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**Tackling Crohn's disease using
deep learning**

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Abstract

This is the abstract about this thesis.

Acknowledgements

Thanks mum!

Contents

List of Figures	3
1 Introduction	4
1.1 Crohn’s Disease	4
1.2 Motivation	5
1.3 Machine Learning Challenges	6
1.4 Objectives	6
2 Related Work	8
2.1 Automatic Detection and Segmentation of Crohn’s Disease Tissues from Abdominal MRI	8
2.2 Automatic Detection of Bowel Disease with Residual Networks	9
2.3 Leveraging Machine Learning Methods for Accurate Predic- tion of Intestinal Damage in Crohn’s Disease Patients	10
3 Background	12
3.1 Image Segmentation	12
3.1.1 More on Semantic Segmentation	12
3.2 Manual Segmentation	13
3.3 Threshold-based Methods	13
3.4 Region-based Methods	14
3.5 Deep Learning Methods	15
4 Dataset Analysis	17
5 Methodology	18
6 Evaluation	19
7 Ethical Discussion	20
8 Conclusion	21

9 Future Work	22
Bibliography	23

List of Figures

1.1	The gastrointestinal tract of a Human	5
3.1	Different Image Segmentation Tasks	13
3.2	An example of the U-net architecture. Each blue box in the figure represents a multi-channel feature map, and on the top of each box indicates the number of channels. The x - y -size is shown at the lower left edge of the box. Each white box represents a copied feature maps. The arrows denote the different operations.	15
3.3	The pipeline representation of nn-UNet.	16

Chapter 1

Introduction

1.1 Crohn's Disease

Crohn's Disease [1, 2] is one of the primary types of Inflammatory Bowel Disease (IBD) [3], which is characterised by its chronic nature with inflammation in the gastrointestinal (GI) tract, as indicated in Figure 1.1 [4]. This condition can lead to long-term damage and complications, such as strictures, fistulas, and abscesses. Many people worldwide are struggling with IBD, and the management remains a challenge for medical professionals to address. A study from the University of Nottingham [5] reports that more than half a million individuals in the UK are affected by Crohn's Disease and Ulcerative Colitis, another significant IBD subtype. Unlike Ulcerative Colitis, which is limited to the colon and rectum, Crohn's disease can potentially develop lesions anywhere within the GI tract. Consequently, patients may experience diverse symptoms, including abdominal pain, diarrhoea, fatigue, and weight loss.

Although numerous research initiatives have been undertaken [6, 7], the precise aetiology of Crohn's disease remains elusive, rendering it incurable. However, fortunately, early diagnosis and appropriate treatment can alleviate patients' symptoms and substantially improve their quality of life. Various diagnostic methods are employed by clinicians, such as enteroclysis, endoscopy, colonoscopy, and radiographic techniques (including barium contrast X-rays, Computed Tomography (CT), and Magnetic Resonance Imaging (MRI)) to assist in the early diagnosis of the disease. MRI has become increasingly popular among radiographic techniques due to its non-invasive nature and enhanced imaging capabilities compared to CT. Nevertheless, manual MRI scan analysis remains a challenge since it is a time-consuming and labour-intensive process. Additionally, medical experts must examine each scan slice

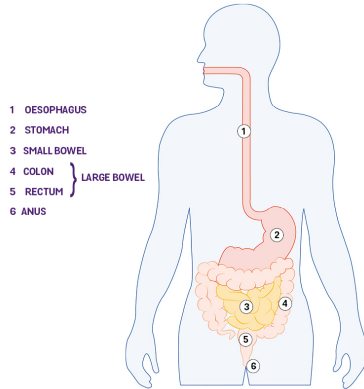


Figure 1.1: The gastrointestinal tract of a Human

by slice painstakingly.

1.2 Motivation

The advancement of Machine Learning and Deep Learning technologies, notably Convolutional Neural Networks (CNNs), offers powerful means for automatic feature extraction from input imaging data, thereby supporting medical professionals in diagnostic tasks. One crucial aspect of Crohn’s Disease diagnosis is the examination of the terminal ileum. Holland et al.’s study [8] in 2019 proposed a residual network specifically targeting the terminal ileum to facilitate automated detection of Crohn’s Disease using MRI scans. The authors claimed that the efficacy of their framework was contingent upon the degree of localisation during the preprocessing stage. Consequently, they advocated for incorporating terminal ileal ground-truth segmentations to enhance the localisation of the terminal ileum and improve the performance of automated detection techniques.

In a subsequent study, Abidi et al. [9] advanced this line of research by developing an innovative deep-learning tool based on the nnU-Net architecture [10]. This approach enabled the automatic localisation of critical regions, particularly the terminal ileum, essential for radiologists during diagnostic assessments. The researchers addressed the previously identified limitations regarding the high dependence on localisation during the preprocessing phase [8]. Furthermore, their findings established a solid foundation for a multi-class terminal ileum segmentation algorithm that combines transfer learning strategies with the nnU-Net architecture.

Inspired by the insights from [8, 9], this project aims to create a binary

segmentation model capable of accentuating terminal ileum regions more accurately by incorporating advanced transfer and semi-supervised learning methodologies. The successful accomplishment of this objective will significantly aid clinicians in diagnosing Crohn’s disease, ultimately contributing to enhanced patient outcomes.

1.3 Machine Learning Challenges

The efficacy of deep learning models is intrinsically linked to the training data’s quality, quantity, and diversity. One of the principal challenges faced in this project is the limited availability of training data. The dataset at our disposal is relatively small, comprising only 233 patient cases, which pales compared to those utilised in other industry-leading deep learning systems. Furthermore, since the region of interest (ROI) occupies a minor portion of the MRI scan, additional preprocessing techniques, such as localisation and cropping, must be considered for enhancing the segmentation model’s performance, as suggested by [9]. Another major challenge is the necessity for manual segmentation by clinical experts to develop gold-standard labels or point-wise centerlines for patient data, which is a complex, laborious, and inefficient endeavour. Consequently, acquiring high-quality and abundant patient data and gold-standard annotations poses significant challenges.

To mitigate these concerns, we propose a proxy training task employing weak supervision to generate coarse-grained segmentation masks as a compromise for the scarcity of gold-standard segmentations. Upon completion of the proxy task, gold-standard segmentations will be integrated into the training process to produce the final segmentation model. However, prior research [9] indicates that training from scratch using the nnU-Net framework for proxy tasks is inefficient due to long convergence times and unstable performance. Implementing transfer learning for proxy training [11] or incorporating a related pre-training job may serve as potential solutions to address these limitations.

1.4 Objectives

The primary goal of this project is to leverage deep learning methodologies, building upon previous research, to devise an advanced segmentation model for the terminal ileum, employing sophisticated transfer and semi-supervised learning strategies. The objectives of this project include:

- Implementing a nnU-Net-based baseline segmentation model, incorpo-

rating relevant data preprocessing techniques to ensure optimal performance.

- Generating coarse-grained weak masks for data lacking ground-truth annotations, based on prior work, to establish the proxy training task.
- Training the proxy model using weak masks and utilising the proxy model and fully annotated data to develop the target segmentation model.
- Enhancing the weak mask generation step by integrating the **SegmentAnything** Model [12] from Meta AI and training a refined model accordingly.
- Evaluating the performance of the developed models quantitatively by comparing the Dice Similarity Coefficient (DSC), training efficiency, and generalisation gap.

Chapter 2

Related Work

2.1 Automatic Detection and Segmentation of Crohn’s Disease Tissues from Abdominal MRI

The origins of applying deep learning techniques to medical image analysis can be traced back to approximately a decade ago. In 2013, Mahapara et al. [13] pioneered a machine learning-based method for segmenting bowel regions to detect Crohn’s disease tissues in MRI scans.

The proposed pipeline begins with the over-segmentation of the input MR image test volume into supervoxels. Sequentially, Random Forest (RF) classifiers are employed to identify supervoxels containing diseased tissues, subsequently defining the Volume of Interest (VOI). Within the VOI, voxels are further examined to segment the affected region. An additional set of RF classifiers is applied to the test volume to generate a probability map, which delineates the likelihood of each voxel being classified as diseased tissue, normal tissue, or background.

Empirical results demonstrate that this approach achieved satisfactory segmentation performance, as evidenced by a Dice metric value of 0.90 ± 0.04 and a Hausdorff distance of 7.3 ± 0.8 mm. The significance of this research lies in the development of an automated pipeline for segmenting diseased bowel sections in abdominal MR images. This pipeline assists medical experts in identifying affected tissues, thereby facilitating the diagnosis and treatment of Crohn’s Disease. The clinical validation of the results, showcasing high segmentation accuracy, further underscores its utility in supporting medical professionals in their work.

Nevertheless, the method is limited by computational inefficiency and

complexity due to extended testing times for each instance, fine-tuning requirements for each pipeline stage, and ample opportunities for architectural improvements. Moreover, the research does not delve into finer details, such as the terminal ileum, which is particularly crucial for comprehensive analysis and early diagnosis.

2.2 Automatic Detection of Bowel Disease with Residual Networks

Building on several years of research in the field, Holland et al. [8] put forth a pioneering approach in 2019 to automate the detection of Crohn’s disease from a limited dataset of MRI scans. The authors employed an end-to-end residual network [14], equipped by a soft attention layer [15]. This layer essentially magnified salient local features and added a layer of interpretability, providing a clearer understanding of the analytical process.

In a strategic departure from semantic segmentation strategies typically employed, their approach exclusively targets the terminal ileum. This focus served to underscore the potential feasibility of deep learning algorithms for the precise identification of terminal ileum Crohn’s Disease within abdominal MRI scans.

The method’s robustness is reflected in its experimental results. Under conditions of localized data within a semi-automatic setting, the model achieved a commendable weighted-f1 score of 0.83. This score is particularly noteworthy given its close correlation with the MaRIA [16] score, a clinical standard that enjoys widespread acceptance in the medical community. Beyond its performance metrics, the researchers accentuated the relative efficiency of their model, which necessitated only a fraction of the preparation and inference time compared to standard procedures. This aspect underlines the potential for significant time-saving benefits in a clinical context.

However, the research did reveal certain limitations. Notably, when applied in a fully automatic setting, the model’s performance exhibited a marginal decrease in efficiency. Although this does not detract from the overall achievements of the study, it does highlight an area where further refinement and improvement could be pursued.

Reiterating their discoveries, Holland et al. proposed a strong correlation between model performance and the degree of localisation in the training data. They suggested the collection of gold-standard segmentation of the terminal ileum could prove beneficial as an antecedent task in efforts to enhance automatic detection performance. This proposition opens up in-

triguing possibilities for research, including the work presented in this thesis, which explores these aspects in greater detail.

Their insights illuminate the synergistic potential between manual analysis and automated methods in enhancing diagnostic capabilities. Importantly, they establish a pathway for integrating deep learning techniques to detect Crohn’s disease from limited datasets, indicating a promising approach to tackle one of the significant challenges in machine learning: data scarcity. By leveraging soft attention mechanisms to intensify salient local features and augment interpretability, they provide a valuable tool for medical professionals to comprehend better the results generated by the algorithm.

These findings, particularly the proposed use of gold-standard segmentation of the terminal ileum, provide a solid foundation for the work pursued in this thesis.

2.3 Leveraging Machine Learning Methods for Accurate Prediction of Intestinal Damage in Crohn’s Disease Patients

In 2020, Enchakalody et al. [17] embarked on an innovative study exploring the potential of machine learning methodologies to enhance the precision and reliability of diagnosing and monitoring Crohn’s Disease. They applied these techniques to a small dataset of 207 CT-Enterography (CTE) scans, an approach that mirrors our own research focus. Their comprehensive analysis involved the intricate examination of cross-sectional views of small intestine segments and detailed detection of diseased tissues. Utilising two distinct classifier types - Random Forest (RF) with ensemble techniques and Convolutional Neural Network (CNN) algorithms, they quantitatively evaluated intestinal damage related to Crohn’s Disease on each mini-segments.

The efficacy of both RF and CNN techniques was compellingly demonstrated in the experimental results, achieving accuracy rates of 96.3% and 90.7%, respectively, for classifying diseased and normal segments. Remarkably, these techniques mirrored the effectiveness of expert radiologists in distinguishing between diseased and normal small bowel tissue. This underscores the immense potential of machine learning, even when applied to small datasets, in elevating the precision of Crohn’s Disease diagnoses.

The research conducted by Enchakalody et al. is particularly insightful for our work. It not only demonstrates the successful application of deep learning techniques on small datasets but also opens the door to potentially revolutionising the diagnosis and treatment of Crohn’s disease through ma-

chine learning. It highlights the possibility of a more precise and automated approach to detecting intestinal damage in such patients, a focus that aligns closely with our current research aims.

While it should be noted that this study primarily focused on data derived from CT-Enterography, differing slightly from our focus on MRI data, the methodology and findings offer valuable insights. As of the time of writing this report, despite the progress made, achieving a fully automatic approach for diagnosing Crohn’s disease based on cross-sectional imaging that equates to the proficiency of expert radiologists continues to be an exciting area of ongoing research.

Chapter 3

Background

3.1 Image Segmentation

When we talk about "Image Segmentation", what exactly are we talking about? Suppose we have a picture of two birds; the segmentation task, or more precisely the "**semantic segmentation**" task, is to separate the whole image into different regions with different colour codes, where the regions represent the exact position of birds covered on the image and the background.

3.1.1 More on Semantic Segmentation

The word "semantic" means we always assign a word label (a **semantic meaning**) to the segmented region, representing what this region refers to. For example, for the example we mentioned above, the regions we segmented for the bird will be assigned with the label "bird", and the background region will be labelled as "background".

Note. Semantic segmentation is different from the tasks based on "pure" clustering of images to coherent regions. The regions we are looking to have their value or semantic meaning from the task we defined.

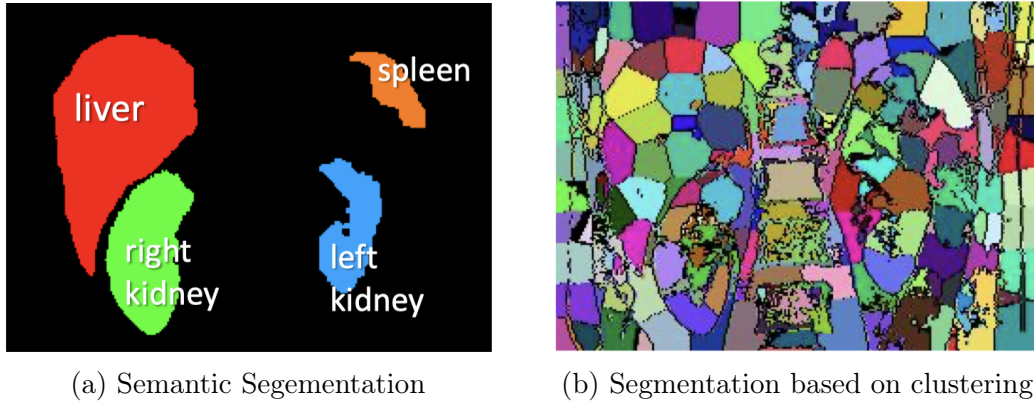


Figure 3.1: Different Image Segmentation Tasks

After getting a glance at **Semantic Segmentation**, we will discuss the methods for segmentation tasks in the following sections.

3.2 Manual Segmentation

Manual Segmentation must be the most straightforward method we can come up to our mind. It refers to a process that lets human experts as an observer make gold standard labels based on their background knowledge. It is clear to see that the segmented labels are confirmed to be validated. However, it might take a long time for human observers to create such labels due to the time cost of training and the amount of data required to be labelled.

Furthermore, inter or intra-observer variability may bring a concern to the validity of the labelled data by manual segmentation since there might be disagreement between different human observers and/or disagreement from one observer but on different occasions. Also, the bias from human experts might cause problems. We still need the assistance of computers to utilise intelligence for performing the segmentation task.

3.3 Threshold-based Methods

Thresholding is one of the simplest and most popular segmentation techniques used in the industry. This method is based on the assumption that intensity distribution has multiple modes. That is to say, the grayscale intensity of the pixels can be divided into two (or more) clusters, and we can pick thresholds from the "gaps" between the clusters to segment the background and foreground. The segmentation can be achieved by setting the

pixels with an intensity lower than the threshold background and those with an intensity equal to or greater than the threshold foreground. It is also accepted to select multiple thresholds to select pixels within a specific range only for segmentation.

The algorithm is simple and fast, yet the algorithm can only be applied when regions (of interest) are homogeneous and distinct. That is to say, the pixels in the same region should have similar intensity values. Also, finding consistent threshold frequencies across different images is different, since the intensity of pixels will vary from image to image.

3.4 Region-based Methods

The region-growing method is a typical region-based method. The algorithm is based on the assumption that the segmented regions are homogeneous. The algorithm starts with a seed pixel, and then it will grow the region by adding pixels similar to the seed pixel. The algorithm will stop when the region reaches a specific size or when the region is homogeneous, where interpreted as the neighbouring pixels are too dissimilar with each other in comparison [18].

Applying the region-growing method is usually very efficient, yielding a connected region from the seed point. Unlike thresholding, region-growing methods achieve segmentation without the explicit use of image properties. However, the region-growing method is not robust to noise since the algorithm will keep growing the region even if the neighbouring pixels are not similar to the seed pixel.

Another major issue that the region-growing method has is that the initial seed point selection is significant. If the seed point is not selected correctly, the algorithm will not be able to grow the region properly. Consequently, this initial step is time-consuming and inaccurate to find the optimal seed point, and it also requires human intervention to evaluate the choice of seed point.

To address this problem in medical imaging, Poonguzhali et al. proposed an automatic region growing method for ultrasound images [19]. They adopt an automatic seed point selection based on textural features such as co-occurrence features and run length features without human intervention. The experimental results showed the feasibility and effectiveness of the proposed region-growing algorithm in selecting seed points and segmenting the ROI without manual intervention.

3.5 Deep Learning Methods

U-Net [20] is a deep learning method for image segmentation. It is a fully convolutional network (FCN) [21] that uses a contracting path to capture image context and a symmetric expanding path that enables a precise level of localization. The network is trained end-to-end from raw pixels to pixel-wise segmentation masks. The network architecture is shown in Figure 3.2.

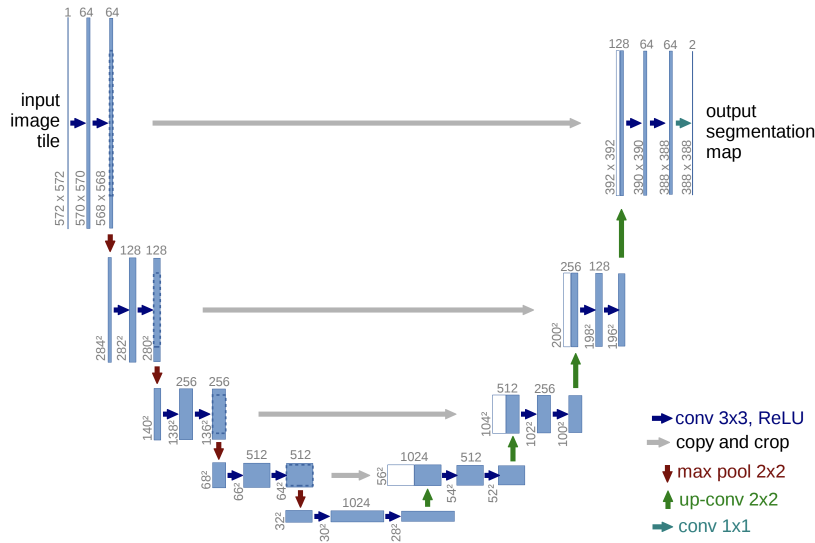


Figure 3.2: An example of the U-net architecture. Each blue box in the figure represents a multi-channel feature map, and on the top of each box indicates the number of channels. The x - y -size is shown at the lower left edge of the box. Each white box represents a copied feature maps. The arrows denote the different operations.

In the contracting path of the network (on the left), the network consists of a series of repeated applications. Each step starts with two 3x3 convolutions, and each convolution doubles the number of feature maps. Then the network applies a rectified linear unit (ReLU) as activation, followed by a downsampling step via a 2x2 max pooling operation with a stride of 2.

The expansive path (on the right) starts with an upsampling of the feature map followed by a 2x2 convolution, halving the number of feature channels. The feature maps are then concatenated with the corresponding crops of the contracting path. After that, two 3x3 convolutions are applied to the image, and a ReLU activation follows each convolution. The reason for cropping the

convolution results from the contraction path is the loss of border pixels in every convolution. At the final layer, the network used a 1x1 convolution to map each 64-component feature vector to the desired number of classes.

nnU-Net [10], a framework based on U-Nets, is a self-configuring segmentation framework that can automate the configuration of the preprocessing, network architecture, training, and post-processing of a segmentation pipeline. The selected configuration is depending on the medical data used for training. The framework provides a fully automated segmentation workflow that can be trained and inferred on any medical dataset.

For determining hyperparameters, nnU-Net uses "data-fingerprints" with heuristic rules to select the best hyperparameter configuration for a given dataset before processing the training data. The framework also uses data fingerprints to generate pipeline configurations including the inferred parameters (image resampling, normalisation, batch, and patch size), and the blueprint parameters (loss function, optimiser, architecture).

Combined with pre-selected hyperparameters and the pipeline configurations, the pipeline generates network training for 2D, 3D full-resolution, and 3D-Cascade U-Nets [22]. The optimal performance (e.g. average dice coefficient) is obtained by ensembling the configurations of the three networks. After that the optimal configuration will be deployed and evaluated on test dataset. The pipeline architecture is shown below.

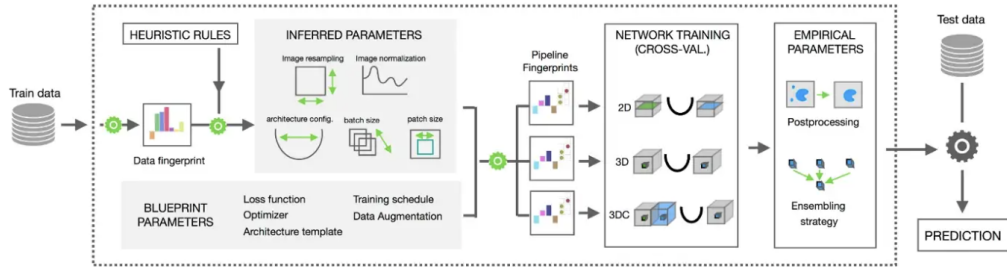


Figure 3.3: The pipeline representation of nn-UNet.

The nnU-Net has achieved the state-of-the-art performance on a variety of medical imaging tasks, including brain tumour segmentation, prostate segmentation, and liver segmentation [23].

Chapter 4

Dataset Analysis

Chapter 5

Methodology

Chapter 6

Evaluation

Chapter 7

Ethical Discussion

In this project, ethics were carefully considered. The project involves further processing of the previously collected medical data, including image registration and data augmentation, and merging of the existing datasets as well.

However, all MRI scans were processed and approved by clinical radiologists at St Mark Hospital. All sensitive personal data, such as names, genders, ages and ID numbers, were removed. Consequently, patients' identities can not be traced back from the medical data.

For the model-training procedure, since we are using the nnU-Net framework with convolutional layers involved, the model learns from data by extracting features. The model will not store original training data but create feature maps in this case. In other words, the training data cannot be recovered from the model, so personal data privacy is preserved.

Chapter 8

Conclusion

Chapter 9

Future Work

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