Evaluation of AVMs in 4D-CTA

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Abstract

The aim of this bachelor thesis is to improve the evaluation of arteriovenous malformations (AVM) in 4D computed tomography angiography (4D-CTA) using Matlab. For this evaluation anonymised AVM datasets from patients from the UMC St Radboud are loaded into Matlab. With this loaded data an automatic evaluation of the AVM will be developed. The AVM datasets have been made Matlab compatible and afterwards they were cropped. The cropping reduces the size of the data and makes Matlab perform better. Following the blood vessels are segmented using a mask image to filter the surrounding irrelevant tissue. These images of solely blood vessels are aligned and played in a movie where the vascular filling is shown. To continue placing a mark near the nidus to indicate and visualize the AVM can be a valuable progress. Next to this visualization it would be useful to look at navigation for the treatment of an AVM.
keywords: AVM, arteriovenous malformation, 4D CTA, 4D computed tomography, Matlab, navigation, DSA, digital subtraction angiography

Contents

I. Introduction

I. Arteriovenous Malformations (AVM)

AVMs are anomalies of the circulatory system. There are different types of congenital vascular anomalies: haemangioma, capillary malformations, venous malformation, lymphatic malformations and arteriovenous malformations. *[Radboud, 2015a] & [HEVAS, 2015]*These anomalies can occur anywhere in the body: as well in the brain (central) as somewhere else in the body (peripheral). In this thesis the focus is on the peripheral AVMs and their evaluation. AVMs arise during development in the embryonic or foetal stage caused by a genetic mutation or hereditary factors. *[NIH, 2011]* Most of the time AVMs do not manifest at birth, but at an older age. *[Radboud, 2015a] & [HEVAS, 2015]* In some rare cases an AVM occurs after a trauma. When both the artery and the vein are cut, they might merge and form an AVM. *[Schultze Kool, 2015a]*

An AVM can occur when a high amount of arteries in a specific part of the body, conduct too much blood to the organ. The veins will dilate to be able to drain the blood. *[Radboud, 2015a]* A blood vessel wall consists of three layers: the tunica intima on the inside, the tunica media in the middle and the tunica adventitia on the outside. The tunica media contains circulary arranged smooth muscles cells. *[Junqueira and Carneiro, 2010]* This layer is thicker in arteries than in veins, because artery walls need to withstand higher pressures. This is why a vein dilates easier than an artery. The dilated blood vessel is called a nidus and can be fed by one or several arteries. A nidus can have different sizes. The size variation of a nidus can lead to a larger circulating blood volume up to 20 litres in severe cases. *[Schultze Kool, 2015b]*

Due to the AVM an anomalous inflow and outflow of blood is present in the nidus and a short circuit occurs. *[Schultze Kool, 2015b]* As a result the pressure drops and surrounding capillaries will receive less blood.

I.1 Symptoms

The symptoms and risks of an AVM depend on the location and severity of these congenital malformations. *[NIH, 2011]* Symptoms can appear at any time and vary from person to person. Most often these symptoms are found in people in their twenties to forties. *[NIH, 2011]*

Symptoms for AVMs are staged in the Schobinger Scale. *[Covey et al., 2015]* At stage I, or in quiescence AVMs, skin warmth and a cutaneous blush is seen. Also, an arteriovenous shunt is shown with Doppler ultrasound (US). The next stage, stage II or expansion AVMs, includes a darkening blush and a pulsating lesion. Due to the pulsating lesion vascular murmur is audible. At stage III, or destruction AVMs, distal ischemia, pain, dystrophic skin changes, ulceration, necrosis and tissue changes occur. These symptoms are caused by the Steal syndrome. In the Steal syndrome the blood flows through the malformation which leads to a reduced blood flow in the surrounding tissue and capillaries. At the final stage, stage IV or decompensation AVMs, a high-output cardiac failure appears, caused by an increased circulatory volume.

I.2 Treatment

An AVM is mostly found by coincidence, when a patient visits the hospital with indistinct symptoms. Sometimes these symptoms clearly indicate an AVM. However in most cases, as discussed above, the symptoms of an AVM are very widespread. The large range of symptoms can lead to several differential diagnoses. A CT scan can rule out some of the differential diagnoses. The scan will visualise the AVM in the patient. However, this CT image is not optimal to determine an AVM due to a static image. In addition, an AVM is sometimes found if the patient is suffering from other illnesses or diseases. This happens when a patient gets for example a CT scan due to another medical condition.

In addition to a CT scan, an angiography is made. This angiography facilitates the eval-

uation of the AVM by visualizing the blood flow in the nidus. The angiogram shows the inflow and outflow of blood in the malformation. The angiogram gives a better evaluation of the nidus opposed to the static CT image. In the next subsection the angiogram is elaborated.

In the angiogram a malformation of the blood vessels is shown. Using this real time image an evaluation of the vascular malformation can be made. After the diagnosis a risk assessment is done: what risk has the patient living with an AVM? The AVM can, for instance, spontaneously start bleeding. This rupture can have a wide range of complications depending on its location. The symptoms of a patient play an important part in the decision whether to treat or not. It is hard to cure an AVM as a whole that is why the aim of most treatments is to denature parts of the AVM to decrease the symptoms. *[Schultze Kool, 2015a]*

When the malformation is diagnosed as a peripheral AVM there are four possible interventions. Endovascular embolization and percutaneous embolization are used in the UMC St Radboud. *[Schultze Kool, 2012]* Treatments which are not used in the UMC St Radboud are stereotactic radiation with the Gammaknife and the surgical treatment to remove the AVM. These treatments are not discussed in this thesis.

In the UMC St Radboud the primary treatment of peripheral AVMs is percutaneous embolization. During this treatment the location of the nidus is found by injecting a needle with a fluid with fluoroscopic tracking. This location is determined by the angiogram in combination with a contrast medium. The angiogram is not precise enough to have an exact location of the AVM. It is difficult to find the exact depth and origin of the nidus, due to the small variations that can occur. A difference of 100 micrometres matters. *[Schultze Kool, 2015b]*

With a percutaneous approach a fluid is injected in the nidus. This fluid, containing 96% ethanol, causes the endothelial proteins to denature. During the treatment ethanol is injected up to a maximum of 1 millilitres per kilogram body weight, since larger volumes can be toxic. The denaturation of the proteins activate the coagulation system, which causes the nidus to close. *[Yakes and Baumgartner, 2014]*

The endovascular embolization treatment is used when the AVM cannot be reached percutaneously. The physician enters the inguinal artery with a catheter. The catheter is moved up the arteries to the location of the AVM. When the catheter is at the desired position of the AVM, onyx or histoacryl is injected through the catheter. Onyx is a substance which contains ethylene-vinyl alcohol copolymer, dimethyl sulfoxide (DMSO), and tantalum. The fluid, Onyx, makes the nidus dissolve if they are rather small or shrink when they are over three centimetres. The blood vessels react with the alcohol in the onyx. The alcohol causes the dissolvement and shrinking by denaturing the proteins in the vascular wall. The histoacryl contains n-Butyl-2 Cyanoacrylate. Histoacryl is a liquid that causes the nidus to selectively obliterate due to the carbon groups in this molecule. *[Rooij et al., 2007] & [Rosen and Contractor, 2004]*

In some cases coils or guidewires are inserted endovascular into the nidus to help blocking the blood flow by injecting the substance afterwards. The coil or guidewire contributes to the coagulation. Immediately after injecting the substance a change can be seen on the DSA image. The process of denaturation continues after the procedure. Therefore the actual outcome can only be seen after a couple hours. *[Schultze Kool, 2015a]*

Patient

During the treatment the patient will need to lie still. Since this is difficult with a patient when conscious a general anaesthesia is used. The patient will not move during the treatment, which makes the plan of treatment more trustworthy. The general anaesthesia is done during both percutaneous and endovascular treatments. Furthermore the embolization causes a pain sensation for the patient. The pain will be reduced by the anaesthesia and pain killers. However the anaesthesia and the toxicity of the 96% ethanol substance have disadvantages. One of these disadvantages is the day admis-

sion of the patient in the hospital. The day admission is needed to guard the patient while recovering. *[Schultze Kool, 2015a]*

In endovascular embolization the catheter inserted in the inguinal artery causes a wound. The recovery of this wound takes a couple of days. The patient needs to be careful due to this wound. The patient needs to recover for a couple of days post procedure.

II. Diagnostics

II.1 Digital Subtraction Angiography (DSA)

Nowadays the DSA is the gold standard in AVM diagnostics. *[Willems et al., 2012]* DSA is a fluoroscopy technique. This technique is used in interventional radiology for the diagnosis of vascular diseases. DSA is used to visualize blood vessels surrounded by bone or soft tissues. These other tissues cover the blood vessels in an X-ray photo. *[Ota, 1985]*

To visualize the blood vessels iodinated contrast medium is used. In a traditional angiogram this contrast agent is visible as it flows through the blood vessels. However, when imaging a bony environment, the overlying bone structures cause problems due to their high density. *[Ota, 1985]* In order to obtain an image of the blood vessels, first a precontrast image is acquired. After this an image is created with the contrast agent injected. *[Oosterom and Oostendorp, 2008]* Both images are uploaded to a computer. The computer subtracts the precontrast image from the images in which the contrast agents are added. The overlying structures are eliminated by the computer and only the blood vessels remain visible. *[Oosterom and Oostendorp, 2008]*

During the DSA procedure every second 1 up to 6 images are taken. This series of images lead to a real time video of the contrast agent movement in the blood vessels of interest. This short film shows how the blood flows from the arteries into the veins. When an AVM is present a short circuit is visible with an anomalous flow. The anomalous flow most likely indicates the nidus. Figure 1 shows an AVM on DSA.

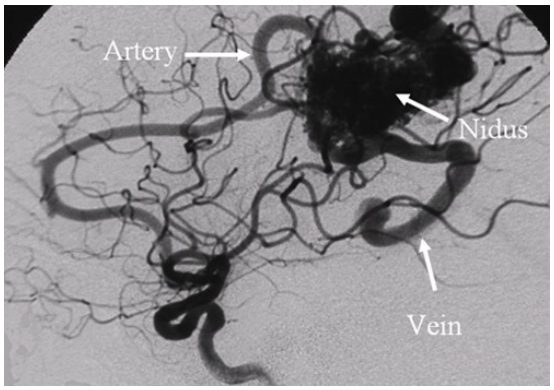

Figure 1: *DSA image of an AVM. The image shows the feeding artery, the nidus and a dilated vein. [Manual, 2015]*

DSA is a dynamic imaging technique. Its spatial and temporal resolution are rather high and therefore useful for the current medical standards. *[Tamargo and Huang, 2012]* However DSA has some disadvantages as well. For example it is difficult to determine the nidus size based on the 2D angiogram. This is hard while the 2D image is made from a 3D structure. The overlapping blood vessels in the image make it harder to interpret the information. *[Tamargo and Huang, 2012]* Beside that, DSA does not show adjacent tissue. Another scan will be necessary to evaluate the relationship and involvement of the blood vessels and the surrounding tissue. *[Tamargo and Huang, 2012]* Also there is, depending on the duration of the intervention, a large radiation exposure for both the patient and the operator. *[Kortman et al., 2014]* A standard fluoroscopy fluoroscopy leads to an average effective radiation dose of 3.6 mSv compared to normal background radiation exposure over a year of 2.5 mSv. *[Milieu, 2015]*

Also DSA is an invasive diagnostic tool, because the contrast medium is locally injected through a catheter inserted in the inguinal region with local anaesthesia. Because of this invasiveness the patients have to be admitted in the hospital for one full day of recovery. The whole procedure has to be done steril and takes up to six hours. Also the patient has to be fasting for this intervention and the contrast agent

can cause nausea. *[Schultze Kool, 2015b]*

II.2 Four Dimensional Computed Tomography Angiography (4D-CTA)

4D-CTA (four dimensional computed tomography angiography) is a minimal invasive tool for vascular imaging of the human body. In the UMC St Radboud it is currently used to replace the invasive imaging procedure for arteriovenous malformations. The current procedure consists of two components: CT and angiography. These components are fused together and enhanced within 4D-CTA.

2D

A CT scanner consists of a gantry and a patient table. The gantry consists of an X-ray tube and a detector ring. As in radiography an image is acquired using the X-ray tube and the detector. In CT the X-ray tube and the detector rotate. During the rotation the X-rays are emitted towards the detector. From multiple angles an attenuation coefficient is detected. These coefficients are combined into a 2D image by an algorithm. *[Goldman, 2007] [Ketcham and Carlson, 2001]*

An X-ray is excited in the X-ray tube. This tube consists of a cathode and an anode covered in Wolfram. The cathode and anode are located in a vacuum. The cathode is heated and the electrons originating from the Wolfram form an electron cloud around it. An electric field is established. The anode is given positive potential compared to the cathode, so the electron cloud is attracted to the anode. When the electrons reach the anode, an X-ray beam is formed. *[Oosterom and Oostendorp, 2008]*

Not every imaging technique requires the same properties of an X-ray beam. When a radiograph is acquired, an image with great details is taken quickly. However, in fluoroscopy a long screening is desirable without a high radiation dose. The properties are regulated by the tube voltage, the tube current and the exposure time. The tube voltage determines the penetrating power of the radiation. The tube current determines the radiation quantity. Especially the tube current has an important role in the radiation dose. By varying these properties X-ray can be used for different applications. The tube current for example could be hundred times less in fluoroscopy as in a radiograph. *[Hobbie and Roth, 2007]*

The X-ray beam is detected by a digital detector. The detector consists of scintillators, photodetector diodes and a analog-to-digital converter. When an X-ray photon reaches the detector it interacts with the scintillators and some of its energy becomes a visible photon. Subsequently the photodetector diodes transforms the visible photons into an electrical signal. Then the electrical signal is converted into a digital signal by an analog-to-digital converter. This signals can be reconstructed as a CT image. *[Scampini, 2010]*

Nowadays an algorithm based on backprojection reconstructs an image. The detectors measure the attenuation value. This detected value is divided evenly along its ray path with backprojection. At multiple angles this algorithm will be repeated. When all the backprojections are put together an image of the slice will appear. *[Goldman, 2007] [Ketcham and Carlson, 2001]* In figure 2 filtered backprojection is shown.

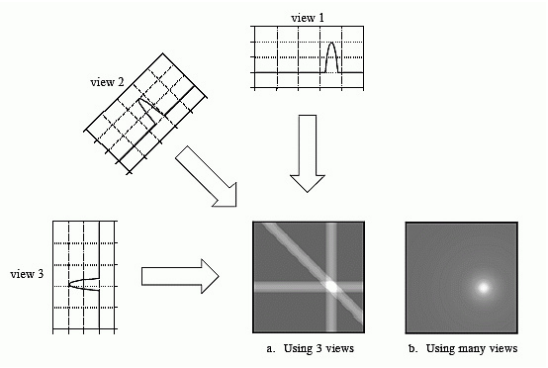

Figure 2: *An image is reconstructed using backprojection combining the attenuation coefficients from different angles. [Smith, 1997]*

A disadvantage of this technique is that the image will be blurred. To clear the image the raw data or the sinogram will be filtered before the backprojection. The filter will eliminate the noise by filtering the low frequencies from the sinogram (convolution). After backprojection

the image will be less blurred. With this technique an image with less noise will be made after reconstruction. *[Goldman, 2007]*

To reduce the noise further a new method is upcoming named iterative reconstruction. This uses the filtered backprojection image after which algorithms are implemented to reduce the noise. *[Berlamont, 2011]* Simply, a comparison between the filtered back projection data and the raw measured data is made. The average of these two is determined and an image will be reconstructed out of the new data using backprojection. This procedure will be repeated. The new data will be matched to the raw data until the stop criteria for the image is matched. Since iterative reconstruction has less noise the radiation dose can be decreased. However when the dose is decreased the noise will increase again. Thus, with iterative reconstruction there is a choice of less noise for the same radiation dose or less radiation dose for the same noise. *[Beister et al., 2012]* In figure 3 the loop of iterative reconstruction is shown.

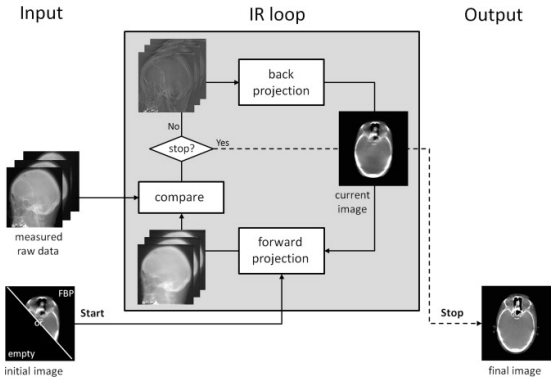

Figure 3: *This figure shows the loop of iterative reconstruction. [Beister et al., 2012]*

3D

The method to create a 2D image has been discussed above. In order to get a three dimensional image, the 2D slices need to be stacked on each other. There are a several visualization techniques. To visualise this 3D data, the data needs to be rendered. There are several rendering techniques used, a few will be discussed.

A rendering technique consists of three steps: volume formation, classification and image projection. Volume formation contains the acquisition of data, combining the data and preprocessing. In classification the tissue type is determined, depending on the structures that have to be visualised. The tissue classification can be binary or continuous. Examples of binary techniques are surface-based or threshold-based reconstructions. In binary reconstructions a voxel contains a specific tissue type. Examples of the continuous based techniques are percentage-based or semi-transparent volumes-based reconstructions. This means that the voxel contains a combination of tissue types. The final step, image projection, consists of projecting the classified volume. *[Fishman et al., 2006]*

SS-VRT

Shaded surface display volume rendering (SS-VRT) is an example of a 3D visualization technique. In this technique a range of Hounsfield units is selected, which determine whether voxels are included in a surface. Several types of tissue can be segmented by selecting different ranges and tissue types. After that the surface borders are calculated by defining the boundary between voxels of two tissue types. SS-VRT therefore is a binary rendering technique. A visualization is then formed by casting a virtual beam through the voxels from a selected perspective. When the ROI is resized, many details can be shown in structures with a specific density. Because of that this technique is often used in virtual endoscopy and to visualize articular surface fracture lines. *[Perandini et al., 2010]*

MIP

Another binary projection technique is maximum intensity projection (MIP). As the name suggests voxels with a high Hounsfield unit are projected. *[Perandini et al., 2010]* This means that for every ”X” and ”Y” coordinate the highest Hounsfield unit along the Z-axis is represented. Consequently all structures with a high attenuation coefficient are selected and processed in a 2D image. This technique is often used for the imaging of blood vessels. However, other structures with a high Hounsfield unit, for example bone, can cause difficulties. Overlapping causes a disturbed visibility of the

blood vessels.

Minimum intensity projection (MinIP) works according to the same principle, but instead of the voxel with the highest Hounsfield unit, the voxel with the lowest Hounsfield unit is chosen. This is profitable if an image of the lungs is made. The lungs contain air, which has a low Hounsfield unit. Due to the black environment the white blood vessels are less visible. If MinIP is used the blood vessels become black and the air in the lung turns white.

In current vascular radiology an inverted MIP is used. Inverted MIP is MIP but the highest Hounsfield unit will be black and the lowest in the window will be bright white. The hospitals use inverted MIP for it has almost the same appearance as an angiogram. *[Van der Woude, 2015]*

Volume rendering

Volume rendering is another 3D projection technique and is explained by Fishman et al. *[Fishman et al., 2006]* This technique does not use a threshold, it uses percentage classification. Percentage classification enables a combination of different tissue types per voxel. The amount of a tissue type in a voxel is expressed as a percentage. To determine this percentage a trapezoid, or ramp, is used. There are two types of trapezoids: single, open ended, ramps and double ramps. Which trapezoid will be used depends on the tissue type which has to be visualized. To adjust the levels of the trapezoids a window level and a window width are chosen. The window level determines the most important Hounsfield unit in the images. The window width determines the reach of Hounsfield units, which are represented in the image.

In a single ramp trapezoid, for example used for bony structures, the ramp covers the window width with the window level as central value. Every voxel below the window width appears black, because it contains 0% bone. Every voxel above the width appear white and is assigned 100% bone. Every voxel in the ramp gets a grey colour from the greyscale determined by a percentage between 0-100% of bone. This principle makes it possible to focus on the voxels in the window width. *[Fishman et al., 2006]* This ramp is shown in figure 4.

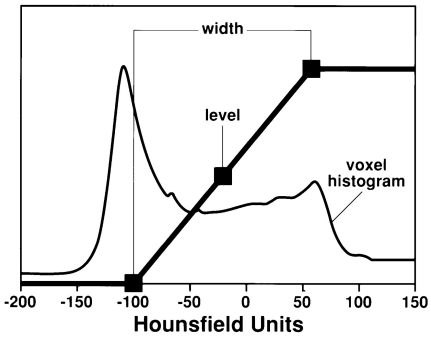

Figure 4: *In this diagram the impact of the window width and level are shown. The window width affects the image contrast. When the window width increases, the contrast distinction decreases. The window level affects the data inclusion and the attenuation of certain voxels. [Calhoun et al., 1999]*

For soft tissues a double ramp trapezoid is used, because the difference between the attenuation values is rather small. To create a better contrast between different soft tissues two window widths are chosen. The first window is chosen for the lower values and have a percentage from zero to hundred percent. The second window is chosen for the higher values and the percentage is adjust from hundred to zero percent. The values outside these windows will have a percentage of zero and thus get no soft tissue value. The zero percentage voxels will appear black on the image. The values between the both windows will have hundred percent and will appear bright white on the image. *[Fishman et al., 2006]*

Every tissue has its own trapezoid, which leads to overlap. This is why a voxel has a percentage for every tissue. This tissue has its own colour and in every voxel a transparency percentage. Now a 3D image can be composed by casting a simulated beam of rays through the voxels. This leads to a 3D representation of the tissues. [Fishman et al., 2006]

Comparison

All three techniques have advantages and disadvantages. SS-VRT, for example, is a useful

technique for the visualization of details and surfaces. However, it is not necessary to study the surface of a blood vessel wall. MIP is a more common technique in CTA. This technique increases the visibility of the smaller blood vessels due to the high intensity in these vessels. However veins are represented more posterior than their anatomical location. This phenomenon occurs due to the fading of the contrast. The fading of the contrast happens due to the flow of the arterial blood into the veins. The contrast medium enters the larger lumen of the vein where it can dissolve in a larger volume. This results in a smaller intensity of the contrast medium in the image. This smaller intensity of the contrast causes a small displacement of the veins. Because MIP shows the larger intensities more in front. The displacement of the veins in the image makes it harder to comprehend the vascular anatomy. MIP also requires filtration of the bone tissue in the image where volume rendering does not. In addition volume rendering visualizes the vascular anatomy best of these three techniques in 3D. While MIP focuses solely on the blood vessels, volume rendering enables studying of the soft tissue, which gives additional information. The best evaluation is obtained by combining both rendering techniques. *[Fishman et al., 2006]*

CT Angiography

CT scans are used to visualize different structures in the human body. The vasculature can be shown as well. However, blood vessels are soft tissues, which are not displayed well on a CT scan. To enhance the visualization of the vasculature a contrast medium is added. Iodinated contrast medium is injected in the arm vein via a cannula. The contrast medium is distributed over the blood vessels in the body. Iodine has a high electron density and an high atomic number. For this it absorbs X-ray well and leads to a high attenuation coefficient. When a CT-scan is performed, blood vessels become visible.

4D

Most CT-scans are helical scans. The detector and X-ray rotate while the patient is moved through the gantry. In this way a static 3D image is acquired. However to get a dynamic image time is needed as a fourth dimension. To acquire time, a volume mode scan is performed. With a volume mode scan the patient is fixated to prevent movement artefacts in the acquired data. The fixed body part lies in the gantry, while the gantry turns around the patient. Every second several images are acquired, up to twenty frames per second. 4D-CT scans thereby enable the visualization of the human anatomy in time. Movements of tissues and or fluids become visible. A limitation of this technique is the gantry width, because this width determines the maximum scan area.

II.3 DSA vs 4D-CTA

4D-CTA seems to be a promising technique compared to the current gold standard, DSA, in diagnosing and evaluating AVMs. 4D-CTA is able to show adjacent tissue, which is not possible in DSA. Besides that, 4D-CTA enables the radiologist to study the 3D structure of the AVM, while DSA only shows the AVM in a 2D plane. Although the evaluation of an AVM in a 4D image by 4D-CTA gives more information it is not used widespread.

DSA is a very invasive diagnostic tool compared to 4D-CTA. The AVM is approached by a catheter, which is inserted in the inguinal artery. Via this catheter the contrast medium is locally injected in the AVM. Because of the local anaesthesia which is needed for a DSA and the catheter insertion a day admission at the hospital is needed. For using anaesthesia the patient has to be fasting. The catheter wound requires the patient to recover for several days. In addition, the procedure itself has a duration up to six hours, because of its preparation and the complexity of anatomical structures. 4D-CTA is a simple diagnostic tool. The contrast medium is injected via a cannula in the arm vein and a CT scan is performed. Altogether, the 4D-CTA takes twenty minutes (this is further explained in section I.III.1).*[Van der Woude, 2015]* Therefore 4D-CTA is a less invasive diagnostic tool. For the same reasons 4D-CTA is

also more cost-effective.

III. Data

III.1 Obtaining data

In the UMC St Radboud a protocol for 4D-CTA in cerebral AVMs is used. *[Radboud, 2015b]* A protocol for peripheral AVMs is not available. A protocol is of no use if the location of the AVM varies. The treatment is custommade for every patient. This is resembling to the cerebral AVM protocol.

A 4D-CTA is made if an interventional radiologist suspects an AVM. First an intravenous cannula is inserted in the arm of the patient. During the scan Xenetix 300 or Iomerion 300, iodinated contrast media, alternated with NaCl to rinse, is injected via the cannula. The location of the AVM in the patient determines the position of the patient in the CT scanner. When the patient is positioned he or she is instructed not to move to reduce the movement artefacts on the scan. *[Radboud, 2015b]*

First a scanogram is acquired to determine the most optimal gantry position. Second an artery near the AVM is selected, this is the region of interest for the procedure (ROI). Third the time of arrival of the contrast medium in the AVM is determined. The determination of the time of arrival is done by sending a test bolus to the AVM. The test bolus contains fifteen millilitres of contrast medium and is injected at five millilitres per second. The cannula is rinsed with five millilitres NaCl. Meanwhile the scan is started. *[Radboud, 2015b]*

The density is measured at the ROI. The measurements are graphed into a Time Density Curve. This curve indicates the density of the contrast in time. When an increase of density is registered the contrast medium is arrived at the region of interest. After arrival the time delay is calculated. To make sure none of the contrast bolus is missed a margin of one second will be added. This adjustment makes sure the scan starts on time. *[Radboud, 2015b]* The average time of arrival in most cases is about ten seconds after the bolus injection, so the scan has to start after nine seconds.

If all the settings are obtained and set, the final scans are performed. These final scans are two dynamic volume scans. To make these final scans a bolus of fifty millilitres contrast medium is injected at five millilitres per second. After the complete injection of the bolus a rinse with five millilitres NaCl is done. Meanwhile two seconds after injecting the first bolus volume, a mask image is acquired. The acquirement of the mask image is done during the ten seconds of injecting the contrast bolus. The mask makes the tissue of the ROI visible while it does not contain the contrast medium yet. This step is considered as the first dynamic volume scan. The second volume is acquired at the calculated starting time. *[Radboud, 2015b]* This volume is continuously acquired during twelve seconds with a frame rate of three up to ten frames per second.*[Van der Woude, 2015]* Following the obtained data are processed. The images will be processed into inverted MIP as described above. *[Radboud, 2015b]*

In 4D-CTA a volume scan is made using the Toshiba Aquilion One Vision CT scanner. The Toshiba Aquilion One series are some of the first CT scanners enabling dynamic volume scans. The gantry of the Aquilion One exists of three hundred and twenty slices with each a size of five hundred micrometres thick. By this a maximum of sixteen centimetres is scanned because the aquilion one is a non-helical scan. Every five hundred milliseconds the gantry rotates three hundred and sixty degrees. *[Van der Woude, 2015]*

III.2 Evaluation

After obtaining the data the interventional radiologist studies the CT data in Vitrea, a product by Toshiba, to find and understand the nidus. He studies the nidus for evaluation of the blood vessels. He tries to distinguish if there is more than one connection between the artery and the vein. At first the evaluation is done by examining the slices in 2D from different perspectives. The slices are rendered in ”X”, ”Y” and ”Z” direction. When a suspicion for an transition of artery to vein arises, the

radiologist uses the 4D rendering to study the blood flow. The AVM can be found examining the flow of contrast. When the contrast moves from the narrow artery into the dilated vein, the contrast dilutes and becomes less dense on the scan. The evaluation becomes more difficult when there are more conducting arteries. Finding the first artery which enters the nidus, is relatively simple, because there is not yet contrast medium in the nidus. If a second artery enters the nidus, the nidus already contains contrast medium. This makes it more difficult to evaluate the origin of the second artery due to the lower difference in colour caused by the already present contrast. Also the draining vein should be found. This is mostly done by following the contrast medium through the blood vessels. It is also possible to evaluate the nidus backwards. Sometimes it takes hours to study all blood vessels and to gain insight in the AVM. *[Schultze Kool, 2015a]*

After the evaluation of the AVM the interventional radiologist develops a custommade treatment. To plan the treatment the interventional radiologist uses his experience and the information he obtained from the 4D-CTA data. It is difficult to make a reproducible plan for the treatment due to the continuously shifting blood vessels. The interventional radiologist cannot fully rely on the plan for the treatment due to these changes.

IV. Issue and Objectives

The treatment of an AVM has difficulties to endure. First the evaluation of the nidus is a difficult task for the interventional radiologist and it sometimes takes hours. Second the treatment is complicated, because every AVM is different and a standard approach does not exist. The radiologist uses his experience to develop a custommade treatment, however this still has uncertainties which have to be reckoned with.

To reduce the uncertainties in the treatment of AVMs a few improvements should be made. There are several ways to eliminate some of these insecurities. First the process of evaluating the nidus should be better facilitated. For example, the data should become easier to process for Vitrea and a regular computer. This will result in a less time consuming rendering process of the data and thereby a faster evaluation can be made. Next to the evaluation process, the treatment too can be enhanced. More of the acts in the procedure should not be left up to chance and become standardised. These problems in the complete procedure and treatment lead to the following research question: In what way could the evaluation of peripheral AVMs in 4D-CTA data be improved?

This research question leads to several objectives for this thesis. First the 4D-CTA data, made available by the UMC St Radboud, will be adjusted to make the data compatible with Matlab. When the Matlab compatible data is obtained it will be visualized as an image by a viewer. The viewer displays the data in 2D and 3D, the 3D is rendered with the maximum intensity projection technique. The data will be manipulated in Matlab to make it easier to manage. When it is more manageable a 4D data set will be created. The 4D dataset will be made into an image. This 4D image will show the flow of the contrast by colours. This 4D with colouring will make the evaluation of the nidus easier and faster.

II. Materials and Methods

At first the 4D-CTA datasets with an AVM need to be viewed. The UMC St Radboud delivered the datasets for this thesis in a DICOM format. To locate and evaluate the AVM, the DICOM files will be viewed on a laptop at the University of Twente. Therefore a DICOM viewer needs to be used. A DICOM viewer is an application specially designed for the imaging of DICOM files. When the AVM is found, the 4D-CTA datasets need to be made compatible with Matlab. The Matlab compatibility is necessary to be able to manipulate the 4D-CTA data. The datasets need to be in matrices of at least two or three dimensions. These matrices in the DICOM file will be converted from a .dcm into a .mat file.

Then the datasets will be uploaded to Matlab. When the datasets are in Matlab they will be viewed by a viewer which can display the .mat format in 2D and 3D. After the datasets are made visible the 3D will be rendered with the maximum intensity projection technique.

In the Matlab viewer the AVM can be evaluated again. This new evaluation can be compared to the AVM evaluation which will be done in the DICOM viewer.

After the 3D viewer is used and the data set is compatible, the data can be adjusted to smaller sizes for a better performance of Matlab.

After creating more manageable datasets, the data will be filtered until only the blood vessels are visible. The visualization of only the blood vessels will make the AVM evaluation become easier. To do so the blood vessels need to be segmented and thus the surrounding tissue can be eliminated.

To make a segmentation of the blood vessels an evaluation of the voxel values and the voxel attenuation coefficients need to be made. The voxel values of the blood vessels will be measured at every time. These values change the most since the contrast medium has a high density value. With the measured voxels a window can be made to filter the data. With the filter the surrounding tissues are removed.

When the 3D data set of the AVMs blood vessels only is created it will be put in a 4D matrix. This 4D matrix is created and shall be viewed in Matlab. The animation that arises will show the flow of the contrast fluid through the blood vessels. To take a small step further a clearer view of the flow can be made by adding colours to the flow. A 5D dataset is created with this step.

Besides the use of colours research can be done if there are other properties of the AVM to make it possible to quantify its nidus. This can be applied with the 3D and 4D matrices. Thereby the static images from 3D can be used for calculations of distances and since the 3D datasets are smaller than the 4D datasets the calculations shall be executed faster. Furthermore the use of time of 4D gives the possibility to use the flow of the contrast through the blood vessels to evaluate the nidus. The changing density values of the voxel values can be of use with that.

Next to processing data the protocols for treating an AVM will be evaluated. In addition the process of AVM detection and evaluation done by the interventional radiologist in the 4D-CTA data will be reviewed.

This is done to get a better understanding how the interventional radiologist inspects the AVM. When this is known a script can be made to automatically detect and find the AVM with Matlab. With the goal to replicate the proceedings of the interventional radiologist as much as possible.

Also there will be looked at the intensiveness of treating an AVM and it procedures. All of this will be done to get a better understanding of the clinical value of 4D-CTA in the treatment of AVMs.

III. Results

I. Evaluation of the AVM

Three timeframes are used to evaluate the AVM: timeframe 4, 9 and 14. At time frame 4 the contrast is visible for the first time, at frame 9 the contrast medium is highest and frame 14 is the last frame from the series. Figure 5 shows the different frames in axial and coronal plane.

The red circle contains two blood vessels, presumably an artery and a vein. The left blood vessel is probably a vein, because its intensity is low compared to the right blood vessel. The right blood vessel has a high intensity compared to the left vessel at frame 14 and is probably an artery. The right blood vessel will be followed through the slices. A red circle indicates the location of the blood vessel in both the axial and the coronal slice.

When following the right encircled blood vessel, its diameter changes. It is doubtful whether the vessel is an artery or a vein. As mentioned earlier veins dilate as a result of the high blood pressure caused by the large

amount of blood feeded by the arteries. Due to the diameter it is assumed the right blood vessel is a vein. The enlargement is shown in figure 6.

The encircled blood vessel is followed distally. The green circle shows a possible connection from the nidus and the vein. This is shown in figure 7.

In figure 8 the connection between the vein and the nidus is shown in the coronal plane.

The blue circle in figure 9 shows another connection to the avm. It is not clear if the nidus connects with an artery or a vein.

Figure 10 shows another connection to the AVM. It is assumed that the connected blood vessel is an artery based on the anatomy of the blood vessel in the hand. The vascular anatomy of the hand is shown in figure 11.

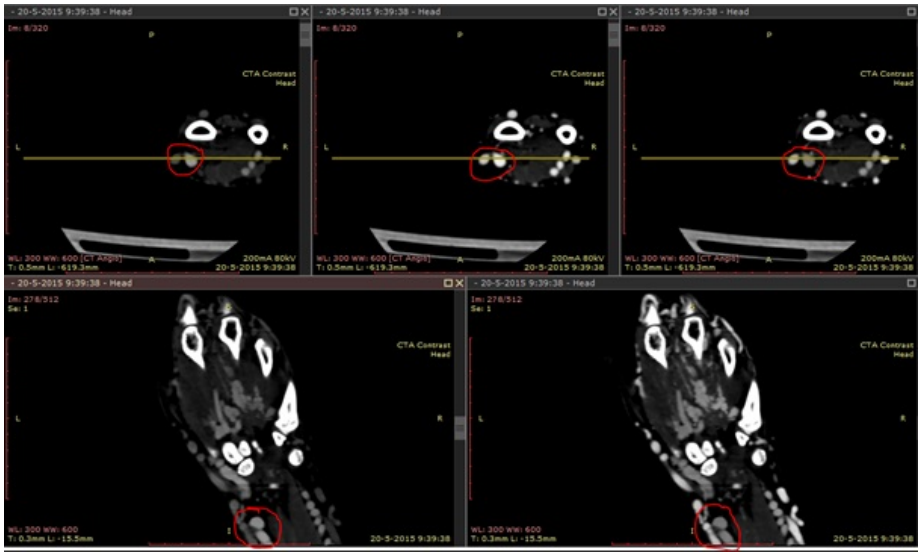

Figure 5: *Axial slices at time frame 4 (left), 9 (middle) and 14 (right). Coronal slices at 4 (left) and 14 (right). The yellow line indicates the location of the coronal slice on the axial slice.*

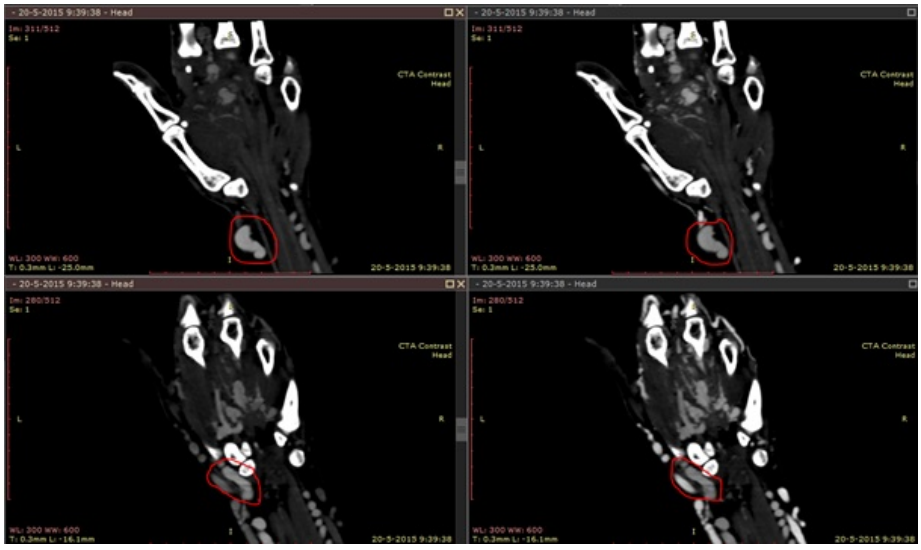

Figure 6: *The diameter of the right encircled blood vessel increases.*

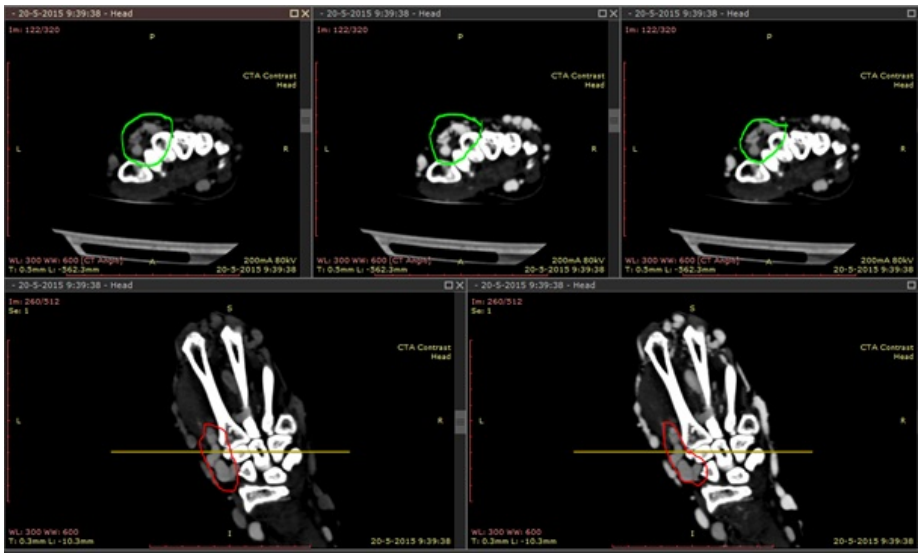

Figure 7: *The green circle shows a possible connection from the nidus and the vein.*

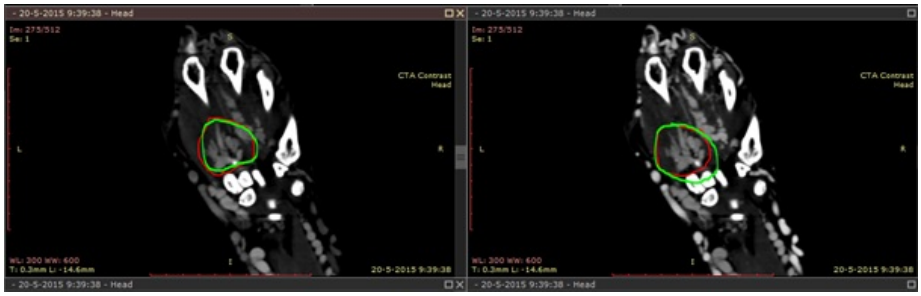

Figure 8: *The location of the connection in the coronal plane.*

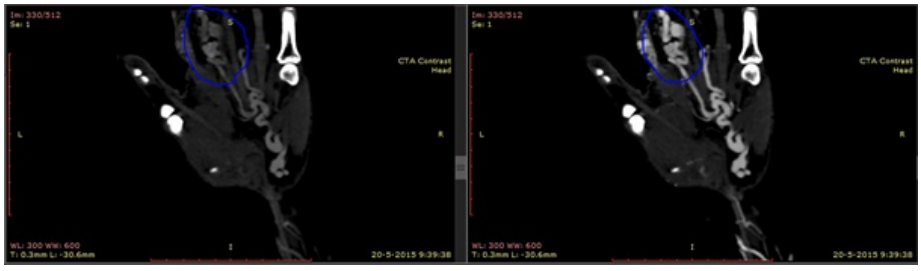

Figure 9: *Another connection is encircled in blue.*

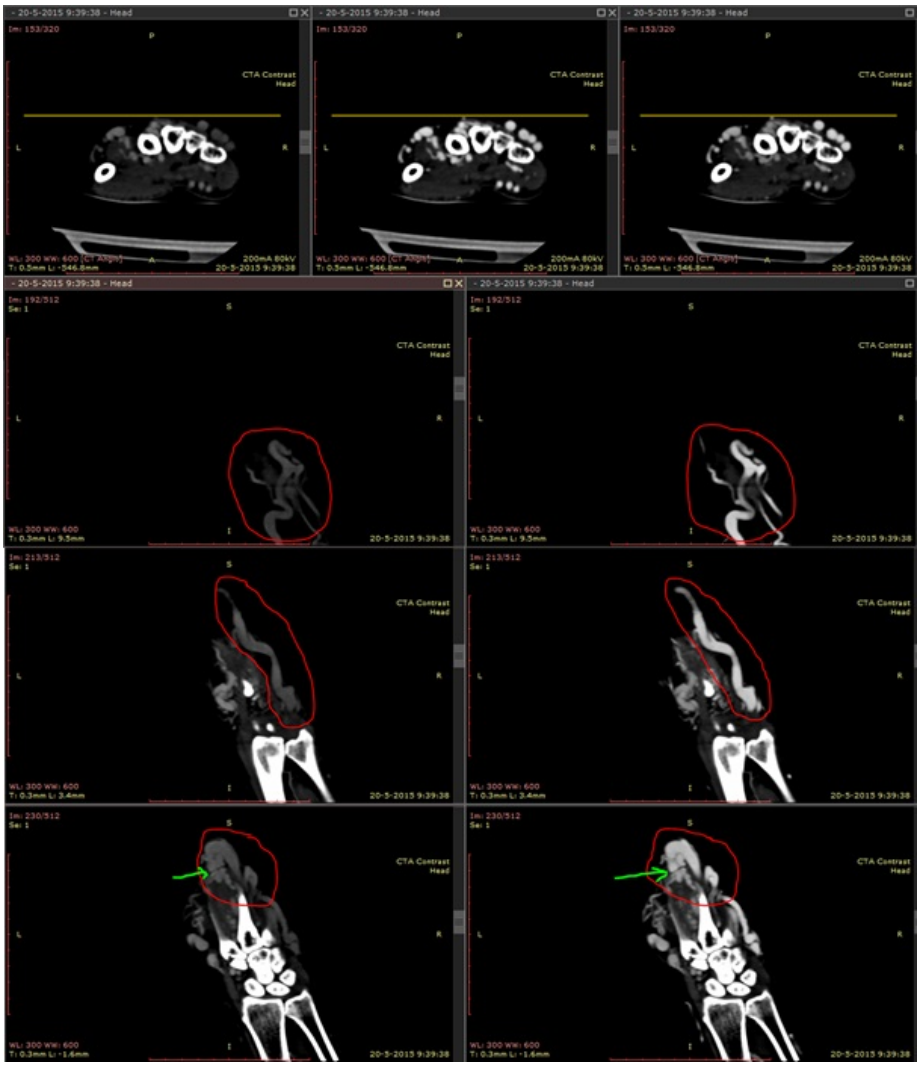

Figure 10: *Mask image of the bones in the hand.*

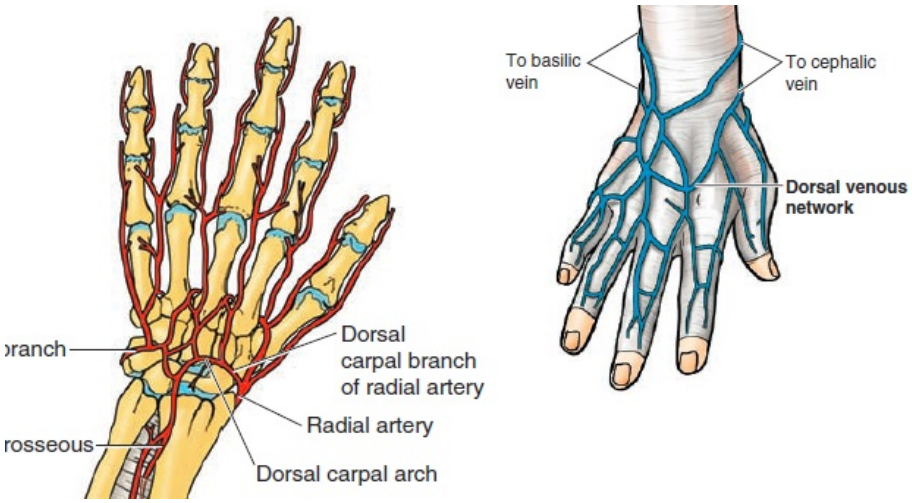

Figure 11: *Dorsal vascular anatomy of the hand. [Moore et al., 2010]*

II. Image processing software

The evaluation of an AVM is performed using image processing software. In the UMC St Radboud Vitrea, a product of Toshiba, is used to examine the 4D-CTA data sets. This version of Vitrea is adapted to the Aquilion One CT scanner also made by Toshiba, especially for examining the dimension of time, which is used in scans of AVMs. The data sets created by the CT scanner are very well compatible with Vitrea. However, Vitrea performs sufficiently for evaluating the AVM, but unfortunately the computer encounters problems loading the data due to the large files. In addition Vitrea is not available for home use. In this thesis one data set of an AVM of a wrist will be used for image processing.

To view the DICOM files, with the format of .exec DICOM, at home a specific reader is needed. Many of these DICOM readers are available, but several readers demand payment. Some programmes were found useful to evaluate the AVM datasets at the University of Twente. For example RadiAnt was found. This is a useful tool for examining CT data in the ”X”, ”Y” and ”Z” plane, but it does not have the option to visualize the data in 3D, nor in 4D. Also OsiriX Lite (Mac only) was found. Osirix has segmentation tools and can show images in 3D, though 4D is not available in the free version.

The DICOM readers were used to evaluate the AVM, but it is not possible to add new functions as for example automatically locating the AVM. This is where Matlab comes in and plays an important role. Several functions are needed to automate the evaluation. The plan is to first segment the blood vessels, because the surrounding tissue is not needed to find the nidus. At Matlab Central many useful scripts for different proceedings can be found to evaluate the AVM. These scripts available at Matlab Central were combined to process the obtained data.

III. Matlab

III.1 DICOM to Matlab

Before the data is compatible with DICOM viewers in Matlab the .exec DICOM files need a different format. To make these DICOM files the right format the DICOM toolbox by Dirk-Jan Kroon from Matlab Central is used. *[Kroon, 2011a]* The toolbox has two scripts for the process of .exec conversion to .dcm, which are Matlab compatible. These two scripts have been automated to create the .dcm files with a 512 by 512 dimension continuously for every time sequence.

To create 3D images a three dimensional matrix needs to be made from all the 320 .dcm images of one time sequence. This is done by writing a script which contains a loop to stack the 2D slices and form a 3D image. A file called ct3d"nr".mat is created with the script ct3d_05_auto.m. This file is a matrix of 512 by 512 by 320. At this moment the data are 3D and with viewer3d by Dirk-Jan Kroon the 3D image is viewed. *[Kroon, 2011b]* The image can be viewed in "X", "Y" and "Z" plane and it can be rendered into a maximum intensity projection as well. The 3D image shows a lot of information which is not necessary for the image processing. The viewer shows an excess of data which does not contain tissue and therefore can be eliminated from the data.

To eliminate this information the 512 by 512 by 320 is cropped. The boundaries for the crop can be set in the script ct3d_05_auto_crop.m. This script executes the same as ct3d_05_auto.m, but only between the selected boundaries of the crop. The name of the file in the workspace will not change (ct3d"nr".mat). The cropped data will be used in Matlab for image processing. An advantage of the cropping of the data is the faster processing, because there is less information to process.

The fourteen 3D matrices created by ct3d_05_auto_crop.m will be put together to create a fourth dimension. These 3D matrices combined make a 4D matrix of 512 by 213 by 320 by 14. Creating this 4D matrix in Matlab goes rather fast. An almost two year old laptop with an Intel CoreTM i5 processor with a RAM of 8 gigabytes takes about half an hour to obtain a 4D matrix. However this large .mat file takes more time to process in several experimental scripts for image processing. For this reason the processing of the images is mainly done with 3D files.

III.2 Image processing with Matlab

The cropped 3D data still contain data which are not directly necessary for the goal of this thesis. To get a clear view of the blood vessels, the bone and other soft tissue are removed as much as possible. This is done by a new written script where the voxels in the zero contrast image, containing bone information, are saved. (see ct3d_06_bone_mask_create.m). This is called the bone mask and will be used to subtract as many bone as possible from the other images with the script: ct3d_07_bone_subtraction.m. Figure 12 shows an image of a bone mask. The new 3D matrices which are created are now called ct3d"nr"sub.

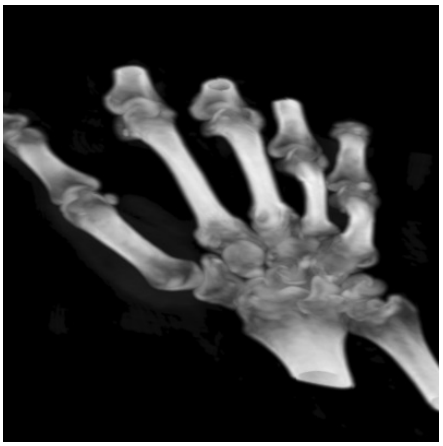

Figure 12: *Mask image of the bones in the hand.*

The next step after clearing almost all bone tissue, is the elimination of the soft tissue. To save only the blood vessels a mask is made by a new written script called ct3d_08_mask_create.m. The zero contrast boneless 3D dataset will be subtracted from the high contrast boneless 3D dataset. After subtraction only the voxels with the information of the blood vessels remain with a higher value. These voxels will get the number "1" applied by an "if" loop and the remaining voxels will get the number '0'. When multiplying this mask with the 3D dataset of every time sequence, only the voxels which are multiplied with "1" remain. This is done by running ct3d_09_mask_filter.m.

It is possible the patient makes a movement during the 4D-CTA scan. Due to this movement some high valued pixels of the bone tissue stay visible after subtraction. These high valued pixels are made visible by the mask which has been created for the blood vessels.

These artefacts of bone could disturb the visibility of the blood vessels. To prevent these artefacts to disturb the ”blood vessel mask” a script called, ct3d_10_mask_filter_adjust.m, is used. ct3d_10_mask_filter_adjust.m erases every pixel with a value lower than ”0” and higher than ”800”. These pixel values are determined by research of the pixel values of the 3D image. Any pixel value above 800 is bone and any pixel value below 0 is considered as irrelevant, because a blood vessel has only pixel values above 0. After the ”mask filter adjust” the name of the dataset is changed to ct3d”nr”maskfilt.mat.

In the ct3d”nr”maskfilt.mat file another problem occurs. Due to difference in contrast density the minimum and maximum voxel values differ between the 3D datasets. Since the greyscale is determined by these minimum and maximum value a script is written to give two voxels a new minimum and maximum. These values are equal in every 3D dataset. By this the grey scales are identical and the three dimensional images are easier to compare to each other.

With viewer3d.m the 3D datasets were viewed and at every time sequence a ”save picture” was executed. The created .png files were aligned and saved as an .avi file. The .avi file is a video which is played to give the 3D datasets their fourth dimension ”time”. With the fourth dimension the flow of the contrast fluid becomes visible. All of the scripts described above are found in the appendix.

IV. Discussion

I. Setbacks of 3D

During this thesis several setbacks have occurred, especially in the 3D imaging since most of the image processing has been done with these matrices. For example the MIP function of viewer3d needs time to load the image after every angle rotation with the mouse. For a quicker and easier evaluation a 3D viewer should be updated and enhanced for larger files. The 3D viewers used at UMC St Radboud, Vitrea and Osirix, are much faster. However as discussed above, these viewers are not adaptable. For this thesis Matlab was chosen, since this is a known multi-paradigm numerical computing environment which could help to resolve the research question of this thesis.

II. Alternatives to CTA

In this thesis mainly the focus lays at 4D-CTA. However there are several alternatives to the 4D-CTA. For instance Magnetic Resonance Angiography (MRA), Doppler Ultrasound and more. In this part of the discussion a few possibilities of these alternatives are given.

II.1 MRA

Magnetic Resonance Angiography is an imaging technique based on MRI. The main principle of MRI is the activation of a magnetic field. This magnetic field aligns the hydrogen atoms in the body with each other. After the alignment the magnetic field is disabled and the hydrogen atoms will move to their relaxed state. The energy these atoms emit during their movement to their relaxed state is caught by a detector. This detector translates the energy which was emitted by the atoms and sends the acquired data to a computer. The computer filters and constructs an image out of the data. In case of an AVM a contrast agent is added to the bloodstream. The contrast agent injection follows the same principles as in CTA. *[Schad et al., 1996]*

An example of a contrast agent in MRA is arterial spin labelling (ASL). ASL is a technique where a part of the blood of the patient gets a magnetic spin altering to the magnetic field which is induced by the MRI magnet. This spin is given to blood in an artery. The targeted artery needs to be in front of/before the region of interest. After a short delay this blood arrives at the region of interest and will be brighter compared to unlabelled blood on the images. In this way the AVM and its nidus can be evaluated better. *[Osch and Lu, 2011]*

This MRA technique is non-invasive. In comparison with DSA this is a great bene-

fit. Though MRA has several disadvantages as well. Firstly, it is insensitive to intracranial AVMs with low blood flow. Secondly, the time coverage is relatively short to detect the complete blood flow of the AVM. *[Yu et al., 2012]* Finally, the venous blood vessels are stretched and have a faster blood flow. Since ASL is dependant of blood flow the arteries and veins are hard to distinguish from each other. This is called contamination by venous blood vessels and can give a wrong judgment about the AVM. *[Schmid et al., 2014]*

II.2 Doppler

Another way to detect the nidus is by studying the blood flow. Since the nidus is a short circuit between artery and vein a disturbed blood flow occurs. The blood flow can be visualized using Doppler. Doppler is used to investigate larger blood vessels in the body. Images of these blood vessels are coloured to evaluate the flow. For different velocities of the flow different colours will be used. The different velocities are labelled by the measured time delays of the moving objects created by the US.

However the average Doppler is not able to detect a blood flow which has a velocity lower than 4.35 millimetre per second. *[Roy et al., 2012]* In addition an AVM has many blood vessels close to each other. This makes an US image difficult to read.

V. Recommendations

Following to the objectives of this thesis several new views arose to approach the problem sketched by L.J. Schultze Kool of the UMC St. Radboud. More ways to find and evaluate the nidus in the datasets were found. Next to the different approaches the visualization of the nidus could also become marked. After the AVMs are found in the data it is possible to add navigational techniques to the treatment.

I. AVM detection approaches

I.1 Density of the contrast

The quantity of contrast medium in the AVM (density) can be used to detect the nidus. The AVM exists of one or several arteries, which enter a dilated vessel, also known as the nidus. When the contrast medium enters the nidus through a conducting artery, the contrast fades out. The contrast fades out due to the increase of blood volume. This process can be detected in Matlab by looking at the attenuation coefficient of the voxels. In the artery this value is rather constant and fairly high. However when the flow enters the nidus, these voxel values drop. To quantify this value drop the voxels should be compared to adjacent voxels. It may indicate the start of the nidus when a voxel value suddenly differs a lot from an adjacent voxel.

The voxel values comparison is only needed in the blood vessels. Thus the surrounding tissue can be left out. To filter the surrounding tissue the blood vessels should be segmented. Several segmentation principles exist. Most segmentation techniques work with a density or colour scale. An easy way of segmentation is the threshold-based segmentation. *[Saleh et al., 2011]* Since the radiodensity of AVMs is higher than in the surrounding tissue, it is possible to detect grayscale differences in the data. The contrast medium in the blood vessels has a high Hounsfield unit (HU), but the surrounding tissue has not, except for the lower values of bone. The known HU values allow to set a threshold to divide the blood vessels from adjacent tissue. The threshold creates a binary picture which can be used as a mask for the other datasets. For example the threshold is set at 200 to 500 HU. All voxels with a HU of 500 or higher will be visualized white, while voxels with a HU of 200 or lower will be black. A drawback of this segmentation technique is that not only the blood vessels will be visible but also the bones. This happens due to the high density of bone, for example 450 to 2500 HU. Thus bone will also turn white. The bone parts in the image will disturb the visibility of

the blood vessels.

I.2 Diameter of the vessels

A second way to detect and evaluate the nidus is by comparing the diameter of the blood vessels in the AVM. As mentioned before the artery feeds a large dilated vein. The dilatation of the blood vessel can be detected and measured. To detect the dilatation it can be more useful to use 2D images. For measuring the blood vessel diameter the other tissue is not necessary. To eliminate the irrelevant tissue segmentation of the blood vessels can be used. After segmentation of the images the contrast difference could be converted to binary information. However, before the image is converted to binary the bone and soft tissue need to be filtered and be completely deleted. Changing the image to binary follows the same procedure as described above, only for a 2D dataset. In this altered 2D image only the blood vessels will be shown as a white region.

The size of the blood vessels can be determined by counting the white pixels of the selected region. Meanwhile the counting of the pixels is done, the blood vessels can be quantified automatically. The quantification gives information to compute the area of the blood vessel in 2D. This area gives information about the blood vessel to make an evaluation of this vessel. This evaluation determines if the larger areas in the image are veins and the smaller ones arteries. After aligning the images of the same slice in different time frames change can become visible. The size of a blood vessel changes due to the density of contrast. This higher density could show a larger blood vessel on the angiogram. This change of size can get a colour and makes an in- or decrease of the blood vessel visible.

This approach has some disadvantages too. For example a blood vessel is not often placed in the same direction as the measurement is done. The blood vessel can appear as an oval on the 2D image or even as a tube. This can trouble the distinguishing between the veins and arteries and should strongly be taken into consideration.

This problem can be reduced by measuring the size of the blood vessels in a 3D image. This can even result in quantification of the blood vessels and therefore elimination of irrelevant blood vessels can become easier.

I.3 Blood flow quantification

The nidus also can be detected when studying the flow in the AVM. The shortcut located in the AVM disturbs the blood flow. This disturbance of the flow can also be detected in Matlab. However this detection will only be possible when the (fourth) dimension of time is easy to obtain and view.

Currently the flow can for example already be evaluated by a Doppler colouring system. This system can be used to show the blood flow in metres per second. This imaging technique could show the flow disturbance right at the nidus where the flow is altered by entering a larger vascular lumen of the vein. This means it is possible to obtain this information out of a 4D-CTA dataset as well.

The three possibilities described above can be used to evaluate and visualize the nidus. However the vascular system consists of many complex structures and the anatomical variations are high. In these complex structures parts could be wrongly indicated as an AVM. To create a more reliable system for evaluation, all three techniques should be combined. In this program the techniques can check each other for truth of an AVM.

II. Visualization of data

Inverted MIP is used to visualize an AVM in Vitrea, because this resembles a DSA image best. The visualization of the 4D-CTA data stays the same. However in this inverted MIP the nidus should be indicated. Indication of the nidus creates an easier view of the connected blood vessels. There are several ways for indication, for example with arrows or colours. The image is already crowded due to the complex structure. Therefore it is not wise to use a wide range of colours and arrows.

An option is to indicate the nidus by colouring the blood vessels. However only the feeding artery or the nidus itself should be coloured. This should be done to keep an overview of the image.

For an even better evaluation of the AVM it can be useful to simplify the structure and limit the image to only the nidus. After subtraction of the surrounding tissue the surrounding blood vessels which are not a part of the AVM could be filtered. For this only the nidus and its feeding and draining blood vessels will only be visible. To create an image with only the nidus a late frame should subtracted. This late frame with the abducting veins shown, should be subtracted from a frame somewhere in the middle of the time sequence. This middle frame shows almost all blood vessels. In this way the nidus stays visible and the surrounding blood vessels will be deleted.

III. Improving therapy

III.1 Navigation

When treating an AVM, DSA is used to verify if the needle or catheter is in the right location to inject ethanol. It is hard to determine whether the right blood vessel is reached due to a 2D image. For this reason the physician should be rather experienced in placing the needle at the exact right spot. A 3D image of the tissue with the exact location and angle to insert the instrument would be very helpful for this intervention. This is where navigation could play an important role.

Navigation is mainly used in neurosurgery, because the brain consists of many vital structures, which may not get damaged. It is important to know which structures need to be treated and which structures should be avoided. For this reason a navigation system that calculates the route and navigates to a particulate structure is useful. Also, navigation enables to visualize the anatomical location of the instrument by tracking it. Altogether navigation improves the safety of interventions and makes them less invasive. *[Mezger et al., 2013]*

Surgical navigation consists of a couple of steps. *[Maier-Hein et al., 2007a]* First a preoperative scan is made. This could be a CT - or MR scan. Afterwards the target is determined. Prior to the operation registration takes place. This process is performed to establish a relation between the virtual coordinate system, the image and the real coordinate system, the patient. *[Mezger et al., 2013]* A stereoscopic camera emitting infrared light is used to determine the 3D position using marker spheres. These marker spheres are attached to the surgical instruments and the patient. The coordinate systems are matched by linking the marker sphere to its location in the scan data. After this process navigation with real time tracking is possible. *[Mezger et al., 2013]*

The problem of navigation in soft tissue is movement. Due to respiration, muscle tone, heartbeat, patient movement and more the morphology of the tissue changes over time. A CT scan made a week before the procedure, can be useless at the time of this intervention. It is best when the scan is made directly prior to the intervention and the patient is not moved during. But even then the usage of instruments at the intervention can cause differences in the morphology. Therefore scans could also be acquired intraoperatively. However it is still expensive and difficult. . An MR scan, for example, takes time to prepare and hinders the workflow. Also the instrumentation should be MR proof. CT is more approachable, but also copes with work flow problems.

Maier-Hein et al (2007) described a way to improve soft tissue navigation by using needles as navigation aids in phantoms. *[Maier-Hein et al., 2007b]* First the target is encircled with a couple of needles and a preoperative CT scan is acquired. Afterwards the registration takes place: the navigation aids are located in the planning CT. Also the position of the target structure relative to the navigation points is defined. Subsequently the intervention takes place with a trackable instrument. Afterwards the needles are removed.

Next to needles, other objects could also be used as navigation aids. In some AVMs coils or guidewires are already inserted in the

nidus. These structures could work as a navigation aid. In this case a specific point on the object should be chosen as navigation aid and it is important that the object does not move. Treatment of an AVM most of the time includes a series of treatments. In these cases it may be useful to position navigation aids for a longer time. Gold fiducial seeds are already used as markers in image guided radiation therapy. *[Fawaz et al., 2014]* Because gold is a noble metal and it is diamagnetic, it will not cause a metal artefact. *[Mathew et al., 2013]* But in CT metal artefacts cause problems. This might be a problem when a second 4D-CTA should be made to evaluate the AVM, because the blood flow cannot be studied properly. Although, metal artefact reduction software (MARS) can improve the image quality. Brook et al (2012) used this software and successfully improved the abdominal tumour visibility in the vicinity of gold fiducial seeds. *[Brook et al., 2012]* This software was developed by GE Medical Systems combined with gemstone spectral imaging hardware. This combination corrects for beam hardening and photon starvation. The Toshiba Aquilion ONE family also features metal artefact reduction software. Single Energy Metal Artefact Reduction (SEMAR) virtually eliminates metal artefacts by adding it to the scan protocol. *[Systems, 2015]*

To improve the treatment of an AVM it can be useful to project the targeted structure on the exterior of the patient. Riva et al (2015) projected the superficial temporal artery on the skin in vascular brain surgery. *[Riva et al., 2015]* This technique was used to visualize the superficial temporal artery and to remove it to use it as a bypass. Preoperative CTA or MRA scans were combined with reference points to start navigation with high accuracy. When the skin was not moved between the preoperative scan and surgery the artery turned out to be projected at its location. This technique could be a supportive tool in puncturing the AVM. However, the depth of the nidus is not displayed. The location of the needle can be tracked using navigation.

As said before treating the AVM with fluoroscopy is difficult, however navigation creates opportunities for improvement. The radiation dose for navigation is lower, because only one standard CTA is required prior to the intervention instead of continuous imaging. In addition contrast medium is no longer needed to determine the position of the needle. The contrast medium is only needed in the CTA scan.

Implementation

Soft tissue navigation could be a promising new technique. Though it is difficult to implement in the workflow in the radiology department in the UMC St Radboud. In the first place a sterile CT room should be built. In this hybrid operating room the preoperative scans can be acquired and the treatment can be started without moving the patient. Also the physicians should be trained to work with the navigation system during the procedure. Before implementation more research should be done on this topic.

III.2 3D printing

Another way to increase understanding in the structure of an AVM is by creating a 3D structure. 3D printing can be of good use to the interventional radiologist since it can create difficult structures. An AVM should not be a problem to print. A printed AVM can attribute to an increased understanding of the specific AVM. The printed AVM can be evaluated by the interventional radiologist in real life. The radiologist can look at every different angle he needs. Next to this evaluation he can prepare an approach of treatment based on this model. It has to be taken into account that the model does not resemble the morphology of the human body. So changes due to respiration, muscle tone, heartbeat, patient movement and more should be taken into account.

3D printing of vascular models has already been used in preoperative planning. Itagaki et al (2015) printed a model of the splenic artery. *[Itagaki, 2015]* The CT scan of the patient, 3D printing software and 3D printing services were used to print a 3D model of the splenic artery aneurysm. The 3D model was used

to plan the splenic artery aneurysm surgery. Though it is not yet possible to manufacture hollow small blood vessel models, since the blood vessel walls are not visible on a CTA scan. It is possible to print the blood vessel lumen as a tube. However this tube does not resemble the anatomical shape of the blood vessel wall. Itagaki et al (2015) used this kind of hollow model preoperatively to practice the intervention and test the equipment. They also used a second model intraoperatively as a reference. *[Itagaki, 2015]*

Although in splenic artery aneurysm surgery understanding in the blood vessel lumen has to be created, in AVM treatment the location of the blood vessels is important. A 3D model can be formed by segmenting the blood vessels and 3D print this structure. It has to be taken into account that the 3D model represents the lumens of the blood vessels. The walls of the blood vessels are not represented in the model, since these are not visible on the scan.

VI. Glossary

4D: Dimensions X, Y, Z and time, displaying a 3D structure in time
4D CTA: Imaging blood vessels as a 3D structure in time using volume mode CT and a iodinated contrast agent
Angiography: Medical imaging technique to visualize blood vessels in 2D using a iodinated contrast medium
Arteriovenous malformation (AVM): Anomaly of the circulatory system which consists of one or several arteries feeding a dilated vein
Attenuation coefficient: Unit to characterize how easy a structure can be penetrated by an X-ray beam
Backprojection: CT reconstruction technique
Computed tomography angiography: Imaging blood vessels in 3D using CT and a iodinated contrast agent
DICOM file: File format for handling, storing, printing, and transmitting information in medical imaging
Digital subtraction angiography: Medical imaging technique to visualize blood vessels in 2D by eliminating overlying structures
Embolization: Process to close a blood vessel by injecting an embolization fluid, which causes the endothelial proteins to denature, which also activates the coagulation system
Fluoroscopy: Imaging technique which uses X-rays to obtain real-time images of a structure
Iterative reconstruction: CT reconstruction technique
Hounsfield unit (HU): Quantitative scale for describing radiodensity
Mask image: Dataset of a certain structure which can be subtracted from another dataset to obtain a dataset without this structure
Matlab: Multi-paradigm numerical computing environment and programming language
Region of interest (ROI): Subset of samples in a dataset selected for a particular purpose
Scanogram: A scan made to determine the location of the patient in the scan
Sinogram: Visual representation of raw CT data of the attenuation coefficient in CT
Surgical navigation: Medical technique for tracking instruments in real-time in the body during an intervention
Volume mode CT scan: Type of CT scan in which all slices of the gantry scan parallel
Volume rendering: A technique to represent CT data in 3D
Voxel: Three dimensional pixel

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VII. Appendix

In the following pages the used Matlab scripts are included.

ct3d_01_dicom_folder_info.m

```
function datasets=dicom_folder_info(link,subfolders)
% Function DICOM_FOLDER_INFO gives information about all Dicom files
% in a certain folder (and subfolders), or of a certain dataset
%
% datasets=dicom_folder_info(link,subfolders)
%
% inputs,
%   link : A link to a folder like "C:\temp" or a link to the first
%          file of a dicom volume "C:\temp\01.dcm"
%   subfolders : Boolean if true (default) also look in sub-folders for
%          dicom files
%
% ouputs,
%   datasets : A struct with information about all dicom datasets in a
%           folder or of the selected dicom-dataset.
%             (Filenames are already sorted by InstanceNumber)
%
%
% Example output:
%  datasets=dicom_folder_info('D:\MedicalVolumeData',true);
%
%  datasets =  1x7 struct array with fields
%
%  datasets(1) =
%             Filenames: {24x1 cell}
%                 Sizes: [512 512 24]
%               Scales: [0.3320 0.3320 4.4992]
%             DicomInfo: [1x1 struct]
%     SeriesInstanceUID: '1.2.840.113619.2.176.2025'
%     SeriesDescription: 'AX.  FSE PD'
%            SeriesDate: '20070101'
%            SeriesTime: '120000.000000'
%              Modality: 'MR'
%
%  datasets(1).Filenames =
%   'D:\MedicalVolumeData\IM-0001-0001.dcm'
%   'D:\MedicalVolumeData\IM-0001-0002.dcm'
%   'D:\MedicalVolumeData\IM-0001-0003.dcm'
%
% Function is written by D.Kroon University of Twente (June 2010)

% If no Folder given, give folder selection dialog
if(nargin<1), link =  uigetdir(); end

% If no subfolders option defined set it to true
if(nargin<2), subfolders=true; end

% Check if the input is a file or a folder
if(isdir(link))
    dirname=link; filehash=[];
else
    dirname = fileparts(link);
    info=dicominfo(link);
    SeriesInstanceUID=0;
```

```
    if(isfield(info,'SeriesInstanceUID')),
SeriesInstanceUID=info.SeriesInstanceUID; end
    filehash=string2hash([dirname SeriesInstanceUID]);
    subfolders=false;
end

% Make a structure to store all files and folders
dicomfilelist.Filename=cell(1,100000);
dicomfilelist.InstanceNumber=zeros(1,100000);
dicomfilelist.ImagePositionPatient=zeros(100000,3);
dicomfilelist.hash=zeros(1,100000);
nfiles=0;

% Get all dicomfiles in the current folder (and sub-folders)
[dicomfilelist,nfiles]=getdicomfilelist(dirname,dicomfilelist,nfiles,filehash,
subfolders);
if(nfiles==0), datasets=[]; return; end

% Sort all dicom files based on a hash from dicom-series number and folder
name
datasets=sortdicomfilelist(dicomfilelist,nfiles);

% Add Dicom information like scaling and size
datasets=AddDicomInformation(datasets);

function datasets=AddDicomInformation(datasets)
for i=1:length(datasets)
    Scales=[0 0 0];
    Sizes=[0 0 0];
    SeriesInstanceUID=0;
    SeriesDescription='';
    SeriesDate='';
    SeriesTime='';
    Modality='';
    info=dicominfo(datasets(i).Filenames{1});
    nf=length(datasets(i).Filenames);

    if(isfield(info,'SpacingBetweenSlices')),
Scales(3)=info.SpacingBetweenSlices; end
    if(isfield(info,'PixelSpacing')), Scales(1:2)=info.PixelSpacing(1:2); end
    if(isfield(info,'ImagerPixelSpacing ')),
Scales(1:2)=info.PixelSpacing(1:2); end
    if(isfield(info,'Rows')), Sizes(1)=info.Rows; end
    if(isfield(info,'Columns')), Sizes(2)=info.Columns; end
    if(isfield(info,'NumberOfFrames')), Sizes(3)=info.NumberOfFrames; end
    if(isfield(info,'SeriesInstanceUID')),
SeriesInstanceUID=info.SeriesInstanceUID; end
    if(isfield(info,'SeriesDescription')),
SeriesDescription=info.SeriesDescription; end
    if(isfield(info,'SeriesDate')),SeriesDate=info.SeriesDate; end
    if(isfield(info,'SeriesTime')),SeriesTime=info.SeriesTime; end
    if(isfield(info,'Modality')), Modality=info. Modality; end
    if(nf>1), Sizes(3)=nf; end
    if(nf>1)
        info1=dicominfo(datasets(i).Filenames{2});
        if(isfield(info1,'ImagePositionPatient'))
```

```
            dis=abs(info1.ImagePositionPatient(3)-
info.ImagePositionPatient(3));
            if(dis>0), Scales(3)=dis; end
        end
    end
    datasets(i).Sizes=Sizes;
    datasets(i).Scales=Scales;
    datasets(i).DicomInfo=info;
    datasets(i).SeriesInstanceUID=SeriesInstanceUID;
    datasets(i).SeriesDescription=SeriesDescription;
    datasets(i).SeriesDate=SeriesDate;
    datasets(i).SeriesTime=SeriesTime;
    datasets(i).Modality= Modality;
end

function datasets=sortdicomfilelist(dicomfilelist,nfiles)
datasetids=unique(dicomfilelist.hash(1:nfiles));
ndatasets=length(datasetids);
for i=1:ndatasets
    h=find(dicomfilelist.hash(1:nfiles)==datasetids(i));
    InstanceNumbers=dicomfilelist.InstanceNumber(h);
    ImagePositionPatient=dicomfilelist.ImagePositionPatient(h,:);
    if(length(unique(InstanceNumbers))==length(InstanceNumbers))
        [temp ind]=sort(InstanceNumbers);
    else
        [temp ind]=sort(ImagePositionPatient(:,3));
    end
    h=h(ind);
    datasets(i).Filenames=cell(length(h),1);
    for j=1:length(h)
        datasets(i).Filenames{j}=dicomfilelist.Filename{h(j)};
    end
end

function [dicomfilelist
nfiles]=getdicomfilelist(dirname,dicomfilelist,nfiles,filehash,subfolders)
dirn=fullfile(dirname);
if(~isempty(dirn)), filelist = dir(dirn); else filelist = dir; end
for i=1:length(filelist)
    fullfilename=fullfile(dirname,filelist(i).name);
    if((filelist(i).isdir))
        if((filelist(i).name(1)~='.')&&(subfolders))
            [dicomfilelist nfiles]=getdicomfilelist(fullfilename
,dicomfilelist,nfiles,filehash,subfolders);
        end
    else
        if(file_is_dicom(fullfilename))
            try info=dicominfo(fullfilename); catch me, info=[]; end
            if(~isempty(info))
                InstanceNumber=0;
                ImagePositionPatient=[0 0 0];
                SeriesInstanceUID=0;
                Filename=info.Filename;
                if(isfield(info,'InstanceNumber')),
InstanceNumber=info.InstanceNumber; end
```

```
if(isfield(info,'ImagePositionPatient')),ImagePositionPatient=info.ImagePositi
onPatient; end

                if(isfield(info,'SeriesInstanceUID')),
SeriesInstanceUID=info.SeriesInstanceUID; end
                hash=string2hash([dirname SeriesInstanceUID]);
                if(isempty(filehash)||(filehash==hash))
                    nfiles=nfiles+1;
                    dicomfilelist.Filename{ nfiles}=Filename;
                    dicomfilelist.InstanceNumber( nfiles)=InstanceNumber;

dicomfilelist.ImagePositionPatient(nfiles,:)=ImagePositionPatient(:)';
                    dicomfilelist.hash( nfiles)=hash;
                end
            end
        end
    end
end

function isdicom=file_is_dicom(filename)
isdicom=false;
try
    fid = fopen(filename, 'r');
    status=fseek(fid,128,-1);
    if(status==0)
        tag = fread(fid, 4, 'uint8=>char')';
        isdicom=strcmpi(tag,'DICM');
    end
    fclose(fid);
catch me
end

function hash=string2hash(str,type)
% This function generates a hash value from a text string
%
% hash=string2hash(str,type);
%
% inputs,
%   str : The text string, or array with text strings.
% outputs,
%   hash : The hash value, integer value between 0 and 2^32-1
%   type : Type of has 'djb2' (default) or 'sdbm'
%
% From c-code on : http://www.cse.yorku.ca/~oz/hash.html
%
% djb2
%  this algorithm was first reported by dan bernstein many years ago
%  in comp.lang.c
%
% sdbm
%  this algorithm was created for sdbm (a public-domain reimplementation of
%  ndbm) database library. it was found to do well in scrambling bits,
%  causing better distribution of the keys and fewer splits. it also happens
%  to be a good general hashing function with good distribution.
%
```

```
% example,
%
%  hash=string2hash('hello world');
%  disp(hash);
%
% Function is written by D.Kroon University of Twente (June 2010)


% From string to double array
str=double(str);
if(nargin<2), type='djb2'; end
switch(type)
    case 'djb2'
        hash = 5381*ones(size(str,1),1);
        for i=1:size(str,2),
            hash = mod(hash * 33 + str(:,i), 2^32-1);
        end
    case 'sdbm'
        hash = zeros(size(str,1),1);
        for i=1:size(str,2),
            hash = mod(hash * 65599 + str(:,i), 2^32-1);
        end
    otherwise
        error('string_hash:inputs','unknown type');
end

ans = infop;
```

ct3d_02_dicom_read_header.m

```
function info=dicom_read_volume(filename)
% function for reading header of Dicom volume file
%
% info = dicom_read_header(filename);
%
% examples:
% 1,  info=dicom_read_header()
% 2,  info=dicom_read_header('volume.dcm');

% Check if function is called with folder name
if(exist('filename','var')==0)
    dirname='C:\Users\Admin\Desktop\4D DSA\MediaManager-
201505201006289706\DICOM\ST00001';
    [filename, dirname] = uigetfile( { '*.*', 'All Files (*.*)'}, 'Select a
dicom file',dirname);
    if(filename==0), return; end
    filename=[dirname filename];
end

% Read directory for Dicom File Series
datasets=dicom_folder_info(filename,false);
if(isempty(datasets))
    datasets=dicom_folder_info(filename,true);
end
```

```
if(length(datasets)>1)
    c=cell(1,length(datasets));
    for i=1:length(datasets)
        c{i}=datasets(i).Filenames{1};
    end
    id=choose_from_list(c,'Select a Dicom Dataset');
    datasets=datasets(id);
end

info=datasets.DicomInfo;
info.Filenames=datasets.Filenames;
info.PixelDimensions=datasets.Scales;
info.Dimensions=datasets.Sizes;
```

ct3d_03_Dicom_read_volume_playlist.m

```
for i=1:19; %change number of subfolders depending on the struct files infop
    num2=num2str(i);
    numzeros2='00';
    numstr2=[numzeros2(1:end-length(num2)) num2];

    dicom_read_volume(eval(['infoIM', numstr2]));

    j = ['volp', numstr2];
    eval([j '=ans;']);

end
```

ct3d_04_Dicom_write_volume_playlist.m

```
h = waitbar(0,'Please wait ...!');
for i=1:19;
    num2=num2str(i);
    numzeros2='00';
    numstr2=[numzeros2(1:end-length(num2)) num2];


    mkdir('C:\Users\Admin\Documents\MATLAB\MDO\images\Ingelade data',['SE000'
numstr2 ]);
    cd(['C:\Users\Admin\Documents\MATLAB\MDO\images\Ingelade data\SE000'
numstr2 ]);
    dicom_write_volume(eval(['volp', numstr2]),'IM',[0.5 0.5
0.5],eval(['infoIM', numstr2]));

    waitbar(i/19,h)
end
```

ct3d_05_auto_crop.m

```
% CT3D Auto is een script waarin geautomatiseerd alle dicom files van een
% map in ??n .mat file worden gezet.
% Instructies:
%   - rgl 14: Zet achter cd de pathway waar de ct3d.mat workspace files
%   opgeslagen dienen te worden.
%   - rgl 22: verander de img_dir naar de pathway waarin alle .dcm files
%   zijn opgeslagen. Houdt daarbij (['.../SE000' numstr3]); intact.
%   - rgl 39-44: Om overbodige data weg te halen, is er de mogelijkheid de
%   afbeeldingen die worden ingeladen direct bij te snijden. Vul de X, Y en
%   Z grenzen van het bijgesneden plaatje in op deze regels.
%   - run het programma.

h = waitbar(0,'Please wait...');
cd('/Users/jeroenmol/Documents/MATLAB/MDO/Toolbox Kroon/CT3D Hand');
for jj=1:14; %change number of subfolders
    num3=num2str(jj);
    numzeros3='00';
    numstr3=[numzeros3(1:end-length(num3)) num3];

N = 320;
img_dir = (['/Users/jeroenmol/Documents/MATLAB/MDO/Toolbox Kroon/Data/SE000'
numstr3]);

% read the first image separately just to get the size
strfile = 'IM0000001.dcm';
img = dicomread(fullfile(img_dir, strfile));
siz_img = size(img);

% create result matrix:
eval(['ct3d', numstr3, '= NaN([siz_img N]);']);
eval(['ct3d', numstr3,'(:,:,1) = img;']);

% load all the remaining images and put them in the matrix
for ii=2:N
    strfile = sprintf('IM000%04d.dcm',ii);
    eval(['ct3d', numstr3,'(:,:,ii) = dicomread(fullfile(img_dir,
strfile));']);
end

%Boundaries for the crop of the imgage
X1 = ...;%Lowest X-axes boundary
X2 = ...;%Highest X-axes boundary
Y1 = ...;%Lowest Y-axes boundary
Y2 = ...;%Highest Y-axes boundary
Z1 = ...;%Lowest Z-axes boundary
Z2 = ...;%Highest Z-axes boundary

eval(['ct3d', numstr3,' = ct3d', numstr3, '(', X1, ':', X2, ',', Y1, ':', Y2,
',', Z1, ':', Z2, ');']);
save(['ct3d', numstr3], ['ct3d', numstr3]);
waitbar(jj/14,h,['Please wait...(', numstr3,')'])
end
%sprintf('IM0000%04d.dcm',ii)
```

```
close all
```

ct3d_06_bone_mask_create.m

```
%Fill in the pathway to the clean 3D image
load('C:\Users\Admin\Documents\MATLAB\MDO\images\Ingelade data hand\croped
data\ct3d01')
BOT = ct3d01;


% the for loop is built in such away as the pic is 213*512
for h = 1:213 %X-array of the dataset
    for i = 1:512 %Y-array of the dataset
        for j = 1:320 %Z-array of the dataset
        pv = BOT(h,i,j);
        if (pv <125) %Change the pixelvalue above which everything is deleted.
            BOT(h,i,j)=0;
        end

        end
    end
end
```

ct3d_07_bone_subtraction.m

```
W = waitbar(0,'Please wait...');
for k=1:14; %change number of subfolders
    num=num2str(k);
    numzeros='00';
    numstr=[numzeros(1:end-length(num)) num];

    eval(['ct3d',numstr,'sub = ct3d',numstr,'-BOT;']);

    waitbar(k/14,W,['Please wait until it is done...(', numstr,')']);
end
waitbar(k/14,W, 'Ready')
```

ct3d_08_mask_create.m

```
%Fill in the pathway to the clean 3D image
load('C:\Users\Admin\Documents\MATLAB\MDO\images\Ingelade data hand\croped
data\ct3d01')
IMG0 = ct3d01sub;
%Fill in the pathway with the contrast 3D image
load('C:\Users\Admin\Documents\MATLAB\MDO\images\Ingelade data hand\croped
data\ct3d09')
IMG1 = ct3d09sub;
%Create the boundaries of the mask.
MASK = IMG1 - IMG0; %This mask is not yet the mask which is needed.
```

```
% the for loop is built in such away as the pic is 213*512
for h = 1:213 %X-array of the dataset
    for i = 1:512 %Y-array of the dataset
        for j = 1:320 %Z-array of the dataset
        pv = MASK(h,i,j);
        if (pv >465) %Change the pixelvalue above which everything is deleted.
            MASK(h,i,j)=0;
        end
        if (250<pv<465) %Set the pixelvalue which is needed to make a mask of.
            MASK(h,i,j)=1;
        end
        if (pv <250) %Change the pixelvalue below which everything is deleted.
            MASK(h,i,j)=0;
        end
        end
    end
end
```

ct3d_09_mask_filter.m

```
W = waitbar(0,'Please wait...');
for k=1:14; %change number of subfolders
    num=num2str(k);
    numzeros='00';
    numstr=[numzeros(1:end-length(num)) num];

    eval(['ct3d',numstr,'maskfilt = ct3d',numstr,'sub.*MASK;']);

    waitbar(k/14,W,['Please wait...(', numstr,')']);
end
waitbar(k/14,W, 'Ready')

pause(5);

%% Leuk om 's nachts te draaien of met supercomputer
W=waitbar(0,'Please wait...');
for h = 1:213 %X-array of the dataset
    for i = 1:512 %Y-array of the dataset
        for j = 1:320 %Z-array of the dataset
        eval(['pv = ct3d', numstr, 'maskfilt(h,i,j);']);
        if (pv <0) %Change the pixelvalue below which everything is deleted.
            eval(['ct3d', numstr, 'maskfilt(h,i,j)=0;']);
        end
        if (pv >1000) %Change the pixelvalue above which everything is
deleted.
            eval(['ct3d', numstr, 'maskfilt(h,i,j)=0;']);
        end
        end
    end
    hs = num2str(h);
    waitbar(h/213,W,['Please wait...(', hs, ')']);
end
waitbar(h/213,W, 'Ready');
```

```
%%
%for h = 1:213 %X-array of the dataset
 %       for i = 1:512 %Y-array of the dataset
  %          for j = 1:320 %Z-array of the dataset
   %        if (pv <0) %Change the pixelvalue above which everything is
deleted.
%             eval(['ct3d',numstr,'(h,i,j) = 0;']);
 %            end
  %              %for m = 1:(14*213*512*320)
%                 %ks=num2str(k);
 %                %hs=num2str(h);
  %               %is=num2str(i);
%                 %js=num2str(j);
 %                %waitbar(m/(14*213*512*320),W,['Please wait...(', ks, ':',
hs, ':', is, ':', js,')'])
  %              %end
%             end
 %       end
  %  end
```

ct3d_10_mask_filter_adjust.m

```
%% ??n per keer
W=waitbar(0,'Please wait...');
for h = 1:213 %X-array of the dataset
    for i = 1:512 %Y-array of the dataset
        for j = 1:320 %Z-array of the dataset
        pv = ct3d01maskfilt(h,i,j);
        if (pv <0) %Change the pixelvalue below which everything is deleted.
            ct3d01maskfilt(h,i,j)=0;
        end
        if (pv >799) %Change the pixelvalue above which everything is deleted.
            ct3d01maskfilt(h,i,j)=0;
        end
        end
    end
    hs = num2str(h);
    waitbar(h/213,W,['Please wait...(', hs, ')']);
end
waitbar(h/213,W,['Ready']);
```

ct3d_11_contrast_adjust.m

```
W=waitbar(0,'Please wait...');
for k=1:14
    num=num2str(k);
```

```
    numzeros='00';
    numstr=[numzeros(1:end-length(num)) num];

    for h = 1:213 %X-array of the dataset
        for i = 1:1 %Y-array of the dataset
            for j = 1:320 %Z-array of the dataset
            eval(['ct3d', numstr, 'maskfilt(h,i,j) = 0;']);
            end
        end
    end

    for h = 1:213 %X-array of the dataset
        for i = 2:2 %Y-array of the dataset
            for j = 1:320 %Z-array of the dataset
            eval(['ct3d', numstr, 'maskfilt(h,i,j) = 800;']);
            end
        end
    end

    waitbar(k/14, W, ['Please wait...(', numstr, ')']);

end

waitbar(k/14, W, 'Ready')
```

ct3d_12_permute_xyz.m

```
W = waitbar(0,'Please wait because you need to...');
%% [x z y]
for k=1:14; %change number of subfolders
    num=num2str(k);
    numzeros='00';
    numstr=[numzeros(1:end-length(num)) num];

    eval(['ct3d',numstr,'maskfilt_xzy = permute( ct3d', numstr, 'maskfilt ,
[1,3,2]);']);

    waitbar(k/70,W,['Please wait...(', numstr,')']);
end;
%% [y x z]
for l=1:14; %change number of subfolders
    num=num2str(l);
    numzeros='00';
    numstr=[numzeros(1:end-length(num)) num];

    eval(['ct3d',numstr,'maskfilt_yxz = permute( ct3d', numstr, 'maskfilt ,
[2,1,3]);']);

    waitbar((k+l)/70,W,['Please wait...(', numstr,')']);
end;
%% [y z x]
for m=1:14; %change number of subfolders
    num=num2str(m);
```

```
    numzeros='00';
    numstr=[numzeros(1:end-length(num)) num];

    eval(['ct3d',numstr,'maskfilt_yzx = permute( ct3d', numstr, 'maskfilt ,
[2,3,1]);']);

    waitbar((k+l+m)/70,W,['Please wait...(', numstr,')']);
end;
%% [z x y]
for n=1:14; %change number of subfolders
    num=num2str(n);
    numzeros='00';
    numstr=[numzeros(1:end-length(num)) num];

    eval(['ct3d',numstr,'maskfilt_zxy = permute( ct3d', numstr, 'maskfilt ,
[3,1,2]);']);

    %waitbar((k+l+m+n)/70,W,['Please wait...(', numstr,')']);
end;
%% [z y x]
for o=1:14; %change number of subfolders
    num=num2str(o);
    numzeros='00';
    numstr=[numzeros(1:end-length(num)) num];

    eval(['ct3d',numstr,'maskfilt_zyx = permute( ct3d', numstr, 'maskfilt ,
[3,1,2]);']);

    waitbar((k+l+m+n+o)/70,W,['Please wait...(', numstr,')']);
end;


waitbar((k+l+m+n+o)/70,W, 'Ready');
```

ct3d_20_create_avi.m

```
cd ('C:\Users\Admin\Documents\MATLAB\MDO\images\tests\test2'); %choose desired
map to save the avi

writerObj = VideoWriter('subtract.avi');% choose desired name
open(writerObj);
for K = 1 : 28
  dirname = 'C:\Users\Admin\Documents\MATLAB\MDO\images\tests\test2'; %fill in
folder with PNG files
  filename = sprintf('MIP%02d.png', K);  %name of first file and number of
digits
  FullFile = fullfile(dirname, filename);
  thisimage = imread(FullFile);
  writeVideo(writerObj, thisimage);
end
close(writerObj);
```

ct3d_auto.m

```
% CT3D Auto is een script waarin geautomatiseerd alle dicom files van een
% map in ??n .mat file worden gezet.
% Instructies:
%   - rgl 11: Zet achter cd de pathway waar de ct3d.mat workspace files
%   opgeslagen dienen te worden.
%   - rgl 18: verander de img_dir naar de pathway waarin alle .dcm files
%   zijn opgeslagen. Houdt daarbij (['.../SE000' numstr3]); intact.
%   - run het programma.

h = waitbar(0,'Please wait...');
cd('C:\Users\Admin\Documents\MATLAB\MDO\images\Ingelade data hand\CT3D Hand');
for jj=1:14; %change number of subfolders
    num3=num2str(jj);
    numzeros3='00';
    numstr3=[numzeros3(1:end-length(num3)) num3];

N = 320;
img_dir = (['C:\Users\Admin\Documents\MATLAB\MDO\images\Ingelade data
hand\SE000' numstr3]);

% read the first image separately just to get the size
strfile = 'IM0000001.dcm';
img = dicomread(fullfile(img_dir, strfile));
siz_img = size(img);

% create result matrix:
eval(['ct3d', numstr3, '= NaN([siz_img N]);']);
eval(['ct3d', numstr3,'(:,:,1) = img;']);

% load all the remaining images and put them in the matrix
for ii=2:N
    strfile = sprintf('IM000%04d.dcm',ii);
    eval(['ct3d', numstr3,'(:,:,ii) = dicomread(fullfile(img_dir,
strfile));']);
end

save(['ct3d', numstr3], ['ct3d', numstr3]);
waitbar(jj/14,h,['Please wait...(', numstr3,')'])
end
%sprintf('IM0000%04d.dcm',ii)
close all

ct4d_auto
```

ct4d_auto.m

```
[rows cols dimen1] = size(ct3d01);
h = waitbar(0,'Please wait...');
for i=7:8
    num4=num2str(i);
    numzeros4='00';
```

```
    numstr4=[numzeros4(1:end-length(num4)) num4];
    ct4d(:,:,:,i) = eval(['ct3d', numstr4]);

    waitbar(i/14,h,['Please wait...(', numstr4,')'])
end

close all
cd('C:\Users\Admin\Documents\MATLAB\MDO\images\Ingelade data hand\CT3D Hand');
save ct4d
```

dicom_read_volume.m

```
function voxelvolume = dicom_read_volume(info)
% function for reading volume of Dicom files
%
% volume = dicom_read_volume(file-header)
%
% examples:
% 1: info = dicom_read_header()
%    V = dicom_read_volume(info);
%    imshow(squeeze(V(:,:,round(end/2))),[]);
%
% 2: V = dicom_read_volume('volume.dcm');

if(~isstruct(info)), info=dicom_read_header(info); end

voxelvolume=dicomread(info.Filenames{1});
nf=length(info.Filenames);

% Convert dicom images to voxel volume
h = waitbar(0,'Please wait...');
if(~isempty(strfind(info.ImageType,'MOSAIC')))
    if(isfield(info,'Private_0019_100a'))
        nSlices=single(info.Private_0019_100a);
    else
        sInfo=SiemensInfo(info);
        nSlices=single(sInfo.sSliceArray.lSize);
    end
    mimg=ceil(sqrt(nSlices));
    realwidth=single(info.Width)/mimg;
    realheight=single(info.Height)/mimg;

    % Initialize voxelvolume
    voxelvolume=zeros(realwidth,realheight,nSlices,nf,class(voxelvolume));
    for i=1:nf
        waitbar(i/nf,h)
        I=dicomread(info.Filenames{i});
        J=blockproc(I,[realwidth realheight],@(x)block(x));
        J=reshape(J,realwidth,realheight,[]);
        voxelvolume(:,:,:,i)=J(:,:,1:nSlices);
    end
else
    % Initialize voxelvolume
    if((size(voxelvolume,3)*size(voxelvolume,4))>1), return; end
```

```
    voxelvolume=zeros(info.Dimensions,class(voxelvolume));
    for i=1:nf,
        waitbar(i/nf,h)
        I=dicomread(info.Filenames{i});
        voxelvolume(:,:,i)=I;
    end
end
close(h);

function y=block(x)
y=x.data(:);
```

dicom_write_volume.m

```
function dicom_write_volume(Volume,filename,volscale,info)
% This function DICOM_WRITE_VOLUME will write a Matlab 3D volume as
% a stack of 2D slices in separate dicom files.
%
% dicom_write_volume(Volume,Filename,Scales,Info)
%
% inputs,
%   Volume: The 3D Matlab volume
%   Filename: The name of the dicom files
%   Scales: The dimensions of every voxel/pixel
%   Info: A struct with dicom tags and values
%
% Function is written by D.Kroon University of Twente (May 2009)

% Check inputs
if(exist('filename','var')==0), filename=[]; end
if(exist('info','var')==0), info=[]; end
if(exist('volscale','var')==0), volscale=[1 1 1]; end

% Show file dialog if no file name specified
if(isempty(filename))
    [filename, pathname] = uiputfile('*.dcm', 'Save to Dicom');
    filename= [pathname filename];
end

% Add dicom tags to info structure
if(~isstruct(info))
    info=struct;
    % Make random series number
    SN=round(rand(1)*1000);
    % Get date of today
    today=[datestr(now,'yyyy') datestr(now,'mm') datestr(now,'dd')];
    info.SeriesNumber=SN;
    info.AcquisitionNumber=SN;
    info.StudyDate=today;
    info.StudyID=num2str(SN);
    info.PatientID=num2str(SN);
    info.PatientPosition='HFS';
    info.AccessionNumber=num2str(SN);
```

```
    info.StudyDescription=['StudyMAT' num2str(SN)];
    info.SeriesDescription=['StudyMAT' num2str(SN)];
    info.Manufacturer='Matlab Convert';
    info.SliceThickness=volscale(3);
    info.PixelSpacing=volscale(1:2);
    info.SliceLocation=0;
end

% Remove filename extention
pl=find(filename=='.'); if(~isempty(pl)), filename=filename(1:pl-1); end

% Read Volume data
disp('Writing Dicom Files...');
for slicenum=1:size(Volume,3)
    filenamedicom=[filename number2string(slicenum) '.dcm'];
    % Add slice specific dicom info
    info.InstanceNumber = slicenum;
    info.SliceLocation = info.SliceLocation+volscale(3);
    % Write the dicom file
    disp(['Writing : ' filenamedicom]);
    dicomwrite(Volume(:,:,slicenum), filenamedicom, info) ;
    if(slicenum==1),
        info2=dicominfo(filenamedicom);
        info.StudyInstanceUID=info2.StudyInstanceUID;
        info.SeriesInstanceUID=info2.SeriesInstanceUID;
    end
end


function numstr=number2string(num)
    num=num2str(num);
    numzeros='000000';
    numstr=[numzeros(length(num):end) num];
```

Tool_Filter_ct3d.m

```
h = waitbar(0,'Please wait...');
for kk=1:13; %change number of ct3d files 'minus 1'
    num5=num2str(kk);
    numzeros5='00';
    numstr5=[numzeros5(1:end-length(num5)) num5];

    num6=num2str(kk+1);
    numzeros6='00';
    numstr6=[numzeros6(1:end-length(num6)) num6];

    eval(['ct3dfilt', numstr5, '= ct3d', numstr5, '- ct3d', numstr6,';'])

waitbar(kk/13,h)
end

close all
```

```
%% IMSHOW3D of Filter
for kk=1:2; %change number of ct3d files 'minus 1'
    num5=num2str(kk);
    numzeros5='00';
    numstr5=[numzeros5(1:end-length(num5)) num5];

    figure
    imshow3D(eval(['ct3dfilt', numstr5]))
end
```

Tool_SliceFilm.m

```
%Return rows cols and dimensions
[rows cols dimen1 dimen2] = size(ct4d);

count = 0;
%Loop through each image
for i = 1:dimen1
for j = 1:dimen2
count = count + 1;
image = ct4d(:,:,i,j);
tmimg=uint8(image);
img=reshape(tmimg,cols,rows);
images{count} = img;
figure
imagesc(img); colormap('gray')
pause(.05);
end
pause(1);
end
```