Deep learning for automated analysis of cardiac imaging: applications in Cine and 4D flow MRI

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Chapter 1 General Introduction

Cardiovascular disease (CVD) is the leading cause of death globally, taking an estimation of 17.9 million lives each year, representing 32% of all deaths worldwide [1]. Echocardiography, computer tomography (CT) and magnetic resonance imaging (MRI) are the prevailing non-invasive imaging techniques for CVD diagnosis in clinical practice. Compared to the other two modalities, due to its excellent image quality and good soft tissue contrast, cardiac magnetic resonance (CMR) established itself as the reference standard for quantification of cardiac dimensions and function, including assessment of left ventricular volume, ejection fraction (EF) and myocardial mass. These clinical parameters can be derived with high precision from cine MRI. Other hemodynamic parameters, including trans-valvular blood flow, peak velocities, kinetic energy and wall shear stress, which also greatly aid in the diagnosis and prognostication of CVD, can be derived from the four-dimensional (4D) flow MRI.

In recent years, deep learning (DL), especially convolution neural network (CNN), has been successfully applied to automatically analyze medical images and derive clinical measures. Therefore, this thesis investigated deep learning techniques and its applications in both cardiac cine and 4D flow MRI.

1.1. Cine cardiac MRI

Cine cardiac MRI is typically obtained by repeatedly imaging the heart at a single slice location at multiple time points throughout one cardiac cycle. To fully image the whole heart, multiple slices at various locations must be obtained. Therefore, cine cardiac MRI provides a complete 3D visualization of the heart supporting detailed analysis of cardiac function. The short-axis (SAX) view and long-axis (LAX) four-chamber (4-CH) and two-chamber (2-CH) views, as shown in Figure.1.1, are routinely obtained anatomical views in cine cardiac MRI [2]. The images in the long-axis view are extracted as imaging planes parallel to a line extending from the cardiac apex to the center of the mitral valve. The SAX sequences are acquired as a stack of multiple 2D slices from the apex to the base of the heart perpendicular to the LAX view. The SAX view provides an excellent cross-sectional view of left ventricle (LV) and right ventricle (RV). Therefore, the images in SAX view are routinely considered as the standard approach to derive volumetric measurements for LV function assessment [3]. The end-diastolic (ED) and end-systolic (ES) phases, i.e. the phases with the largest and smallest LV blood volume, are two crucial phases in the cardiac cycle. ED volume (EDV) and ES volume (ESV) can be used to measure the stroke volume (SV) and ejection fraction (EF) which are important parameters quantifying global cardiac function [4].

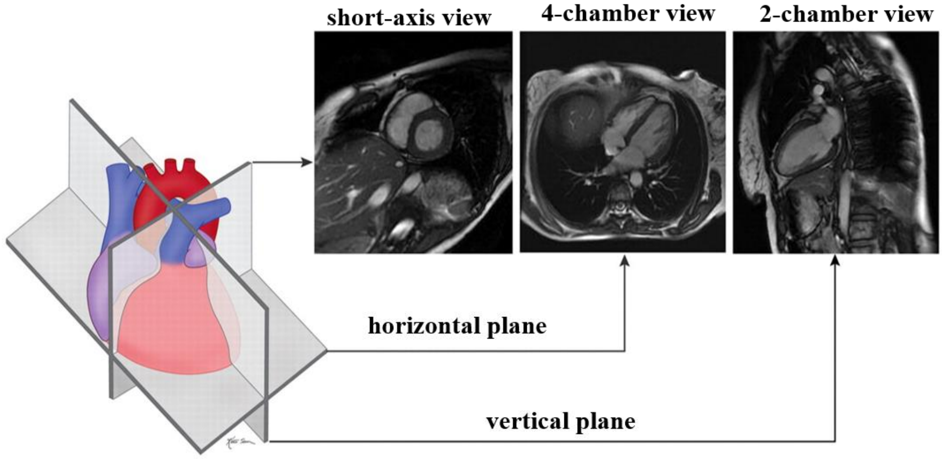

Figure.1.1 Major cardiac imaging planes and their corresponding views in cine cardiac MRI.

There are still some significant barriers to widespread use of cardiac MRI [5,6]. Poor breath-holding related respiratory motion, which is common in patients with heart failure, may introduce artifacts, resulting in low quality images. Additionally, numerous applications of cardiac MRI have been relying on segmentation of the cardiac structures. Manual image segmentation is tedious and time-consuming work and also prone to inter-observer variability. Therefore, in this thesis we address two aspects including the image quality and data analysis in cine MRI.

1.2. 4D flow cardiac MRI

2D cine cardiac MRI allows quantification of volumetric clinical parameters, but it cannot be used to identify hemodynamic markers in the heart or great vessels. 4D flow MRI is a state-of-the-art MR imaging technique encoding time-resolved three-directional velocities, allowing to visualize and quantity the flow direction, peak velocity and flow volume. 4D flow MRI provides sets of 3D volumes over time. Each 4D flow volume contains one magnitude volume and three velocity volumes. 4D flow MRI is particularly used to derive relevant flow parameters, such as flow components, kinetic energy, pulse wave velocity and pressure gradient, to evaluate various cardiovascular conditions and help guide diagnosis treatment and follow-up care for patients.

4D flow MRI shows promising applications in clinical practice, however, it has not been widely used yet. One of the main limitations is that the post-processing takes time and labor. Quantitative analysis relies on segmentation of anatomical regions in the images. But the extremely poor contrast between the heart chamber and surrounding tissues aggravates the difficulty of manual segmentation. As shown in Figure.1.2, the prevailing segmentation approach in 4D flow MRI depends on the registration between cine MRI and 4D flow data. However, the registration is computationally expensive, resulting in long runtimes. Additionally, differences in heart rate and spatial resolution between those two MRI acquisitions will introduce some misalignment during the registration. Therefore, fully automatic segmentation methods for 4D flow MRI segmentation are needed. The relatively long scan time, ranging from 5 to 20 minutes and limited spatial resolution, are other barriers of 4D flow MRI, which also restrict its analysis.

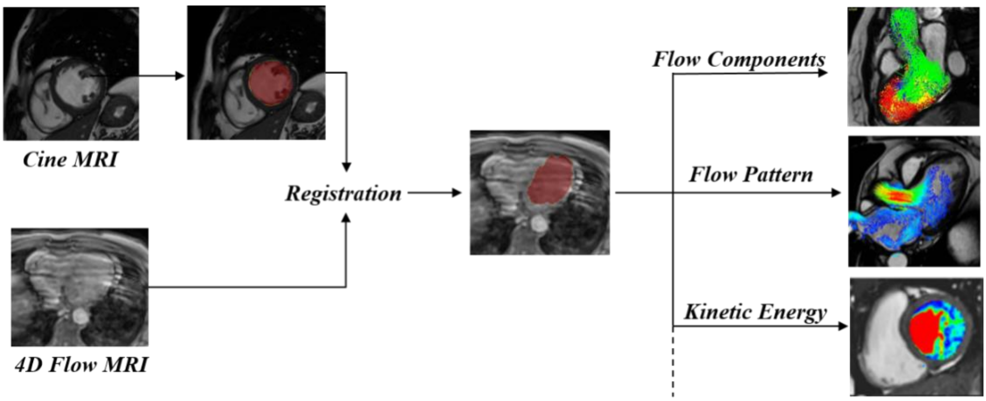

Figure.1.2. Existing workflow of quantitative analysis of 4D flow data. It requires two MRI sequences, firstly generates the mask on cine MRI, then registration is introduced to propagate the segmentation mask from cine MRI to 4D flow MRI.

1.3. Deep learning in cardiac MRI analysis

Based on the availability of the labels in the given data, DL can be divided into unsupervised learning and supervised learning. Unsupervised learning, where the labels are not available, tries to reveal the structure within the data on its own. In supervised learning, the model aims to mimic human performance by learning a mapping from the input data to the annotated labels. Supervised learning is the most commonly used approach in the field of CMR.

CMR has been a crucial technique in the evaluation of cardiac function and disease diagnosis. However, the analysis of CMR is complicated and time-consuming, requiring expert knowledge. Recently with the advance of DL, a variety of DL-based methods have been proposed enabling automated analysis of medical images, including cardiac MRI. For instance, given the manual segmentation, many DL-based frameworks were proposed for automated cardiac MR image segmentation [7-11] enabling quantification of volumetric parameters. As summarized in Figure1.3, the developments of DL relevant to cardiac MRI provide an efficient and effective way in the areas of image acquisition, reconstruction, image quality assessment, segmentation and diagnosis evaluation. The review [12] provides more details about the applications of DL in cardiac MRI analysis.

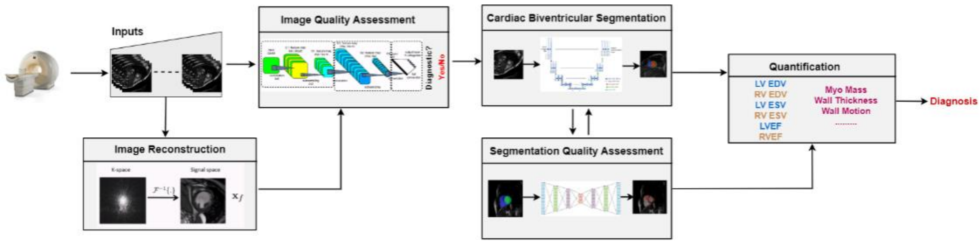

Figure.1.3. Deep learning applications for cardiac function diagnosis including image reconstruction, image quality assessment, segmentation and segmentation quality control [6].

Although deep learning has achieved immense success in the field of medical images, there is still a long way ahead to deploy them to real-world applications. Compared to natural images, medical images are less widely available, especially for cases with rare diseases and expert annotations are expensive. Additionally, model's generalization is another limitation for the deployment in real world, due to the data distribution heterogeneity across multiple modalities, scanners and centers.

1.4. Thesis outline

The work described in this thesis aims to develop deep learning based techniques to achieve fully automatic analysis of cine and 4D flow cardiac MRI. The research topics and connections between each chapter are summarized in the Figure.1.4.

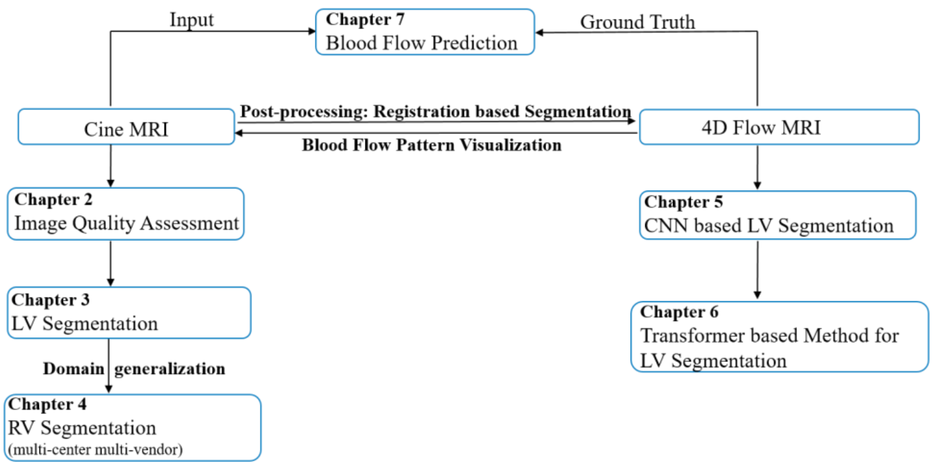

Figure.1.4 Overview of the research topics in the this thesis.

Chapter 2-4 present our work on cine MRI. Motion-related artifacts may result in non-diagnostic image quality. We first propose a method to automatically classify the image quality. Then, we investigate methods for left ventricular segmentation in short-axis cine images to derive LV volumetric parameters, which can be used for disease classification. A common issue with deep learning based models is that a model trained on one dataset does not generalize well to other unseen datasets due to the distribution heterogeneity between the data sets from various centers or vendors. Therefore, chapter 4 focuses on domain generalization.

Chapter 2 presents a method for cardiac MR image quality assessment combining data augmentation and deep learning network. Given the limited dataset, three specially designed data augmentation techniques are proposed. We also introduce a CNN model to mimic the sample inspection. The method has been evaluated on a public data set and achieved a promising results, ranking the 4^{th} in an international challenge.

Chapter 3 proposes two stack modules to integrate the temporal or spatial information from neighboring slices for left ventricle segmentation in short-axis view. A stack attention module is presented to weigh the features in the channel dimension. The stack attention module can be inserted into the U-Net to improve the segmentation performance. The approach was evaluated on two data sets, one in-house data set and one public data set.

Chapter 4 studies domain generalization in cardiac MR segmentation. **Chapter 3** solves the segmentation task given a specific single-center, single-vendor data set. Instead the use of fine-tuning or adaption to train a new model for a new data set, **Chapter 4** introduces a registration-based method to generate more pseudo data to enlarge the dataset. Additionally, the stack model, introduced in **Chapter 3,** is also applied to explore more features for the segmentation. The trained model is directly validated on an unseen data set.

Chapters 5 and 6 describe methods for LV segmentation in cardiac 4D flow MRI. Due to the poor contrast in 4D flow MRI, conventional segmentation in 4D flow MRI relies on the registration between cine and 4D flow MRI. **Chapter 5** investigates the feasibility of LV segmentation directly from 4D flow data without the use of any additional cine MRI. In contrast to previous studies, this is the first work to fuse the features from two modalities in 4D flow MRI to automate LV segmentation via deep learning. In this chapter we also compared the impact of different network structures and data pre-processing methods on the performance of LV segmentation from 4D flow MRI.

Chapter 6 extends the work of **Chapter 5** into an efficient feature fusion module to aggregate the information from magnitude and velocity images. The proposed module contains a Transformer based cross- and self-fusion layer to explore the inter-relationship between two modalities and the intra-relationship within the same modality. The clinical parameters derived from the proposed segmentation method are in good agreement with the ground truth.

Chapter 7 aims to build a bridge between cine and 4D flow MRI. 4D flow MRI provides quantitative information on intra-cardiac blood flow, but quantification requires complicated post-processing. A novel deep learning-based approach is presented to predict intra-cardiac blood flow directly from long-axis cine MRI. The intensity fluctuations within the cardiac cavities provide a visual clue about the global blood flow pattern. The model takes temporal neighboring frames as the input and the velocity field derived from 4D flow MRI as the ground truth. The prediction is validated against 4D flow data.

Chapter 8 summarizes the achievements of this thesis and provides a future outlook.

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