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Deep learning for vascular segmentation and tissue characterization in CT images

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General Introduction

With the rapid advances in CT acquisition technology over the past decade, CT Angiography has now become commonplace in diagnostic and interventional radiology. CTA is primarily used to depict complex vasculature, providing detailed insights in disease processes such as atherosclerosis. In addition, CTA also provides valuable insights into individual anatomical features of patient vasculature, and as such may help in planning interventional procedures. However, the 3D nature and complexity of vascular anatomy necessitates analysis and visualization methods that assist the radiologist in the interpretation of large CTA datasets. Such methods should work automatically and reliably, such that the time expenditure for the radiologist to analyze CTA data is minimized.

A large body of prior research has been performed on automating the analysis of CT Angiography data. These methods are still suboptimal in their segmentation performance and robustness, and a fully automatic and reliable method remains a technical challenge. However, the recent emergence of AI methods such as deep learning holds promise for further automating this analysis, and for improving robustness of this automation. This thesis focuses on enhancing CTA image analysis and interpretation using the latest deep learning technologies. The overarching aim of this thesis is to overcome existing technical limitations in the automated analysis of CTA imaging data by developing advanced deep learning methods for two CTA application domains: coronary computed tomographic angiography (CCTA) and CTA of liver vasculature. In the following sections, we first introduce CT Angiography in more detail, followed by an introduction on the clinical context of the two applications addressed in this thesis and a detailed outline of the thesis.

1.1 Vessel CTA

CTA is one of the commonly used imaging modalities for diagnosing vascular diseases, offering a minimally invasive approach that reduces patient risk[1, 2]. Spatial resolution, temporal resolution, and volume coverage are three key image quality metrics of concern in CTA data acquisition[3]. To achieve faster image acquisition and greater scan volume coverage, multidetector-row computed tomography (MDCT)[4] was developed, which has greatly facilitated the clinical use of CTA. In addition to the

requirement for advanced CT techniques, contrast medium enhancement is a crucial component of CTA acquisition. A contrast medium with a high iodine concentration is considered ideal for clinical use [3]. Following intravenous injection, the injected contrast medium travels through the arm veins to the right heart chambers, passes through the lungs, and then enters the left heart chambers before reaching the arterial system[1]. After being distributed throughout the organs via the vascular system, the contrast medium returns to the right heart in a process known as recirculation [1]. The vascular lumen can be distinguished from the vessel wall based on the enhancement properties of the contrast medium.

1.2 Coronary plaque detection

Coronary Artery Disease (CAD), the leading cause of cadiovascular mortality and morbidity worldwide[5, 6, 7], is a pathological process of atherosclerotic plaque accumulation within the epicardial coronary arteries[8]. Atherosclerotic plaques can be categorized as either stable or vulnerable plaques and can be represented by various phenotypes. Stable plaque phenotypes contain larger calcium deposits which is significantly associated with suboptimal results of coronary interventions[8]. Vulnerable plaque phenotypes include a large lipid-rich necrotic core, thin fibrous cap, and spotty calcifications. An increased size in the lipid-rich necrotic core is highly correlated with an increased risk of Major Adverse Cardiovascular Event (MACE)[8], and the thin-fibrous caps that cover the lipid-rich cores may lead to plaque rupture[9]. Vulnerable plaques with these characterizations are high-risk plaques (HRP) shown in Fig. 1.1 and can develop into culprit lesions associated with acute coronary syndrome (ACS)[10]. Large observational studies show that patients with vulnerable plaques are five times more likely to experience MACE than patients without[8]. Thus, identifying high-risk features is clinically significant for individuals at high risk for future cardiovascular events.

Coronary plaque imaging modalities can be broadly classified as either invasive or noninvasive. Invasive imaging modalities shown in Fig. 1.2, such as intravascular ultrasound (IVUS), optical coherence tomography (OCT) and near infrared spectroscopy (NIRS), are considered the gold standard for plaque quantification and characterization[11]. IVUS is normally combined with post-processing methods, such as virtual histology intravascular ultrasound (VH-IVUS), to assess plaque composition. VH-IVUS can distinguish between fibrous, fibrofatty, necrotic core, and dense calcium[11], but its limited efficacy in identifying vulnerable plaques and low resolution limit its effectiveness[13, 14]. Although OCT can provide higher-resolution images than IVUS, assessing lipid cores with OCT may lead to up to 20% false positives because macrophages and calcifications have similar signal representations compared to lipid cores in OCT images[15]. Additionally, OCT's limited tissue penetration makes

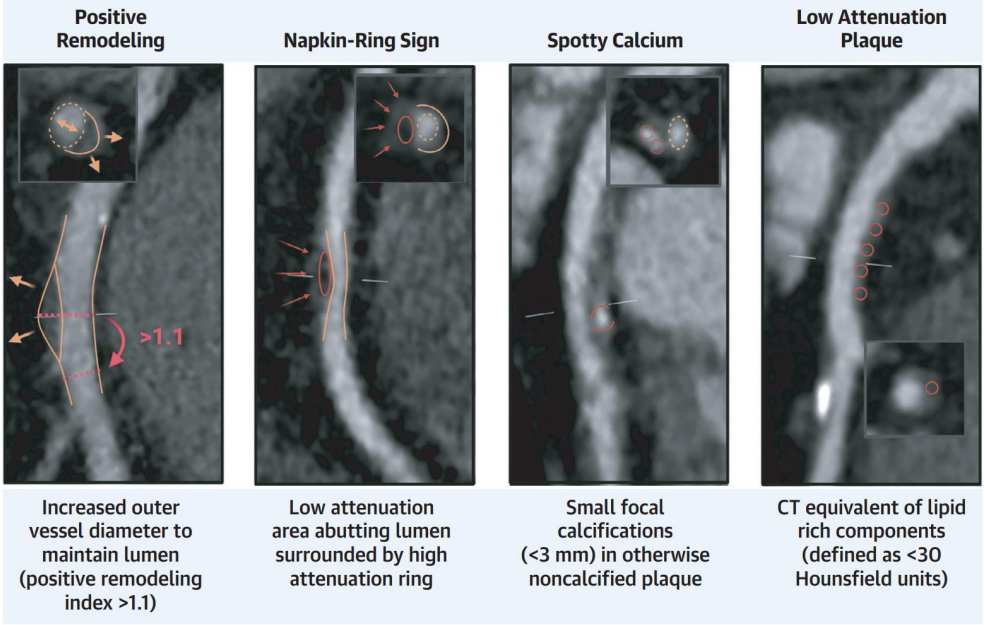

Figure 1.1: High-risk plaque features. (Figures reproduced from [11] under the CC BY-NC license)

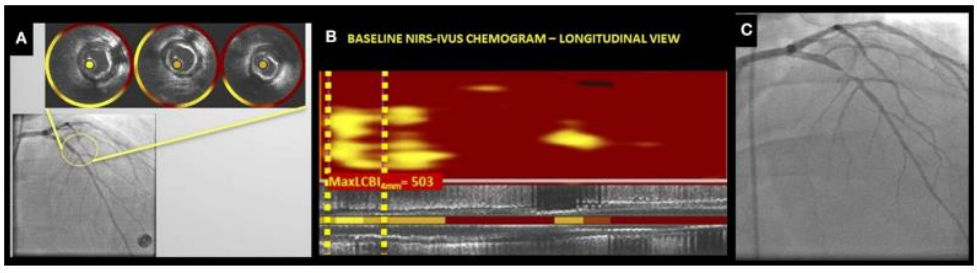

Figure 1.2: NIRS-IVUS imaging modality. (A) IVUS cross-sections and NIRS-IVUS rings, (B) NIRS-IVUS chemogram in longitudinal view, (C) vessel angiogram. (Figures reproduced from [12] under CC BY license.)

volumetric quantification of lipid plaque burdens difficult because the abluminal border of lipid pools cannot be detected.[8]. NIRS can accurately identify lipid areas based on their spectral properties. However, it cannot distinguish non-lipid components[8, 16], such as fibrous or calcified tissues, nor can it provide anatomical information about vessels. To overcome the limitations of IVUS and take advantage of NIRS, a combined NIRS-IVUS imaging modality shown in Fig. 1.2 has been proposed. This modality accurately detects lipid-rich plaque and visualizes lumen and plaque structures[13, 17]. However, all these invasive modalities increase the risk of harm to the patient.

Recent developments in noninvasive cardiac imaging modalities, such as computed tomography angiography (CTA), enable precise plaque phenotyping with minimal invasiveness. Coronary CTA can provide quantification of calcified, non-calcified, and low-attenuation plaque, as verified by intravascular imaging and histology[18, 19]. Noninvasive CTA can identify various high-risk features of vulnerable plaque, such as areas of low attenuation (<30 Hounsfield units (HU)) on CT scans and napkin-ring sgins, which are low-attenuation central areas surrounded by peripheral hyperattenuation[8]. Thus, CTA is a safe and efficient alternative for plaque characterization compared to invasive imaging modalities. However, HU-based plaque components differentiation is unreliable due to the significant overlap between the HU range of lipid-rich or fibrous plaque and that of the surrounding myocardial tissue[20, 21]. Some unclear cases still require more accurate invasive assessment[8], and a reduction in the dependence on HU ranges when differentiating coronary plaque components based on CTA images.

1.3 Liver anatomy

Advances in hepatic surgery are significantly facilitated by exploring intrahepatic anatomy. Claude Couinaud (1922-2008) demonstrated that hepatic functional anatomy depends on vascular and biliary relationships rather than external surface anatomy[23, 24]. As shown in Fig. 1.3, the liver can be divided into eight functionally independent segments based on the distribution of the hepatic and portal veins in the liver[25], each segment has its own vascular inflow and outflow. The three hepatic veins divide the liver into four sections: the right lateral section, the right medial section, the left medial section, and the left lateral section. The planes containing the portal pedicles further divide the right lateral, right medial, and left lateral sections into upper and lower segments, resulting in segments II to VIII. In addition, segment I (the caudate lobe) lies posteriorly and functions independently from the other segments, receiving branches from both the right and left portal veins. These functionally independent segments provide critical anatomical guidance for liver surgery, enabling precise preoperative planning. Further details on preoperative planning for liver surgery are discussed in the following section.

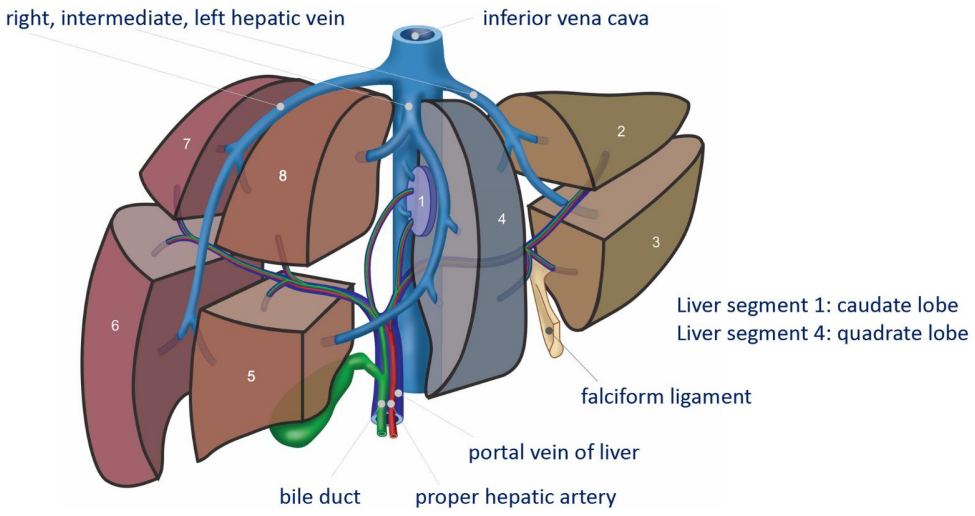

Figure 1.3: Segmental anatomy of liver organ. Eight functionally independent segments are divided based on the distribution of liver veins. (Figures reproduced from [22] under CC BY-NC-SA license.)

1.4 Preoperative planning for liver surgery

Clinical treatments for Hepatocellular carcinoma (HCC) and and colorectal cancer (CRC) are highly dependent on accurate preoperative planning[27, 28]. There are two key tasks in the preoperative planning of liver surgery. One involves identifying the relative positions of other organs, vessels, and tumor locations. The other involves planning the cutting path for liver resection or the puncture path for percutaneous radiofrequency ablation (RFA). Currently, computer-aided diagnosis systems are normally used for preoperative planning and surgery risk assessment. Designing an appropriate computer-assisted diagnosis system requires 3D visualization of liver anatomy as shown in Fig. 1.4, including main liver vessels, tumors, and self-contained liver segments, etc. For instance, during liver resection surgery, image segmentation of the liver and its internal structures is necessary for navigating the procedure and ensuring that the remaining liver percentage after resection is sufficient[27, 29]. Through preoperative planning, surgeons can identify the liver segment at risk to guide the resection of the tumor and the surrounding tissue[30]. The tumor cannot be resected by making an arbitrary cut because the hepatic or portal vein could be cut. Accidentally cutting the main hepatic vein could negatively affect blood drainage from the cancerous part of the liver, and cutting the portal vein could cut off the supply path from the other parts of the liver[31, 32, 33]. As with resection treatment, accurate preoperative planning is necessary for RFA treatment to minimize the risk of main

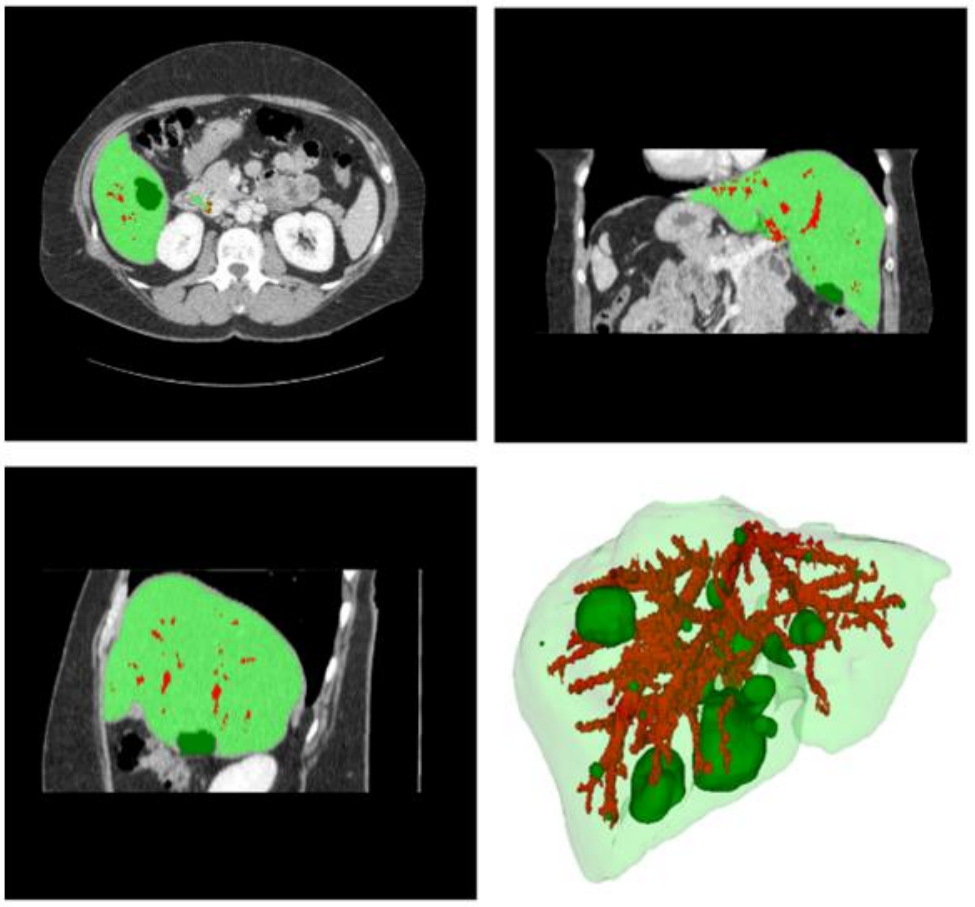

Figure 1.4: Spatial locations of liver vessels and tumors. (Figures reproduced from [26] under CC BY-NC-ND.)

vessel penetration and ensure proper needle placement[28, 34, 35]. Therefore, in order to perform precise surgical navigation and minimize the risk of cutting a major vessel, it is essential to divide the liver into functionally independent segments and accurately segment the liver vessels. However, accurately segmenting liver vessels and functional segments is challenging. The main challenges for accurate liver vessel segmentation are the complex vascular structures, thin branches, and small vessels. Inaccurate liver vessel segmentation can negatively impact the segmentation of the functional liver segments.

1.5 Deep learning in CTA images

Coronary CTA is currently the most frequently used noninvasive method for diagnosing coronary artery disease (CAD), providing information on stenosis quantifica-

tion, plaque classification, and plaque component characterization[36, 37, 38, 39]. However, CTA image interpretation remains a subjective task that depends on the experience of clinical experts[36]. To make CTA-based diagnosis more reliable and reproducible, convolutional neural networks (CNNs) have proven to be powerful tools for feature-based automated image analysis. CNN-based methods for CTA image analysis can be roughly divided into morphological analysis, including automatic coronary segmentation and centerline extraction[40, 41, 42], as well as functional analysis, such as coronary stenosis quantification and plaque characterization[43, 44, 45]. Despite the great success of deep learning in these tasks, noninvasive CTA still cannot replace invasive modalities for diagnosis, especially in ACS patients with ambiguous intravascular features on CTA images, such as low-attenuation lipid-rich tissue and other non-calcified plaque components mentioned in Fig. 1.1. Thus, to reduce the reliance on invasive modalities for diagnosis, exploring deep learning methods to learn the feature mapping between noninvasive CTA and invasive imaging has significant clinical value.

In addition to deep learning methods specifically developed for CTA images, many advanced techniques designed for general medical image analysis across other imaging modalities can also be adapted to the CTA domain. Medical image segmentation is one of the most widely studied tasks in this field. It plays a crucial role in medical image analysis by aiming to identify pixel-level associations with specific organs or lesions [46]. Numerous studies have demonstrated that CNN-based deep learning methods achieve accurate medical image segmentation with reduced sensitivity to image quality and significantly outperform traditional mathematical models and conventional machine learning techniques[47]. In addition to the well-known CNN-based methods, many advanced models from the field of computer vision, such as graph convolutional network (GCN)[48], point-based convolutional network (PCNN)[49], generative adversarial network (GAN)[50], and denoising diffusion probabilistic model (DDPM)[51], can be effectively adapted for downstream medical image segmentation tasks, such as the widely studied multi-organ segmentation[52, 53, 54, 55], etc. However, due to the inherently three-dimensional nature of most medical imaging modalities, extensive model optimization is often required to preserve anatomical completeness and continuity, unlike segmentation tasks in natural image processing.

1.6 Thesis outline

The overarching goal of this thesis is to overcome existing technical limitations and develop advanced deep learning methods for coronary plaque characterization, liver vessel segmentation, and Couinaud segmentation. All of the methods proposed in the thesis were developed using CTA modalities. This thesis is guided by the following three specific aims:

1. To investigate whether coronary plaque can be accurately detected and characterized using CTA images, thereby eliminating the need for invasive diagnostic procedures.

2. To explore the potential of 2D deep learning models to improve the continuity of 3D liver vessel segmentation.

3. To examine whether Couinaud liver segments can be delineated without relying on vessel priors, using deep learning-based approaches.

Specific Aim 1 is addressed in Chapter 2, which presents two methods for the detection and characterization of lipid-rich and calcified plaques in coronary CTA images. The two methods learn to map plaque features between gold-standard yet risky invasive modalities and the safe, non-invasive CTA modality. Unlike existing deep learning methods for plaque detection, we first propose predicting the plaque occurrence angle in the cross-sectional view to achieve a finer visualization of the angular distribution of coronary plaque.

Specific Aim 2 is addressed in Chapter 3 and Chapter 4. Chapter 3 presents a novel graph-attention guided diffusion model for continuous and complete liver vessel segmentation in CT images. We use the graph anatomy to constrain the diffusion model, which generates liver vessel segmentation with good 3D connectivity.

Chapter 4 presents a novel top-k maximum intensity projection (MIP) prior for continuous liver vessel segmentation in CT images. We mimic 3D segmentation as a CT reconstruction process. We use a latent diffusion model to learn the mapping between the top-k maximum intensity projections (MIPs) and the integral projections (IPs) of the ground truth liver vessel masks. Liver vessel segmentation can be reconstructed using the filtered back projection method based on the generated IPs.

Chapter 5 addresses thesis aim 3 by presenting a vessel-prior-free graph reasoning point net for Couinaud segmentation in CT images. Unlike the liver vessel-dependent delineation used in clinical practice, the graph reasoning module learns implicit graph embeddings instead of using explicit liver vessels for Couinaud segmentation.

Chapter 6 discusses the studies in this thesis in the context of the envisioned clinical applications and provides insights for further related research.

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