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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

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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 accuracy and the consistency of the segmentation of the ventricles, hence the process is done under extreme caution in order to minimize the risks of any possible error. However, the process of turning this task into an automated one presents a number of challenges that need to be mitigated. First of all, the signal-to-noise ratio (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 and the differences in the hardware used for the imaging introduces inconsistencies. Finally, there is a lack of a standardized definition of the shape of the LV and 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 data. The proposed architecture achieves over 4% improvement over a number of metrics in segmentation and classification against the benchmarked state-of-the-art (SOTA) approaches used 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) plays an important role in the process of non-invasive assessment of the coronary artery disease (CAD). Considering 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 critical information about the perfusion status of the heart, which helps in the early detection and planning the treatment which 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 is also non-invasive, in order to identify 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 regarding 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 also functions as an important tool for mitigating 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 established standard clinical protocols hence it is the

prefers 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 ^{201}Tl Chloride, $^{99\text{mTc}}$ Tetrofosmin, and $^{99\text{mTc}}$ 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 parameters 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 detailed 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 the 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, multiple 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 existing solutions fall short when they are applied to the newer reconstruction paradigms, especially in the situations where there are only a limited number of labeled patients datasets. In order to mitigate these limitations faced by the current solutions and to increase the generalization capabilities of the models under limited 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 resolve 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 contributing 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 model to infer the left ventricular structure in relations to the surrounding regions of the anatomy. This holistic approach increases the robustness of the model, specifically in cases where abnormalities in the patterns could possibly interfere with the more localized analysis.

In order to mitigate the limitations that are associated with single convolutional neural networks (CNN), specifically 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 specifically developed for tasks pertaining to volumetric medical imaging. It allows the network to learn global reasoning over the 3D structures which offers 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 available data is limited. Using the shape priors, the model is made to learn meaningful 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 segmentation process of MPI SPECT represent steps that are essential for the accurate and efficient diagnosis and 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 assessment from SPECT. This extremely integrated system gives access to an automated processing tool for analysis and reporting which is 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 thickening, used for functional assessment, and a very advanced display function that allows to display 3D volumes for image fusion. The Cedars-Sinai approach [14] focuses 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 functional abnormalities, which address the challenges faced by the process by multiple 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 be 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 volumetric SPECT. This method integrates adaptive thresholding for initialization with the evolution of variational level set for the determination of the final contour. Very effective performance has been demonstrated using this approach as compared to the manual delineation through ROC analysis. More advanced LSM techniques [17] developed a 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 eliminated 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 handle the concavities in the segmentation label volumes. Later, [19] proposed a novel approach that combined the shape and appearance priors using a constraint with level set deformable models, hence implementing a soft-to-hard probabilistic constraint that provided a lot more flexibility as compared to rigid shape constraints alone. This approach proved to be particularly effective 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 that 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 efficiency. 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 still 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 have driven the more recent exploration of the machine and deep learning techniques in the field of nuclear car-

diology. Early machine learning 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, demonstrating that the approach can be comparable to expert performance in SPECT alignment, at the same time reducing the dependence 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] presents a specific discussion about the transformative impact of using convolutional neural networks (CNNs) on the task of LV segmentation, 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. Building 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 myocardium. 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 prevalent in the analysis 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 architecture with a self-attention mechanism which is employed at the bottleneck. This allows for better inclusion of the global contextual information throughout the volumetric data.

Chapter 3

User documentation

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3.1 Enumerations and lists

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3.1.1 Lists with narrow spacing inbetween items

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3.2 Images and figures

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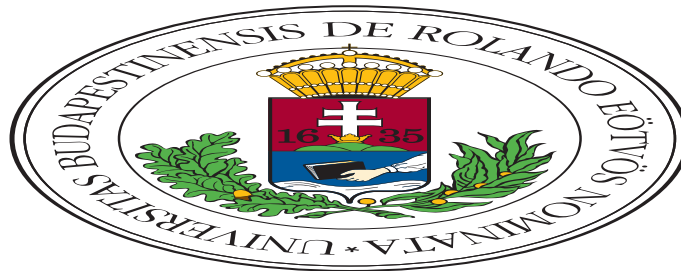


Figure 3.1: Quisque ac tincidunt leo

3.2.1 Framing figures

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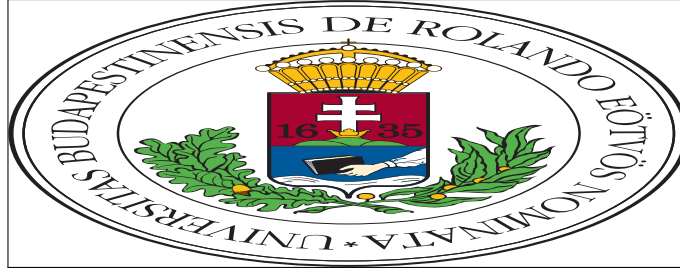


Figure 3.2: Quisque ac tincidunt leo

3.2.2 Subfigures

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Figure 3.3: Aenean porttitor mi volutpat massa gravida

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3.3 Tables

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3.3.1 Multi rows and multi columns

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Vel	9,60 MB	100%	564 KB	5,74%	292 KB	2,97%
Auge	78,2 MB	100%	52,3 MB	66,88%	3,22 MB	4,12%

Table 3.2: Vivamus ac arcu fringilla, fermentum neque sed, interdum erat. Mauris bibendum mauris vitae enim mollis, et eleifend turpis aliquet.

3.3.2 Long tables over multiple pages

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Table 3.3: Praesent ullamcorper consequat tellus ut eleifend

Chapter 4

Developer documentation

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4.1 Theorem-like environments

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Remark. Nunc ornare mi at augue vulputate, eu venenatis magna mollis. Nunc sed posuere dui, et varius nulla. Sed mollis nibh augue, eget scelerisque eros ornare nec. Praesent porta, metus eget eleifend consequat, eros ligula eleifend ex, a pellentesque mi est vitae urna. Vivamus turpis nunc, iaculis non leo eget, mattis vulputate tellus.

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Note. Aliquam vehicula luctus mi a pretium. Nulla quam neque, maximus nec velit in, aliquam mollis tortor. Aliquam erat volutpat. Curabitur vitae laoreet turpis. Integer id diam ligula.

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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:

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

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

Proin tempor risus a efficitur condimentum. Cras lobortis ligula non sollicitudin euismod. Fusce non pellentesque nibh, non elementum tellus. Omissa numeratione aliquarum aequationum:

$$\begin{aligned} f(u) &= \sum_{j=1}^n x_j f(u_j) \\ &= \sum_{j=1}^n x_j \sum_{i=1}^m a_{ij} v_i \\ &= \sum_{j=1}^n \sum_{i=1}^m a_{ij} x_j v_i \end{aligned} \tag{4.4}$$

4.2 Source code samples

Nulla sodales purus id mi consequat, eu venenatis odio pharetra. Cras a arcu quam. Suspendisse augue risus, pulvinar a turpis et, commodo aliquet turpis. Nulla aliquam scelerisque mi eget pharetra. Mauris sed posuere elit, ac lobortis metus. Proin lacinia sit amet diam sed auctor. Nam viverra orci id sapien sollicitudin, a aliquam lacus suscipit. Quisque ac tincidunt leo.

```
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++

```
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

Func 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  $lb f(X)$  ▷ Bounding rule
5:     if  $X$  cannot be eliminated then ▷ Elimination rule
6:         Divide  $X$  into  $X^j$ ,  $j = 1, \dots, p$ , subintervals ▷ Division rule
7:         for  $j = 1, \dots, p$  do
8:             if  $X^j$  satisfies the termination criterion then ▷ Termination rule
9:                 Store  $X^j$  in  $\mathcal{L}_Q$ 
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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Acknowledgements

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Appendix A

Simulation results

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