| | |
|---|---|
| **Title** | Vessel Segmentation in Medical Image Analysis |
| **Student name:** | Matthew De Vries |
| **Supervisor name:** | Dr Xiaohao Cai |

## *Aims/research question and Objectives*

The main aim of this project is to **aid clinical fields** such as oncology, ophthalmology and neurosurgery in diagnosis, both planning and actual treatment, as well as evaluation and follow up. To this end, this project will explore automatic vessel segmentation techniques which can be broadly used across vessels in different parts of the anatomy and varying imaging modalities. Several actualities inspire this idea.

Firstly, manual segmentation of blood vessels carries an **exorbitant** price in terms of time. Along with this, it lacks both inter- and intra-operator reproducibility and repeatability. Using a typical deep-learning approach across the board as a tool for semi-automatic or automatic segmentation of blood vessels will **significantly decrease this time** as well as lean towards a more robust, and reproducible method gaining the trust of more doctors.

Secondly, vessel co-option is a non-angiogenic process (when a tumour does not need an angiogenic sprout to obtain an efficient blood supply) through which malignant tumour cells utilise existing blood vessels to support survival and growth of the tumour. A wide range of malignant tumours growing in various tissues such as the lungs, brain, liver, and lymph nodes adopt vessel co-option. The importance of analysing vessel co-option is that it is implicated in patient outcomes and resistance to cancer treatments regimes. Analysis of vessel co-option requires **precise** and **accurate** segmentation of the blood vessel across numerous regions of the body.

Thirdly, medical images such as histopathological slides or whole slide images consist of **huge** files with hundreds of thousands of pixels per image. Given it remains **unmanageable** to process pathology slides in their entirety, deep learning models have performed inference few individual patches extracted from the image. This requires a large amount of computation and may result in ignoring potentially relevant contextual and spatial information. The ability to process larger input patches and locate discriminatory regions more efficiently could help **improve** both computational and task-specific performance. For this reason, we propose **attention-based/gated networks**. Furthermore, existing deep learning models have mostly relied on local appearances learned on the normal image grid, without considering the graphical structure of the vessel shape. Effective use of the strong relationship that exists between vessel neighbourhoods can help improve the vessel segmentation accuracy. Here, we propose the use of **graphical neural networks**.

Finally, algorithms which work well on vessel segmentation can usually be extended to other tubular structures in either medical image analysis or other computer vision problems.

The following research questions will be considered in order to understand which segmentation techniques and deep learning architectures are best suited for segmentation of tubular structures across the board:

1. Can an end-to-end deep-learning vessel segmentation approach for different anatomical regions and various imaging modalities be used?
2. Can graph neural networks efficiently and effectively exploit the relationship that exists between vessel neighbourhoods?
3. Is there a benefit in incorporating attention into segmentation networks in terms of computational and task-specific performance of segmentation of whole slide images?
4. Can these approaches be transferred to the segmentation of pathological vessels?

According to these aims and research questions above, the following objectives have been outlined:

- Familiarisation with the **techniques** and **limitations** in medical image analysis.
- Familiarisation with the **principals** in the design of automatic segmentation algorithms.
- Familiarisation with the principals in the design of deep-learning-based segmentation algorithms.
- Selection of suitable current state-of-the-art techniques in order to establish baseline results.
- Selection of suitable datasets covering **different** imaging modalities and anatomical regions.
- Implementation of current state-of-the-art on datasets.
- Understanding **why** these models work.
- Design and experimentation **original** methods using techniques described above.
- Thorough analysis and comparison between methods.
- Extension to other tubular structures.
- Test final, best-achieving method on range of datasets.
- Write thesis and **publish** review paper as well as original article with code.

## *Summary of proposed research and analysis methodology*

Before any major project, it is essential to **gain familiarity** with the research domain. Medical image computing is a large interdisciplinary topic involving aspects of computer science, physics, mathematics, and medicine. **Thorough research** and study of the medical side of this topic will greatly benefit its overall outcome and translational ability. This will be done through an in-depth study of numerous journal articles gathered in the forms of a literature review.

Following this initial study, it is possible to **narrow down** to the specific task at hand, which is segmentation. The segmentation process is at the core of the vessel segmentation workflow, which partitioned into four main categories:

- **Vessel enhancement**
- **Machine learning**
- Tracking
- Deformable models

Vessel enhancement improves the quality of vessel perception, where the vessel contrast is increased with respect to other non-informative structures. Numerous vessel enhancement techniques already exist, including vesselness-based approaches and **Wavelet filtering**. This research will begin by **reviewing** the literature and **experimenting** with these different techniques. This is usually followed by a thresholding step in order to obtain a binary mask of the medical image. These enhanced versions of the vascular structures can then be used to extract features on which to classify with the use of **deep learning algorithms**, to guide vascular tracking, or to define the forces which constrain vessel model deformation. A post-processing step may then also be used as a means to reconnect vascular segments or remove too small segmented areas which may correspond to noise. This research will not look into tracking and deformable models but will instead focus on an **end-to-end deep learning mechanism**.

In the medical image analysis domain, there exist a rich literature of segmentation techniques. This will lead to the **exploration** and **evaluation** of the current state-of-the-art techniques used across multiple imaging modalities. It is important to understand **why** U-net architectures have achieved outstanding results and build onto this in a way which is backed by evident findings. Thorough experimentation will be done, which may involve the use of **neural architecture searches** where we would allow the network to design itself in a way, to see if anything can be learnt from this. To this end, differentiable architecture search (**DARTS**) may be used, which addresses the scalability issue of architecture search by formulating the problem in a differentiable manner. Unlike other approaches of applying evolution or reinforcement learning over a discrete and non-differentiable search space, DARTS is based on the continuous relaxation of the architecture representation, allowing efficient search of the architecture using gradient descent. This is an **exciting** topic which can be used across deep learning problems and may prove useful in this study.

For exploiting the **graphical structure** and the strong relationship existing between vessel neighbourhoods, techniques from **graph neural networks** in medical image analysis will be adapted and explored. A thorough understanding of graph neural networks and spatial analysis will be gained with research which may focus on different domains.

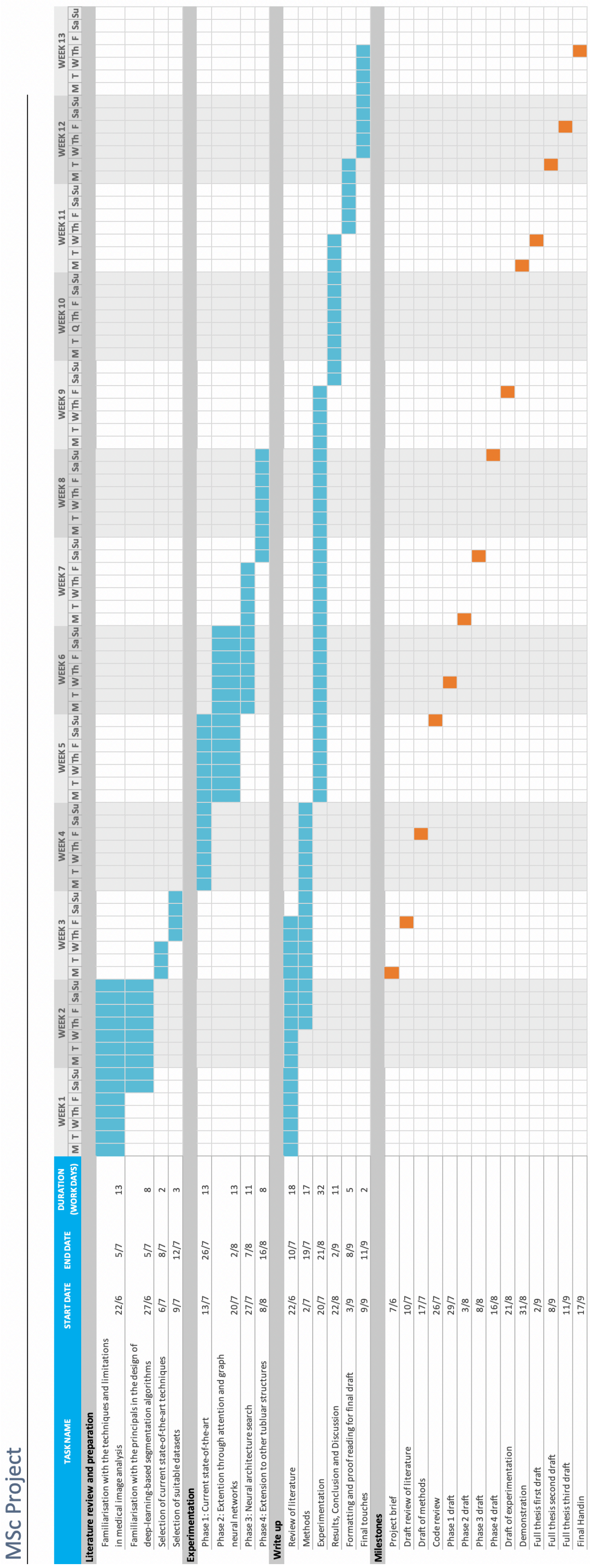
Recently, convolutional neural networks (CNNs) have shown **promising** performance in medical image segmentation tasks. However, this can often result in **ignoring** potentially relevant spatial and contextual information. Being able to locate discriminatory regions more **efficiently** could help improve both computational and task-specific performance. For this reason, it may be beneficial to explore **attention-based/gated networks**. Attention Gates (AGs) are commonly used in segmentation tasks. The attention modules infer attention maps along different dimensions, which help focus the CNNs on critical image regions, as well as highlight discriminative feature channels while suppressing the irrelevant information with respect to the segmentation task. AGs can be **integrated easily** into standard CNN models such as U-net increasing the model sensitivity and prediction accuracy with minimal computational overhead.

From this, it may be necessary to break this project into a number of sub-compartments or phases. **Phase 0** will be the **research** into the broad field of segmentation in medical image analysis through a thorough review of the literature with **preliminary implementations** of techniques on a few datasets. This is defined as a **preface** as will be done prior to the start of the summer. **Phase 1** will then include **reimplementation**, **experimentation** and analysis of the **current state-of-the-art**, looking to **explain** why certain methods work as well as establishing baseline results. **Phase 2** will include the incorporation of **attention gates** into these models as well as the use of **graph neural networks**. **Phase 3** will include **neural architecture search**. Finally, **phase 4** will be exploring how these found methods may be **extended to other tubular structures**.

Current state-of-the-art models have been built in **Python** using libraries such as **PyTorch** and **Tensorflow**. I will use these libraries to build upon these models as well as when designing new models. The data will be provided by Southampton General Hospital and is already available along with labelled training data. There are a number of publicly available datasets which may also be used in this project, e.g. the Medical Image Repositories[1]. Finally, throughout the project, I will use thorough software engineering practices including **version control**, **documentation of code, and automated testing**.

[1] https://www.ucl.ac.uk/child-health/support-services/library/resources-z/medical-image-repositories.

## *Research plan – Gantt chart or Pert chart*



## *Ethical statement*

Artificial intelligence (AI) has great potential to significantly **benefit** the medical industry through **guiding** medical professionals to data-driven decisions. It has great potential to increase accuracy and **efficiency** throughout medical image analysis however, it also carries pitfalls and biases. These systems provide sensitive services that, when performed by a radiologist, require years of training and certification. This raises questions concerning the standards to which these AI systems are held. Unrestricted use of AI in radiology may increase the risk of systematic errors which carry enormous consequences as well as highlights complex ethical and societal issues. Ultimately, **radiologists should remain responsible** for patient care and may need to acquire new skills in an AI ecosystem.

The use of AI in healthcare carries with it multiple ethical issues. Algorithms may find **biased links** from patient data which may lead to outcomes of a **discriminatory** nature. Many algorithms search for **correlations** between variables rather than **causation**. Although this is not looking at diagnosis, these models may be extended to do so. Thus, it is imperative that model **explainability** is largely incorporated into the use of AI in radiology.

Finally, the use of patient data may inflict **privacy issues** which can be used in a number of negative ways, including unjust insurance premiums for certain groups of people. Ultimately AI in healthcare needs to be **highly regulated** and used as an **aiding tool** rather than to replace the decisions of healthcare professionals.

## *Legal and commercial aspects*

Legal aspect:

In the UK, the definition of a medical device is given in [1]. This term is used for any instrument, including any kind of software, intended by the manufacturer to be used for human beings for the purpose of diagnosis, prevention, monitoring, alleviation of treatment of disease. The European regulatory regime requires manufacturers to ensure that the devices they produce are **fit for the purpose** for which they are intended, meaning they must comply with a number of essential requirements set up by the directives in [1, 2, 3]. Furthermore, there are data protection issues governed by the General Data Protection Regulation. According to this, all data processing and use should be **opt-in**, and consumer consent for data use should be clear.

Commercial aspect:

AI is anticipated to **transform** the healthcare industry, with imaging-enabled specialities such as pathology and radiology set to be early adopters. As outlined in the previous report as well as in the aims of this report, there is a **high demand** for blood vessel segmentation techniques which can be used across imaging modalities. The final model could be incorporated directly into varying medical procedures with the potential to generate a **large income** if a series of tests are passed. Furthermore, this research will be **essential to future research** in this domain. Adding **explainability** into AI models for healthcare is an important issue and realising why some models work better over others could have a significant impact on the direction of future research.

References:

[1] European Economic Community (1993) 93/42/EEC - Council Directive concerning Medical Devices. Official Journal of the European Communities. Available via http://ec.europa.eu/growth/single-market/european-standards/harmonised-standards/medical-devices_en

[2] European Commission (2018) MDCG 2018–2 Future EU medical device nomenclature – Description of requirements. Available via https://ec.europa.eu/docsroom/documents/28668

[3] European Economic Community (1990) 90/385/EEC - Council Directive on the approximation of the laws of the Member States relating to active implantable medical devices. Council Directive. Available via https://ec.europa.eu/growth/single-market/european-standards/harmonised-standards/implantable-medical-devices_en