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Cardiac radiomics: an interactive approach for 4D data exploration

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Abstract: Cardiac diseases manifest in a multitude of interconnected changes in morphology and dynamics. Radiomics approaches are a promising technique to analyze such changes directly from image data. We propose novel features to specifically describe moving cardiac structures, and an interactive 4D visualization method to explore such data. Prototypical tests with an open data set containing different diseases show that our approach can be a fast and useful tool for the 4D analysis of heterogeneous cohort data.

Keywords: cardiac function; cardiac imaging; parallel coordinates; radiomics.

Problem

Cardiac diseases, such as myocardial infarction and cardiomyopathy are the world's leading causes of death [1]. Currently, physicians mostly rely on echocardiography and cardiac magnetic resonance imaging (CMR) to estimate basic diagnostic features such as left ventricular (LV) volume or left ventricular ejection fraction (LVEF). However, the inclusion of novel diagnostic features extracted from the imaging data might improve early detection and treatment of cardiac diseases [2]. Especially the analysis of parameters derived from 4D CMR data have provided new insights into the pathologies of heart diseases recently [3].

In radiomics, large numbers of features are extracted from medical images and processed using data clustering and classification algorithms. The underlying premise is that patterns in morphology and texture of the imaged structures that are hard to discern with the bare eye can differentiate subgroups of a patient cohort. Radiomics has initially been employed for oncological applications but is an emerging technique in the cardiovascular field, especially with CMR [4, 5]. Several studies have shown the potential of cardiac radiomics (cf. section Related work), but reproducibility and robustness of the features are still a concern to be resolved [6].

In the heart, global and regional changes in morphology, structure, and motion patterns are associated with specific diseases and disease progress. We propose to extend existing radiomics approaches by shape descriptors that reflect the nature of the heart as a hollow organ, by features that reproduce cardiac dynamics, and by an approach that allows the exploration of complex 4D feature data.

Related work

Previous studies analyzed the applicability of CMR-based radiomics approaches for disease classification with cine MRI [7, 8], and CMR T1 and T2 sequences [9]. The authors could identify suitable shape, intensity and texture features for the recognition of diseases such as myocardial infarction. To support users in understanding the meaning of radiomics features and their application in cohort characterization, radiomics have been combined with visual analytics. Bannach et al. combined electronic health records (EHR) and image data for the visual analytics of head-and-neck cancer cases in order to enable the exploration of image characteristics for patient cohorts with certain properties [10]. The iVAR system for the analysis of lung cancer with CT enables linked views of 3D image data and feature exploration tools [11]. Tautz et al. suggested a hierarchical exploration of morphological features of the interventricular septum (IVS), including temporal properties to support the analysis of the interplay of left and right ventricle in dependence of physical stress [12].

Because radiomics have been developed for the analysis of tumors, there is a clear lack of features to describe the morphology and dynamics of non-compact structures

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in existing toolboxes. For interactive visualization, the suggested approaches provide only limited ways of incorporating temporal information, which is crucial for the characterization of functional properties.

Materials and methods

Our radiomics pipeline consists of three major workflow steps: a machine learning (ML) segmentation approach and expert preprocessing of the MRI image data, feature extraction, and interactive exploration of the 4D feature data.

Data

We include three sources of data for ML training, processing, and validation. Firstly, we utilized the ACDC challenge data set [13], a public data set containing image data of 150 patients in five subgroups. The subgroups include healthy subjects (NOR), patients with previous myocardial infarction (MINF), dilated cardiomyopathy (DCM), hypertrophic cardiomyopathy (HCM), and abnormal RV (RV). The image data was acquired as a series of short-axis slice stacks on 1.5 T and 3.0 T MRI scanners (in-plane resolution 1.37–1.92 mm²/pixel, 13–40 images per series). For details on the data acquisition, the reader is referred to the ACDC publication. The provided end-diastolic and end-systolic segmentations were used in the training of our segmentation model. Secondly, a medical expert manually segmented the remaining time points on 10 cases each from the normal, MINF, DCM, and HCM groups (40 cases in total), which also contributed to the training. Lastly, expert segmentations on 18 cine MRI data sets acquired at the German Heart Center Berlin (DHZB) were included in the training (in-plane resolution 1.219–1.632 mm²/pixel, 25 images/series). An expert curated all segmentations.

Data preprocessing

First, the relevant structures are segmented from the image data using an ML approach [14]. A U-net convolutional neural network is trained on the

the prepared datasets. The trained model is then used to segment the left and right ventricular blood pools (LVBP and RVBP), and the left ventricular myocardium (LVM) (Figure 1). Additionally, the ML algorithm calculates a map indicating the certainty of each voxel's belonging to the respective structure. A medical expert inspects the segmentation in a web-based software tool and corrects them where necessary. In addition, the expert defines landmarks for the standardized AHA model.

Feature extraction

Next, radiomics features are extracted directly from the images based on the curated segmentations. We extract two groups of features: a set of commonly used features from the PyRadiomics library [15], and a set of custom features designed to capture specific morphological and dynamic characteristics of the heart in non-quantitative MRI data.

From the standard radiomics features, we include *VoxelVolume*, *Elongation*, *Compactness1*, *Compactness2*, *glcm.ClusterTendency*, *glrlm.GrayLevelNonUniformityNormalized* and *glszm.GrayLevelNonUniformityNormalized* to describe shape, deformation and uniformity of the relevant structures, namely myocardium and bloodpools.

We hypothesize that different contraction and trabeculation patterns manifest in the appearance of the blood pool region. We add three intensity-based features to characterize the left blood pool further. The region is segmented into foreground and background using Otsu's method. We extract the mean intensity of each subregion, and the distance between the means (Figure 2).

The tortuosity of the left ventricle centerline, defined as the ratio of true centerline length to the Euclidean distance between the centerline end points, is an additional descriptor of ventricle shape (Figure 3, left).

Features associated with interventricular septum (IVS) and respiration dynamics, as presented in Ref. [12], including the in-slice heart diameter, the IVS thickness and the relative IVS thickness (normalized to the heart diameter) are calculated from the LV and RV segmentations (Figure 3, right).

Eventually, simple geometric and non-image features are added: the areas of the segmented structures on each slice, patient age, weight and height, and the length of the heart cycle.

Figure 1: Image processing: left and right ventricular bloodpool as well as the myocardium are segmented on all time frames. The segmentation is used to calculate the feature curves.

Figure 2: Left: Otsu segmentation of the LV blood pool (yellow delineation) into foreground (red) and background (blue) areas. Right: Corresponding histogram of foreground and background areas, with mean intensity of each area indicated by a vertical line.

Figure 3: Left: Illustration of LV center line tortuosity. Straight distance between centerline ends (blue), compared to true centerline (red). Exemplary short-axis slice for reference. Right: Illustration of IVS features. Heart diameter (yellow) and IVS diameter (green).

Interactive exploration

For the exploration of the extracted features, we provide an interactive web-based, hierarchical exploration tool (Figure 4). There are three main viewing areas that are coordinated with each other. A parallel coordinates

plot (PCP) serves as the starting point for the exploration and shows all features aggregated by case and by time point. Temporal curves of all cases selected in the PCP and for a specific feature are shown in a diagram. A 2D image viewer displays the underlying MRI slices, with overlays showing the segmentation result and the segmentation uncertainty.

Figure 4: Exemplary screenshot of the exploration tool, with DCM cases selected (red range on the right-most axis). Visualization areas highlighted by dashed lines. Orange: Parallel coordinates plot. Green: Classes of the data set. Blue: Temporal curves for a specific feature. Red: Patient/case selection and 2D image slice with segmentation class probability overlaid. Purple: Schematic heart anatomy indicating the current slice.

Figure 5: Result of visual exploration and differentiation of the DCM subgroup. Note the data range selection on two PCP axes (red areas). Close-up of brushed axis areas (green box).

Within the PCP, data lines can be selected by brushing a range on a feature axis (Figure 5). The user can brush several axes, as well as multiple ranges on the same axis, enabling a fine-grained selection of the data. In the curves diagram, a slider allows to select a time point, which in turn is linked with the image viewer. A navigation viewer shows the relative position of the currently viewed slice in a schematic heart anatomy.

implementation of our exploration concept to analyze the processed cases. To evaluate the interactive approach, we defined two tasks for the operator.

Results

We processed the 40 cases curated by the medical expert (cf. section Data), extracted features and combined the data for exploration. A medical expert used a prototypical

Task 1: differentiate diseases using the extracted features

The operator used PCP brushing to restrict the cases gradually. The *Avg. Left Blood Pool Intensity Line Non-Uniformity* and *Max. Left Blood Pool Voxel Volume* features

Figure 6: Result of visual exploration and analysis of the HCM and DCM subgroups. Note the feature distributions in the PCP, and the features curves.

helped to distinguish the DCM cases visually (Figure 4). Analysis of the data took ~5 min.

Task 2: develop a plausible hypothesis to link features and a disease

The operator used PCP brushing several times, combined with inspecting the curves of *Left Blood Pool Voxel Volume* and *Relative Septum Thickness* to build a hypothesis about the existing disease classification. The visual appreciation of PCP clustering, curves and the image data supported the contribution of ventricle geometry and dynamics to the classification (Figure 6). Analysis of the data took ~10 min.

Discussions

The expert could fulfill the tasks sufficiently in a short time. There is no preceding clustering of correlated features or filtering of potentially unimportant features. Automatic clustering of correlated features could help to choose the features that are displayed in the PCP, and to highlight remarkable data ranges.

The additional septum features helped to describe ventricular dynamics. The blood pool intensity and tortuosity features showed different dynamic patterns for the diseases, but not enough for visual differentiation. Additional analysis is needed to evaluate their potential for disease classification.

Our approach can be extended to explore of multi-cycle real-time CMR data, for example, the analysis of inter-cycle feature variation in arrhythmia patients.

Conclusions

We presented a proof of concept for novel features describing cardiac morphology, and a method to extract and interactively explore 4D features to differentiate cohort subgroups. The presented use cases show the potential for analysis of heterogeneous patient cohorts, and for disease differentiation. Further research is needed to validate the new 4D features, and to optimize the exploration concept.

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