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Towards Clinical Deployment of Automated Anatomical Regions-Of-Interest

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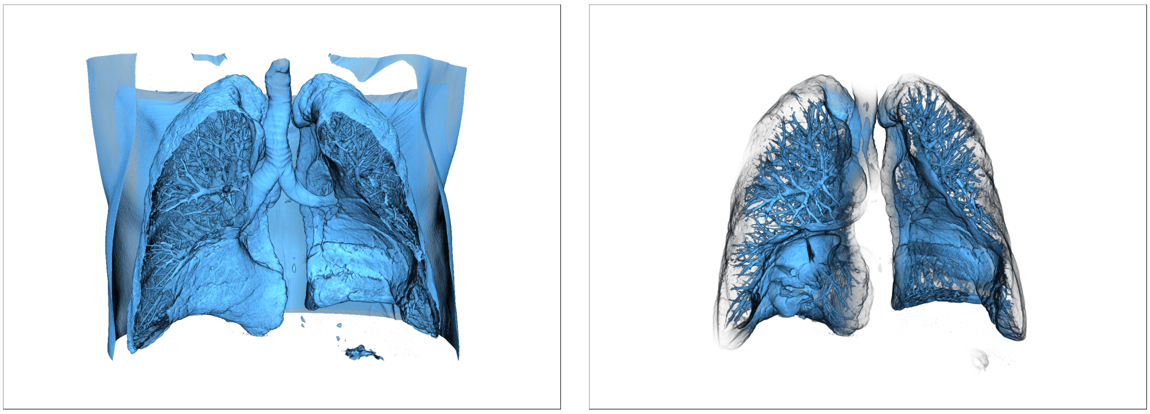

Figure 1: *Region Of Interest (ROI) selection is an important part of three-dimensional visualization [AWK*11]. Here, both images show overview visualizations of the bronchial tree of human lungs.* (Left): *Clip-plane ROI selection.* (Right): *Anatomical ROI selection. Our investigation shows that the combination of automatic image registration and Distance-Based Transfer Functions [TPD06, KHS*10] could be a clinically feasible method for selection of anatomically related ROIs.*

Abstract

The purpose of this work is to investigate, and improve, the feasibility of advanced Region Of Interest (ROI) selection schemes in clinical volume rendering. In particular, this work implements and evaluates an Automated Anatomical ROI (AA-ROI) approach based on the combination of automatic image registration (AIR) and Distance-Based Transfer Functions (DBTFs), designed for automatic selection of complex anatomical shapes without relying on prohibitive amounts of interaction. Domain knowledge and clinical experience has been included in the project through participation of practicing radiologists in all phases of the project. This has resulted in a set of requirements that are critical for Direct Volume Rendering applications to be utilized in clinical practice and a prototype AA-ROI implementation that was developed to addresses critical points in existing solutions. The feasibility of the developed approach was assessed through a study where five radiologists investigated three medical data sets with complex ROIs, using both traditional tools and the developed prototype software. Our analysis indicate that advanced, registration based ROI schemes could increase clinical efficiency in time-critical settings for cases with complex ROIs, but also that their clinical feasibility is conditional with respect to the radiologists trust in the registration process and its application to the data.

Categories and Subject Descriptors (according to ACM CCS): Computer Graphics [I.3.6]: Methodology and Techniques—Computer Graphics [I.3.7]: Three-Dimensional Graphics and Realism—Computer Graphics [I.3.8]: Applications—

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1. Introduction

It is widely accepted that Direct Volume Rendering (DVR) is useful for clinical purposes by facilitating the understanding of three-dimensional (3D) structures and in creating "gestalt" case overviews [AWK*11]. It is today successfully used in certain situations, but is despite its benefits still not an everyday tool for most radiologists.

One of the fundamental challenges in clinical use of DVR is the isolation of targeted Region Of Interests (ROIs). The dominating approach today is use of the clip-plane. This works well for simple selections but becomes prohibitively cumbersome for more complex regions requiring multiple planes and corresponding interaction. Distance-Based Transfer Functions (DBTFs) [TPD06, KHS*10] presents a promising alternative, but is hindered by its reliance on segmented data, resulting in high per-patient costs.

In this work, we present an approach based on the idea of obtaining anatomical information by registering the patient specific volume with an atlas using automatic image registration (AIR). This enables user based high-level anatomical ROI selection. The atlas information, and user ROI selection, is then used to modify the effect of the transfer function used in DVR. The method facilitates effective selection and provides the full capabilities of DVR, and at the same time avoids expensive per-patient segmentation procedures.

We present in turn: an analysis of the shortcomings of current ROI solutions, the developed approach for Automated Anatomical ROI (AA-ROI) visualization, and a feasibility study of the developed approach in a clinical environment through a radiologist user study.

2. Background

This work relates to a broad selection of literature, here discussed in two sections: TFs methods that utilize spatial information and registration.

Material classification and feature delineation are important regardless if a ROI is selected or not. For a broader spectrum of methods we direct the reader to available surveys [EHK*06, AD10] while we here limit ourselves to works that more directly relate to the AA-ROI approach. First, there are numerous works that consider spatial information but do not rely on pre-segmented data. Spatialized TFs [RBS05] automatically derive color components from the spatial location of a sample. Spatial conditioning of TFs [LLL*10] similarly achieves selective tissue separation but is limited to materials that are separable in attribute space. Two areas of TF literature that perform more extensive pre-processing are topology-based and segmentation-based methods. Topology based TF approaches strive to express the spatial relations between features in the data [TTF04, WDC*07]. Disadvantages of existing topological methods include prohibitive time consumption and weak relations to anatomical features or purely conceptual regions. Segmentation based TF approaches are used for medical diagnostic, pre-operative or surgical purposes [SBZ*09, SSE*09]. A common drawback for these methods is that most processing and interaction steps need to be repeated for every patient. More generic segmentation based approaches have also been presented, aiming at improving image quality instead of focusing on specific medical tasks. DBTFs [TPD06] allows the user specify the distance to some pre-classified objects as a second attribute when designing TFs. This was later extended to weighted distance fields [KHS*10] to create focus and context renderings. DBTFs are used in this work but with a lower degree of parameterization than proposed in the original works. The idea of compartmentalized TFs based on pre-registered models has been proposed for two-dimensional (2D) slices [FLAK11] but was only evaluated by showing pre-rendered images to a set of clinical experts.

The AA-ROI approach applies image registration on scanned patient data. The large variability in the human anatomy makes it necessary to employ non-rigid registration methods. Surveys of registration in medical imaging with particular focus on non-rigid registration can be found in [Hol08, RA10]. In our work we have utilized two existing non-rigid registration methods: the Demons [Thi98] and the Morphons [KA05]. The Demons and Morphons algorithms are fully automatic methods for non-rigid registration based on optical flow and phase-difference respectively. Demons is arguably the more wide spread of the two but is intensity dependent and therefore less suited for Magnetic Resonance Imaging (MRI) data or synthetic models. The Morphons is intensity-invariant and, thus, handle larger differences between patient and model data. Both methods have been shown to perform well in evaluations [LJR*08, KAA*09], and have also been implemented on the GPU [GPL*10, FEAK11].

3. Prerequisites for DVR in clinical practice

As a starting point for our work we conducted focused discussions with the radiologists participating in the project to analyze the apparent under-utilization of DVR in clinical practice. In this way limitations of available tools such as TFs, clip-planes and segmentation, were articulated in terms of classification capability and ease of use. Five central requirements for medical DVR were identified that were not sufficiently fulfilled by any of their current tools. In summary, the radiologists requested a concept that is *Efficient*, *Anatomical*, *Generic*, *Robust*, and *User-controlled*. These requirements are described in the following typical but challenging situation:

> The radiologist receives previously unseen image data along with a non-standard diagnostic task *(Genericness)*. The region necessary to review is of a complex shape and related to multiple organs and other anatomical landmarks *(Anatomi-*

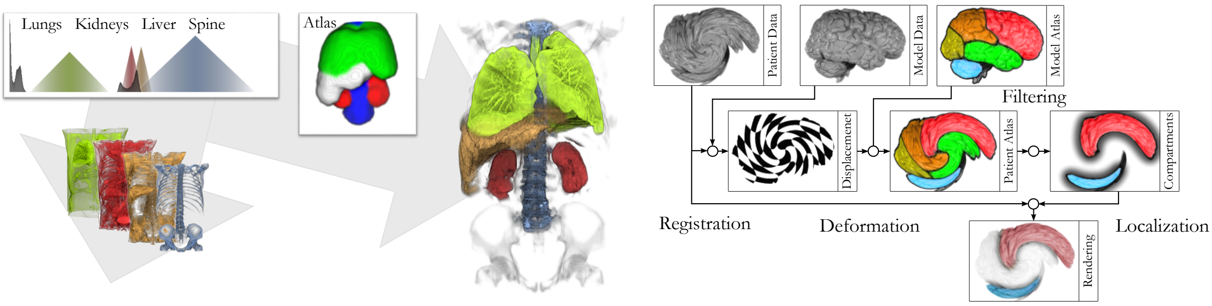

Figure 2: Left: *Conceptual overview showing the difference between traditional global TF methods and our local atlas based method.* Right: *State-of-the-art registration methods help alleviate the hurdles that prevent clinical efficiency for atlas based methods by providing reasonably accurate delineation of anatomy for individual patients.*

cal), whose boundaries and positions cannot be precisely identified even with advanced segmentation methods *(Robustness)*. The radiologist need interactive tools *(User Control)* and can spare two minutes to create an informative visualization *(Efficiency)*.

While there are existing methods targeting this situation, significant challenges remain. Findings by Lundström and Persson [LP11] indicate that exploratory approaches are necessary in radiology image review and that efficiency is the single greatest challenge in radiology image review. Our findings indicate that anatomical delineation is important to make exploratory approaches more efficient. This is further supported as the dominant solution in clinical environments of manually controlled clip-planes becomes problematic as the number of planes increase [TKAM06].

4. Automatic Anatomical ROI Selection

The concept of AA-ROI visualization is illustrated in Figure 2 (left), where each primitive of the TF is localized to its corresponding anatomical parts using a registered atlas. A more detailed overview of the registration pipeline is available in Figure 2 (right). The pipeline consists of four main parts: *Registration*, *Deformation*, *Processing*, and *Localization*. The objective of the registration and deformation steps is to arrive at the patient-specific atlas through the use of generic model and atlas data (Section 4.1). Next, compartments of the atlas are extended with transitional regions in the *Processing* part of the pipeline (Section 4.3). For the user, this introduces the concept of verification zones, which are used to verify the integrity of the visualization and yield user trust. The final step is *Localization* (Section 4.4), where semantic labels are used to connect TF widgets to atlas compartments and limit the TF response to the compartments and their associated verification zones.

4.1. Anatomical Registration of Patient Data

The first parts of the AA-ROI pipeline are *Registration* and *Deformation*. The goal of the registration step is to estimate a displacement field that describes the geometric alignment between model and patient data. Once the displacement field is known, a patient-specific atlas is obtained by applying the field to the model atlas. Many registration methods are unable to operate directly on label atlas values. Hence, it is often necessary to acquire separate model data in addition to the model atlas. For Computed Tomography (CT) data, we primarily employ an external atlas-generating software called XCAT [SSM*10] (Version 2) to produce the input: the model data and the model atlas. XCAT generation time varies from 30 seconds to two minutes depending on the resolution. As this is a one-time cost which does not effect per patient time consumption it is not included in any timings reported in this paper.

4.2. Registration Inaccuracy

In this work we employ either the Demons or the Morphons algorithm depending on the characteristics of the data. Both are well documented and have previously been successfully used and evaluated for medical imaging [KAA*09,LJR*08]. Inaccuracies are, however, inevitable and need to be addressed in order to maintain user trust and fulfill the requirements set by the radiologists. Yet it is important to realize that for the purpose of ROI selection, a registration does not need to be precise in order to be useful. In a ROI scenario, only underestimation is critical with respect to user trust as it can lead to a loss of important structures. This work use verification zones to address registration inaccuracies.

4.3. Per-Compartment Verification Zones

The verification zones extend from the binary atlas compartments and acts as buffer zones in case the registration underestimates the targeted feature. Inside the verification zones, the opacity of the associated TF is gradually reduced through a *localization function* to form a DBTF.

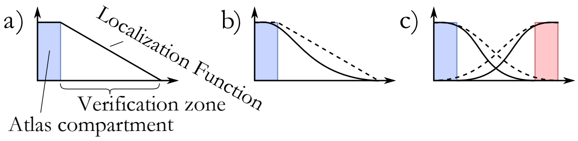

Figure 3: *Overview of the processing and creation of localization functions: a) distance fields, b) mapping, and c) overlap normalization. Illustrations are in 1D while computations are performed on discrete 3D grids.*

The localization functions, denoted Λ_i, are derived from three dimensional discrete Euclidean Distance Transforms (EDTs) [SKW09]. EDTs are performed at the same resolution as the registration using the binary atlas compartments as inputs. The EDTs are regularized with a small box filter (3-5 voxels depending the active resolution and voxel size). The purpose of the regularization is to increase the robustness and predictability of the DBTF by preventing the TF from being modulated too rapidly from one voxel to the next. Note that this does not affect high frequencies in the data, but only limits at which frequencies the response of the TF is allowed to be modulated spatially.

All filtered EDT values are then mapped with a monotonically decreasing function of the form

$$\Lambda_i = \left(1 - \frac{\mathrm{Box}(\mathrm{EDT}_i)}{\kappa_{\mathrm{A}}}\right)^{5/2} \quad \text{with } \Lambda_i \in [0,1]. \tag{1}$$

where κ_{A} is a user accessible parameter controlling the size of the verification zone. Feedback from pilot testing showed κ_{A} proportional to 30% of the targeted structure size to be a reasonable starting point, equating to 40–60mm range for major organs in full body CT scans. The exponent in Equation 1 is used to extend the perceived range of semi-transparency. More extensive approaches were considered [KHS*10] but not used here in view of the decreased interaction efficiency they would infer.

If two or more functions are non-zero and overlap after the mapping, a normalization is applied to limit the total output according to Equation 2

$$\Lambda'_i = \Lambda_{\max} \frac{(\Lambda_i)^x}{\sum_{j=1}^{N_C} (\Lambda_j)^x} \tag{2}$$

where $\Lambda_{\max}$ is the maximum value for any single compartment. The mapping consists of a linear normalization raised to the power of x. We use $x = 2$, effectively favoring higher compartment weights. The normalization is illustrated in Figure 3 (c) and Λ'_i corresponds to the final localization function.

The final localization functions are stored in three-dimensional textures to facilitate access during rendering, fitting up to four compartments in a four-channel RGBA texture. For our examples we use resolutions between 128^3 and 256^3 for registration and maintain the EDTs at the same resolution.

4.4. TF Widget Association and Opacity Modulation

Association between atlas compartments and TF components is performed directly in the TF editor where semantic label, such as *head* or *chest*, are added to individual widgets. Semantic labels are assumed to be available together with the atlas model. Label associations are stored with the TF presets and typically does not need to be altered for a given case once set, keeping per patient interaction costs to a minimum.

The DBTFs are realized by multiplying the localization function, Λ'_i, onto the opacity channel of the associated TF widget, α_{TF}, as

$$\alpha_i = \Lambda' \alpha_{\mathrm{TF}}, \tag{3}$$

where α_i is the modulated opacity blended into the buffer. Λ' is in this stage linearly interpolated from neighboring values. If more than one widget produces a non-zero output, such as in overlapping verification zones, the individual contributions are sequentially blended to the buffer using accumulation level intermixing as categorized by Cai and Sakas [CS99].

4.5. Parameterizations and Interaction

The user parameter κ_{A} introduced earlier controls the size of the verification zone. A second parameter, κ_{B}, provides the user with a representation of uncertainty originally proposed by Lindholm *et al.* [LLL*10]. The technique offers a choice between opacity reduction or chromatic desaturation. The reader is referred to the original paper for further discussion and comparisons. Both parameters are global and thus affect all atlas compartments identically. Individual parameterizations was considered but rejected due to the inevitable increase in interaction complexity.

5. Results

In this section, we present a series of cases which demonstrate the utility and versatility of AA-ROIs. This is followed by a study of the potential for AA-ROIs in a clinical environment in Section 6.

5.1. Rendered Cases

Detailed descriptions of AA-ROI benefits for each rendering are provided below, while technical data and individual process timings can be found in Table 1. All cases demonstrate, from a clinical perspective, feasible efficiency with registration and processing times well under 30 seconds total.

TORSO (CASE 1) Figure 2. Simultaneous visualization of multiple anatomical features. This CT case contains both

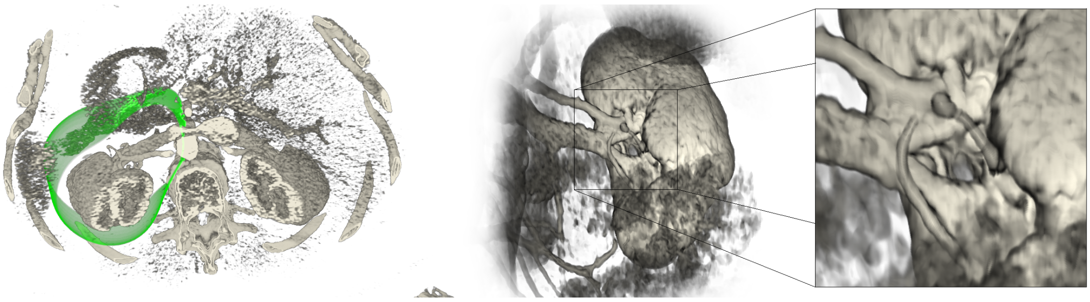

Figure 4: Left: *Axial view of deformed atlas compartment (green).* Middle: *AA-ROI visualization of arteries between the left kidney and the aorta.* Right: *Close-up of thin vessels for surgical planning. The AA-ROI selection effectively isolates the targeted region and, as a result, no clip-plane interaction is needed and the sensitivity of the TF parameters is reduced.*

Table 1: *Performance timing, in seconds, of the registration and compartment processing for our test cases.*

	Reg.	Proc.	Reg. Size	Method
TORSO	17s	1.3s	$256 \times 128 \times 256$	Demons
TORSO	20s	1.3s	$256 \times 128 \times 256$	Morphons
KIDNEYS	9.5s	1.1s	$128 \times 96 \times 64$	Demons
LUNGS	5.0s	0.3s	$128 \times 128 \times 128$	Demons

classification challenges (overlaps in attribute space and partial volume effects) as well as conceptual region differentiation (spine over other bone). Unlike solutions found in current radiology software, AA-ROIs can be used to address the challenges without costly segmentation or extensive clip-plane interaction.

KIDNEYS (CASE 2) Figure 4. Visualizations of the blood supply for the left kidney. AA-ROIs are particularly useful when purely conceptual anatomical regions are targeted; in this case the wedge shaped area between the kidneys and the aorta. Two separate atlas compartments, both including the area of the aorta, provides a semantic 'one-click' solution that would otherwise require extensive interaction with manually oriented clip-planes.

LUNGS (CASE 3) Figure 1. Overview of the interior of both lungs. The case demonstrates the usefulness of the freedom in compartment design that comes with atlas registration. In this case, the lung compartment is made smaller than the actual lungs, which provides a way to efficiently cut away not only the surrounding misclassified tissue but also the lung wall.

The total observed decrease of rendering performance induced by using AA-ROI visualization over standard DVR was 15%–20% due to one extra texture lookup and additional computations per sample point. Performing empty space skipping based on the mapped EDT data could potentially increase the performance additionally but was not implemented in our prototype software. Renderings were performed with volumetric illumination techniques [RDRS10].

6. Radiologist Study

In order to assess whether the developed approach fulfilled the defined objectives, a qualitative study was carried out in a clinical environment.

The prototype implementation used in the study is described in Section 4. The only exception relates to parameter κ_A^* which, in the study, modulated the amplitude of the localization function. The use of parameter κ_A^* was changed based on feedback from the study and is presented in this manuscript in its revised form as κ_A, controlling the size of the verification zone.

6.1. Materials and Methods

Five radiologists were involved in the study, four of which had not participated in the initial discussions and thus were new to the AA-ROI approach. The participants all use DVR in clinical practice to varying extents. The scenarios used were clinical cases where traditional DVR methods are not feasible due to inadequate resulting renderings or need for extensive TF and clip-plane tailoring. The three cases described in Section 5 were used in the study. The visualization tasks given to the participants were the following: First, the participants attempted to solve the given tasks using their regular medical DVR application. They were then given an introduction to the AA-ROI prototype software and informed about how the tasks could be addressed with the AA-ROI approach. Following this, the participants executed a hands-on session to explore the interaction possibilities of the AA-ROI approach in the context of the given tasks. TF presets were available for the respective applications, including semantic labels for the AA-ROIs.

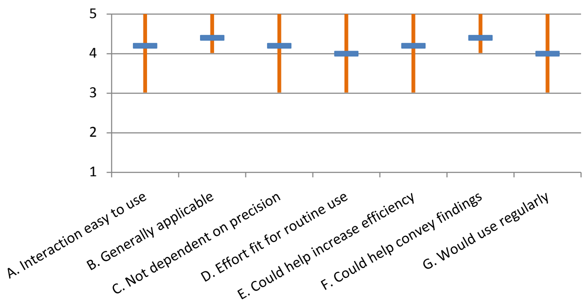

Figure 5: *Five radiologists assessed whether they agreed with qualitative statements about AA-ROIs. The answer scale ranged from* Strongly disagree *(1) to* Strongly agree *(5). The horizontal dashes are average values and the vertical lines show the min-max span. The radiologists were positive to the method for all aspects studied.*

6.2. Questionnaire

After the hands-on session, the participants were asked to grade the strength of their opinions for a set of statements related to the five requirements of *Genericness*, *Anatomical delineation*, *Robustness*, *User Control* and *Efficiency*.

The questionnaire used a five-degree Likert scale (1: Strongly disagree, 2: Disagree, 3: Unsure, 4: Agree, 5: Strongly agree) for which the quantitative results are shown in Figure 5. The statements answered, covering the objectives defined (Section 1), read as follows:

A. The AA-ROI interaction was easy to use
B. The AA-ROI approach is applicable to many parts of the anatomy
C. The usefulness of the AA-ROI approach does not depend on a precise registration (millimeter precision)
D. The time and effort needed to use the AA-ROI approach appears low enough to allow routine use
E. As a complement to DVR, the AA-ROI approach could help increase efficiency in my clinical work
F. As a complement to DVR, the AA-ROI approach could help to better convey findings to other physicians
G. If it was available, I would use the AA-ROI approach regularly in my clinical work

Finally, interviews were conducted with the participants, discussing their general qualitative impressions. They were also encouraged to provide further detail on the questionnaire.

6.3. Requirements for clinical deployment

Regarding the *User-controlled* requirement, the radiologists expressed a positive sense of staying in control of the visualization, attributed to the interaction possibilities and to the fact that the method did not employ automatic binary decisions. User parameter κ_A was used extensively and the fact that the parameter gradually transitions towards "standard" DVR was appreciated. Parameter κ_B was used more sparingly and could potentially be removed to further simplify interaction. The questionnaire answers related to the requirements of *Generic* and *Robust* scored well but several of the radiologists noted the importance of verifying that the final size of the verification zone sufficiently covers errors introduced by the registration. This feedback led to the change of parameter κ_A to directly express the size of the verification zone. The radiologists also expressed a necessity to thoroughly test each combination of examination type and choice of registration algorithm. While this implies an additional one-time cost of manual validation it should not effect time consumption on a per patient basis.

One limitation that was brought up in the study was the reliance on labeled atlas data, as it is not feasible that a single atlas is sufficient for all cases. Rather, a library of atlases for common cases would be more realistic. This issue is helped by the fact that atlases can be created both from synthetic models or from manual segmentation of acquired data sets, and also that AA-ROIs can be constructed with any registration method with sufficiently low interaction and computation costs. Further advances in registration research would also enable the AA-ROI approach to reach higher levels of general applicability. Overall the radiologists were very positive of the anatomical connection provided by the AA-ROI approach, drawing references to an appreciated "table removal" feature in their existing software. They were also positive that the processing times were low enough to not hinder clinical deployment for verified case types once integrated into their existing tools.

7. Conclusions

The starting point for this work was an analysis of why DVR still is seen as a peripheral tool by many radiologists. The registration based AA-ROI approach was developed with the objective to provide anatomical localization to DVR without introducing costs preventing wide-spread clinical practice. The results of the user study confirm that the combination of AIR and DBTFs presents an improvement regarding these objectives relative existing solutions. Thus, there is reason to believe that further research towards advanced, registration based ROI approaches could help reduce the underutilization of DVR and enable clinical benefits. Future efforts will be directed towards the points raised by the radiologists, primarily focusing on examination-type specific evaluations of registration accuracy and atlas availability.

Acknowledgments

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