Myocardial Perfusion Imaging using Vision Transformers

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Declaration

I hereby declare that this thesis titled "Myocardial Perfusion Imaging with Vision Transformers" and the work presented in it is my own original research. I confirm that:

- This work was done wholly or mainly while in candidature for a research degree at Eötvös Loránd University.

- Where I have consulted the published work of others, this is always clearly attributed.

- Where I have quoted from the work of others, the source is always given.

- I have acknowledged all main sources of help.

- This thesis has not been submitted for any other degree or professional qualification.

Signed: Haris Ali

Date: 13th April, 2025

Acknowledgements

Contents

Abstract

The manual delineating the left ventricle (LV) in Myocardial Perfusion Imaging (MPI) is one of the most labour-intensive and time consuming tasks in nuclear cardiology and radiology. The outcome of the diagnosis of the MPI is extremely dependent on the accuracyand the consistency of the segmentation of the ventricles, hence the process is done under extreme caution in roder to minimize the risks of any possible error. However, the process of turning this task into an automated one present a number of challenges that need to bbe mitigated. Fist of all, the signal-to-noise ration (SNR) is mostly low and the resolution of the image is limited, complicating the process of detecting the boundaries. Secondly, the high disparity in both the cardiac traces uptake ad the differences in the hardware used for the imaging introduces inconsistencies. Finally, their is a lack of a standardized definition of the shape of the LV and the there is no standard shape that can be traced based purely on image data, which introduces a lot more ambiguity in the task.

This thesis proposes a novel method built to address the limitations mentioned above by using a Transformer-based architecture, integrating statistical shape prior (SSP) technique. This approach is specifically used to mitigate the data-hungry nature of the transformers in case of limited deta. The proposed architecture achieves over 4% improvementover a number of metrics in segmentation and classification against the benchmarked state-of-the-art (SOTA) approaches use for LV segmentation, both on the synthetic data and the real-world clinical scans.

In addition to the improvements in the quantitative metrics, the incorporation of the prior shape information enabled the model to learn insights into the variability and the structural patterns of the LV anatomy in MPI single-photon emission tomography (SPECT) imaging. This deeper understanding of the LV enhances the reliability of the AI-powered automatic segmentation of the LV and also the general comprehension of the morphology of the LV in clinical practice.

Chapter 1

Introduction

Myocardial Perfusion Imaging (MPI) using single-photon emission computed tomography (SPECT) pllays an important role in the process of non-invasive assessment of the coronary artery disease (CAD). Considerig cardiovascular diseases being one of the leading causes of mortality all across the world, the need for an efficient, accurate and accessible tool for diagnosis is at a high demand. MPI SPECT provides critial information about the perfusion status of the heart, which helps in the early detection and planning the treatment wich improves the outcomes of the patients.

Radionuclide MPI under a specific condition, such as stress, is majorly regarded as one of the most effective diagnosis technique, which ia also non-invasive, in order to identify the or detect the coronary artery disease (CAD). Using the application of MPI SPECT, clinicians become equipped to diagnose and detect the functionally relevant coronary stenoses with a relatively high level of specificity This actually enables them to make decisions that are informed and possibly the right ones recarding the pathways of the patients' treatment [1]. By visualizing the perfusion process of the heart muscles, clinicians can detect the areas of the heart where there is a presence of coronary stenoses or obstructions which may be the causing issue for inducible perfusion deficits under the conditions of stress or rest.This ability of diagnosis is not only essential to identify the patients with CAD but aso functions as an important tool for mitigaing patient risk and guiding the decision making process of the clinicians.

MPI using SPECT has emerged as both an effective and economically viable modality for the purpose of diagnosis. MPI based SPECT offers both the advantages of being accessible and having establined standard clinical protocools hence it is the

preferres choice of a number of diagnostic processes. One of the major strengths of MPI is the adaptability of the technique, as it can incorporate a number of radiopharmaceutical agents, such as 201Tl Chloride, 99mTc Tetrofosmin, and 99mTc Sestamibi, which basically is dependant upon the imaging protocols and imaging needs. The mentioned agents are typically administered intravenously before the image acquisition part, and then the collected image data are later reconstructed using techniques which are dedicatedly designed for cardiac imagery. The last, and possibly the most crucial, stages in the diagnostic process involves the segmentation of the anatomical structures relevant to the diseases and then the reorientation of this segmented volumetric data. This part of the diagnostic is usually performed by trained clinical professionals in order to ensure precision, better reliability and to mitigate the risks of errors.

Beyond the usage of the perfusion imaging alone, there are additional functional parameters, which are valuable, that can be derived when gated acquisition techniques are applied. These marameters include end-systolic volume (ESV), end-diastolic volume (EDV), and the left ventricular ejection fraction (LVEF). All of the mentioned parameters are essential in order to indicate the performance of the heart. The values of these parameters are computed through the precise delineation of the myocardial boundaries of the LV,, which makes the task of segmentation even more crucial in the whole pipeline. The perfusion and the functional analysis collectively provide a detaled understanding of not only the vascular but also the mechanical health of the heart.

Efficient and accurate quantitative analysis of the 3D MPI SPECT data is extremely sensitive to a number of factors that are involved in the full end-to-end imaging and reconstruction pipeline, as mentioned above. All of these factors together contribute not only to the reliability of the evaluation of the data, but also to the detection of a range of cardiac abnormalities [2]. The important step in this process is the segmentation and reorientation of the LV, which basically refers to the determination of te spatial alignment of the LV and its segmentation based on the anatomical midline. The tasks of both reorientation and the segmentation within MPI SPECT imaging have been acknowledged, for a long time, as one of the central yet difficult challenges. Over the course of years, mutltiple commercial systems have been developed in order to counter these issues, but more often relying on very extensive and curated datasets in order to ensure reliable performance in clinical

environments [3], [4], [5].However, the eixisting solutions fall short when they are applied to the newer reconstruction paradigms, especially in the situations where there are only a limited number of labled patients datasets. In order to mitigate these imitations faced by the current solutions and to increase the generalization capabilities of the models under llimited data conditions, approaches incorporating self-supervised learning and few-shot learning have gained popularity. Nevertheless, the effectiveness of these strategies is most of the times overshadowed by the high costs associated with the expert annotations. In addition to this the lack of consensus regarding a standard segmentation protocol also complicate the practical application of the processes.

In the recent years, within the field of MPI SPECT imaging, the adoption of Deep Learning (DL) techniques are looking at a significant revival [6]. This renewal is basically driven in part by the development of the novel radiotracers and also the growing clinical demand to minimize the amount of administered radiation dose and also the image acquisition time of the performed procedures [7]. As a consequence, the modern methods of reconstruction have been focusing on configurations that are based on low photon count data, sparse acquisition views and reduced amount of injected doses [8], [9], [10]. But inspite all that, the advancements do not fully rosolve the challenges which are inherent to the segmentation tasks of MPI SPECT. Despite using state-of-the-art neural network based reconstruction strategies, the segmentation accuracy is still heavily relied on the underlying reconstructed images. When working with lower-dose inputs, the images mostly lack proper structural clarity, which diminishes the benefits which are offered by the DL based reconstruction methods. Even in situations where the image reconstruction achieves are visual equivalence to a full-dose filtered back projection methods, the issues of low Signal-to-Noise Ratio (SNR), Poisson noise characteristics, and the impact of partial volume effect (PVE) continue to affect the generalization capabilities and hence the reliability of automated segmentation models.

In this work, is proposed a novel approach in order to solve the aforementioned bottlenecks of the segmentation task, all the while also constributing further detailed insights into the anatomical characteristics of the MPI SPECT LV. Contrary to the previous approaches employed for the task, where the use of isolated pre-processed regions, or usage of cropped volumes, is common, the method in this study makes use of the entire reconstructed image volumes, hence incorporating all of the contextual

spatial cues which are available within the full field-of-view (FOV). The choice of this design makes sure that no information that is diagnostically relevant is discarded, hence allowing the moel to infer the left ventricular structure in relations to the surrounding regions of the anatomy. This holistic approach increases the robustness of the model, specifilcally in cases where abnormalities in the patterns could possibly interfere with the more localized analysis.

In order to mitigate the limitations hat are associated with singg convolutional neural networks (CNN), specifilcally their receptive field being restricted which hinders them from learning long-range dependencies, the proposed method employs a fully transformer based architecture called nnFormer [11]. This architecture is specifilcally developed for tasks pertaining to volumetric medical imaging. It allows the network to learn global reasoning over the 3D structures which offeres a significant advantage over the traditional CNNs in situations where the boundaries of the organs are not sharply defined such as SPECT. But there is a limitation to using transformer architectures, which is that they require a huge amount of data in order to learn acceptable global representations and have a good generalization ability. Hence, in order to overcome such a limitation, the proposed method incorporates Statistical Shape Priors (SSP) as a regularization technique. Such shape priors introduce an anatomical consistency into the DL model which acts as a guidance signal during the training of the model. This approach helps the models in situations where the amount of avaiable data is limited. Using the shape prios, the model is made to learn meaningfull and spatially coherent segmentation outputs even with minimal amount of supervision. This whole process bridges the gap between the traditional rule-based segmentation models and the fully data driven DL approaches.

Chapter 2

Related Work

The automatic reorientation and segmntation process of MPI SPECT represent steps that are essential for the accurate and and efficient diagnosis andd the quantitative analysis of the heart. A number of commercial softwares have been developed in order to perform these tasks and are widely adopted in clinical practices. The Corridor4DM [12], which was developed at the university of Michigan ,provides a platform for the comprehensive quantitative analysis for Myocardial Perfusion and the functional assesment from SPECT. This extremely integrated system gives access to an automated processing tool for analysis and reporting which si specifically developed to meet the increasing demands of such tools. In a similar way, the Emory Cardiac Toolbox (ECTb) [13] implements an extensive pipeline of quantitative tools which are developed as a result of very extensive research and its validation. It features a database of normal perfusion with more than 150 patients each, the fourier analysis of regional thikening, used for functional assesment, and a very advanced display function that allows to display 3D volumes for image fusion. The Cedars-Sinai approach [14] fouses on an end-to-end automatic expert system which is based on mathematical algorithms and rules based on logic reasoning. The presented QGS software is been used at more than 20 thousand locations all across the globe. The yale method [15] is focused on the quantification process of both the MPI and specifically the LV funcctional abnormalities, which adress the challenges faced by the process by muultiple factors such as background of images and the defects of perfusion using specialized processing techniques.

Other than the mentioned commercial solutions for the tasks, there is significant amount of research efforts that have been devotedly carried out to develop more ad-

vanced approaches and algorithms for MPI SPECT segmentation and reorientation. The Level-Set Methods (LSMs) have been proved to me one of the most developed methods in the field. The research by [16] presented an automatic method for the segmentation of the LV based on variational level sets in volumetri SPECT. This methos integrates adaptive thresholding for initialization with the evolution of variational level set for the determination of the finall contour. Very efective performance has been demonstrated using this approach as compared to the manual delineation through ROC analysis. More advanced LSM techniques [17] developeda model for implicit level sets representations which is based on 4D statistical shape analysis that combined the temporal information gotten from gated SPECT sequences. This eliminatedd the need for challenging point correspondences, at the same time outperforming 3D models with a better characterization of the evolution of the temporal shape.

Multiple hybrid approaches have also been developed in order to address some specific challenges in MPI SPECT analysis. The charged contour model presented in [18] is designed specifically to handlle the concavities in the segmentation label volumes. Later, [19] proposed a novel approach that combined the shape and appearance priors using a constraint with levels set deformable models, hence implementing a soft-to-hard parobabiitic constraint that provided a lot more flexibility as compared to rigid shape constraints alone. This approach proved to be particularly efective for LV segmentation in 4 dimensional gated SPECT, even if there were perfusion defects present. [20] developed hybrid active contour model for Myocardial D-SPECT volumes thar combined local image fitting models with the region-scalable fitting energy functions in order to mitigate the inhomogeneity issues, all the while maintaining the computational effciency. More earlier work by [21] developed a statistical model-based approach with the usage of 3D Active Shape Models (ASM) which combined both the geometric shape and the information depicted by the grey-level appearance from training data for the purpose of achieving robust segmentation of gated SPECT MPI.

Despite all the advances in the research, the traditional approaches stil continue to face great challenges in order to achieve the globally optimal point especially when processing the complete field-of-view volumes with a varying amount of image quality and variability in the anatomy. Such limitations has drived the more recent exploration of the machine and deep learning techniques in the field of nuclear car-

diology. Early machine larning applications in the domain were specifically focused on sub-tasks of the whole segmentation pipeline. [22] showed the effectiveness of using support vector machines (SVMs) for predicting the optimal valve positioning, demonstraing that the approach can be comparable to expert performance in SPECT alignment, at thesame time reducing the dependance on users for quantification. This study highlighted how even the conventional machine learning approaches can improve some specific aspects of the workflow of cardiac analysis. The study done in [23] presents a comprehensive review showing that deep learning solutions have shown remarkable promise across multiple aspects of PET and SPECT imaging, from the quantitative analysis to the instrumentation part of it all. [24] presentes a specific discussion about the transformative impace of using convolutional neural networks (CNNs) on the task of LV segmentaion, showing their ability to learn and interpret complex features directly from images.

The dawn of deep learning in the world brought forward even more comprehensive solutions to the task of LV segmentation. [25] proposes an end-to-end fully CNN based architecture that directly learns the segmentation mapping from the SPECT images taken as input. This approach eliminated the need to process the volumes in multiple stages for the segmentation map. This way the approaches using deep learning in order to handle the entire segmentation task could be developed, replacing the traditional way, with a unified framework. Buiding on the same idea [26] implemented a U-Net [27] based CNN architecture that outperformed significantly their own previous dynamic programming solution presented in [28], and it particularly improves handling the complex variations of shape of the Lv myocardim. More recently, there have been an increasing number of studies in even more sophisticated network architectures that are tailored to some of the unique challenges that are prevelant in the analaysis of cardiac SPECT. [29] introduced convolutional long-short term memory (LSTM) units in the skip connections of a V-Net architecture [30], which enabled an effective way of extracting temporal features from gated SPECT sequences. This novel approach addressed an essential need to leverage the presence of temporal information in higher dimensional volumes of SPECT. In a similar way, [31] enhances the usual 3D U-Net arhitecture with a self-attention mechanism which is amployed at the bottleneck. This allows for better inclusion of the global contexual information throughout the volumetric data.

The usage of shape priors have been identified as one o the efficient strategies,

valuable for improving the accuracy of segmentation models. [32] proposes a method that includes the shape priors, which are generated using a dynamic programming algorithm into a 3D V-Net network using a spatial transformer network (STN) which proved to give extremely good resuts al the whhile maintaining anatomical consistency. Despite the research, there is still a lot of unexplored room when it comes to shape priors and their use in the segmentation process [25]. The existing solutions rely heavily on a number of factors. The first one being the availability of a huge dataset size available with labels in order to train a model. Secondly, the focus within the architecture have been convolutional neural networks and thirdly, even the use of hybrid mechanisms which include attension systems have at least one convolutional layer component. While being effective, these approaches most of the time require substantial training data or very complex model architecture that might limit clinical applicability.

Chapter 3

User documentation

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3.2 Images and figures

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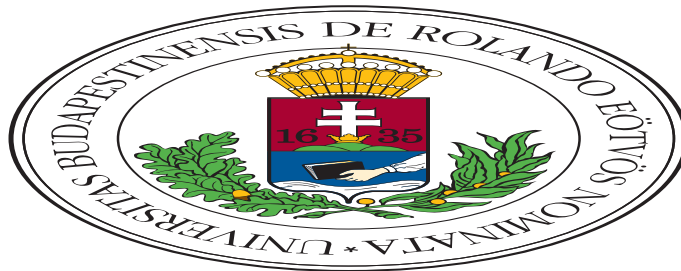

Figure 3.1: Quisque ac tincidunt leo

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Figure 3.2: Quisque ac tincidunt leo

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Chapter 4

Developer documentation

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4.1 Theorem-like environments

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4.1.1   Equations, formulas

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$$a^2 + b^2 = c^2$$

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In mathematica, identitatem Euleri (equation est scriptor vti etiam notum) sit aequalitatem Equation.:

$$e^{i \times \pi} + 1 = 0 \tag{4.1}$$

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tionis signum:

$$A = \frac{\pi r^2}{2} \tag{4.2}$$

$$= \frac{1}{2}\pi r^2 \tag{4.3}$$

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$$f(u) = \sum_{j=1}^{n} x_j f(u_j)$$

$$= \sum_{j=1}^{n} x_j \sum_{i=1}^{m} a_{ij} v_i$$

$$= \sum_{j=1}^{n} \sum_{i=1}^{m} a_{ij} x_j v_i \tag{4.4}$$

4.2   Source code samples

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```
1  #include <stdio>
2
3  int main()
4  {
5    int c;
6    std::cout << "Hello World!" << std::endl;
7
8    std::cout << "Press any key to exit." << std::endl;
9    std::cin >> c;
10
11   return 0;
12 }
```

Code 4.1: Hello World in C++

```csharp
1 using System;
2 namespace HelloWorld
3 {
4   class Hello
5   {
6     static void Main()
7     {
8       Console.WriteLine("Hello World!");
9
10       Console.WriteLine("Press any key to exit.");
11       Console.ReadKey();
12     }
13   }
14 }
```

Code 4.2: Hello World in C#

4.2.1 Algorithms

A general Interval Branch and Bound algorithm is shown in Algorithm. An appropriate selection rule is applied in. Source of example: Acta Cybernetica (this is a hyperlink).

Algorithm 1 A general interval B&B algorithm

Funct IBB(S, f)

1: Set the working list $\mathcal{L}_W := \{S\}$ and the final list $\mathcal{L}_Q := \{\}$
2: **while** ($\mathcal{L}_W \neq \emptyset$) **do**
3:      Select an interval X from $\mathcal{L}_W$ ▷ Selection rule
4:      Compute $lbf(X)$ ▷ Bounding rule
5:      **if** X cannot be eliminated **then**   ▷ Elimination rule
6:          Divide X into X^j, $j = 1, \ldots, p$, subintervals   ▷ Division rule
7:          **for** $j = 1, \ldots, p$ **do**
8:              **if** X^j satisfies the termination criterion **then**   ▷ Termination rule
9:                 Store X^j in $\mathcal{L}_W$
10:             **else**
11:                 Store X^j in $\mathcal{L}_W$
12:             **end if**
13:          **end for**
14:      **end if**
15: **end while**
16: **return** $\mathcal{L}_Q$

Chapter 5

Conclusion

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Appendix A

Simulation results

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