University of Twente

A method for calculating the breast volume of lactating and non-lactating breasts using T1-weighted MRI scans.

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Bachelor thesis

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1 Samenvatting

Borstvoeding is belangrijk voor de gezondheid van zowel moeder en kind, omdat het, onder andere, het kind bescherming biedt tegen ziektes zoals diarree. Ondanks verscheidene voordelen begint slechts ongeveer 50% van de vrouwen met borstvoeding geven na hun bevalling, en dit percentage daalt naarmate tijd verstrijkt. Een belangrijke reden hiervoor is lactatie-insufficiëntie; hierbij produceren vrouwen onvoldoende melk om borstvoeding te geven, of ze hebben het gevoel dat dit het geval is, wat leidt tot het stoppen of verminderen van borstvoeding geven. Er is nog niet veel bekend over fysiologische processen die invloed hebben op lactatie; daarom was het doel van deze thesis om een methode te ontwikkelen waarmee het volume van de borst bepaald kan worden met behulp van Magnetic Resonance Imaging (MRI) beelden, opdat uiteindelijk volumes van bijvoorbeeld bloedvaten in de borst vergeleken kunnen worden met het gehele volume. Met vier datasets is een methode ontwikkeld om het borstvolume te bepalen met MATLAB. De verkregen MRI beelden zijn echter van het gehele lichaam rondom de borst en daarom was de eerste stap om de borst te isoleren. Dit is gedaan door op drie verschillende slices zeven punten in te tekenen. Vijf punten volgen de contour van de borstholte om alleen de anteriore kant van het lichaam te behouden, en twee extra punten zorgen ervoor dat alleen het mammaire weefsel in beeld blijft. Alle overgebleven voxels die een intensiteit hadden hoger dan 10% van de maximale intensiteit van de slice werden opgeteld en vermenigvuldigd met het volume van een voxel, waarmee het totale borstvolume berekend werd. Het script werd getest door één gebruiker die driemaal het script uitvoerde en door drie gebruikers die het script eenmaal uitvoerden. Hieruit volgde dat de inter-persoon variabiliteit maximaal 3,75% afweek van de genormaliseerde waarde en de intra-persoon variabiliteit maximaal 8,79%. In deze thesis is het bloedvolume niet bepaald, maar er is wel gekeken naar 'maximum intensity projections' om een beeld te krijgen van de hoeveelheid bloedvaten in de borst. Concluderend is in deze thesis een methode ontwikkeld waarmee het volume van de borst bepaald kan worden aan de hand van MRI-beelden, wat een eerste stap is in de richting om een relatie te vinden tussen borstvolume en lactatie.

2 Abstract

Breastfeeding is important for the health of both mother and child, since it provides, among other things, protection against diseases like diarrhea. Despite diverse benefits, only about 50% of the women start breastfeeding after giving birth, and this percentage declines over time. An important reason for this is lactation insufficiency; this means that not enough breast milk is produced, or that women believe they don't produce enough milk. There is not much known yet about the physiological processes that influence lactation; that's why the goal of this thesis was to develop a method that can be used to calculate the volume of the breast when using Magnetic Resonance Imaging (MRI) scans so that eventually, volumes of, for example, blood vessels in the breast can be compared to the total volume of the breast. Using four datasets, a method is developed to determine the volume of the breast in MATLAB. The MRI scans were, however, from the entire body around the breast and therefore, the first step was to isolate the breast. This was done by selecting seven points on three different slices. Five points followed the contour of the thoracic cavity and the pectoralis major to only maintain the anterior side of the body, and two extra points made sure that only the mammary tissue was left. All remaining voxels that had an intensity of more than 10% of the maximum intensity of the slice were added together and multiplied by the volume of a voxel, which gave the total breast volume. The script was tested by one user who performed the script thrice and by three users who performed the script once. The results showed that the inter-person variability had a maximum of 3.75% from the normalized mean value and the intra-person variability had a maximum of 8.79%. In this thesis, the volume of the blood vessels is not determined, but there has been looked at 'maximum intensity projections' to indicate the amount of blood vessels in the breast. In conclusion, this thesis has developed a method that can be used to calculate the volume of the breast using MRI scans, which is a first step toward understanding the relationship between breast volume and lactation.

3 Introduction

Breastfeeding is important for both the child's and the mother's health [1]. It is recommended by professional organizations, such as the World Health Organization (WHO), that women exclusively breastfeed during the first 6 months after giving birth, and continue breastfeeding, with complementary foods, until the infant is 2 years old [2, 3]. This is because breast milk is among other things of high nutritional value and contains antibodies that help to protect the child against diseases such as diarrhea [1]. On top of that women who breastfeed are also less likely to get sicknesses like cancer or diabetes type II [1]. Despite these and other benefits, not all women breastfeed [1]. Studies have shown that about 50% of women start breastfeeding postpartum, but this prevalence declines over time [1, 4]. A reason for these relatively low numbers can be that women experience lactation insufficiency; this means that not enough breast milk is produced to maintain infant growth or that women believe their milk supply is insufficient [5, 6]. About 10-15% of women are not able to produce enough milk, while about 60-90% of women believe that this is the case [7].

Research on the physiological aspects of why some women can produce more breast milk than other women is still limited. Research has shown that the diameter of the Internal Mammary Artery (IMA) is significantly bigger in the lactating breast than in the non-lactating breast, with a corresponding increase in flow volume [8]. Despite blood having the important role in the body of transporting nutrients and oxygen and removing waste, the relationship between blood volume and milk production in a lactating breast has not been researched so far. Since a higher blood volume indicates more nutrition and oxygen, a higher blood volume might also be an indicator of higher milk production.

To say something about the blood volume in the breast, the total volume of the breast needs to be known. With this information, the blood volume can be related to the total volume. This research will therefore focus on calculating the total breast volume of (lactating) breasts from T1-weighted Magnetic Resonance Imaging scans.

3.1 Breast Anatomy

The breast's base overlies the 2nd to 6th rib [9, 10]. An overview of the contours of the breast is seen in Figure 1a. The upper two-thirds of the breast overlies on the pectoralis major, seen in Figure 1b and the rest of the breast makes contact with the serratus anterior and the upper part of the abdominal oblique [9, 10].

The breast is composed of skin, superficial and deep fascia, breast parenchyma, and the nipple-areola complex [11]. The main components of the parenchyma are adipose tissue and fibroglandular breast tissue [11, 12] and this makes up for the biggest part of the volume of the breast [13]. The fibroglandular tissue is split into 15-20 lactiferous ducts, whose origins are lobules, where milk is made, and converge at the nipple [13]. A duct is associated with a lobe, consisting of 20-40 lobules, consisting of 10-100 alveoli that secrete milk. The ratio between adipose and glandular differs between women [14, 15] and can influence the milk storage capacity; the amount of milk a breast can hold is representative of the amount of glandular tissue, so more adipose tissue may indicate a lower storage capacity than expected [15]. However, 24-hour milk production has not correlated with factors such as the amount of glandular tissue or storage capacity [15]. Breasts do often increase in size during pregnancy, because of the expansion of glandular tissue and the differentiation of lactocytes to produce milk [15]. In Figure 1b an overview of the breast is visible. It shows the different components of the breast and the boundary between the breast and the rest of the body. This Figure also shows the size difference of secretory lobes with alveoli between a non-lactating and a lactating breast.

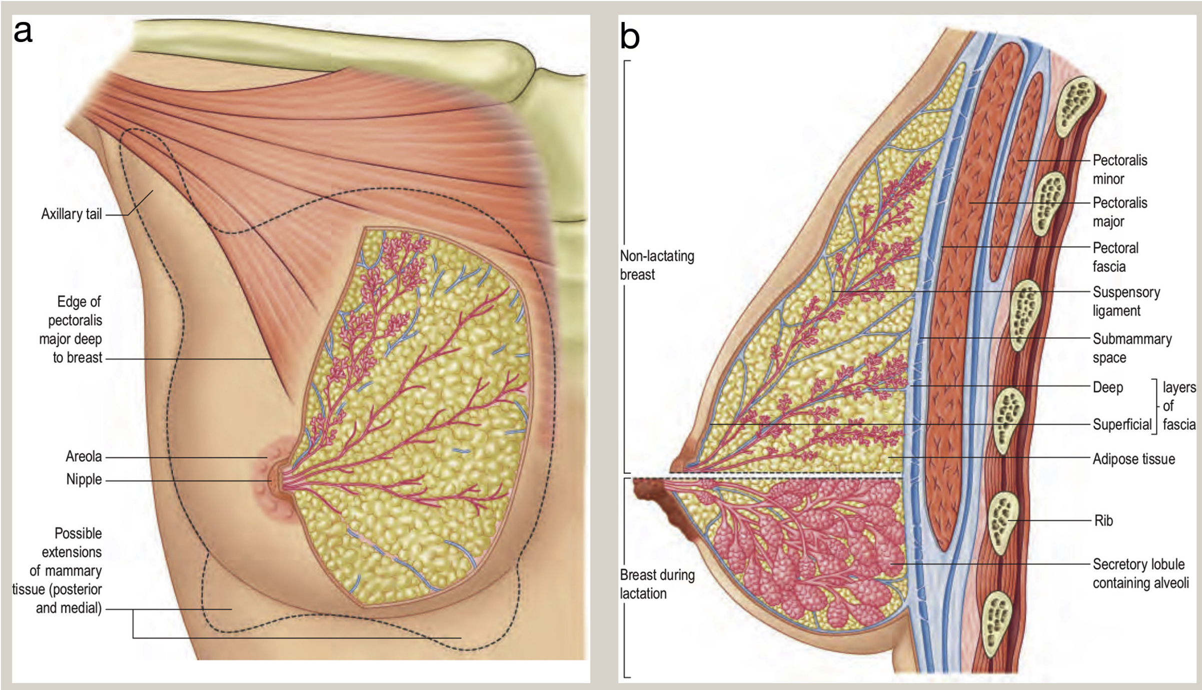


Figure 1: (a) shows the contours of the breast, viewed from the anterior aspect. The nipple-areola complex is also partially visible with its connection to secretory lobes. (b) shows a more detailed overview of the components of the breast. The boundary between the breast and the body, namely the pectoralis major, is important. The size difference between secretory lobules between a lactatling and a non-lactating breast is also shown [9].

3.1.1 Nipple-Areola Complex

On the breast lays the nipple-areola complex; the areola enlarges during pregnancy and contains sweat and sebaceous glands. This complex is visible in 1a and b. The Montgomery glands are also visible on the areola; these provide lubrication during lactation and therefore protect the areola from the mechanical stress of sucking and infections [10, 13, 14].

3.1.2 Blood Supply

Three major arterial routes supply the breast with blood; the internal thoracic artery, the axillary artery, and the posterior intercostal arteries [10]. About 60% of the breast's blood supply comes from the anterior perforating intercostal branches that rise from the internal thoracic artery. This supplies the medial and central sections of the breast. It is also a significant contributor to the nipple-areola complex. The axillary artery is the origin of the lateral thoracic artery and branches of the thoracoacromial artery, which supply the upper outer part of the breast [10, 13]. These account for about 30% of the breast's blood supply. The remaining 10% of the breast's blood comes from the posterior intercostal arteries. These penetrate the deep surface of the breast. An overview of the blood vessels in the breast is seen in Figure 2, where the arteries that contribute to the three arterial routes are mentioned in bold. The venous anatomy in the breast is variable and doesn't directly mirror the arterial supply, even though it resembles the arterial anatomy [16].

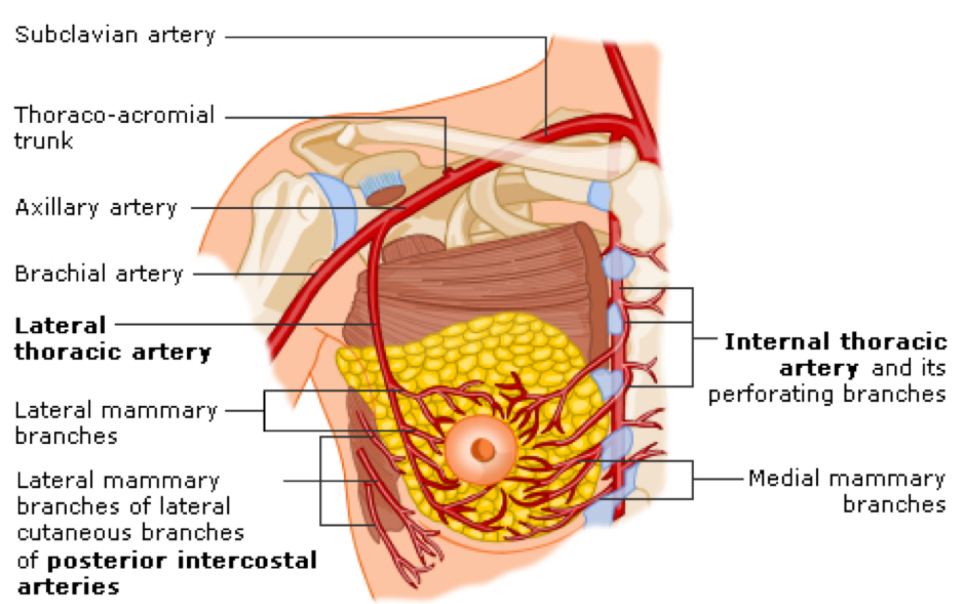


Figure 2: This figure shows the arteries that play a role in the blood supply of the breast. Three major routes provide the breast with blood and the corresponding arteries are shown in bold. [17]

3.1.3 Breast Volumes

Breast volumes differ a lot between women. A study [18] calculated the left and right breast volumes of 400 women using MRI scans. This gave a range of a minimum of 55 ml and a maximum of 4670 ml for the left breast and a minimum of 64 ml and a maximum of 4777 ml for the right breast. A mean volume was found of 979 ml and 973 ml for the left and right breast, respectively.

Since women have different breast volumes, comparing breast volumes between non-lactating and pregnant/lactating women does not give information about milk production. A study [19] researched the maternal breast volume and its changes during pregnancy and showed that the breast volume increases during pregnancy, on average 263 ml between the first and third trimester of pregnancy.

3.2 Magnetic resonance imaging

MRI makes use of the principles of nuclear magnetic resonance (NMR) to create images. Atomic nuclei, such as hydrogen, have the characteristic of 'spin', that induces a magnetic moment. Normally these nuclei and their magnetic moments are distributed randomly [20], but they align parallel or perpendicular to the external field after an external magnetic field (B_0) is applied [21], see Figure 3. This results in a net magnetization vector Mz parallel to B_0. However, to be able to measure magnetization, this equilibrium state must be disturbed, which is achieved by radiofrequency (RF) pulses. After this RF signal, two phenomena happen: (1) some protons absorb energy and go from the parallel state to the perpendicular state and (2) Mz flips 90° from the z-axis to the transverse plane [20].

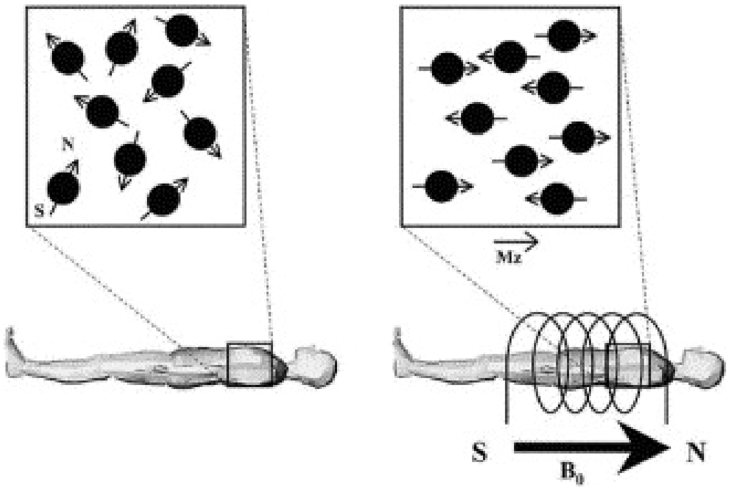


Figure 3: The left image shows that normally, nuclei and their magnetic moments are distributed randomly. The right image shows that when an external magnetic field B_0 is applied, the nuclei align parallel or perpendicular to this external field. This results in a magnetization vector parallel with B_0 [20].

There are two important characteristics of a tissue regarding MRI, namely the T1 and T2. The T1 is the longitudinal relaxation time and tells how long it takes for the Mz to recover to 63% of its value before. The T2 time is the transverse relaxation time and is the amount of time after Mxy is at 37% of its value [22]. Aqueous tissues have a high T1 and appear dark on T1-weighted MRI images, while aqueous tissues also have a high T2 but appear bright on T2-weighted MRI images [23].

3.2.1 Breast MRI

Out of all imaging modalities, MRI scans show the highest contrast between tissues in the breast [24]. That's why MRI is often used to evaluate the breast for conditions such as breast cancer [25, 26], but its application to get information about milk production is still limited. MRI is named by multiple review articles as the most reliable imaging method to calculate the volume of the breast [27, 28].

3.2.2 Dixon method

Fat and glandular tissues are often not both important in the same image; to distinguish fat and fluids in the breast, fat-only and water-only images can be made using the Dixon method. These images improve the visibility of the structures of the breast [29]. The Dixon method gives four different scans, namely in-phase, opposed-phase, water-only, and fat-only. The in-phase images are created with using an echo time when the water and fat protons are in phase. The opposed-phase images are then performed using an echo time when the water and fat protons are out of phase [30]. The water- and fat-only images are then formed by adding and subtracting the in-phase and opposed-phase images, respectively. This can be seen in Equation 1. Figure 4 shows the four outcomes of the Dixon method.

$$\text{In-phase} = \text{Water} + \text{Fat} \tag{1a}$$

$$\text{Opposed-phase} = \text{Water} - \text{Fat} \tag{1b}$$

$$\text{Fat-only} = (\text{In-phase} - \text{Opposed-phase})/2 \tag{1c}$$

$$\text{Water-only} = (\text{In-phase} + \text{Opposed-phase})/2 \tag{1d}$$

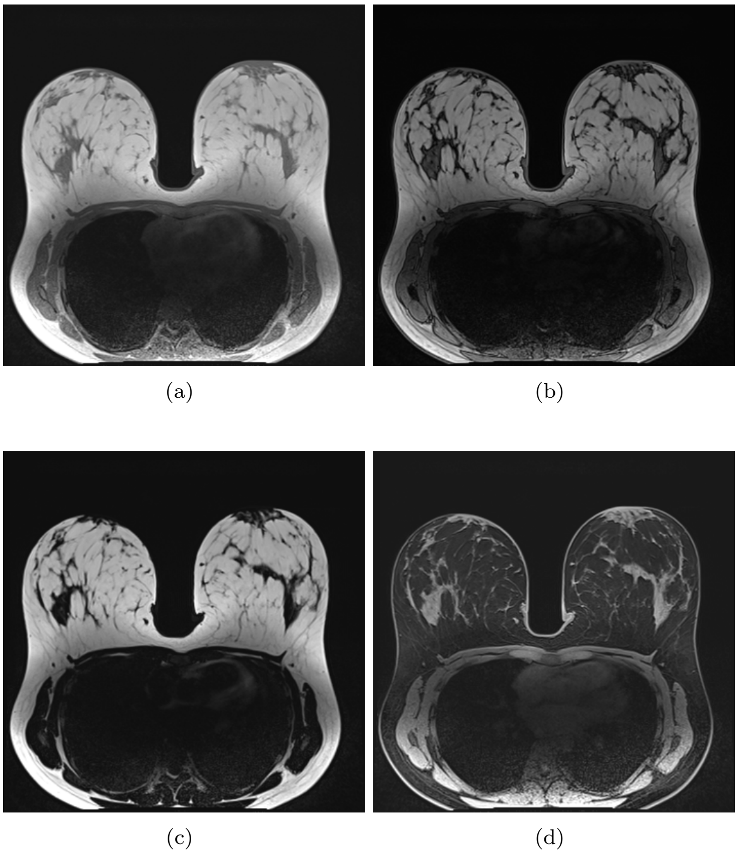


Figure 4: This figure shows the four outcomes of the Dixon method on T1 weighted images. (a) shows the in-phase image, (b) the opposed-phase, (c) the fat-only, and (d) the water-only.

3.2.3 Contrast agent

While making a breast MRI, a contrast agent is often used. A contrast agent is used to shorten the T1 time and therefore have a high signal on T1-weighted images [31]. This is done because most breast MRI scans are done to check for breast cancer and blood vessels can indicate breast cancer [11]. During pregnancy, a contrast agent is not used, since this can cross the placenta. It is safe to use a contrast agent during lactation, but since the background parenchymal enhancement is increased, the sensitivity is limited [11].

3.2.4 Maximum intensity projection

A way commonly used to show vascular structures on MRI scans is a maximum intensity projection (MIP) [32]. An MIP projects three-dimensional data on a two-dimensional plane [33]. This is done by determining the pixel with the highest value in the desired direction that gets projected on the two-dimensional plane [32]. Figure 5 shows that two objects get projected on a plane, where the object with the highest data volume gets projected over objects with a lower data volume. It is not visible from the viewpoint that the two objects have an area where they overlap.

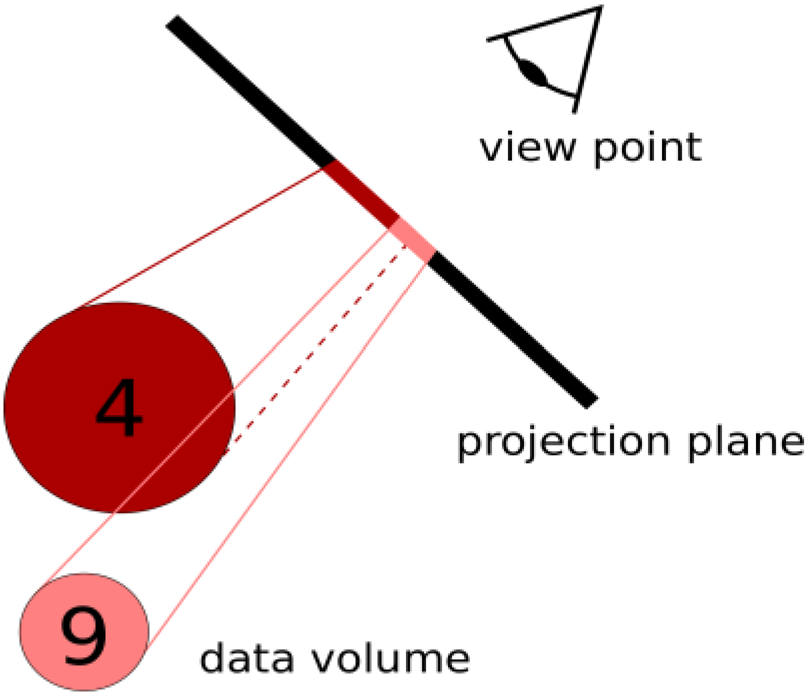


Figure 5: Schematic overview of MIP rendition [34]. This shows that the object with the highest value gets projected on the projection plane, over an object with a lower value. From the viewpoint, it is not visible that the object with a lower value and the object with a higher value have overlapping projection areas.

3.3 Problem Definition

Overall, this research aims to gain knowledge about blood supply and lactation in the breast by looking at the segmentation of blood vessels on MRI scans. This is done by calculating the volume of the blood vessels in the breast and the total volume of the breast. This research doesn't use a contrast agent so the procedure is non-invasive. This, however, increases the difficulty of finding blood vessels in the breast.

Overall, this research aims to develop a method to calculate the breast volume of lactating and non-lactating breasts. This volume can eventually be compared to, for example, blood vessel volume in the breast to gain insight into lactation.
This all leads to the following research question with its secondary questions.

3.4 Research Question

How can the the volume of the (lactating) breast be calculated from non-contrast 1.5T T1-weighted MRI images, after segmenting the breast?

3.5 Secondary Questions

- How can the breast be distinguished from the rest of the body on MRI scans?
- What method can be used for automating the segmentation of the whole breast from the rest of the body on MRI scans?
- How can the total breast volume be determined from MRI scans, after the segmentation?

4 Method

4.1 Data Acquisition

This thesis made use of MRI scans from different women, lactating and non-lactating. The participants and the investigator signed an informed consent form and the study was approved by the Medical Research Ethics Committee (METC) Oost-Nederland, registered under number NL84865.091.23. The study thus far consisted of 4 scans of non-lactating breasts and 1 scan of lactating breasts, that were made between November 2023 and February 2024. The study was advertised via flyers placed at locations where often a lot of breastfeeding mothers are, such as lactation rooms, or were electronically distributed, through social media for example.

4.2 Image Acquisition

All scans were made with a 1.5T MR scanner (Magnetom Aera, Siemens Healthcare, Erlangen, Germany) with a dedicated breast coil (Siemens Breast 18 Coil, Siemens Healthcare, Erlangen, Germany), which can be seen in Figure 6. The participant was lying on her anterior side with her breasts in the coil, without a bra or any clothing that could compress the breasts and her arms along her head. Multiple sequences were used, namely: T2-dixon-Turbo spin echo (TSE), T1-vibe-dixon, and T2-TSE, but this thesis only made use of the T1-vibe-dixon (in-phase) to calculate the volume of the breast and T2-dixon-TSE (water only) to create MIPs. These were chosen because on the T1-vibe-dixon (in-phase) images, all tissues have an intensity and the T2-dixon-TSE (water only) images show the blood vessels in the breast the clearest when creating MIPs. Table 1 shows each sequence's characteristics.

Table 1: MRI sequence characteristics

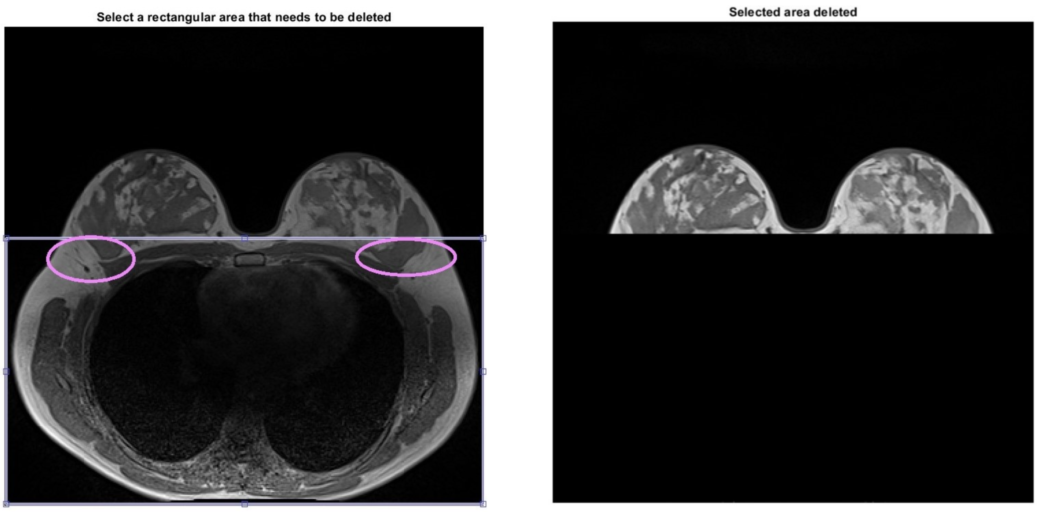
Characteristic	T1_DIXON_IN	T2_TSE_DIXON_W
Echo time (ms)	4.77	81
Repetition time (ms)	6.76	4750
Resolution (mm)	1.0227x1.0227	0.9375x0.9375
Slice thickness (mm)	1	2
Matrix size	352x352	384x384
Acquisition time (min:sec)	4:40	2:48

Figure 6: The Siemens Breast 18 Coil [35]

4.3 Defining the breast borders on MRI

The first thing that needed to be done to be able to calculate the volume of the breast was defining the breast on the MRI scans. Those parts of the MRI scan that corresponded to the breast had to be isolated to perform an adequate volume estimation of the breast. This involved excluding the body's muscles and the excessive fat around the body from the scans. To achieve this, the first attempt was with a rectangle. This rectangle would be placed as seen in Figure 7a. Everything in this rectangle would then be deleted, as visible in Figure 7b. However, parts of the breast that still provided information and were important for the total volume also got deleted, as the ellipses in Figure 7a indicate.

A more effective way was to follow the contour of the Pectoralis Major and the thoracic cavity. Only following this contour was, however, not enough, since there is still extra-mammary fat that got counted as part of the breast. Another spot was needed to cut off this fat so that only the adipose tissue of the breast was taken into account. Since the breast made a small curve with the body, this was a reproducible place for that spot. This spot is seen in Figure 9 as points 6 and 7. This method was suitable for segmenting the whole breast from the body, with as little extra-mammary tissue as possible. Therefore it was chosen to apply this method in the segmentation process described in this thesis.



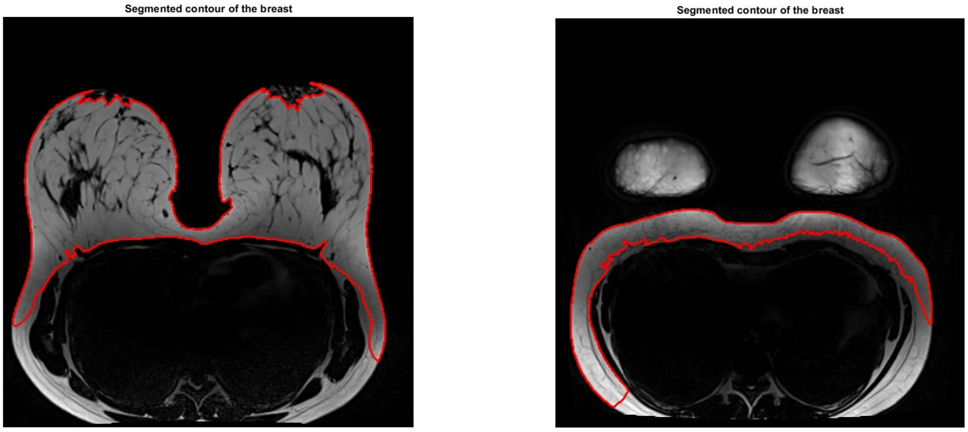
(a) (b)

Figure 7: This figure shows using a rectangle to isolate the breasts from the rest of the body. (a) shows an example of how the rectangle can be drawn. The ellipses show parts of the breasts that provide information about the breasts but are deleted now. After drawing this rectangle, the deleted version is seen in (b).

4.4 Trials for Volume Estimation of the Breast

Multiple methods were tested to define which one would be suitable to use in this thesis to calculate the volume of the breast. The first method was using the Medical Imaging Interaction Toolkit (MITK). The segmentation part of this toolkit was applied, but the interpolation between slices didn't work as expected. Since this was a new method, properly understanding the toolkit would have taken a long time, and therefore, it was decided to not use this method for calculating the breast volume.

After trying the MITK, MATLAB(R2024a) was selected as the programming language for further processing and development. The first method to segment the breast was the active contour method, also known as snakes, a MATLAB commando (`activecontour`). This commando starts with a region that grows with each iteration until it finds the boundaries of an object; in this case, the outline of the breast. This can be seen in Figure 8a. Unfortunately, this segmentation method also segmented around darker areas inside the breast, where milk ducts and blood vessels were, instead of only the outer contour. The script was changed to only segment the largest area. This, however, did not work on image slices at the very top or bottom of the breast where the breast was not connected to the rest of the body on the MR image, as seen in Figure 8b. This method was performed on the full MRI scans, so it was still needed to isolate the region of interest; namely the breast. That's why it was decided to not use this method anymore.



(a) (b)

Figure 8: Segmentation of breasts on two different slices. (a) shows the segmented breast, excluding the areola. (b) shows the biggest segmented area, which excludes the two parts of the breast.

4.5 Segmentation of the breast

In this thesis, a method was developed to isolate the breast in MRI scans. This method was written in the programming language MATLAB to create a spline to follow the contour of the pectoralis major and thoracic cavity. Two extra lines were added to cut off the extra-mammary fat. The flowchart below shows an overview of each subsequent step of the method. All figures in this flowchart are shown and explained further in this thesis.

Multiple people have tested this script; the used protocol can be found in Appendix C.

Overview of all steps of the method

Legend

- Before running the script
- User action
- Script output
- Extra information
- End result
- Extra information about the script
- Order of script
- Example

Select start- and end-slice

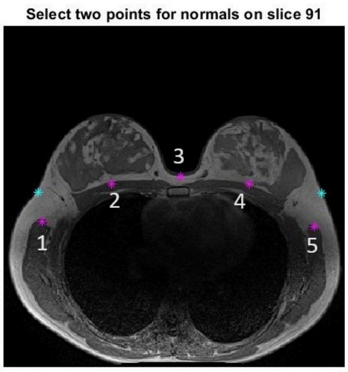
Run script

Fill in start- and end-slice number

A figure opens with an MR slice where points need to be selected on

Select 5 points to define the border of the breast

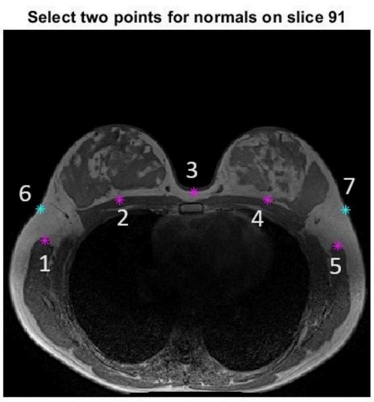
1. On the upper part of the latissimus dorsi
2. On the pectoralis major
3. In the middle between the two breasts
4. On the pectoralis major
5. On the upper part of the latissimus dorsi



Repeat this for start-, middle and end-slice

Select 2 more points to define the outline of the breast

6. On the left sidehere the breast makes a curve with the rest of the body
7. Repeat 6 on the right side



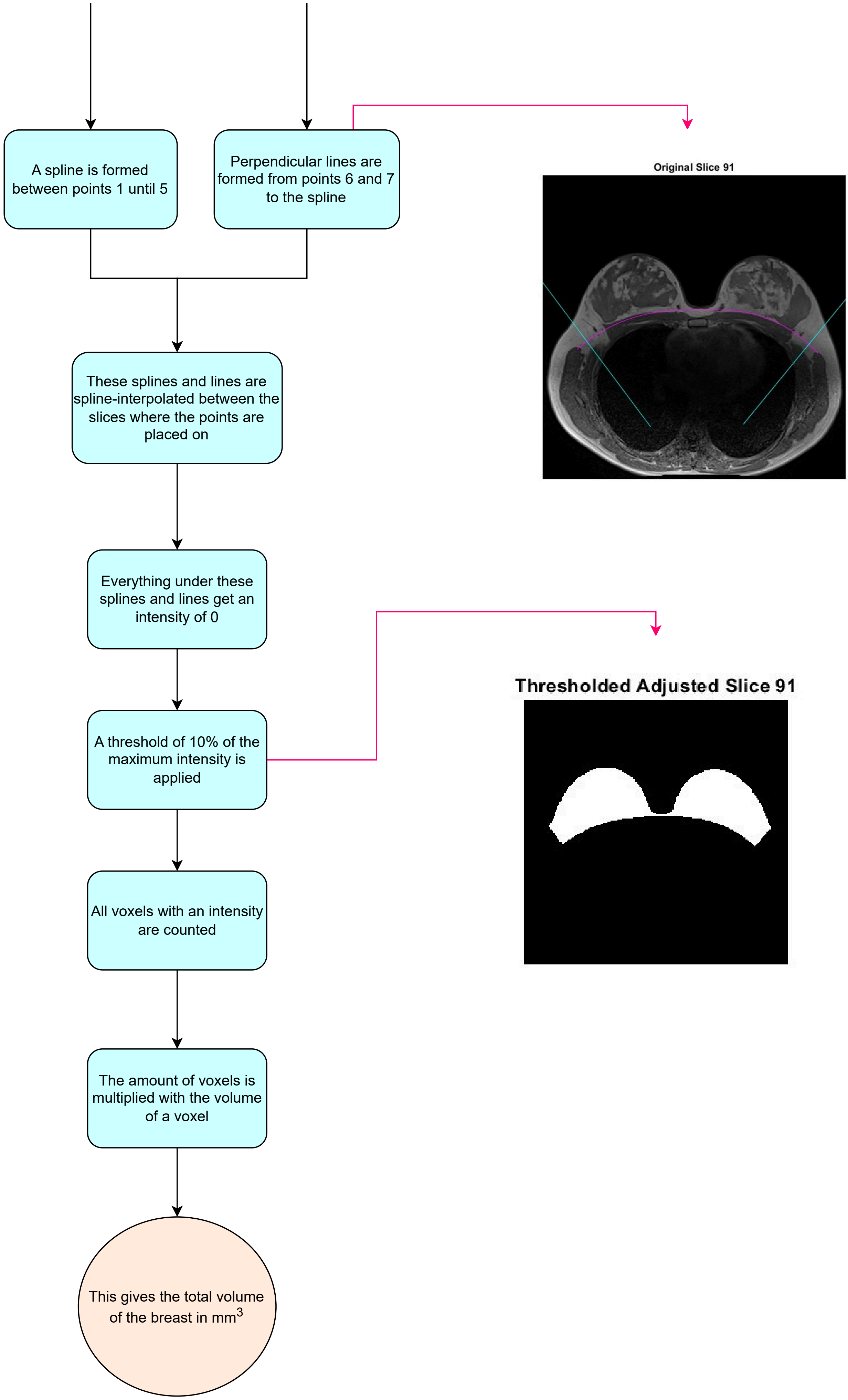

A spline is formed between points 1 until 5
Perpendicular lines are formed from points 6 and 7 to the spline
Original Slice 91
These splines and lines are spline-interpolated between the slices where the points are placed on
Everything under these splines and lines get an intensity of 0
A threshold of 10% of the maximum intensity is applied
Thresholded Adjusted Slice 91
All voxels with an intensity are counted
The amount of voxels is multiplied with the volume of a voxel
This gives the total volume of the breast in mm^3

Figure 9 shows the selected points described in the flow chart. Points 1 until 5, the magenta stars, are for the splines, and points 6 and 7, the cyan stars, are for the perpendicular lines on the splines. Figure 10 shows the created splines and lines after the points are selected. Figure 11 shows then that everything under the lines and splines gets an intensity of zero. There is, however, still a part of the body visible on the last slice, indicated with an arrow, that is supposed to have an intensity of zero. After this, a binary image is created, and everything that has an intensity above a threshold of 10% will get a value of 1 in this binary image and everything below this threshold gets a value of 0; this is visible in Figure 12. These voxels then get counted and multiplied by the voxel volume of the used MRI sequence to get the volume of the breast.

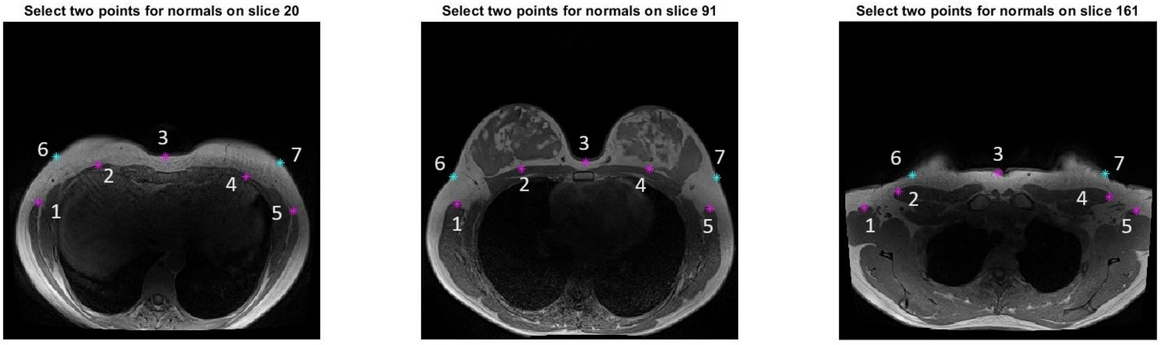


Figure 9: This figure shows the 7 selected points on the start-, middle- and end-slice. Points 1 until 5 are for creating the splines that get interpolated. Points 1 and 5 are placed on the highest part of the latissimus dorsi muscle, points 2 and 4 are placed on the pectoralis major muscle in such a way that this muscle is below the spline, and point 3 is placed in the middle between the two breasts. Points 6 and 7 are for the perpendicular lines on the splines. The points are placed where the breast makes an edge with the rest of the body on the outer left and right side, respectively.

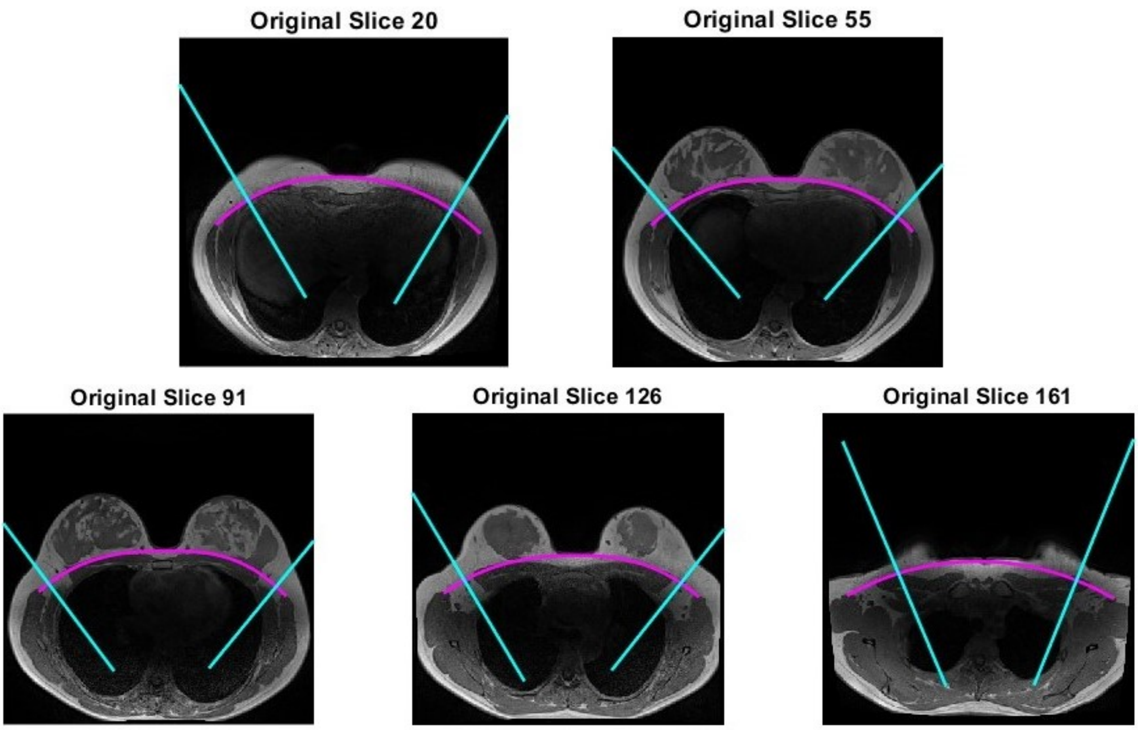


Figure 10: This figure shows 5 slices, namely the start-, middle, and end-slice, and two slices in between slices to show the interpolation of the splines and lines between the start-, middle, and end-slice. The splines and lines that are created with the points placed as seen in Figure 9 are shown.

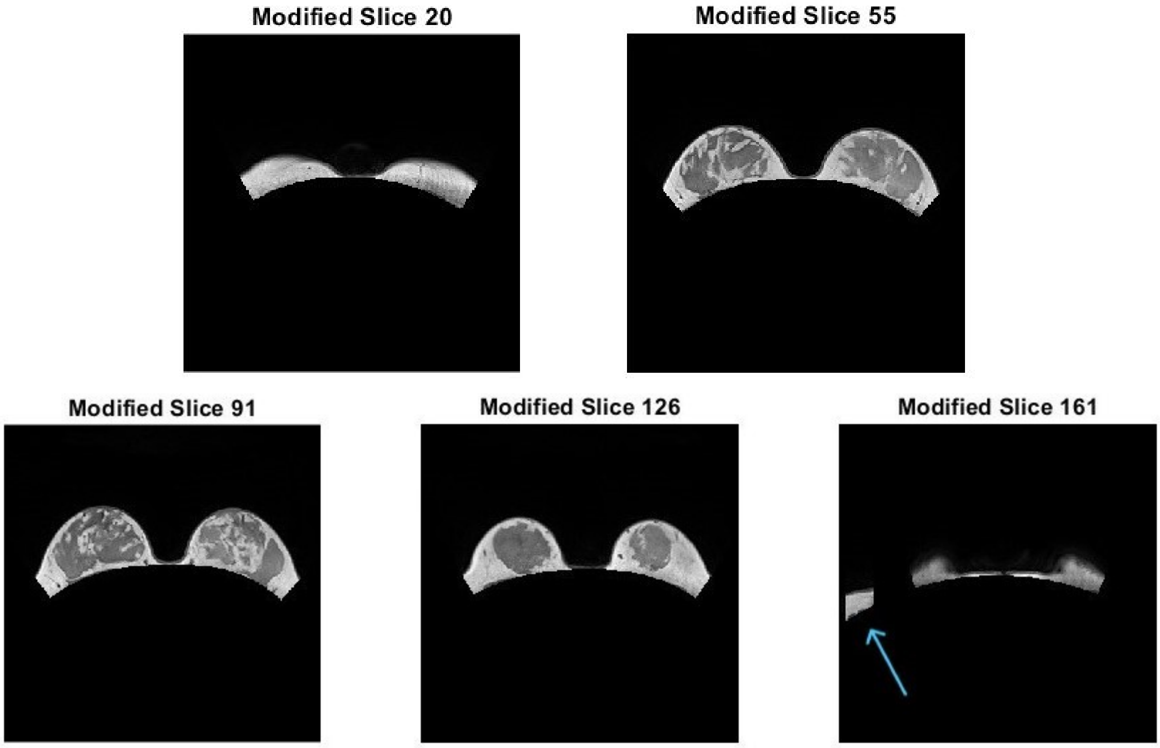


Figure 11: This figure shows 5 slices, namely the start-, middle, and end-slice, and two slices in between these slices when everything under the lines and splines, as seen in Figure 10, gets an intensity of 0. The blue arrow on the last slice shows a part of the body that should have an intensity of 0 but is still visible.

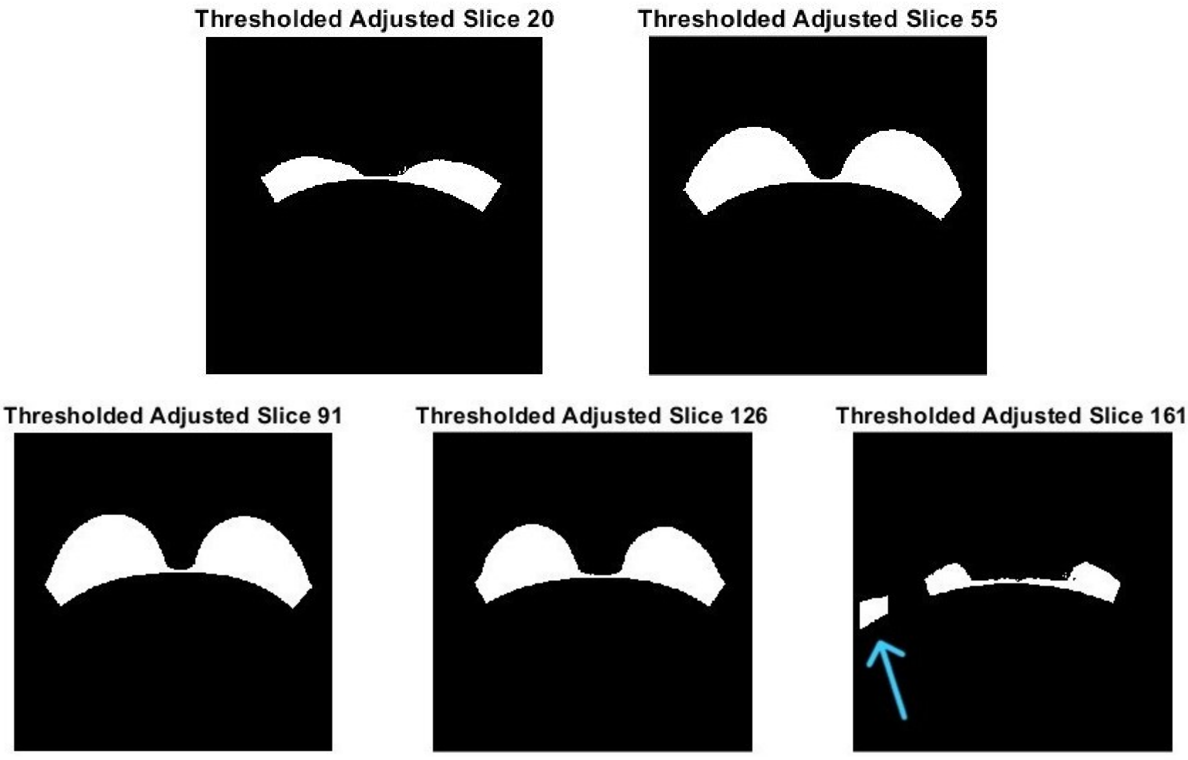


Figure 12: In this figure, binary images are shown. In white all voxels with an intensity above a threshold of 10% of the maximum intensity of each slice are visible. The arrow on the last slice points to a part of the body that should be black but it's still visible.

4.6 Parallel study

Lonneke Heerkes (Bachelor thesis, 2024) has created a method to calculate the volume of fat and non-fat tissue in the breast, based on the same datasets as in this thesis. In that thesis, an ellipse was drawn over the pectoralis major, thoracic cavity, and extra-mammary tissue so these parts of the images does not get taken into account when calculating the volume. Two extra points were selected to create perpendicular lines to the ellipse; the same as in this thesis. This needed to be done on five different slices and the ellipses and lines were then interpolated between these slices. Thresholds were then used to distinguish the fat and non-fat tissues and their volumes were calculated. These two volumes could then be added together to calculate the entire volume of the breast.

4.7 Blood vessel segmentation

For gaining insight into the amount and volume of blood vessels in the breast, MIPs were made of different datasets. The diameter of a blood vessel in the left breast near the edge of the breast was measured in Weasis for three non-lactating breasts. This blood vessel was not visible on the scans of the lactating breast, so the diameter of a blood vessel that resembled the other blood vessel in the right breast was measured. The slice thickness to create the MIPs was chosen in such a way that the blood vessel could clearly be distinguished from the rest of the breast and was the biggest it could be.

5 Results

The script was tested in multiple ways and this gave different volumes of the breast. In this section, the inter- and intra-person variability is shown where the values are normalized. In Table 4 in Appendix B the absolute values are shown.

5.1 Inter-person variability

Figure 13 shows the results of 1 user testing the script thrice and the difference between these measurements. The values are normalized, where the mean value of the three calculated volumes is set to 1. The biggest difference between a data point and the mean value is 0.0375 and the smallest is 0.0012.

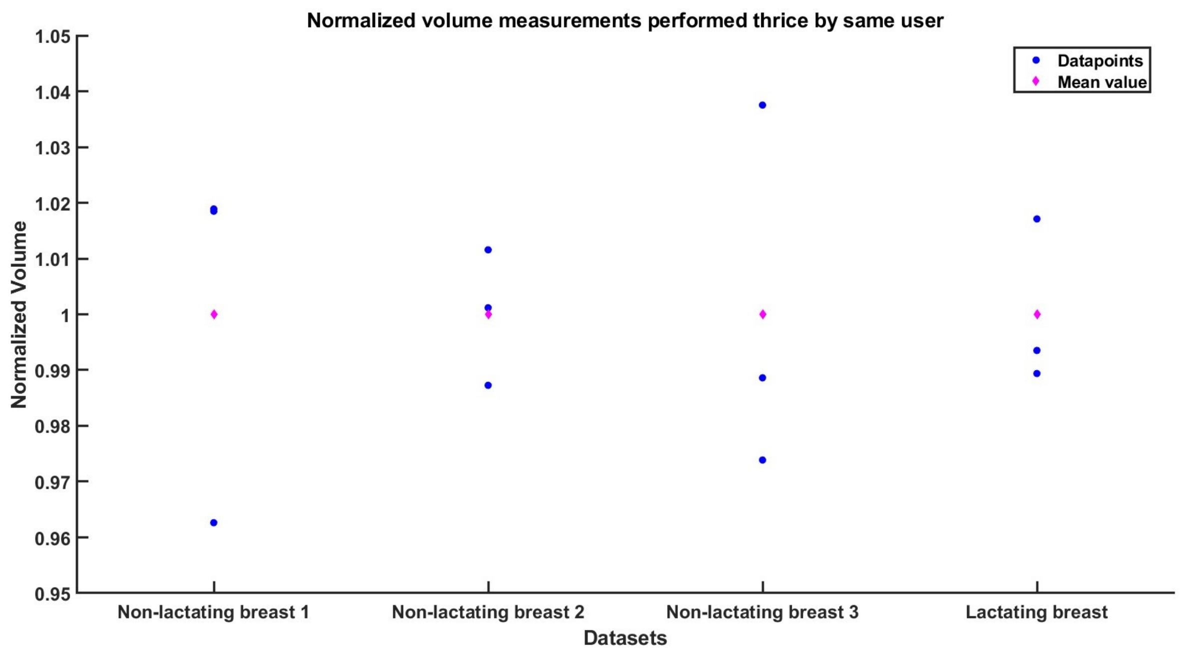


Figure 13: This figure shows the normalized values of calculated volumes when the same user performs the script thrice. The mean value is set to 1 and the calculated volumes are normalized to this mean value.

5.2 Intra-person variability

Figure 14 shows the results of 3 users testing the script once, based on the protocol found in Appendix C. The volumes calculated by each user are represented with different colors and the mean value is set to one. The other volumes are normalized to the mean value. The biggest difference between a data point and the mean value is 0.0879 and the smallest difference is 0.0158.

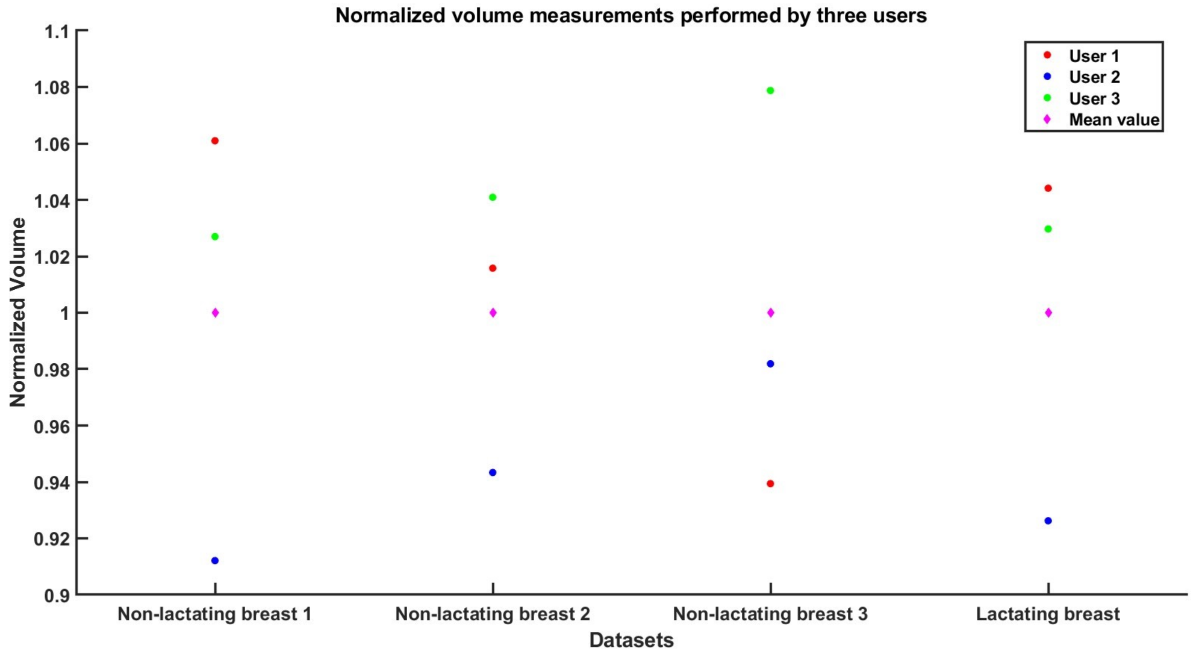


Figure 14: This figure shows the normalized values of calculated volumes when tested by three different users. The mean value is set to 1 and the calculated volumes are normalized to this mean value.

5.3 Parallel study

Table 2: This table shows the different volumes calculated in this study and in the parallel study. Volume A is the volume calculated in this study, and volume B is the volume calculated in the parallel study. The percent difference between these two is also shown.

	Non-lactating breast 1	Non-lactating breast 2	Non-lactating breast 3	Lactating breast 1
Volume A (ml)	739.4	3956.4	793.4	1742.9
Volume B (ml)	665.6	3950.0	718.0	1513.0
Percent difference (%)	10.5	0.2	10.0	14.1

5.4 Blood Vessels

Figures **??** and **??** show two MIPs of two datasets. In both Figures, (a) shows the full image of the breast and (b) shows the breast with a zoomed-in part of the area around the blood vessel. The diameter of a blood vessel is measured for these two

Figure 15 shows MIPs of the four used datasets in this thesis. The diameters of the measured blood vessel differ between 2.3 mm and 4.2 mm.

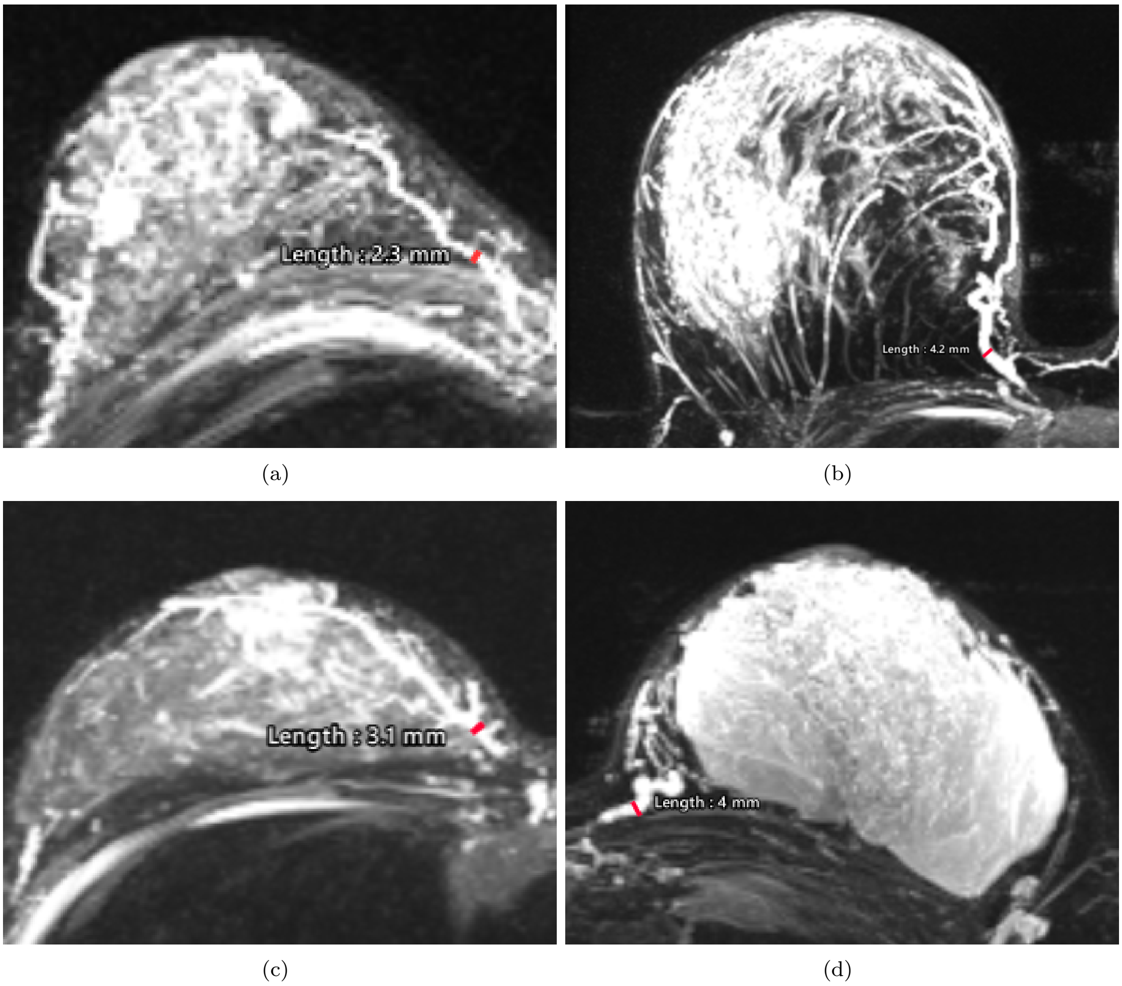


Figure 15: This figure shows MIPs of all datasets. (a) shows the breast with a diameter of 2.3 mm of a blood vessel. This MIP has a slice thickness of 78 mm. (b) shows the left breast of non-lactating breast 2. The diameter of the blood vessel is 4.2 mm. The MIP has a slice thickness of 58 mm. (c) shows the left breast of non-lactating breast 3 with a measured diameter of 3.1 mm of the blood vessel. The MIP has a slice thickness of 50 mm. (d) shows a lactating breast with a measured diameter of 4.0 mm of the blood vessel in the right breast. This MIP has a slice thickness of 50 mm.

6 Discussion

The main goal of this thesis was to determine the volume of the blood vessels in the breast, so this could be compared to the total volume of the breast. In this thesis, the first step for this comparison has been achieved; a method to define the breast volume has been created.

6.1 Inter-person variability

It was chosen to show the normalized values of the calculated volumes instead of the absolute values, to show the reproducibility of the script. Comparing the absolute values of the volumes does not give information about the script, since all breast volumes are different. The start- and end-slices were selected each time and despite the same user selecting these slices, these still differed in each measurement. The start-slice was in the 20s of the slices, except for the third measurement of non-lactating breast 3, and the end-slice in the late 150s, except for the second measurement of non-lactating breast 3. The biggest difference in start-slice numbers was 9 slices and in end-slice numbers 11 slices. The actual slice numbers are shown in Table 5 in Appendix B.

Differences in the calculated volumes show that the same volume won't be calculated every time. This also means that the user can redo the script if they do not agree with the created splines and lines. This can be done until the user is satisfied and can use the saved points after that, when necessary.

6.2 Intra-person variability

The results of three users testing the script are further apart than the results of one user testing the script three times. When comparing the slice numbers of the same user, these numbers were all close to each other. This was however different when multiple users tested the script, mainly for the start-slice numbers. The biggest difference in the start-slice number is 35 slices and in the end-slice number is 14 slices. The differences between the selected slices of the different users are bigger for the start slices than for the end slices. Appendix ... shows the actual numbers of these slices. User 3 always started around slice 15, while user 2 started around slices 30-35. This can explain why user 2's calculated volume was always lower than user 3's calculated volume. User 1's start slices changed from 25 to 50; the measurement with 50 as the start slice is the only time user 1 had the lowest calculated volume. When comparing inter- and intra-person variability, it makes sense that the inter-person variability is less than the intra-person variability. This is because one person will look for the same characteristics to select slices and the same points to select.
While testing the script, the users gave feedback on the protocol to make it more clear. A revised protocol was made after obtaining all results and is seen in Appendix D. This revised protocol is clearer and might give a smaller intra-person variability.

6.3 Parallel study

When comparing the volumes in Table 2, it's seen that the volumes from the parallel study are all lower than the volumes from this study. This difference can come from the way the breast is defined in the two studies and the way the volume is calculated. In this study, the volume is calculated by counting all voxels with an intensity above a threshold of 10%. In the parallel study, the volume is calculated by adding the volumes of the calculated volumes of the fat and non-fat tissue in the breast. Some voxels, however, were part of the fat and non-fat volumes, while other voxels were part of none. Calculating how many voxels were part of none, was not possible, since these voxels did not get a label. That's why it is not possible to conclude something about the impact of double-labeling and not-labeling of the voxels on the total volume of the breast.

6.4 Blood vessels

The measured diameters of the blood vessel differ between the datasets, but the order from less to more volume is the same as smaller diameter to bigger diameter and the difference in diameters is about 1.8 times, but the difference in volume is about 5 times. The lactating breast did not have a visible blood vessel in the left breast, so the diameter was measured in the right breast. The other datasets, however, had a less clear blood vessel in their right breast.

6.5 Comparison to other research

Breast volumes are not the same for every woman. That makes it difficult to compare the calculated volumes in this thesis with volumes calculated in other studies. That's why the volumes are compared to ranges calculated in other studies. However, this does not mean that if a volume does not fall in the range calculated in a study, the calculation is incorrect.
This study was not the first to calculate the volume of the breast with MRI scans. Another study was performed to calculate the breast volume of 400 women, where the segmentation was done manually by a single radiologist [18]. The anatomical boundaries they applied were mentioned in the article, but there was only one user who performed the segmentation. That study split the volume into the left and right breast, where the smallest breasts had a volume of 55 and 66 mL and the largest breast had a volume of 4670 and 4777 mL, respectively. The mean average breast volume was 976 mL. Comparing these volumes with the calculated volumes in this study, the calculated values here are in the range of volumes between the smallest and biggest breasts, namely 55-4777 mL.

Another method to calculate the breast volume is to measure water displacement [36]. This research [36] used this method and had an average volume of 642 and 643 mL for the left and right breast, respectively and the maximum volume they found was 1900 mL for one breast. This is lower than the research mentioned before. This is, first of all, dependent on the women who join the research and the way of calculating the volume is much different. With water displacement, only the outside part of the breast is taken into account, but when making use of MRI scans, there is also extra-mammary tissue that is part of the volume.

6.6 Limitations

In Figures 11 and 12 on the last slice a part of the body that should have an intensity of 0, is still visible, indicated with an arrow. It can be seen that the spline gets extrapolated and everything under the extrapolated spline gets an intensity of 0. It looks like the upper end of the line goes to the visible end as seen in Figure 10 and everything that is above the spline but not under the line still has an intensity.

A threshold of 10% was chosen to get rid of background noise, but in some cases, voxels that were part of the breast had a too low intensity for this threshold For some voxels, that are part of the region of interest, the threshold of 10% is too high. This means they are not counted with the total amount of voxels when they should be. This is, however, rarely the case and when it happens, it's about a small amount of voxels, that should not have a big influence on the total volume. Lowering the threshold means that more background noise voxels will also be counted for the volume.

The points are manually selected and even though the protocol stays the same, it can change between users, or between multiple times of the same user, where the points are placed. Saving the data points is partially a solution since the user can then use their previously selected points and get a constant volume.

A total of five datasets was acquired, but calculating the volume of this dataset gave unreliable results. This was because it was very difficult to find the muscle where points one and five needed to be placed. Despite this difficulty, it was tried one time, but because of the threshold, background noise turned white on the binary images and a part of the breast turned black. This means that the calculated volume was not the breast volume and it was, therefore, decided to leave this dataset out of the test datasets.

The reliability of the results cannot be determined, since only four datasets were used, but comparing the results of this thesis with other research, as mentioned above, does show that the results are within the same range as other calculated volumes.
This research does not make use of a contrast agent, what increases the difficulty of finding blood vessels in the breast. Reasons for not using a contrast agent are that it can cross the placenta and despite it being safe during lactation, the sensitivity is limited due to the background parenchymal enhancement is increased [11].

6.7 Outlook

As mentioned before, it was not possible to calculate the volume of the blood vessels in the breast. MIPs are a way to show the blood vessels and give an insight into the amount of blood vessels in the breast. Because MIPs are 2D projections of a 3D image, calculating the volume of blood vessels while making use of MIPs is not the preferred method. MIPs can, however, indicate the volume of the blood vessels in the breast.

Right now, the total breast volume of two breasts is calculated. However, calculating the volume of the left and right breasts separately from each other gives more information about the breasts and their relation to lactation. This is useful because not all moms breastfeed with both breasts [37] and women rarely have two breasts that are the same size [13]. In the method, there is already one point between the two breasts. This point can be used to divide the image into the left and right sides, so the volume can be calculated of both breasts together and apart.

6.8 Relevancy

In this thesis, a method to calculate the volume of lactating and non-lactating breasts has been created. With this information, other volumes in the breast can be compared to the total volume, such as the blood volume. Since there isn't a lot of knowledge yet about the physical influences on lactation, being able to compare volumes of the breast is a small step into closing this knowledge gap.

7 Conclusion

The goal of this thesis was to develop a method to calculate the volume of (non-)lactating breasts using MRI scans so these volumes could eventually be compared to, for example, the volume of the blood vessels in the breast. A method to calculate the volume of the breast is created using MATLAB and is done by the user manually selecting points in such a way that the breast gets isolated from the rest of the body on the MRI scans and the volume of the breast can be calculated. This method is a promising first step in being able to compare other volumes of components of the breast to gain more insight into the physiological aspects of lactation.

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A AI Disclosure

During the preparation of this work, I used Grammarly and ChatGPT to improve the writing style of this report and ChatGPT to help with the MATLAB code. After using this tool/service, I thoroughly reviewed and edited the content as needed, taking full responsibility for the final outcome.

B Data

Table 3: The calculated volumes and their average of the same user, performing the script thrice.

	Non-lactating breast 1	Non-lactating breast 2	Non-lactating breast 3	Lactating breast 3
Volume 1 (ml)	711.8	4,002.1	823.1	1,724.3
Volume 2 (ml)	753.4	3,961.0	784.3	1,772.7
Volume 3 (ml)	753.1	3,906.1	772.7	1,731.6
Average (ml)	739.4	3,956.4	793.4	1,742.9

Table 4: The calculated volumes and their average of users 1, 2, and 3 as volumes 1, 2, and 3, respectively.

	Non-lactating breast 1	Non-lactating breast 2	Non-lactating breast 3	Lactating breast 3
Volume 1 (ml)	802.7	4,136.1	729.4	1,785.8
Volume 2 (ml)	690.1	3,841.3	762.4	1,584.2
Volume 3 (ml)	777.0	4,239.5	837.6	1,761.1
Average (ml)	756.6	4,071.9	776.5	1,710.4

Table 5: The start and end slice number of the same user performing the script three times. n-l stands for non-lactating breast, and l for lactating breast.

Test	Start n-l 1	End n-l 1	Start n-l 2	End n-l 2	Start n-l 3	End n-l 3	Start l 1	End l 1
1	24	154	25	157	24	159	21	157
2	23	157	26	159	25	147	20	158
3	26	156	27	159	33	158	21	158

Table 6: The start and end slice number of users 1, 2, and 3. n-l stands for non-lactating breast, l for lactating breast.

User	Start n-l 1	End n-l 1	Start n-l 2	End n-l 2	Start n-l 3	End n-l 3	Start l 1	End l 1
1	31	155	25	159	50	152	35	156
2	35	147	30	159	32	151	35	155
3	17	161	15	161	15	162	13	161

C Protocol

Protocol

Calculating the volume of the breast can be done with the following two scripts:
1. save_datapoints.m
2. use_save_datapoints.m

When using a new dataset, the first script is used. After points are selected and saved, the rest of the time the second script can be used. By doing so, the user doesn't have to choose points each time and the volume is the same each time the script is used.

To give a summary of what the script does: the user selects two slices and between these two the volume of the breast is calculated and then has to select a few points to create a spline and two lines. These are then used to make sure that everything under these, the intensity of the image becomes 0. This way, after an intensity threshold of 10% of the maximum intensity of each slice, every voxel that still has an intensity is counted and multiplied by its volume. This then gives the entire volume of the breast.

There are a few things that need to be manually changed before using the scripts, namely:

```
dicom_folder = 'route_to_DICOM_folder';
```

```
save('data_points_name_of_dataset_t1ort2.mat', …);
```

in save_datapoints.m

and

```
dicom_folder = 'route_to_DICOM_folder';
```

```
load('data_points_name_of_dataset_t1ort2.mat');
```

in use_saved_datapoints.m

The following protocol is for save_datapoints.m, since use_saved_datapoints.m works automatically.

When running the code, the first input is the number of the starting and ending slices of the dataset. These slices are chosen by the user, based on the images of the dataset. While choosing these slices, it's important to select slices that contain breast and the breast has started to get its shape already. The breast should also make a small edge with the body since this is necessary later.

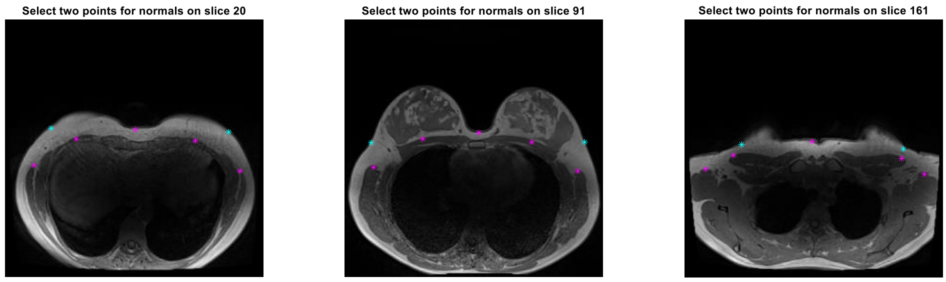
After these slices are chosen, MATLAB will open a figure and show the chosen beginning slice. Here, the user needs to select 5 different points, going from left to right in the image. These points are necessary so that only the breast volume is calculated and parts such as muscles are not part of this calculation. This might help to place the second and fourth point. The points will not show up immediately after clicking, but show up all at once after pressing 'Enter'.

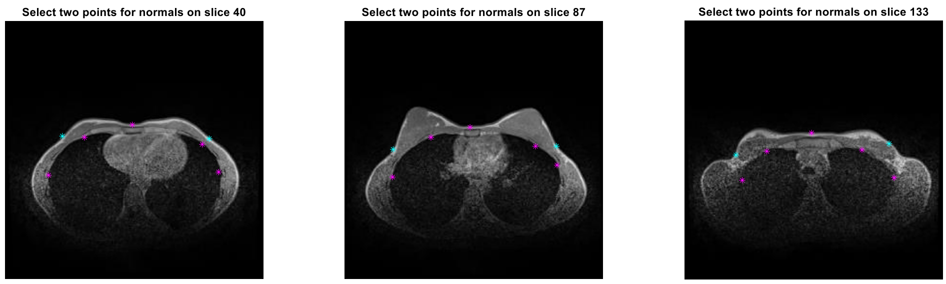
- The first is placed on the left highest part of the Latissimus Dorsi muscle
- The second on the Pectoralis Major
- The third in the middle of the breasts on the edge of the body
- the fourth and fifth ones on the Pectoralis Major and Latissimus Dorsi again, but on the right side of the body this time.

See the figure below for an example of where these points should be (magenta stars). In the case of the last slice, it can be difficult to determine where the points should be placed since the muscle's shape changes. Make sure to click on the lateral (outer) upper part of the muscle, as illustrated. In case the muscles are not clearly visible, click on the most lateral part of the lungs for the first and fifth points; this is shown in the second figure.

After clicking the 5 points, press 'Enter' and the figure will ask to select 2 more points. These points need to be where the breast starts to make an edge with the body. It is not necessary to press 'Enter' after these points. This can also be seen in the figure below (cyan stars). This process needs to be done 3 times for 3 different slices.

The figure below is an example of how the slices should look and where the points should be placed.

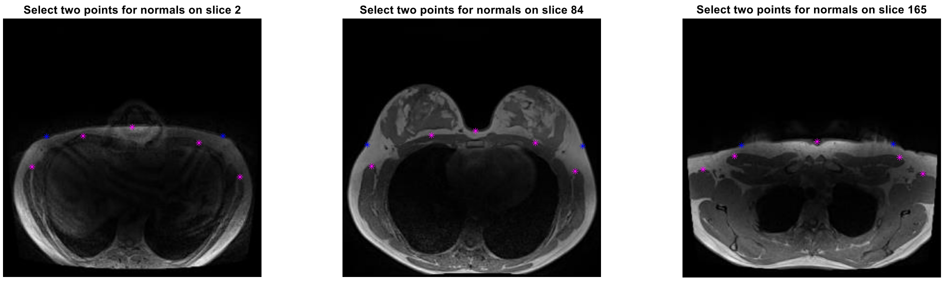




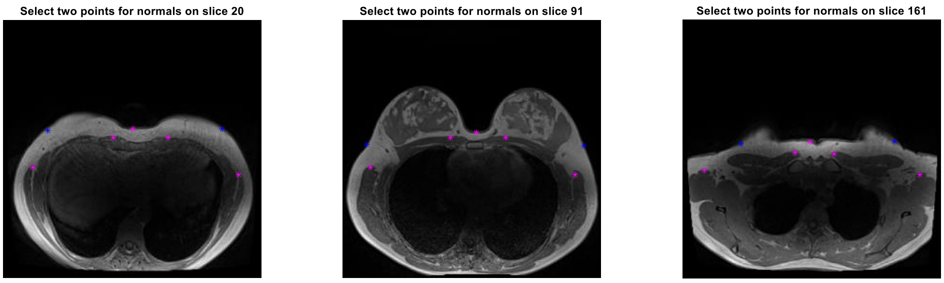
When these are selected, the script will show 5 slices of the dataset with the created splines and lines and will also show a figure of slices that show black and white slices, where white means that that part of the slice is selected. All these voxels are counted and multiplied with the volume of each voxel and the volume of the breast will then be calculated and shown in the command window of MATLAB. When all is done correctly, three figures are displayed, one with the selected points, one with the slices with splines and lines and what of the slices becomes dark and one that shows slices what voxels are counted.

Below a few bad examples are shown to prevent making these mistakes, since these mess up the calculation of the volume.

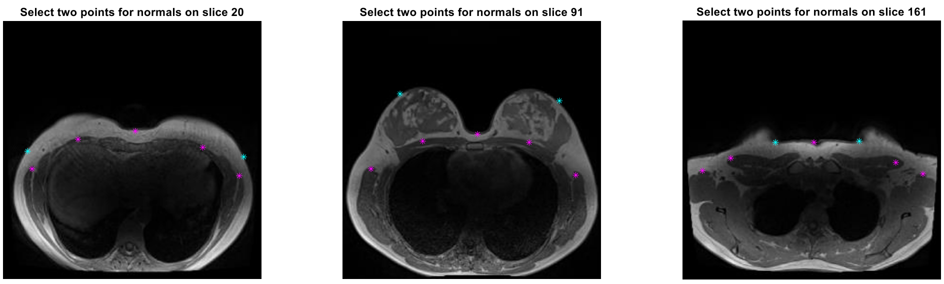
The figure below shows that the slices are chosen wrong, since on the first and last slice, the breasts are not or barely visible.



In the figure below, the points on the Pectoralis Major are too close to the middle point what creates incorrect splines and lines. Especially on the last slice, the placement can be difficult, so make sure to click on the lateral part of the muscle.



When selecting the points where the breast makes an edge with the body, make sure to not click too low, too high or too far to the middle, as seen in the figure below on the left, middle and right slice respectively.



D Improved Protocol

Protocol

General information

Calculating the volume of the breast is performed by the following two scripts in MATLAB:

1. save_datapoints.m
   This script is used to select the points and calculate the breast volume.
2. use_save_datapoints.m
   This script is used after the points are selected and saved and can be repeatedly used with the same volumes.

To give a summary of what the first script does: the user selects two slices and between these two the volume of the breast is calculated and then has to select a few points to create a spline and two lines. These are then used to make sure that everything under these, the intensity of the image becomes 0. This way, after an intensity threshold of 10% of the maximum intensity of each slice, every voxel that still has an intensity is counted and multiplied by its volume. This then gives the entire volume of the breast.

This protocol assumes that the user has access to the MRI scans that are loaded in the script. The script does not show the images.

Practical information

There are a few things that need to be manually changed before using the scripts, namely in save_datapoints.m:

```
Line 6: dicom_folder = 'route_to_DICOM_folder';
```

```
Line 97: save('name_of_dataset.mat', …);
```

and in use_saved_datapoints.m:

```
Line 2: dicom_folder = 'route_to_DICOM_folder';
```

```
Line 35: load('name_of_dataset.mat');
```

The following protocol is for save_datapoints.m.

The script use_saved_datapoints.m works automatically after using save_datapoints.m and changing the lines of code mentioned above.

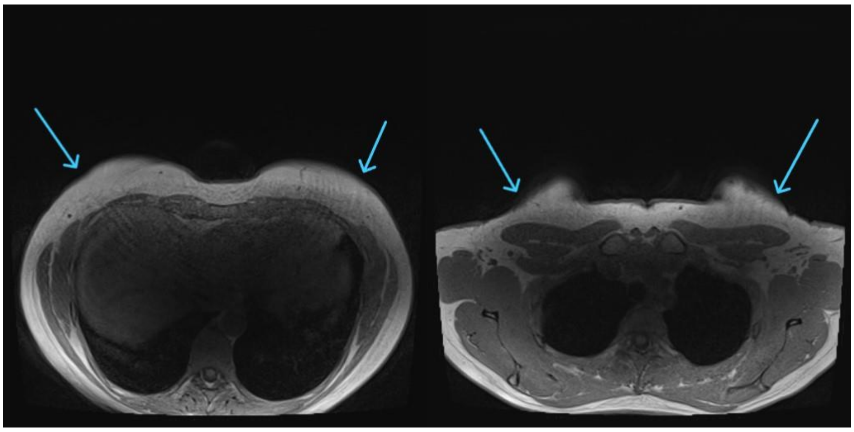
Step-by-step guide

Text shown in italics is done by MATLAB without user input at that step.

The next section shows examples of what can go wrong using the script.

1. Before running the script, two slices need to be selected, namely the start- and end-slice. It is important that the selected slices show the beginning/end of the breast and

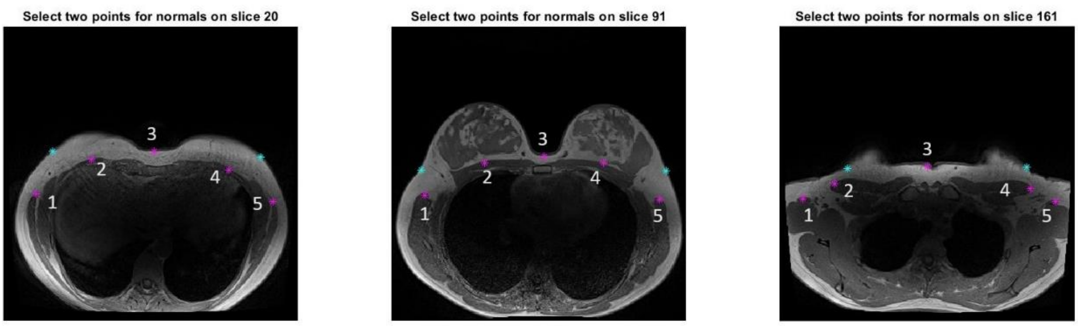
the breast starts to get its shape already. The breast needs to make a curve with the rest of the body, indicated with arrows in the figures below.



start end

2. Put in the start and end slice numbers they have chosen before running the script. Note: the start number has to be lower than the end number!
3. *A figure opens and shows the chosen start slice.*
4. Select 5 different points from left to right (see the figure below for an example):
   I. The first is placed on the left highest part of the Latissimus Dorsi muscle
   II. The second on the Pectoralis Major
   III. The third in the middle of the breasts on the edge of the body
   IV. The fourth one on the Pectoralis Major on the right side of the body
   I. The fifth one on the Latissimus Dorsi again, but on the right side of the body

   Note: in the case of the last slice, it can be difficult to determine where the points should be placed since the muscle's shape changes. Make sure to click on the lateral (outer) upper part of the muscle, as illustrated.

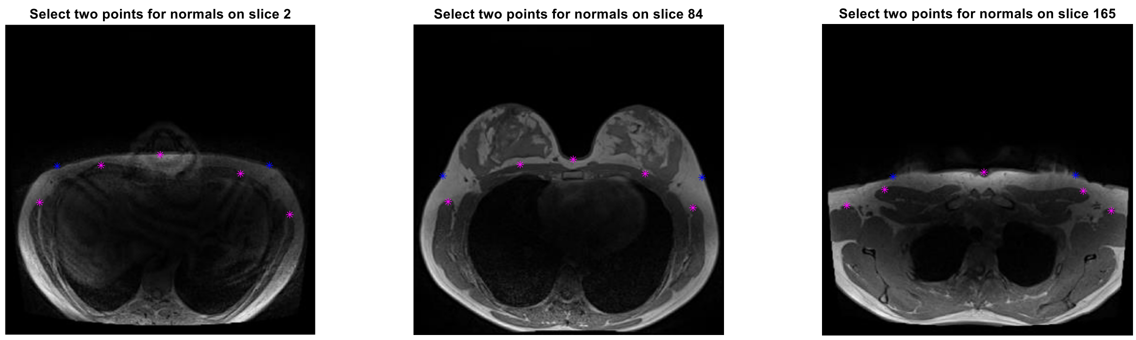


5. Press 'Enter' after selecting the five points.
6. Select 2 more points, on the place where the breast makes an edge with the body. These are points 6 and 7 in the example below.
7. Repeat this process for the two other slices.
8. *After this, two more figures show and MATLAB will give the calculated volume as output.*

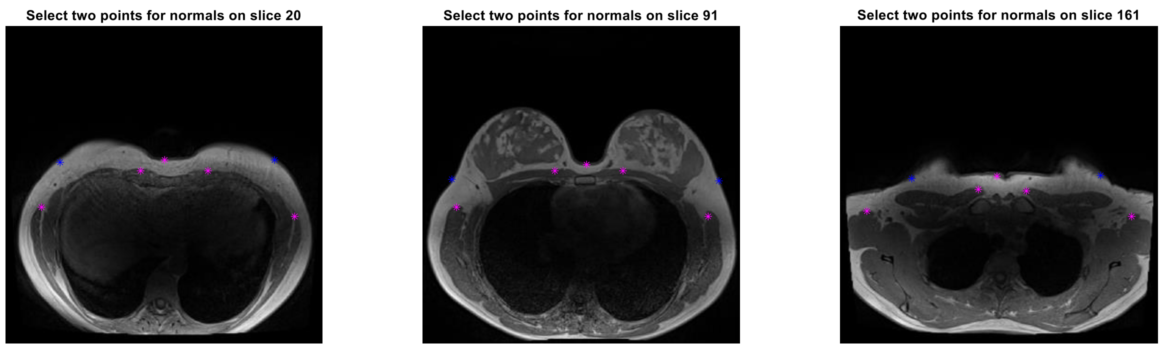
Bad examples

Below a few bad examples are shown to prevent making these mistakes, since these mess up the calculation of the volume.

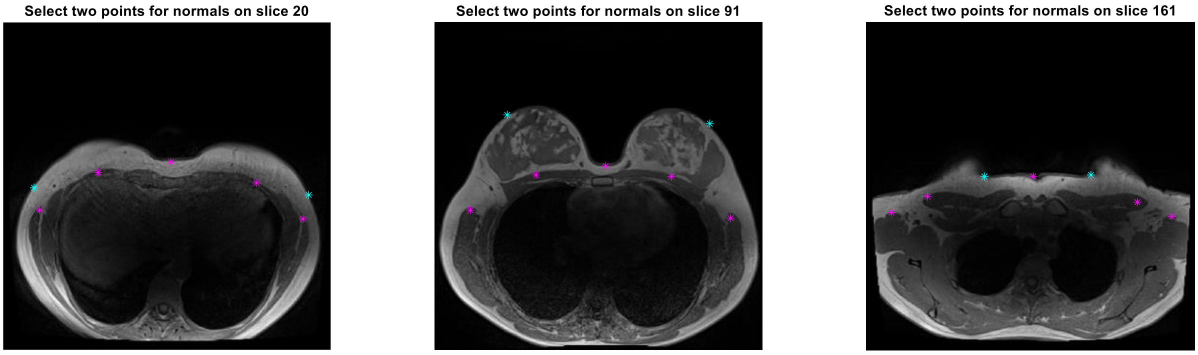
The figure below shows that the slices are chosen wrong, since on the first and last slice, the breasts are not or barely visible.



In the figure below, the points on the Pectoralis Major are too close to the middle point what creates incorrect splines and lines. Especially on the last slice, the placement can be difficult, so make sure to click on the lateral part of the muscle.



When selecting the points where the breast makes an edge with the body, make sure to not click too low, too high or too far to the middle, as seen in the figure below on the left, middle and right slice respectively.


Select two points for normals on slice 20
Select two points for normals on slice 91
Select two points for normals on slice 161