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Original article

Multi-atlas-based segmentation of prostatic urethra from planning CT imaging to quantify dose distribution in prostate cancer radiotherapy

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ABSTRACT

Background and purpose: Segmentation of intra-prostatic urethra for dose assessment from planning CT may help explaining urinary toxicity in prostate cancer radiotherapy. This work sought to: i) propose an automatic method for urethra segmentation in CT, ii) compare it with previously proposed surrogate models and iii) quantify the dose received by the urethra in patients treated with IMRT.

Materials and methods: A weighted multi-atlas-based urethra segmentation method was devised from a training data set of 55 CT scans of patients receiving brachytherapy with visible urinary catheters. Leave-one-out cross validation was performed to quantify the error between the urethra segmentation and the catheter ground truth with two scores: the centerlines distance (CLD) and the percentage of centerline within a certain distance from the catheter (PWR). The segmentation method was then applied to a second test data set of 95 prostate cancer patients having received 78 Gy IMRT to quantify dose to the urethra.

Results: Mean CLD was 3.25 ± 1.2 mm for the whole urethra and 3.7 ± 1.7 mm, 2.52 ± 1.5 mm, and 3.01 ± 1.7 mm for the top, middle, and bottom thirds, respectively. In average, 53% of the segmented centerlines were within a radius < 3.5 mm from the centerline ground truth and 83% in a radius < 5 mm. The proposed method outperformed existing surrogate models. In IMRT, urethra DVH was significantly higher than prostate DVH from V74 Gy to V79 Gy.

Conclusion: A multi-atlas-based segmentation method was proposed enabling assessment of the dose within the prostatic urethra.

In prostate cancer radiotherapy (PCRT), dose increase is limited by toxicity in organs at risk [1]. While gastrointestinal (GI) toxicity has been relatively reduced by the introduction of highly conformal image-guided radiotherapy techniques, genitourinary (GU) toxicity remains relatively stable, with a 5-year rate of Grade ≥ 2 toxicity of approximately 15–20% [2,3]. Urinary toxicity is a challenging issue, not only due to the variety of associated irritating or obstructive symptoms, but also owing to the limitations of dose descriptors and difficulties identifying the regions at risk responsible for those symptoms [4–6]. The bladder, for example, presents the largest inter-fraction shape variations, causing geometric and dose uncertainties that limit the possibility of accurately modeling the dose–volume response concerning GU toxicity [4,7–9]. Most existing models address urinary toxicity by computing the dose to the bladder using either the dose parameters extracted from volumes (whole bladder or bladder wall), surface maps or localized sub-regions via spatial dose descriptors [1,6,10–14] which partially have revealed global or local dose–effect relationships. Although there is evidence in prostate cancer brachytherapy that some urinary symptoms are related to urethra damage [15–17] this has not yet been shown in external-beam radiotherapy. Quantifying the delivered dose to the urethra may therefore improve our understanding of urinary toxicity or at least some of the related symptoms if we can accurately identify the organ from the planning CT. Thus, segmenting the urethra from the planning CT in order to assess the dose it receives, would pave the way for further studies on urinary toxicity prediction considering both the bladder and urethra.

To our knowledge, a formal segmentation of the intra prostatic urethra from CT images has not been addressed yet. However, indirect surrogate models for estimating the urethra position have been previously proposed [18,19]. They are nevertheless based on empirical considerations with respect to the prostate midplane. Segmenting the urethra from CT scans is fairly challenging. Not

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only is there already poor contrast between soft tissues like the prostate, bladder, and rectum, thus rendering segmentation difficult for planning, but the intra-prostatic urethra itself is completely invisible. These issues restrict the use of classic intensity-based segmentation methods. Atlas-based approaches, widely discussed in the literature [20–26], are common methods for organ segmentation. In atlas-based methods, precomputed segmentation in a template space is propagated onto the image to be segmented via spatial normalization (registration) as depicted in Fig. A1 (supplemental material). Several individuals from a population can be used to constitute the atlas (multi-atlas). This allows to overcome the inter-individual variability and registration issues. Previous works have shown the benefits of combining multiple atlases in improving segmentation accuracy [20,22,23,27–29].

In this paper, we propose a weighted Multi-Atlas-Based Urethra Segmentation strategy, herein called MABUS, from planning CTs. Our goal is to provide a method that could be applied to a different set of patients receiving external-beam radiotherapy in order to assess the dose to the urethra and relate with toxicity effects.

Material and methods

This study is divided into three main parts: i) a description of MABUS, the multi-atlas-based urethra segmentation method which illustrates the whole implemented framework, from the atlas construction to the final urethra segmentation, ii) the evaluation of the method's accuracy with respect to the urethra ground truth in a leave one out cross validation framework, and comparison with the existing surrogates proposed by Bucci [18] and Waterman [19] and finally iii) the computation of the dose received by the urethra in a different series of patients with prostate cancer IMRT which aims to introduce the way in which the method may be used in toxicity studies.

Multi-atlas based urethra segmentation (MABUS) method description

In general, as depicted in Fig. A1 in supplemental material atlas-based segmentation relies on the registration of a template I_i to the query image I_q, in order to obtain a transformation $T_{I_i \to I_q}$, which maps a set of generated labels ζ_i onto I_q. If the mapping is anatomically correct, the yielded segmentation is accurate and anatomically meaningful. Multi-Atlas based segmentation builds upon this idea by extending the number of atlases thereby reducing the interindividual variability issues.

Following the multi-atlas concept, the proposed MABUS was devised and can be divided into seven steps as depicted in Fig. 1. In summary, an atlas dataset was first built from manually-delineated CTs including the urethra, thanks to the presence of a urinary probe (Step 1). The query image to be segmented I_q was then rigidly aligned with the same template I_T as the atlas database (Step 2) and features were extracted $F_q = \{f_{1q}, .., f_{5q}\}$ (Step 3). By comparing the features, the atlases were ranked according to their similarity to the query image (Step 4). The labels $\zeta_i = \{urethra\}$ from the top $n = 10$ ranked atlases were then propagated to the query image using an accurate non-rigid registration method (Step 5) designed to match the prostate anatomies. Finally, the urethra segmentation was obtained by combining different labels in a weighted-fusion process (Step 6), followed by centerline detection (Step 7). The image segmentation methods were developed in C++ using the Insight Toolkit libraries (ITK) [30] and python [31] open source technologies. We made the atlas database as well as the whole code available for further studies.

Atlas building from training data (Step 1)

For the atlas building, we used an initial series of CT scans (512×512 0.63×0.63 mm axial pixels and 3 mm slices) from 55 patients treated for localized prostate cancer with Iodine-125 brachytherapy. All the patients were fitted with urinary catheters, enabling urethra segmentation. The prostate, bladder, and urethra were delineated by the same radiation oncologist, constituting the set of atlases I_i, with the label $\zeta_i = \{urethra\}$.

Template selection and rigid registration (Step 2)

A first average patient I_T was selected as a common coordinate system. This patient was the closest to all others in terms of prostate volume. The whole population was then rigidly registered to this patient by aligning the prostate centroids followed by a fine alignment of bony anatomy. This enabled geometrical descriptors to be generated and compared in the same common space. The central lines of the manually delineated catheters were computed by extracting their centroid at each slice.

Feature extraction (Step 3)

A simplified geometrical description of the anatomy (prostate/bladder) was generated to characterize each individual. Hence, a vector $F_{i\in[1,..,N]} = \{f_{1i}, .., f_{5i}\}$ describes the individuals in terms of i) prostate volume ii) distance between prostate and bladder centroids, iii) the extension of the bladder in the anterior posterior direction, and iv) the orientation of the bladder with respect to the prostate centroid, regarding two angles (φ) and (θ), which respectively describe the anteroposterior and lateral directions. The descriptors were then normalized across the population with a z-score.

Query image and atlas selection (Step 4)

For an image I_q to be segmented, the two previously described steps (2 and 3) were applied as for the training database. Thus, rigid registration to the common template I_T and characterization yield for I_q the vector $F_q = \{f_{1q}, .., f_{5q}\}$, exhibiting similar features as computed for the atlas dataset. Following z-score normalization, the Euclidean distances $d_{i-q} = \|F_i - F_q\|$ between features enabled the individuals from the atlas I_i to be ranked in terms of similarity to the query image I_q. In our multi-atlas strategy, only the top ($n = 10$) ranked atlases were selected as the closest to the query image I_q, with all remaining atlases discarded. Since their configuration is similar to that of the query image, the urethra is expected to lie inside the prostate in a similar position. The number of atlases ($n = 10$) was selected as a tradeoff between computational time and optimized results in a leave-one-out segmentation process in which the top 1,2,..,n atlases were tested.

Non-rigid registration (Step 5)

In this step, the labels ζ_i from the n most suitable previously-selected atlases were non-rigidly propagated to the prostate of the query image. To register each prostate from the best atlases to the prostate of the query image I_q we applied a Laplacian-based registration method, built upon our previous work [32], but here only considering the prostate. In our implementation, instead of using the central line, we selected the centroid Cp of the prostate for computing a scalar field $u(x, y, z)$ by applying Laplace's equation inside the prostate volume, demarcated by an external boundary F_{Ext}, here the prostate surface, and an internal boundary, here the prostate centroid Cp, as:

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