Delineation of Pelvic Lymph Nodes for Image Guided Radiotherapy of Pelvic Cancer

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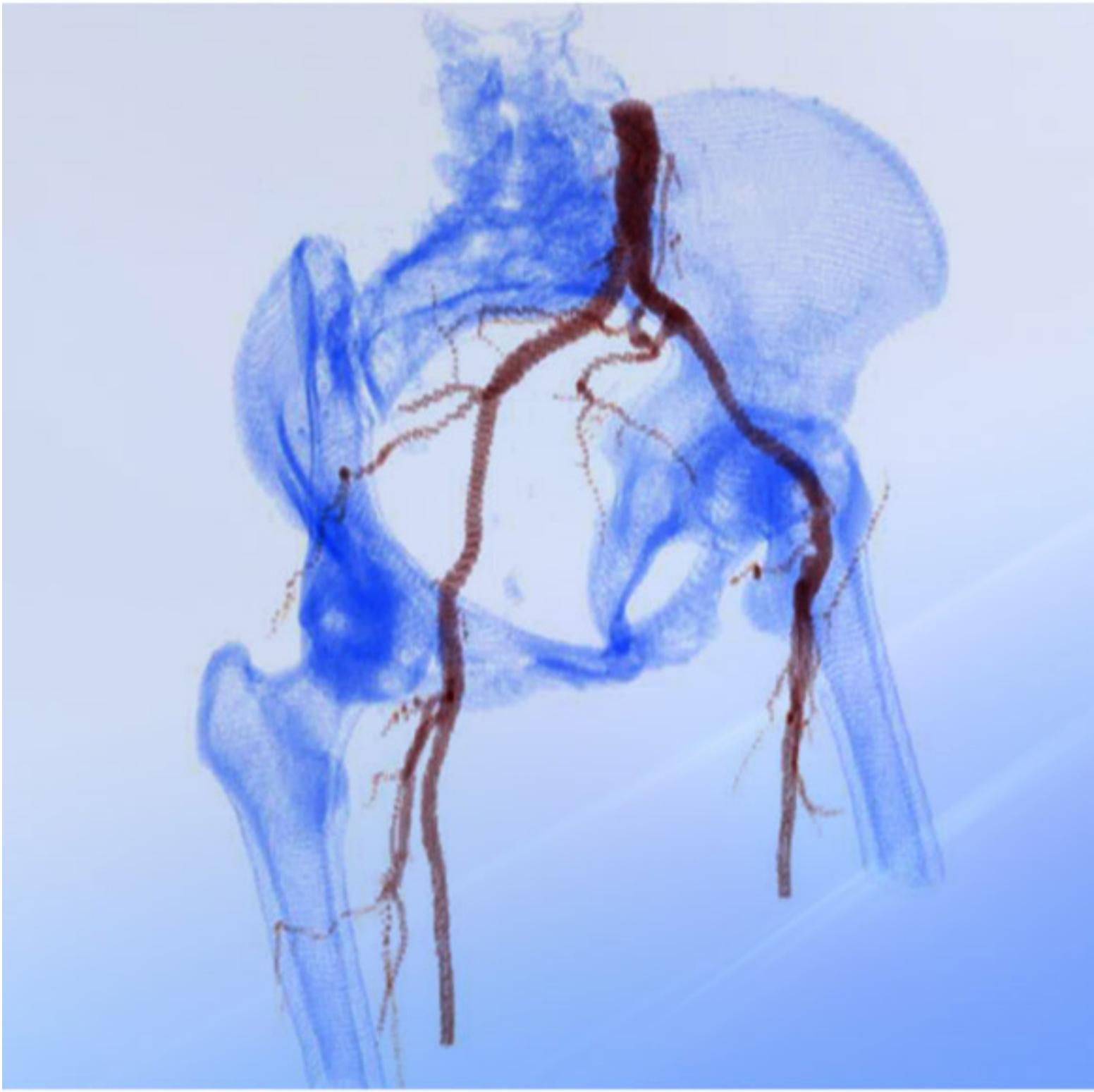

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Synopsis:

Pelvic cancer is a severe disease which can be treated with Image guided radiotherapy (IGRT). IGRT is widely used for treatment of cancerous tumors. The goal of the IGRT process is to improve the accuracy of the radiation field, and to reduce the exposure of healthy tissue during radiation treatments. This is obtained by acquiring 3D medical images of the patient and from the images delineate the tumor clinical target volume (CTV). An accurate delineation of the CTV allows an increased dose of radiation to the target, while reducing the exposure to the surrounding healthy tissue. Delineation of pelvic lymph nodes is important for treatment of several types of cancer in the pelvic region including cervical, prostate, colon, and rectal cancer. The pelvic lymph nodes are located adjacent to the arteries and their branches and are not visible in standard CT or MRI. However the iliac arteries are visible and can be used as a target for the lymph nodes by adding a margin to the vessels.
AIM and SOLUTION: Based on CT images a segmentation of iliac arteries and there branches must be performed in order to define a target for the lymph nodes. This is done by using region growing with 26 neighbours based on intensity and edge detection as the primary segmentation method as well as a removal of bone based on simple morphology. This segmentation method was constructed from knowledge of five datasets from patients with cancer in the pelvic region. The method was afterwards tested on nine datasets in order to demonstrate the delineation of CTV.

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Preface

This thesis was written by Anders Heebøll-Holm and Yang Li in the 10th semester in health science and technology, with specialization in medical informatics, at Aalborg University. The source code for the project can be obtained by contacting one of the authors. Notice that all abbreviations and the general notation used can be found in the beginning of the thesis. References are cited in square brackets, with author's last name and publication year.

The report consists of six parts and two appendices. Part I contain the introduction while part II-V contains a preliminary analysis, an analysis, method, and tests and results of the developed method. Part VI constitute the synthesis and finally part VII constitutes the appendices. The appendices contain background knowledge on the project i.e. Cancer staging.

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Abbreviations

CT	:	Computed Tomography
CTA	:	Computed Tomography Angiography
CTV	:	Clinical Target Volume
EBT	:	External Beam Therapy
GTV	:	Gross Target Volume
HU	:	Hounsfield Unit
IGRT	:	Image Guided Radiotherapy
IMRT	:	Intensity Modulated Radiotherapy
IPS	:	Inferior Pelvic Subsite
LPS	:	Lateral Pelvic Subsite
MLC	:	Multileaf Collimator
MRI	:	Magnetic Resonance Imaging
PVE	:	Partial Volume Effect
PTV	:	Planning Target Volume
PPS	:	Posterior Pelvic Subsite

Part I

Introduction

1 Pelvic cancer

In this chapter cancer and specifically pelvic cancer is defined to give the background information for the imaging techniques addressed in this thesis.

Cancer definition

A malignant tumour or 'cancer' is a term used for a group of cell diseases which are caused by mutations that disrupt normal cellular control mechanisms and produce potentially malignant cells [Martini(2006a)]. The two main characteristics of cancer are uncontrolled growth of the cells in the body and the ability of these cells to migrate from the original site and spread to distant sites (metastases) through the circulatory or lymphatic system [Martini(2006b)]. Cancer can be classified by the location of the tumour and by the microscopic appearance of the tumour cells. Thus pelvic cancer is defined as cancer that arises in the pelvis, which is the large, bony, basin-shaped cavity where the hips and legs join the lower part of the body. In this project the term 'pelvic cancer' includes colon cancer, rectal cancer, prostate cancer, bladder cancer and gynecologic cancers such as cervical cancer, uterus cancer, and ovarian cancer [Pizarro(2009), Inc.(2010)].

Pelvic cancer

1 of 3

One out of three people in developed countries will suffer cancer, and one out of four will die from it [Airley(2009)]. In the years 1996 - 2000, pelvic cancer corresponded to 27.9% of all patients with cancer in Denmark [I. Clemmensen et. al(2006)]. Death may occur as a result of the compression of vital organs when nonfunctional cancer cells have killed or replaced the healthy cells in those organs, or when the cancer cells have starved normal tissue of essential nutrients. [Martini(2006a)] As around one third of all cancer patients are suffering from pelvic cancer, an improved method of treatment will benefit the healthcare system and society.

To diagnose a patient with suspected pelvic cancer, the clinical history is studied. The focus is on symptoms like unusual bleeding and diarrhea, fatigue, frequent nocturnal urination, blood in urine or from rectum, and pain in the pelvic region. [I. Clemmensen et. al(2006), Britannica(2010e), Schroeder *et al.*(2007a), Schroeder *et al.*(2007b)] Laboratory tests are performed, such as a complete blood count, an urine analysis, biopsy, and other possible tests to complete a physical examination. The examination includes vaginal examination, ano-rectoscopy, and in many cases sigmoidoscopy. [Britannica(2010b)] To assist these results, diagnostic imaging is used. Depending on which type of cancer, X-ray, ultrasound, CT, PET, SPECT, or MRI scanning technology can be applied.[Britannica(2010b)]

Knowing the stage of the cancer is not only one of the most important factors in selecting treatment options, but also a major factor in predicting a prognosis [Britannica(2010b)].

TNM

A standardized classification system is the TNM staging system. The TNM system describes the extent of the primary tumour, where T refers to the size of the primary tumour, N to the presence and extent of lymph node metastases, and M to the presence of distant metastases. To know more about TNM staging system, see appendix A.2 on page 84 [(NCI)(2010a), Mette Tandrup Hansen and Elisabeth Kjems(2010)].

The progression of cancer depends on the type of tumour and the situation of the individual patient. Whenever a cancer spreads to the lymph nodes (stage II, III, and IV), this results in an increased risk of distant metastasis and death. Lymph nodes are of special interest, because cancer spreads locally through direct infiltration into soft tissues, or at a distance by invading vascular structures, then migrating through the lymphatic or blood flow. Although cancer cells carried in the blood can end in virtually any corner of the body, lymphatic migration is usually stepwise, through successive nodal stops, which can temporarily delay further progression. In radiotherapy, irradiation of lymphatic paths relevant to the localization of the primary tumour has been common practice for decades. Similarly, extinction of cancer is often completed by lymphatic dissection [Lengele and Scalliet(2009)]. Therefore advanced knowledge of the lymphatic pathways relevant to any tumour location is important in both radiotherapy and in surgery for treatment preparation and execution. [Lengele and Scalliet(2009)]

LYMPH NODES

Lymph nodes are small lymphoid organs ranging in diameter from 1-25 mm. When lymph nodes are infected, they enlarge due to an increase in lymphocytes and macrophages. A lymph node is considered pathologic when proven with a biopsy or when the diameter of the short axis of the node is greater than 1 cm.[van de Bunt *et al.*(2006), Martini(2006c), cancer support(2009)] Particularly, lymph node metastases are a common site of spread in patients with pelvic cancer [Dinniwell *et al.*(2009)]. Thus it is important to treat lymph nodes in the near area of the cancer and verify the regress of cancer cells spreading, whatever treatment is employed. [Chao and Lin(2002), Taylor *et al.*(2005), Dinniwell *et al.*(2009)]

Part II

Preliminary analysis

2 Treatment

In this chapter different means of treating cancer are outlined with special emphasis on radiotherapy because it relates most closely to the imaging produced by scanning, though other kinds of treatment - specifically localized treatments - can benefit greatly from more precise imaging depicting the cancer and the immediate surroundings.

There are various ways of treating pelvic cancer depending on the type and stage. The main categories are surgical, radiation and medical treatment. [Schroeder *et al.*(2007b)]

2.1 Surgical therapy

Surgical therapy is the oldest method of cancer treatment. Surgical therapy also plays a key role in the diagnosis of cancer and finding the stage, since more information about the tumour will be available after the operation. Surgical therapy is usually applied as the first treatment in many cases, especially at the early stage in an attempt to remove the tumour or stop the spreading of it. [Britannica(2010b), of Iowa Hospitals and Clinics(2008)]

To cure a cancer with an operation as the only treatment, the tumour has to be confined to a small region of cancerous tissue without metastasis. The removal of the cancerous tissue or organ may not have any influence on the vital function of the body, and if so the function of the vital elements and processes can be replaced in some clinical way. In the surgical removal of cancerous tissue, lymph nodes will also be removed if they are connected with or close to the cancerous tissue. Removing the lymph glands (along with the organ with the tumour) improves the chance of cure. [of Iowa Hospitals and Clinics(2008)]

Removal of cancer

2.2 Radiotherapy

Radiotherapy can be applied to treat cancer alone or in combination with other forms of treatment, most often surgery or chemotherapy. The purpose of radiotherapy is to kill cancerous cells or stop their growth. For the most used radiotherapy, external radiation, the body is exposed to an external source of high-energy X-ray that penetrate internally. [Christensen.(2005), cancer.dk(2010), Slowik(2009)]

Kill or stop growth

Radiotherapy is an effective treatment, because exposure to radiation makes the cancer cells chemically unstable, affecting their ability to multiply and survive. The principle is

that the radiation reacts with water in the cells causing damages to the DNA or genetic material in the cell that controls cell growth. Normally, cells can repair themselves and continue growing; this is not the case for cancerous cells exposed to radiation. This results in a greater amount of decay among cancer cells than healthy cells. [Christensen.(2005), cancer.dk(2010), Slowik(2009)]

2.3 Medical treatment

There are several types of treatment, in which various drugs or chemicals are used to treat the cancers in different stages. The most common ones are chemotherapy and hormone therapy. [(NCI)(2010b), (NCI)(2006a), (NCI)(2006b), (NCI)(2006c)].

Chemotherapy

Chemotherapy is the use of chemicals to destroy cancerous cells, is commonly employed for almost all kinds of cancers. One or more chemotherapy drugs may be administered intravenously, sometimes intramuscularly or orally. When drugs are absorbed through the blood stream distributed to the whole body, cancer cells can be affected, this is called systemic chemotherapy. Another way to use chemotherapy is regional chemotherapy, in which the drugs are placed directly into the an organ, or even a body cavity, so that the main effects arise in the local area. By using regional chemotherapy, the side effects can be greatly reduced, since the exposure of other body tissues to the drugs is limited. The way the chemotherapy is given depends on the type and stage of the cancer, and the condition of the individuals. [(NCI)(2006a), Britannica(2010b)]

DISTRIBUTION TO THE WHOLE BODY

Hormone therapy

Hormone therapy is another form of systemic therapy. It is most often used as an adjuvant therapy to help reduce the risk of cancer recurrence after surgery, although it can be used as neoadjuvant treatment as well. In the case of prostate cancer, synthetic hormones or other drugs may be given to block the body's natural hormones which cancerous cells need during growth. It is effective in treatment for some types of pelvic cancer. [Britannica(2010c), Britannica(2010g), Society(2009)]

BLOCK HORMONES

There are several other opportunities of medicinal treatment, e.g. biological therapy, targeted therapy, in which drugs or other substances are used to identify and attack specific cancer cells without harming normal cells [(NCI)(2010b), (NCI)(2006a), (NCI)(2006c)]. More information about treatments of pelvic cancer with specification of various types of cancer will be found in appendix B on page 85.

Surgical treatment is generally employed for patients with cancer at an early stage, and it will not help removing the lymph node metastases without a combination of other treatments such as radiotherapy. Chemotherapy does not show a satisfactory result in some

treatment of pelvic cancers, such as prostate cancer [Britannica(2010c)]. Hormone treatment is employed with the limitation that it is efficient for hormone-affected cancers such as cancers in the uterus. More than half of the patients receive radiotherapy in some connection with their treatment [Institute(2004)]. Furthermore whole pelvic nodal radiotherapy has a key role in the management of many pelvic malignancies and may improve both locoregional control and survival. [Taylor *et al.*(2005)]. Thus the focus of this project is on radiotherapy.

3 Standard radiotherapy

IN THIS CHAPTER RADIOTHERAPY AND THE DIFFERENT IMAGING TECHNIQUES WILL BE PRESENTED IN MORE DETAIL IN ORDER TO EXPLAIN BOTH THE TREATMENT AND THE WAY THE MEDICAL STAFF OBTAINS INFORMATION ABOUT THE LOCATION AND SPREAD OF THE TUMOUR. IT IS THE METHOD OF TREATING AND HENCE EXTRACTING INFORMATION FROM THESE IMAGES IN RELATION TO PELVIC CANCER THAT IS THE MAIN OBJECT IN THIS THESIS.

Standard treatment for pelvic cancer at Aalborg Hospital follows the conventional method for planning radiotherapy[Carl(2010)]. This involves ”planning radiation” of the primary tumour, which is the mass of cells in which a cancer cell initially developed, and the pathologic lymphatic nodes[Martini(2006a)]. The conventional method uses a uniform intensity beam, which means that the tissue in the area receives the same intensity. The idea of the method is to mark a box around the target, in order to confine the treatment to the target area. It is possible to plan more boxes for adequate coverage of lymphatic nodes and the primary tumour.

CONVENTIONAL METHOD

To plan the treatment margins, image guiding techniques such as computed tomography (CT), magnetic resonance (MR) imaging, and positron emission tomography (PET) are used. The principle and utility of these imaging techniques will be explained later in section 3.1 on the following page. From these images, margins are drawn. The treatment margins are the margins of the primary tumour, gross tumour volume (GTV) and external areas taking internal motion and tumour regression into account, i.e., the clinical target volume (CTV) and planning target volume (PTV) expansions. PTV can expand to include CTV plus a margin of 0.5 cm or 1 cm in all directions. Likewise all critical organs are defined as bladder, rectum, and bowel, so that these can be avoided. [van de Bunt *et al.*(2006)] In figure 3.1 on the next page, the conventional treatment is shown.

TREATMENT MARGINS

The lymph nodes are included in the radiation target volume when the tumour stage and grade indicate a significant risk of microscopic nodal metastases or if overt node involvement is already present. Unenlarged nodes may still contain tumour deposits; therefore, it is necessary to include all lymph nodes within the draining regions in the CTV [Taylor *et al.*(2005)].

LYMPH NODES

Even though radiotherapy is performed to minimize radiation side effects still occur. All the side effects are caused by the ’double effect’ of radiotherapy, since it may stop spread of cancerous cells and simultaneously damage the healthy tissues or organs. Side

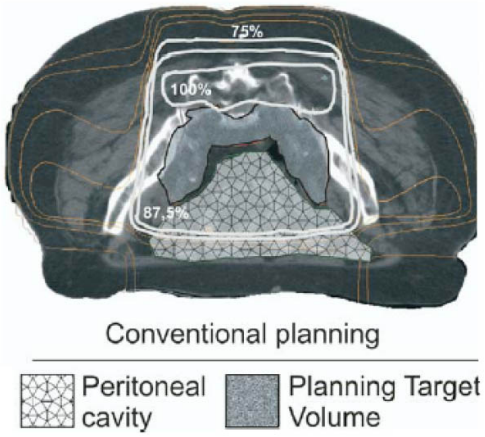

Fig 3.1: Transverse plane of a conventional plan. It is possible to make more boxes for adequate coverage of lymphatic nodes, the uterus, the cervix and the vagina. The three borders indicate the areas to irradiate [Roels *et al.*(2006)].

SIDE EFFECTS

effects depend mainly on the amount of radiation given and the part of the body that is treated. The more healthy tissues or organs are damaged by radiation, the more side effects can occur. The complications of radiotherapy to the abdomen and pelvis may include fatigue, nausea, vomiting, diarrhea, low blood count, urgent bowel movements or urinary problems, urinary incontinence or retention. For females, premature menopause, bladder irritation, or narrowing of the vagina due to scar tissue buildup may be caused by the radiotherapy. Besides, some general side-effects like hair loss, weight loss, weakness, drop in blood cell counts or skin disorders may occur. [Britannica(2010b), Britannica(2010a)] Though conventional treatment is planned to minimise radiation to critical organs, it can still be improved. [van de Bunt *et al.*(2006), Portaluri *et al.*(2004)]
As metioned above medical imaging technologies are employed to improve radiotherapy. Depending on how the image is obtained, and with various goals, medical imaging technology can be used in different situations, such as in the diagnosis of pelvic cancers, see 1 on page 3, and planing of treatment.

3.1 Medical imaging technology

The aim of medical imaging is to establish shape, structure, size, and spatial relationships of anatomical structures within the patient, and to give the spatial information about the body's function and pathology or abnormality. Medical imaging technology is widely used in healthcare, especially in the treatment of cancer: a) to diagnose and stage cancer, b) to guide cancer treatments, c) to evaluate the treatment, d) to monitor the effect of new drugs or new therapeutic innovation [Hajnal *et al.*(2001)].

Functional medical imaging technology, such as CT, PET, fMRI, has contributed to cancer care in many ways: It makes detection of cancer at an early stage possible; moreover,

the diagnosis and treatment could be less invasive, if supported by imaging technology such as Image Guided Radiation Therapy (IGRT). Medical imaging helps cancer care to improve the efficiency in treatment by giving more precise shape and location of the tumour. At last, the follow-up process will be more effective as well; science imaging technology gives a description of presence or spread of cancer or so called visualised response of treatment. [Hajnal *et al.*(2001)] At Aarhus university hospital, Aalborg Sygehus Syd CT is used for therapeutic scanning for the planning of radiotherapy.[Carl(2010)] Thus the following section will address CT imaging technology. Explanations of other imaging techniques can be found in appendix B.4 on page 90

Computed tomography (CT)

A CT scanner is an X-ray device capable of cross sectional imaging. Cross sectional images are obtained by passing the patient through a doughnut shaped gantry where a rotating X-rays source coupled to a bank of detectors produce diagnostic image of the patients body. This results in 2D X-ray transmitted images, known as slices. These 2D slices are then stacked to produce a 3D image of the inside of the patient by means of computer-intensive reconstruction techniques.[Carver(2006)]

X-RAY

In order to obtain good quality images, noise should be kept to a minimum. Several factors influence the noise level on the image, the primary ones being slice thickness, patient size, and applied mAs. Here is a trade-off to since images can be produced with almost no noise, but at the cost of increased dose as the noise level is related to the applied mAs. The slice thickness is changed compared to the amount of detail desired. As such conventional thick slices would be used for general soft tissue use. More photons contribute to image quality so noise is lower, a larger area is covered more quickly, the dose is reduced, and examination time is faster. Thinner slices are reserved for areas where high resolution was required; fewer photons contribute to the image, therefore noise level is higher, and to achieve a similar image quality to the thicker slice, the dose administered needs to be increased to improve the signal to noise ratio. More slices are also needed to cover the same area.[Carver(2006)]

The advantage of CT is its ability to differentiate overlying structures as well as show good contrast (spatial) resolution, and excellent bone detail. However even though good contrast is produced it can be difficult to separate e.g. vessels from other soft tissue given a very low contrast difference between these.

Data from a CT scan can be enhanced in several ways to show internal structure, e.g. by employing a contrast agent orally or through veins (as a bolus injection), when the patient is about to be scanned. How the contrast agent is administered depends on the target structure and the indications for the scan. Image intensity varies from structure to structure in CT images, due to the density of the different tissues. High-density tissue produce white areas on CT images while less dense tissue produces darker intensities. The contrast agent further weakens the X-ray in that region, resulting in higher intensities. [eHealthMD(2010), Hajnal *et al.*(2001)]

3.2 Image-guided radiotherapy(IGRT)

IGRT DIRECT RADIOTHERAPY

With assistance of a CT imaging technique, IGRT is implemented, which makes development of more sophisticated approaches to radiotherapy possible. IGRT is a process using frequent multiple dimensional imaging to direct radiotherapy with higher precision and accuracy. This process involves all steps in the treatment such as patient immobilization, CT simulation, treatment planning, verification and correction of patient setup, and delivery of radiation. Thus radiotherapy can be improved to reduce radiation of critical organs and tissues such as bladder. [of North America(2010), Huntzinger *et al.*(2006)] Patient management and outcomes have been improved significantly by such technical and clinical advances in radiotherapy. Radiation fields can be shaped by means of several techniques and approaches, e.g. intensity modulated radiotherapy that reduces volume of normal tissues and organs receiving high dose, comparing with conventional radiotherapy in pelvic region. [Taylor *et al.*(2005)]

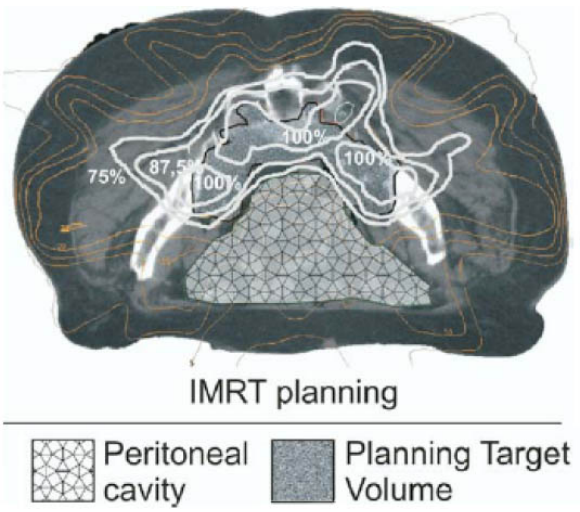

Fig 3.2: Transverse plane for an IMRT plan. The intensity of the radiation beam is controlled to focus a higher dose on the cancerous tissues and to spare the adjacent normal tissues. Several intensity-modulated fields are combined from different beam directions to produce a radiation dose that maximizes the dose of the region with cancer, and minimizes the dose to the healthy tissue. [Roels *et al.*(2006)]

3.3 Intensity modulated radiotherapy (IMRT)

IMRT

IMRT is an advanced method used to tailor the radiotherapy to the body structures of patients. It utilizes X-ray accelerators to deliver a precise radiation dose to a specific region of the body. The radiation dose is designed to conform a 3D shape of the region. The intensity of the radiation beam is controlled to focus a higher dose on the cancerous tissues and to spare the adjacent normal tissues. Several intensity modulated fields are combined from different beam directions to produce the tissue sparing treatment. Because of

the intensity-modulated fields, it is possible to irradiate the region with a higher dose than when using the conventional method. It is also documented that IMRT remains superior in overall sparing of the critical organs. On figure 3.2 on the facing page, an IMRT is shown. [van de Bunt *et al.*(2006), Schwarz(2010)]

Challenges

IMRT is gaining increased interest due to its ability to focus the dose of radiation while reducing the exposure to the surrounding healthy tissue. However it is difficult it implement as a standard treatment. This can be due to changing organizational and economical aspects from one procedure to another. The planning procedure is different from patient to patient, and for the same patient over time, which makes the dose calculations difficult and time consuming. [Schwarz(2010)]

Software improvement is needed as well in the treatment planning and verification process. One of the primary factors is reducing time in planning of volume delineation, and treatment planning. [Schwarz(2010)]

An obstruction to widespread implementation of IMRT for patients with pelvic cancer is the absence of an objective description of lymph node locations in three dimensional space, which can make radiotherapy planning of pelvic cancers easier. [Dinniwell *et al.*(2009)]

4 Problem statement

THIS CHAPTER OUTLINES THE GENERAL PROBLEM AREA, THAT IS THE SUBJECT OF THIS THESIS, AND ADDRESSES PRECISELY THE PROBLEM.

Pelvic cancer affects many patients and results in a decrease in length and quality of life. When pelvic cancers spread to lymph nodes in pelvis, it makes the situation more complex. Treatment can be performed with radiotherapy either to cure patient or to relieve pain. The treatment at Aalborg hospital, Sygehus Syd, is the conventional treatment. Radiotherapy is used to treat pelvic cancer with risk of damage in the healthy tissue around the site of treatment. Therefore, IMRT, an advanced treatment, which can spare the healthy tissue, would be preferable. However, it is very time consuming and complex to plan dose calculations here off. Furthermore, it is difficult to visualise lymph nodes. The pelvic lymph nodes lie adjacent to the iliac arteries and their branches, which indicates that these blood vessels with a margin can be used to locate the lymph nodes. The margin is estimated to 7 mm to ensure coverage of the lymph nodes [Taylor *et al.*(2005), Taylor *et al.*(2007)]. Therefore segmentation of the blood vessels is important in planning IMRT in pelvis. Thus if the arteries are segmented, a volume delineation of the margins with the artery and lymph nodes can be performed. This would improve the treatment and reduce time spent on planning. CT imaging with contrast agent given as a bolus is widely used at Aablorg Sygehus Syd to visualise vessels, since this provide enhanced vessels of a high resolution.

In this report, we investigate methods for precise segmentation of pelvic arteries with the use of vessel enhanced CT images. This is the key for decreasing the region of CTV. Furthermore, [J.Suri *et al.*(2002)] expressed in a review article of vessel segmentation the need for a technique which can track vessels to the second and third layers of branching.

Delimitation

The focus of this research is to produce a model for segmenting the arteries and thus locate the lymph nodes. Since 27.9 % of cancers occur in the pelvic region, and spreading to the lymph nodes has an increased mortality, cancers from this region will be focused. The treatment of interest is radiotherapy, which has been described in section 3.3 on page 14.

Part III

Analysis

5 Anatomy of arteries in the pelvic region

In this chapter an outline of the arteries in the pelvic region is presented and their importance is explained in relation to cancer in different regions of the pelvis. The focus of this investigation it the Iliac artery and its branching.

Lymph nodes are significant in diagnosis, in treatment planning, under treatment, and even in follow-up examination, because they are parts of the immune system and the lymphatic system, and they are important in classification of cancer staging. Especially for patients with pelvic cancer, the lymph node status is extremely important in determining the prognosis. [Chao and Lin(2002)]

The current medical imaging techniques are not good at visualising lymph nodes, but by using the knowledge that the pelvic lymph nodes are located adjacent to the arteries and their branches in pelvis, it is possible to delineate the CTV of lymph nodes. Because arteries in pelvic region can be shown in e.g. CT image by using contrast enhanced bolus, if the structure of these arteries can be extracted separately from image, the location of lymph nodes will be defined afterwards.

Because the arteries can be used to locate lymph nodes, a short description of arterial anatomy in the pelvic region is given. The major arteries have a shape similar to an upside down 'Y' which branch into smaller arteries in a tree-like structure. Abdominal aorta splits into three branches, Inferior mesenteric artery, right common iliac, and left common iliac. From left and right common iliac, a further branching occurs into internal iliac, and external iliac. These further branch into smaller arteries. [Martini(2006d)]

The thoracic aorta tapers approximately to 20-23 mm, depending on age, gender, and body surface area. The gender difference in aortic root dimension is not entirely explained by body surface area. The abdominal aorta narrows from thoracic aorta to 17-19 mm in its distal portion. At the point of bifurcation to common iliac it narrows to 13-16 mm. In common iliac, the diameter is between 7-10 mm. Inferior mesenteric, a branch from abdominal aorta, at the distal portion attached to rectum, has a diameter of around 4 mm at its origin and narrow to 2.5 mm at the distal end of the superior rectal artery. The smallest vessels in the pelvic region are down to 0.5 mm. The aorta and arteries of males are larger than those of females, and aortic root dimension increases with age, height, and weight. [Fuster *et al.*(2004), Cowan *et al.*(1991), Shatapathy and Aggarwal(1997)]

A detailed view of vessels in the pelvic region can be seen on figure 5.1

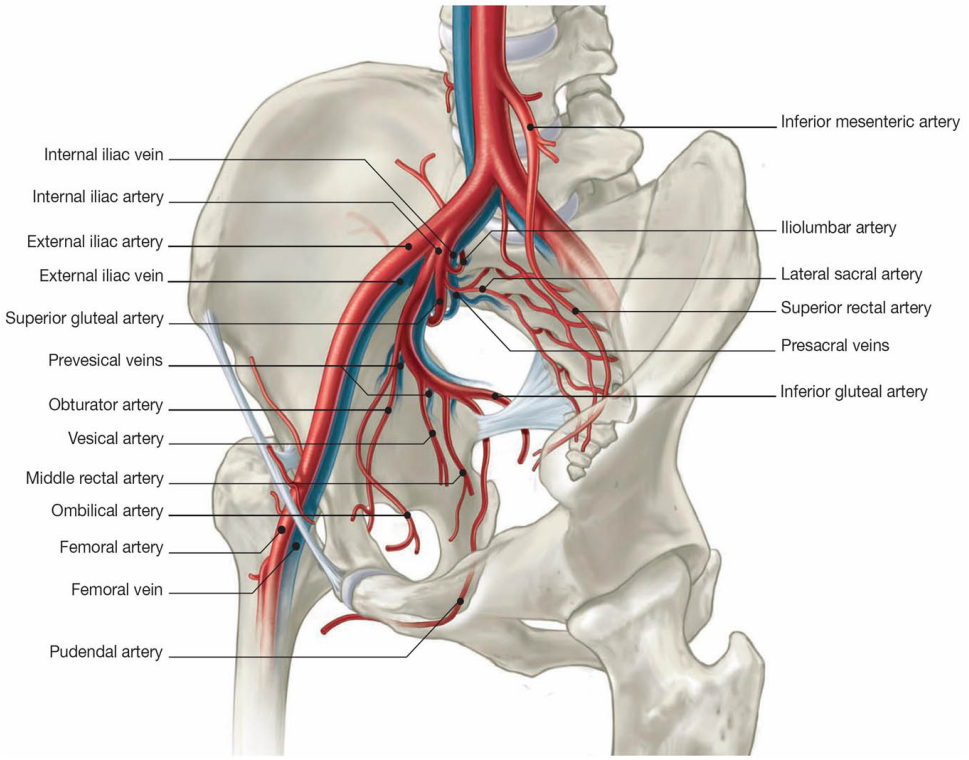

Fig 5.1: Anatomical description of main pelvic arteries and veins [Geeraerts(2007)]

To verify which vessels would be important to segment, a correspondence with the oncology department of Sygehus Syd was performed. The consensus for now is an increased interest in the small arteries in pelvic region, for instance, superior gluteal artery, and superior rectal artery, since they provide oxidized blood to the rectal area (rectal cancer), and thus it is expected that lymphatic vessels aliened to these arteries have a higher risk of cancer, if the patient suffers from rectal cancer. [Carl(2010), Taylor *et al.*(2005), Andreasen(2010)]

Which part of the iliac arteries that is of interest depends on the particular case. For instance a patient with bladder cancer, the delineation of the part from the internal iliac artery down to inferior gluteal artery, would be helpful in radiotherapy [Carl(2010), Taylor *et al.*(2005), Chao and Lin(2002), Martini(2006d)].

In the pelvic region, all organs have connection to some arteries descending from abdominal aorta. The table 5.1 on the facing page shows these connections.

BIG VESSELS
SMALL VESSELS

In this project, 'big vessels' are defined as abdominal aorta, the first branch of vessels from aorta, and internal iliac of second branch. 'Small vessels' are defined respectively as second, and third branch from aorta, and the connective arteries to the organs.

This table shows the most of interesting vessels. Furthermore, the connection in the table makes a more concrete goal for the segmentation, since the small vessels such as superior rectal artery is one of the targets of interest. The vessels that have connections with colon can not be seen on figure 5.1, but on the figure 5.2 on the facing page.

First branch	Second branch	Third branch	Connective artery	Organ
Inferior mesenteric	Left colic artery		Colic artery	Colon
Inferior mesenteric	Superior rectal artery	Sigmoid artery	Colic artery	
Inferior mesenteric	Superior rectal artery	Middle rectal artery	Inferior rectal artery	Rectal
Common iliac	Internal iliac	Superior gluteal artery	Middle rectal artery	
Common iliac	Internal iliac	Pudendal artery	Interal pudendal artery	Rectum and anus
Common iliac	Internal iliac	Inferior gluteal artery		Bladder
Common iliac	Internal iliac	Middle rectal artery	Deferential artery	Prostate
Common iliac	Internal iliac	Vesical artery	Deferential artery	
Common iliac	Internal iliac		Ovarian artery	Ovary
Common iliac	Internal iliac	Obturator artery	Uterine artery	Uterine cavity
Common iliac	Internal iliac	Pudendal artery	Vaginal artery	Vagina

Tab 5.1: Connection between organs in pelvic region and vessels descended from abdominal aorta. [B-Lynch *et al.*(2006), Mallandur(2008), Martini(2006d)]

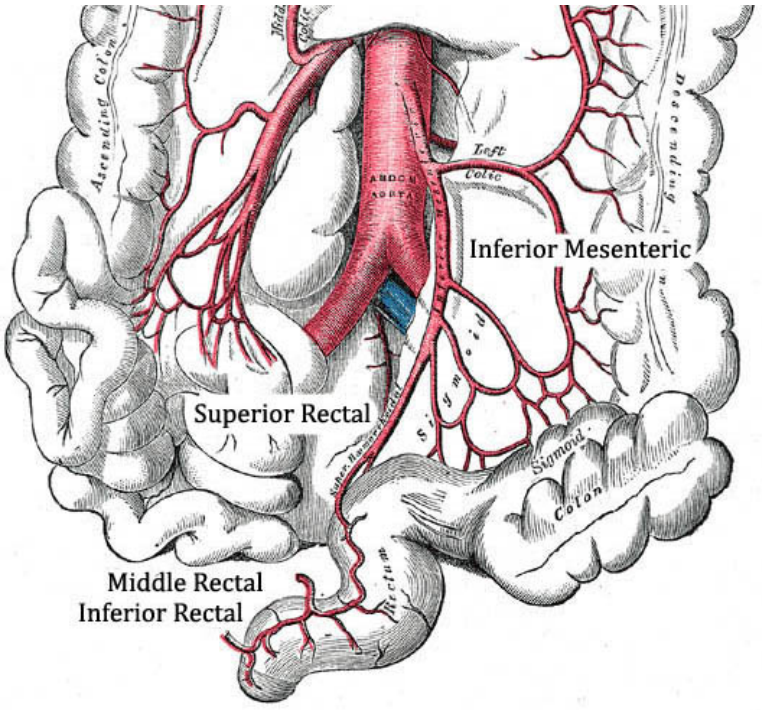

Fig 5.2: Anatomical description of colic arteries [Gray(1858)].

6 Data analysis of CT images

In this chapter the data obtained from the CT scan are analysed, and the possible challenges and bias are presented. This result in a summary of the most important topics.

Our goal is to extract the vascular tree of the pelvic region and provide a complete geometric description of the extracted tree compared to organs in this region. In this project, the data are obtained from 14 patients scanned with two types of CT scanners. All patients are elderly (age 60 to 80) and have cancer in the pelvic region. Vessels are enhanced with a radiographic contrast agent (Imeron or Omnipaque), injected as a bolus into the a vein. When the contrast agent passes down aorta to the pelvic region, the CT scanning process starts, this provides enhanced arteries. [Carl(2010)] The spatial resolution of a voxel is $1x1x2.5mm^3$, obtained with a 12 bit resolution, providing intensities from 0 to 4095. DATASET

Research in this field often assume the follow:

- Images are degraded due to Partial volume effect (PVE) [Wan *et al.*(2000)].
- As vessels are enhanced, it is assumed that contrast-enhanced vessels are brighter than their direct neighbourhood [Lesage *et al.*(2009)].
- Intensity values along the tree may vary due to the contrast medium's inconsistent spreading [Wan *et al.*(2000)].
- The vascular tree is a connected structure [Lesage *et al.*(2009), Martini(2006d)].

It is expected that the data obtained for this project are subject to the same assumptions; however a data analysis is performed to clarify this. The data analysis is associated with several challenges regarding PVE, image intensities, size and shape of vessels, and artifacts.

6.1 Partial volume effect

PVE is a limitation to the data since a single voxel can contain a mixture of multiple tissue values. Since the axial dimension of the scanned images is greater than the dimensions in the slice plane, this dimension provides the greatest limitation of PVE. [Mudry *et al.*(2003)] PVE occur due to the scanner being unable to differentiate between a small amount of high density material (e.g. bone) and a larger amount of lower density (e.g., cartilage), in a given voxel volume. The processor tries to average out the two densities or structures, and information is lost. This results in a smoothing of anatomical structures which effect

borders, as well as limiting segmentation of small arteries. [a. Kalender(2005)] Arteries in the pelvic region varies in diameter from abdominal aorta of 17-19 mm; common iliac of 7-10 mm, inferior mesenteric of 4-2.5 mm, to small arteries of 0.5 mm. [Fuster *et al.*(2004), Cowan *et al.*(1991)] See section 5 on page 21 for further information. This means that the smallest arteries can not be visualised. A finer spatial resolution will diminish the PVE and provide possibilities for more detailed segmentation of arteries. Thus the assumption that our data is degraded due to PVE is valid.

6.2 Image intensity

HOUNSFIELD UNITS

The intensities of voxels in CT images are described with Hounsfield units (HU). HU describe the amount of X-ray attenuation of each 'voxel' in the 3D image. Our data are represented as 12-bit binary numbers, and therefore have $2^{12} = 4096$ possible values. These values are arranged on a scale from -1024 HU to +3071 HU, calibrated so that -1024 HU is the attenuation produced by air having digital intensity value 0, and 0 HU is the attenuation produced by water, having digital intensity value 1024. [Radiography(2010), Encyclopedia(2010), Schneideryx *et al.*(1996)] This gives the following values for body structures seen in table 6.1.

Structure	Digital intensity value
Air	0
Fat	924–974
Water	1024
Muscle	1034–1064
Kidney	1054
Blood	1064
Bone	1260–2024
Skeleton– spongiosa	1260
Skeleton– sacrum	1413

Tab 6.1: HU Intensity values of body structures in the digitalized data. [Radiography(2010), Schneideryx *et al.*(1996)]

POSSIBLE BIAS

Because blood is enhanced with contrast agent, it is unsure which HU values blood has. This is affected by the amount of contrast agent used, as well as the CT scanners ability to follow blood induced with contrast agent through all slices. Thus further analysis of the data is required.

The different structures in the CT images are fat, muscle, organs, vessels enhanced with contrast agent, and bone. Histograms are used to obtain an overview of how the above mentioned structures are interconnected. The structures are shown from three histograms seen in figure 6.1 on the next page.

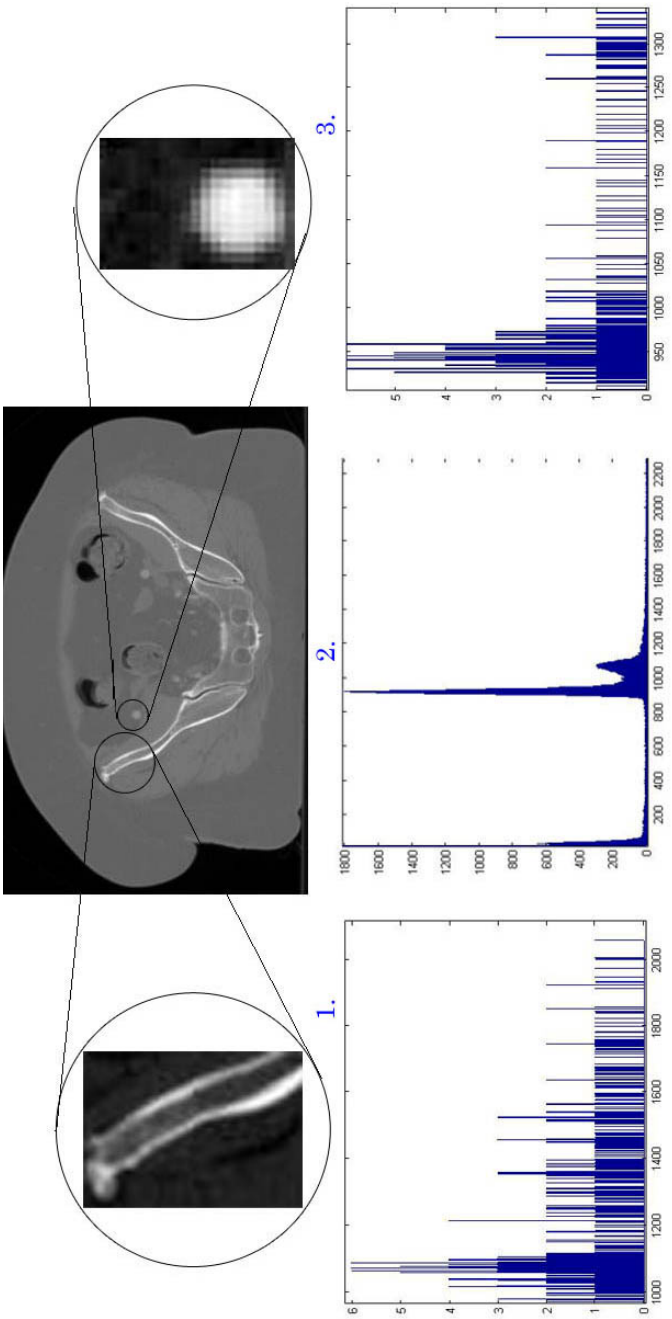

Fig 6.1: (1.) a cropped version of the centre image where bone, bone marrow, and muscle are included. Below this image is the histogram of the cropped image (the x axis shows intensities, while the y axis show the frequency of a pixel with a given intensity value).(2.) A CT image in the transverse view, below the image is its histogram. (3.) a cropped version of the centre image, where an enhanced artery, and fatty tissue are included, below the images is its histogram.

From the centre histograms 2 of figure 6.1, there can be seen three different intensity peaks; one sharp peak near zero, one narrow near 950, and one peak near 1100 flattening towards 1400. According to table 6.1 on the preceding page the first peak is produced by

air, the second by fat, the third by muscle, organs, vessels, and spongy bone. Due to the close interconnection between the different structure intensities, it is necessary to perform revised histograms where there only exists a small variation of identified structures.

On histogram 1, a cropped image is performed of the bone, spongy bone and muscle. From the histogram, a high peak is observed from 1000 to 1150, and a flatter positive skewed from 1200 to 2000. Because muscle produces the lowest intensity value in the image, it is expected that the first peak is a product of this. The second peak is a product of bone and spongy bone. Note from the image of the bone that the border between bone and muscle called periosteum, consisting of outer fibrous layer, and an inner cellular layer, is less compact than the circumferential lamellae of the bone [Martini(2006e)]. Together with PVE, this results in a darker gray near the border than the rest of the compact bone.

On the histogram 3 a cropped image is performed of an enhanced vessel and fat. From the histogram a peak is observed from 900 to 1000, and a flatter negative skewed from 1100 to 1400. Since fat produces lower intensity than enhance vessels, the first peak is assumed to be fat, while the second is assumed to be enhanced vessel.

LAMINAR FLOW

Visualisation of vessels show that there are higher intensities at the center of the vessels, see figure 3 in figure 6.1 on the preceding page. This is due to a laminar effect of the vessel walls. Friction near the vessel walls make the blood flow decrease, thus a higher amount of contrast is observed near the center resulting in the higher intensity. Furthermore it is expected that thinner vessel likewise will have a lower intensity due to the laminar effect in the circulatory system. This can be seen from figure 6.2. [Despopoulos and Silbernagl(2003)]

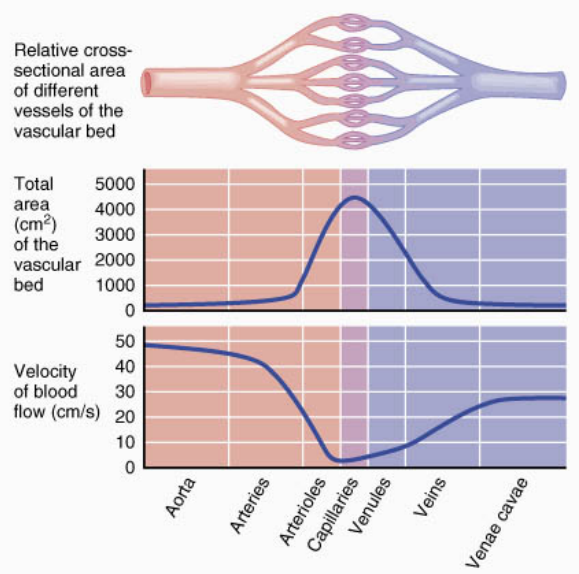

Fig 6.2: Laminar effect in the blood circulatory system [Despopoulos and Silbernagl(2003)]

From the histograms an illustration is constructed to show the interconnection of tissue, muscle and organ, arteries, and bone. See figure 6.3 on the facing page.

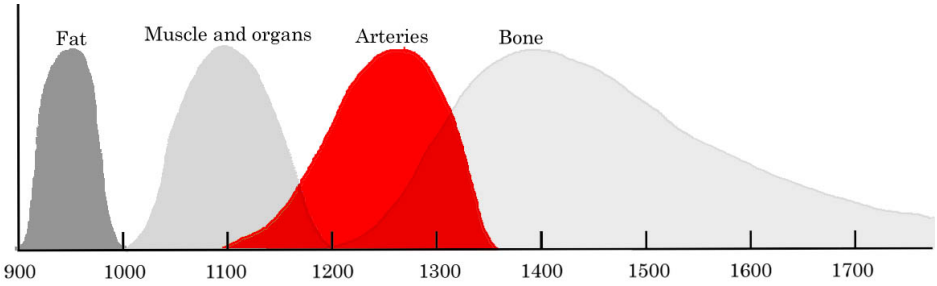

Fig 6.3: Illustration of the structures intensity distributed

The data of vessels obtained for this project varies in intensity range, having a closer interconnection to bone then muscle and organs, see histograms in appendix C on page 93. This can in part be due to intra-variation in data acquired from two different CT scanners with two different contrast agents as a bolus, and an anatomical inter-variation in arteries. Thus the assumption that contrast-enhanced vessels are brighter than their direct neighbourhood is partially true.

Contrast agents can produce different HU intensities depending on the chemical structure of it. However it is beyond this project to analyse the difference of these contrast agents. It is observed that vessel calcification (sclerosis) can influence flow of blood induced with contrast [Woodcock(1976)]. see figure 6.4.

Furthermore it is expected that an increased heart rate as well as laminar flow can affect the images due to an increased flow of blood, resulting in a higher exposure of contrast in the slices, thus producing higher intensities. Therefore the assumption that intensity values along the tree may vary due to the contrast medium's inconsistent spreading, is true in the data used.

VARYING INTENSITY

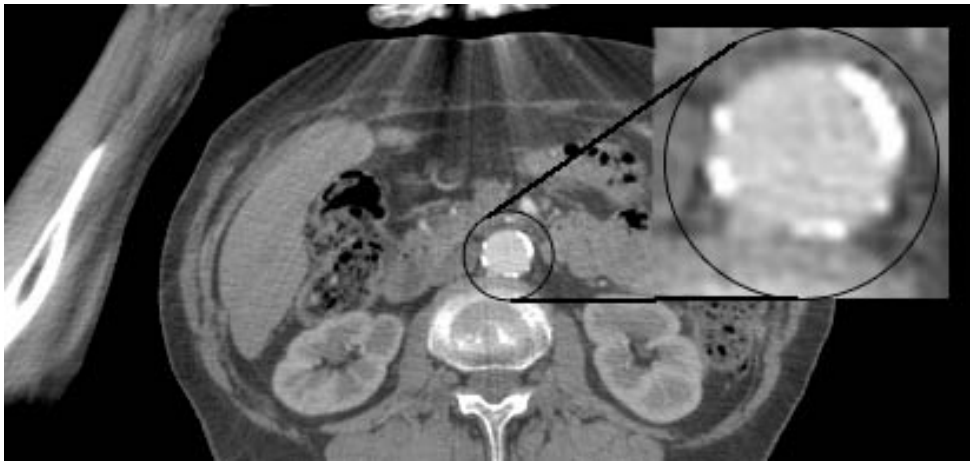

Fig 6.4: Calcification in aorta shown as the white high intensity blobs near the vessel walls

6.3 Size and shape

Vessels in the pelvic region have a structure similar to a tube, which in some cases curves. When vessels bifurcate, the structure will change at these points. Thus a segmentation method needs to address the challenge of curving connected vessels of different sizes in three dimensions as well as handle the change of bifurcation. This can be seen in figure 6.5 which also verify the assumption that the vessels in the pelvic region is a connected tree branching structure.

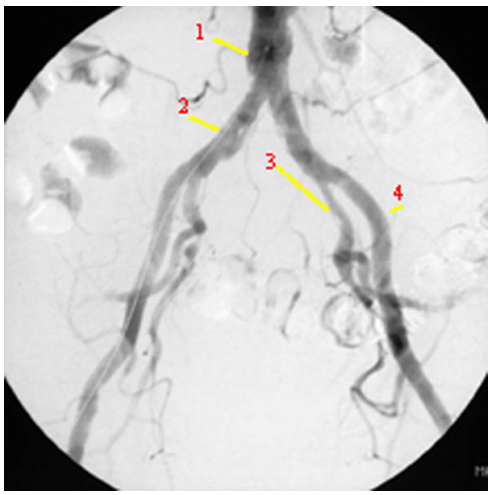

Fig 6.5: Angiogram of 1. Aortic bifurcation, 2. Common Iliac Artery, 3. Internal Iliac Artery, 4. External Iliac Artery. From the figure, bifurcation, and vessel characteristics are seen[of Vascular and Radiographers(2010)].

In figure 6.6, a small artery is shown localized close to bone structure. This has been seen in several datasets. Since intensity intervals of vessel and bone are overlapping and the physical location of vessel and bone are close, the segmentation of vessel can be challenging.

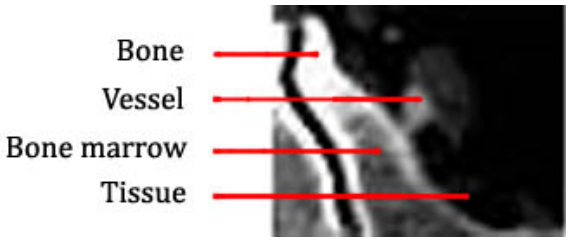

Fig 6.6: CT image with intensities from 1000 to 1500 of a vessel near the bone. The borders of compact bone and the vessel have similar intensities.

6.4 Artefacts

In some images, artifacts arising from rings, watches, or prosthesis do not only result in noise, but also affect the inherent information from the images. This can change the gradient between vessels and tissue or vessels and bone. See figure 6.7.

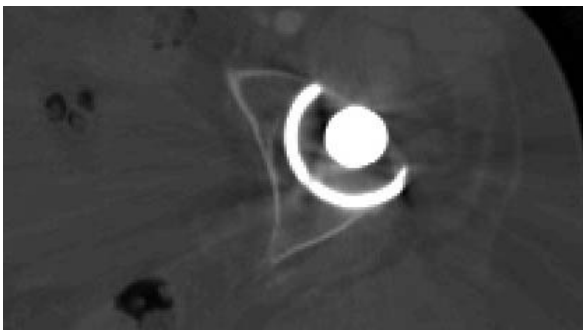

Fig 6.7: Artefacts occurring from metallic prosthesis

Artifacts produced by implants are inevitable and thus a segmentation method is needed which is less affected by that kind of noise.

Summary

From the data analysis the initial assumptions were partially verified and the following challenges for segmentation of vessels were identified:

1. Vessel intensities change from dataset to dataset
2. Vessel contrast change in the same dataset
3. Vessel and bone intensities have a close interconnection
4. Vessel and bone are spatially close in some slices
5. Vessel width changes
6. Artefacts

These challenges are based on PVE, laminar flow, intravariation from two CT scanners and two different contrast agents, and intervariation due to anatomical differences as well as prosthesis.

7 Current research

THIS CHAPTER DESCRIBES SEGMENTATION OF VESSELS IN MEDICAL IMAGING

Vessel segmentation challenges have been approached in many ways. Challenges like varying vessel width, bifurcations, noise and changing contrast are among the basic problems. [J.Suri *et al.*(2002)] expressed in a review article the need for a vessel segmentation technique which can track vessels to the second and third layers of branching.

An overview of segmentation techniques has been provided by [Lesage *et al.*(2009)]. In this review article three segmentation methods were identified.

- Region growing
- Active contour
- Centreline based

All these three segmentation methods are summarized by the similar primary principles used in the research. However there are different ways to use the same primary principle, which means that even though methods might be classified as the same, there may be significant differences.

7.1 Region growing

Region growing approaches, are based on segmenting an object by recruiting neighbouring voxels founded on some low level inclusion criteria. This is performed from an initial points or regions located inside a vessel. Classical region growing methods are based on a simple intensity threshold as performed by [Boskamp *et al.*(2004)] or on growth-limiting criteria proposed by [Metz *et al.*(2007)] to lessen risks of leakage. Besides the classical region growing, adaptive methods have been developed to cope with potential over- and under segmentation by dynamically adjusting parameter such as inclusion thresholds [Lorenz *et al.*(1997)].
With these approaches, the inputs are generally provided manually, which does not influence the popularity of the methods, because of their simplicity and computational efficiency.

7.2 Active contour

Active contours segment an object by evolving a contour through differnet forces:

External forces, derived from the image, and interna, model based forces. Since classical implementation of active contours in 3D have some problems with e.g. using curvature-based regularization that prevent the capture of thin, elongated surfaces, some other developed active contours have been presented: parametric and implicit active contours. Parametric active contours (snakes) are dependent on a precise Lagrangian formulation of a contour evolution, and some of these methods are specifically designed for vessel segmentation like topology-adaptive snakes. Snakes allows a better capture of thin and branching structures by controlling contour splitting and merging [McInerney and Terzopoulos(1996)].

Implicit active contours, especially level-set techniques, have been popular to a degree. The level-set framework does not have parametrization problems inherent, and topology changes are handled implicitly. A vessel-dedicated method called Curves evolves a 1D curve on a 3D domain; this has proved to be well adapted to vascular segmentation [Lorigo *et al.*(2001)].

7.3 Centerline based

Centerline-based techniques focus on directly extracting the vessel centerline, which can be difficult, while the complete volume information is usually not part of the final result. Thus in most cases, a rough volume segmentation can be acquired by means of centerline. Most centerline tracking techniques follow one branch at a time, relying on manual reseeding to extract a complete tree. To automatize bifurcation handling, some authors have proposed to perform the segmentation of the lumen locally and rely on topological criteria, similar to region growing.

There are several other kinds of centerline-based methods: model-based optimization between two points, and minimal path techniques.

In segmentation by model-based centerline optimization, knowledge of both start and end points will give some advantages; a method to solve this problem is using fixed boundary conditions [Lesage *et al.*(2009)]. Such methods balance data through the parametrization of the energetic formulation.

Minimal path techniques are particularly popular for centerline extraction, global optimality is a key motivation in these and results in good robustness even in case of corrupted data. Classical vessel-dedicated minimal path algorithms focus on extraction the centerline curve, and with a new idea of incorporation an additional dimension corresponding to the vessel radius, [Lesage *et al.*(2009)] used multiscale feature to improve the minimal path technique.

An intuitive way to solve vessel segmentation is through the use of region growing,

since this method is simple as well as effective for structures, which branch into different directions. It was chosen to use region growing since this offers several advantages. The wanted region will never contain too much of the background, so long as the parameters are defined correctly. The borders of regions found by region growing are perfectly thin by using the simple concept, and it is stable to produce connected edges. The algorithm is also very stable with respect to noise. Most importantly, membership in a region can be based on multiple criteria. [Gonzalez *et al.*(2004)]

There are, however, several disadvantages to region growing. First and foremost, it is very expensive computationally. It takes both serious computing power (processing power and memory usage) and a decent amount of time to implement the algorithms efficiently. Secondly, the method sometimes cannot distinguish the shading of the real image by using the single type information of the image. At last, holes or over segmentation could appear causing noise or variation of intensity. [Gonzalez *et al.*(2004)]

[Boskamp *et al.*(2004)] proposed in 2004 a segmentation method based on region growing for vessel segmentation of vessel enhanced CT images, which solves some of the basic problems like varying vessel width, bifurcations, and noise. [Boskamp *et al.*(2004)]'s method is based on intensity differences of enhanced vessels and neighbouring tissue. To avoid leakage to other areas, [Boskamp *et al.*(2004)] used varying intensity thresholds, thus adapting the threshold to the data. However, when interfering structures e.g. bone are close to vessels spatially as well as in intensity, it can be difficult to exclude the interfering structure based on region growing with intensity as a similarity parameter alone. [Boskamp *et al.*(2004)] handled this challenge by applying a watershed technique to separate vessels from bone. Our work is inspired by this study.

Part IV

Method

8 Vessel segmentation

IN THIS CHAPTER THE VESSEL SEGMENTATION IS PRESENTED AS WELL AS THE NECESSARY CONSIDERATIONS AND THEORY FOR EACH METHOD APPLIED. 14 DATASETS ARE AVAILABLE. THE METHOD FOR VESSEL SEGMENTATION IS DEVELOPED ON FIVE OF THESE DATASETS AND THE VALIDATION OF THE METHOD IS BASED ON THE NINE REMAINING DATASETS

The segmentation method is developed in MATLAB R2010a. The aim of the vessel segmentation is to achieve a 3D image of the vessels in the pelvis. In order to obtain this, an initial segmentation is performed, followed by an extended segmentation. The purpose of the initial segmentation, is on the macro level, to ensure connectedness of the vessels in the final 3D image. The purpose of the extended segmentation is to obtain an improved 3D image of all vessels. It is primarily the small vessels that are of interest since these could be located near lymphatic nodes. However, in order to improve the planning of IMRT it is also necessary to know where the larger vessels are located.

Region growing can be performed in many ways, however all forms of region growing follows the principle of growing from one or more seed points to regions by comparing the neighbouring voxel similarity [Gonzalez *et al.*(2004)]. From CT images with contrast-enhanced vessels, it is most plausible to use intensity as a parameter for similarity. Thus in this study it is chosen to focus on intensity based region growing like [Boskamp *et al.*(2004)] as the primary segmentation method. From the data analysis in chapter 6 on page 25 some challenges were identified. The following challenges will be addressed:

CHALLENGES

1. The contrast of the vessel vary throughout the dataset
2. Vessel and bone intensities are similar
3. Vessel and bone are spatially interconnected in some slices

The first challenge is addressed in both the initial and the extended segmentation methods through the use of region growing with an adaptive threshold, while the other two are addressed solely in the extended segmentation with morphological image processes which will be described in section 8.2.1 on page 44.

In figure 8.1 on the following page the vessel segmentation method is illustrated. The input is the original images recorded in the transverse plane, after cropping.

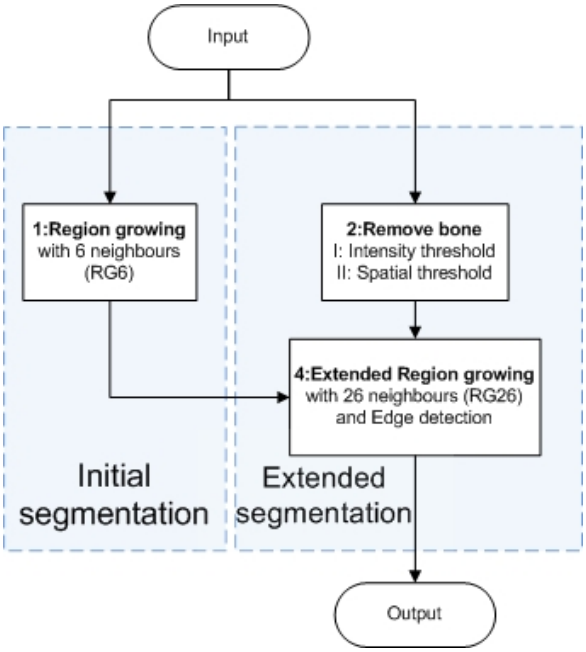

Fig 8.1: The vessel segmentation is illustrated with functions in a consecutive order.

8.1 Initial segmentation

The purpose of the initial segmentation is to produce a primitive segmentation of the vessels and thus ensure connectivity of the vessels before further image processes are applied. The initial segmentation is based on a region growing method with six neighbours and an adaptive threshold. Connectivity is one of the key words for region growing. When the vessels have a continuous structure, region growing can handle the challenge of bifurcation and different widths of vessels as long as the vessels are connected - in our case to aorta.

8.1.1 Region growing

REGION-BASED Region growing is a simple region-based image segmentation method, where the pixels are grouped into larger regions with predefined criteria for growth. As a region-based segmentation method, region growing can be explained by the following formulations:

- (a) $\bigcup_{i=1}^{n} R_i = R$
- (b)Ri is a connected region, i = 1, 2, ...,n
- (c)$R_i \bigcap R_j = \phi$ for all i = 1, 2,...,n
- (d)P(Ri) = TRUE for i = 1,2,...,n
- (e)P($R_i \bigcap R_j$) = *FALSE* for any adjacent region Ri and Rj

R represents the entire image region, R1, R2,, Rn represent the subregions in R. P(Ri) is a logical predicate defined over the points in set P(Rk) and ϕ is the null set.

A region growing approach examines neighbouring voxels of one or more initial 'seed points' and determines whether the voxel neighbours should be added to the region. In the same manner as general data clustering algorithms, the process is iterative for each boundary voxel in the region. Region growing exploits the important fact that voxels which are close together have similar gray values. The substantial process is described as below:

1. Choose the initial seed voxel(s)
2. Check the neighbouring voxels and add them to the region if they are similar to the seed
3. Repeat step 2 for each of the newly added voxels
4. Stop if no more voxels satisfy the criteria for inclusion in the region

Neighbouring voxels

Neighbouring voxels can in 3D be 6, 18 or 26 voxels, compared to the distance to the centre voxel. A distance of 1 would equal 6 neighbours, distance $\sqrt{2}$ equals 18, and $\sqrt{3}$ equals 26. More neighbours result in higher sensitivity but also a less time efficient region growing. Likewise the increased amount of voxels can result in connectedness to bone with voxel intensity values similar to the vessels. In figure 8.2 an illustration of 6, 18 and 26 voxels neighbours is shown.

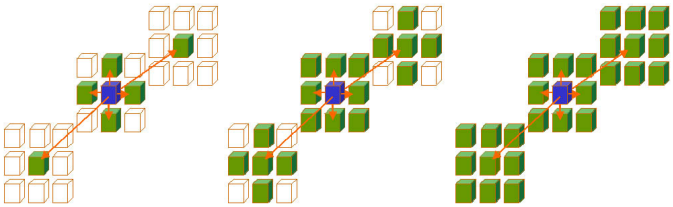

Fig 8.2: [Left:] A 6 neighbour model. [Middle:] An 18 neighbour model. [Right:] A 26 neighbour model. The blue voxel represents the center voxel, the green are neighbouring voxels and, white voxels have no connection to the centre voxel. Orange arrows are used to show the connection to the centre.

Due to the removal of large bone an increased threshold can be used to segment vessels. However with an increased threshold value, over segmentation arise from tissues with similar intensity as low contrast vessels. To limit the over segmentation, edge detection is used as an exclusion criterion.

Region growing with six neighbours

The region growing implemented in the initial segmentation is based on an initial user interaction by selecting a seed point where aorta is clear. From this seed point the inclusion of voxels is performed iteratively by comparing all unallocated neighbouring voxels to the

region. Comparison is performed by calculating the difference between the neighbouring voxel intensity and the respective regions mean intensity. The neighbouring voxel with the smallest measured difference is allocated to the region. This process stops when the intensity difference between the mean value of the region, and new voxels become larger than a certain intensity threshold TH. The formulation of is as follows:

MEAN VALUE

$$|M - X| < TH \tag{8.1}$$

Where M is the mean intensity value of the voxels in the region, and X is the intensity value of the new voxel, which is considered to be included or excluded.

To meet the challenge of changing vessel contrast, the region growing use an adaptive global threshold, which change iteratively by calculating a new mean value for the region after inclusion of a new voxel. The algorithm for computation of the mean value is as follows:

$$M_1 = \frac{M_0 \cdot n + X}{n + 1} \tag{8.2}$$

M_1 is the new mean, M_0 is the old mean, n is the amount of voxels included in the region, and X is the intensity of the newly added voxel.

Threshold value - TH

TH is changed from dataset to dataset due to different intensity interval of vessels in the datasets. It was observed from the first seven datasets that volumes from the best manually chosen thresholds were between 9258 to 22336 voxels with a mean value of 15958. For most datasets there would be a 'leap' in the voxel amount after the best manually chosen threshold to around 50000 and above, due to over segmentation, see figure 8.3 on the facing page. Thus it was chosen to produce an upper threshold of 50000 voxels which would prevent further additions of neighbours in the region growing method and improve system efficiency by stopping unfortunate over segmentation.

For every dataset a graph is computed with the amount of voxels segmented on the y-axis compared to a given threshold value on the x-axis.

SEMI-AUTOMATIC

To avoid manually laborious work by finding the right TH value, a semi-automatic method is integrated to provide an initial suggestion of the best threshold. This is performed by iteratively running the region growing method with changing TH value until over segmentation occur. The last segmentation before the voxel amount exceeds 50000 is visualised. If this segmentation is satisfactory, e.g. no visual bone or tissue is included, it is assumed to be the best segmentation.

By using this initial segmentation, the big vessels are segmented without bone. To obtain more vessel structures, TH should be increased. However, the greater TH, the larger the risk of over segmentation.

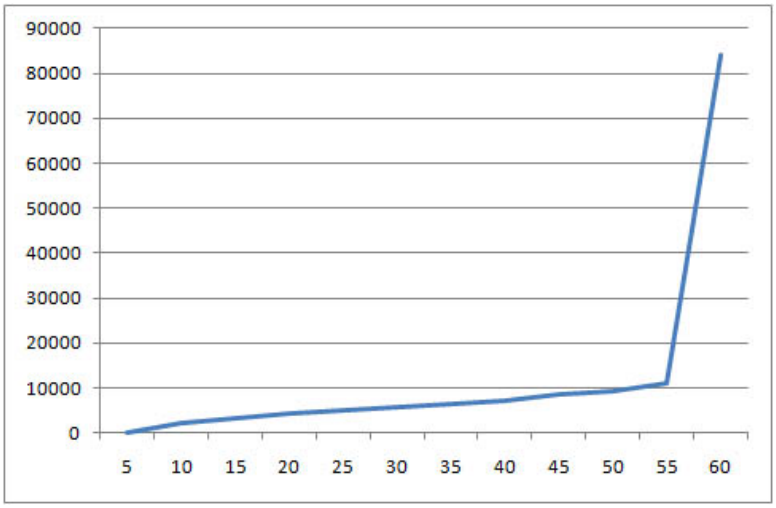

Fig 8.3: The x-axis show the TH and the y-axis the amount of voxels segmented to the given TH

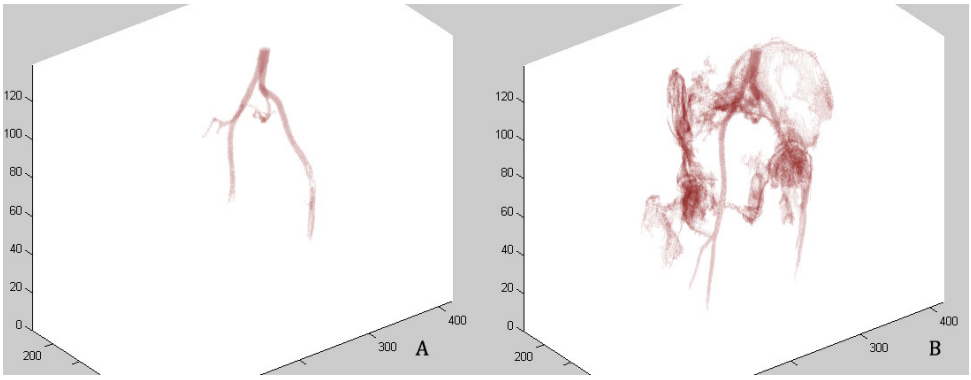

Fig 8.4: A. show the initial segmentation of vessels with a TH of 55, while B show an over segmented image with TH 60.

As can be noted from figure 8.4, a greater TH can result in segmentation of bone as well. Bone are close to vessels spatially as well as in intensity, thus it can be difficult to exclude the interfering structure based on region growing with intensity as a similarity parameter alone. Thus, an extended segmentation is needed to include smaller vessels while removing disturbing structures like bone.

The initial segmentation is capable of making a rough blueprint of the large vessels without including bone structure. However, this segmentation is not sufficient. If the smaller vessels should be segmented along with the larger ones, there is a risk that the region growing would spread to bone structure and fail to include the smaller vessels. The initial segmentation is however of crucial importance, since the extended segmentation (in 'Remove bone') might eliminate some big vessels in some slices, and thereby connectivity of a vessel could be lost. This problem will be explained in 'Remove bone' under the Extended segmentation.

8.2 Extended segmentation

The purpose of the extended segmentation is to produce a more detailed segmentation of small vessels. However due to interconnection of bone and vessel both spatially as well as in intensity, the region growing method may most likely result in segmentation of both bone and vessels. Thus, it is necessary to remove bone structure near vessels before a more detailed segmentation of vessels is possible.

8.2.1 Remove bone

Removal of bone is based on prior knowledge of bone and tissue being separated in HU intensities. Furthermore bones are larger structures than vessels. This knowledge is used to separate bone from the images. Thus, the method consists of two simple steps: 'Intensity threshold' to exclude tissue and thereby make bone the largest structure in the images, and 'Spatial threshold' to remove structures (e.g. bone) larger than a pre set value.

Intensity threshold

Intensity threshold is performed by comparing voxel intensities with a pre set intensity value, thus dividing the image into two values. Values above the threshold are 1, while values below are 0. Generally bone intensity is well separated from intensities of other tissues. [a. Kalender(2005)] However, if a patient suffer from a degenerative bone disease like Osteoporosis, intensities of bone in the CT images can thereby be lowered, that makes it more difficult to separate bone from tissue or vessel.

In data analysis in section 6 on page 25, bone intensity was studied. No bone intensity below 1200 was observed, and therefore this value is used as the threshold which will separate bone structure from other tissues. Thus it is assumed that the lower intensity boundary of bone is 1200, making this value adequate to separate bone structure from other tissues except enhanced vessels. The result of this step is an image with bone and some vessels. See figure 8.5 or figure 8.6 on the facing page for an illustration of the result.

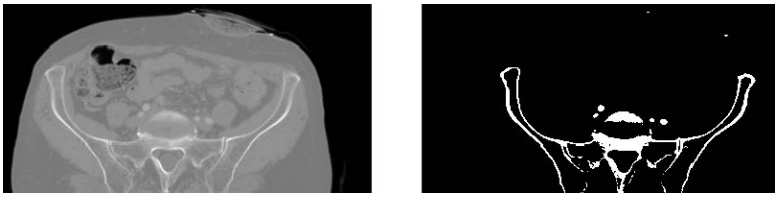

Fig 8.5: [Left:] A CT image in 2D from the pelvic region in a transverse plane. [Right:] A global high pass thresholding of the CT image.

Spatial threshold

The next step after intensity thresholding is a morphological removal of bone in 2D images, known as a spatial threshold. Bones can be separated from slices in the transverse plane, by

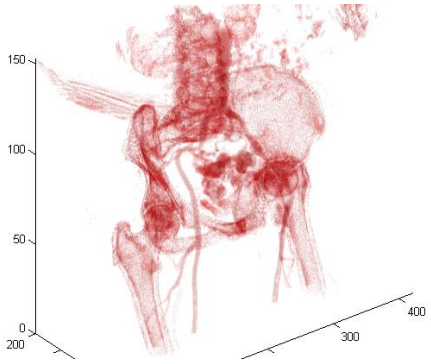

Fig 8.6: A globally thresholded CT image in 3D.

exploiting that bone is a larger structure than vessels.

The applied morphological image process is based on theory of connected component with adjacency of pixels. Adjacency is the connectivity of neighbouring pixels with intensities within a given range, e.g., in a binary image, adjacency can be defined either as one or zero, connecting all neighbours with this pixel value. A connected component (region) is a subset of adjacent pixels, all connected with consisting pixel intensities, for instance, one in binary images. If regions are separated, they are treated as different regions in the image. [Gonzalez *et al.*(2004)]

After partitioning an image into regions, an exclusion of unwanted regions can be performed. This exclusion criterion is based on finding regions larger than a given threshold and then invert the image. The inverted image is then superimposed with the original image. This gives the original intensities of the image, while excluding regions larger than a given threshold. A spatial threshold was set empirically to 200, as regions larger than this are more probable to be bone structures than vessels. If the value is too big, bones close to vessels will not be removed; if the value is too small, unnecessary removal of vessels can occur. On figure 8.7,the result of the method is shown.

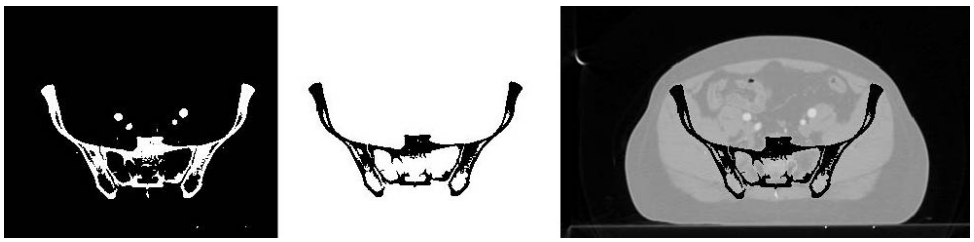

Fig 8.7: [Left:] The result from intensity threshold. [Middle:] The inverted image where large connected components are excluded. [Right:] The image after it has been superimposed with the original image

Removal of connected components in 3D is difficult, because this would lead to removal of both bone and the vessels. However, because bone and vessel only touch in some slices, removal in 2D ensures that only the connected vessel in the respective slice would

be removed instead of the whole vessel tree.

8.2.2 Extended region growing with 26 neighbours

The purpose of this method is to segment the vessel tree and especially the small vessels, which cannot be segmented with the 'Initial segmentation'. It is based, like the previous region growing, on the same semi-automatic intensity thresholding, but with larger values. However the method uses comparison of 26 neighbouring voxels. Furthermore, edge detection in 3D is included as a parameter to restrict growth into tissues with similar intensity as low contrast vessels.

In some slices from the output of the step "Rome bone", vessels could be removed as a large region due to e.g. a vessel is aligned along the transverse plane or touch bone. However, because the initial segmentation already has segmented the big vessels, this segmentation of vessels can supplement the extended segmentation by adding lost vessel information to the output from 'Remove bone'. This is performed by comparing all voxels from the two images. If a voxel is 1 in the initial segmentation and 0 in the 'Remove bone' output, this information is added. Figure 8.8 illustrate the effect of this step.

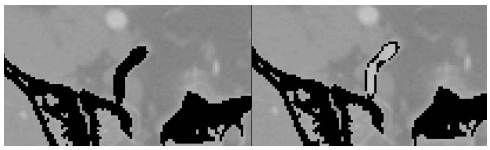

Fig 8.8: [Left:] the output after removal of bone. [Right:] The output after including soft initial segmentation to A

As mentioned earlier intensity intervals of vessels change notably from dataset to dataset, requiring different threshold values. To obtain the best result, the data is segmented with different threshold values in the same manner as explained in section 8.1.1 on page 41. In figure 8.9 on the facing page a table of the segmented volumes are shown for a dataset.

The best segmentation without edge detection is at TH of 110. Note that there are only few small vessels segmented. When TH is increased, leakage occur, this is shown in 2D in figure 8.10 on the next page.

Edge Detection

Edge detection in all directions in 3D, can in theory result in a closed boundary for the arterial tree in pelvis. This is the foundation of this parameter, since region growing would grow from the inside of the artery with the initial seed point. The use of edge detection is based on the assumption that contrast-enhanced vessel have a higher intensity than its neighbouring structures. [Lesage *et al.*(2009)]

Edge detection is employed to detect changes in intensity. This is based on strength and direction at a location (x,y,z) of a dataset. First and second order derivatives can be used to enhance edges. However, second order derivatives have a stronger response to fine detail,

SECOND ORDER DERIVATIVES

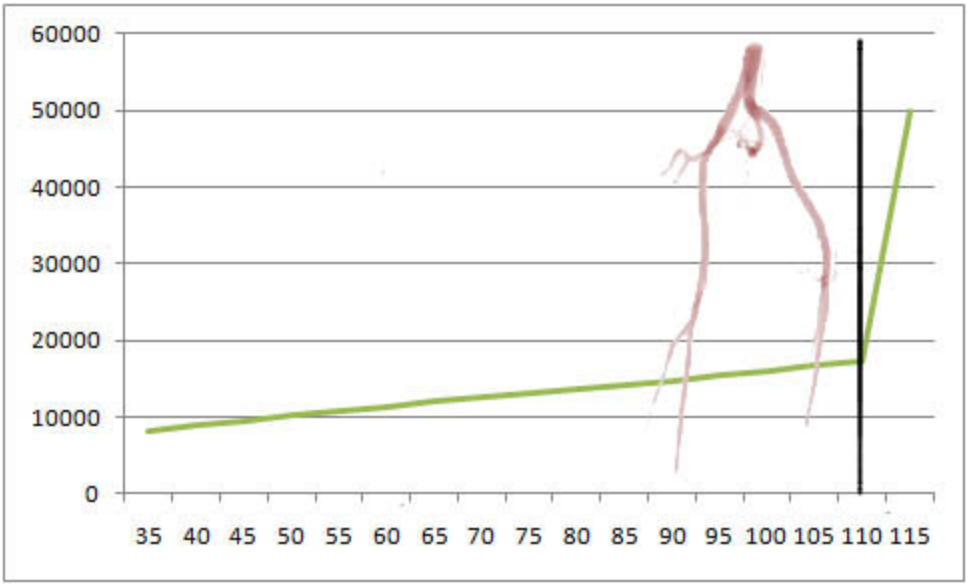

Fig 8.9: The x-axis show the threshold value TH and the y-axis the amount of voxels segmented to the given TH. The vessel tree is the best segmentation with TH 110

Fig 8.10: The segmentation with region growing with 26 neighbours, without edge detection

such as thin lines like vessels, and isolated points. Derivatives of a digital function are defined in terms of differences. To approximate these differences, second order derivatives must be zero in areas of constant intensity, nonzero at the onset and end of an intensity step or ramp and zero along intensity ramps. To compute second order derivatives, spatial masks of 3x3 can be used as seen in figure 8.11. 3D edge detection is performed by using the four masks on the xy, xz, and yz plane, this provided a 3D boundary.

0	0	0		0	1	0		1	0	0		0	0	1			
1	-2	1		0	-2	0		0	-2	0		0	-2	0			
0	0	0		0	1	0		0	0	1		1	0	0			

Fig 8.11: Horizontal, Vertical, and two diagonal masks

The mathematical function is as follows:

$$\frac{\partial^2 f}{\partial x^2} = f''(x) = f(x+1) + f(x-1) - 2f(x) \tag{8.3}$$

Furthermore, it is noted that second order derivatives produces a double edge response at ramp and step transitions in intensity. This produces a voxel at the border with high positive intensity and one inside the border with high negative intensity. In small vessels all voxels will be negative while the border is positive. This characteristic of second order derivatives is used as an inclusion criterion. As long as voxels are negative in the edge detected planes, the region grows. In large vessels this results in holes near the centre of a vessel.

An example of the result from the four masks on a 2D image can be seen on figure 8.12.

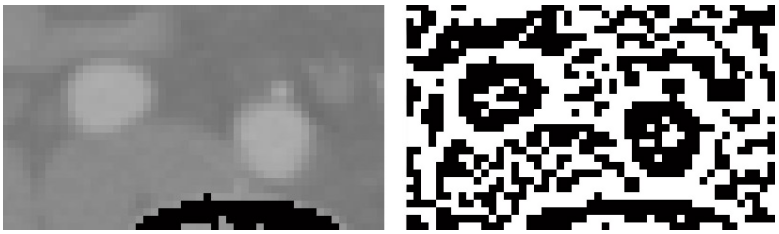

Fig 8.12: [Left:] A CT-vessel enhanced image. [Right:] An edge detection where negative values are shown as black

'Extended region growing' have an increased sensitivity to segment vessels due to the higher threshold and increased neighbours while excluding other structures.

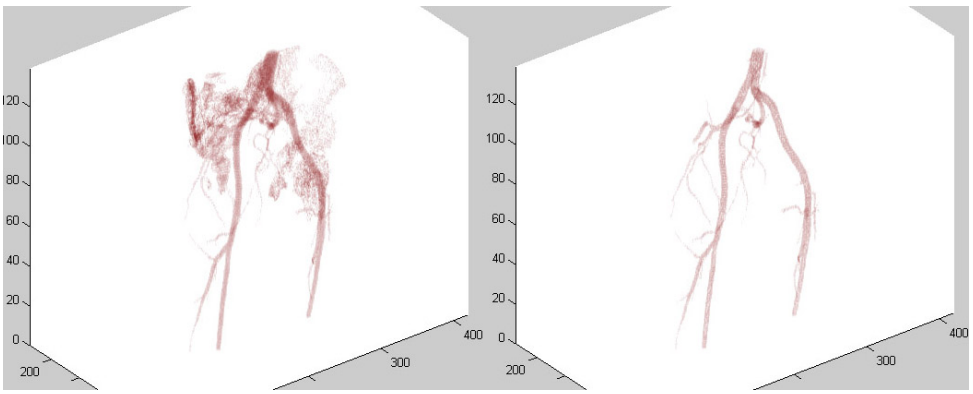

Fig 8.13: [Left:] A region growing segmentation without edge detection at TH 130. [Right:] A region growing segmentation with edge detection

The segmentation shown in figure 8.13 was performed with a TH value of 130. However, it was chosen to stop the segmentation of the region growing without edge detection when it exceeded an inclusion of more than 50000 voxels, because of computational complications. It is noted that the edge detection parameter restrict the region growing to produce holes in the large vessels. Since this only occur in the large vessels which already have been segmented in the initial segmentation, information from the initial segmentation can reused to fill these holes. Thus if some vessel information would be lost due to the edge detection restriction, this could be included in the final result. The result can be seen in

figure 8.14

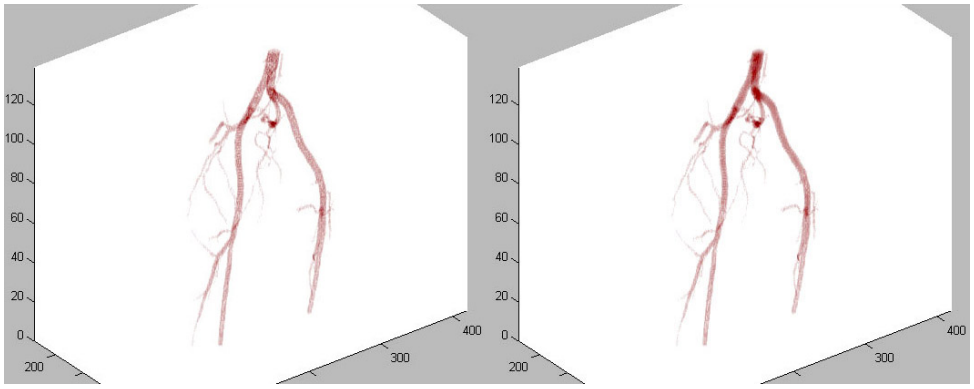

Fig 8.14: [Left:] The output from 'Extended region growing with 26 neighbours'. [Right:] The result after 'initial segmentation' output is merged with 'Extended region growing with 26 neighbours'

Figure 8.15 show one of the tables for the extended region growing with 26 neighbours where the amount of voxels are shown, compared to there respective TH. It is noted that there is an improvement in the amount of voxels included while avoiding segmentation of bone.

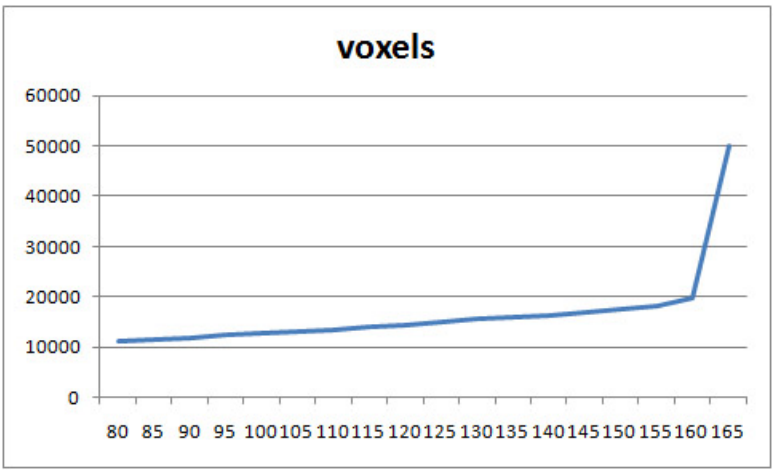

Fig 8.15: The x-axis show the threshold value and the y-axis the amount of voxels segmented to the given threshold.

The amount of voxels were calculated from the seven test datasets with the best chosen TH, without visual bone. These vary from 13081 to 30830 voxels with a mean value of 23847.

Part V

Test

9 Test

In this chapter, the vessel segmentation method will be tested, the results of the tests will be shown as well.

The test is divided into three parts. First, the different steps of the method will be tested separately. Secondly, there will be tests of the complete method, where accuracy and consistency is tested. At last, there will be a qualitative test to verify if the segmented vessels are arteries and which of them can be identified as the vessels of interest.

The first test of the different steps is divided into three steps to extract the vessels: initial segmentation, segmentation in removing bone structure, and extended region growing. Thus, every step needs to be tested.

9.1 Test of initial segmentation

The purpose of this test is to verify whether the initial segmentation can extract the big vessels without over segmentation, and if the initial segmentation provides the connective vessel structure.

The test of extracting the big vessels is performed through observation in 2D images by comparing the output of the initial segmentation with the original image.

The test of providing connective vessel structure is performed by observing the 3D output to confirm or dismiss the connectivity.

Figure 9.1 shows one of the results for the test of extracting the vessels.

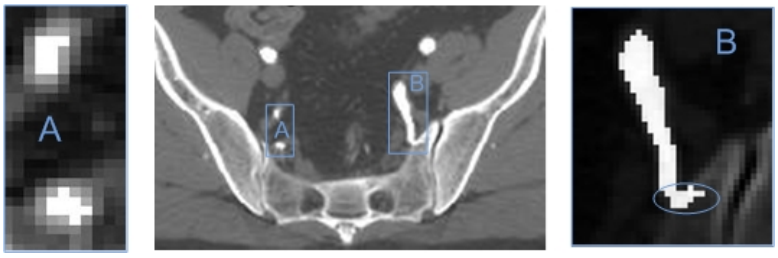

Fig 9.1: [Middle:] The initial segmentation in 2D from dataset 8 , where the segmented image is highlighted (white) in the original image . [Left:] Under segmentation of the edge of vessels (gray areas around the white ones). [Right:] Over segmentation of bone and bone marrow (the white areas in the ellipse).

For the test of providing connective vessel structure, one of the results is shown in

figure 9.2 .

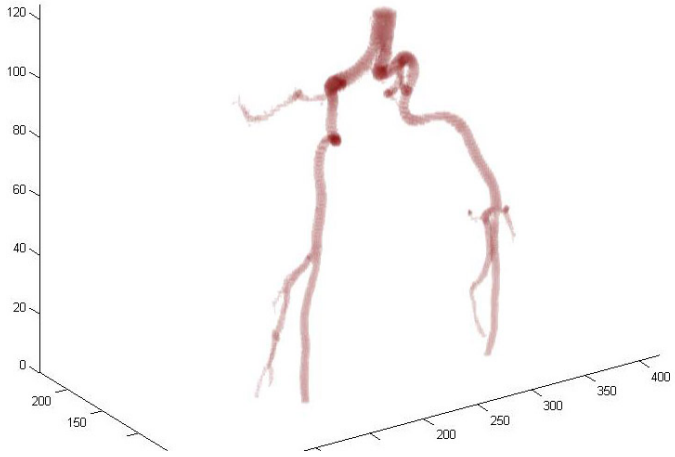

Fig 9.2: The initial region growing segmentation shown in 3D for dataset 8

It is confirmed that most segmentations can extract the big vessels without over segmentation. Furthermore, it is confirmed that big vessels are segmented in all datasets providing connectivity.

9.2 Test of segmentation in removing bone structure

The aim of this test is to test whether the step that removes bone structure has separated vessel from bone.

The test was performed by observing the output from step 'Remove bone' in the transverse plane.

It was observed that there were no connected vessels and bones in all the slices for all datasets. In the case that remaining vessel and removed bone were close in a slice, the intensities of the pixels in the area between them was recorded. An example of this in 2D is showed in figure 9.3.

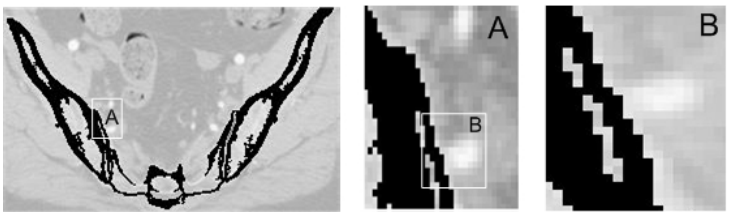

Fig 9.3: [Left:] Output of the segmentation step. [Middle:] 'A' is the magnified image of the output. [Right:] 'B' is the magnified image of 'A'. Notice the bright areas of 'B' between the removed bone (black) and the vessel (white). Here connection to bone would have occurred previously.

By analysing the recorded intensity values together with the intensity values obtained from surrounding area of the corresponding area in the original image, the area was con-

firmed to be the edge of bone, which has intensity under 1200 but close to the vessel intensity. Thus, this area (remained bone edge) could be included as a part of vessel later in the segmentation. This could cause the over segmentation of bone structure at last.

9.3 Test of extended region growing

This test consists of two parts:

- Effect of different neighbouring voxels
- Effect of edge detection

The separated tests will be described as followed.

9.3.1 Effect of different neighbouring voxels

The various amounts of neighbouring voxels gives different sensitivity for the region growing method, therefore it will be tested whether there are different effects of using 6, 18 or 26 neighbours.

All three region growing methods were performed on the same dataset with the same seedpoint and the same TH value, the only difference was the numbers of neighbours.

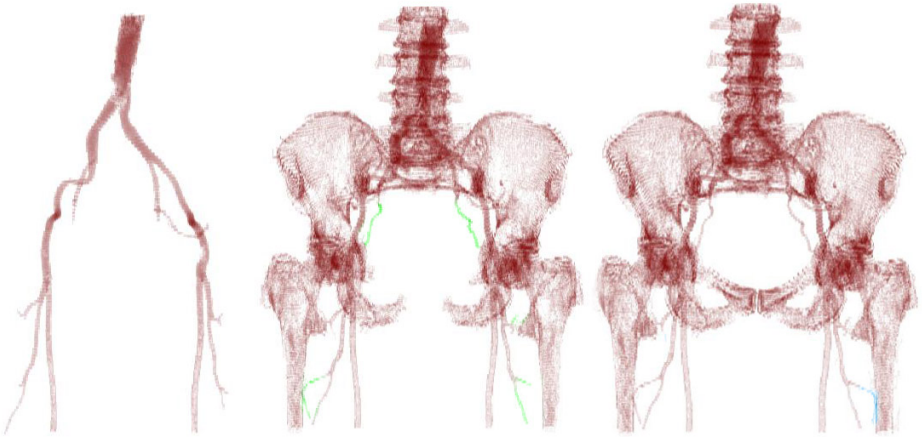

Fig 9.4: [Left:] A 6 neighbour region growing model. [Middel:] An 18 neighbour region growing model where vessel improvement compared to 6 neighbours, has been highlighted with green. [Right:] A 26 neighbour region growing model, where vessel improvement compared to 18 neighbours, has been highlighted with blue.

As can be seen from figure 9.4 and increased number of neighbours improves extracted details of vessels. Thus, region growing with 26 neighbours is more sensitive and prone to over segmentation of bone structure, which has the similar intensity as the vessels, than region growing with six neighbours.

9.3.2 Test of edge detection

For the extended RG, we have used edge detection as an exclusion criterion. Thus, this test has the purpose to verify whether edge detection has an improved effect to limit the region growing.

In this test, the vessels in all datasets are segmented by region growing 26 with and without edge detection. One of the most satisfactory segmenation results (of dataset 14) is shown, see figure 9.5.

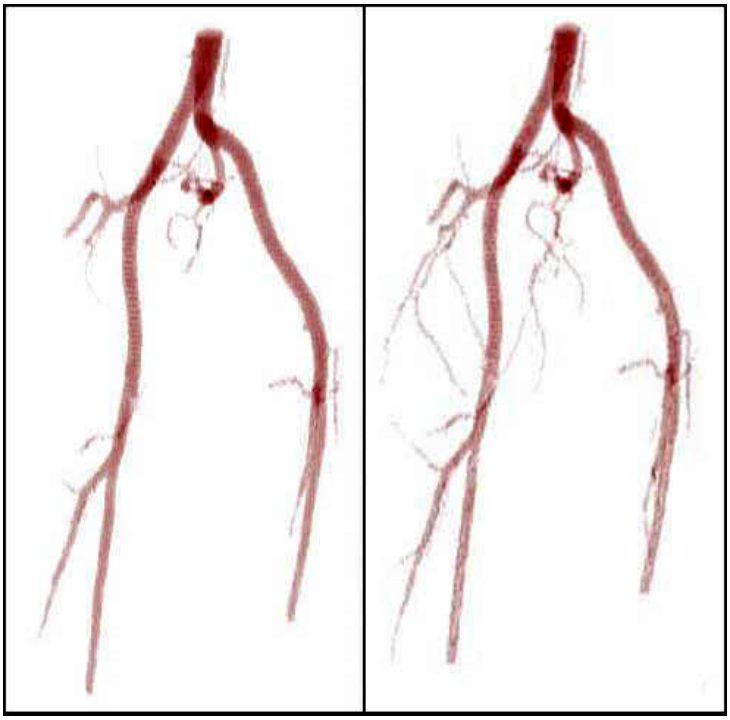

Fig 9.5: [Left:] The best result from data set 14 without edge detection. [Right:] The best result from data set 14 with edge detection.

A bar chart shows segmented volumes for all test datasets with and without edge detection, see figure 9.6 on the facing page.

From figure 9.5 it can be observed that the region growing with edge detection improves segmentation compared to without edge detection. The bar chart is shown to confirm that extra vessels are included without over segmentation for all these datasets.

9.4 Test of the complete segmentation

The test of the complete segmentation is divided into two main categories: accuracy and consistency. Accuracy is tested through a closer inspection of over and under segmentation and the semi-automatic initial TH value. While consistency is verified by testing if the method segments the same amount of voxels when different seed points have been applied.

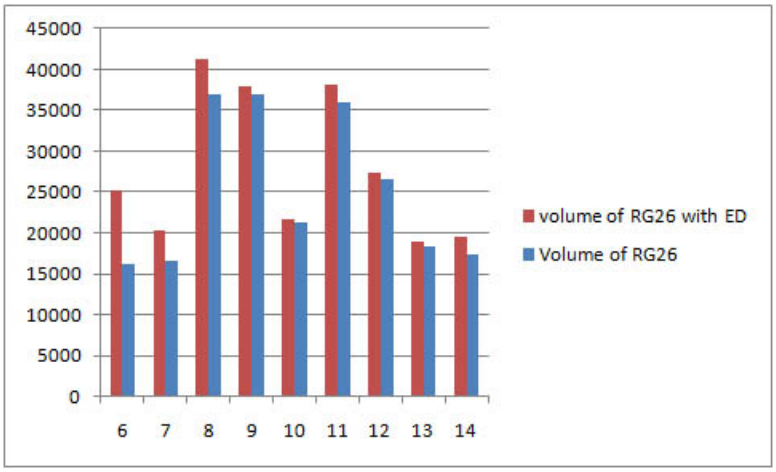

Fig 9.6: The amount of voxels from the finest segmentation result with and without edge detection for all test data sets. x-axis: dataset number; y-axis: volume amout. 'RG26' in the bar chart means 'Region growing with 26 neighbours'.

9.4.1 Accuracy

OVER- AND UNDER SEGMENTATION

The purpose of this test is to verify whether there are over- and under segmentation in the results. Over segmentation arises when other structures than vessels are extracted, while under segmentation arises when omitting portions of vessel structure. Because the precise segmentation without over- and under segmentation is almost impossible to find, an exact corresponding TH value is thereby difficult to obtain. Thus, the standard for over- and under segmentation is only presented to a relative.

The test is performed by comparing the segmented result to the original image in 2D. The volume count of 'finest segmetnation' results are employed besides the observation to assess if there are obvious over segmentation.

The following table shows the boundary TH values and volume counts of applied segmentation results for all test datesets. These so called 'finest segmentation' are desided by finding the TH value and volume just before visible over segmentation (in 3D) arises for all test datasets.

Dataset no.	6	7	8	9	10	11	12	13	14
TH	135	125	145	145	100	165	135	195	130
Volume	25104	20213	41237	37892	21758	38173	27256	18868	19597

Tab 9.1: Threshold and volume of finest segmentation before over segmentation for all test datasets.

The test result shows that over- and under segmentation could occur. However, this is unfrequently. The over segmentation arose when some bone sturctures that have not been removed by the earlier segmentation step. Under segmentation arose when the boundary of vessels are not included in the segmented structure. In figure 9.7 on the following page, the

over- and under segmentation is shown.

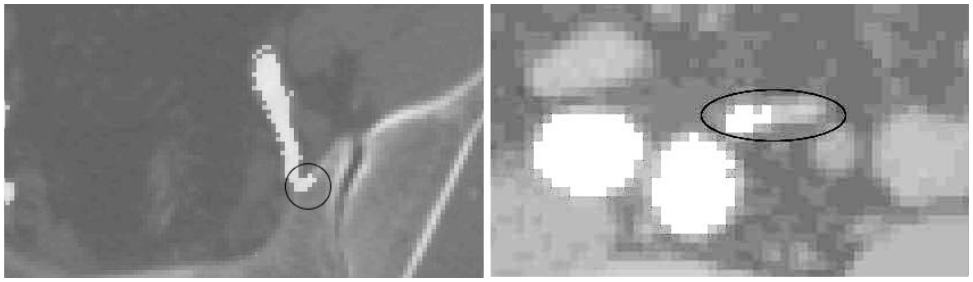

Fig 9.7: The segmented vessels are highlighted in the figures. [Left:] A slice where over segmentation occurs shown in the circle. [Right:] The Oval shows a location (the gray area) where vessels should have been segmented.

9.4.2 Effect of semi-automatic TH

The test has the purpose to veriry if semi-automatic TH can find the finest segmentation result. This is performed by comparing the TH value and volume count obtained by the semi-automatic TH with the corresponding values used in the test of over- and under segmentation 9.1 on the previous page, called 'Finest TH' and 'Finest volume'.

It has been tested that the initial setting of upper boundary for volume count, 50000, has been effective, as over segmentation arose for all datasets when the volume count exceeded 50000.

Thus, the last TH value and the volume count just before the segmentation was stopped, were taken as the 'Auto TH' and 'Auto volume',

Dataset no.	6	7	8	9	10	11	12	13	14
Auto TH	135	*150*	145	145	100	165	135	195	130
Auto volume	25104	*27740*	42216	37892	21758	38173	27256	18868	19597
Finest TH	135	*125*	145	145	100	165	135	195	130
Finest volume	25104	*20213*	42216	37892	21758	38173	27256	18868	19597

Tab 9.2: Threshold and volume count of finest segmentation, before over segmentation for all test datasets.

The result shows that, the semi-automatic TH has been able to find the eight right TH values of nine datasets.

9.4.3 The reliability of the vessel segmentation

The vessel segmentation using region growing starts with the manual input - the seed point, which might change from time to time. Therefore, it is necessary to test if the different input can affect the segmentation result, thereby the reliability of the segmentation can be verified.

This is done by applying 10 different seed points in aorta for one test dataset (data 14) under the same conditions such as TH, the voxel volume of each is counted to observe if there is a variation among the results.

Seed point	(103,232)	(103,231)	(105,230)	(106,230)	(104,230)
Volume	19597	19597	19597	19597	19597
Seed point	(105,235)	(110,231)	(108,230)	(110,232)	(105,232)
Volume	19597	19597	19597	19597	19597

Tab 9.3: The result of segmentation extracted from different seed points with TH value 130

The test shows that, the different input would not affect the the segmentation result. It is possible that the reliability can be affected by using a lower TH value, since the inclusion criterion thereby will be stricter. This was not tested, because the boundary TH for all datasets are relatively high, over 100 for all datasets, seen from table 9.1 on page 57.

9.5 Quantitative Validation

A quantitative validation of segmentation was performed to se whether the segmentation structures were vessels, and if they were the required vessels.

A doctor was asked to execute the manual comparison of segmented vessels with the anatomical atlas for all test datasets. The figures presented in report 5 on page 21, figure 5.1 on page 22, fugure 5.2 on page 23 and table 5.1 on page 23, together with the book 'Clinical Anatomy for Medical Students' are applied as references. In the validation, the various small vessels were identified. The table 9.4 shows the names of vessels that could be identified in the segmentation results in all test datasets.

Artery/Dataset no.	6	7	8	9	10	11	12	13	14
Inferior mesenteric artery (1)	X	X	X	X	X	X	X	X	X
Left colic artery (2)	X	X	X	X	X		X	X	X
Sigmoid arteries (3)		X						X	
Anterior division of internal iliac (4)	X	X	X	X	X	X	X	X	X
Middle rectal artery (5)	X	X	X	X		X	X	X	X
Internal pudendal artery (6)	X	X	X	X	X	X	X	X	X
Inferior gluteal artery (7)	X		X	X	X	X	X	X	X
Posterior division of internal iliac (8)	X	X	X	X	X	X	X	X	X
Iliolumbar artery (9)	X		X	X		X	X	X	X
Lateral sacral artery (10)	X		X	X		X		X	
Superior gluteal artery (11)	X	X	X	X		X		X	X

Tab 9.4: The identified vessels of the vessel segmentation output. [Snell(1973a), Snell(1973b)]

In the table, 'X' means that the vessel can be identified. The vessels '*Anterior division of internal iliac*' and '*Posterior division of internal iliac*' are listed in the table in order to give a clearer view of the result, since they are upper classes of the vessels of interest as well as '*Inferior mesenteric artery*'. [Snell(1973b)]

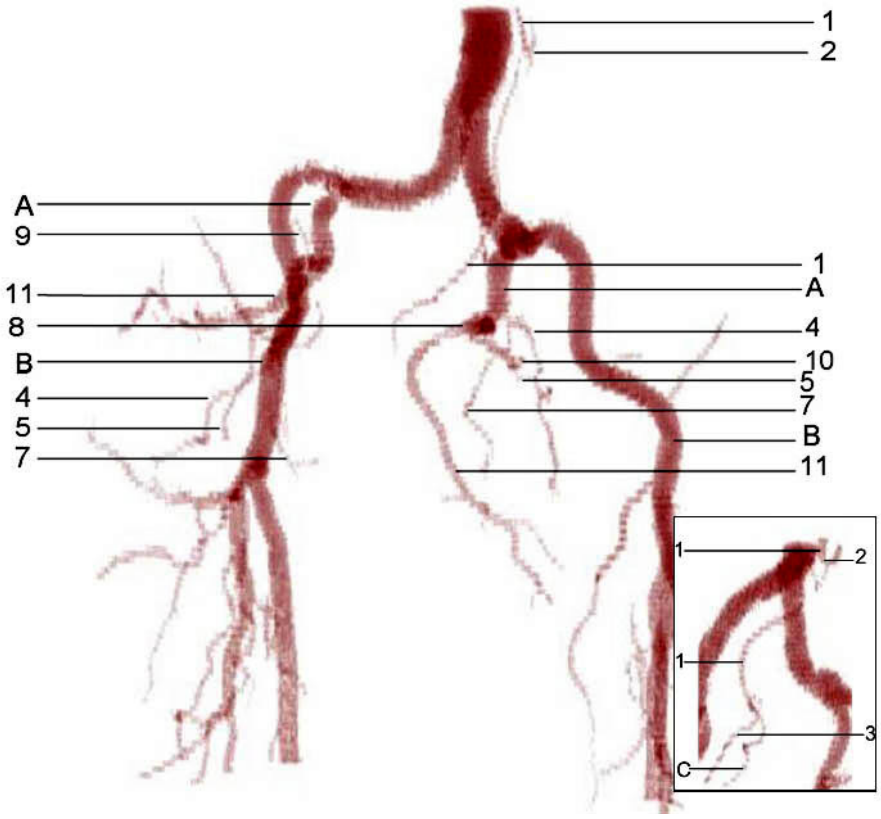

Fig 9.8: The final segmentation result, view point is right rear. The big figure shows the identified vessels listed in the table 9.4 on the preceding page with the corresponding numbers, some of them can not been seen clearly, the figure 9.9 on the next page will give a better view of these vessels. The figure in the lower right corner show the segmented Inferior mesenteric artery and the branches of it, which cannot be shown well from this view point.

In the figure 9.8, the vessels 'A' are Internal iliac arteries, and 'B' are External iliac arteries. These vessels are indentified to confirm the symmetrical structure of the segmentation result as well as to give a clear view of the structure of vessels. 'C' is Superior rectal artery, which has not been identified in most of datasets.

As figure 9.8 and figure 9.9 on the facing page showed, the visible structure has not only the form of vessel but also the characters of curving and branching, which supports that the segmented results are vessels. Moreover, under the comparison, the symmetry of left- and right external/internal iliac are detected as well as the branches from both the internal iliacs. This symmetry can be substantiated by the anatomical knowledge, which confirms the segmented structures are vessels and not other substances.

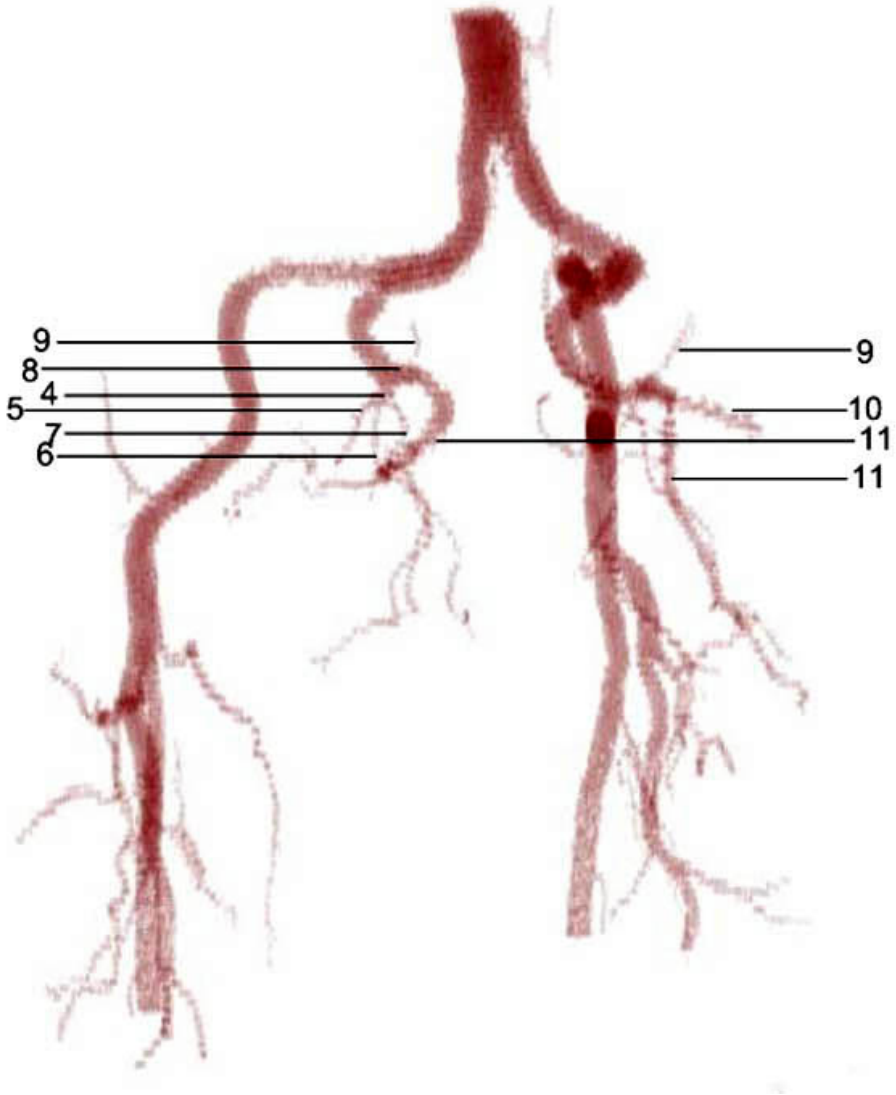

Fig 9.9: The same segmentation result as figure 9.8 on the preceding page show, but with the left rear view point. The name of vessels can be found in the table 9.4 on page 59.

The whole results showed that the segmentation structures were vessels, and most of the required vessels could be found.

Part VI

Discussion and Conclusion

10 Discussion

THE PRELIMINARY ANALYSIS CONTAINS SEVERAL CONSIDERATIONS, ALL RELATED TO THE TREATMENT OF CANCER IN THE PELVIC REGION. THE MOST IMPORTANT CONSIDERATIONS ARE DISCUSSED IN THE FIRST SECTION OF THIS CHAPTER. AFTERWARDS THE DEVELOPED METHOD FOR SEGMENTATION OF VESSELS IS DISCUSSED AS WELL AS THE RESULTS AND THE DATA, FROM WHICH THE RESULTS ARE OBTAINED.

One out of three people in developed countries will suffer from cancer. 27.9 % of cancer patients suffer from pelvic cancer in Denmark. Whenever a cancer spreads to the lymph nodes, the result is an increased risk of distant metastasis and death. More than half of cancer patients receive radiotherapy in some connection with their treatment. Conventional radiotherapy is often used resulting in overexposure of X-ray to sensitive organs. This can be improved with IMRT. However this is often not used due to its complicated planning. It is expected that IGRT of arteries can improve the complicated planning of lymph nodes.

In this project, IGRT image sare obtained from vessel enhanced CT images. This was performed to improve segmentation of vessels. The segmentation of vessels was based on region growing due to its ability to extract thin connected structures. Tests of the method were performed in a systematic order. The test was performed to ensure if all steps of the segmentation fulfilled their purposes. Then the test was performed to verify accuracy and consistency of the method. After testing this, a qualitative validation was done with the aid of a doctor to test the method's ability to segment vessels by comparing the segmented vessels to anatomical atlas.

When using all image segmentation methods the problems of over- and under segmentation have to be considered to some degree. In medical environments where the segmented results are used either to diagnose or for treatment, it is important to produce a precise result, since this can affect the diagnosis or treatment. Therefore, accuracy of the segmentation is required.

In this project, over segmentation was defined as inclusion of bone or tissue and under segmentation as exclusion of important vessels. However, validation can be difficult to perform, and the result of validation is often subjective due to the need of a manual observation and analysis of segmented vessels.

Segmentation is affected by the quality of the original images. Thus if an image is

influenced by artefacts, it can impact the result of the segmentation. Data acquired in this project was produced by two CT scanners where vessels were enhanced with contrast bolus. The CT scanner measures the intensity in abdominal aorta and then starts when a specific intensity equal to the contrast intensity is obtained. However the scanners were not designed to follow the contrast the whole way down in the body, which means that the scanning sometimes could be out of phase with bolus peak. This would result in a lower intensity of the vessels that produces datasets with changed intensity of vessels from slice to slice, this was also observed from the datasets. If this problem was handled e.g. by tracking the bolus through the pelvic region, it is expected that the intensity of the data would be more consistent. If data is obtained from other CT scanners, it is expected that the contrast of different structures will likewise vary respectively. However by adding an adaptive TH value to region growing, this variation is less important for the segmentation.

The segmentation method developed in this project is based on the following assumptions which will be introduced in the different parts of the evaluation of the results.

1. Bone is separated from tissue in intensity interval
2. Large bone structure can touch vessels
3. Vessels are brighter than the neighbouring tissue

10.1 Evaluation of results

We have presented an approach based on classic region growing similar to the method presented in [Boskamp *et al.*(2004)], however we have implemented edge detection as a restricting parameter, as well as removing of bones that are spatially close to vessels.

10.1.1 Part segmentation

The initial segmentation was verified to be able to extract big vessels and to provide the connective vessel structure. However, in a few cases, the lower part of vessels could not be included in the region due to a low TH value, chosen to avoid over segmentation. This could affect the final segmentation of some important vessel structures, if these vessels were removed in the 'Remove bone' step, due to loss of connectivity. Nevertheless, in lower part of pelvis, bone and vessel structures are well separated for all test datasets, thus, these big vessels would be extracted by the further segmentation.

Though the connectivity of vessel can be kept in the big vessels, some vessels could become a little smaller in diameter than the corresponding ones from the original images caused e.g. by calcification or the effect of laminar flow that makes blood intensities near the vessel walls lower than near the central axis of the vessel. This could induce under segmentation in the final segmentation result as well as a disconnection to small vessels.

The segmentation in removing bone structure has been confirmed to be able to separate vessel from bone, though in few cases the small vessels that are connected with bone are removed, as well as bone structure. Thus, the lost small vessels might not be extracted again in the further segmentation process. The worst case would be that aorta or other big vessels are removed instead of bone. This problem was addressed by including the information from the output of initial segmentation, but as mentioned previously, the vessel diameter might become smaller.

The application of an intensity threshold of 1200 was based on the assumption that intensity of bone and tissue could be separated by using this value. However, some bone structures such as bone marrow are left in the image because of their lower intensity values. The effect of this could be a separation of bone structures into two or more relative small bone regions. The separation of bone regions could produce a problem when the spatial threshold is used. By using a lower intensity, this separation might be removed, but this could also increase the risk of removing vessels, which might not be reconstructed by the initial segmentation, as more connections between bone and vessels are created.

The spatial threshold of 200 connected pixels in 2D was based on the assumption that bone structure is larger than vessel structure in the transverse plane. A bigger spatial threshold value would result in less removal of bone structures, while a smaller one would result in removal of more vessel structures.

As the anatomical structure is consistent for all human bodies, it is expected that these threshold values would not necessarily be adaptive. When bone structures were removed, some vessels would likewise be removed. This choice of removing bone and some vessel was based on the weighting of extracting more vessels, while avoiding over segmentation.

It might be possible that the vessel segmentation can be carried out without removal of bone, if there are other better methods to limit the growth of region from vessel to bone with respect to both spatial closeness and the closeness of intensity interval.

The region growing method with 26 neighbours has been considered to be more sensitive in growth of a region than that with six neighbours. This is the reason why region growing with 26 neighbours was not employed as the initial segmentation: it was difficult to find the boundary TH, as the over segmentation arose with a very low TH value, which would result in less satisfactory segmentation of the big vessels.

The application of edge detection has been considered to be useful, because the edges found by edge detection has limited the region growing in every slice in three planes. Rather than the global inclusion criterion region growing utilised, the edge detection in local sites made the information of change effective as an exclusion criterion.

To use the local information in images, a region growing with 26 neighbours using a local threshold might be employed, but it will not provide the same robustness as the current vessel segmentation does.

The holes made by the edge detection restriction occurred only in big vessels, which already are segmented in the initial segmentation. Thus it was intuitive to use the informa-

tion from the initial segmentation to improve the image. However, the initial segmentation was not always effective in including voxels of all big vessels, which means that holes still could occur. Another way to solve this problem would be to use morphological processes like a dilation followed by an erosion, or a simple region based method which exploits those holes occurred due to a closed boundary.

10.1.2 Complete segmentation

The complete segmentation method was evaluated through the test of the method's accuracy and consistency. Accuracy was evaluated though over- and under segmentation compared to the chosen TH value. In this project, the choice of TH was based on manual observations from 3D images as well as an initial suggestion based on the amount of included voxels. If bone or tissue was observed, it would be classified as over segmented and a lower TH would be used. To minimise the degree of under segmentation, the last value before over segmentation was used. However, this is a crude test as small parts of tissue or bone near vessels could be interpreted as vessel. An improved way to verify if over- and under segmentation occurs, is by superimposing the segmented result onto the original image. This showed that there were over segmentation in some slices, but the amount of that was very small.

The reason why observations were chosen in 3D, when the best TH values were chosen, was due to the increased overview compared to the laborious work of running through all slices and verifying if over segmentation arises. This method of choosing TH is very subjective. An automatic method should be applied based on an objective parameter. However, this was not possible with the given time, instead a semi-automatic method was applied based on the amount of voxels segmented. The largest amount of voxels below 50000 is chosen. This however was still based on the manual observation in 3D as explained earlier with the same weakness but with the amount of voxels as an extra feature to detect over segmentation.

Consistency of the method is tested by running the method 10 times with various seed points in aorta and then counting the segmented voxels. It was chosen to use the best TH value before over segmentation. The result of this was 100% consistent. It was noted that a high TH value could produce a more robust method than a low TH value could. This is because a greater TH will allow a greater variation in intensity, thereby reducing the effect of the seed point.

10.1.3 Qualitative validation

The qualitative validation was performed by one medical consultant in collaboration with one of the authors of this project. The purpose of author's presence was to assist with the representation of the vessels in 3D with MATLAB. All identifications were then performed by the medical consultant, with the help of different anatomical atlases. Even though the author did not participate in the identification of vessels, it is possible that the assistance

could have biased the identification. To improve the validity of the vessel segmentation, more medical staff should be involved to analyse the segmented results. This should be performed without any assistance from the authors. Furthermore, it is advised to compare the segmented vessels with results of other segmentation methods or a manual segmentation.

10.2 The usage of region growing

Region growing offers several advantages, for instance, it is able to find perfectly thin borders of regions by using the simple concept of including neighbours that are similar to the initial point. Intensity based region growing is supposed to be good at distinguishing the aimed region from other subjects in the image, based on the assumption that the contrast-enhanced vessels are brighter than the neighbouring structures. But, the fact is that it was difficult to separate vessel from bone by a simple region growing based on intensity in the CT image data used in this project. However, region growing allows the use of multiple criteria, thus it was possible to improve the vessel segmentation by means of an extra criterion. Besides, the region growing method is expensive computationally, which has given problems in the developing process, especially when over segmentation arose.

11 Conclusion

THIS CHAPTER WILL CONTAIN THE CONCLUSIONS ON THE AIMS OF THE PROJECT

The purpose of the vessel segmentation was to improve planning of CTV in radiotherapy of lymph nodes in the pelvic region. This was performed by producing an accurate and consistent segmentation of the vessels from which a CTV could be extracted. The goal for the segmentation was to segment the thin vessels close to the different organs which could have cancer. Furthermore, [J.Suri *et al.*(2002)] expressed in a review article of vessel segmentation the need of a technique which can track vessels to the second and third layers of branching, so this has been the further goal of the segmentation method.

In figure 9.8 on page 60, one of the results of the vessel segmentation is shown. Together with the table 9.4 on page 59, it can be concluded that both second and third branches were visualised and in some datasets even the fourth branches as well.

The segmentation method developed in this project is underlined a low level pixel-wise inclusion criterion with a manual initial seed point. It is based on region growing with 26 neighbours and a restriction parameter from edge detection as well as a removal of large bone structures. Moreover, the segmentation is based on a user interaction of choosing the most suitable TH value, since the correction rate of the suggested TH value provided by the method only is 89%.

The method was tested to confirm its consistency, and it can be concluded that the results were the same with different manual seed points in the vessel. In addition, the accuracy of the vessel segmentation was tested. In all test data, there were none or only a small amount of over segmentation in some slices. However, only two datasets could show all vessels while the rest showed almost all vessels of interest.

In the case that the removal of bone structure removed some vessels as well, these would be extracted from the initial segmentation again. However, the re-extracted vessels might not have the same diameter as the original, thus small vessels that branch from the lost edges of these big vessels could not be extracted in the further segmentation.

This problem needs to be addressed either by using another pre segmentation of the big vessels or simply finding another way of resolving the problem of separating vessels from bone.

Furthermore, the segmentation with edge detection produced holes in the vessels, this problem was resolved by using the initial segmentation, however it is concluded that it did

not fill all holes. This problem might be resolved by using a simple region based method to fill all holes in the slices.

The vessel segmentation provides reasonable results regarding both accuracy and consistency, though it does not provide enough information to be included in the treatment planning of CTV as an independent element. Before the implementation of the vessel segmentation, further tests need to be performed to validate the precision of extracted vessels, for instance by comparing the result to a manual segmentation.

12 Future work

IN THIS CHAPTER, SOME OF THE POTENTIAL IMPROVEMENTS FOR THE METHOD WILL BE SHOWN.

The focus of this project has been the segmentation of vessels to improve planning of radiationtherapy for pelvic cancer. However, the segmentation can not be employed as it is. From the segmented arteries, the centerline of vessel should be found. Since the centerline method also can be applied to determine the width of vessels, it can be seen as an opportunity to validate whether the position of the segmented vessels is precise. When the centerline and the width of vessel are identified, a margin in every direction of 7 mm can be added to the known radius of the vessel, this should provide a good measure of lymph nodes for CTV margin. All in all, the use of centerline could be an improvement both for validation and for further development. [Taylor *et al.*(2005), Taylor *et al.*(2007)]

The delineation of the vessels has purpose to benefit determination of CTV margin of lymph nodes, and this is one way to use the result of the segmentation. There are other opportunities in utilizing the segmented vessels such as the classification of the diseases that result in widening of vessels such as aorto-aneurism.

If the vessel segmentation should be included in the planning of treatment, the method should be improved comparing to time efficiency.

Among the discussed current researches, level set has been one of the most popular methods in 3D vessels segmentation, which can provide a robust detection of fine vessels by using contrast-enhanced vessel MR images. It could be of interest to investigate the vessel segmentation of level set in the pelvic region with CT imaging technique. [Lorigo *et al.*(2001)]

Segmentation method of eigenvalue vector analysis based on Hessian matrix with multi-scale (Frangi) also gives an opportunity to handle the problem, since the method offers an excellent result in pelvic vessel segmentation with MR. It is worth to implement the method in the vessel segmentation in pelvic region, since it could be good at finding tube-like structures in all directions. [Frangi *et al.*(1998)]

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Part VII

Appendix

A Cancer staging

A.1 Cancer

Cancer is a term for a group of cell diseases, which are caused by mutations that disrupt normal control mechanisms and produce potentially malignant cells [Martini(2006a)]. The two main characteristics of cancer are uncontrolled growth of the cells in the human body and the ability of these cells to migrate from the original site and spread to distant sites [Martini(2006b)].

There are two types of tumors, benign and malignant. Benign tumors are rarely life threatening, since they remain localized to their arising area and pose little risk to health. These can in some situations evolve to malignant tumors. Malignant tumors spread aggressively, invade and destroy the surrounding healthy tissues by growing. It can affect the whole body by migrating through the circulatory or lymphatic systems. [Britannica(2010b), Martini(2006a)]

From a cancer registration of 23 countries cross the world, with the exception of Africa where no registration was sufficient, the following incidents are shown in figure A.1. Denmark has a high incidence compared to other countries.

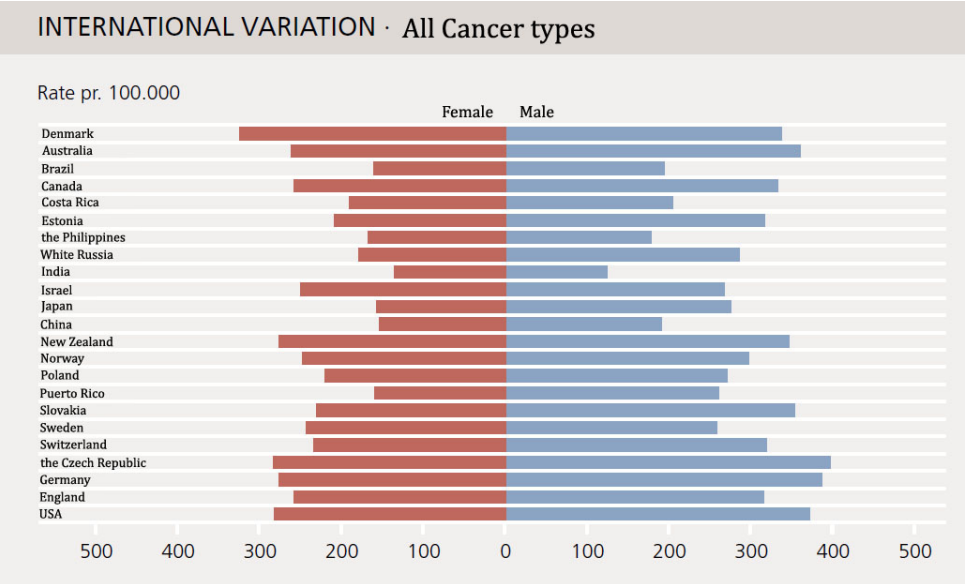

Fig A.1: Age standardised incidents in the period from 1992 to 1998.[I. Clemmensen et. al(2006)]

In Denmark from 2007 there were 32,936 new cancer incidence, 16686 for men and 16,250 for women and it is rising. A reason why more people develop cancer is, population increase, and increasing longevity. The amount of people that live with the diagnosis accounting ill, and post ill patients in Denmark is 205108, 82522 for men and 122586 for women. The cumulative incidence for people at the age to 65 years is 16% for men and 19% for women. At the age of up to 75 years it has risen to 33,3% for men and 32,1% for women. [Niels E. Hansen(2010), I. Clemmensen et. al(2006)]

A relative survival rate diagnosed from 2001-2003 showed that 65-70% survive one year while it drops to 51-59% after three years. From the years 2002 to 2006, there was an annual rate of death of 7817 for men and 7500 for women. [I. Clemmensen et. al(2006), Niels E. Hansen(2010)]

Cancer is classified by the location of the tumor and by the microscopic appearance of the tumor cells. Cancers in different locations are not alike and therefore this project will focus on cancer in the pelvic region. [Pizarro(2009), Inc.(2010)].

A.2 TNM

The TNM system describes the extent of primary tumor, where T refers to the size of the primary tumor, N to the presence and extent of lymph node metastases, and M to the presence of distant metastases. T is categorized as being X(unknown), or 0-4 depending upon site, size, and spread, N as X, or 0-3 depending upon how many lymph nodes that are affected, and M as X, or 0 or 1, depending on existence of distant metastasis. [(NCI)(2010a)] [Mette Tandrup Hansen and Elisabeth Kjems(2010)]

Various types of cancers have their own staging systems. The combinations of TNM correspond to five stages. A numerical staging system is showed in the followed table A.1, and criteria for stages differ for different types of cancer. This means that the same TNM classification for different cancers can mean different stages, for instance, bladder cancer T3 N0 M0 is stage III, but colon cancer T3 N0 M0 is stage II. [(NCI)(2010a)] [(NCI)(2006d)] [Mette Tandrup Hansen and Elisabeth Kjems(2010)]

Stage	Definition
Stage 0	Early cancer that is present only in the layer of cells in which it began
Stage I Stage II Stage III	Higher numbers indicate more extensive disease: greater tumor size, and/or spread of the cancer to nearby lymph nodes and/or extent of the primary tumor
Stage IV	The cancer has spread to another organ

Tab A.1: The clinical staging system of cancer. Stage I is suitable for localized resection; stage II requires regional resection; stage III needs radiotherapy and/or chemotherapy; and stage IV is terminal or preterminal cancer for which only palliative care is possible. [John M. Last(2010)]

B Treatment

There are various ways of treating cancer depending on the type and stage of cancer. Three mainly applied categories of them are surgical, radiation and medicinal treatment. [Schroeder *et al.*(2007b)]

B.1 Surgical therapy

Surgical therapy, the oldest form of cancer therapy, is one of the methods that can cure cancer. Surgical therapy plays also a key role in process of diagnosing of cancer and finding out the stage, since more information about the tumour will be available after the operation. Surgical therapy is usually applied as the first treatment in many cases, especially at the early stage in an attempt to remove the tumour or stop spreading of it. [Britannica(2010b), of Iowa Hospitals and Clinics(2008)]

To cure a cancer with an operation as the only treatment, the tumour has to be confined to the small region of cancerous tissue without metastasis. The removal of the cancerous tissue or organ may not have influence on the vital function of the body or the function of it can be replaced by some clinical way. Lymph nodes will also be removed if they are connected with or close to the cancerous tissue. Particularly, lymph node metastases are a common site of spread in patients with pelvic cancer [Dinniwell *et al.*(2009)]. Removing the lymph glands (along with the organ with the tumour,) improves the chance of cure. [of Iowa Hospitals and Clinics(2008)]

Colorectal cancer is a disease that is primarily treated with surgery. Almost 50% of patients can be cured with surgery alone. For these operations a colonoscopy is used, where a small malignant polyp may be removed from the colon or upper rectum with a colonoscopy. Some small tumours in the lower rectum can be removed through the anus without a colonoscopy. Early colon cancer may be removed with the aid of a thin, lighted tube (laparoscopy). Here three or four tiny cuts are made into the abdomen from which the surgeon sees inside the abdomen with the laparoscopy. The tumour and part of the healthy colon are removed as well as nearby lymph nodes. The surgeon checks the rest of the intestine and the liver to see if the cancer has spread. In some cases an open surgery can be necessary, where the surgeon makes a large cut into the abdomen to remove the tumour and part of the healthy colon or rectum. When colorectal cancer spreads outside the colon or rectum, cancer cells are often found in nearby lymph nodes. If cancer cells have reached these nodes, they may also have spread to other lymph nodes or other organs. Colorectal cancer cells most often spread to the liver. [(NCI)(2006d)]

For patients with bladder cancer, if the cancer has spread to a large region of the bladder, a cystectomy, or removal of bladder tissue, is necessary. A portion of the bladder is removed in a partial cystectomy, and the remaining portion is repaired, whereas removal of the entire bladder or a radical cystectomy is required with more intensive bladder cancer. A radical cystectomy for men usually includes removal of the prostate gland and seminal vesicles, and for women the ovaries, fallopian tubes, and uterus are usually removed. [Britannica(2010a)]

Surgery of prostate cancer is known as prostatectomy, an operation to remove all or part of the prostate gland. Prostatectomy can be used to treat an enlarged prostate gland, which is stopping the flow of urine from the bladder or prostate cancer. Two types of prostatectomy can be performed–transurethral prostatectomy and open prostatectomy. [Care(2006)]

Transurethral prostatectomy is performed on about 90% of all enlarged prostates that require surgery and is done without making an incision. This procedure is done most often in patients whose prostate is moderately enlarged. If the enlargement is greater, then open prostatectomy is usually used. With open prostatectomy, the entire prostate will be removed through an incision beneath the navel. [Care(2006), clinical staff(2009)]

A simple hysterectomy that removes the uterus and cervix can be applied to treat gynecologic cancers at the early stage; and where the cancer has spread, a radical hysterectomy, which also removes underlying connective tissue and ligaments along with the upper portion of the vagina. These surgeries may be done in conjunction with the removal of the fallopian tubes and ovaries depending on cancers spreading and the requirement of the whole treatment. [Britannica(2010f)]

Side effects

Surgery therapy can give some risks e.g. for prostatectomy: impotence, infertility and difficulty controlling urination, as well as other problems related to urinating normally [Care(2006)].

Surgical removal of the uterus or ovaries results in infertility, and removal of the ovaries will also cause women to go immediately into menopause. Lymph nodes may also be removed during surgery, which will have influence in immune system. [Britannica(2010f)]

If an operation cannot be done without damage to the body, there will be removed as much of the cancer as possible. Radiation and/or chemotherapy will be given after the person has healed, to kill the remaining tumour cells. [of Iowa Hospitals and Clinics(2008)]

B.2 Radiation therapy

Radiation therapy can be applied to treat cancer alone or in combination with other forms of treatment, most often surgery or chemotherapy. More than half of all cancer patients receive some radiation therapy as a part of their treatments. Radiation therapy is also called radiotherapy, which is used to kill cancerous cells or stop growth of them. Radiation therapy uses either an internal radiation or an external radiation. For internal radiation a radioactive substances is implanted into the tumours. For external radiation,

the body is exposed to an external source of high-energy rays that penetrate internally. [Christensen.(2005), cancer.dk(2010), Slowik(2009)]

Radiation therapy is an effective treatment, because exposure to radiation makes the cells chemically unstable, affecting its ability to multiply and survive. The principle is that the radiation reacts with water in the cells causing damages to the DNA or genetic material in the cell that controls cell growth. Normally, cells can repair themselves and continue growing; this is not the case for cancerous cells exposed to radiation, resulting in a greater amount of decay among these cells. Although normal cells in healthy tissue are also affected, they repair themselves more effectively. [Christensen.(2005), cancer.dk(2010), Slowik(2009)]

Research has shown that giving many smaller doses of radiation is better than a few large doses. This is called fractionated radiation therapy. Application of fractionated radiation therapy results in less damage to healthy tissue compared to the cancerous cells, since healthy tissue regenerates faster than cancer tissue, so that side-effects are decreased. [Christensen.(2005), cancer.dk(2010), Slowik(2009)]

There are two kinds of ionised radiation that is used in when radiotherapy is performed. These are photon and electron radiation. Photon radiation is used when the cancer is deep in the body. It has changing effectiveness in depth depending upon the amount of energy each photon posses. The higher the energy, the further the radiation can pass before collision. Upon collision photons will cause release of electrons from the atoms in the tissue causing the ionisation in the cells which leads to the cell death. [Christensen.(2005), cancer.dk(2010)]

Electron radiation is used on cancers near the surface. Covering the area with high speed electrons will as photon radiation release electrons upon collision. Since the electrons are larger than photons they will collide with other electrons earlier, giving the short penetration distance. [Christensen.(2005), cancer.dk(2010)]

When treating prostate cancer, an external beam therapy (EBT) is often used. The beam is generated outside the patient, by a linear accelerator and is targeted at the tumour site. The treatment is planned to spare the surrounding tissue. Normally advanced technology is used to tailor the radiation therapy to an individual's body structures. Relying on computerized three-dimensional images of the prostate, bladder and rectum, the x-ray radiation beam is aimed precisely to affect the diseased area.

Bladder cancer may be treated with radiation as well, usually following surgery to destroy small amounts of remaining cancerous tissue. The treatment can be employed with either external beams or internally by surgically implanting radioactive rods or pellets. [Britannica(2010a)]

Radiotherapy is rarely used to treat colon cancer, but it is sometimes used to relieve pain and other symptoms. Nevertheless, radiotherapy may be used both before and after surgery of rectal cancer. Some patients receive radiotherapy before surgery to shrink the tumour, and others receive it after surgery to kill cancer cells that may remain in the area. [(NCI)(2006d)]

To treat gynaecologic cancers, radiation therapy is rarely employed as the primary treatment, but in conjunction with surgery. Both external beam radiation and internal target tissue radiation can be used. [Britannica(2010f)]

Side effects

Side effects depend mainly on the amount of radiation given and the part of the body that is treated. A general side-effect is that the patients are likely to become very tired during radiation therapy, especially in the later weeks of treatment. In addition, the skin in the treated area may become red, dry, and tender. The skin near the anus is especially sensitive. [(NCI)(2006d), Slowik(2009)]

The complications of radiation therapy may include vomiting, nausea, hair loss, weight loss, weakness, drop in blood cell counts, and skin disorders. [Britannica(2010b)]

Radiotherapy to the abdomen and pelvis may in addition to the general side-effects cause nausea, vomiting, diarrhea, low blood count, or urgent bowel movements. It also may cause urinary problems, such as being unable to stop the flow of urine from the bladder.

The side effects of radiation treatment may include vomiting, diarrhea, fatigue, or skin irritations resembling a sunburn. [Britannica(2010a)]

Side effects of pelvic radiation therapy may include diarrhea, fatigue, premature menopause, bladder irritation, or narrowing of the vagina due to scar tissue buildup. [Britannica(2010g)]

Side effects of pelvic radiation therapy may include diarrhea, fatigue, skin irritation, premature menopause, bladder irritation, or a narrowing of the vagina due to scaring of tissue. [Britannica(2010d)]

B.3 Medical treatment

There are several types of treatment, in which vary drugs or chemicals are used to treat the cancers in different stages. The most commonly used ones are mentioned as followed [(NCI)(2010b), (NCI)(2006a), (NCI)(2006b), (NCI)(2006c)].

Chemotherapy therapy

Chemotherapy, the use of chemicals to destroy cancerous cells, is commonly employed for almost all kinds of cancers. One or more chemotherapy drugs may be administered intravenously, sometimes intramuscular or orally. When drugs are taken thought the bloodstream, distributed to the whole body, cancer cells can be affected, this is called systemic chemotherapy. Another way to use chemotherapy is regional chemotherapy, in which the drugs are placed directly into the spinal column, an organ, or even a body cavity, so that the main effects arise in the local area. By using regional chemotherapy, the side effects can be greatly reduced, since the exposure of other body tissues to the drugs is limited. The way the chemotherapy is given depends on the type and stage of the cancer being treated,

and the condition of the individuals. Drugs, chemotherapy employed are able to kill dividing cancer cells, and normal cells to some degree, therefore several side effects can be followed. General side effects can for instance be nausea, vomiting, diarrhea, hair loss, anemia, loss of ability to fight infection, and a greater propensity to bleed may be caused by chemotherapy. [(NCI)(2006a), Britannica(2010b)]

Chemotherapy is not highly effective in treating prostate cancer, but it can, however, slow the growth of the tumour; therefore chemotherapy is applied particularly if surgery or potential hormone therapy fails [Britannica(2010c)].

Chemotherapy may also be employed for treatment of bladder cancer. If the cancer remains localized to the bladder after other treatments, chemotherapeutic agents may be administered directly through a urinary catheter. If the cancer has spread, systemic chemotherapy will be required. [Britannica(2010a)]

For colon cancer, the typical chemotherapy can be employed. And if cancer has spread to the liver, a chemoembolization of the main artery that supplies blood to the liver can be employed. It means the hepatic artery is blocked and anticancer drugs are injected between the blockage and the liver. The drugs will be delivered throughout the liver, which means a higher concentration of drug will be in contact with the tumour for a relative longer time, and only a small amount of the drug reaches other parts of the body. This method can be considered as a regional chemotherapy as well. [(NCI)(2006a)]

Generally, for patients with gynaecologic cancers, chemotherapy is the preferred treatment when the cancer has spread beyond the uterus or ovaries. A systemic chemotherapy is usually required in this stage to destroy as many cancerous cells as possible. Sometimes, chemotherapy may also be used following surgery. [Britannica(2010g), Britannica(2010d)]

Side effects

However, these compounds also attack normal cells to varying degrees and therefore often produce serious side effects such as vomiting, fatigue, mouth or vaginal sores, immune suppression, and hair loss. Several side effects resemble those of radiation therapy as well.

Hormone therapy

To slow or stop the growth of certain cancers, for instance prostate cancer, synthetic hormones or other drugs may be given to block the body's natural hormones, which cancerous cell need during growing. This is called hormone therapy, which is effective in treatment for some type of cancer.

For hormone treatment of prostate cancer, so called LHRH analogs can be used. LHRH analogs that chemically block the production of androgens can be used. And antiandrogens such as Abiraterone that inhibits the activity of an enzyme during the synthesis of testosterone are often used in combination with other forms of hormone therapy. [Britannica(2010c)]

Except these two kinds of drugs, Docetaxel and Sipuleucel-T are used to prolong sur-

vival in different treatments, since Docetaxel inhibits the growth of cancer cells, while Sipuleucel-T is designed to activate the immune system to attack cancer cells. [Britannica(2010c)]

Some uterine cancers, such as endometrial cancer, can be treated in part by using hormonal therapy. Hormone progesterone may be used to slow the growth of the tumour, in cases that the cancer cells are found to contain the progesterone receptor. [Britannica(2010g)]

Side effects

The side effects for prostate cancer could be limited primarily to hypertension, edema, and potassium deficiency. [Britannica(2010c)]

There are several other opportunities of medicinal treatment, e.g. biological therapy, targeted therapy, in which drugs or other substances are used to identify and attack specific cancer cells without harming normal cells [(NCI)(2010b), (NCI)(2006a), (NCI)(2006c)].

B.4 Additional Imageing Methods

The aim of medical imaging is to establish shape, structure, size, and spatial relationships of anatomical structures within the patient, and to give the spatial information about the body's function and pathology or abnormality. Medical imaging technology is widely used in healthcare, especially in the treatment of cancer: a) to diagnose and stage cancer, b) to guide cancer treatments, c) to evaluate the treatment, d) to monitor the effect of new drugs or new therapeutic innovation [Hajnal *et al.*(2001)].

Functional medical imaging technology, such as CT, PET, fMRI, has contributed to cancer care in many ways: It makes detection of cancer at an early stage possible; moreover, the diagnosis and treatment could be less invasive, if supported by imaging technology such as Image Guided Radiation Therapy (IGRT). CT imaging is was used in this project and is therefore part of the rapport, however other methods can also be applied. MR and PET will be briefly explained.

B.4.1 Magnetic resonance (MR)

MR imaging is a medical imaging technique where the atoms of the body are aligned to a super conductive electromagnetic field. Then radio frequencies are applied to force tissues to emit radio frequencies of their own. Since different tissues emit a more or less strong signal based on their chemical composition (basically the content of water), an image of the organs can be reconstructed and displayed. MR imaging is most commonly used in radiology to visualise detailed internal structure of the body. Other than sensitivity to tissue density and atomic composition of CT imaging, MR imaging are related to proton density, relaxation times, flow, and other parameters, which gives better opportunity to distinguish soft tissue. MR's ability to distinguish tissues provides improved possibilities for defining boundaries of a tumour from neighbouring normal tissues. [Hajnal *et al.*(2001)]

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B.4.2 Positron emission tomography (PET)

The PET scan is one of the nuclear medicine imaging techniques in medical research that produces a detailed and excellent 3D image of functional processes in the body. The system detects couples of quanta emitted indirectly by a positron-emitter, which is given by injection into the body on a biologically active molecule, like glucose. Images of tracer concentration in 3D or 4D (time) space within the body are then reconstructed by computer analysis. The radioactive glucose can help in locating a tumour, since cancer cells use glucose more greedily than other tissues in the body. By showing metabolic changes in tissues and tumours, PET images provide an essential tool in cancer therapy. For many common tumours, PET is the most accurate single imaging technique for visualising the spread of tumour or its response to therapy. In modern scanners, this reconstruction is often accomplished with the aid of a CT scan performed on the patient during the same session, in the same machine. PET/CT imaging is widely used in cancer care today. [Hajnal *et al.*(2001)]

C Histograms

Histograms are shown for the first three data sets of slice 1, 50, 100, and the last slice of the dataset. This is done to verify how the data is distributed throughout the slices. There is chosen of window of intensities from 900 to 1700, since it is assumed to ensure that all enhanced vessel are included as well as tissue that interconnect with vessels. Furthermore a cropped dataset is performed on a vessel from the same slices to verify vessel intensity distribution.

Images of data with histograms are displayed in the following order:dataset one, slice 1 body, slice 1 vessel, slice 50 body, slice 50 vessel, slice 100 body, slice 100 vessel, last slice body, last slice vessel. Dataset two, slice 1 body, and so forth.

Dataset 1

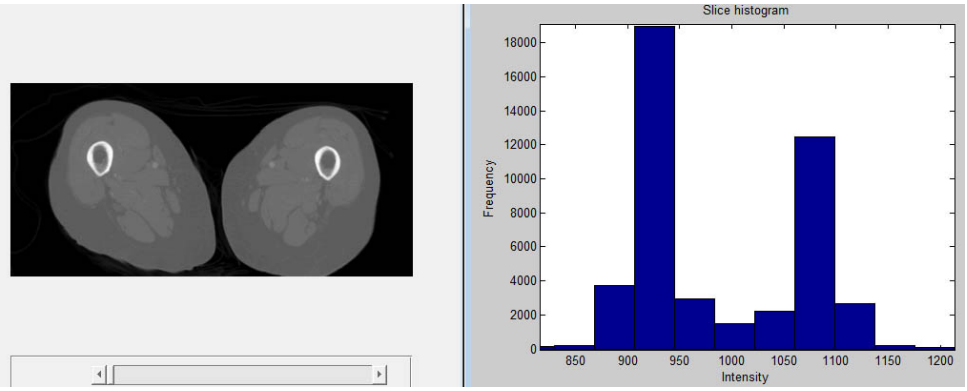

Fig C.1: dataset 1 body slice 1

From the cropped histograms of vessels in dataset 1, it is noticed that vessel are from:

- slice 1: 1150-1300
- slice 50: 1100-1300
- slice 100: 1150-1300
- slice 153: 1100-1550

This is based on Hounsfield units knowledge of the tissues in the cropped images. Since anatomical tissues is assumed to absorb the same amount of x-ray, only the enhanced vessels can change values.

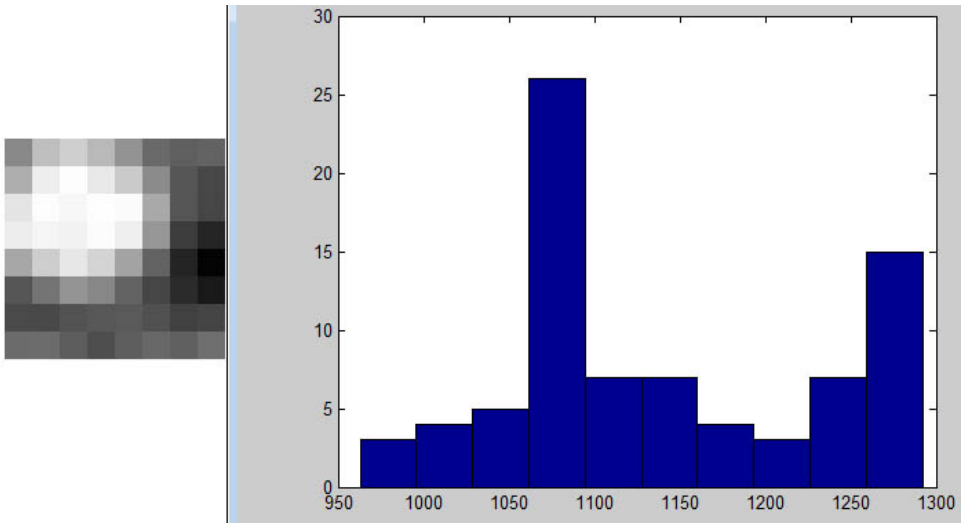

Fig C.2: dataset 1 vessel slice 1

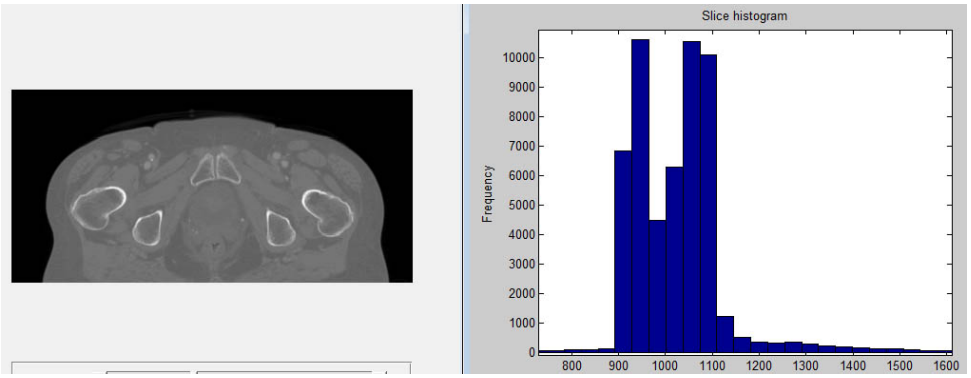

Fig C.3: dataset 1 body slice 50

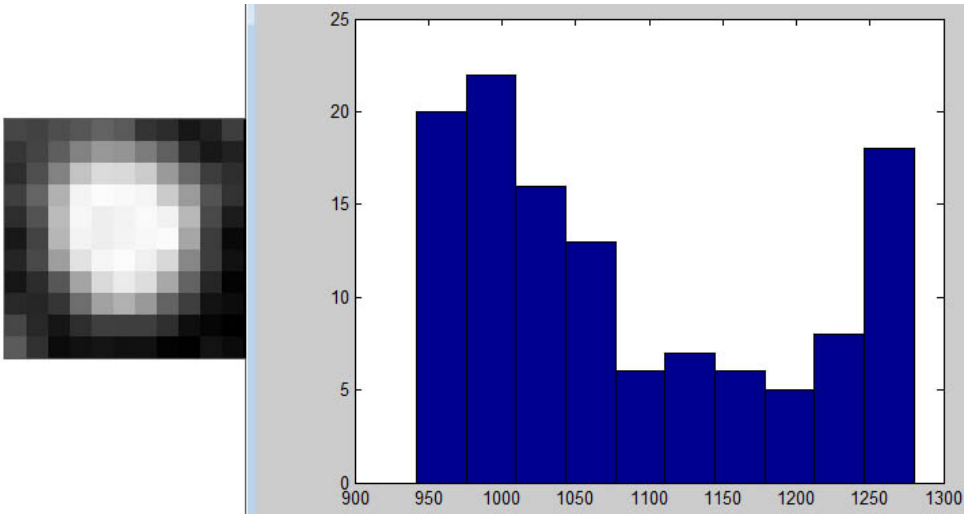

Fig C.4: dataset 1 vessel slice 50

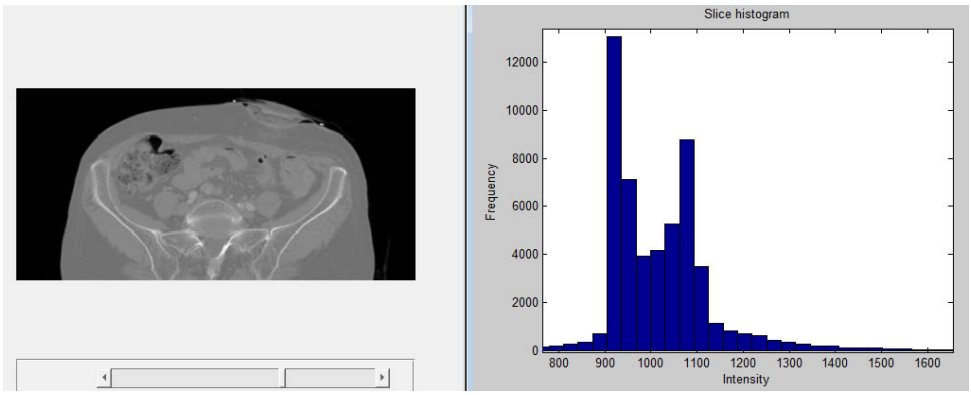

Fig C.5: dataset 1 body slice 100

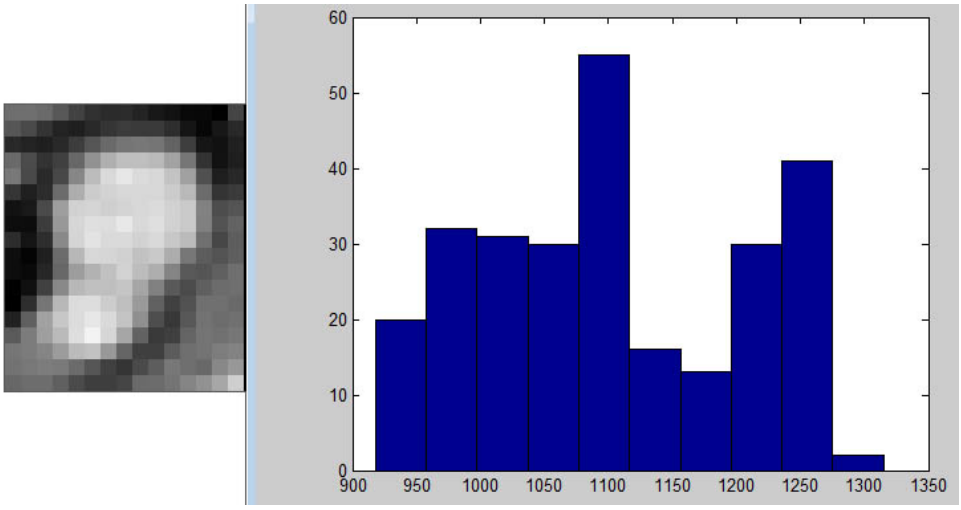

Fig C.6: dataset 1 vessel slice 100

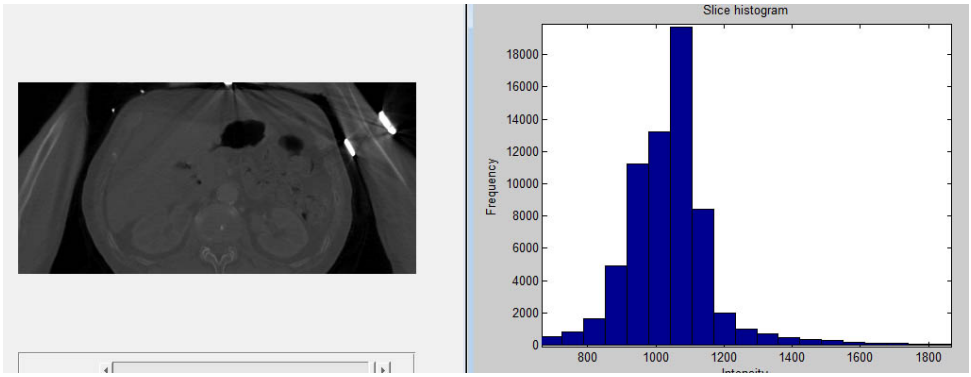

Fig C.7: dataset 1 body slice last slice

Dataset 2

From the cropped histograms of vessels in dataset 2, it is noticed that vessel are from:

- slice 1: 1150-1200
- slice 50: 1250-1550
- slice 100: 1150-1350
- slice 141: 1150-1380

This is based on Hounsfield units knowledge of the tissues in the cropped images. Since anatomical tissues is assumed to absorb the same amount of x-ray, only the enhanced vessels can change values.

Dataset 3

Slice 1:

From the cropped histograms of vessels in dataset 2, it is noticed that vessel are from:

- slice 1: 1200-1600
- slice 50: 1200-1600
- slice 100: 1200-1750
- slice 141: 1200-2100

This is based on Hounsfield units knowledge of the tissues in the cropped images. Since anatomical tissues is assumed to absorb the same amount of x-ray, only the enhanced vessels can change values.

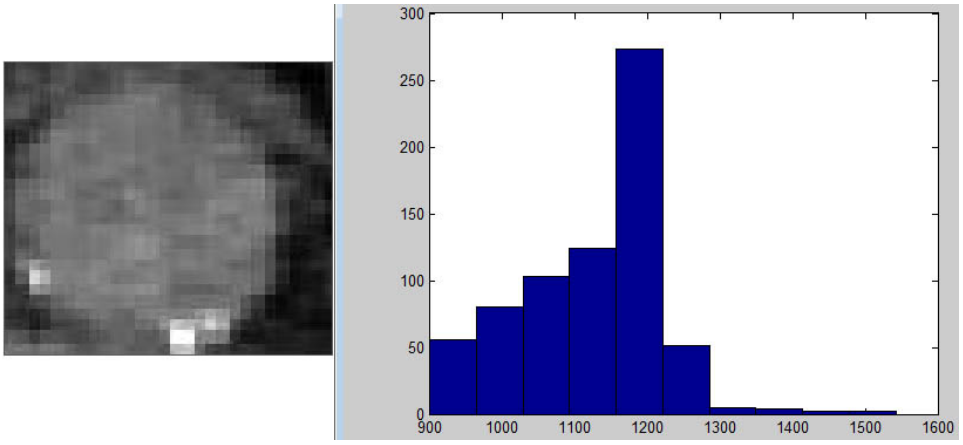

Fig C.8: dataset 1 vessel slice last slice

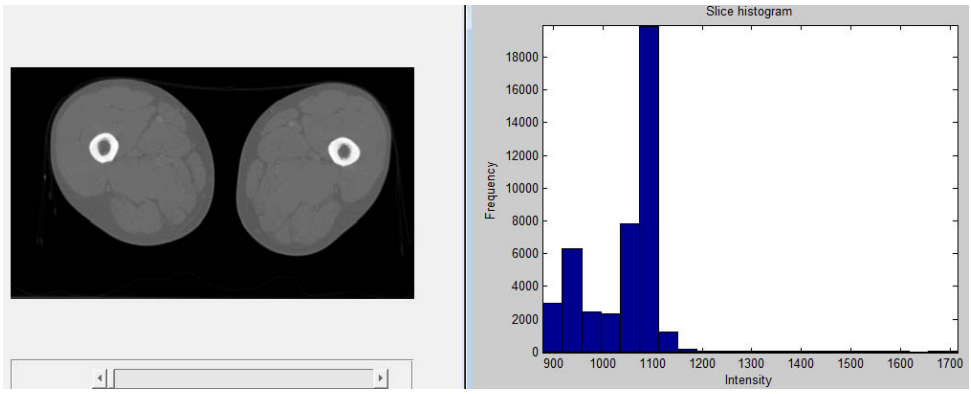

Fig C.9: dataset 2 body slice 1

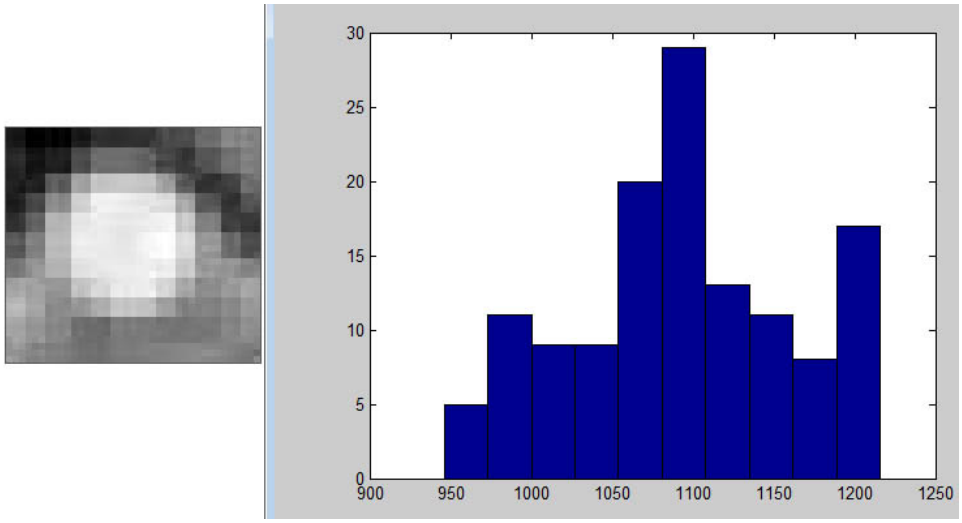

Fig C.10: dataset 2 vessel slice 1

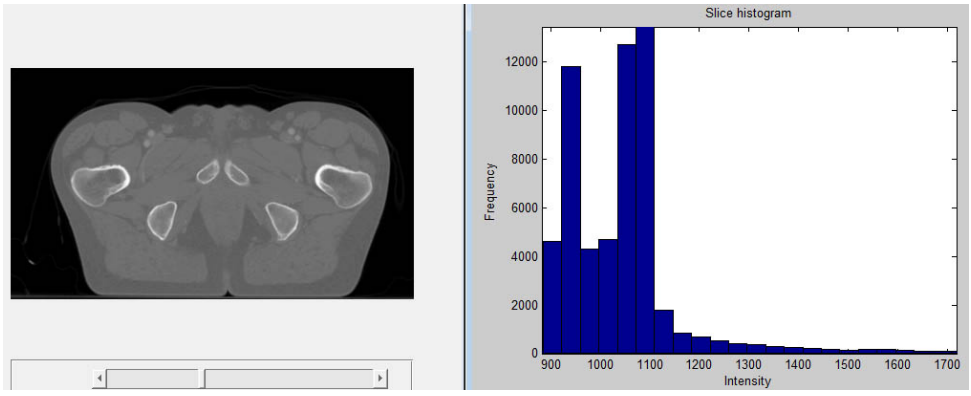

Fig C.11: dataset 2 body slice 50

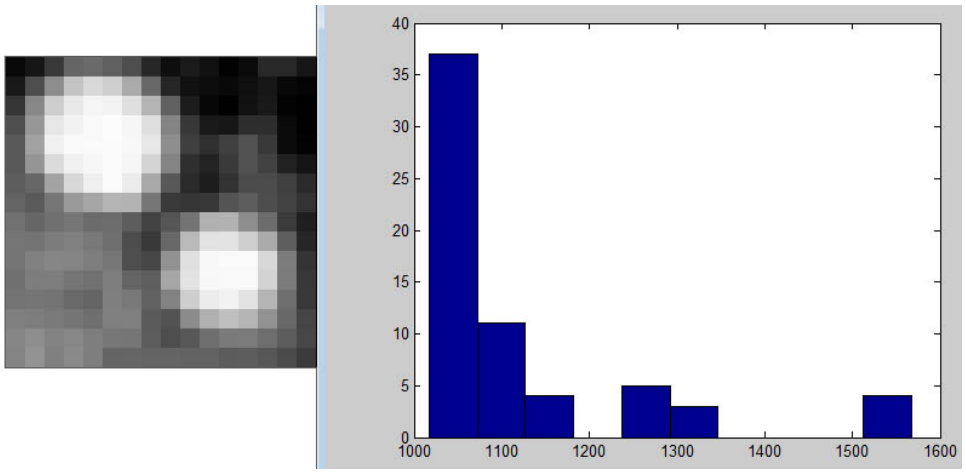

Fig C.12: dataset 2 vessel slice 50

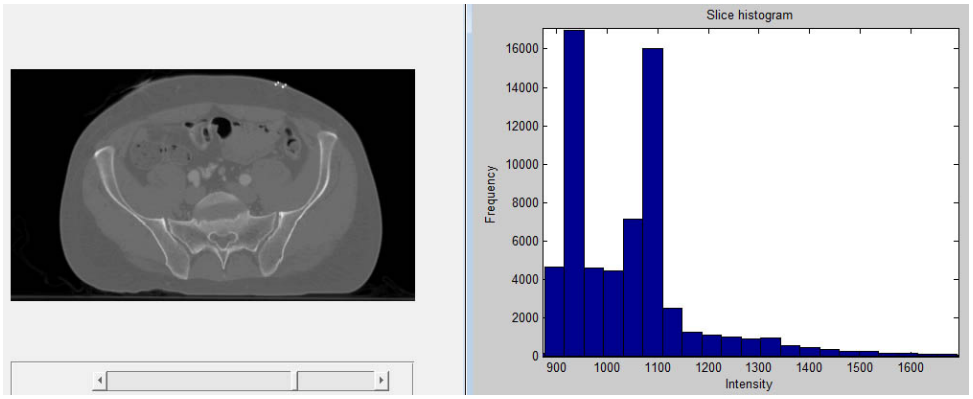

Fig C.13: dataset 2 body slice 100

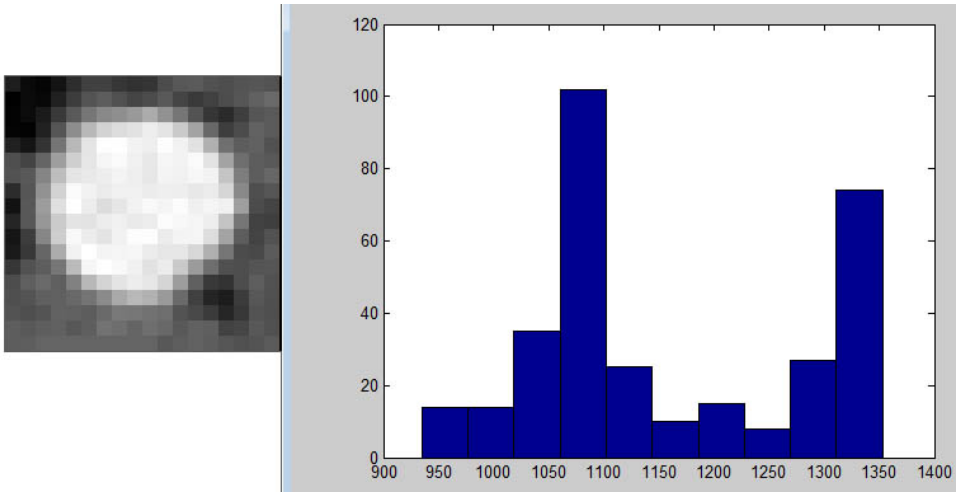

Fig C.14: dataset 2 vessel slice 100

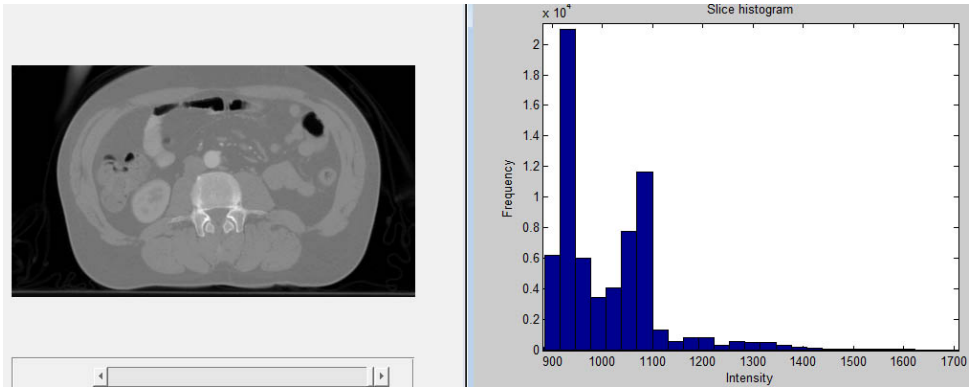

Fig C.15: dataset 2 body slice last slice

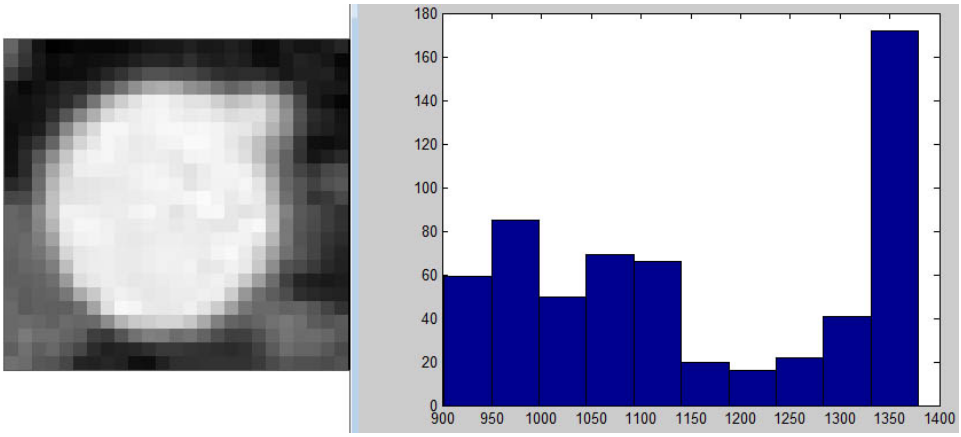

Fig C.16: dataset 2 vessel slice last slice

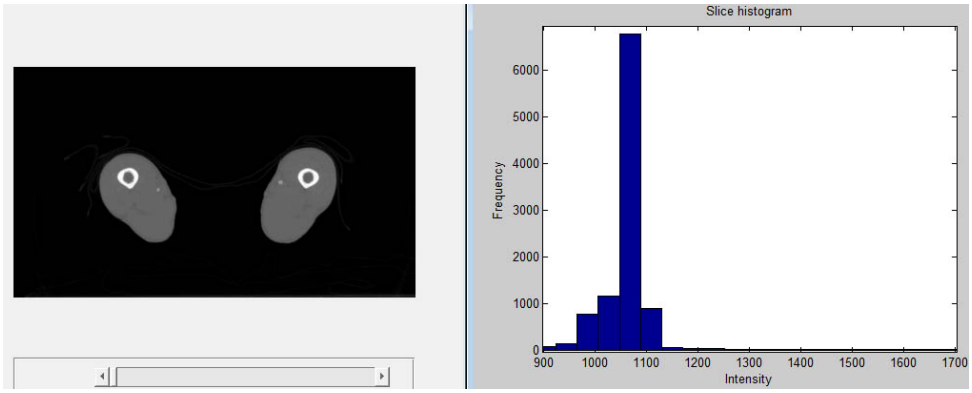

Fig C.17: dataset 3 body slice 1

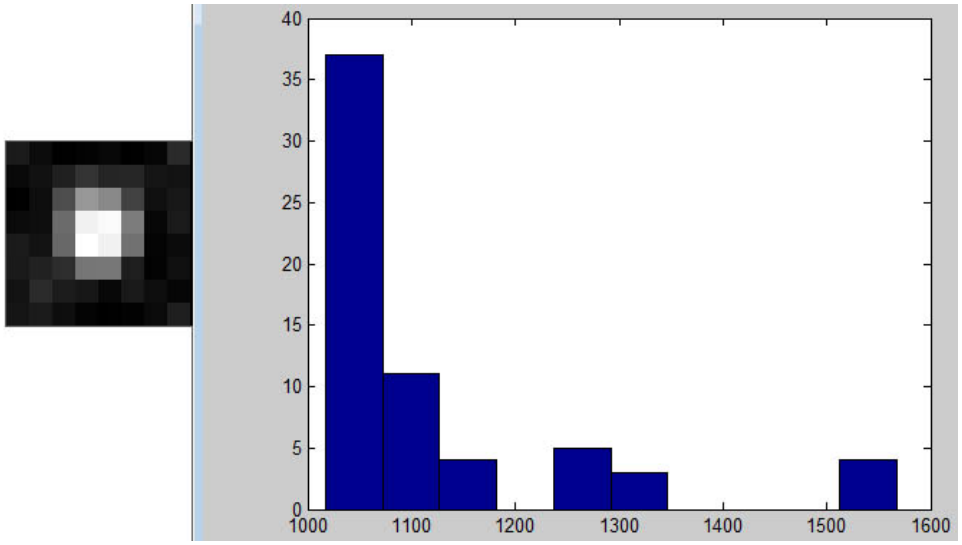

Fig C.18: dataset 3 vessel slice 1

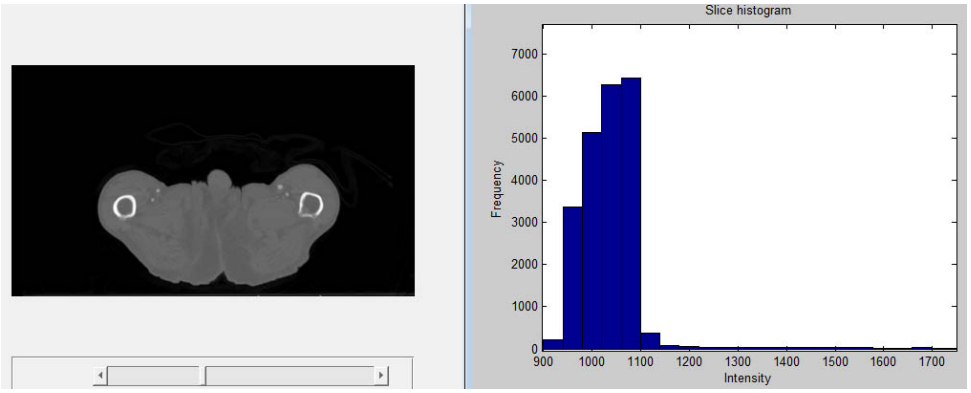

Fig C.19: dataset 3 body slice 50

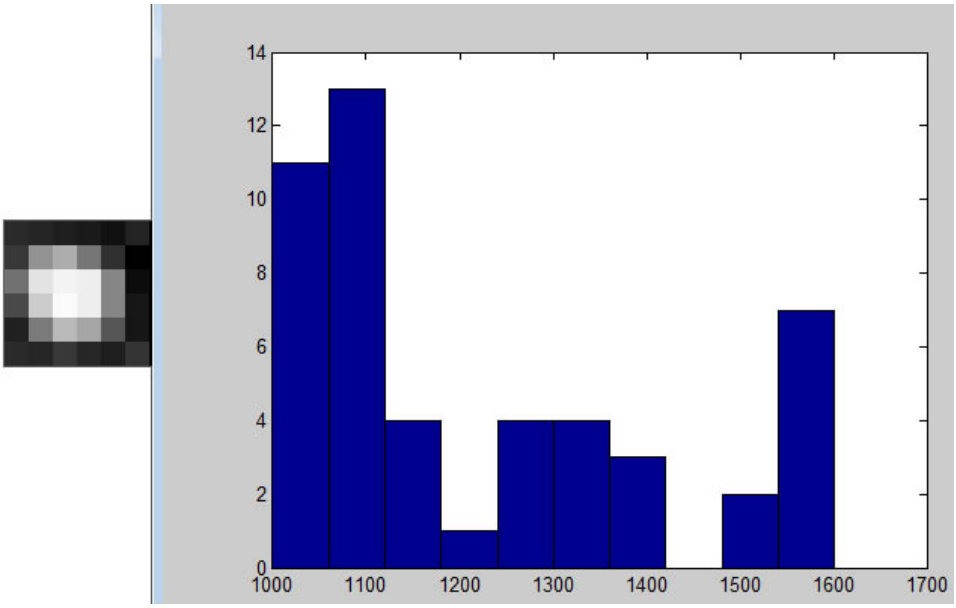

Fig C.20: dataset 3 vessel slice 50

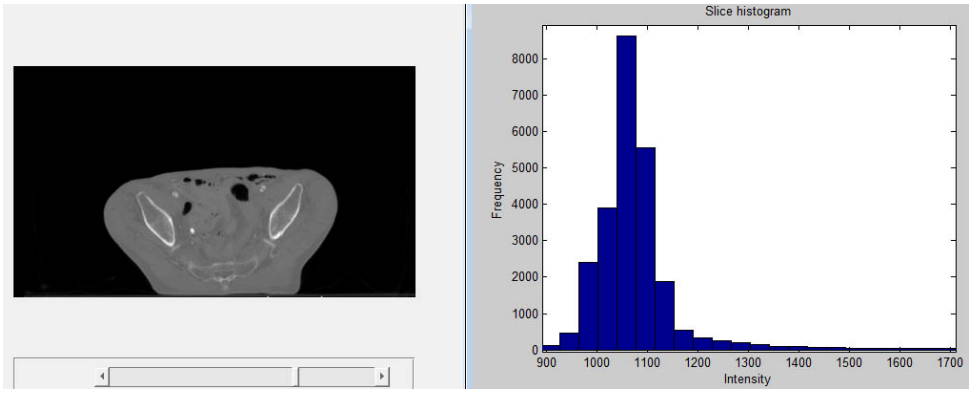

Fig C.21: dataset 3 body slice 100

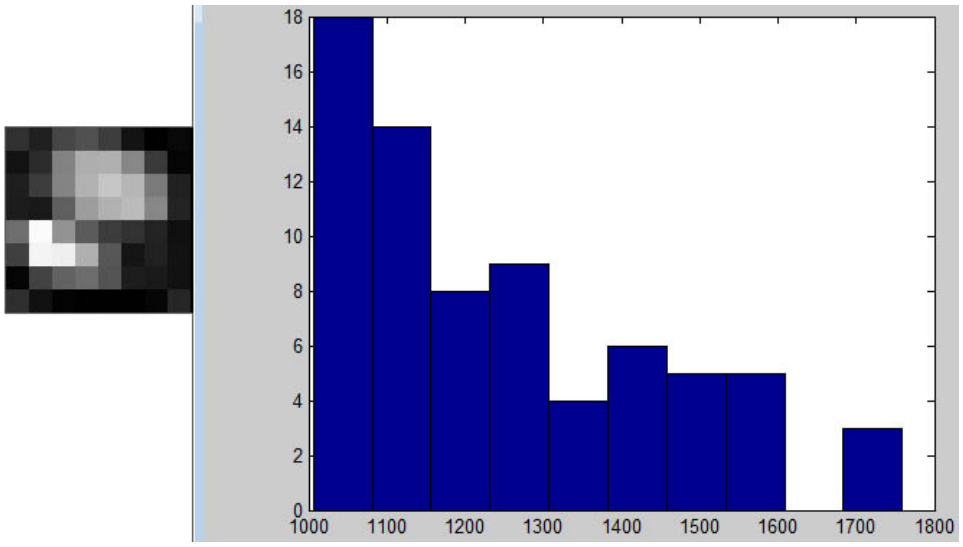

Fig C.22: dataset 3 vessel slice 100

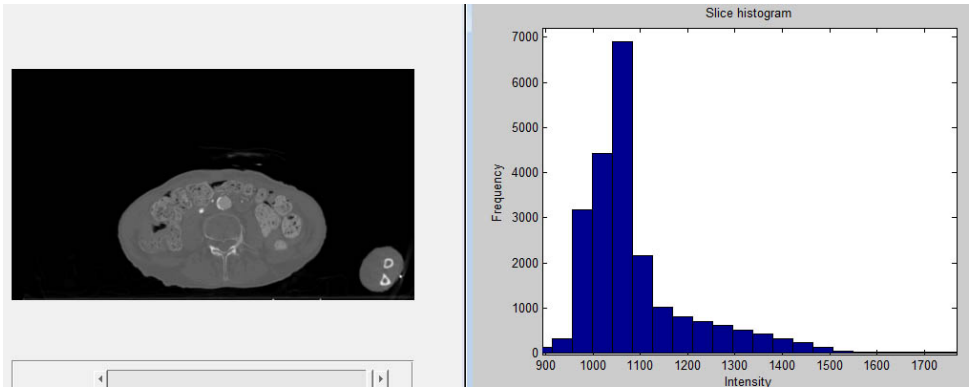

Fig C.23: dataset 3 body slice last slice

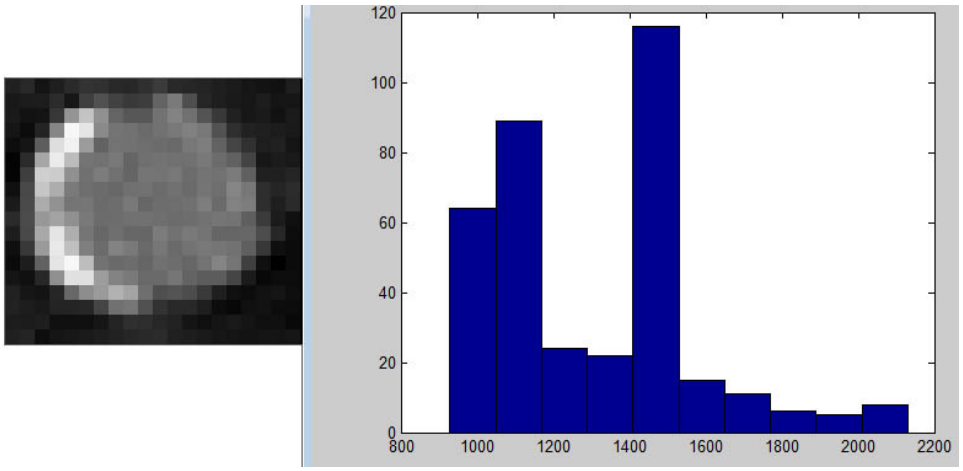

Fig C.24: dataset 3 vessel slice last slice