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Auto-Initialized Cascaded Level Set (AI-CALS) Segmentation of Bladder Lesions on Multi-Detector Row CT Urography

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Abstract

Rationale and Objectives—To develop a computerized system for segmentation of bladder lesions on CT urography (CTU) scans for detection and characterization of bladder cancer.

Materials and methods—We have developed an auto-initialized cascaded level set (AI-CALS) method to perform bladder lesion segmentation. The segmentation performance was evaluated on a preliminary data set including 28 CTU scans from 28 patients collected retrospectively with IRB approval. The bladders were partially filled with intravenous (IV) contrast material. The lesions were located fully or partially within the contrast-enhanced area or in the non-contrast-enhanced area of the bladder. An experienced abdominal radiologist marked 28 lesions (14 malignant and 14 benign) with bounding boxes that served as input to the automated segmentation system and assigned a difficulty rating (DR) on a scale of 1 to 5 (5=most subtle) to each lesion. The contours from automated segmentation were compared to 3D contours manually drawn by the radiologist. Three performance metric measures were used for comparison. In addition, the automated segmentation quality was assessed by an expert panel of two experienced radiologists, who provided quality ratings of the contours on a scale from 1 to 10 (10 = “excellent”).

Results—The average volume intersection ratio, the average absolute volume error, and the average distance measure were $67.2 \pm 16.9\%$, $27.3 \pm 26.9\%$, and 2.89 ± 1.69 mm, respectively. Of the 28 segmentations, 18 were given quality ratings of 8 or above. The average rating was 7.9 ± 1.5 . The average quality ratings for lesions with difficulty ratings of 1, 2, 3, and 4 were 8.8 ± 0.9 , 7.9 ± 1.8 , 7.4 ± 0.9 , 6.6 ± 1.5 , respectively.

Conclusion—Our preliminary study demonstrates the feasibility of using the 3D level set method for segmenting bladder lesions in CTU scans.

Keywords

CT urography; bladder cancer; 3D segmentation; level sets

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1. Introduction

Bladder cancer is a common type of cancer that can cause substantial morbidity and mortality among both men and women. Bladder cancer causes 14,880 deaths per year in the United States [1]. Early detection of bladder cancers is very important. The survival rate for patients whose cancers were detected and treated early is high [1]. Early diagnosis and treatment of these lesions can improve the morbidity, mortality and their attendant costs compared to diagnosis at a later stage when muscularis mucosa invasion and/or regional or distant metastases have developed. However, at the present time, only 75% of cancers are detected in the early localized stage.

Multi-detector row CT (MDCT) urography is a very promising new imaging modality for evaluation of patients with known or suspected urothelial neoplasms [2-5]. It offers the distinct advantage of providing essentially complete imaging of the urinary tract and of the remainder of the abdomen and pelvis in a single study. With MDCT urography, it is expected that the need for other imaging studies (such as intravenous urography, ultrasonography, or MRI) will be substantially reduced. CT urography (CTU), therefore, may spare the patient the considerable effort of undergoing a potentially large number of alternative imaging studies and also reduce health care costs.

Preliminary studies [6] have suggested that CTU may have superior sensitivity in detecting urinary tract lesions compared with all available alternative imaging studies. Recent research has demonstrated that CTU can detect urothelial neoplasms that are very small (measuring as small as 2-3 mm in maximum diameter). It has also been reported that CTU can occasionally identify bladder lesions missed by cystoscopy, a procedure which has been traditionally considered to be the “gold-standard” for non-surgical diagnosis of bladder abnormalities.

Despite these potential benefits, there are a number of technical difficulties related to CTU. Each CT scan for urinary tract produces, on average, about 300 slices at a slice interval of 1.25 mm with a range of 200 to 600 slices. Reformatted images (in the coronal with or without sagittal planes must also be reviewed. As a result, interpretation of a CTU study demands extensive reading time from a radiologist who has to visually track the upper and lower urinary tracts and look for abnormal lesions usually small in size. The interpreting radiologists frequently need to adjust window settings and may use zooming on a display workstation to improve visualization. The possibility of multiple lesions demands that radiologists pay close attention throughout the urinary tract. In addition, reported results in the literature [7, 8] show that substantial interobserver variability exists among radiologists in detection of bladder cancer on MDCTU with reported sensitivity ranging from 59% to 92%.

With the increase in radiologists' workloads, the chance for oversight of subtle lesions is not negligible. Computer-aided detection (CAD) might therefore play an important role in the reading of CTU. We are developing a CAD system for detection of bladder cancer in CTU.

Lesion segmentation is a crucial step in CAD systems for detection and characterization of bladder cancer. It also has potential applications in tracking changes of bladder lesion volume. Li et al [9] and Duan et al [10, 11] analyzed the automatically segmented bladder wall for suspected lesions on magnetic resonance (MR) cystography. In a different study Duan et al [12] proposed an adaptive window-setting scheme for segmentation of bladder tumor surface on MR images. Hadjiiski et al [13] reported preliminary results for segmentation of bladder lesions on CTU scans using level sets. The segmentation of bladder lesions on CTU is challenging. Some lesions are located fully or partially within the contrast-enhanced area and some are located entirely in the non-contrast-enhanced area of the bladder. The boundaries between the lesions and the adjacent normal tissues have very

low contrast. The bladder lesions often are small in size, subtle in contrast and have irregular boundaries. The main goal of this study is to develop a computerized system for segmentation of different type of bladder lesions on CTU scans and to evaluate its segmentation accuracy in comparison with an experienced radiologist's manual segmentation.

2. Materials and methods

With IRB approval, we retrospectively collected a preliminary data set of CTU scans from patient files at the University of Michigan Health System. We developed a level set-based method and performed a pilot study for segmentation of lesions within the bladder. Figure 1 shows a CTU slice of a bladder. The bladder is partially filled with IV contrast material and a lesion is located in the non-contrast-enhanced area.

2.1 Level set segmentation

We have developed an auto-initialized cascaded level set (AI-CALS) method for bladder lesion segmentation. The system consists of three stages: preprocessing, initial segmentation, and 3D level set segmentation. The system was an adaptation of our previously developed method for segmentation of head and neck lesions [14]. A brief description of the AI-CALS method is presented below and the details can be found in a previous report [14].

Level set segmentation generally starts with an initial contour, which is then evolved iteratively to search for the true lesion boundary. A block diagram of the AI-CALS is shown in Fig. 2. The first and second stages of AI-CALS were designed to automatically generate an initial 3D contour [14], which auto-initializes the 3D cascaded level set in the third stage. In the first stage, preprocessing techniques are applied to a predefined volume of interest (VOI) in the original 3D volume. The VOI can be marked by an automated lesion detection program or by a user, and approximately encloses the lesion to be segmented. In this study the VOI was marked by an experienced abdominal radiologist. Smoothing, anisotropic diffusion, gradient filters and the rank transform of the gradient magnitude are applied in 3D to the VOI and are used to obtain a set of smoothed images, a set of gradient magnitude images, and a set of gradient vector images for the slices within the VOI. The smoothed set is used in the second stage, while the latter two sets are used during level set propagation in the third stage.

In the second stage, the AI-CALS system automatically labels a subset of voxels in the VOI for analysis of lesion statistics based on the attenuation, gradient, and location of the voxels. First, the maximal ellipsoid W inscribed in the lesion VOI is defined. The ellipsoid is centered at the VOI and has axis lengths the same as the dimensions of the VOI box. Then, the lesion center is approximated by the ellipsoid $1/2 W$ with radii one half of the inscribed ellipsoid W , forming a binary mask. Then the regions of high gradient are removed from $1/2 W$ by removing all the voxels x for which the percentile value of is in the top 50%. Finally, the voxels which have intensity in the smoothed image below -400 HU are also removed. Additional details can be found in a previous report [14]. After these procedures, a subset S of voxels that belong to smooth (low gradient) areas and are relatively close to the center of the lesion is identified. S is then used as a statistical sample of the full population of voxels in the object of interest and the mean and standard deviation σ of the voxel values from the smoothed image within S are computed. The object region $\tilde{C}$ is obtained after thresholding by including the set of all voxels x falling within 3.0 standard deviations of the mean of the voxel values in the mask S and with values above -400 HU:

$$x \in \tilde{C}: \{|I(x) - \mu| \leq 3.0\sigma, I(x) > -400HU\}, \quad (1)$$

where $I(x)$ is the voxel value. A morphological dilation filter, 3D flood fill algorithm, and morphological erosion filter are applied to $\tilde{C}$ to connect neighboring components and extract an initial segmentation surface C .

In the third stage, the initial segmentation surface C is propagated towards the lesion boundary through a bank of cascading level sets. The first 3D level set slightly expands and smoothens the initial contour. The second 3D level set pulls the contour towards the sharp edges, but at the same time it expands slightly in regions of low gradient. The third 3D level set further draws the contour towards sharp edges. A 2D level set is applied also to every slice of the segmented object to refine the 3D contours. The 2D level set was initialized by the 3D level set contours. The refinement is most important at the top and the bottom of the object where 3D level set does not work well because the intersection of the CT slices with the object change rapidly. The top to bottom direction of the lesion is defined to be the patient's head-to-toe direction. To maintain inter-slice cohesion, the 2D level set is propagated only for a small number of time steps.

2.2 Data set

The AI-CALS system was evaluated on a preliminary data set that included 28 CTUs performed on 28 patients. Excretory phase images, obtained 12 minutes after the initiation of an intravenous contrast injection of 150 or 175 ml of nonionic contrast material (at a concentration of 300 mg iodine per ml) were utilized. CTU images obtained using a thickness of 0.625 were reconstructed at contiguous 0.625 mm intervals. Since patients were not turned prior to image acquisition, dependently layering intravenous (IV) contrast material partially filled the bladder on the CTU images. Twenty eight bladder lesions (14 malignant and 14 benign) were identified by an experienced abdominal radiologist in the 28 CTU scans. The lesions were located fully or partially within the contrast-enhanced area or entirely in the non-contrast-enhanced area of the bladder. The radiologist defined a difficulty rating scale that represented the radiologist's subjective judgment on the overall conspicuity of a lesion, based on the subtlety of its boundary and overall visibility relative to those encountered in clinical practice. Each lesion in our data set was assigned a difficulty rating (DR) from 1 (most obvious) to 5 (most subtle). Figure 3 plots the distribution of the difficulty ratings. It shows that there were no lesions with rating of 5 in this small data set. Each lesion was marked with a bounding box that served as input to our automated segmentation system.

2.3 Evaluation methods

An experienced radiologist provided manual outlines on the CT slices for all lesions using a graphic user interface (GUI). The radiologist outlined the lesion on every 2D CT slice on which the lesion was visible, resulting in a 3D surface contour. Several different performance metrics [14-16] that quantify the similarity of a pair of contours were used for evaluating the system, including the average distance, the volume intersection ratio, and the volume error between the radiologist contours and AI-CALS segmented contours. The average distance between two 3D surface contours G and U is defined as:

$$AVDIST(G, U) = \frac{1}{2} \left(\frac{\sum_{x \in G} \min \{d(x/y) : y \in U\}}{N_G} + \frac{\sum_{y \in U} \min \{d(x/y) : x \in G\}}{N_U} \right), \quad (2)$$

where G is the gold standard 3D surface contour marked by the radiologist and U is the 3D contour being evaluated. N_G and N_U denote the number of points (voxels) on G and U , respectively. The function d is the Euclidean distance. For a given voxel along the contour G , the distance to the closest point along the contour U is determined. The minimum distances for all points in G are averaged. This process is repeated by switching the roles of G and U . The two average minimum distances are then averaged.

The volume intersection ratio is defined as the ratio of the intersection measure and the gold standard measure in 3D:

$$R^{3D} = \frac{V_G \cap V_U}{V_G}, \quad (3)$$

where V_G is the volume enclosed by the gold standard contour G and V_U is the volume enclosed by the contour U . A value of 1 indicates that V_U completely overlap with V_G , whereas a value of 0 implies V_U and V_G are disjoint.

The volume error is defined as the ratio of the difference in the two volumes divided by the volume of the gold standard, i.e.,

$$E^{3D} = \frac{V_G - V_U}{V_G}, \quad (4)$$

where negative error indicates over-segmentation and vice versa. Because the over- and under-segmentation tend to mask the actual deviations from the gold standard when the average is taken, the absolute (unsigned) errors $|E^{3D}|$ is also calculated.

In addition, the segmentation quality of AI-CALS was assessed by an expert panel of two radiologists, who provided quality rating of each segmented lesion. The quality of the contour was rated on a scale from 1 to 10 regarding the closeness of the segmentation to the visual lesion boundary in 3D. Specific descriptor was defined as guideline for each category: 1= “unacceptable or missing”, 2=“very poor”, 4=“poor”, 6=“fair”, 8=“good”, 10=“excellent or perfect”. Odd-numbered ratings were defined to be between the adjacent even-numbered ratings.

3. Results

The histograms of the volume intersection ratio, average distance, and the volume error are presented in Figs. 4, 5, and 6. The average volume intersection ratio R^{3D} was $67.2 \pm 16.9\%$ (Fig. 4). Twelve lesions had R^{3D} higher than 75%. The average distance measure $AVDIST$, averaged over 28 bladder lesions, was 2.89 ± 1.69 mm. Fourteen of the lesions had $AVDIST$ less than 2.5 mm (Fig. 5). The average volume error E^{3D} and the average absolute volume error $|E^{3D}|$ were $4.9 \pm 38.3\%$ and $27.3 \pm 26.9\%$, respectively (Fig. 6). Twelve lesions had an absolute volume error smaller than 15%.

The distribution of the quality ratings for the AI-CALS segmented lesions is plotted in Fig. 7. Of the 28 segmented contours, 18 were given quality ratings of 8 or above. Only 2 were given a rating of under 6 (corresponding to “fair”). The average rating was 7.9 ± 1.5 . Figure 8 shows the radiologists’ quality ratings grouped by lesion difficulty ratings (DR). The average quality ratings for lesions of difficulty ratings 1, 2, 3, and 4 were 8.8 ± 0.9 , 7.9 ± 1.8 , 7.4 ± 0.9 , and 6.6 ± 1.5 , respectively. The automated segmentation performed relatively consistently for the range of lesions from most obvious (DR=1) to subtle (DR=4).

Examples of segmentation results for lesions of four difficulty levels are shown in Figs 9, 10, 11, and 12 respectively. In a given figure, lesions with the same level of difficulty but having segmentation quality ratings ranging from the best to the worst are shown. Figures 9f, 10f, 11f, and 12f represent examples with the worst segmentation for the four levels of difficulty.

4. Discussion

In this study, our AI-CALS segmentation system was applied to a data set containing a wide range of bladder lesions of different characteristics. Some of the lesions were located fully or partially within the contrast-enhanced area and some were located entirely in the non-contrast-enhanced area of the bladder. Our segmentation system performed well for the wide variety of lesions with different sizes, different levels of difficulty, and with lesions present at different locations (Figs. 9, 10, 11, and 12). About half of the lesions had large volume intersection ratio (Fig. 4) and small absolute volume error (Fig. 6). Large lesions within the contrast-enhanced area of the bladder were successfully segmented (Fig. 9a and 9b). Even though the lesions on Figs. 9c and 10c were only partially within the contrast-enhanced area, the computer segmented contours were also rated as good quality (Fig. 9d and 10d). A number of small lesions were located in the non-contrast-enhanced area of the bladder (Figs. 10a, 11a, and 11c). Although most of the boundaries between the lesions and the adjacent normal tissues had very low contrast, the AI-CALS method was able to estimate reasonable boundaries in these cases (Figs 10b, 11b, and 11d, respectively). Even some subtle lesions such as that shown in Fig. 12a were accurately segmented by the AI-CALS method when compared to the radiologist's hand-drawn contour.

However, there were cases for which the AI-CALS method did not produce good contours. For example, the small lesion in the contrast-enhanced area of the bladder in Fig. 12e was over-segmented (Fig. 12f). Due to the strong gradient on the upper half of the lesion, where it bordered with the contrast material, the segmentation system was not able to find the correct lesion boundary with lower gradient on the bottom part, where it bordered with the abdominal background. Some of the lesions had a complex shape (Fig 11e and 12c) or were surrounded by a complex background of perivesical tissue (Fig. 10e), which strongly contributed to the lower quality of the segmentation (Figs. 11f, 12d, and 10f, respectively).

One limitation of this pilot study is the small database. A second limitation is that the AI-CALS method is not able to follow irregular lesion boundaries that have sharp turns and corners such as the example in Fig. 11e. It may be necessary to develop additional local refinement methods for such lesions. Better criteria to prevent leakage into adjacent normal tissue across low contrast boundaries are also needed. We are in a process of collecting a larger database with more samples for each type of lesion characteristics to further improve the bladder segmentation method.

5. Conclusion

The automated segmentation system is capable of producing reasonable 3D segmentations for a wide variety of bladder lesions. The system provides good segmentation for many small lesions. In this study, the average segmentation quality was good with a mean quality rating of 7.9 (with 10 the best). This pilot study demonstrates the feasibility of using our auto-initialized cascaded level set method for segmentation of bladder lesions present on CTU examinations.

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References

1. American Cancer Society. Cancer Facts & Figures 2012. 2012. www.cancer.org 2012
2. McCarthy CL, Cowan NC. Multidetector CT urography (MD-CTU) for urothelial imaging. *Radiology* (P). 2002; 225:237.
3. Noroozian M, Cohan RH, Caoili EM, Cowan NC, Ellis JH. Multislice CT urography: State of the art. *British Journal of Radiology*. 2004; 77:S74–S86. [PubMed: 15546844]
4. Akbar SA, Morteale KJ, Baeyens K, Kekelidze M, Silverman SG. Multidetector CT urography: Techniques, clinical applications, and pitfalls. *Seminars in Ultrasound CT and MRI*. 2004; 25:41–54.
5. Liu WC, Morteale KJ, Silverman SG. Incidental extraurinary findings at MDCT urography in patients with hematuria: Prevalence and impact on Imaging costs. *American Journal of Roentgenology*. 2005; 185:1051–1056. [PubMed: 16177432]
6. Caoili EM, Cohan RH, Korobkin M, Platt JF, Francis IR, Faerber GJ, Montie JE, Ellis JH. Urinary tract abnormalities: Initial experience with multi-detector row CT urography. *Radiology*. 2002; 222:353–360. [PubMed: 11818599]
7. Sudakoff GS, Dunn DP, Guralnick ML, Hellman RS, Eastwood D, See WA. Multidetector computerized tomography urography as the primary imaging modality for detecting urinary tract neoplasms in patients with asymptomatic hematuria. *Journal of Urology*. 2008; 179:862–867. [PubMed: 18221955]
8. Park SB, Kim JK, Lee HJ, Choi HJ, Cho K-S. Hematuria: portal venous phase multi detector row CT of the bladder--a prospective study. *Radiology*. 2007; 245:798–805. [PubMed: 17951346]
9. Li L, Wang Z, Li X, Wei X, L AH, Huang W, Rizvi S, H. M, Harrington DP, Liang Z. A new partial volume segmentation approach to extract bladder wall for computer aided detection in virtual cystoscopy. *Proc SPIE*. 2004; 5369:199–206.
10. Duan C, Liang Z, Bao S, Zhu H, Wang S, Zhang G, Chen JJ, Lu H. A coupled level set framework for bladder wall segmentation with application to MR cystography. *IEEE Trans Med Imaging*. 2010; 29:903–15. [PubMed: 20199924]
11. Duan CJ, Yuan KH, Liu FH, Xiao P, Lv GQ, Liang ZR. Volume-Based Features for Detection of Bladder Wall Abnormal Regions via MR Cystography. *IEEE TRANSACTIONS ON BIOMEDICAL ENGINEERING*. 2011; 58:2506–2512. [PubMed: 21642039]
12. Duan CJ, Yuan KH, Liu FH, Xiao P, Lv GQ, Liang ZR. An Adaptive Window-Setting Scheme for Segmentation of Bladder Tumor Surface via MR Cystography. *Ieee Transactions on Information Technology in Biomedicine*. 2012; 16:720–729. [PubMed: 22645274]
13. Hadjiiski L, Chan H-P, Caoili E, Cohan R, Wei J, Zhou C. Segmentation of Malignant and Benign Bladder Lesions on Multidetector Row CT Urography Using 3D Level Set. *RSNA Program Book*. 2010; SSG13
14. Street E, Hadjiiski L, Sahiner B, Gujar S, Ibrahim M, Mukherji SK, Chan HP. Automated Volume Analysis of Head and Neck Lesions on CT Scans Using 3D Level Set Segmentation. *Medical Physics*. 2007; 34:4399–4408. [PubMed: 18072505]
15. Sahiner B, Petrick N, Chan HP, Hadjiiski LM, Paramagul C, Helvie MA, Gurcan MN. Computer-Aided Characterization of Mammographic Masses: Accuracy of Mass Segmentation and its Effects on Characterization. *IEEE Transactions on Medical Imaging*. 2001; 20:1275–1284. [PubMed: 11811827]
16. Way TW, Hadjiiski LM, Sahiner B, Chan H-P, Cascade PN, Kazerooni EA, Bogot N, Zhou C. Computer-aided diagnosis of pulmonary nodules on CT scans: segmentation and classification using 3D active contours. *Medical Physics*. 2006; 33:2323–2337. [PubMed: 16898434]

Figure 1. CTU slice showing bladder with a bladder lesion (white arrow). This lesion contains a thin rim of peripheral calcification.

Figure 2.
Block diagram of the auto-initialized cascaded level set (AI-CALS) method.

Figure 3. Distribution of the difficulty ratings for the conspicuity of the lesions in the data set (1=most obvious, 5=most subtle). No case was rated as 5 in this pilot data set.

Figure 4.
Histogram of the volume intersection ratio measure R^{3D} . The average was 67.2%.

Figure 5.
Histogram of the average distance measure *AVDIST*. The average was 2.89 mm.

Figure 6.
Histogram of the volume error E^{3D} . The average was 4.9%.

Figure 7.
Histogram for the radiologists' quality ratings of the AI-CALS segmented contours.

Figure 8. Radiologists' quality ratings for the AI-CALS segmented lesions grouped by radiologists' lesion difficulty ratings.

Figure 9.

Segmentation of bladder lesions with difficulty rating of 1: (a), (c), and (e) are the original images; (b), (d), and (f) are the corresponding AI-CALS segmentations (black contours) and radiologist hand outlines (white contours). The segmentation quality for (b), (d), and (f) was 10, 8, and 7 respectively.

Figure 10.

Segmentation of bladder lesions with difficulty rating of 2: (a), (c), and (e) are the original images; (b), (d), and (f) are the corresponding AI-CALS segmentations (black contours) and radiologist hand outlines (white contours). The segmentation quality for (b), (d), and (f) was 10, 8, and 5 respectively.

Figure 11.

Segmentation of bladder lesions with difficulty rating of 3: (a), (c), and (e) are the original images; (b), (d), and (f) are the corresponding AI-CALS segmentations (black contours) and radiologist hand outlines (white contours). The segmentation quality for (b), (d), and (f) was 8, 8, and 6 respectively.

Figure 12.

Segmentation of bladder lesions with difficulty rating of 4: (a), (c), and (e) are the original images; (b), (d), and (f) are the corresponding AI-CALS segmentations (black contours) and radiologist hand outlines (white contours). The segmentation quality for (b), (d), and (f) was 9, 6, and 5 respectively.