Spectroscopy and Learning-based Image processing
for
Cardiac Diagnosis

Thesis submitted in partial fulfillment

for the Award of Degree

Doctor of Philosophy

by

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CHAPTER 8

SUMMARY AND CONCLUSION

Highlights of the Chapter

- *Summary of the research works*
- *Highlights of the methods*
- *Discuss the conclusion*

The thesis has extensively reviewed the existing conventional methods for cardiac biomarker detection for prognosis and diagnosis of CVDs in Chapter 2. In Chapter 3, the literature survey on the different image-based diagnostic methods is explored which are applied on medical images. Fabrication of fiber scanner for imaging of cardiac tissue and spectroscopic analysis of cardiac biomarker is discussed in Chapter 4. Chapter 5 shows the spectroscopic method for detection cardiac specific biomarker (cTnI) and evaluates the performance of double density dual tree dual-tree complex wavelet transform for spike removal and denoising of spectroscopic signals for accurate quantitative and qualitative analysis. Chapter 6 & Chapter 7 contains the cardiac image based diagnosis of the CVDs and mainly concentrates on development of algorithm for accurate segmentation of different cardiac components for extraction of accurate and precise feature for cardiac diagnosis.

Using the conventional method, deformable registration of multimodal abdominal images (Ultrasound and Computed Tomography) is performed in Chapter 4 and Chapter 5. As the liver and its surface shows prominent intensity features, a surface segmentation operation is executed followed by the selection of best matching CT slice from a set of CT images in Chapter 4. Also, a gradient based similarity metric is incorporated in the cost function and utilized for registration. This metric is further used in Chapter 5 for registration refinement along with an algorithm and compared with another refinement algorithm consisting of multilevel B-splines. Performance evaluation with a distance-based measurement indicates better accuracy of the former one, while Levenberg-Marquardt method is found to be more precise than the rest two optimizations utilized. It is also concluded precisely that distance measure is fairly independent of the optimization technique.

In first phase of the work, biomarker-based detection of CVDs is explored using spectroscopy methods. Biomarkers are small molecules that can be quantified and help in the prognosis of the heart condition. Concentration above a certain value for biomarkers represents the changes of occurring of cardiac event in near future or certain heart condition is developed recently. Several spectroscopic methods had been used by different research groups still limitations exist in the method. Major limitations are:

- Method specific and tedious sample preparation
- Long processing and result time
- Requirement of central lab
- Lack of standardization
- Lack of prognosis capabilities and lower detection of limit

Spectroscopy based methods are proved to required no sample preparation method with faster results, and higher detection accuracy. UV-Vis, Raman, and Fourier transform infrared Spectroscopy is mainly investigated in this work for label-free detection of cardiac biomarker Cardiac Troponin I (cTnI). UV-Vis spectroscopy provided a SPR quenching phenomenon when biomarker is conjugated with gold nanoparticles. The 530 nm SPR peak of gold nanoparticles vanished as the concentration of cTnI is increased above certain level. The conjugation of cTnI with gold nanoparticles are further visualized using TEM images. The initial Raman signal for gold conjugated cTnI provided a hint of low concentration detection of the biomarker using multivariate signal processing but the results were initial and no conclusive inference can be drawn. The occurrence of global pandemic and shutdown of the institutes caused the postponement of the project and no further verification can be carried out as sample procurement and instrument handling is highly affected by the global situation. Further, the application of double density dual tree complex wavelet transform is also evaluated and observed that the method is not only able to remove the spikes from the spectroscopy signals but also have better denoising capabilities compared to other state-of-the-art denoising methods.

In the second phase of this work, Image based cardiac diagnosis is investigated mainly focusing on cardiac MR images. Cardiac Magnetic resonance imaging is considered the gold standard for non-invasive cardiac function analysis due to its 3D capabilities and high spatiotemporal resolution. It had been already proved to be an invaluable tool in the diagnosis of complex cardiomyopathies. Cardiac Magnetic resonance not only helps in the visualization of cardiac anatomy but also allows to know the functional behavior of the heart. Clinical implications of cardiac MRI are:

- Quantify coronary blood flow
- Measurement of ventricular volumes, wall thickness, and other parameters.
- Quantify myocardial infarction size.
- Myocardial viability
- Measure blood flow in the myocardium

Cardiac function analysis provides several information related to heart structure and helps in the diagnosis of several pathological conditions like hyper cardiomyopathy. But to accurately extract this information from cardiac function analysis-based modalities especially MRI, accurate segmentation is of the utmost importance. Despite several hardware and software advancements in recent years, several limitations exist like the requirement of ground truth, Image intensity and contrast inhomogeneity, and others. Major difficulties in Image-based diagnosis, regarding MRI, are as:

- Poor contrast between myocardium and surrounding structures
- Brightness heterogeneities in LV and RV chamber due to blood flow
- Presence of trabeculae and papillary muscles with intensity similar to the myocardium
- Inherent noise due to motion and heart dynamics
- Shape and intensity variability of heart structures
- Presence of banding artifact

These problems in the cardiac MR images makes the physicians difficult to do inference regarding the clinical conditions. To augment them, automated segmentation of the images are carried out which is further used to extract features to classify the patient as a normal or abnormal. To do so, accurate segmentation of the images is required for which a transfer learning-based method, a modified U-Net network, and a cascaded model is proposed. Results showed that the methods proposed are well-performed and the cascaded model paved a way to go from supervised learning to unsupervised learning thus removing the need of ground truth which is a hectic task.

Thus, the thesis aims are to improve methods of cardiac diagnostic by improving two of the most used aspects: Image-based diagnosis and Spectroscopy based diagnosis. In this view, this thesis aims to fulfill the following objectives like design and optimization of Raman probe for

Cardiac troponin I detection, validation of the use of spectroscopic methods in Cardiac troponin I detection, spectral signal processing to extract more accurate and quantitative information from the signal, development of an algorithm for more accurate segmentation of CMRI to improve feature extraction for diagnosis of the cardiac pathological condition, and to pave a way towards unsupervised segmentation of cardiac images to exploit the availability of vast unannotated biomedical image data for better diagnosis.

CHAPTER 8

FUTURE SCOPE OF WORK

Highlights of the Chapter

- *Background of the work*
- *Identification of the problem*
- *Probable solutions and future scope*

In this thesis, a part of research work is done on application of spectroscopy method for detection of cardiac biomarkers. Accurate detection of cardiac biomarkers plays an important role in efficient management of patients with heart problems. Several methods had been explored by different research groups around the globe to accurately quantify the cardiac biomarkers. the main issue in this method is limit of detection and variability among different modalities of detection by different manufacturer. This is mainly due the fact that the antibody and chemical process used by different methods varies widely and thus the target fragment of the protein changes leading to different cut-offs. Also, these methods are limited by lower detection limit defined by the binding capacity of the antibody and chemical process used for the proposed methods [1].

In second phase of the thesis work, different algorithms were developed for the efficient segmentation of different cardiac parts. For effective cardiac diagnosis using imaging modality, accurate segmentation of images is required which in turn gives the features and characteristic measures such as volume. In this thesis, weakly supervised method for segmentation of left ventricle in cardiac MR images is evaluated which in turn is a step forward to unsupervised segmentation of images [2]. Also, the algorithms developed for supervised segmentation improved the accuracy and thus improved the feature extraction from the images. For supervised methods, 3D segmentation is the future of algorithms development where 3D segmentation of the different heart chambers can be done.

So, the future work will probably include the following:

- To further use the developed probe for detection of cardiac biomarkers *in vivo* and imaging for diagnosis of the cardiac conditions.
- More advanced wavelet transforms like tunable-Q wavelet tranform can be used for denoising of Raman spectrocopy signals.
- To apply proposed method of quantitative and qualitative analysis to actual acquired real-time signals.
- To develop algorithms based on unsupervised methods so that availability of large unannotated biomedical images can be used.

References

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