the snake model [7] and is expressed as equation (1) [6]:

$$F(c_1, c_2, C) = \int_{\Omega_1=\omega} (u_0(x, y) - c_1)^2 dx dy + \int_{\Omega_2=\Omega-\omega} (u_0(x, y) - c_2)^2 dx dy + v|C| \quad (1)$$

where u_0 is the given image, $C = \delta\omega$ is the parameterized curve with c_1 and c_2 are the unknown constants. The first two terms are described as two forces. The goal is to minimize the energy forces with respect to the constants and curve so that contour C reaches its equilibrium. The first term is the force to shrink the contour while the second term is the force to expand the contour. These two forces get balanced when the contour arrives at the boundary of the desired object. The MRI images were retrieved into MATLAB R2013a (MathWorks, Massachusetts, USA) for ACM segmentation implementation which took around less than 20 minutes for solid subregion segmentation in one sequence of a patient.

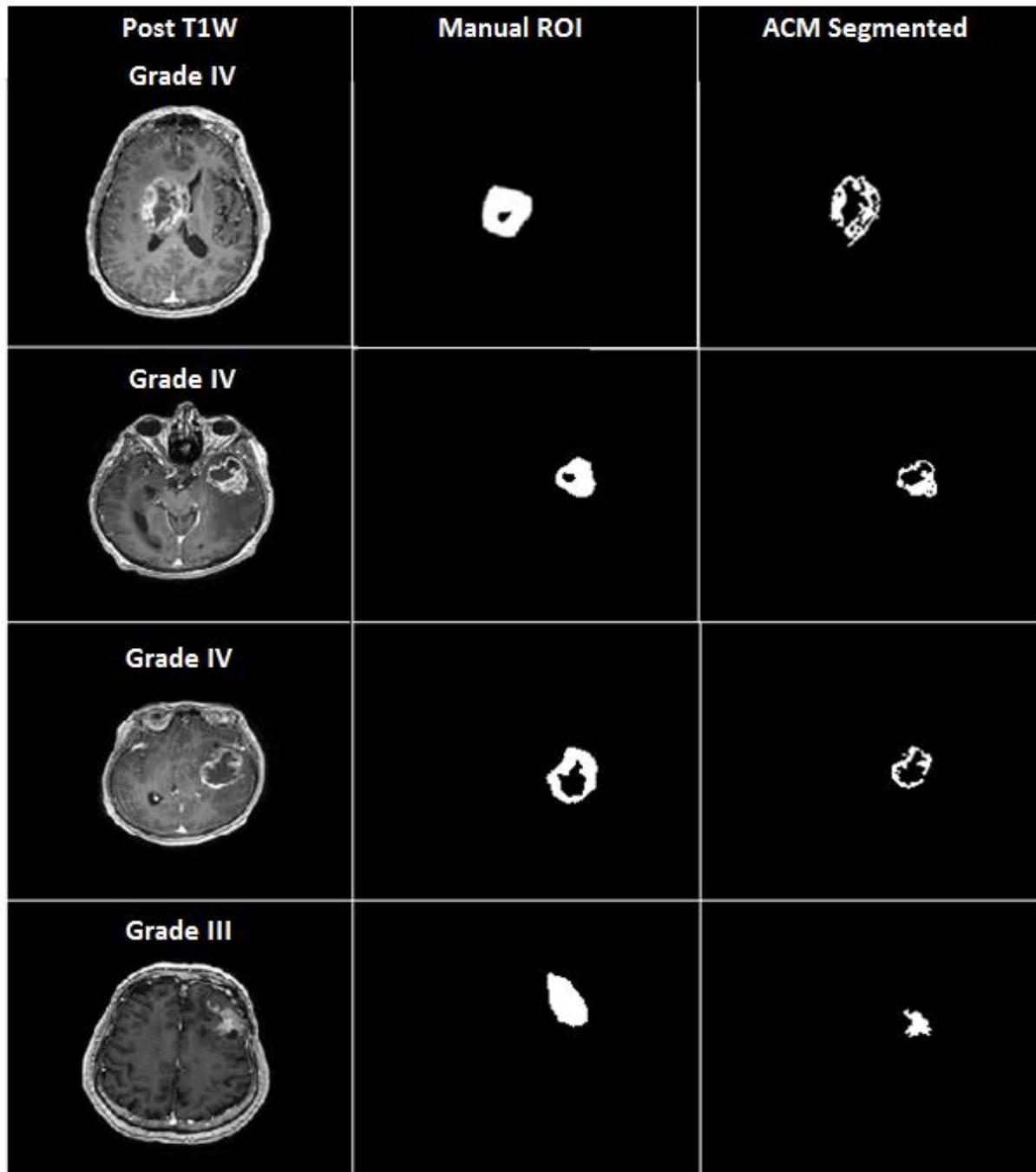


Figure 1. Post-gadolinium T1W MRI images of four high grade glioma patients (left), the manually delineated ROIs of the solid subregions by the radiologist (center) and the ACM segmented solid subregions of the tumour (right). The gliomas grade IV are glioblastoma multiforme (GBM) and the glioma grade III is anaplastic oligodendroglioma. The cystic portion of the grade III patient is too small to be delineated manually.

2.3. Comparison with manual segmentation

Manual delineations of the solid subregions were performed by a trainee radiologist (WMT) for comparison with the ACM segmented results. The average time spent for manual volumetric delineation

of the tumour into its subregions (solid, cystic and edema part) was roughly 1 hour per sequence for one single patient.

2.4. Validation of segmented solid subregions

The manual delineated ROIs and ACM segmented solid subregions were randomized and presented to an experienced neuroradiologist (NR) who was blinded to the segmented results and the histological grades of the images. The neuroradiologist then decided on which segmented results that better represent the enhancing solid subregions. The preferred segmented results serve as the validation of the ACM model.

3. Results and discussion

Figure 1 shows better morphological structures on the solid subregions depicted using ACM segmentation when compared to the manually delineated ROI of the solid portions of all the four images. The segmented solid subregions showed clear boundaries between the solid subregions and the cystic subregions. The region based ACM model make use of the intensity characteristics emphasized from the subtraction process of the pre-contrast from the post-contrast T1W MRI image. Large differences for the pixel areas between the manual and automatic segmented results were obtained (table 1). The pixel area of the manually delineated ROIs were always larger than the ACM segmented solid subregions because the ROIs of the manual delineations are merely estimations of the subregions. Validation by the clinician showed that ACM segmentation was preferred compared to manual segmentation as the ACM segmented results were chosen to best represent the solid subregions in all the four images. Difference ratios describe about the dissimilarities between the manual and the automatic segmented subregions where high difference ratio indicates high dissimilarity between them. The segmentation results for grade III showed the highest difference ratio implying a large difference between the manual and ACM segmented subregions. The current ACM model can be improved for segmentation of cystic and edema subregions.

The subtraction process of the pre-contrast from the post-contrast MRI image facilitates the segmentation technique by accentuating the intensity characteristic of the solid subregion, a feature manipulated by the ACM model to carry out the segmentation of the solid portion of the tumour. The limitation of using the ACM model is that the initialization depends on the placement of the curve and the size of the initial contour. The model works better when the initial contour was placed nearer to the region of the solid portion of the tumour. Other than that, the ACM model does not work so well for the glioma cases which possess high degree of heterogeneity and weak borders between the tumour subregions. ACM segmentation is efficient for lesion segmentation since manual delineation could never achieve such detailed segmentation results that showed clear structures and border of the solid portion as ACM. Furthermore, ACM segmentation is much faster than manual segmentation. Precise manual delineation following the outlines of the enhancing solid subregion is time consuming, laborious and not practical in clinical practice.

Table 1. The validation measures of the four glioma patients for the segmentation of the solid subregions as compared to the manually delineated ROIs. Data 1 till 3 correspond to grade IV gliomas while data 4 refers to grade III glioma. Validation described the decision to choose which segmentation results that best represent the solid enhancing subregions based on the MRI images where value 1 means represent while value 0 means did not represent.

	Segmented Area (pixel number)		Validation by Neuroradiologist		Difference Ratio $\left(\frac{Manual-ACM}{ACM}\right)$
	Manual	ACM	Manual	ACM	
1	973	712	0	1	0.367
2	408	281	0	1	0.452
3	554	227	0	1	1.441
4	722	181	0	1	2.989

4. Conclusion

Preliminary results showed that the ACM model is feasible for time efficient and large scale segmentation of solid enhancing subregion from the tumour core of brain gliomas. The ACM method is a better method to represent the solid enhancing portion of the tumour when compared to manual delineation. Brain tumour segmentation has great impact on diagnosis, monitoring, treatment planning for patients and clinical trials. Improved accuracies and performance in the ACM model will favour the realization of computer aided detection (CAD) for detection and diagnosis of gliomas.

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