

**MENG INDIVIDUAL PROJECT**

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**Transfer Learning for Deep Learning  
Radiotherapy Planning**

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## Abstract

Radiotherapy planning involves outlining the macro and microscopic spreads of a cancer. Previously, bespoke models were trained on sufficient sample sizes of architectures that vary significantly in design to address distinct segmentation objectives. However, this makes models inaccessible to departments with limited datasets, increasing the barrier to experiencing the promised superiority beyond a model's specific use case.

We, therefore, analyse the effectiveness of transfer learning techniques in leveraging knowledge learned from one domain into another. Variants of transfer include zero-shot, few-shot and many-shot transfer learning. The evaluation of n-shot approaches of transfer learning onto the radiotherapy planning objective will clarify whether the transfer is a valid strategy for increasing performance over models learnt from scratch.

We represent three distinct model architectures for each type of transfer. We conclude that a many-shot transfer using TotalSegmentator remains a robust method for transferring knowledge. We find that few-shot transfer using UinverSeg does not apply to the complexity of 3-D volume delineations for cervical cancer. Finally, the finetuning of zero-shot models, represented by MedSAM, offers local bounded improvements on volume delineation independently of tumour localisation when compared to the baseline.

# Contents

<b>1</b>	<b>Introduction</b>	<b>2</b>
1.1	Technical Context . . . . .	2
1.2	Objective and Methodology . . . . .	3
1.3	Outline of Report . . . . .	3
<b>2</b>	<b>Motivation</b>	<b>4</b>
2.1	Clinical Context . . . . .	4
2.1.1	Cervical Cancer . . . . .	4
2.1.2	Radiotherapy Treatment . . . . .	4
2.1.3	CT modality . . . . .	5
2.1.4	Radiotherapy Planning . . . . .	6
2.1.5	International Guidelines . . . . .	6
2.1.6	Data Aquisition . . . . .	7
2.1.7	Delineation classes . . . . .	7
2.1.8	Rules . . . . .	8
2.1.9	Motivation in AI . . . . .	9
2.2	Machine learning for image segmentation . . . . .	9
2.2.1	Image Segmentation . . . . .	10
2.2.2	U-Net . . . . .	11
2.2.3	nnUNet . . . . .	12
2.2.4	TotalSegmentator . . . . .	13
2.2.5	UniverSeg . . . . .	13
2.2.6	SAM . . . . .	14
2.2.7	MedSAM . . . . .	14
2.3	Transfer Learning . . . . .	15
2.3.1	Mathematical Definition . . . . .	15
2.3.2	Shot based learning . . . . .	16
<b>3</b>	<b>Methodology</b>	<b>17</b>
3.1	Transfer Strategy . . . . .	17
3.2	Baseline – nnUNet . . . . .	18
3.2.1	Preprocessing . . . . .	18

3.2.2 Separate Training . . . . .	18
3.3 Many-shot Transfer – TotalSegmentator . . . . .	18
3.3.1 Separate Training . . . . .	19
3.3.2 Region Based Training . . . . .	19
3.4 Few-shot Transfer – UniverSeg . . . . .	21
3.4.1 Preprocessing . . . . .	21
3.4.2 Automated Support Set Sampling . . . . .	21
3.4.3 Supervised Support Set Sampling . . . . .	22
3.5 Zero-shot Transfer – MedSAM . . . . .	23
3.5.1 Preprocessing . . . . .	23
3.5.2 Point based transfer . . . . .	23
3.5.3 Box based transfer . . . . .	24
3.5.4 Evaluation . . . . .	25
3.6 Quantitative Evaluation of Segmentation . . . . .	25
3.6.1 Classification Based . . . . .	25
3.6.2 Spatial Overlap Based . . . . .	26
3.6.3 Surface Based . . . . .	26
3.6.4 Volume Based . . . . .	27
3.6.5 Evaluation . . . . .	27
3.6.6 Estimated Editing Based . . . . .	27
3.6.7 Summary . . . . .	28
<b>4 Results and Discussion</b>	<b>29</b>
4.1 Many-shot Transfer – TotalSegmentator . . . . .	29
4.1.1 Separate Training . . . . .	29
4.1.2 Region-based Training . . . . .	29
4.1.3 Rule enforced Region-based Training . . . . .	29
4.2 Few-shot Transfer – UniverSeg . . . . .	29
4.2.1 Automated Support Set Sampling . . . . .	29
4.2.2 Supervised Support Set Sampling . . . . .	31
4.3 Zero-shot Transfer – MedSAM . . . . .	32
4.3.1 Training Bottlenecks . . . . .	32
4.3.2 MedSAM’s claim to zero-shot transferability . . . . .	32
4.3.3 The performance of a transferred MedSAM model . . . . .	33
<b>5 Conclusion</b>	<b>34</b>
<b>6 Ethics</b>	<b>35</b>
6.1 Patient disclosures . . . . .	35
6.2 Using the tool . . . . .	35

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<b>A Appendix</b>	<b>37</b>
A.1 Ground Truth Organ Delineations . . . . .	37
A.1.1 Organs At Risk . . . . .	37
A.1.2 CTV volumes . . . . .	38
A.1.3 Parametrium, Uteurs, and Vagina . . . . .	38
A.2 Metrics . . . . .	40
A.2.1 Total Segmentator . . . . .	40
A.2.2 Region Based . . . . .	46
A.2.3 UniverSeg Metrics . . . . .	50
A.2.4 MedSAM Box Prompt Metrics . . . . .	56
<b>Bibliography</b>	<b>62</b>

# Chapter 1

## Introduction

### 1.1 Technical Context

Transfer Learning is a technique in which a model trained on one task is repurposed and fine-tuned on a second task. Thus, the model can leverage the knowledge gained from the first task to improve performance on the second task. An accrual of literature across PubMed in 2023-2024 was conducted with a search string displayed in Figure 1.1, which found a gap in technical research surrounding Transfer Learning in the radiotherapy planning domain.

```
"radiotherapy" AND "contour" AND ("cervix" OR "cervical") AND "cancer" AND ("Deep Learning" OR "  
    ↪ DeepLearning" OR "Machine Learning" OR "ML" OR "Artificial Intelligence" OR "AI" OR "  
    ↪ Computer assisted")
```

**Figure 1.1:** Search string used in PubMed accrual in 2023-2024

The conclusion of the accrual confirmed that the most common network structure for radiotherapy planning was the U-Net architecture [1, 2, 3, 4, 5, 6]. However, each segmentation benchmark required modifications such as specialized architectures or bespoke training schemes to achieve competitive performance. These tailored modifications contribute little to the overall development in medical segmentation [7], as it becomes increasingly challenging for researchers to identify methods that live up to their promised superiority beyond the limited scenarios they are demonstrated on [8].

The publications from the accrual also reveal that the bespoke trained model assumes a sufficient sample size, representing the entire population of all individuals under the same circumstances. However, the underrepresented users of these models cannot apply this assumption; most hospital teams work in a specialized medical field with only in-house patients who follow specific hospital guidelines. A simple plug-and-play approach is unsuitable in this scenario because segmentation guidelines often differ between facilities. Therefore, specific recalibration is necessary to effectively use these models because incorrect or inaccurate contours are the primary factors contributing to treatment failures in radiotherapy [5].

We therefore analyse the effectiveness of Transfer Learning in radiotherapy planning. The Transfer Learning approach aims to leverage other trained models with great performance and lift low-level features for the target domain. A PubMed search for publications mentioning transfer learning in the radiotherapy planning field returned no relevant matches. Therefore, research on transfer in the medical domain will also fill the literature gap, which has yet to consider solving the auto-contouring problem for radiotherapy planning volumes.

## 1.2 Objective and Methodology

Firstly, we select a dataset from The Royal Marsden Hospital, which will act as the pillar for advocating the success and use of transfer learning in radiotherapy planning. The real-world clinical dataset provides segmentations for key anatomies and tumours that aid in radiotherapy planning for females with cervical cancer. It has yet to gain exposure to the widespread segmentation challenges and has uncommon and limited segmentation patterns specified by internal team-wide guidelines.

Secondly, we analyse the effectiveness of Transfer learning in radiotherapy planning. To research the application of this technique in the medical context, we study three types of modern training approaches to study their transferability. These types are zero-shot, few-shot, and many-shot learning transfers.

## 1.3 Outline of Report

The report will first discuss the relevant background knowledge required for this project in Chapter 2. Within, we provide a high-level overview of anatomies and the clinical context (Section 2.1) as well as core existing academic knowledge in the Computer-assisted vision in the Medical Imaging field (Section 2.2-3.6).

Then, Chapter 3 describes the experiments used to evaluate how well different architectures transfer knowledge into the target domain, as well as an overview of the results (Chapter 4) and a discussion of their implications (Chapter 4). Finally, we discuss the conclusion and future work in Chapter 5.

# Chapter 2

## Motivation

### 2.1 Clinical Context

This project will have its foundation for experimentation in a dataset provided by the Royal Marsden Hospital [9]. The real-world clinical dataset segments key anatomies and tumours that aid in radiotherapy planning for females with cervical cancer. It has yet to gain exposure to the public eye and has uncommon and limited segmentation patterns. This dataset will act as the pillar for justifying the success of the transferability of knowledge between medical domains.

In this section, we discuss the clinical context behind cervical cancer in the population, the Hospital's pipeline for segmenting patients in preparation for radiotherapy treatment, and the Hospital's motivation for recruiting an AI tool to assist in its treatment pipeline.

#### 2.1.1 Cervical Cancer

Cancer is a burden around the globe that has been a driver for almost one-sixth of the world's mortality in 2022 [10]. In females, cervical cancer makes up 25 countries' leading causes of cancer death, following breast cancer for 157 countries in 2022 [10]. Furthermore, an estimated 1 million maternal orphans who lose their mothers to cancer suffer long-term disadvantages in health and education [11]. Thankfully, cancer screening services provided by hospitals around Europe have been shown to decrease incidence and mortality rates of cervical cancer in women over the recent years [10]. Paired with quality improvements offered by medical imaging models, this forms the motivation for total control over cervical cancer.

#### 2.1.2 Radiotherapy Treatment

A mechanism available for cancer treatment involves radiation therapy. High beams of radiation energy are tuned to hone in to target cancerous cells in a clinically defined 'target area'. The cells killed by the energy experience interphase or proliferative death depending on the cell cycle stage. Death occurs when the damage to genetic material within the cell prevents it from dividing, or the cell's accumulation of genetic aberrations leads to a "mitotic catastrophe" [12]. In Europe, such radiotherapy treatment was used on average for 70% of cases, with a curative rate of 40% [13, 14].

This death is characteristic of any cell subjected to high energy beams, placing much responsibility on the oncologist to deliver an accurate treatment area so that healthy cells are unaffected; any adverse alteration of an organ's standard functionality may cause grave implications for the already compromised patient. Therefore, the precise and complex nature of the task is estimated to take oncologists 90–120 mins to delineate target areas for radiotherapy [4].

This time-consuming endeavour is never favourable for a patient already in a dangerous situation; for mid-low-income countries, where this may not be an available resource, this leaves them with a death rate 18 times that of a higher-income country [15].

### 2.1.3 CT modality

High-resolution and high-contrast computed tomography (CT) machines have further benefited cancer treatment due to their noninvasive nature and ability to view patients' internal organs. X-ray devices rotate around a specified body part, and computer-generated cross-sectional images are produced [16]. Whilst the scanner rotates, the patient's table slowly moves up and down inside the tube to produce different cross-section images. The images show damaged and surrounding soft tissue, allowing physicians to propose clinical target volumes more accurately.

#### Hounsfield Units



(a) Muscle Window (35, 55) [17] (b) Bone Window (300, 400) [18] (c) Fat Window (-120, -90) [17]

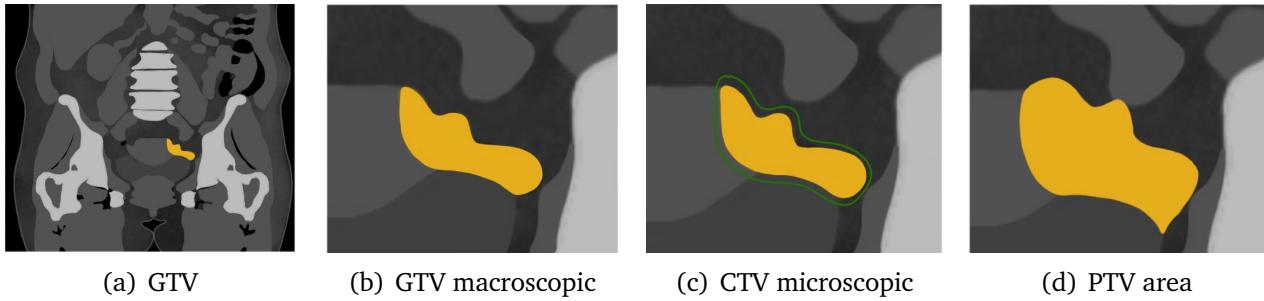
**Figure 2.1:** Coronal view the same image slice of a CT image, with different window cropping (Patient id: 49, slice 251). White (radiopaque) areas represent high-density tissues, and black (radiolucent) areas represent low-density tissues within the window range.

The operator or physician decides the granularity or image slice thickness, which ranges from 1mm to 10mm. Therefore, the precision along each axis creates a cube, or voxel, representing the value on a grid in three-dimensional space. The voxel values are measured in Hounsfield Units (HU) [19].

Contrary to natural images, where pixel values vary from 0 to 255 in 3 channels representing Red, Blue and Green, the Hounsfield scale is a quantitative scale describing radiodensity. The image intensity reflects tissue type; each voxel intensity refers to a specific tissue composition. The positive values (white) result from more dense tissue with greater X-ray beam absorption, and negative values (black) are less dense tissue with less X-ray beam absorption [20].

Therefore, because the HU scale is relative, different windows may be taken for a CT scan to highlight different tissues. Those voxels within the window will likely be tissues of a specific classification. For example, as shown in Figure 2.1, we display three such windows: muscle, cancellous bone and fat.

### 2.1.4 Radiotherapy Planning



**Figure 2.2:** Simplified representation of the clinical target volumes. Figure 2.2(b) shows the visible tumor, Figure 2.2(c) shows microscopic spread of the tumor, Figure 2.2(d) shows area to account for short-term organ misalignment.

oncologists use CT scans to draw clinical volumes by combining their knowledge about the particular cancer to determine target structures, organs-at-risk structures, and areas where the cancer will likely spread to [9]. We provide a simplified representation in Figure 2.2.

The first area is the macroscopic delineated area of the visible tumour area. This Gross Target Volume (GTV) has a high probability of containing the tumour. Secondly, the Clinical Target Volume (CTV) is derived to account for potential microscopic spread. The CTV will be an area at least as big as the GTV with an optional margin surrounding it containing a 'rind' of non-zero probability of tumour spread. Lastly, the Primary Target Volume (PTV) contains residual geometric uncertainties and safety margins surrounding the CTV, ensuring the radiotherapy dose gets delivered to the CTV [21, 22, 2, 23]. The PTV is a necessary extension of the CTV since geometric uncertainties are impossible and not advised to eliminate; after all, static scans are only estimations, subject to short-term organ misalignment, relative movement between structures of reference and tumours, partial volume effects and skewed anisotropic resolution [24].

In parallel, the oncologist constantly considers critical healthy tissue structures that need to be preserved during irradiation. These are referred to as organs-at-risk (ORs). In some specific circumstances, adding a margin analogous to the PTV margin around an OR is necessary to ensure that the organ cannot receive a higher-than-safe dose; this gives a planning OR volume [22].

### 2.1.5 International Guidelines

The final volumes have no internationally agreed-upon guidelines, which leaves it up to the interpretation of the oncologists and Hospitals to use their heuristics when drawing areas. This time-consuming process has high variability, causing it to suffer significantly from inter and intra-observer variability [2].

## 2.1.6 Data Aquisition

The Royal Marsden Hospital provides the dataset as a set of ‘Neuroimaging Informatics Technology Initiative’ files (NIfTI) [16]. It is a lightweight alternative to other formats such as Digital Imaging and Communications in Medicine (DICOM) [16] and eliminates ambiguity from spatial orientation information [25]. Libraries exist for handling these files, such as SimpleITK [26], which we use to read and manipulate the data in this project.

The training data provides 100 female patients that have been diagnosed with similar types of cervical cancer. Each patient comes with seven relevant segmentation classes which contribute to radiotherapy planning for cervical cancer. For reproducibility, all delineated anatomies were labelled consistently by the oncologists to improve chances that an AI model can learn cervical cancer patterns [9].

## 2.1.7 Delineation classes

The clinicians at the Royal Marsden Hospital have provided segmentation labels for seven high-priority regions of interest (ROI). These are the anorectum, bladder, CTVn, CTVp, parametrium, uterus, and vagina. The function of these anatomies is irrelevant to this project and is left to the reader to research further.

### Organs At Risk

An organ at risk is an organ that, despite being healthy, is substantially likely to be within the PTV. Any areas created around the area should actively avoid these organs because overlapping with them risks complicating treatment and compromising the health of functioning organs. The key supplied anatomies at risk are the Anorectum (Figure A.1(a)-A.1(c)) and the Bladder (Figure A.1(d)-A.1(f)).

### CTVp

The CTVp stands for the Primary Clinical Target Volume; see the example at Figure A.2. This is an area comprised from areas where there may be local microscopic spread (uterus, cervix, upper vagina, primary tumour) [9].

### CTVn

The CTVn stands for Nodal Clinical Target Volume; see the example at Figure A.3. This CTV surrounds areas that may contain microscopic spread to lymph nodes. It is drawn based on set margins around pelvic blood vessels and includes pelvic lymph nodes, common iliac lymph nodes and para-aortic lymph nodes [9].

Similarly to CTVp, this is a compound area with three groups of lymph nodes. However, in contrast to the CTVp, in clinical practice the area is drawn depending on the development of the disease.

### Parametrium, Vagina, and Uterus

The Parametrium (or Paravagina) is the tissue surrounding the cervix/vagina at risk of local spread; see Figure A.4. The Parametrium is drawn as a complete structure and edited back to the level of the vagina to be included [9].

Finally, the clinical significance of the Vagina and Uterus is to help define encapsulating structures like the CTVn (see Section 2.1.8). Example for the Uterus and Vagina structures can be seen at Figure A.5(a)- A.1(c) and Figure A.5(d)- A.5(f) respectively.

#### 2.1.8 Rules

The top seven priority structures have been selected to identify and plan an area where radiotherapy should be used. With these structures, there are rules that the clinicians have outlined that affect the final segmentation. They are quoted below. Note, the structures do not refer to more than one patient in one rule.

Let us represent each organ anatomy as the first letter of its name, specifically: (A)norectum, (B)ladder, (C)ervix, (P)arametrium, (U)terus, (V)agina. Further, define:

1. The CTVn and CTVp as  $C_n$  and  $C_p$  respectively
2. The GTVn and GTVp as  $G_n$  and  $G_p$  respectively
3. The Pelvic, Common and Para-aortic Lymph Node as  $L_p$ ,  $L_c$ , and  $L_{pa}$  respectively

#### Relationship between Structures

1. Let the overlap of two structures be denoted by the set intersect symbol  $\cap$ .
2. Let the joint area of two structures be denoted by the set union symbol  $\cup$ .
1. There should be no overlap between the CTVn, CTVp or Anorectum.

$$\forall i, j \in \{C_n, C_p, A\} \text{ with } i \neq j, i \cap j = \emptyset \quad (2.1)$$

2. The Parametrium may overlap with all of the other structures.

$$\forall i \in S, \quad (P \cap S \neq \emptyset) \vee (P \cap S = \emptyset), \quad \text{where } S = \{A, B, C, C_n, C_p, U, V\} \quad (2.2)$$

3. The Bladder may overlap with the CTVn.

$$B \cap C_n \neq \emptyset \vee B \cap C_n = \emptyset \quad (2.3)$$

4. The CTVp is defined as a compound structure containing:

$$C_p = \overbrace{C \cup G_p}^{\text{High Risk CTV}} \cup U \cup V \quad (2.4)$$

However, since we are never explicitly provided with the segmentation maps for the Cervix  $C$  and the GTVp  $G_p$ , we cannot use as strong of a definition as above. Instead,

we operate on the assumption that the union of the Uterus and Vagina is at least as big as the CTVp.

$$U \cup V \subseteq C_p \quad (2.5)$$

5. The CTVn is defined as a compound structure containing:

$$C_n = G_n \cup L_i \cup L_p \cup L_{pa} \quad (2.6)$$

Similarly, we are not provided segmentations for these areas, therefore, operating under no clinical knowledge apart from the provided, cannot make any claims as to the composition of the CTVn.

### 2.1.9 Motivation in AI

The medical sector has been a hotbed for AI research since Convolutional Neural Networks (Section 2.2.1) have been applied on medical image data by researchers. A branch of research dedicated itself to segmentation, which involves labelling individual pixels in the image according to which object or class they belong to. In dense classification, a model assigns every pixel to a specific class. Relevant to the direction of this project is determining the precise location and extent of organs or certain types of tissue, like ORs, CTV volumes, or other anatomies.

The key objective of models trained for delineating target structures for this project is to see if an AI model can learn cervical cancer CTV pattern detection. The decision is complex as clinicians use information beyond the CT-imaging modality, such as how far along the tumour has progressed, and other clinical intuition to make proper judgements about the CTV volumes. Therefore, with this information missing from AI models, it is likely to misjudge target volumes, and a clinician will have to select which components of the CTV are required. However, a clinician will benefit from the time saved and improved consistency with the planning process if a trained model can produce the substructures required within the CTV that a clinician can review [9].

## 2.2 Machine learning for image segmentation

Before the popularization of machine learning, algorithms used to be defined by strict and convoluted rules. These heuristically defined algorithms struggled to scale to complex problems and were often complicated or confusing to maintain. The typical task, however, does not warp easily into human intuition.

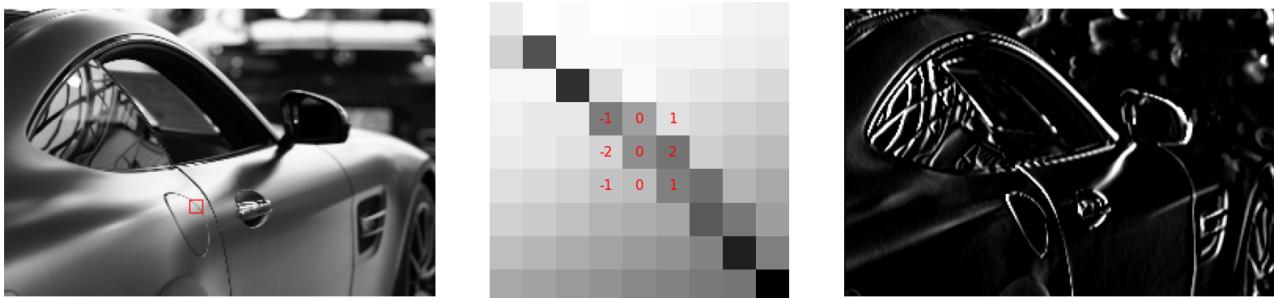
As a consequence of poor scalability, a new genre of algorithms began to emerge that fell into the classification of neural network models. Observations were rephrased and morphed into vectorised inputs, where each constituent of the vector represented a particular feature of the observation. For instance, the California Housing dataset [27] contains an input of 9 features (longitude, latitude, number of bathrooms, ...) and one target feature (house price). After pre-processing and strategising, this input would be vectorised and fed into a network with several layers. Within each layer, sets of tunable parameters would optionally change the number of features and learn a relationship between parameters using weights until the  $1 \times 9$  vector finally translates into a scalar value indicating the house price. After

many repetitions of learning from examples, the model would learn an approximation to the complex objective. These models were termed Multi-Layered Perceptrons (MLPs).

### 2.2.1 Image Segmentation

The current machine learning approach didn't work well with image data. Up until that point, rich structures such as images were neglected, and matrices of gray-scale images were mutilated into flat vectors. This approach was necessary to feed the flattened image representation through the MLP. The issue with vectorising an image is that it loses its spatial context-driven awareness.

At the same time, J. Hull, sponsored by the United States Postal Service, published a Database for Handwritten Text Recognition with the incentive of providing an extensive dataset of images of characters of variable writing mediums, isolation, overlap, and neatness to aid research efforts in developing accurate digit classification algorithms [28]. Yann LeCunn et al. [29] used this database to propose the first Convolutional Neural Network (CNN) for image processing, which preserved the input in its 2D glory by applying convolutions. The fundamental Convolutional Filter is displayed in Figure 2.3.

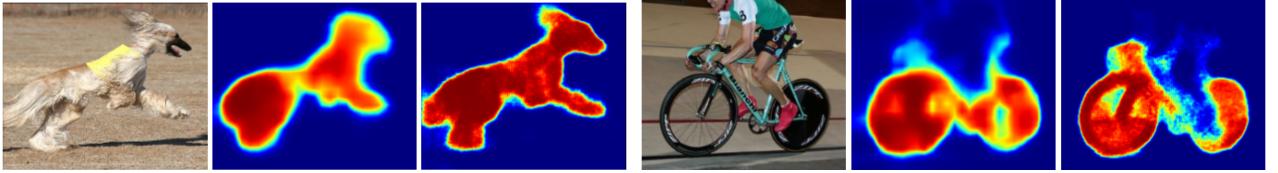


**Figure 2.3:** Example application of a convolution. From left to right, the input image with a region outlined in a red box, the boxed region magnified with a convolutional (Sobel) filter being applied to a part of the magnified region, and lastly the output after the filter has passed over the entire image. The output represents a new feature map encoding features of the original (input) feature.

Convolutional layers are rectangular blocks that are recipes for translating an image (alternatively known as the input feature). The algorithm centres the block over a specific pixel and uses a square radius of neighbouring pixels. It multiplies and sums the pixels along the corresponding pixel positions according to the recipe to produce a transformed resulting pixel that encodes the reference pixel's information and the surrounding receptive field around it. Figure 2.3 demonstrates this concept. Specifically the middle tile, which shows an example  $3 \times 3$  convolutional filter being applied to a zoomed in part of the image. This filter slides across the entire image and encodes it which produces the output on the right of Figure 2.3.

The CNN operates by having multiple learnable convolutional filters stacked on top of each other. The values within the square convolutional filter are *learned* during training; the values learnt are those that, in combination with the layers before and after, encode the image's features according to the training objective the best. When stacked with many other convolutional filters that piggyback off the encoded features produced by filters before it, this allows for dense feature representations that encode the entire image.

This first convolutional network spawned a vicious flurry of convolutional architectures, which followed in their footsteps. The Fully Connected Neural Network (FCN) adapted the



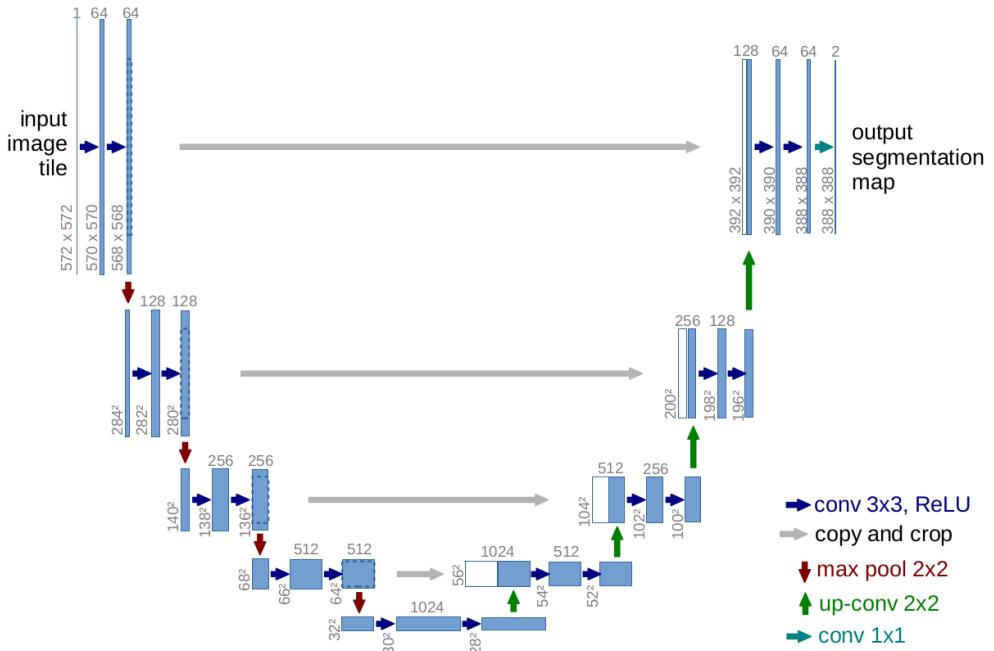
**Figure 2.4:** Comparison of upsampling a base image using FCN [30] and the VGG-16-based DeconvNet [31, 32] architectures.

architecture used by LeCunn et al. [29] for segmentation applications. Previously, convolutions would reduce input image feature vectors into non-spatial classification outputs. However, this paper ‘convolutionalized’ the pipeline to provide a heatmap of segmented objects within the image [30]. The heatmap would describe in a 2D feature the location of each class.

Trivial upsampling through de-convolutional layers allows the heatmap to translate back to the original size. This process would produce a largely inaccurate segmentation with much room for improvement. Therefore, similarly to learning the downsampling, the model learnt to upsample low-level heatmap representations [31]. This way, the deconvolutional network also became “a key component for precise object segmentation”, which improved the base upsampling provided by the FCN. This conclusion is shown in Figure 2.4.

The strategy of downsampling and upsampling for image segmentation is a common theme amongst many segmentation architectures.

## 2.2.2 U-Net



**Figure 2.5:** The U-Net architecture, with contractive side on the left, and expansive side on the right. The feature map follows the arrows and multiplies the number of feature maps twice at each contraction, and halves at each expansion [33].

Simultaneously, a unique architecture was under development. This architecture mirrored the hourglass structure of contracting and upsampling sections of the FCN, only this time, the illustration of its architecture led to its name, the U-Net [33].

The U-Net similarly consists of a contractive and expansive side, with the added feature of so-called ‘skip-connections’. As shown in Figure 2.5, at each stage of the contracting/expansive side, these copy operations help localise high-resolution features from the contracting path [33]. The network yielded great results for a few training images and more precise segmentations.

The U-Net was now very close to being a staple choice in biomedical data for anatomy segmentation. A limitation of its current implementation is that slices along the third dimension would most certainly contain contextual information that would influence the decision of the current design. Therefore, an identical network topology with extended 3D convolutions was proposed by Çiçek et al. [34].

### 2.2.3 nnUNet

The nnUNet is closely related to the U-Net architecture. However, nnUNet’s ability to adapt to the data improves this model performance over the vanilla implementation.

Until now, architectures have operated on data pre-processed to a particular expected distribution and configured to deal with a specific problem. For instance, out-of-the-box configuration has stringent input size requirements, which require image resizing. Furthermore, 3D images commonly produce heterogeneous voxel spacing depending on the parameters chosen by the clinician or the machine from which they were produced [8]. The number of moving parts often leaves a unidirectional dependency on the data depending on the architecture.

#### Automated Method Configuration

Therefore, the nnUNet analyses the fingerprint of the dataset and the device to deliver a tailored experience and force a more codependent relationship; now, the architecture depends on the data and the data is pre-processed to conform to the network [8]. Furthermore, hardware restrictions mean networks may be inaccessible to those with worse specifications or, at the other end of the spectrum, may underutilize powerful computation still available [8]; the nnUNet analyses GPU constraints used to influence batch sizes and more [35].

The automated method configuration is classified into three categories. A dataset fingerprint extracts training data distributions such as shape, spacing and intensity distributions. Rule-based parameters estimate the most common robust parameters for resampling and normalization. Finally, the Empirical Parameters learn parameters, such as ensemble selection, which is not derivable from the dataset fingerprint.

#### Critical Review of the nnUNet

A review of segmentation methods in 2024 reviewed some further developments in segmentation models and found that the convolution-based U-Net architectures continued to outperform Attention-based or Mamba-based approaches six years after the initial publication of the self-configuring network [7]. Isensee et al. concluded that there was a significant mischaracterisation of proclaimed improvements in new strategies such as transformers. Claims of performance improvements over the nnUNet were reviewed through the control of valida-

tion datasets and removals of baseline tampering, which demonstrated the convolution-based performance on datasets with low statistical intra-method standard deviation [7].

The continued performance dominance gives the nnUNet a good foundation for being used as a baseline model for all datasets.

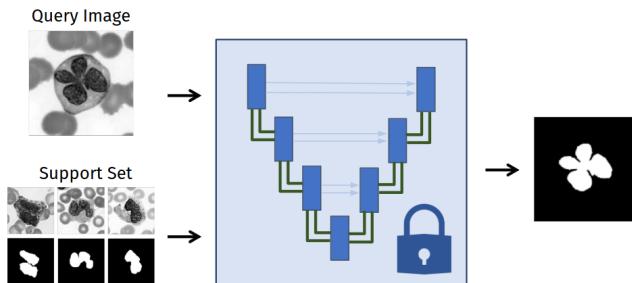
### 2.2.4 TotalSegmentator

TotalSegmentator is a tool based around the nnUNet. TotalSegmentator is pre-trained on 1204 CT examinations to provide plans to segment 104 anatomical structures. The anatomies selected included apparent structures such as skeletal structures, gastrointestinal organs and other major organs. The training data contained many CT images, with differences in slice thickness, resolution, and contrast phase [36]. However, it is important to note that 60% of the scans occurred in a contrast-enhanced environment, which plays a role in how obvious delineations are during scanning, a scanning detail that was omitted during the training data collection for this research project. Furthermore, only an estimated 10% of the data collected from this model contained relevant studies for the abdomen and pelvic areas.

From the segmented organs that total segmentator provides, only the Bladder overlapped with the organs that were of interest in this study.

### 2.2.5 UniverSeg

Convolutional architectures like those discussed above utilize many-shot learning (Section 2.3.2). However, models trained on segmenting a target domain (e.g., bone delineation) do not transfer to other domains (e.g., organ segmentation) without fine-tuning.

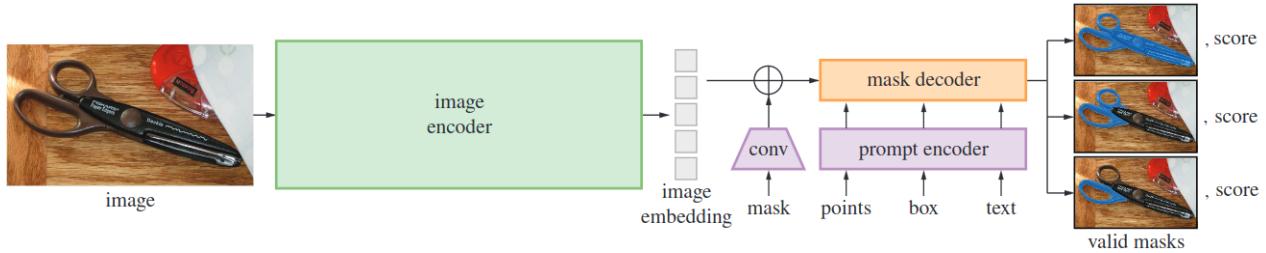


**Figure 2.6:** The UniverSeg architecture [37]. Diagram illustrates the freezing of model parameters while providing a support set of images which follows the query image through the segmentation pipeline.

Butoi et al. present UniverSeg, a model that breaks away from the traditional approach; instead of training a model on a single task (e.g. bone delineation) and freezing parameters during inference, this architecture uses a support set of images to provide a practical few-shot approach to inferring segmentations from input images. Figure 2.6 shows an example of this efficient querying, which manifests itself in a U-Net architecture where the support set passes through the network along the query to influence the final segmentation. This way, Butoi et al. attempt to provide segmentation on a target image based on examples of other samples with the same anatomy contoured in a selection of other images. Therefore, the model can learn to segment both bone and organ segmentation tasks without the need for fine-tuning [37].

This model operates on 2D slices of images and directly avoids the finetuning argument for medical imaging. They argue that finetuning can be unhelpful due to the differences between medical domains, features, and data fingerprints. As such, UniverSeg avoids significant retaining for each subtask.

### 2.2.6 SAM

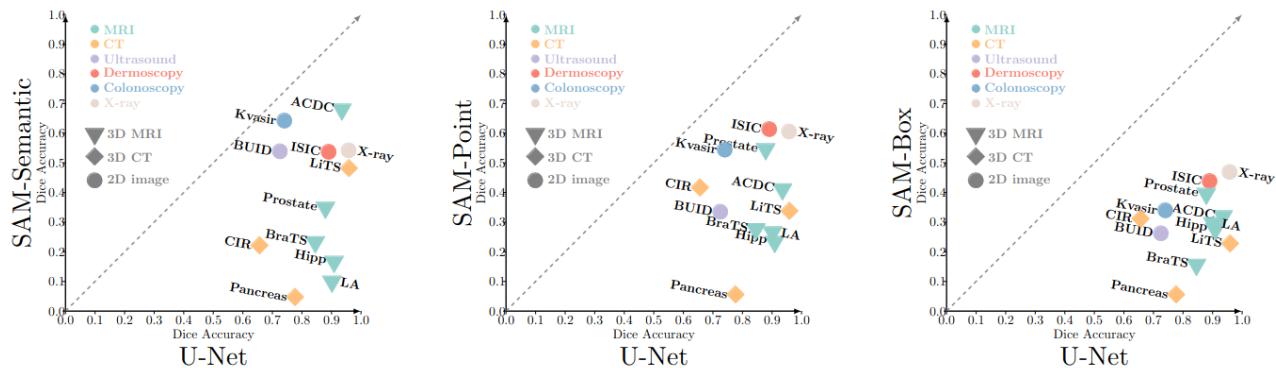


**Figure 2.7:** The SAM model involves a transformer architecture that embeds points and bounding boxes into a promptable encoding, which is used in tandem with the image encoding to produce the most likely segmentation of the described area [38].

Advances in NLP, with attention-based mechanisms, have questioned whether convolutional-based methods like those above are the best approach for segmentation. Transformers from NLP were adapted to form the Vision Transformer (ViT) [39]. This model views the image as a grid of tokens; in the original paper, Dosovitskiy et al. separate the image into a grid of patches and read in these grid cells as individual tokens. The tokens pass through the attention mechanism as with NLP and into a classification mechanism [39].

The SAM (Segment Anything Model) model implemented a modification of the transformer architecture [38] as seen in Figure 2.7. However, the task was reformulated as a promotable segmentation problem to allow for zero-shot generalisation (the model can generalise to unseen examples with no re-training or fine-tuning). As seen in Figure 2.7, the model inputs an image along with either points in the image or boxes. This reduces the search space SAM has to perform to segment an object into an area or a set of points.

### 2.2.7 MedSAM



**Figure 2.8:** Performance of a SAM model across a reference nnUNet baseline when applied to different datasets. The evaluation was considered for semantic, point and box prompts. [40].

SAM trains its network on a collection of natural images, not medical images such as CT and MRI scans. Extensive stress tests performed on SAM concluded that SAM’s out-of-the-box promotable segmentation tool had good baseline performance on large visible objects [41] but required exact prompt segmentation, making it inaccessible to automated contouring. Regarding the number of points required to make a sensible prediction, SAM quantitatively underperformed a nnUNet baseline, with qualitative evaluation showing fuzzy boundaries in medical contexts [42]. Finally, Figure 2.8 shows the performance of SAM against an nnUNet baseline across a set of datasets and imaging modalities [40] which concludes that SAM never outperformed the nnUNet baseline when trained on the 11M natural images [38].

Therefore, Ma et al. enhanced the architecture provided by SAM by training it on a dataset of nearly 500k CT scan test examples to train a model for medical images, named MedSAM [43]. Ma et al. decided to keep close to its original despite medical images being 3-dimensional in CT and MRI scans because of “enhanced flexibility and adaptability” where slices along an axis substitute 3D scans [43]. This model demonstrates an improvement over SAM, nnUNet, and Deepmedic models when MedSAM bounding boxes extracted from the ground truth prompt the model [43].

## 2.3 Transfer Learning

Transfer Learning involves using a model trained on a large dataset. The pre-trained model serves as the starting point for a second task where data acquisition is limited or improbable. Transfer learning is successful because, in the early layers of a model, it typically learns very low-level features. At this scale, the objective of the original domain does not matter; regardless of the initialisation, a model working on a similar problem will inevitably learn similar low-level features.

Arguably, the universality of the parameters learnt in a model with prosperous access to data will have richer and better patterns than another with less data did not have enough information to learn [44, 45].

Transfer Learning has the potential to improve initial performance using only the transferred knowledge before any further learning begins, improve the time it takes to thoroughly learn the target task given the transferred knowledge, and improve the final performance all when compared to initial benchmarks without transfer [46]. Medical contexts have already applied Transfer Learning, which reportedly improved weight initialisation for 332 abdominal liver CT scans and resulted in faster convergence, providing a more robust representation [47].

Transfer Learning has been seen to prevent overfitting in domains where data volume is low and where generality without overfitting is hard to come by. The prevention is because the model has already learnt features likely to be helpful in the second task [48]. Overfitting may still occur if the model is fine-tuned too much on the second task, as it may ‘learn task-specific features that do not generalise well to new data’ [48].

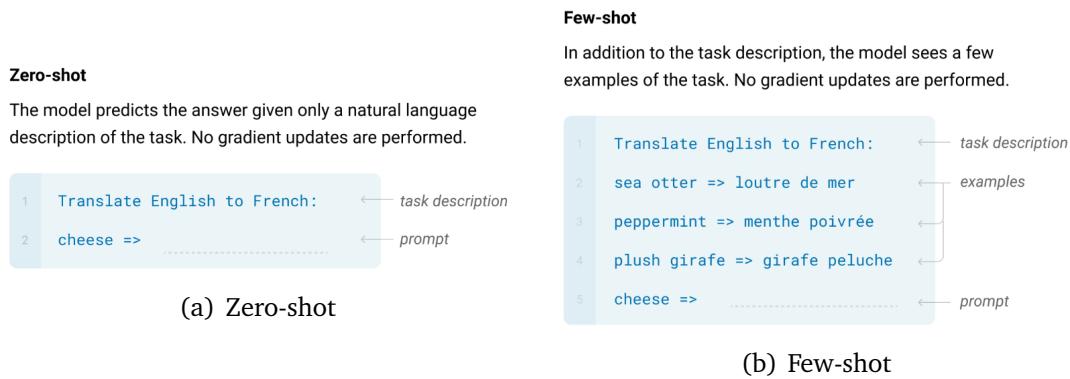
### 2.3.1 Mathematical Definition

Transfer Learning can be formalised mathematically [45, 49].

- Define the starting domain the model trains on initially as  $\mathcal{D} = \{\mathcal{X}, P(X)\}$  with feature space  $\mathcal{X}$  and a marginal probability distribution  $P(X)$ .  $X$  is defined as an instance set, and  $X = \{x_1, x_2, \dots, x_n\} \in \mathcal{X}$ .

- The original task attempts to predict data from domain  $\mathcal{D}$  through a mapping  $\mathcal{T} = \{\mathcal{Y}, f(\cdot)\}$  composed of a label space  $\mathcal{Y}$  and an objective predictive function  $f(\cdot)$ . Given a domain  $\mathcal{D} = \{\mathcal{X}, P(X)\}$  the sample data consists of pairs  $\{x_i, y_i\}$  where  $x_i \in \mathcal{X}$  and  $y_i \in \mathcal{Y}$ . The objective function  $f$  is supposed to learn from sample data to predict the corresponding label for the new instances.  $f$  can be rewritten as  $f(x) = P(y|x)$ .
- The transfer learning task involves a source domain  $\mathcal{D}_S$  with corresponding source tasks  $\mathcal{T}_S$ , and a target domain  $\mathcal{D}_T$  with corresponding target task  $\mathcal{T}_T$ . The goal is to transfer the related knowledge to boost the performance of the target predictive function  $f_T(\cdot)$ .

### 2.3.2 Shot based learning



**Figure 2.9:** Shot based learning captured in the natural language context [50]

The transfer of models is dependent on the strategy the model uses to make predictions. Shot-based learning is a substantial factor. This describes the model's exposure to data in domains and its ability to handle cases it has never seen before. Thus, shot-based learning can be separated into meta-learning tasks or multitask learning.

Instead of learning underlying patterns, meta-learning models learn to *learn* the algorithm itself. This allows it to generalize tasks with few labelled examples of new or rare cases. Otherwise, multitask learning makes predictions for a particular set of tasks [44].

#### Zero-shot Learning

Zero-shot models (Figure 2.9(a)) can generalize to unseen tasks. An example of a model targeted for zero-shot transferability is the SAM model (Section 2.2.6).

#### Few-shot Learning

Few-shot models (Figure 2.9(b)) can generalize to unseen tasks with a few examples. The UniverSeg model is the target model for few-shot transferability (Section 2.2.5).

#### Many-shot Learning

Many-shot models can generalize to unseen tasks with many examples. The nnUNet based models such as the TotalSegmentator is the target model for many-shot transferability (Section 2.2.3).

# Chapter 3

## Methodology

Improvements over the transfer from models trained on other domains could hypothetically allow the segmentation of delineated areas more accurately. To investigate this claim, we iterate over the three types of shot learning, zero-shot, few-shot, and many-shot learning, to determine the effectiveness of transfer learning in the radiotherapy domain.

### 3.1 Transfer Strategy

Transfer learning involves obtaining a pre-trained "base" model, identifying transfer layers, and fine-tuning the remaining layers. Key considerations include preventing overfitting on smaller datasets and making decisive adjustments to learning rates during the fine-tuning phase.

1. Obtain a pre-trained "base" model trained on extensive data which identifies general features and patterns relevant to the target domain.
2. Identify the transfer layers. These layers capture general information relevant to both the new and previous tasks. The selected layers are 'frozen' during training. This means parameters are not changed, preserving the low-level learnt feature functions.

The number of frozen layers depends on how much inheritance is required from the pre-trained model. For unrelated domains, like car vs. face detection, only low-level features should be transferred. However, the amount of information transferred in related domains is more generous, and the quantity is tunable.

3. Fine-tune and retrain the remaining layers. The goal is to preserve the knowledge from the pre-training while enabling the model to modify its parameters to suit the demands of the current assignment better [48].

For smaller datasets, there may be an issue of overfitting because the number of available samples to train on has decreased. Thus, we must set the learning rate to be low; when fine-tuning a new model you want to readjust the pre-trained weights, and if the learning rate is too high, the model may rapidly overfit [48]. Furthermore, this is done for a low number of iterations for the same reasons [44].

## 3.2 Baseline – nnUNet

The provided examples of the objective are enough to train an nnUNet model from scratch. It has been shown that in many biomedical applications, “only very few images are required to train a network that generalises reasonably well” [34]. Therefore, we first train a baseline nnUNet model on the provided examples to establish a benchmark for the transfer models.

### 3.2.1 Preprocessing

Prior to training, necessary normalization must take place to standardize each input. Firstly, CT scans can produce results for different spacings, resolutions, and dimensions. Because the model samples data in batches, the batch properties must align within the model’s body. Therefore, the fingerprint taken by the preprocessing pipeline resamples input data towards the median dimension.

The traditional method of normalization involves normalizing the entire image corpus. However, this method does not take into account the skew that might affect the outcome. This is because the background value occurs most frequently, and artifacts such as metal cause outlier peaks. As a result, traditional normalization could overlook important tissues as it attempts to treat background and outlier values equally with foreground values.

Therefore, the nnUNet avoids this complication by processing voxel properties encased by the ground truth segmentation. The values are clipped to their 0.5 and 99.5 percentile, followed by traditional normalization with the mean and standard deviation. This way, the target structure properties remain relative to their original, and the background label conforms to the normalization inspired by the region of interest.

### 3.2.2 Separate Training

The default strategy is to consider each anatomy separately and attempt to learn segmentation patterns without considering constraints mentioned in Section 2.1.8. These models can be used in an ensemble system to produce thorough segmentations of the target volumes, oblivious to clinical constraints.

We set up the learning pipeline to follow a five-fold cross-validation process. Each fold involves splitting the data into five subsets. Then, the model is trained on four subsets and validated on the fifth subset. The process repeats for each of the five subsets, with each subset used exactly once as the validation set. Cross-validation helps assess the model’s performance and generalize it to new data. Ultimately, the model with the best validation performance represents the anatomy.

## 3.3 Many-shot Transfer – TotalSegmentator

We kickstart the transfer discussion by evaluating the transfer of many-shot models. The candidate model for this is the TotalSegmentator model, which is entirely based on the default implementation of the nnUNet.

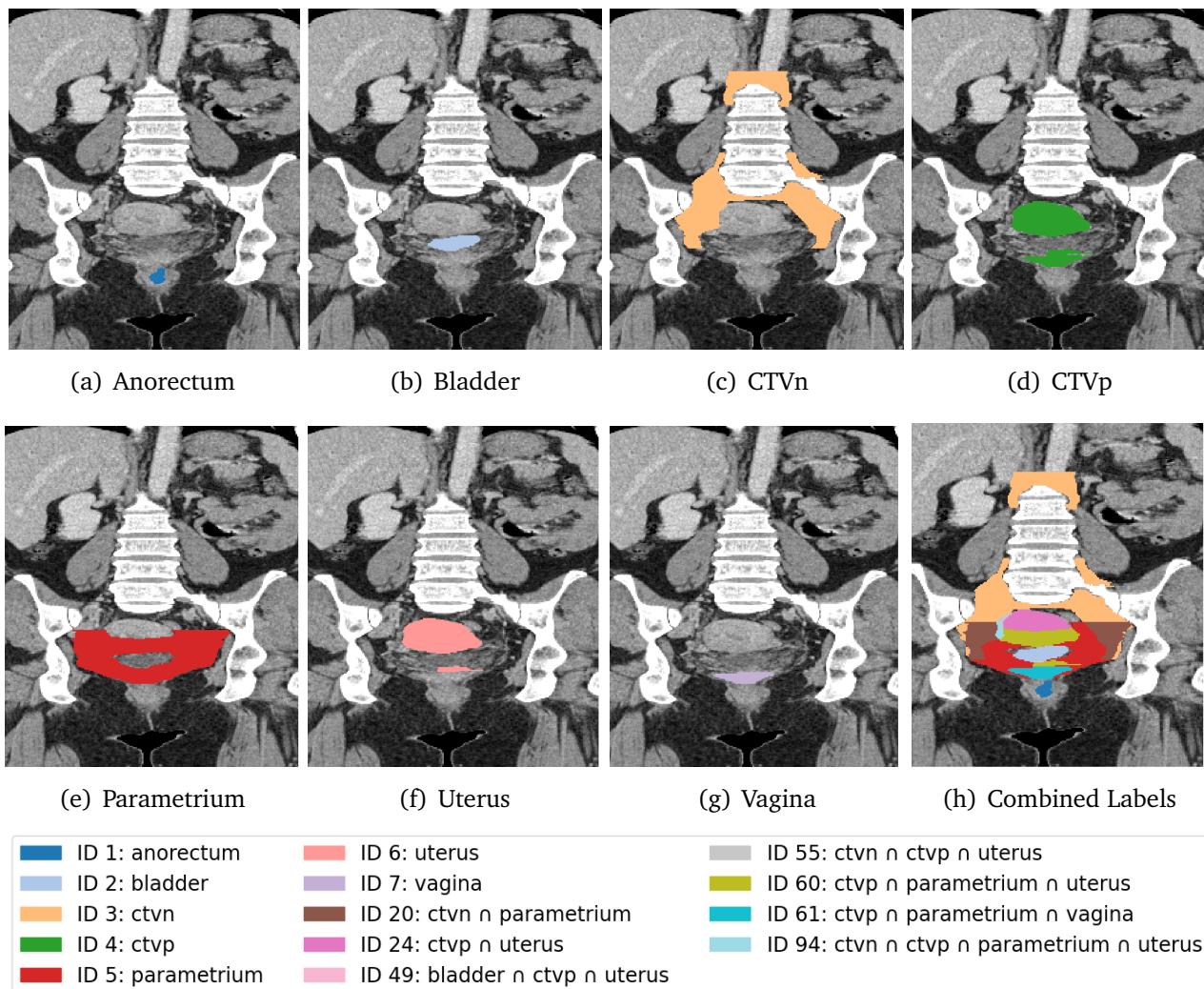
When transferring information, many-shot models are the most obvious choice. These models have the potential to increase the amount of helpful information that can be used to segment

anatomies in the target domain by transferring the original task. The hypothesis is that many-shot transfer models will improve segmentations for clear organ delineations. Additionally, anatomies that have already been segmented (such as the bladder) will fine-tune to become more accurate.

### 3.3.1 Separate Training

Like the nnUNet, we apply the default fine-tuning strategy to a pre-trained TotalSegmentator model. TotalSegmentator has 23 separate nnUNet pre-trained models on different sub-tasks in the anatomical segmentation [51]. These individual models segment structures like the vertebrae, cardiac muscles, rubs, and lung vessels. For this destination delineation task, we chose the 'organ' model trained on a withheld dataset of 1200 CT scans. The only anatomy shared between the two domains is the Bladder which will hypothetically provide a performance improvement for this anatomy due to the additional thousand examples of the bladder.

### 3.3.2 Region Based Training



**Figure 3.1:** New IDs generated for a single slice as a consequence of practical experience show non-conformity to rules in Section 2.1.8.

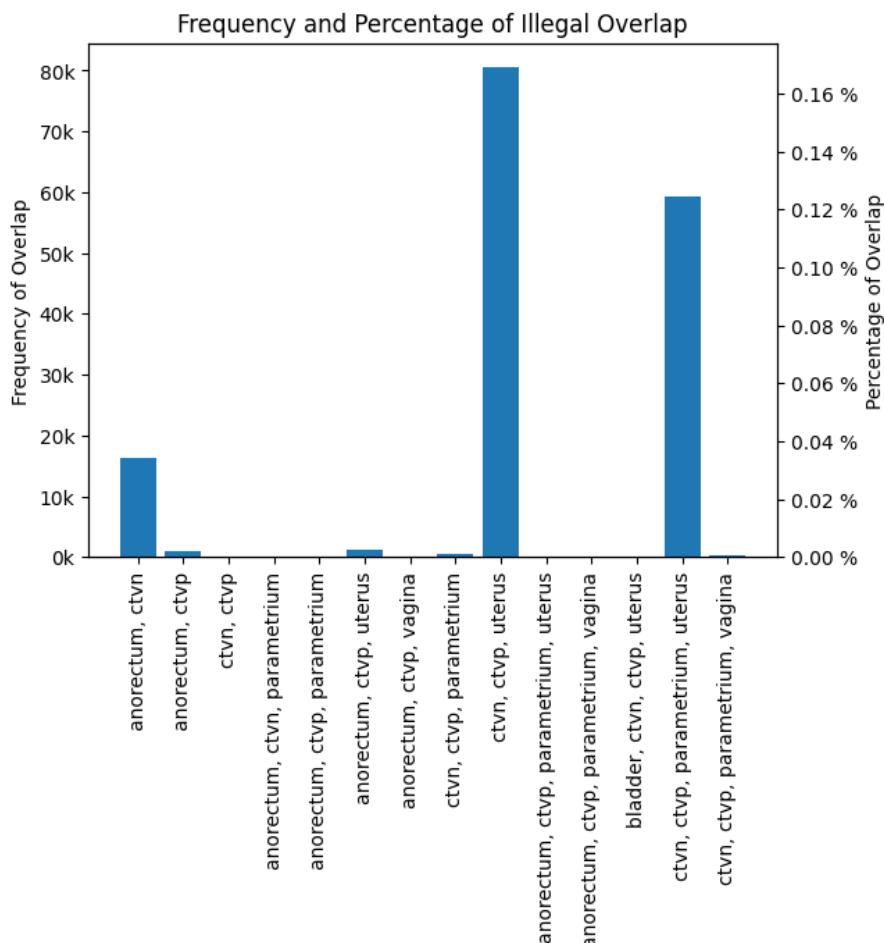
The natural extension of separate training is to consider training each class simultaneously. Region-based training is a noninvasive method offered by the nnUNet. This training style combines the 3D segmentation maps for each of the seven classes into one 3D segmentation by introducing new IDs wherever there is a new overlap. An example slice can be seen in Figure 3.1.

For the purposes of evaluation, the following methods will be applied to the baseline nnUNet model to assess the success.

### No Rule Enforcement

A sensible and calibrated set of ids could be drawn based on the rules in Section 2.1.8. However, practical experience and the recalcitrant and challenging nature of defining logical expressions to generalize something as complex as organs and something as fuzzy as microscopic cancer spread mean that, in practice, these rules cannot be implemented strictly.

Please refer to Equation 2.1 “There should be no overlap between the CTVn, CTVp or Anorectum”. We see marginal overlap between the structures in Figure 3.1(h) in ids 55, 94. These are almost not visible on the figure, but captured by the legend.



**Figure 3.2:** Total frequency and percentage overlap of non-zero occurrences of ‘illegal’ overlap between the CTVn, CTVp, and Anorectum.

When considering the total sample set, the overlap makes up a minimal percentage of the total volume with non-background label classification. Take, for instance, Figure 3.2, which

shows all cases of ‘illegal’ overlap found within the samples. The most frequent culprit overlap that breaks the condition is between the CTVn, CTVp and the Uterus, which makes up the most significant proportion of ‘illegal’ overlap. The Uterus is a necessary subset of the CTVp, which implies that this segmentation of CTVp does not include microscopic spread, including in the Cervix and GTVp. By eliminating this style of error from the model, it might be possible to obtain more general segmentations that align with the clinical team’s rules.

### With Rule Enforcement

We implement the rules with the hypothesis of generalisation despite the rules not strictly followed in practice. Therefore, an augmentation of the nnUNet trainer is necessary to capture this result. Specifically, we introduce an additional loss component dubbed ‘custom\_loss’ during training. This custom loss parameter implements two of the many rules that the Royal Marsden Hospital clinical staff provided. The two rules are thoroughly discussed in Section 2.1.8 and are Equation 2.1 and Equation 2.5.

To consistently include the loss parameter, we have two sub-loss objectives operating on dice loss (Section 3.6.2). The first captures Equation 2.1, which focuses on the strict requirement that the CTVn, the CTVp, and the anorectum do not overlap. The loss term is minimal when the dice score is the lowest, indicating minimal overlap; thus, to calculate this result on the intersection, the implementation of vanilla dice loss applies to the rule’s three permutations independently. Secondly, Equation 2.5 insights more overlap between the vagina and uterus with the CTVp, which is equivalent to 1 minus the previous learning objective. As a hyper-parameter, we attribute a weight of 0.3 to this term, while other loss terms (dice and binary cross-entropy) are assigned weights of 1 to keep the original objective function reasonably unchanged.

We hypothesise that although the rule-free model attempts to approximate the ground truth, which may call for marginal overlap, with the rules in place, this may generalise better over other cases.

## 3.4 Few-shot Transfer – UniverSeg

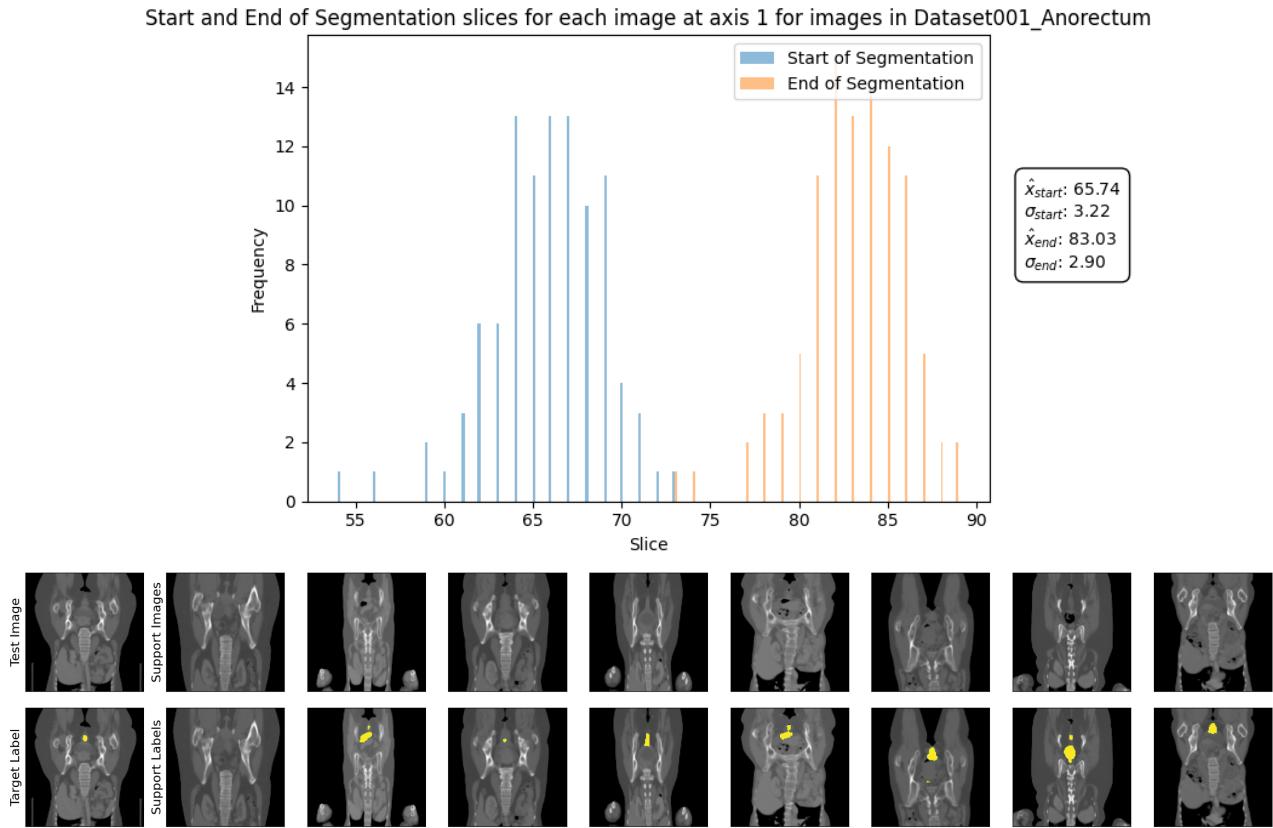
UniverSeg operates on 2-dimensional data. As a result, to provide automatic radiotherapy planning volumes, it is essential to provide slices for the model as input alongside a sufficient support size of similar slices.

### 3.4.1 Preprocessing

Images are normalised to match UniverSeg’s training properties. Specifically, image intensities are clipped to the range  $[-500, 1000]$  and normalised to be between  $[0, 1]$  and finally scaled down to a  $128 \times 128$  resolution [37]. Slice pre-processing is repeated along each axis to evaluate the effectiveness of one slice over another.

### 3.4.2 Automated Support Set Sampling

The most screaming disadvantage of such a model when applied to a three-dimensional unseen segmentation task is tumour localisation; we do not know where the tumour starts or



**Figure 3.3:** The distribution of the start and ending slices of the tumor in a normalized batch of images across axes 1 (sagittal dimension) and the corresponding sampled support extracted.

ends. The tumour’s location can only be determined by referring to assisting models that provide estimates or make assumptions about tumour location based on previous examples. In a secluded environment where only one’s model transferability is assessed, we instead analyse the properties of the tumour from the examples.

We begin by analysing the tumour locations along each axis. The intuition is that the pre-processed images of equal dimensions and spacings should contain the tumour at approximately the same location. Figure 3.3 shows the tumour’s distribution of start and end slices and the corresponding sampled support set.

By sampling a support set concerning slice positions, we include an approximation of a binary classification of ‘does this slice contain a tumour or not’; if for slice n there is a 20% chance that the support contains a tumour, then we can also assume that for an unseen patient, this chance is also the same. However, this does not generalise to boundary cases where tumours or organs may begin sooner or later than all others, which may cause a misclassification.

### 3.4.3 Supervised Support Set Sampling

To consider the overall transfer ability of this model, we also consider a supervised setting; the model is fine-tuned on each axis of every anatomy across a spectrum of tumour locations across a specific axis. The main difference from the previous implementation is that we always expect a contour to be produced from the query, and we always know the support will have variable segmentations across the axis.

## 3.5 Zero-shot Transfer – MedSAM

MedSAM is the final algorithm in the shot-learning strategies that will be covered. Specifically, MedSAM is being evaluated on the provided dataset, both with and without transfer, to test the claim of transferability.

Zero-shot learning, a promising feature of MedSAM, could potentially enable it to handle tasks it has never encountered before. However, the assertion that it can seamlessly transfer without refinements is a bit of a stretch. This is because certain contours, like the CTVn, delineate tiny tumor spread throughout the lymph node system. Therefore, it is unlikely that MedSAM, trained in such cases, would be used for these specific tasks. It would typically be used for more straightforward volume delineations, such as organs.

### 3.5.1 Preprocessing

MedSAM takes two-dimensional images as input, much like UniverSeg. Therefore, we similarly preprocess the data to a resolution of  $1024 \times 1024$  along each slice where the ground truth is present. We clip the ranges of the CT scan to Hounsfield units centred around the 40 value, with a window radius of 400 units and later normalized to the range of  $[0, 1]$ . In contrast to UniverSeg, we resize a slice after selecting the index instead of resizing the whole image. Thus, we do not introduce any anisotropic uncertainties along our sampling axis.

Further, in contrast to previous strategies, the MedSAM preprocessing step also removes ground truth segmentations that occupy an area below a specified threshold. The idea here is that the challenge with locating the small areas of the region of interest is an entirely different classification of the problem; the issue is with object detection instead of object segmentation [38, 43]. This detail of the preprocessing is critical to consider for discussion and use as this would increase the proposed surface distance along an axis.

### 3.5.2 Point based transfer

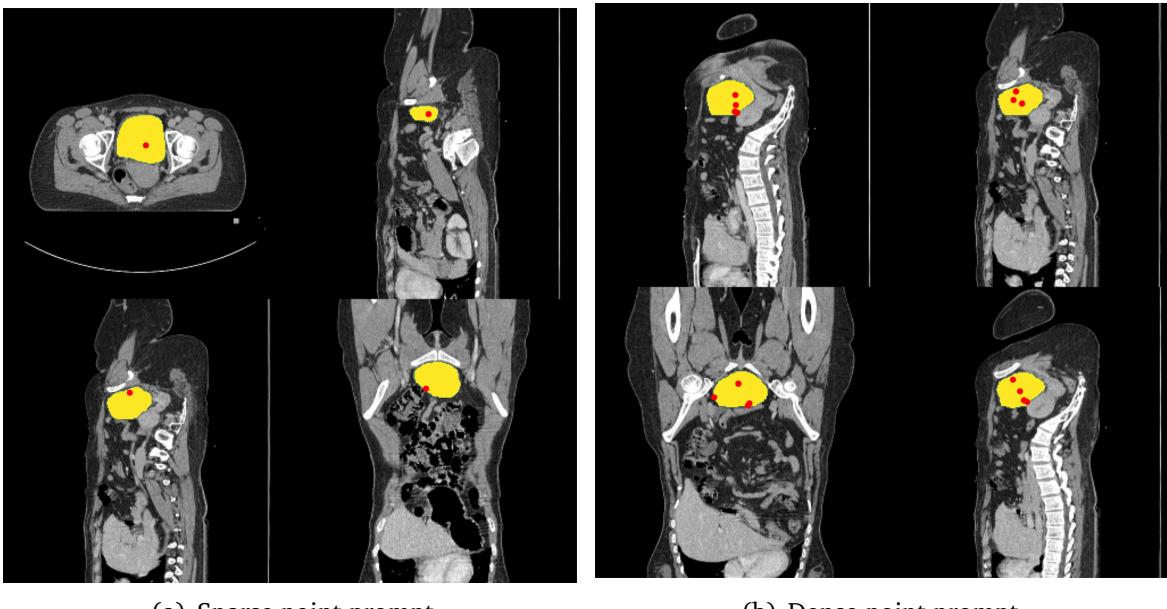
We first experimented with the MedSAM architecture to test the effectiveness of prompting on points. The baseline MedSAM implementation offers a point based prompt and also a box based prompt. To consider both mediums of prompt encoding, we can consider a sparse and dense point planning.

The two strategies are shown in Figure 3.4. The sparse point prompt is a single point in the image, while the dense point prompt is a set of  $n$  points randomly sampled from the ground truth segmentation.

The hypothesis is that point prompts may work well with structures such as the bladder which are trivial to identify. However, for the CTV, the point prompt may not segment the full extent of the structure.

Points are sampled with a higher probability of being towards the centre of the segmented area by calculating the Euclidean distances of all points from the centroid. This heuristic dispels any ambiguity that may be caused when selecting points closer towards the outline of the segmentation, which may occur when boundaries of different objects bleed into one another, causing a higher error.

This strategy, however, is not enough; the MedSAM model often provides wispy boundaries in a response to the point prompts as it must work harder at guessing the boundaries of the object. Therefore, this strategy is dispelled from consideration.



(a) Sparse point prompt

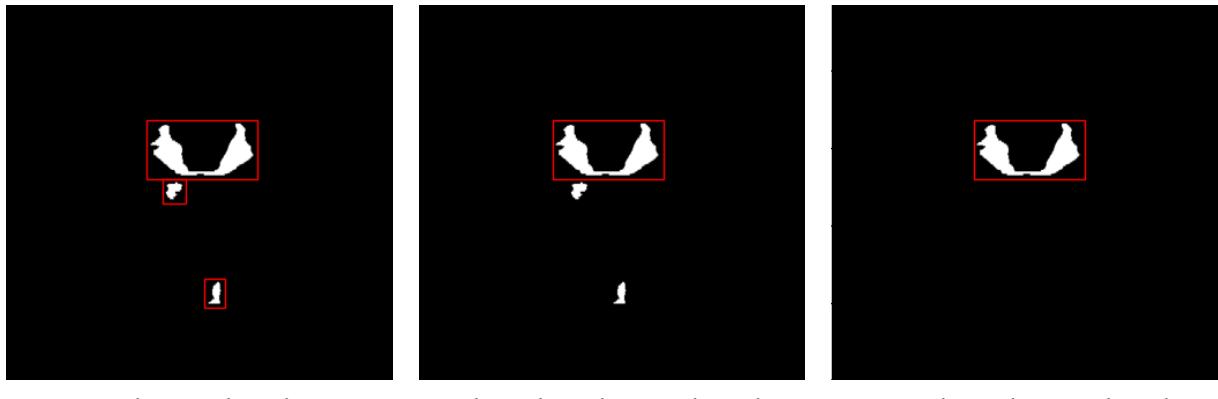
(b) Dense point prompt

**Figure 3.4:** The two strategies for sampling structures in the MedSAM model.

### 3.5.3 Box based transfer

A box prompted solution will define the area where the tumour is likely to be. Box prompts for training are obtained from the ground truth, with a margin surrounding the box.

For training, only one box may be fed into the model for inference. Therefore, we select a random structure from the boxes encompassing the tumour for a given slice. Figure 3.5 demonstrates the tumour box selection at training time.



(a) Boxed ground truth image

(b) Selected tumor boxed

(c) Adjusted Ground truth

**Figure 3.5:** The process of selection bounding box for a given boxed tumor with an augmented ground truth used at training time for the MedSAM box-based prompt model.

Furthermore, images are augmented with a random rotation, scaling, and translation to improve generalisation. Data augmentation ensures that the model does not overfit the training data and can generalise to unseen examples.

### 3.5.4 Evaluation

During training, the test set is divided by ID to ensure that a portion of an image is not both trained and validated. This way, the model’s transferability is not questioned because it is trained on a disjoint set of patients; otherwise, quantitative measurements would skew and not represent the model’s adaptability to unseen data.

Secondly, the MedSAM architecture selects points and boxes for inference from the ground truth. Because MedSAM is an interactive tool, its application will likely adapt as an assisting tool for clinicians. However, for unseen examples, the concept of auto planning is uncertain. The authors of the paper measure performance according to the ground truth [38, 43]. Refining the model pipeline to include bounding box predictions extracted from a baseline like nnUNet is possible, where MedSAM acts as a refinement to an already reasonably accurate guess. This allows for noise to be permeated into the model, thus allowing for a better auto-contour planning pipeline.

## 3.6 Quantitative Evaluation of Segmentation

Calculating the difference between the provided labelled data would be one way to determine if a contour can be used in a clinical context. However, we have different ways to evaluate this measure in a delineation context.

If we were attempting to fit a model onto a line in 2D space, the performance of our model would be the total minimum distance between each point and the prediction. Our objective would be to drive the model’s distance metric as close to 0 without overfitting. Here, the points act as a ‘ground truth’, alternatively referred to as the gold standard, which represents the actual measured value.

The reasoning above extends to 3D and 2D in a segmentation context with variants to measure other quantities, like the minimum distance between prediction and truth or the extent of volume overlap between the two. These are examples of geometric measures, which Mackay et al. has found to be the most popular measure in segmentation tasks [52].

### 3.6.1 Classification Based

Assesses if voxels within and outside the auto-contour have been correctly labelled [52]. To begin, we define ‘positive’ to mean that the voxel selected indeed needs radiotherapy treatment and ‘negative’ to mean that the voxel classifies as healthy.

A standard measure of classification is accuracy. It measures the total number of correct predictions vs. the total predictions it made. However, more than this measure is needed to fully capture a model’s bias because it does not tell the whole story with class-imbalanced data when there is no even number between positive and negative labels.

$$\text{Accuracy} = \frac{TP + TN}{TP + TN + FP + FN}$$

Better measures are Precision and Recall scores. The Precision (also known as the Positive Predictive Value [53]) measures the proportion of successfully correct predictions. The Recall (also known as True Positive Rate [53]), on the other hand, “measures the portion of positive voxels in the ground truth that is also identified as positive by the segmentation being evaluated”.

$$\text{Precision} = \frac{TP}{TP + FP}, \quad \text{Recall} = \frac{TP}{TP + FN}$$

### 3.6.2 Spatial Overlap Based

Similarly to classification-based metrics in Section 3.6.1, an overlap-based metric measures the extent of overlap between an auto-contour and a reference structure [52].

The scores above combined into a more general score  $F_\beta$  to give

$$F_\beta = (1 + \beta^2) \cdot \frac{\text{Precision} \cdot \text{Recall}}{\beta^2 \cdot \text{Precision} + \text{Recall}}$$

A specific case of this equation with  $\beta = 1$  is mathematically equivalent to the DICE Similarity Coefficient. A review found that DICE is the most popular evaluation metric amongst 2021 studies [52, 53, 54].

$$F_1 = \text{DICE} = \frac{2 \cdot \text{Precision} \cdot \text{Recall}}{\text{Precision} + \text{Recall}} = \frac{2 \cdot TP}{2TP + FP + FN} = \frac{2|S_g \cap S_p|}{|S_g| + |S_p|}$$

Where  $S_g$  is the ground truth segmentation and  $S_p$  is the predicted segmentation. From this relationship, the DICE score has found popularity in image segmentation for similar reasons that the  $F_1$  score has found its popularity in classical machine learning; it can provide a fair result for imbalanced datasets. This mentality is applicable in our scenario because a tumour will make up very little of the total volume of the domain space. This argument extends to a Volumetric DSC by considering the above in all three dimensions [55].

Another popular related evaluation method is the Jaccard Index, which measures the intersection over the union of two sets:

$$\text{JAC} = \frac{TP}{TP + FP + FN} = \frac{|S_g \cap S_p|}{|S_g \cup S_p|} \iff \frac{\text{DICE}}{2 - \text{DICE}}$$

Since the numerator for the Jaccard Index is smaller than the DICE (since we avoid the issue of counting the intersecting sections twice), the JAC is always larger than the DICE score.

### 3.6.3 Surface Based

Also commonly known as Boundary-Distance-Based Methods [56] compares the distance between two structure surfaces. These can be maximum, average or distance at a set percentile of ordered distances [53].

A typical example is the Haussdorf Distance. Here, a directed distance metric is the maximum distance from a point in the first set to the nearest point in the other between two individual voxels [56]. Therefore, the better the HD metric, the smaller the value it returns. Here, the distance is typically Euclidian distance.

$$\text{HD}(A, B) = \max(h(A, B), h(B, A)), \quad \text{and directed } h(A, B) = \max_{a \in A} \min_{b \in B} \|a - b\|$$

The HD is generally sensitive to outliers; therefore, direct HD application gives uninspiring results because noise and outliers are common in medical segmentations [56]. Therefore, we can calculate the average directed Haussdorf Distance.

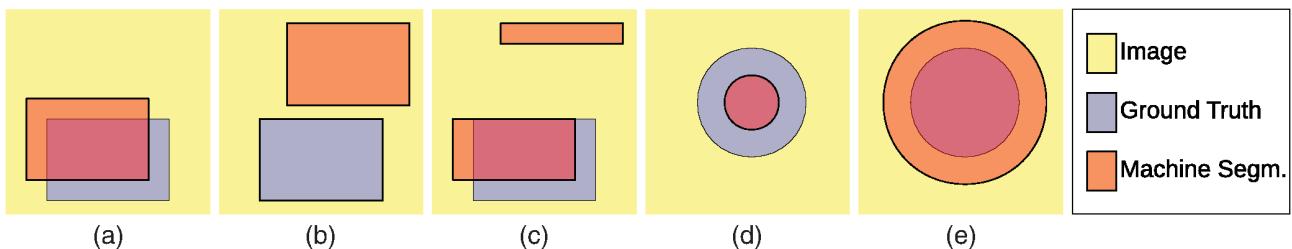
### 3.6.4 Volume Based

Volume-based metrics consider only the volume of the segmentation [57, 52, 56]. However, its poor spatial descriptions make it more commonly used jointly with other metrics.

$$\text{Relative Volume Difference (RVD)} = \left| \frac{|S_g| - |S_p|}{|S_g|} \right|$$

### 3.6.5 Evaluation

All these methods can be advantageous in some places rather than others. To decide which segmentation is best, we can list some challenging scenarios.



**Figure 3.6:** Figure from [56] illustrating cases of segmentation to aid with explanation of setbacks of certain evaluation metrics

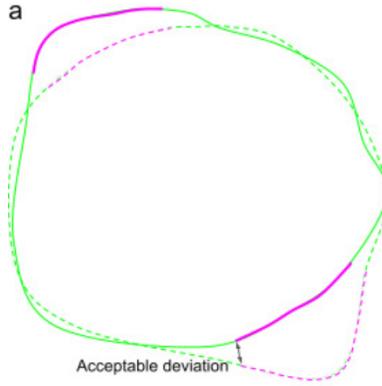
- Classification Based (Section 3.6.1) and Spatial Overlap Based (Section 3.6.2) are similar; they are concerned with the number of correctly classified or misclassified voxels without taking into account their spatial distribution. Here, Figure 3.6(a) and Figure 3.6(c) would achieve similar results despite Figure 3.6(a) being locally bound to a better area.
- With Haussdorf Distance (Section 3.6.3) output segmentations generated by Figure 3.6(d) and Figure 3.6(e) will result in the same score, which is not favourable in a radiotherapy planning environment where an organ-at-risk is involved.
- Figure 3.6(b) would score flawlessly when using volumetric score estimation. However, it does not consider spatial placement, making this measurement poor when used individually.

### 3.6.6 Estimated Editing Based

Selecting a measurement that can reflect a clinician's acceptability score is difficult. A study found a lack of correlation between a geometric index and expert evaluation, with the JAC score having a 13% False Positive Rate. The study's conclusion summarised that scores such as JSC and volumetric DSC "provide limited clinical context and correlation with clinical or dosimetric quality" [54].

#### Surface DSC

The study at [54] helped drive an initiative to combine aspects of surface Based evaluation (Section 3.6.3) and Spatial Overlap Based evaluation (Section 3.6.2) into a Surface DICE which assesses the specified tolerance instead of the overlap of the two volumes.



**Figure 3.7:** Taken from [58]. Illustrates the computation of the surface DICE, where the continuous line is the predicted surface, and the dashed line is the ground truth. The black arrows show the maximum deviation tolerated without penalty; therefore, in pink are the unacceptable deviations and green otherwise.

We can formulate the Surface DSC score in a mathematical definition [54] with its corresponding illustration in Figure 3.7.

$$\text{Surface DSC} = \frac{|S_p \cap B_{g,\tau}| + |S_g \cap B_{p,\tau}|}{|S_p| + |S_g|}$$

This definition measures the agreement between just the surfaces of two structures above a clinically determined tolerance parameter,  $\tau$ . Here,  $B_{p,\tau}$  represents the boundary region of the predicted surface within a maximum margin of deviation  $\tau$  and similarly for  $B_{g,\tau}$  for the ground truth.

### Added Path Length

Similarly, the APL score predicts “the path length of a contour that has to be added” [55]. APL achieved similarly by considering the number of added voxels required between the prediction and the gold standard with no regard to tolerance as a pose to Surface DSC (Section 3.6.6)

### 3.6.7 Summary

For this project, we shall select an evaluation measurement more biased towards conservative boundary estimates not to touch the organs at risk. The clinician’s review pipeline, in part, influenced this choice; it would be easier to correct Figure 3.6(d) instead of Figure 3.6(e) because correcting the latter would likely take a considerable amount of time as it would require redrawing almost all of the boundary, whereas the former could be corrected much faster [58].

This is why we settle at the Surface DSC (Section 3.6.6), which prioritizes deviation along the boundary to a certain degree while measuring the fraction of the surface that needs to be redrawn. Furthermore, to keep in tradition with previous studies, we will also report the DICE and RVD scores to broaden the scope of evaluation into all three categories of evaluation metrics discussed above.

# Chapter 4

## Results and Discussion

In this chapter, we present the results and discussion regarding the experiments carried out with each type of transfer learning strategy. The baseline in each will be displayed alongside the model performance for evaluation. Finally, we step back and consider the performance of different transfer strategies across the anatomies.

### 4.1 Many-shot Transfer – TotalSegmentator

#### 4.1.1 Separate Training

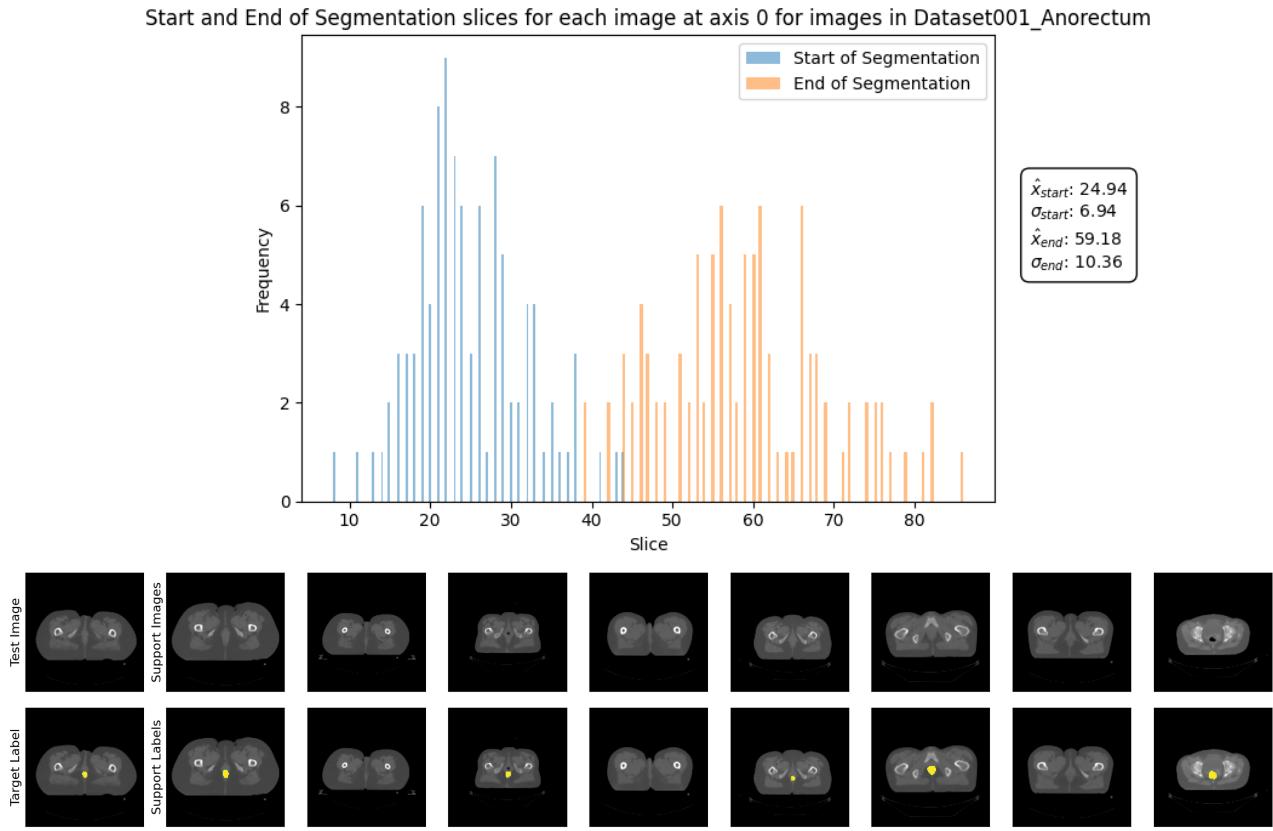
#### 4.1.2 Region-based Training

#### 4.1.3 Rule enforced Region-based Training

### 4.2 Few-shot Transfer – UniverSeg

#### 4.2.1 Automated Support Set Sampling

Automated support set sampling is not a successful technique for unseen patients. First, there is significant variability, and limited examples do not fully address non-trivial segmentations. Provided is an additional plot for the distribution of starting and ending slices for the Anorectum class at Figure 3.3.



**Figure 4.1:** The distribution of the start and ending slices of the tumor in a normalized batch of images across axes 0 (axial dimension) and the corresponding sampled support extracted.

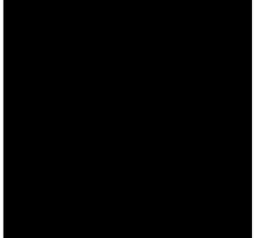
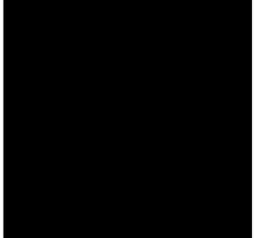
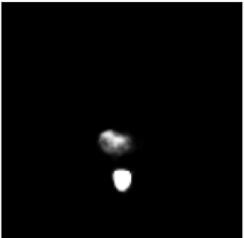
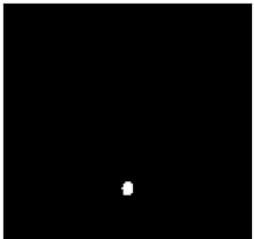
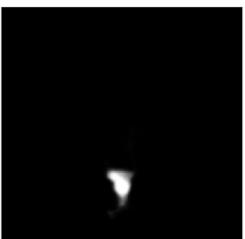
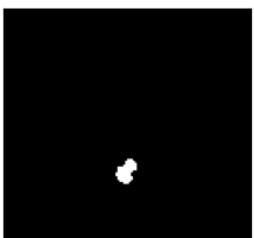
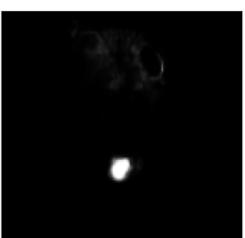
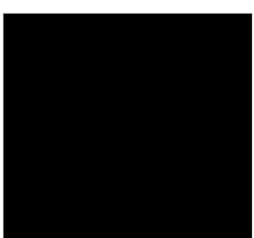
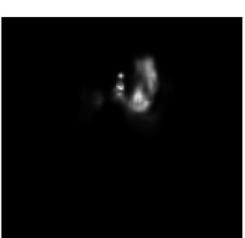
Overlapping regions in the distribution of slice numbers for the support set indicate significant variability in where tumours become visible and disappear across different patients. This overlap suggests that the tumours' start and end points are inconsistent, leading to challenges in creating a reliable support set for segmentation. When the tails of these distributions significantly overlap, it means that for some patients, the end of a tumour in one slice might coincide with the beginning of a tumour in another, or there could be significant gaps between the start and end points of tumours across different slices. This variability can confuse the model, as the support set may not provide clear and consistent examples of tumour boundaries, reducing segmentation accuracy.

Second, automatic slice generation can often lead to confusion, as the UniverSeg model was always trained to predict a segmentation. That is, their training procedure for CT was to take the central slice of anatomy, thus ignoring more complex and ambiguous areas of the anatomy.

A qualitative assessment of the technique as a whole concludes that it is not applicable and that a more supervised approach is required for the UniverSeg architecture, because examples fuel the prediction process.

We provide for review a selection of slices in Table 4.1 from an example inference on a single patient. An additional example of a support set is provided at the appendix at Figure ??.

**Table 4.1:** Qualitative assessment of UniverSeg inference for a random patient

	query	label	prediction
slice 42			
slice 65			
slice 69			
slice 80			
slice 87			

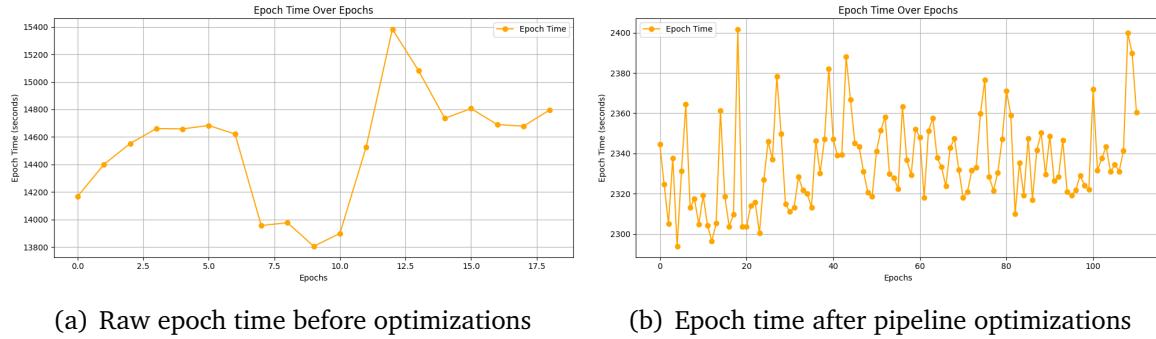
## 4.2.2 Supervised Support Set Sampling

The total summary of results for the Supervised UniverSeg architecture is available at the Appendix; Metric Tables A.16- A.20 aggregate the results along the different metrics discussed in Section 3.6, and Figure A.27- A.33 aggregate metric results along the anatomy level discussed in Section 2.1.7. The relevant figures and diagrams are lifted out of the appendix for discussion.

## 4.3 Zero-shot Transfer – MedSAM

The total summary of results for the MedSAM architecture is available at the Appendix; Metric Tables A.16- A.20 aggregate the results along the different metrics discussed in Section 3.6, and Figure A.27- A.33 aggregate metric results along the anatomy level discussed in Section 2.1.7. The relevant figures and diagrams are lifted out of the appendix for discussion.

### 4.3.1 Training Bottlenecks



**Figure 4.2:** Comparison of epoch times for an expensive MedSAM model before and after pipeline optimizations.

This model requires three channels of  $1024 \times 1024$  image slices, making each input image in its raw state a costly sample to send over the network especially after considering that each channel is a duplicate to match the requirements of the SAM model. This makes training on commodity hardware a difficult thing to accomplish. Training times can be very long without adding changes to the training pipeline. Figure 4.2 compares training pipelines and performance improvements.

Firstly, image slices were stored in a  $(1 \times 512 \times 512)$  resolution and upsampled before the forward pass. Furthermore, caching [59] stored these smaller images on the training node to avoid repeated and expensive reads over the network. This improved training epoch times by 50 times.

### 4.3.2 MedSAM’s claim to zero-shot transferability

The authors of MedSAM engineer the model to be zero-shot transferable by providing a secondary input domain. The domain studied is the box-based spatial prompt. Results across anatomies show that a baseline model cannot outperform the segmentation scores of the nnUNet.

#### Obvious Delineations

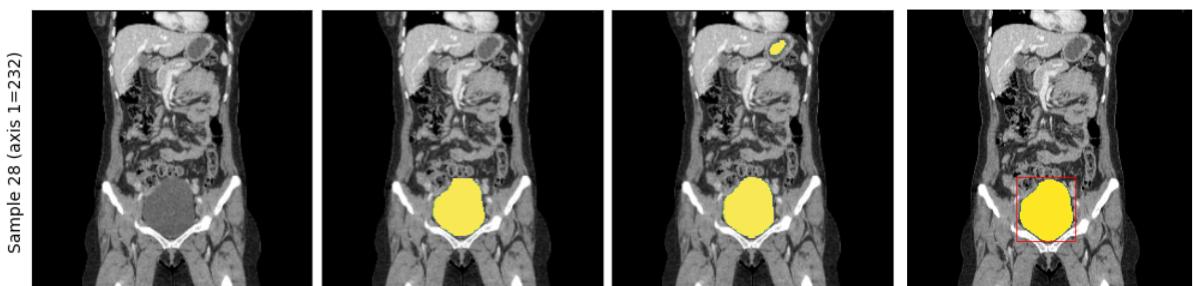
Arguably, the most apparent organ delineation within the dataset is the bladder. Across the range of metrics used to evaluate the segmentation’s performance, the bladder consistently performed worse apart from the Haussdorf Distance metric. Table 4.2 aggregates data at Appendix A.2.4 from Figure A.28.

**Table 4.2:** Performance of models on the bladder delineation.

Anatomy	nnUNet baseline			MedSAM out-of-the-box			MedSAM Fine-tuned		
	Mean	Std Dev	Median	Mean	Std Dev	Median	Mean	Std Dev	Median
Added Path Length	1.21	2.06	0.71	9.12	13.14	3.52	3.59	6.98	0.00
DICE	0.94	0.06	0.97	0.92	0.08	0.94	0.95	0.05	0.97
Haussdorf Distance	77.16	71.94	96.79	3.09	1.55	2.54	3.00	7.69	2.00
Relative volume difference	-0.04	0.12	-0.02	-0.05	0.13	-0.04	-0.03	0.09	-0.01
Surface DSC	0.97	0.06	1.00	0.54	0.16	0.55	0.68	0.14	0.69

This promising performance spike over the non-finetuned model is due to the nature of the box prompts supplied to the model during inference. The MedSAM model heavily relies on good supervision. Otherwise, invalid or imprecise definitions of areas of interest will lead to wrong results. Therefore, this result alone cannot be used to determine the transferability of this model when put into the context of the other metrics; this metric is heavily influenced and biased by the ground truth object’s location. Therefore, areas segmented by the MedSAM model at any fine-tuning stage will return masks close to the gold standard.

The Haussdorf discrepancy with the baseline is explained by its difficult objective of also localising the search area to the region where the tumour is; where this was provided for MedSAM, the baseline model had to learn to locate and segment the object. An example has been provided in Figure 4.3 which shows how the nnUNet has hallucinated a bladder in the stomach, thus causing a huge spike in the Haussdorf distance metric. This problem would not appear in the MedSAM model because the box prompt would have localised the search area to the region around the pelvis.



**Figure 4.3:** From left to right, a slice of a patients CT scan, the ground truth overlayed onto the slice in yellow, and the nnUNet prediction overlayed onto the slice, MedSAM prediction

### Niche Delineations

#### 4.3.3 The performance of a transferred MedSAM model

# **Chapter 5**

## **Conclusion**

Transfer works!

# **Chapter 6**

## **Ethics**

The lack of effort to protect the identities and confidentiality of patients during research projects may result in “stigma, embarrassment, and discrimination” [60] if the data is misused. This project involves the intimate and personal information of many female patients whose privacy must be protected before research occurs.

### **6.1 Patient disclosures**

Researchers may collaborate with third parties, such as Imperial College London, by providing anonymised data that third parties cannot reverse-engineer to identify the patient. The collaborating hospital, The Royal Marsden Hospital, does not require “explicit consent” for sharing collected clinical data with outside entities as long as the patient is made aware of the ways their “de-identified/anonymised” data may be used. [61]. Imperial College’s Medical Imaging team also arranges formalities, such as acting as “ethical data stewards” [62].

The MIRA team acts as responsible data stewards by storing anonymised data within a folder on the college network. They received all provided data in the NIfTI file format, which discloses no personally identifiable information, as defined by the GOV website [63]. Specific access rights limit data availability in this folder, ensuring security measures. Moreover, taking the data outside this folder reduces individual patient risk through the exchange of de-identified data.

Without such disclosure, anonymisation, and a security guarantee of the data, patients may be reluctant to provide candid and complete disclosures of their sensitive information, even to physicians, which may prevent a complete diagnosis if their data is not maintained anonymously.

### **6.2 Using the tool**

The applications of this tool bode well in the healthcare ecosystem as the community slowly accepts the involvement of AI-powered medical tools. Radiology is one application that has been most welcoming of the new technological advances as there is potential for substantial aid by reducing manual labour, increasing precision and freeing up the primary care physician’s time [64].

However, it is too early to take the results of the medical tool as gospel. For current cervical radiotherapy delineation tools, only 90% of the output is acceptable for clinical use [6].

Therefore, The remainder can potentially cause more harm than good if not checked properly. For example, the overlap of a PTV with an organ-at-risk may invoke a cascade of adverse effects for the patient. The remaining 10% of outputs may score incorrectly because the model uses a single modality, but physicians may base their final judgement on a multivariate analysis. Therefore, clinicians should use the tool as a second opinion rather than a primary source of information. Otherwise, an ethical dilemma of establishing the responsible party for incorrect decisions made by DL tools should also be determined [65].

Clinicians can fall into the trap of automation bias as AI becomes more commonplace in clinical environments [66]. However, many models of this age codify the existing bias in common cases, which often will fail those patients who do not fit the majority's expectations.

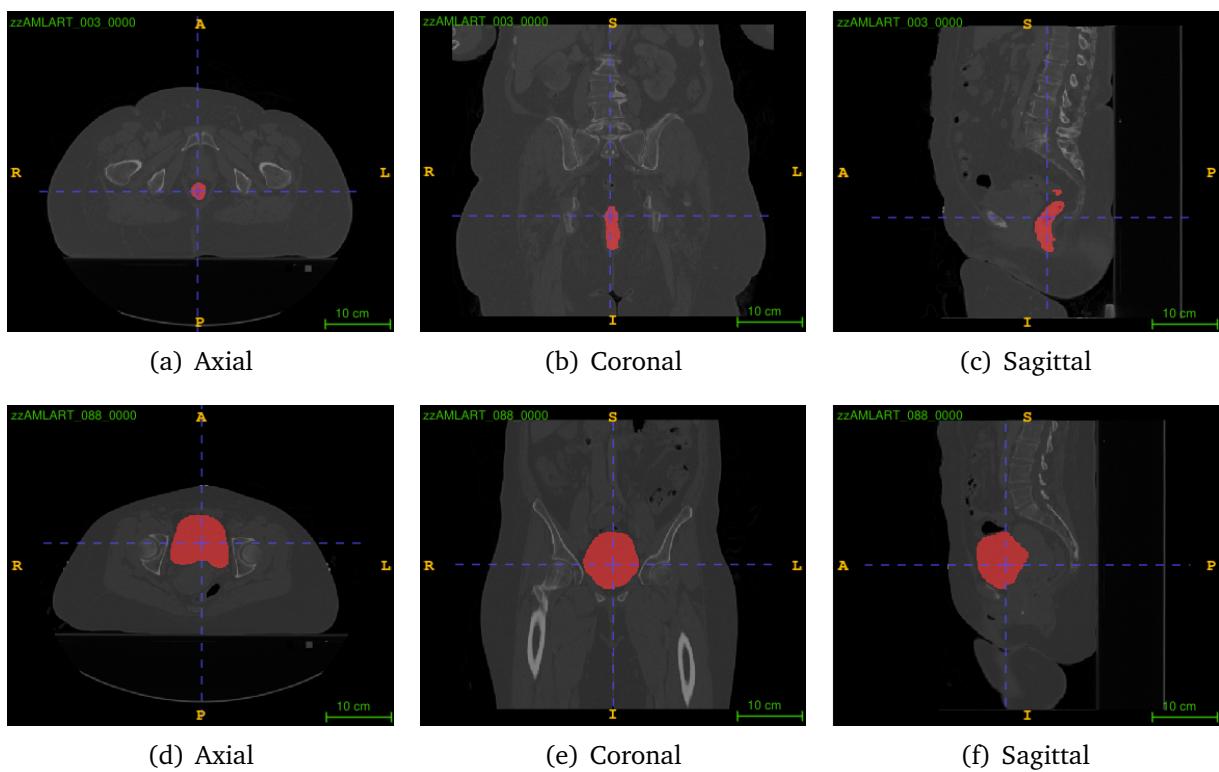
Therefore, before integrating tools into workflows, a committee must establish the degree of supervision required from physicians if this tool is to be used in practice. Currently, oncologists will be required to reverse-engineer the 'black box' results to verify why a decision has been made.

# Appendix A

## Appendix

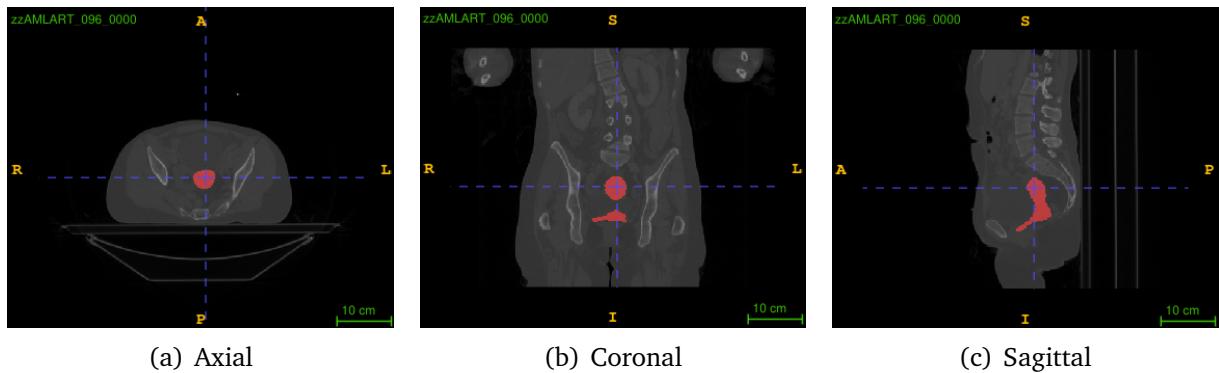
### A.1 Ground Truth Organ Delineations

#### A.1.1 Organs At Risk

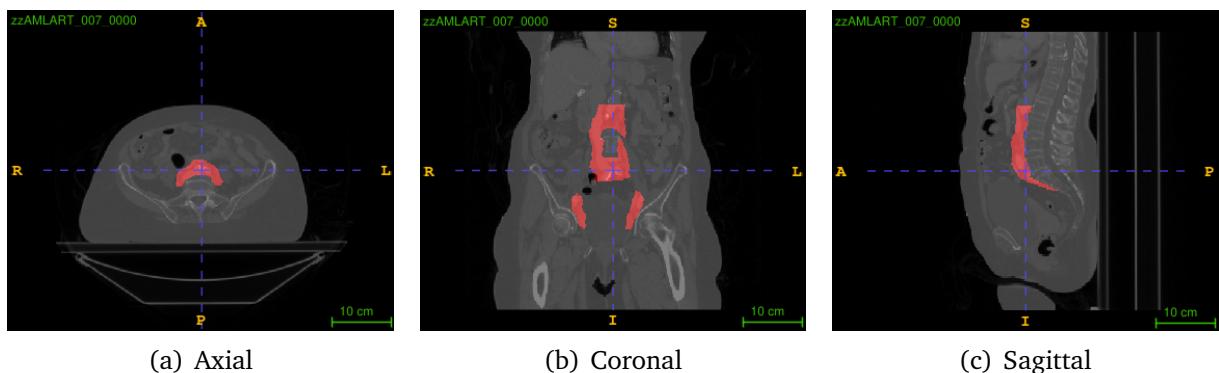


**Figure A.1:** Views of the segmentation (in red) of the Anorectum (A.1(a)-A.1(c)) and the segmentation (in red) of the Bladder (A.1(d)-A.1(f)) of an arbitrary patient

### A.1.2 CTV volumes

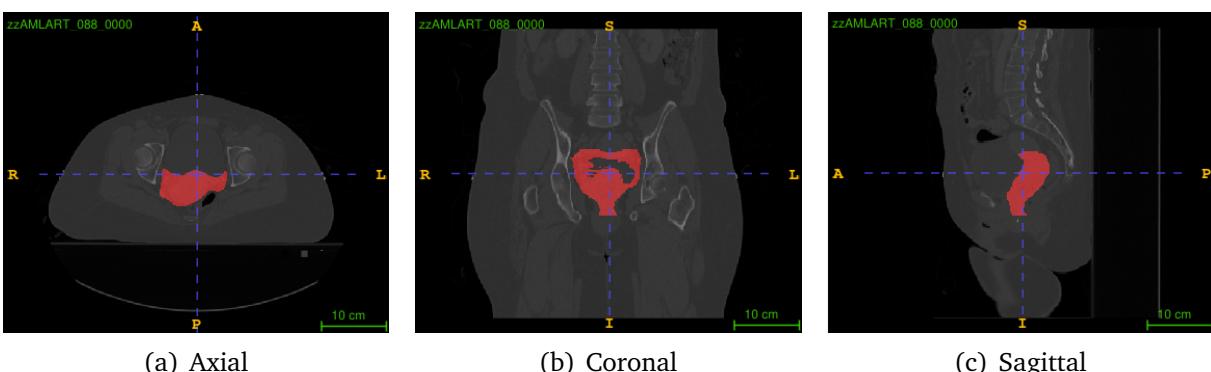


**Figure A.2:** Views of a segmented (in red) CTVp of an arbitrary patient

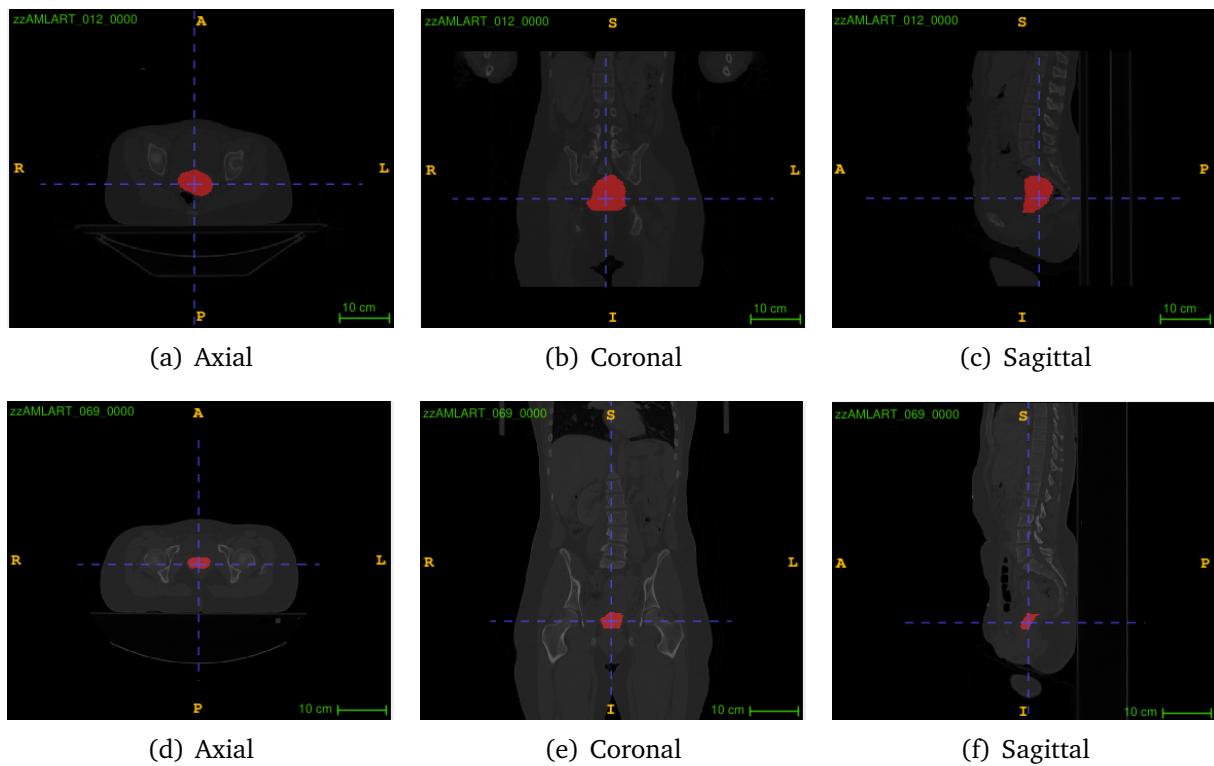


**Figure A.3:** Views of a segmented (in red) CTVn of an arbitrary patient

### A.1.3 Parametrium, Uteurs, and Vagina



**Figure A.4:** Views of a segmented (in red) Parametrium of an arbitrary patient



**Figure A.5:** Views of the segmentation (in red) of the Uterus (A.5(a)-A.5(c)) and the segmentation (in red) of the Vagina (A.5(d)-A.5(f)) of an arbitrary patient

## A.2 Metrics

### A.2.1 Total Segmentator

**Table A.1:** Added Path Length scores across each anatomy

Anatomy	nnUNet baseline			TotalSegmentator out-of-the-box			TotalSegmentator Fine-tuned		
	Mean	Std Dev	Median	Mean	Std Dev	Median	Mean	Std Dev	Median
Anorectum	1.06	1.96	0.45	-	-	-	0.66	1.02	0.31
Bladder	1.21	2.06	0.71	5.87	4.98	4.18	1.32	1.72	0.76
CTVn	3.89	3.01	3.07	-	-	-	4.02	4.01	2.65
CTVp	1.25	1.51	0.80	-	-	-	1.58	1.74	1.05
Parametrium	2.97	2.14	2.45	-	-	-	2.90	3.22	1.72
Uterus	1.11	1.17	0.80	-	-	-	1.51	1.59	0.93
Vagina	0.34	0.42	0.20	-	-	-	0.41	0.97	0.10

**Table A.2:** DICE scores across each anatomy

Anatomy	nnUNet baseline			TotalSegmentator out-of-the-box			TotalSegmentator Fine-tuned		
	Mean	Std Dev	Median	Mean	Std Dev	Median	Mean	Std Dev	Median
Anorectum	0.91	0.03	0.92	-	-	-	0.92	0.04	0.93
Bladder	0.94	0.06	0.97	0.90	0.13	0.94	0.95	0.10	0.97
CTVn	0.93	0.01	0.94	-	-	-	0.94	0.01	0.94
CTVp	0.94	0.01	0.94	-	-	-	0.93	0.02	0.94
Parametrium	0.93	0.01	0.93	-	-	-	0.93	0.04	0.94
Uterus	0.94	0.01	0.94	-	-	-	0.93	0.02	0.94
Vagina	0.89	0.04	0.90	-	-	-	0.86	0.10	0.90

**Table A.3:** Haussdorf scores across each anatomy

Anatomy	nnUNet baseline			TotalSegmentator out-of-the-box			TotalSegmentator Fine-tuned		
	Mean	Std Dev	Median	Mean	Std Dev	Median	Mean	Std Dev	Median
Anorectum	12.14	27.81	5.05	-	-	-	6.37	5.73	4.30
Bladder	77.16	71.94	96.79	8.26	8.35	5.39	15.66	37.98	3.74
CTVn	8.92	2.90	8.30	-	-	-	8.81	2.71	8.31
CTVp	8.88	26.86	5.92	-	-	-	7.33	7.68	6.40
Parametrium	11.28	19.53	8.06	-	-	-	9.85	15.19	7.42
Uterus	6.01	2.61	5.79	-	-	-	6.71	3.25	6.04
Vagina	6.75	21.72	4.12	-	-	-	5.61	4.09	4.12

**Table A.4:** Relative volume difference across each anatomy

Anatomy	nnUNet baseline			TotalSegmentator out-of-the-box			TotalSegmentator Fine-tuned		
	Mean	Std Dev	Median	Mean	Std Dev	Median	Mean	Std Dev	Median
Anorectum	0.04	0.06	0.03	-	-	-	-0.00	0.06	0.00
Bladder	-0.04	0.12	-0.02	-0.07	0.19	-0.03	0.01	0.21	0.00
CTVn	-0.01	0.03	-0.01	-	-	-	0.00	0.02	0.00
CTVp	-0.01	0.04	-0.00	-	-	-	-0.00	0.04	-0.00
Parametrium	0.01	0.03	0.01	-	-	-	0.00	0.06	0.01
Uterus	0.00	0.05	0.00	-	-	-	-0.00	0.05	-0.00
Vagina	0.11	0.09	0.09	-	-	-	-0.02	0.16	-0.00

**Table A.5:** Surface DSC across each anatomy

Anatomy	nnUnet baseline			TotalSegmentator out-of-the-box			TotalSegmentator Fine-tuned		
	Mean	Std Dev	Median	Mean	Std Dev	Median	Mean	Std Dev	Median
Anorectum	0.99	0.02	1.00	-	-	-	0.99	0.03	1.00
Bladder	0.97	0.06	1.00	0.95	0.11	0.99	0.98	0.10	1.00
CTVn	0.99	0.01	0.99	-	-	-	0.99	0.01	1.00
CTVp	0.99	0.01	0.99	-	-	-	0.99	0.01	0.99
Parametrium	0.99	0.01	0.99	-	-	-	0.98	0.04	1.00
Uterus	0.99	0.01	0.99	-	-	-	0.99	0.02	0.99
Vagina	0.99	0.01	1.00	-	-	-	0.98	0.06	1.00

Segmentation metrics for the Anorectum class TotalSegmentator analysis

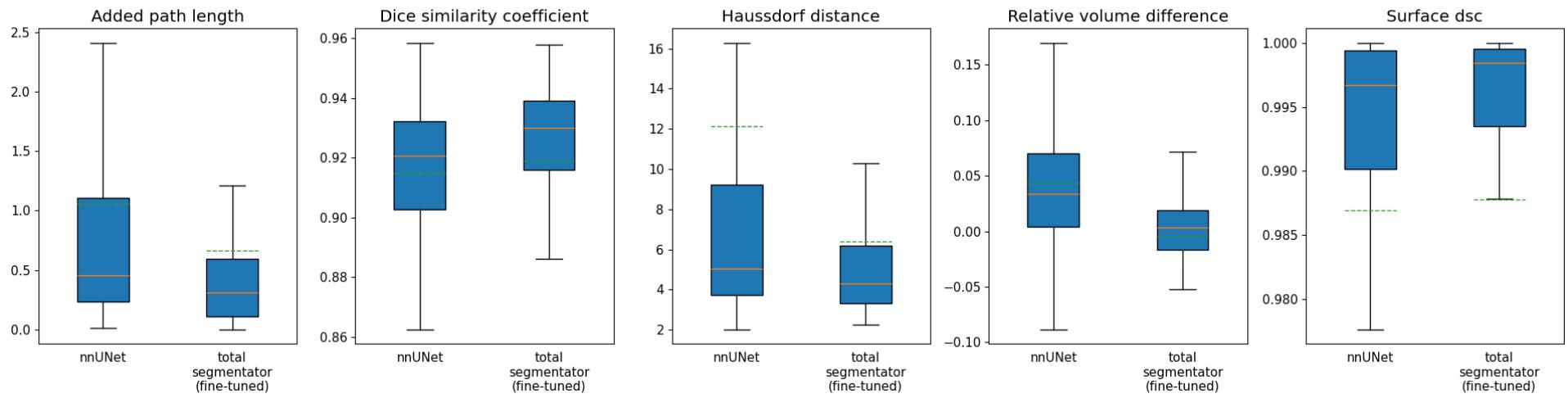


Figure A.6: Anorectum Metrics

Segmentation metrics for the Bladder class TotalSegmentator analysis

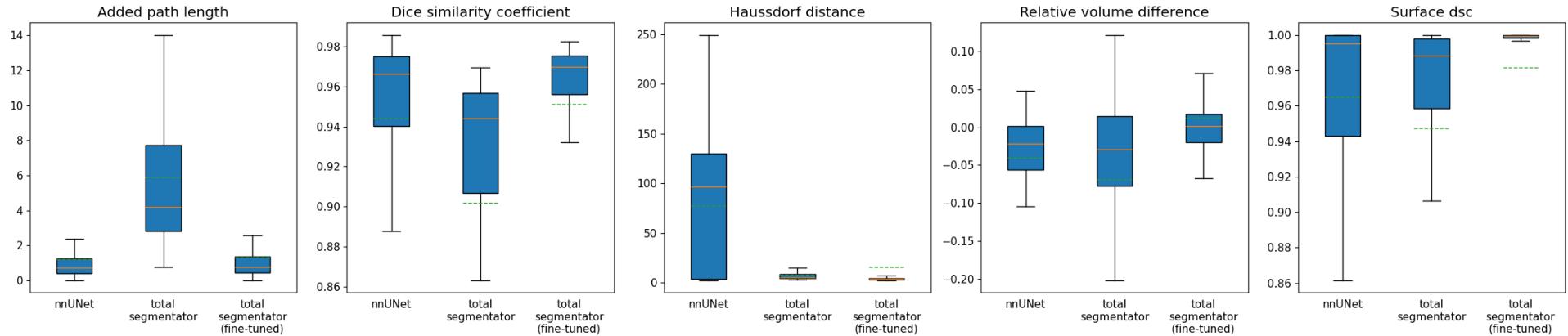


Figure A.7: Bladder Metrics

Segmentation metrics for the Ctvn class TotalSegmentator analysis

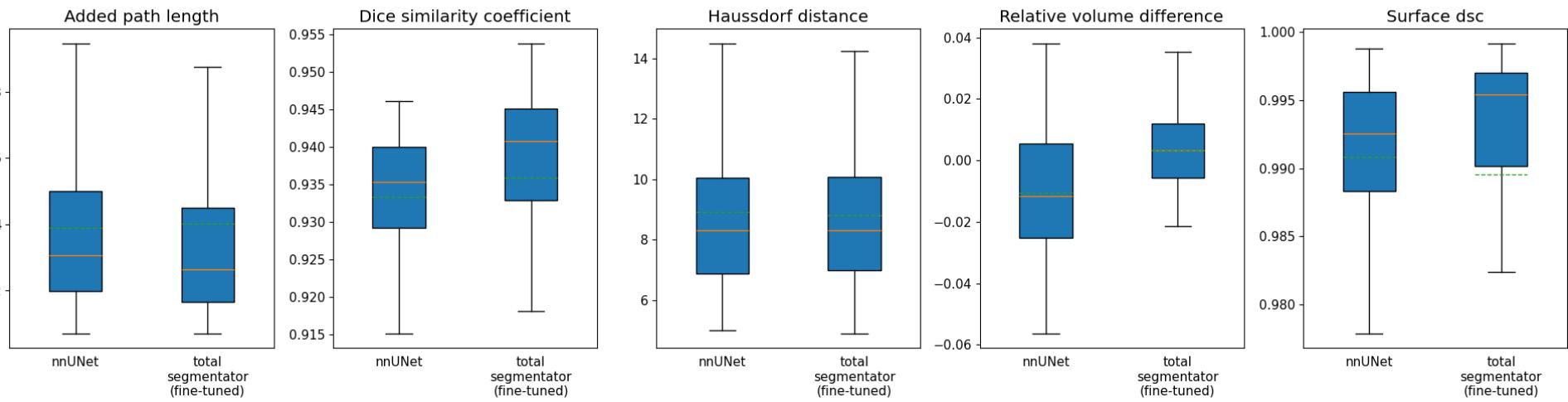


Figure A.8: CTVn Metrics

Segmentation metrics for the Ctvp class TotalSegmentator analysis

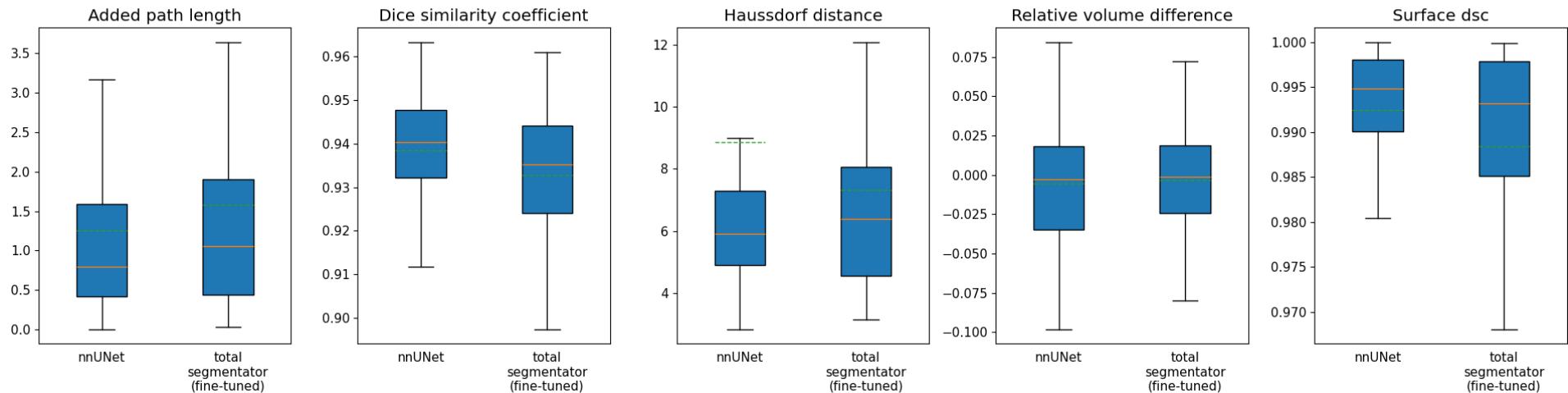


Figure A.9: CTVp Metrics

Segmentation metrics for the Parametrium class TotalSegmentator analysis

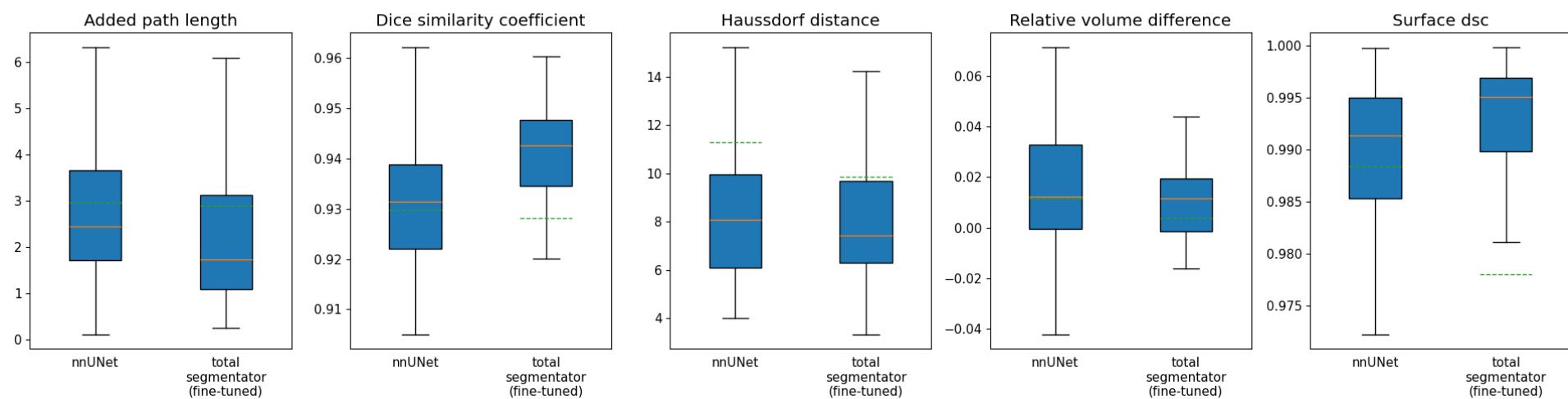


Figure A.10: Parametrium Metrics

Segmentation metrics for the Uterus class TotalSegmentator analysis

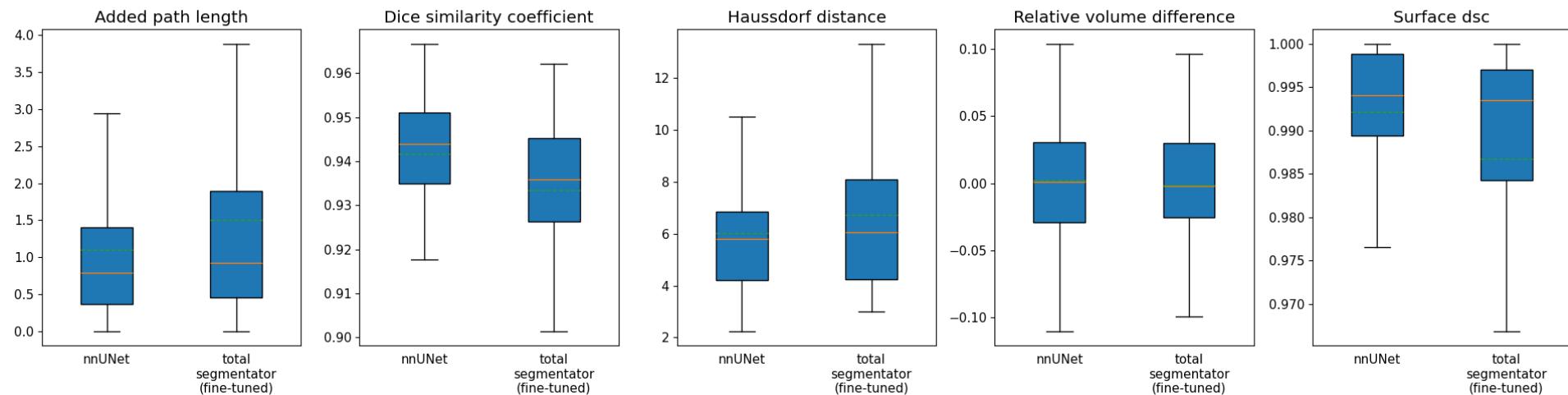


Figure A.11: Uterus Metrics

Segmentation metrics for the Vagina class TotalSegmentator analysis

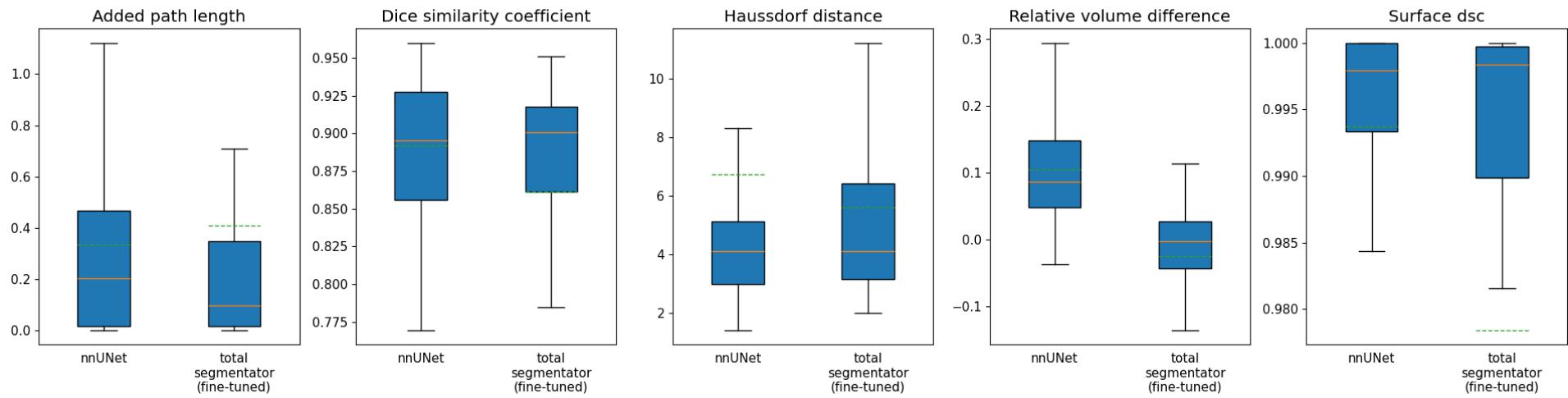


Figure A.12: Vagina Metrics

## A.2.2 Region Based

**Table A.6:** Added Path Length scores across each anatomy (TS = TotalSegmentator (fine-tuned), RB = Region Based, CL = Custom Loss)

Anatomy	nnUNet baseline			nnUNet RB			nnUNet RB CL			TS RB			TS RB CL		
	Mean	Std Dev	Median	Mean	Std Dev	Median	Mean	Std Dev	Median	Mean	Std Dev	Median	Mean	Std Dev	Median
Anorectum	1.06	1.96	0.45	0.82	0.92	0.50	1.19	3.75	0.37	1.05	1.34	0.52	1.14	3.96	0.29
Bladder	1.21	2.06	0.71	0.85	0.99	0.52	0.86	1.54	0.48	0.94	1.14	0.64	0.86	1.62	0.51
CTVn	3.89	3.01	3.07	6.90	4.40	5.60	7.09	5.75	5.51	7.68	4.22	6.45	6.28	5.65	5.03
CTVp	1.25	1.51	0.80	0.98	1.47	0.51	1.09	2.13	0.46	1.16	1.96	0.68	1.15	2.37	0.40
Parametrium	2.97	2.14	2.45	5.14	3.52	4.10	4.14	3.69	3.12	4.81	3.63	3.93	3.90	3.53	2.96
Uterus	1.11	1.17	0.80	0.84	1.15	0.45	0.80	1.28	0.38	0.89	1.55	0.45	0.86	1.54	0.37
Vagina	0.34	0.42	0.20	0.50	0.86	0.27	0.64	1.67	0.09	0.68	1.09	0.40	0.57	1.48	0.05

**Table A.7:** DICE scores across each anatomy (TS = TotalSegmentator (fine-tuned), RB = Region Based, CL = Custom Loss)

Anatomy	nnUNet baseline			nnUNet RB			nnUNet RB CL			TS RB			TS RB CL		
	Mean	Std Dev	Median	Mean	Std Dev	Median	Mean	Std Dev	Median	Mean	Std Dev	Median	Mean	Std Dev	Median
Anorectum	0.91	0.03	0.92	0.91	0.02	0.91	0.91	0.06	0.93	0.91	0.03	0.92	0.91	0.06	0.93
Bladder	0.94	0.06	0.97	0.97	0.02	0.97	0.97	0.02	0.97	0.96	0.02	0.97	0.97	0.02	0.97
CTVn	0.93	0.01	0.94	0.91	0.01	0.92	0.92	0.01	0.92	0.91	0.01	0.92	0.92	0.01	0.93
CTVp	0.94	0.01	0.94	0.94	0.02	0.95	0.94	0.03	0.95	0.94	0.02	0.94	0.94	0.02	0.95
Parametrium	0.93	0.01	0.93	0.91	0.02	0.91	0.91	0.05	0.93	0.91	0.03	0.91	0.91	0.05	0.93
Uterus	0.94	0.01	0.94	0.94	0.03	0.95	0.94	0.04	0.95	0.94	0.03	0.95	0.95	0.04	0.95
Vagina	0.89	0.04	0.90	0.87	0.06	0.88	0.86	0.13	0.91	0.85	0.08	0.87	0.87	0.12	0.92

**Table A.8:** Haussdorf scores across each anatomy (TS = TotalSegmentator (fine-tuned), RB = Region Based, CL = Custom Loss)

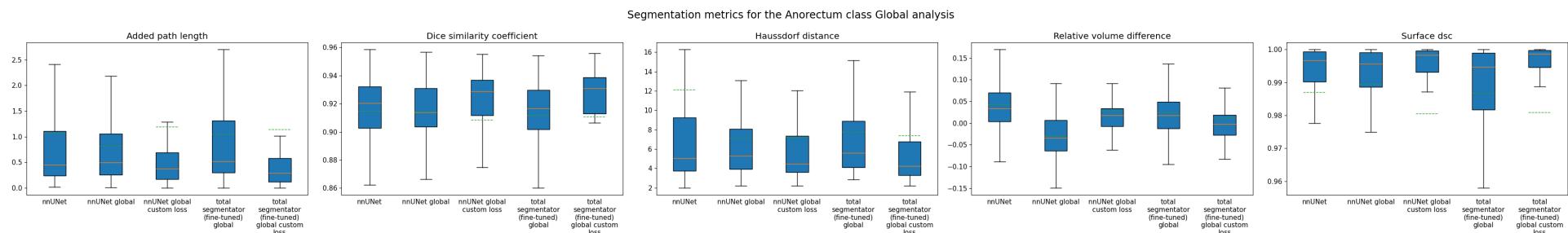
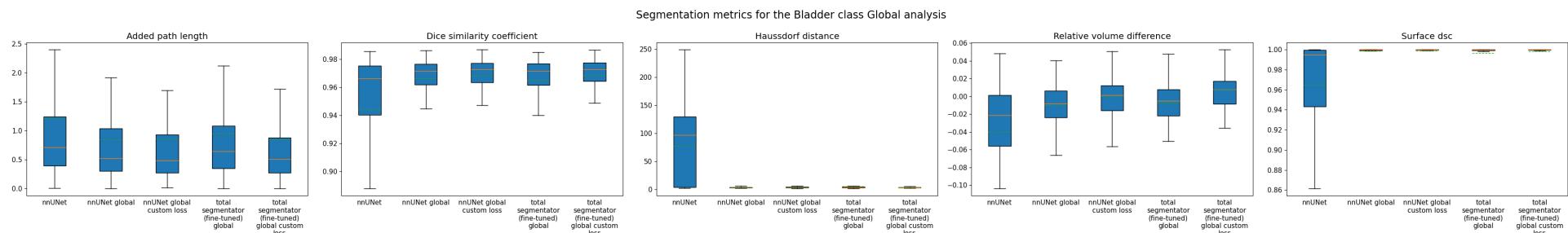
Anatomy	nnUNet baseline			nnUNet RB			nnUNet RB CL			TS RB			TS RB CL		
	Mean	Std Dev	Median	Mean	Std Dev	Median	Mean	Std Dev	Median	Mean	Std Dev	Median	Mean	Std Dev	Median
Anorectum	12.14	27.81	5.05	7.13	5.14	5.29	7.28	7.29	4.47	7.76	5.51	5.61	7.40	8.11	4.24
Bladder	77.16	71.94	96.79	3.98	3.40	3.32	3.77	2.08	3.32	5.12	10.42	3.46	3.70	2.02	3.16
CTVn	8.92	2.90	8.30	10.04	2.73	9.49	10.20	3.08	9.49	10.31	2.79	9.85	9.78	2.83	9.16
CTVp	8.88	26.86	5.92	5.54	2.25	5.00	5.88	3.22	5.10	5.63	2.42	5.00	6.17	3.12	5.43
Parametrium	11.28	19.53	8.06	12.24	15.14	10.30	11.33	15.21	9.08	11.47	15.21	9.57	10.85	15.23	8.54
Uterus	6.01	2.61	5.79	5.69	2.44	5.00	5.77	3.27	4.69	5.77	2.89	5.00	5.95	3.19	5.00
Vagina	6.75	21.72	4.12	5.34	4.10	4.24	4.97	3.52	4.00	6.09	4.33	5.00	5.08	3.67	4.00

**Table A.9:** Relative Volume Difference across each anatomy (TS = TotalSegmentator (fine-tuned), RB = Region Based, CL = Custom Loss)

Anatomy	nnUNet baseline			nnUNet RB			nnUNet RB CL			TS RB			TS RB CL		
	Mean	Std Dev	Median	Mean	Std Dev	Median	Mean	Std Dev	Median	Mean	Std Dev	Median	Mean	Std Dev	Median
Anorectum	0.04	0.06	0.03	-0.03	0.06	-0.03	0.03	0.12	0.02	0.02	0.06	0.02	0.01	0.11	-0.00
Bladder	-0.04	0.12	-0.02	-0.01	0.03	-0.01	0.00	0.03	0.00	-0.01	0.04	-0.00	0.01	0.03	0.01
CTVn	-0.01	0.03	-0.01	-0.03	0.04	-0.03	-0.01	0.03	-0.01	0.01	0.04	0.01	-0.00	0.03	0.00
CTVp	-0.01	0.04	-0.00	0.02	0.03	0.01	-0.00	0.05	0.00	-0.01	0.04	-0.01	0.02	0.04	0.02
Parametrium	0.01	0.03	0.01	0.04	0.06	0.03	-0.01	0.10	0.01	0.00	0.07	-0.00	-0.01	0.10	0.00
Uterus	0.00	0.05	0.00	0.01	0.06	0.01	-0.01	0.08	-0.00	-0.02	0.07	-0.02	0.01	0.07	0.02
Vagina	0.11	0.09	0.09	0.07	0.13	0.03	0.05	0.15	0.01	0.08	0.18	0.05	0.04	0.13	0.02

**Table A.10:** Surface DSC across each anatomy (TS = TotalSegmentator (fine-tuned), RB = Region Based, CL = Custom Loss)

Anatomy	nnUNet baseline			nnUNet RB			nnUNet RB CL			TS RB			TS RB CL		
	Mean	Std Dev	Median	Mean	Std Dev	Median	Mean	Std Dev	Median	Mean	Std Dev	Median	Mean	Std Dev	Median
Anorectum	0.99	0.02	1.00	0.99	0.02	1.00	0.98	0.05	1.00	0.99	0.02	0.99	0.98	0.06	1.00
Bladder	0.97	0.06	1.00	1.00	0.00	1.00	1.00	0.00	1.00	1.00	0.02	1.00	0.01	1.00	1.00
CTVn	0.99	0.01	0.99	0.98	0.01	0.98	0.98	0.02	0.98	0.98	0.01	0.98	0.98	0.02	0.99
CTVp	0.99	0.01	0.99	0.99	0.01	1.00	0.99	0.03	1.00	0.99	0.02	1.00	0.99	0.02	1.00
Parametrium	0.99	0.01	0.99	0.97	0.04	0.98	0.97	0.05	0.99	0.97	0.05	0.98	0.97	0.05	0.99
Uterus	0.99	0.01	0.99	0.99	0.02	1.00	0.99	0.03	1.00	0.99	0.03	1.00	0.99	0.03	1.00
Vagina	0.99	0.01	1.00	0.99	0.04	1.00	0.97	0.08	1.00	0.98	0.06	0.99	0.98	0.07	1.00

**Figure A.13:** Anorectum Metrics**Figure A.14:** Bladder Metrics

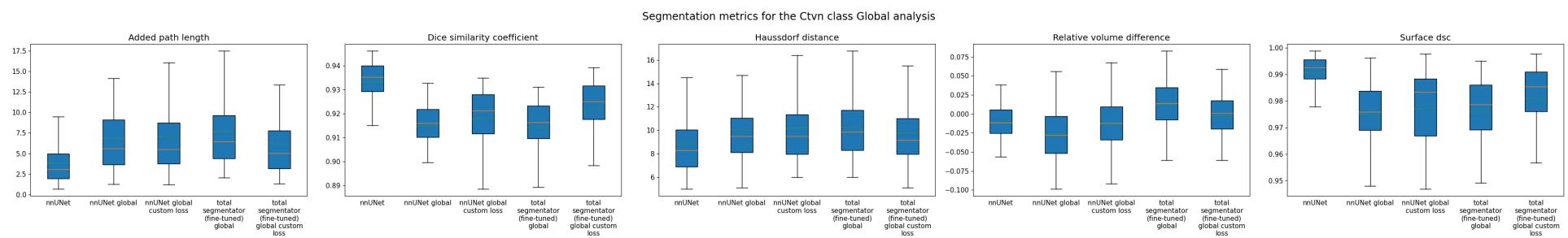


Figure A.15: CTVn Metrics

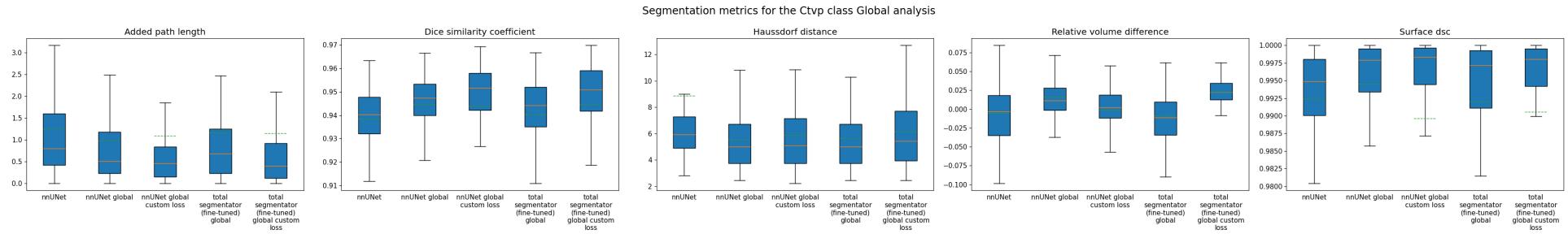


Figure A.16: CTVp Metrics

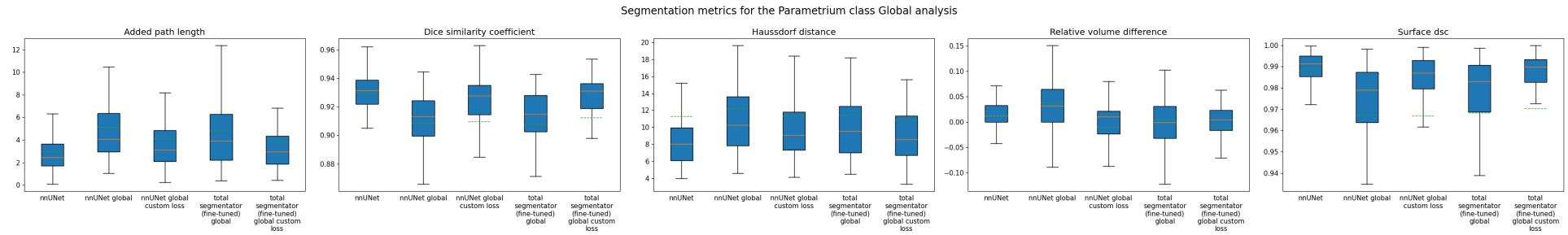


Figure A.17: Parametrium Metrics

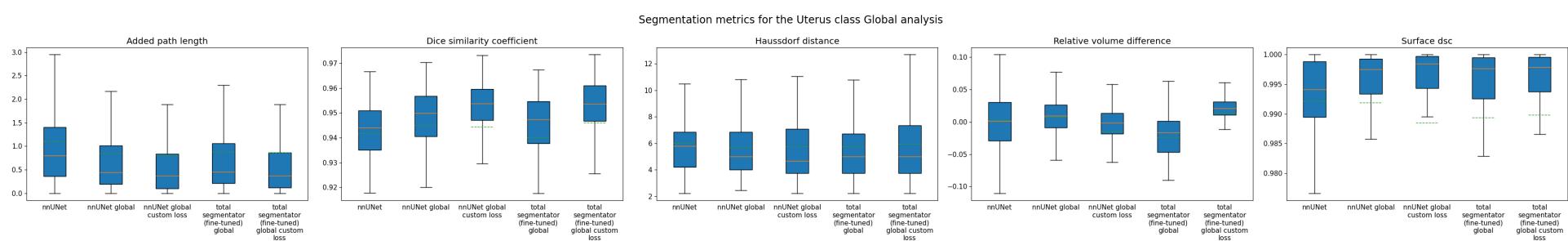


Figure A.18: Uterus Metrics

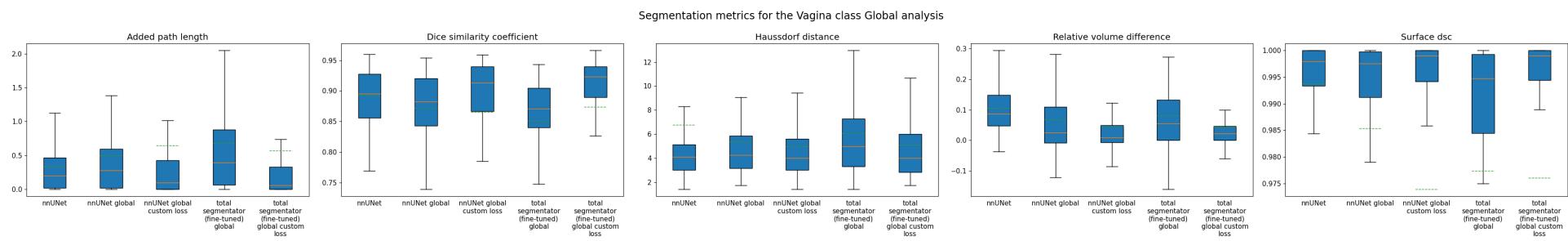


Figure A.19: Vagina Metrics

### A.2.3 UniverSeg Metrics

**Table A.11:** Added Path Length scores across each anatomy

Anatomy	nnUnet baseline			UniverSeg out-of-the-box			Universeg Fine-tuned		
	Mean	Std Dev	Median	Mean	Std Dev	Median	Mean	Std Dev	Median
Anorectum	1.06	1.96	0.45	4.15	9.72	0.00	2.65	6.11	0.00
Bladder	1.21	2.06	0.71	1.37	4.30	0.00	0.61	3.11	0.00
CTVn	3.89	3.01	3.07	9.45	15.54	2.00	7.80	14.94	0.00
CTVp	1.25	1.51	0.80	2.78	6.97	0.00	1.29	3.93	0.00
Parametrium	2.97	2.14	2.45	6.94	9.89	3.00	3.87	7.11	0.00
Uterus	1.11	1.17	0.80	2.24	6.27	0.00	0.65	2.64	0.00
Vagina	0.34	0.42	0.20	1.59	4.67	0.00	0.23	1.28	0.00

**Table A.12:** DICE scores across each anatomy

Anatomy	nnUnet baseline			UniverSeg out-of-the-box			Universeg Fine-tuned		
	Mean	Std Dev	Median	Mean	Std Dev	Median	Mean	Std Dev	Median
Anorectum	0.91	0.03	0.92	0.55	0.23	0.59	0.68	0.17	0.73
Bladder	0.94	0.06	0.97	0.81	0.23	0.91	0.89	0.15	0.94
CTVn	0.93	0.01	0.94	0.63	0.20	0.69	0.74	0.15	0.78
CTVp	0.94	0.01	0.94	0.70	0.22	0.78	0.83	0.14	0.88
Parametrium	0.93	0.01	0.93	0.62	0.21	0.67	0.71	0.18	0.77
Uterus	0.94	0.01	0.94	0.74	0.21	0.81	0.85	0.14	0.89
Vagina	0.89	0.04	0.90	0.52	0.21	0.55	0.72	0.15	0.75

**Table A.13:** Haussdorf scores across each anatomy

Anatomy	nnUnet baseline			UniverSeg out-of-the-box			Universeg Fine-tuned		
	Mean	Std Dev	Median	Mean	Std Dev	Median	Mean	Std Dev	Median
Anorectum	12.14	27.81	5.05	7.11	5.67	5.39	6.16	5.42	4.24
Bladder	77.16	71.94	96.79	4.17	4.87	2.24	2.38	2.72	1.41
CTVn	8.92	2.90	8.30	13.97	14.28	7.62	7.74	8.08	5.00
CTVp	8.88	26.86	5.92	6.77	6.20	4.47	3.67	3.90	2.24
Parametrium	11.28	19.53	8.06	7.23	4.92	6.00	5.70	4.50	4.24
Uterus	6.01	2.61	5.79	5.95	5.55	4.00	3.11	3.04	2.00
Vagina	6.75	21.72	4.12	4.68	3.08	4.00	2.53	1.80	2.00

**Table A.14:** Relative volume difference across each anatomy

Anatomy	nnUnet baseline			UniverSeg out-of-the-box			Universeg Fine-tuned		
	Mean	Std Dev	Median	Mean	Std Dev	Median	Mean	Std Dev	Median
Anorectum	0.04	0.06	0.03	-0.33	0.60	-0.35	-0.13	0.44	-0.10
Bladder	-0.04	0.12	-0.02	-0.24	0.43	-0.10	-0.04	0.26	-0.03
CTVn	-0.01	0.03	-0.01	-0.35	0.44	-0.29	-0.11	0.35	-0.08
CTVp	-0.01	0.04	-0.00	-0.28	0.47	-0.19	-0.07	0.29	-0.03
Parametrium	0.01	0.03	0.01	-0.33	0.49	-0.28	-0.10	0.44	-0.03
Uterus	0.00	0.05	0.00	-0.25	0.44	-0.16	-0.09	0.29	-0.04
Vagina	0.11	0.09	0.09	-0.41	0.51	-0.46	-0.17	0.36	-0.14

**Table A.15:** Surface DSC across each anatomy

Anatomy	nnUnet baseline			UniverSeg out-of-the-box			Universeg Fine-tuned		
	Mean	Std Dev	Median	Mean	Std Dev	Median	Mean	Std Dev	Median
Anorectum	0.99	0.02	1.00	0.82	0.21	0.88	0.90	0.14	0.96
Bladder	0.97	0.06	1.00	0.92	0.19	1.00	0.97	0.10	1.00
CTVn	0.99	0.01	0.99	0.82	0.20	0.88	0.91	0.12	0.96
CTVp	0.99	0.01	0.99	0.86	0.20	0.95	0.96	0.10	1.00
Parametrium	0.99	0.01	0.99	0.81	0.20	0.86	0.89	0.15	0.95
Uterus	0.99	0.01	0.99	0.87	0.20	0.97	0.96	0.11	1.00
Vagina	0.99	0.01	1.00	0.87	0.19	0.95	0.98	0.07	1.00

Segmentation metrics for the Anorectum class UniverSeg analysis

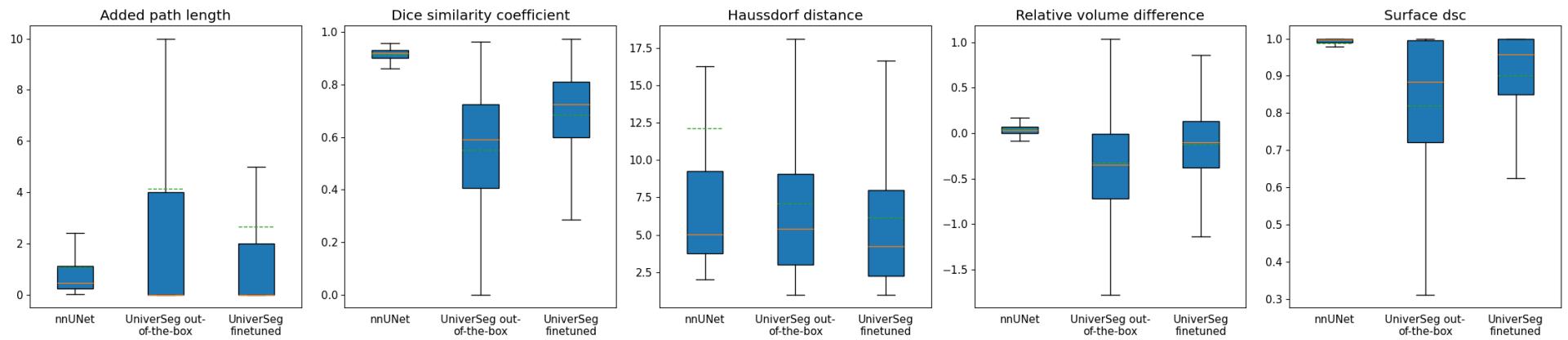


Figure A.20: Anorectum Metrics

Segmentation metrics for the Bladder class UniverSeg analysis

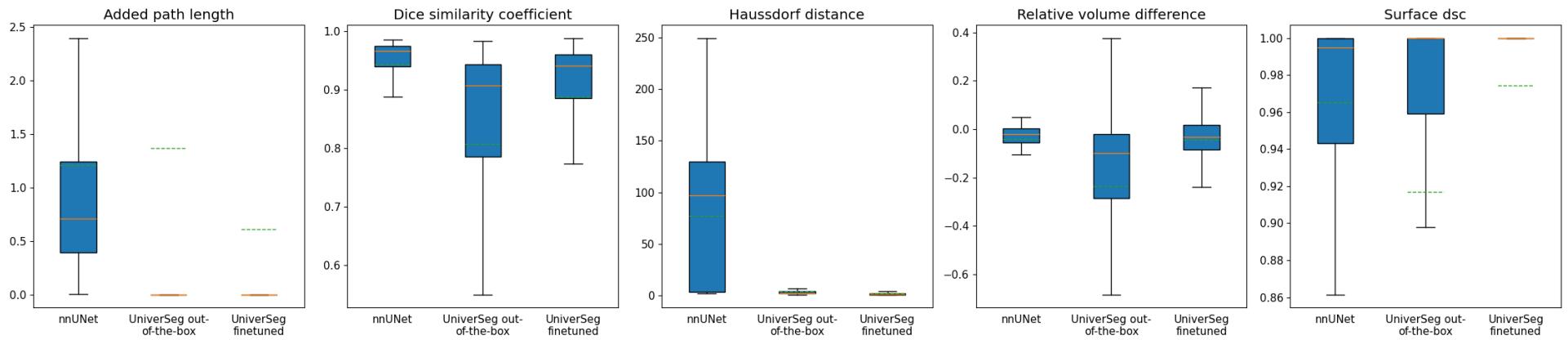


Figure A.21: Bladder Metrics

Segmentation metrics for the Ctvn class UniverSeg analysis

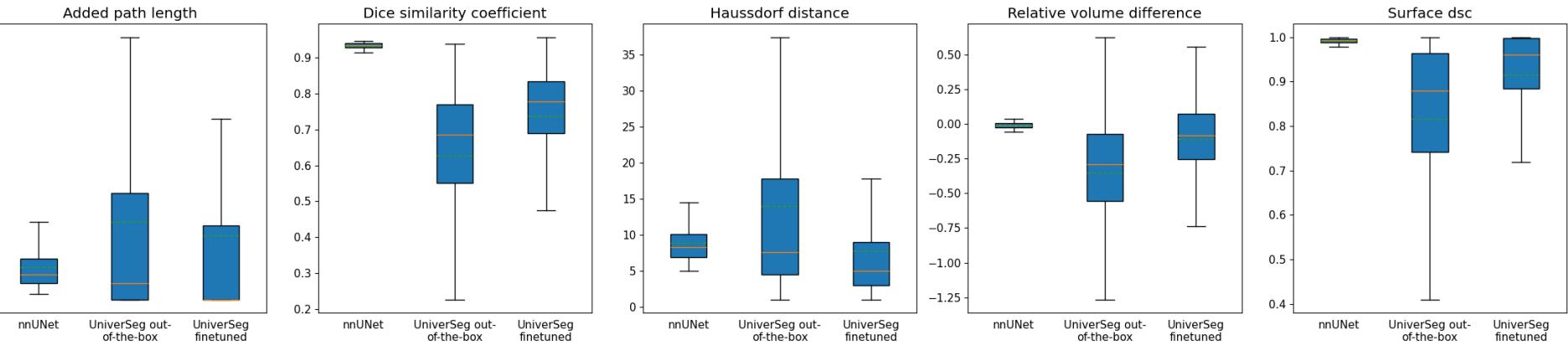


Figure A.22: CTvn Metrics

Segmentation metrics for the Ctvp class UniverSeg analysis

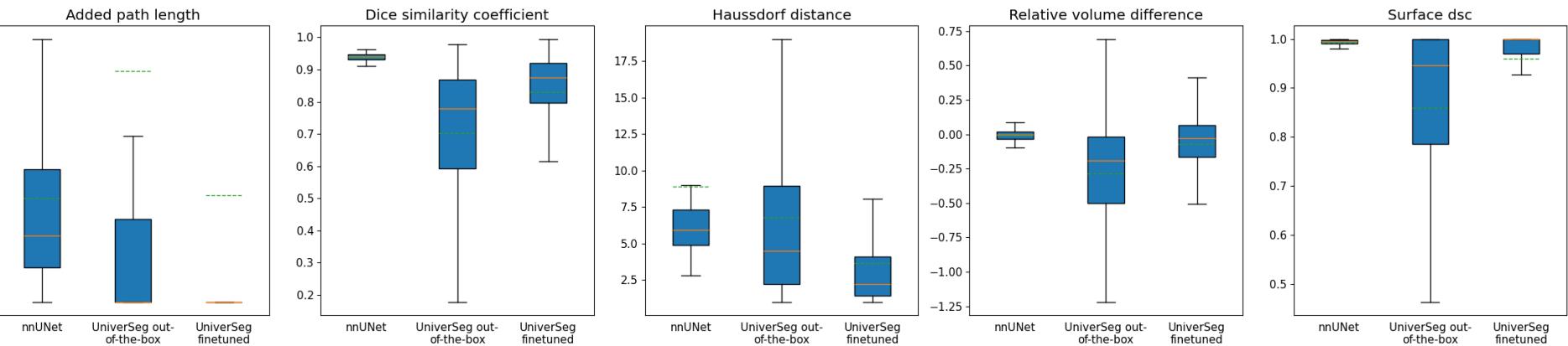


Figure A.23: CTvp Metrics

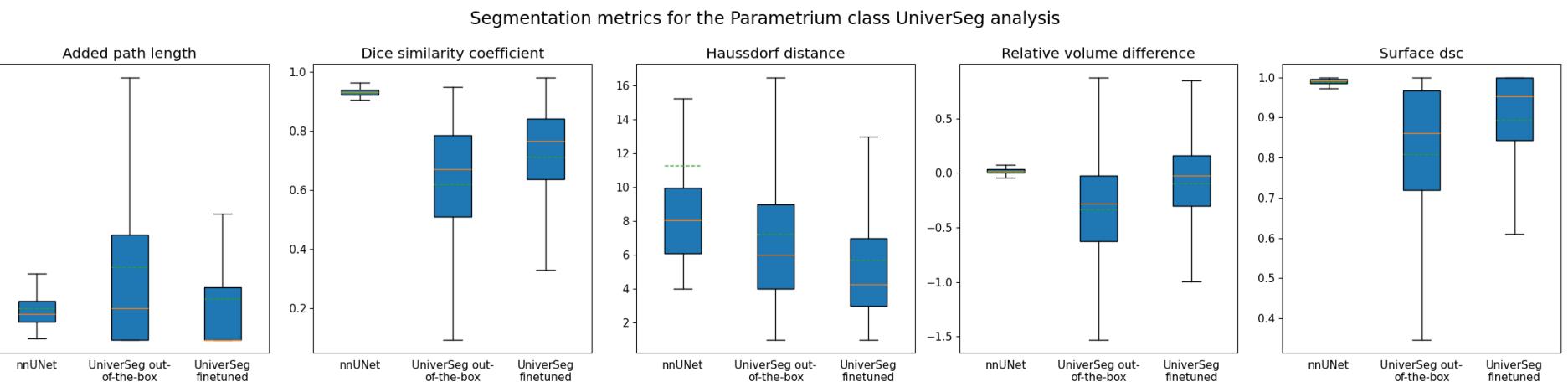


Figure A.24: Parametrium Metrics

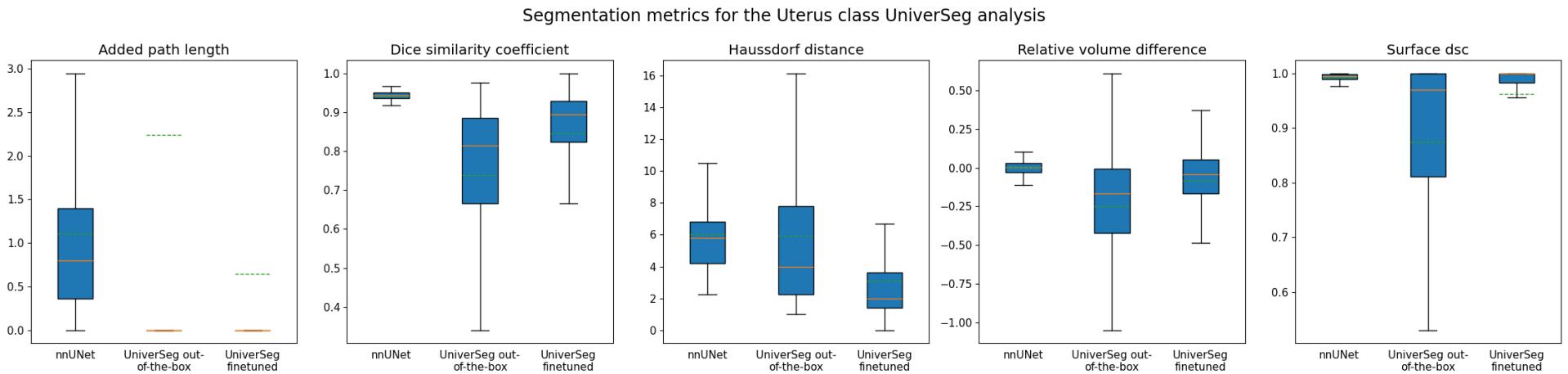


Figure A.25: Uterus Metrics

Segmentation metrics for the Vagina class UniverSeg analysis

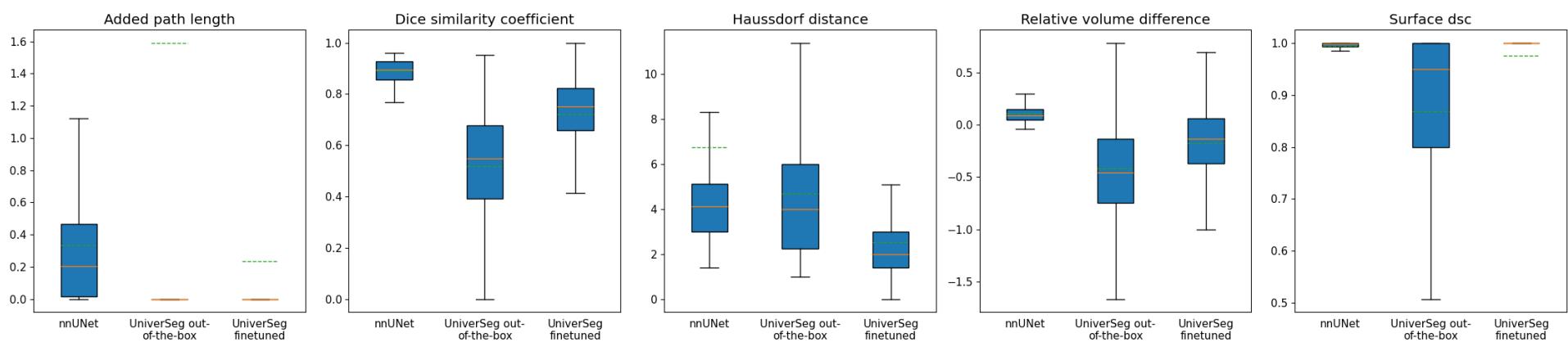


Figure A.26: Vagina Metrics

### A.2.4 MedSAM Box Prompt Metrics

**Table A.16:** Added Path Length scores across each anatomy

Anatomy	nnUnet baseline			MedSAM out-of-the-box			MedSAM Fine-tuned		
	Mean	Std Dev	Median	Mean	Std Dev	Median	Mean	Std Dev	Median
Anorectum	1.06	1.96	0.45	23.98	26.87	15.00	6.94	11.51	1.00
Bladder	1.21	2.06	0.71	13.88	13.99	10.00	5.46	8.52	2.00
CTVn	3.89	3.01	3.07	115.82	74.00	102.00	29.49	36.71	17.00
CTVp	1.25	1.51	0.80	25.73	22.11	20.00	9.86	12.95	5.00
Parametrium	2.97	2.14	2.45	61.40	33.76	57.00	21.80	20.76	16.00
Uterus	1.11	1.17	0.80	22.75	20.33	18.00	8.49	10.85	4.00
Vagina	0.34	0.42	0.20	19.05	10.79	17.00	5.19	6.90	2.00

**Table A.17:** DICE scores across each anatomy

Anatomy	nnUnet baseline			MedSAM out-of-the-box			MedSAM Fine-tuned		
	Mean	Std Dev	Median	Mean	Std Dev	Median	Mean	Std Dev	Median
Anorectum	0.91	0.03	0.92	0.78	0.14	0.81	0.91	0.05	0.92
Bladder	0.94	0.06	0.97	0.92	0.07	0.94	0.95	0.05	0.97
CTVn	0.93	0.01	0.94	0.52	0.13	0.53	0.89	0.05	0.90
CTVp	0.94	0.01	0.94	0.82	0.12	0.85	0.91	0.06	0.92
Parametrium	0.93	0.01	0.93	0.66	0.14	0.68	0.87	0.07	0.88
Uterus	0.94	0.01	0.94	0.85	0.08	0.87	0.92	0.05	0.93
Vagina	0.89	0.04	0.90	0.65	0.14	0.67	0.83	0.07	0.85

**Table A.18:** Haussdorf Distance across each anatomy

Anatomy	nnUnet baseline			MedSAM out-of-the-box			MedSAM Fine-tuned		
	Mean	Std Dev	Median	Mean	Std Dev	Median	Mean	Std Dev	Median
Anorectum	12.14	27.81	5.05	4.83	3.35	3.61	2.36	1.61	2.00
Bladder	77.16	71.94	96.79	2.96	1.60	2.24	2.82	7.93	2.00
CTVn	8.92	2.90	8.30	12.24	5.44	10.77	4.34	3.24	3.61
CTVp	8.88	26.86	5.92	5.38	3.70	4.24	2.89	1.83	2.24
Parametrium	11.28	19.53	8.06	8.92	3.60	8.49	4.30	2.63	3.61
Uterus	6.01	2.61	5.79	4.79	3.08	4.00	3.16	6.11	2.24
Vagina	6.75	21.72	4.12	4.81	1.60	5.00	2.48	1.35	2.24

**Table A.19:** Relative volume difference across each anatomy

Anatomy	nnUnet baseline			MedSAM out-of-the-box			MedSAM Fine-tuned		
	Mean	Std Dev	Median	Mean	Std Dev	Median	Mean	Std Dev	Median
Anorectum	0.04	0.06	0.03	0.04	0.29	0.02	-0.00	0.11	0.01
Bladder	-0.04	0.12	-0.02	-0.05	0.12	-0.04	-0.03	0.08	-0.01
CTVn	-0.01	0.03	-0.01	0.33	0.50	0.37	-0.06	0.10	-0.05
CTVp	-0.01	0.04	-0.00	0.05	0.22	0.04	-0.02	0.10	-0.01
Parametrium	0.01	0.03	0.01	0.31	0.33	0.32	-0.05	0.14	-0.03
Uterus	0.00	0.05	0.00	0.09	0.19	0.07	-0.02	0.09	-0.01
Vagina	0.11	0.09	0.09	0.13	0.36	0.11	-0.03	0.18	-0.02

**Table A.20:** Surface DSC across each anatomy

Anatomy	nnUnet baseline			MedSAM out-of-the-box			MedSAM Fine-tuned		
	Mean	Std Dev	Median	Mean	Std Dev	Median	Mean	Std Dev	Median
Anorectum	0.99	0.02	1.00	0.35	0.15	0.33	0.58	0.15	0.58
Bladder	0.97	0.06	1.00	0.44	0.13	0.44	0.59	0.12	0.60
CTVn	0.99	0.01	0.99	0.12	0.06	0.11	0.48	0.13	0.47
CTVp	0.99	0.01	0.99	0.35	0.13	0.35	0.53	0.14	0.52
Parametrium	0.99	0.01	0.99	0.19	0.09	0.18	0.41	0.12	0.41
Uterus	0.99	0.01	0.99	0.37	0.14	0.36	0.54	0.14	0.53
Vagina	0.99	0.01	1.00	0.29	0.12	0.28	0.51	0.14	0.52

Segmentation metrics for the Anorectum class MedSAM analysis

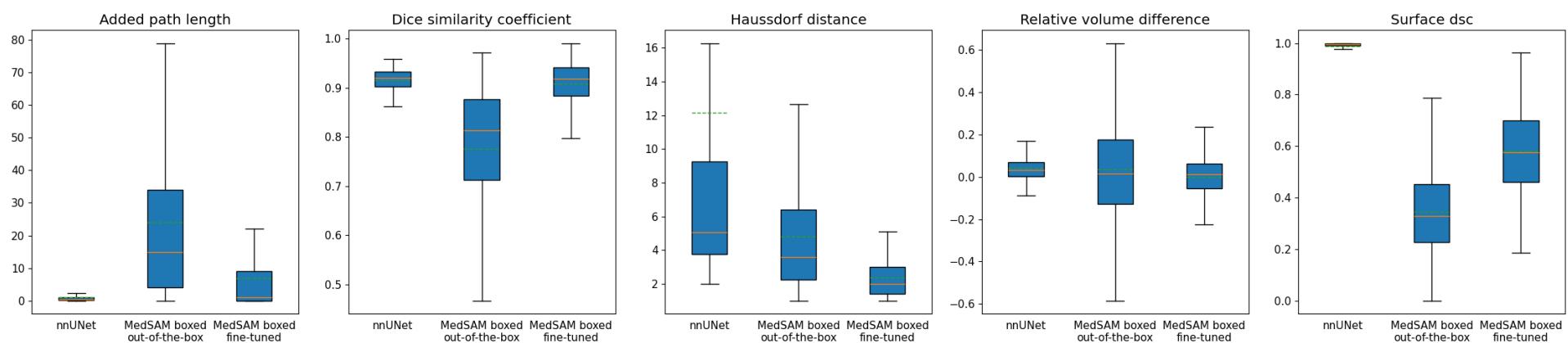


Figure A.27: Anorectum Metrics

Segmentation metrics for the Bladder class MedSAM analysis

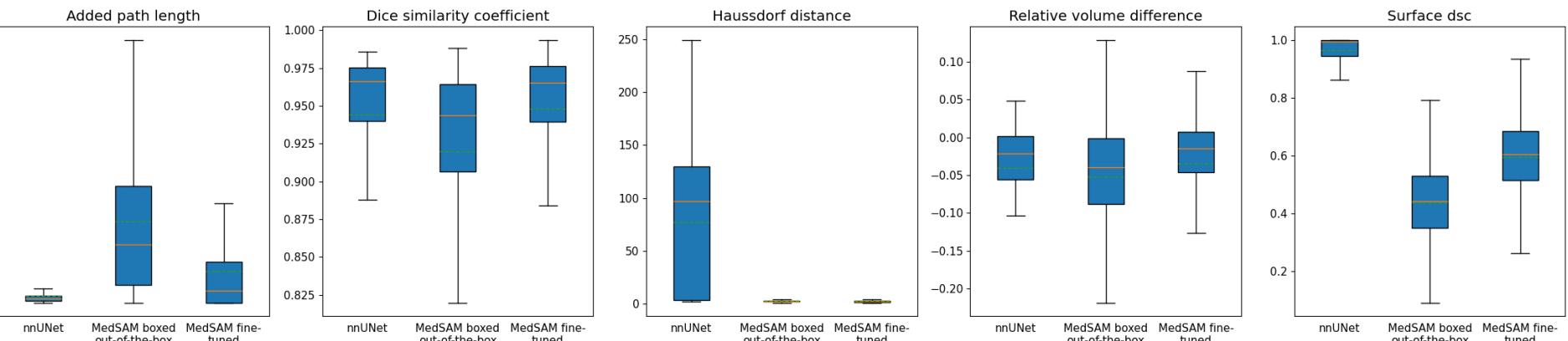


Figure A.28: Bladder Metrics

Segmentation metrics for the Ctvn class MedSAM analysis

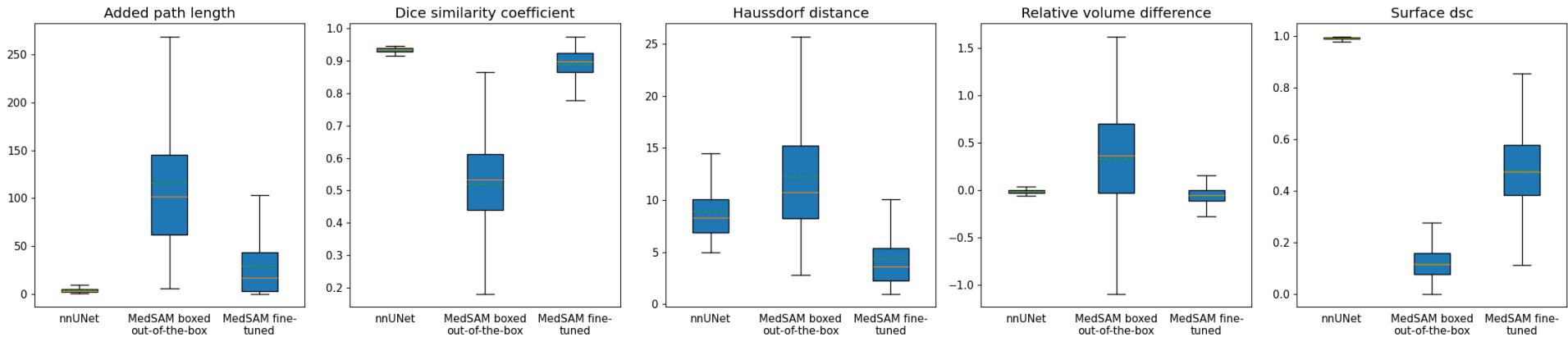


Figure A.29: CTVn Metrics

Segmentation metrics for the Ctvp class MedSAM analysis

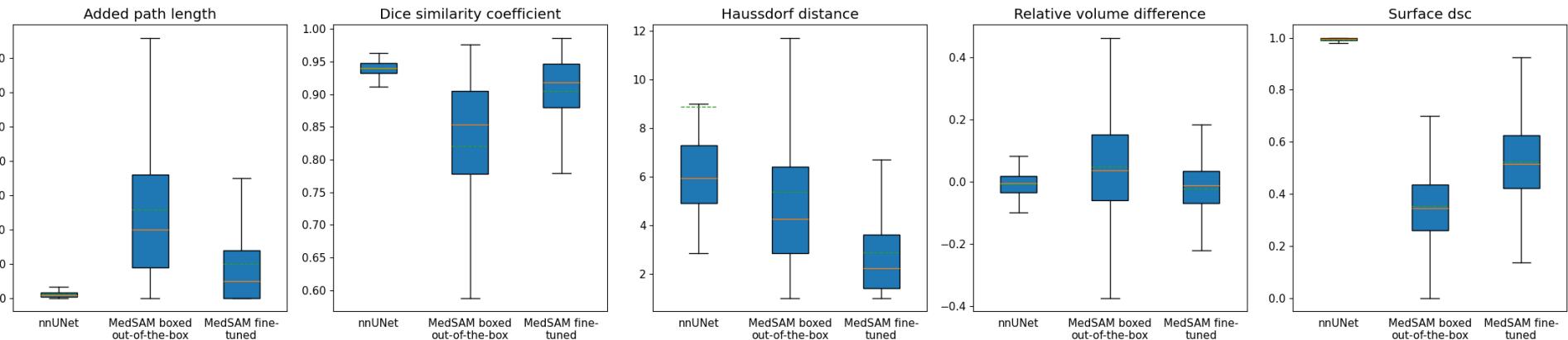


Figure A.30: CTVp Metrics

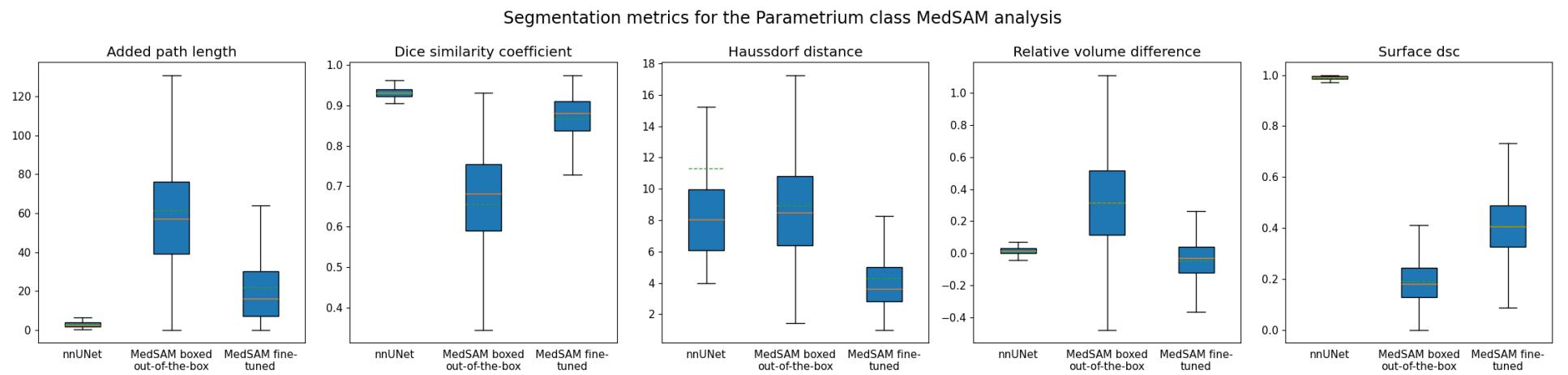


Figure A.31: Parametrium Metrics

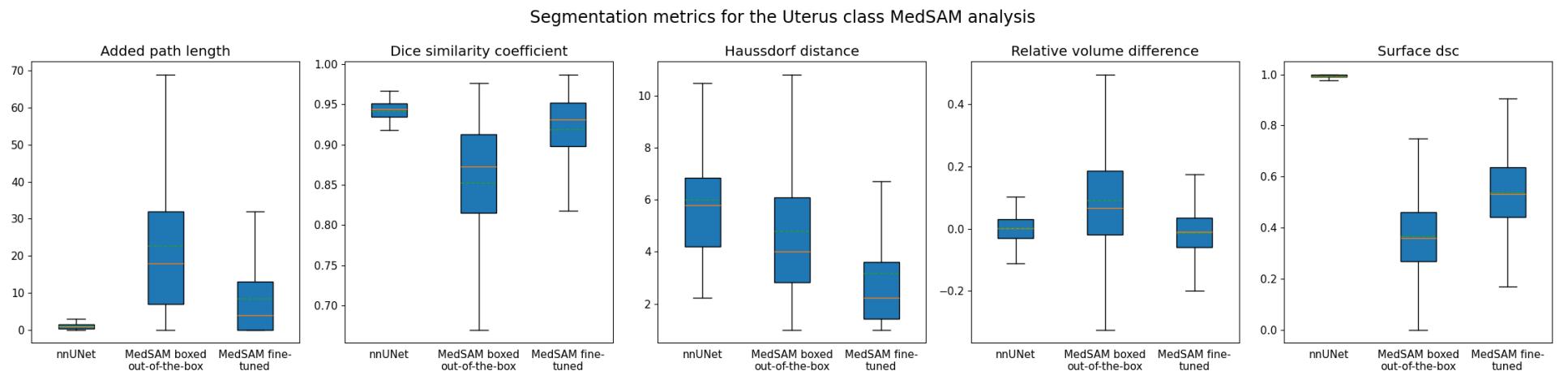
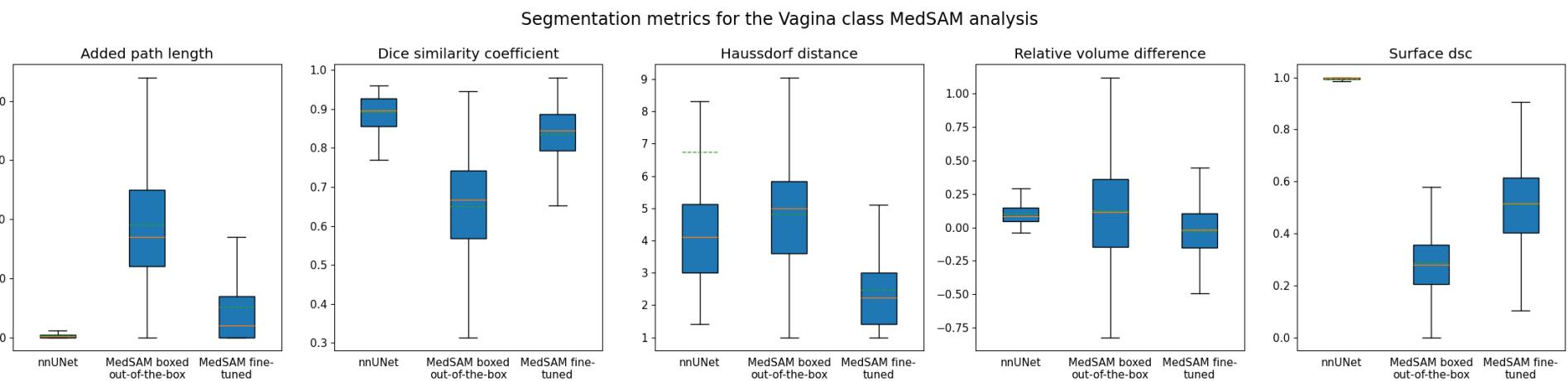


Figure A.32: Uterus Metrics



**Figure A.33:** Vagina Metrics

# Bibliography

- [1] Gihan Samarasinghe, Michael Jameson, Shalini Vinod, Matthew Field, Jason Dowling, Arcot Sowmya, and Lois Holloway. Deep learning for segmentation in radiation therapy planning: a review. *J Med Imaging Radiat Oncol*, 65(5):578–595, July 2021. URL <https://pubmed.ncbi.nlm.nih.gov/34313006/>. pages 2
- [2] Hui Lin, Haonan Xiao, Lei Dong, Kevin Boon-Keng Teo, Wei Zou, Jing Cai, and Taoran Li. Deep learning for automatic target volume segmentation in radiation therapy: a review. *Quant Imaging Med Surg*, 11(12):4847–4858, December 2021. URL <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8611469/>. pages 2, 6
- [3] Hanna Sartor, David Minarik, Olof Enqvist, Johannes Ulén, Anders Wittrup, Maria Bjurberg, and Elin Trägårdh. Auto-segmentations by convolutional neural network in cervical and anorectal cancer with clinical structure sets as the ground truth. *Clin Transl Radiat Oncol*, 25:37–45, September 2020. URL <https://pubmed.ncbi.nlm.nih.gov/33005756/>. pages 2
- [4] Zhikai Liu, Xia Liu, Bin Xiao, Shaobin Wang, Zheng Miao, Yuliang Sun, and Fuquan Zhang. Segmentation of organs-at-risk in cervical cancer ct images with a convolutional neural network. *Physica Medica*, 69:184–191, 2020. ISSN 1120-1797. doi: <https://doi.org/10.1016/j.ejmp.2019.12.008>. URL <https://www.sciencedirect.com/science/article/pii/S1120179719305290>. pages 2, 5
- [5] Dong Joo Rhee, Anuja Jhingran, Bastien Rigaud, Tucker Netherton, Carlos E Cardenas, Lifei Zhang, Sastry Vedam, Stephen Kry, Kristy K Brock, William Shaw, Frederika O'Reilly, Jeannette Parkes, Hester Burger, Nazia Fakie, Chris Trauernicht, Hannah Simonds, and Laurence E Court. Automatic contouring system for cervical cancer using convolutional neural networks. *Med Phys*, 47(11):5648–5658, October 2020. URL <https://pubmed.ncbi.nlm.nih.gov/32964477/>. pages 2
- [6] Zhikai Liu, Xia Liu, Hui Guan, Hongan Zhen, Yuliang Sun, Qi Chen, Yu Chen, Shaobin Wang, and Jie Qiu. Development and validation of a deep learning algorithm for auto-delineation of clinical target volume and organs at risk in cervical cancer radiotherapy. *Radiotherapy and Oncology*, 153:172–179, 2020. ISSN 0167-8140. doi: <https://doi.org/10.1016/j.radonc.2020.09.060>. pages 2, 35
- [7] Fabian Isensee, Tassilo Wald, Constantin Ulrich, Michael Baumgartner, Saikat Roy, Klaus Maier-Hein, and Paul F. Jaeger. nnu-net revisited: A call for rigorous validation in 3d medical image segmentation, 2024. pages 2, 12, 13
- [8] Fabian Isensee, Jens Petersen, Andre Klein, David Zimmerer, Paul F. Jaeger, Simon Kohl, Jakob Wasserthal, Gregor Köhler, Tobias Norajittra, Sebastian Wirkert, and Klaus H. Maier-Hein. nnu-net: Self-adapting framework for u-net-based medical image segmentation. 2018. URL <https://arxiv.org/pdf/1809.10486.pdf>. pages 2, 12

- [9] Institute of Cancer Research and The Royal Marsden Hospital. Amlart data. [Last Accessed: 2023-12-28]. pages 4, 6, 7, 8, 9
- [10] Freddie Bray, Mathieu Laversanne, Hyuna Sung, Jacques Ferlay, Rebecca L. Siegel, Isabelle Soerjomataram, and Ahmedin Jemal. Global cancer statistics 2022: Globocan estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA: A Cancer Journal for Clinicians*, 74(3):229–263, 2024. doi: <https://doi.org/10.3322/caac.21834>. URL <https://acsjournals.onlinelibrary.wiley.com/doi/abs/10.3322/caac.21834>. pages 4
- [11] Florence Guida, Rachel Kidman, Jacques Ferlay, Joachim Schüz, Isabelle Soerjomataram, Benda Kithaka, Ophira Ginsburg, Raymond B. Mailhot Vega, Moses Galukande, Groesbeck Parham, Salvatore Vaccarella, Karen Canfell, Andre M. Ilbawi, Benjamin O. Anderson, Freddie Bray, Isabel dos Santos-Silva, and Valerie McCormack. Global and regional estimates of orphans attributed to maternal cancer mortality in 2020. *Nature Medicine*, 28(12):2563–2572, Dec 2022. ISSN 1546-170X. doi: 10.1038/s41591-022-02109-2. URL <https://doi.org/10.1038/s41591-022-02109-2>. pages 4
- [12] Yunfei Jiao, Fangyu Cao, and Hu Liu. Radiation-induced cell death and its mechanisms. *Halth Phys.*, 2022. URL <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9512240/pdf/hpj-123-376.pdf>. pages 4
- [13] Rajamanickam Baskar, Kuo Ann Lee, Richard Yeo, and Kheng-Wei Yeoh1. Cancer and radiation therapy: Current advances and future directions. 2012. URL <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3298009/>. pages 4
- [14] Mareike K. Thompson, Philip Poortmans, Anthony J. Chalmers, Corinne Faivre-Finn, Emma Hall, Robert A. Huddart, Yolande Lievens, David Sebag-Montefiore, and Charlotte E. Coles. Practice-changing radiation therapy trials for the treatment of cancer: where are we 150 years after the birth of marie curie? *British Journal of Cancer*, 119(4):389–407, Aug 2018. ISSN 1532-1827. doi: 10.1038/s41416-018-0201-z. URL <https://doi.org/10.1038/s41416-018-0201-z>. [Last Accessed: 2024-06-01]. pages 4
- [15] William Small, Monica A. Bacon, Amishi Bajaj, Linus T. Chuang, Brandon J. Fisher, Matthew M. Harkenrider, Anuja Jhingran, Henry C. Kitchener, Linda R. Mileshkin, Akila N. Viswanathan, and David K. Gaffney. Cervical cancer: A global health crisis. *Cancer; An international interdisciplinary journal of American Cancer Society*, 123(13), 2017. URL <https://acsjournals.onlinelibrary.wiley.com/doi/10.1002/cncr.30667>. pages 5
- [16] Michele Larobina and Loredana Murino. Medical image file formats. *Journal of Digital Imaging*, 27, 2013. URL <https://link.springer.com/article/10.1007/s10278-013-9657-9>. pages 5, 7
- [17] Lucas Haase, Jason Ina, Ethan Harlow, Raymond Chen, Robert Gillespie, and Jacob Calcei. The influence of component design and positioning on soft-tissue tensioning and complications in reverse total shoulder arthroplasty. *The Journal of Bone and Joint Surgery*, 12(4), 2024. doi: 10.2106/JBJS.RVW.23.00238. pages 5
- [18] Herbert Lepor. *Prostatic Diseases*. W B Saunders Co Ltd, 1999. ISBN 978-0721674162. pages 5

- [19] D.R. Dance, S. Christofides, A.D.A. Maidment, I.D. McLean, and K.H. Ng. *Diagnostic Radiology Physics*. International Atomic Energy Agency, 2014. pages 5
- [20] DenOtter TD and Schubert J. *Hounsfield Unit*. StatPearls Publishing, Jan 2024. URL <https://www.ncbi.nlm.nih.gov/books/NBK547721/>. pages 5
- [21] C. F. Njeh. Tumor delineation: The weakest link in the search for accuracy in radiotherapy, 2008. URL <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2772050/>. [Last Accessed: 2023-12-29]. pages 6
- [22] Neil G Burnet, Simon J Thomas, Kate E Burton, and Sarah J Jefferies. Defining the tumour and target volumes for radiotherapy, 2004. URL <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1434601/pdf/ci040153.pdf>. [Last Accessed: 2023-12-29]. pages 6
- [23] David Bernstein, Alexandra Taylor, Simeon Nill, and Uwe Oelfke. New target volume delineation and ptv strategies to further personalise radiotherapy, 2021. [Last Accessed: 2023-12-29]. pages 6
- [24] Marcel van Herk. Errors and margins in radiotherapy. *Seminars in Radiation Oncology*, 14(1):52–64, 2004. ISSN 1053-4296. doi: <https://doi.org/10.1053/j.semradonc.2003.10.003>. URL <https://www.sciencedirect.com/science/article/pii/S1053429603000845>. High-Precision Radiation Therapy of Moving Targets. pages 6
- [25] Xiangrui Li, Paul S. Morgan, John Ashburner, Jolinda Smith, and Christopher Rorden. The first step for neuroimaging data analysis: Dicom to nifti conversion. *Journal of Neuroscience Methods*, 264, 2016. URL <https://pubmed.ncbi.nlm.nih.gov/26945974/>. pages 7
- [26] Richard Beare, Bradley Lowekamp, and Ziv Yaniv. Image segmentation, registration and characterization in r with simpleitk. *Journal of Statistical Software*, 86(8):1–35, 2018. doi: 10.18637/jss.v086.i08. URL <https://www.jstatsoft.org/article/view/v086i08>. pages 7
- [27] R. Kelley Pace and Ronald Barry. Sparse spatial autoregressions. *Statistics & Probability Letters*, 33(3):291–297, 1997. doi: 10.1016/S0167-7152(96)00140-X. [Last Accessed: 2024-06-01]. pages 9
- [28] J.J. Hull. A database for handwritten text recognition research. *IEEE Transactions on Pattern Analysis and Machine Intelligence*, 16(5):550–554, 1994. doi: 10.1109/34.291440. [Last Accessed: 2024-06-01]. pages 10
- [29] Y. Lecun, L. Bottou, Y. Bengio, and P. Haffner. Gradient-based learning applied to document recognition. *Proceedings of the IEEE*, 86(11):2278–2324, 1998. doi: 10.1109/5.726791. [Last Accessed: 2024-06-01]. pages 10, 11
- [30] Jonathan Long, Evan Shelhamer, and Trevor Darrell. Fully convolutional networks for semantic segmentation. Technical report, Berkley, 2015. URL <https://arxiv.org/pdf/1411.4038.pdf>. pages 11
- [31] Hyeonwoo Noh, Seunghoon Hong, and Bohyung Han. Learning deconvolution network for semantic segmentation, 2015. [Last Accessed: 2024-06-01]. pages 11

- [32] Karen Simonyan and Andrew Zisserman. Very deep convolutional networks for large-scale image recognition. *arXiv preprint arXiv:1409.1556*, 2014. [Last Accessed: 2024-06-01]. pages 11
- [33] Olaf Ronneberger, Philipp Fischer, and Thomas Brox. U-net: Convolutional networks for biomedical image segmentation. *CoRR*, abs/1505.04597, 2015. URL <http://arxiv.org/abs/1505.04597>. pages 11, 12
- [34] Özgün Çiçek, Ahmed Abdulkadir, Soeren S. Lienkamp, Thomas Brox, and Olaf Ronneberger. 3d u-net: Learning dense volumetric segmentation from sparse annotation. *CoRR*, abs/1606.06650, 2016. URL <http://arxiv.org/abs/1606.06650>. [Last Accessed: 2024-06-03]. pages 12, 18
- [35] Fabian Isensee, Paul F. Jaeger, Simon A. A. Kohl, Jens Petersen, and Klaus H. Maier-Hein. nnu-net: a self-configuring method for deep learning-based biomedical image segmentation. 2021. URL <https://www.nature.com/articles/s41592-020-01008-z>. pages 12
- [36] Jakob Wasserthal, Hanns-Christian Breit, Manfred T. Meyer, Maurice Pradella, Daniel Hinck, Alexander W. Sauter, Tobias Heye, Daniel T. Boll, Joshy Cyriac, Shan Yang, Michael Bach, and Martin Segeroth. Totalsegmentator: Robust segmentation of 104 anatomic structures in ct images. 2023. URL <https://arxiv.org/pdf/2208.05868.pdf>. pages 13
- [37] Victor Ion Butoi, Jose Javier Gonzalez Ortiz, Tianyu Ma, Mert R. Sabuncu, John Guttag, and Adrian V. Dalca. Universeg: Universal medical image segmentation. 2023. URL <https://arxiv.org/pdf/2304.06131.pdf>. pages 13, 21
- [38] Alexander Kirillov, Eric Mintun, Nikila Ravi, Hanzi Mao, Chloe Rolland, Laura Gustafson, Tete Xiao, Spencer Whitehead, Alexander C. Berg, Wan-Yen Lo, Piotr Dollar, and Ross Girshick. Segment anything. Technical report, Meta AI Research, 2023. URL <https://arxiv.org/abs/2304.02643>. [Last Accessed: 2023-12-28]. pages 14, 15, 23, 25
- [39] Alexey Dosovitskiy, Lucas Beyer, Alexander Kolesnikov, Dirk Weissenborn, Xiaohua Zhai, Thomas Unterthiner, Mostafa Dehghani, Matthias Minderer, Georg Heigold, Sylvain Gelly, Jakob Uszkoreit, and Neil Houlsby. An image is worth 16x16 words: Transformers for image recognition at scale. *CoRR*, abs/2010.11929, 2020. URL <https://arxiv.org/abs/2010.11929>. [Last Accessed: 2024-06-04]. pages 14
- [40] Sheng He, Rina Bao, Jingpeng Li, Jeffrey Stout, Atle Bjornerud, P. Ellen Grant, and Yangming Ou. Computer-vision benchmark segment-anything model (sam) in medical images: Accuracy in 12 datasets, 2023. [Last Accessed: 2024-06-04]. pages 14, 15
- [41] Ruining Deng, Can Cui, Quan Liu, Tianyuan Yao, Lucas W. Remedios, Shunxing Bao, Bennett A. Landman, Lee E. Wheless, Lori A. Coburn, Keith T. Wilson, Yaohong Wang, Shilin Zhao, Agnes B. Fogo, Haichun Yang, Yucheng Tang, and Yuankai Huo. Segment anything model (sam) for digital pathology: Assess zero-shot segmentation on whole slide imaging, 2023. [Last Accessed: 2024-06-04]. pages 15
- [42] Chuanfei Hu, Tianyi Xia, Shenghong Ju, and Xinde Li. When sam meets medical images: An investigation of segment anything model (sam) on multi-phase liver tumor segmentation, 2023. [Last Accessed: 2024-06-04]. pages 15

- [43] Jun Ma, Yuting He, Feifei Li, Lin Han, Chenyu You, and Bo Wang. Segment anything in medical images. *Nature Communications*, 15(1):654, Jan 2024. ISSN 2041-1723. doi: 10.1038/s41467-024-44824-z. URL <https://doi.org/10.1038/s41467-024-44824-z>. [Last Accessed: 2024-06-04]. pages 15, 23, 25
- [44] Christopher M. Bishop and Hugh Bishop. *Deep Learning, Foundations and Concepts*. Springer, 2023. pages 15, 16, 17
- [45] Sinno Jialin Pan and Qiang Yang. A survey on transfer learning. 2009. URL <https://ieeexplore.ieee.org/abstract/document/5288526>. pages 15
- [46] Lisa Torrey and Jude Shavlik. Transfer learning. Technical report, University of Wisconsin, 2009. URL <https://ftp.cs.wisc.edu/machine-learning/shavlik-group/torrey.handbook09.pdf>. pages 15
- [47] Michal Heker and Hayit Greenspan. Joint liver lesion segmentation and classification via transfer learning. Technical report, 2020. URL <https://arxiv.org/pdf/2004.12352.pdf>. pages 15
- [48] What is transfer learning? URL <https://www.geeksforgeeks.org/ml-introduction-to-transfer-learning/>. pages 15, 17
- [49] Abolfazl Farahani, Behrouz Pourshojae, Khaled Rasheed, and Hamid R. Arabnia. A concise review of transfer learning. Technical report, 2021. URL <https://arxiv.org/abs/2104.02144v1>. pages 15
- [50] Tom B. Brown, Benjamin Mann, Nick Ryder, Melanie Subbiah, Jared Kaplan, Prafulla Dhariwal, Arvind Neelakantan, Pranav Shyam, Girish Sastry, Amanda Askell, Sandhini Agarwal, Ariel Herbert-Voss, Gretchen Krueger, Tom Henighan, Rewon Child, Aditya Ramesh, Daniel M. Ziegler, Jeffrey Wu, Clemens Winter, Christopher Hesse, Mark Chen, Eric Sigler, Mateusz Litwin, Scott Gray, Benjamin Chess, Jack Clark, Christopher Berner, Sam McCandlish, Alec Radford, Ilya Sutskever, and Dario Amodei. Language models are few-shot learners. *CoRR*, abs/2005.14165, 2020. URL <https://arxiv.org/abs/2005.14165>. [Last Accessed: 2024-06-08]. pages 16
- [51] wasserth, lassoan, fedorov, cnicolasgr, and Arputikos. URL <https://github.com/wasserth/TotalSegmentator>. pages 19
- [52] K. Mackay, D. Bernstein, B. Glocker, and A. Taylor K. Kamnitsas. A review of the metrics used to assess auto-contouring systems in radiotherapy, 2023. URL [https://www.clinicaloncologyonline.net/action/showPdf?pii=S0936-6555\(23\)00021-3](https://www.clinicaloncologyonline.net/action/showPdf?pii=S0936-6555(23)00021-3). [Last Accessed: 2023-12-29]. pages 25, 26, 27
- [53] Abdel Aziz Taha and Allan Hanbury. Metrics for evaluating 3d medical image segmentation: analysis, selection, and tool. *BMC Medical Imaging*, 15(1):29, Aug 2015. ISSN 1471-2342. doi: 10.1186/s12880-015-0068-x. URL <https://doi.org/10.1186/s12880-015-0068-x>. [Last Accessed: 2024-01-13]. pages 25, 26
- [54] Michael V Sherer, Diana Lin, Sharif Elguindi, Simon Duke, Li-Tee Tan, Jon Caciuccedo, Max Dahele, and Erin F Gillespie. Metrics to evaluate the performance of auto-segmentation for radiation treatment planning: A critical review. *Radiother Oncol*, 160:185–191, May 2021. URL <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9444281/>. pages 26, 27, 28

- [55] Femke Vaassen, Colien Hazelaar, Ana Vaniqui, Mark Gooding, Brent van der Heyden, Richard Canters, and Wouter van Elmpt. Evaluation of measures for assessing time-saving of automatic organ-at-risk segmentation in radiotherapy. *Phys Imaging Radiat Oncol*, 13:1–6, December 2019. pages 26, 28
- [56] Varduhi Yeghiazaryan and Irina Voiculescu. Family of boundary overlap metrics for the evaluation of medical image segmentation. *Journal of Medical Imaging*, 5(1):015006–015006, 2018. pages 26, 27
- [57] Ying-Hwey Nai, Bernice W. Teo, Nadya L. Tan, Sophie O'Doherty, Mary C. Stephenson, Yee Liang Thian, Edmund Chiong, and Anthonin Reilhac. Comparison of metrics for the evaluation of medical segmentations using prostate mri dataset. *Computers in Biology and Medicine*, 134:104497, 2021. ISSN 0010-4825. doi: <https://doi.org/10.1016/j.combiomed.2021.104497>. URL <https://www.sciencedirect.com/science/article/pii/S0010482521002912>. pages 27
- [58] Stanislav Nikolov, Sam Blackwell, Alexei Zverovitch, Ruheena Mendes, Michelle Livne, Jeffrey De Fauw, Yojan Patel, Clemens Meyer, Harry Askham, Bernadino Romera-Paredes, Christopher Kelly, Alan Karthikesalingam, Carlton Chu, Dawn Carnell, Cheng Boon, Derek D'Souza, Syed Ali Moinuddin, Bethany Garie, Yasmin McQuinlan, Sarah Ireland, Kiarna Hampton, Krystle Fuller, Hugh Montgomery, Geraint Rees, Mustafa Suleyman, Trevor Back, Cían Owen Hughes, Joseph R Ledsam, and Olaf Ronneberger. Clinically applicable segmentation of head and neck anatomy for radiotherapy: Deep learning algorithm development and validation study. *J Med Internet Res*, 23(7):e26151, July 2021. pages 28
- [59] *Stochastic Caching*. URL <https://github.com/Charl-AI/stochastic-caching>. [Last Accessed: 2024-06-10]. pages 32
- [60] Nass SJ, Levit LA, and Gostin LO. Beyond the hipaa privacy rule: Enhancing privacy, improving health through research. page 18, 2009. doi: 10.17226/12458. pages 35
- [61] The Royal Marsden NHS Foundation Trust. Privacy note. URL [https://rm-d8-live.s3.eu-west-1.amazonaws.com/d8live.royalmarsden.nhs.uk/s3fs-public/2023-10/T22020ac\\_Revisedprivacypolicy\\_V1\\_AW\\_WEB.pdf](https://rm-d8-live.s3.eu-west-1.amazonaws.com/d8live.royalmarsden.nhs.uk/s3fs-public/2023-10/T22020ac_Revisedprivacypolicy_V1_AW_WEB.pdf). pages 35
- [62] David B Larson, David C Magnus, Matthew P Lungren, Nigam H Shah, and Curtis P Langlotz. Ethics of using and sharing clinical imaging data for artificial intelligence: A proposed framework. *Radiology*, 295(3):675–682, March 2020. doi: 10.1148/radiol.2020192536. pages 35
- [63] *Data Protection Act 2018*. URL <https://www.legislation.gov.uk/ukpga/2018/12/contents/enacted>. pages 35
- [64] Amisha, Paras Malik, Monika Pathania, and Vyas Kumar Rathaur. Overview of artificial intelligence in medicine. *J Family Med Prim Care*, 8(7):2328–2331, July 2019. doi: 10.4103/jfmpc.jfmpc\_440\_19. pages 35
- [65] Zi-Hang Chen, Li Lin, Chen-Fei Wu, Chao-Feng Li, Rui-Hua Xu, and Ying Sun. Artificial intelligence for assisting cancer diagnosis and treatment in the era of precision medicine. *Cancer Communications*, 41(11), 2021. doi: 10.1002/cac2.12215. pages 36

- [66] Isabel Straw. The automation of bias in medical artificial intelligence (ai): Decoding the past to create a better future. *Artificial Intelligence in Medicine*, 110:101965, 2020. ISSN 0933-3657. doi: 10.1016/j.artmed.2020.101965. pages 36