CHARACTERISATION OF AGAROSE GEL AS BREAST MIMICKING MATERIAL

By

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Dissertation Submitted in

Partial Fulfillment of the Requirements for the

Degree of Master of Science (Medical Research)

UNIVERSITI SAINS MALAYSIA

JANUARY 2016

DECLARATION

I hereby declare that I am the sole author of this thesis entitled 'Characterisation of Agarose Gel as Breast Mimicking Material'. I declare that this thesis is being submitted to Universiti Sains Malaysia (USM) for the purpose of the award of Master of Science (Medical Research). This dissertation is the result of my own research under the supervision of Dr. Rafidah Zainon except as cited in the references. The dissertation has been accepted for the study performed and is not concurrently submitted in candidature of any other degree.

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ACKNOWLEDGEMENT

All the praises and grateful to Allah S.W.T, with His guidance and assistance giving me opportunity to complete this research successfully although a lot of obstacles and joyful experience has been gone through. This dissertation was prepared for Advance Medical and Dental Institution to complete the postgraduate program that leads to obtaining the Master Science degree of Medical Research.

Firstly, I would like to dedicate my highest gratitude to Dr. Rafidah Zainon as my supervisor for her valuable support, dedicated and guidance during my entire research duration. She had given her great effort by providing much valuable information, suggestions and guidance in helping me to complete my research. I really appreciate all of her suggestion and ideas when confronted with problems related to this study. Utmost thanks to Advance Medical and Dental Institute (AMDI) for giving me an opportunity to use the laboratory equipment and materials and also using the Magnetic Resonance Imaging (MRI) in Radiology Unit, Clinical Trial Complex (CTC). Thank you to all radiographers and physicists in Radiology Unit and laboratory assistances in Animal Research Center (ARC) for their time and willingness to teach and guide me in using research equipment.

Last but not least, deepest thanks to my family, friends, and others for their cooperation, encouragement, constructive suggestion and full of support for helping me to complete this research successfully. Thank you for those who have directly and indirectly helping me all the times. Thank you very much!

PENCIRIAN GEL AGAROSA SEBAGAI BAHAN MEMIMIK PAYUDARA

ABSTRAK

Payudara MRI telah menjadi elemen yang penting dalam pengimejan payudara. Fantom adalah jisim bahan yang digunakan untuk mengkaji kesan radiasi ke atas manusia. Tujuan kajian ini adalah untuk mereka fantom agarosa sebagai bahan memimik payudara untuk MRI dan menilai kepekatan gel agarosa yang mempunyai masa santaian SPGR T_1 dan T_2 untuk tisu payudara yang normal dan tidak normal. Bahan memimik payudara terdiri daripada campuran agarosa dan gelatin sebagai larutan latar belakang yang memimik tisu payudara. Larutan latar belakang terdiri daripada 30% larutan agarosa dan 70% larutan gelatin. Kepekatan agarosa yang berbeza telah ditetapkan pada 0.5%, 1.0%, 1.5%, 2.0%, 2.5%, 3.0% dan 3.5%. Selain itu, terdapat pelbagai jenis bahan yang digunakan untuk memimik ciri-ciri tisu tidak normal di dalam sampel seperti tanah kristal poliakrilamida (PCS) untuk memimik sista, kulit telur untuk memimik kalsifikasi dan kulit telur hancur (CrE) untuk memimik mikrokalsifikasi. Pemilihan parameter MRI adalah berdasarkan protokol rutin klinikal pengimejan MRI payudara yang menggunakan SPGR T_1 dan T_2 untuk 1.5T. Pada masa santaian SPGR T_1, kumpulan 2.0% kepekatan agarosa memberikan nilai yang paling rendah berbanding dengan kumpulan yang lain. Masa santaian SPGR T_1 untuk sampel kawalan, PCS, CrE dan kulit telur masing-masing adalah 48.18 ms, 43.41 ms, 47.15 ms dan 44.38 ms. Pada masa santaian T_2, kumpulan 3.0% kepekatan agarosa memberikan nilai T_2 yang paling rendah berbanding dengan kumpulan yang lain. Masa santaian T_2 untuk sampel kawalan, PCS, CrE dan kulit telur masing-masing adalah 1134.2 ms, 2839.1 ms, 185.5 ms dan 265.2 ms. Walau bagaimanapun, tiada kumpulan sampel yang memberikan

masa santaian yang sama dengan masa santaian T_2 seperti yang dilaporkan dalam kajian sebelum ini. Gelatin merupakan bahan yang tidak sesuai untuk memimik lemak kerana tiada imej lemak yang muncul dalam SPGR T_1WI dan T_2WI. Di samping itu, NaCl boleh bertindak sebagai kekonduksian dan pengubahsuaian kepada kepekatan agarosa. Pemilihan bahan dan saiz yang sesuai perlu dipertimbangkan untuk fabrikasi fantom bagi mendapatkan masa santaian yang sama dengan tisu payudara.

CHARACTERISATION OF AGAROSE GEL AS BREAST MIMICKING MATERIAL

ABSTRACT

Breast MRI has become an essential element in breast imaging. A phantom is a mass of materials that are used to investigate the effects of radiation on human. The aims of this study were to fabricate an agarose phantom as breast mimicking material for MRI and to evaluate agarose gel concentration that has a similar SPGR T_1 and T_2 relaxation times for normal and abnormal breast tissues. The breast mimicking materials consisted of agarose and gelatine mixture as the background material, which mimics the breast tissue. The background solution composed of 30% of agarose solution and 70% of gelatine solution. Different concentrations of agarose were set at 0.5%, 1.0%, 1.5%, 2.0%, 2.5%, 3.0% and 3.5%. Besides, there are different types of materials that were used to mimic abnormal tissue characteristics in the sample such as polyacrylamide crystal soils (PCS) to mimic cysts, eggshells to mimic calcifications and crushed eggshells (CrE) to mimic microcalcifications. Selection of the MRI parameters was based on routine clinical MRI breast imaging protocols that used SPGR T_1 and T_2 for 1.5T. In SPGR T_1 relaxation time, 2.0% of the agarose concentration batch gave the lowest value compared to other agarose concentration batches. The SPGR T_1 relaxation time for control, PCS, CrE and eggshell samples were 48.18 ms, 43.41 ms, 47.15 ms and 44.38 ms, respectively. In T_2 relaxation time, 3.0% of agarose concentration batch gave the lowest T_2 value compared to other batches. The T_2 relaxation time for control, PCS, CrE and eggshell samples were 1134.2 ms, 2839.1 ms, 185.5 ms and 265.2 ms, respectively. However, no sample batches give similar T_2 relaxation time as reported in

previous studies. Gelatine was not a suitable material to mimic fat because no fat images appear in SPGR T_1WI and T_2WI. In addition, NaCl can act as conductivity as well as a modifier to the agarose concentration. Selection of the suitable material and its size also needs to be considered for phantom fabrication to get a similar relaxation time to those of breast tissue.

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LIST OF ABBREVIATIONS

AMDI	Advanced Medical and Dental Institute
ARC	Animal Research Centre
$CaCO_3$	Calcium carbonate
CrE	Crushed egg shells
CTC	Clinical Trial Complex
DCE-MRI	Dynamic Contrast-Enhanced MRI
DICOM	Digital Imaging and Communication in Medicine
ETL	Echo Train Length
FRFSE	Fast Recovery Fast Spin Echo
FSE	Fast Spin Echo
FSE-XL	Fast Spin Echo-Extra Large
IDEAL	Iterative Decomposition of water and fat with Echo Asymmetry and Least-squares estimation
MRI	Magnetic Resonance Imaging
M3D	Merge three-dimensional
NaCl	Sodium chloride
PCS	Polyacrylamide crystal soil
PDWI	Proton density-weighted image
QA	Quality Assurance
QC	Quality Control
RF	Radio frequency
ROI	Region of Interest
SE	Spin echo

SNR	Signal-to-noise ratio
SPAIR	Spectral Attenuation Inversion Recovery
SPGR	Spoiled Gradient Recalled Echo
SPIR	Spectral Presaturation with Inversion Recovery
STIR	Short T_1 Inversion Recovery
TE	Time of echo
TR	Time of repetition
T_1WI	T_1-weighted image
T_2WI	T_2-weighted image
USM	Universiti Sains Malaysia
VIBRANT	Volume Image Breast Assessment

CHAPTER 1

INTRODUCTION

This chapter generally contains the background of study, problem statement, objectives and chapter outline which related to this research that can be referred.

1.1 Background of study

Breast magnetic resonance imaging (MRI) is a medical imaging technique that produces tomographic images of breast tissue by using magnetic fields and radio frequency waves. MRI involves in analysing tissue characteristics which include hydrogen (proton) density, T_1 and T_2 relaxation times of tissue and blood flow within the tissue (William & Clyde, 1999) which is useful to investigate or diagnose soft tissues such as organs and muscles as it can scan through water (State Government of Victoria, 2015). As known worldwide, MRI is a non-invasive imaging technique for detecting and characterising breast carcinomas. MRI uses the magnetic field for lining up hydrogen nuclei inside the body to compose an image. The MRI modality interest differs from other medical imaging modality.

A phantom is a mass of materials that are used to investigate the effects of radiation on human (Mosby, 2012) and to explore the limitations in prototype imaging systems (Madsen *et al*., 2006). A phantom can be made from water to complex chemical mixtures that faithfully mimic the human body as it would interact with radiation. As stated by Hornaks (2014), a phantom usually composed of materials that have a magnetic resonance signal as the bearing substances such as aqueous paramagnetic, paramagnetically doped gels, organic doped gels and reverse micelle solutions. The common paramagnetic solutions that are used as the phantom materials are agarose, gelatine, silicone and polyvinyle alcohol.

1.2 The operation of Magnetic Resonance Imaging (MRI) machine

Water molecule composes of two hydrogen atoms and one oxygen atom. Hydrogen nuclei have a quantum physics property which is called “spin” that can be oriented in a certain way. A strong magnetic field makes the spin to line-up along the magnetic field direction. The hydrogen nuclei with low energy are in the same direction of the magnetic field and the hydrogen nuclei with high energy are in the opposite direction of the magnetic field.

Then, the MRI machine will apply a current with a resonant frequency through the radio frequency (RF) coil for a short period. The resonant frequency releases energy within a specific frequency to be absorbed by the nuclei and the energy given from frequency below or above the specific frequency will not be absorbed by the nuclei. The resonant frequency depends on the magnetic field strength wherein the magnetic field strength is directly proportionally to the resonant frequency. This makes the MRI machine able to scan the

organ by section at a time. At this time, the nuclei with low energy will absorb the energy sent from RF coil and change their energy state and spin direction. These nuclei with low energy will become nuclei with high energy. Next, the RF energy will stop and these nuclei release their energy in the form of waves. The MRI machine works with the receiver coil to receive the energy waves sent out by the nuclei. Consequently, these nuclei will return to their origin state of energy (Avada, 2012). The MRI used in this research was SIGNA™ HDxt 1.5T GE Healthcare that available in Clinical Trial Complex (CTC) as shown in Figure 1.1.

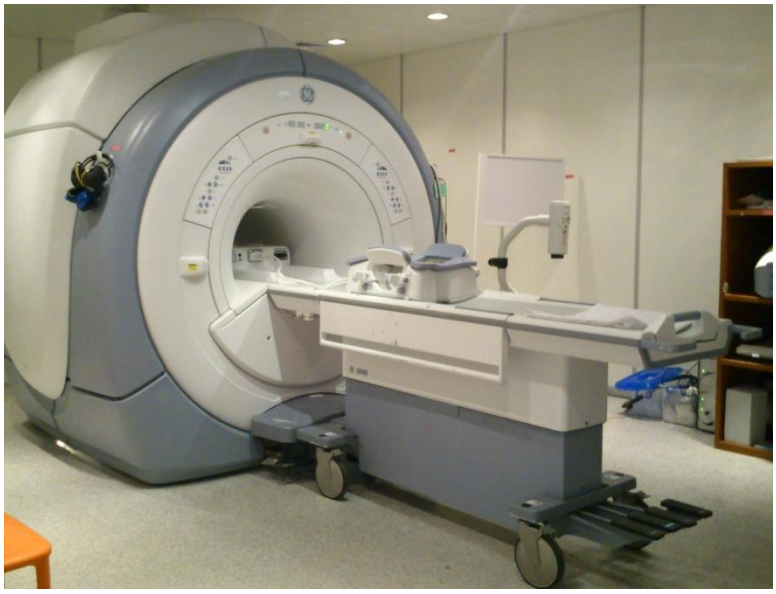

Figure 1.1: SIGNA™ HDxt 1.5T GE Healthcare

The receiver coil converts the energy waves into electrical signals to enable the MRI machine detect hydrogen nuclei in the body and compose an image. A coil is used as a signal receptor to enable the MRI captures the image of the target organ. The selection of

coils to be used in the MRI needs to be considered so that the image of the scanned organ can be captured. Figure 1.2 shows the HD 8-channel breast coil used in this study.

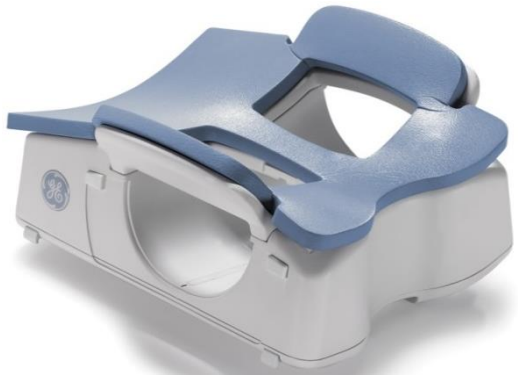

Figure 1.2: SIGNA^{TM} 1.5T GE Healthcare HD 8-Channel breast array MRI coil

1.3 Problem statement and rationale of the study

Breast MRI has become an essential element in breast imaging. Breast MRI imaging has a better diagnosis for patients who have a pre-invasive stage breast cancer compared to mammographic and ultrasound screening (Kuhl *et al.*, 2010). Nevertheless, there is a need for breast phantom to improve the ability for diagnosing breast cancer, which has implications for patient treatment and patient outcome (Kuhl, 2007). The breast phantom has to be suitable for quality performance purposes, evaluating new imaging techniques and sequences instead of quality assurance (QA), quality control (QC) and improvement of magnetic resonance properties such as image resolution, image contrast and image quality. (Friedman & Glover, 2006, Chen *et al.,* 2004 & Wang *et al.,* 2011). The established breast MRI phantoms were only suitable for testing system performance and functional studies

(Friedman & Glover, 2006). The QA phantoms are heavy, large, difficult to handle, some phantoms are made from carcinogenic material such as $NiCl_2$ and expensive. Therefore, the desired characteristics of the agarose phantom include comparable relaxation times to those of human tissue without using contrast agents, non-hazardous and cost effective. Figure 1.3 shows the breast MRI phantom for SIGNA^{TM} 1.5T GE Healthcare.

Figure 1.3: Breast MRI phantom for SIGNA^{TM} 1.5T GE Healthcare

In this study, the tissue mimicking material for human breast was a mixture of agarose and gelatine solution. Different concentrations of agarose solution were set at 0.5%, 1.0%, 1.5%, 2.0%, 2.5%, 3.0% and 3.5%. Each concentration of agarose was 30% of the solution and remaining 70% was the concentration of gelatine solution. On the other hand, different types of tissue mimicking materials were used to mimic abnormal tissue characteristics such as polyacrylamide crystal soil mimic cysts, eggshells mimic calcifications and crushed eggshells (CrE) mimic microcalcifications. The most suitable sample that has similar T_1 and T_2 relaxation times with a normal breast tissue will be chosen as the breast phantom material.

1.4 Objectives

General objective: To fabricate and characterise the agarose phantom as breast mimicking material for Magnetic Resonance Imaging (MRI).

Specific objectives:

i. To fabricate an agarose phantom as breast mimicking material for Magnetic Resonance Imaging (MRI).
ii. To evaluate agarose gel concentration that has a similar SPGR T_1 and T_2 relaxation times for normal and abnormal breast tissues.

It is expected that this study will contribute some knowledge about breast phantom fabrication that using agarose and gelatine mixture as a background solution to mimic normal breast tissue as well as polyacrylamide crystal soils (PCS), crushed eggshells (CrE) and eggshells to mimic abnormal breast tissue. Hopefully, this study can be used as a reference to improve breast phantom fabrication.

1.5 Chapter outline

Chapter 1 describes the introduction of the research and the structure of the dissertation. This chapter consists of the background, general knowledge on how the MRI machine works, problem statements and objectives.

Chapter 2 is literature reviews, which discusses on similar studies perspectives and findings related to this research. It explains the principle of MRI and techniques in breast MRI.

Chapter 3 discusses the materials used in this research as well as methods that have been carried out in this research. This chapter explains the details of the experimental procedures on sample production, MRI study protocols, data acquisition and data analysis.

Chapter 4 focuses on the results obtained from the MRI weighted images. In this chapter, the mean signal from Spoiled Gradient Recalled Echo (SPGR) T_1- and T_2-weighted images are measured and compared to relaxation time for normal and abnormal breast tissue. Discussion on the results also included in this chapter.

Chapter 5 contains the summary of the research, the limitation encountered in this research and recommendation for future improvement.

CHAPTER 2

LITERATURE REVIEW

This chapter discusses the similar studies perspectives and findings related to this project. It explains the basic principles of Magnetic Resonance Imaging (MRI), techniques in breast MRI, MRI parameters, breast composition and materials, as well as techniques used in previous studies to fabricate the breast phantom.

2.1 Basic principles of Magnetic Resonance Imaging (MRI)

In simplest terms, MRI is based on the ability of some protons within the body to absorb and emit radio wave energy when the body is placed within a strong magnetic field. Hydrogen nuclei have a precession that produces small magnetic moment due to their charged particles (Mackiewich, 1995). Most of the hydrogen nuclei aligned themselves with the direction of the magnetic field in the presence of a strong magnetic field. The hydrogen nuclei precess with the direction of the magnetic field is called Larmor precession. The Larmor frequency is directly proportional to the applied magnetic field strength and defined as:

$$\omega_0 = \gamma\beta_0 \qquad \text{(Eq. 1)}$$

ω_0 = the angular frequency of precession of protons

γ = gyromagnetic ratio

β_0 = the strength of the applied magnetic field

The gyromagnetic ratio for hydrogen nuclei is constant, $\gamma = 42.6$ MHz T^{-1}. The strength of the magnetic field applied in this study is 1.5 Tesla. Thus, the Larmor frequency is 63.9 MHz.

The protons will align their spin in the direction of the magnetic field when the external magnetic field, **B** is presence, thus, a net magnetisation in the system will appear. However, this magnetisation does not occur instantaneously but the time taken for a system to reach its maximum net magnetisation after being placed in an external field is called the spin-lattice relaxation and is denoted as T_1 (Vesci *et al.*, 2011). The external magnetic field is supposed to supply in the z-direction. This process of attaining magnetisation is given by:

$$\frac{dM_z}{dt} = \frac{M_0 - M_z}{T_1} \qquad \text{(Eq. 2)}$$

Then, another external magnetic field is supposed to supply in the x-direction. A fully net of magnetisation in the x-y plane is resulted from a right amount of time supplied in this field. This leads to the introduction of an orthogonal **B** field to alter the alignment of the spins is called a pulse. A pulse is created by using a radio frequency (RF) that transforms a

magnetisation in the z-direction into a magnetisation in the x-y plane is called a π/2 pulse. If this pulse is applied for twice the amount of time, the net magnetisation resides in the z-direction and is called π pulse. This pulse is needed to observe the spin-spin relaxation and is denoted as T_2:

$$\frac{dM_{x(y)}}{dt} = \frac{M_{x(y)}}{T_2} \quad \text{(Eq. 3)}$$

A work published by Bloch *et al*. (1946) introduced T_1 and T_2 relaxation times to account for the reestablishment of thermal equilibrium of the nuclear magnetisation after generation of the nuclear magnetic resonance signal. T_1 reflected the regrowth of the longitudinal magnetisation (M_z), whereas T_2 characterised the decay of the transverse components (M_x and M_y). The equation of motion, M during return to equilibrium (after π pulse) is:

$$M_x(t) = M_0 e^{-\frac{t}{T_2}} \sin(\omega t) \quad \text{(Eq. 4)}$$

$$M_y(t) = M_0 e^{-\frac{t}{T_2}} \cos(\omega t) \quad \text{(Eq. 5)}$$

$$M_{xy}(t) = M_0 (e^{-\frac{t}{T_1}}) \quad \text{(Eq. 6)}$$

$$M_z(t) = M_0 (1 - e^{-\frac{t}{T_1}}) \quad \text{(Eq. 7)}$$

Therefore, the longitudinal relaxation time, T_1 represents the time required to M_z to increase from 0 to (1-1/ e) or about 63% of its final value (M_0). The transverse relaxation time, T_2 represents the time required for M_x and M_y to decay or decrease to (1/ e) or about 37% of its initial maximum value (M_0). The graphical presentation of T_1 and T_2 relaxation times are shown in Figure 2.1.

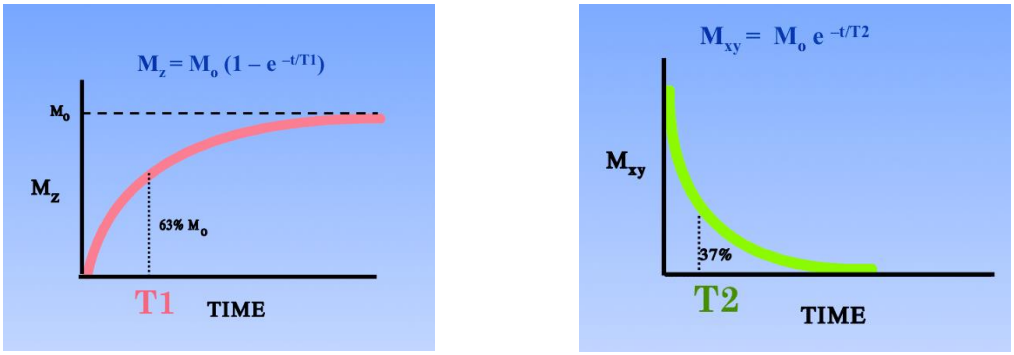

Figure 2.1: Graphical presentation of T_1 relaxation time (left) and T_2 relaxation time (right) [Source: http://mri-q.com/bloch-equations.html]

2.2 Techniques in breast Magnetic Resonance Imaging (MRI)

T_1 is a measure of a proton's ability to exchange energy with its surrounding chemical matrix. It is a measure of how quickly a tissue can become magnetised. T_1-weighted image (T_1WI) optimally shows the soft-tissue anatomy and fat to detect a fat-containing mass. T_2 conveys how quickly a given tissue loses its magnetisation. T_2-weighted image (T_2WI) optimally shows fluid and abnormalities (William & Clyde, 1999). T_1WI and T_2WI are very important for characterising abnormalities because both of them provide complementary information by which different tissues absorb and release radio wave

energy at different, detectable and characteristic rates. In T_1WI, fat has high signal intensity, so it will appear bright. On the other hand, fluids or water has low signal intensity, so it will appear dark. In contrast, fat has low signal intensity and fluid or water has high signal intensity on T_2WI (MSD Manual, 2015).

There are various techniques in acquiring a suitable and useful signal in breast MRI screening nowadays. Each technique has its own purpose to get a clear image of the scanned organ. Among them include Spoiled Gradient Recalled Echo (SPGR), Short T_1 Inversion Recovery (STIR), Volume Image Breast Assessment (VIBRANT), Fast Spin Echo (FSE), Fast Spin Echo-Extra Large (FSE-XL), Fast Recovery Fast Spin Echo (FRFSE), Iterative Decomposition of water and fat with Echo Asymmetry and Least-squares estimation (IDEAL) and many more. One of the widely used methods in fat-suppression is fat-saturation (Fat-Sat). Fat-Sat saturates fat protons to produce a negligible signal prior to acquiring data as in standard sequences. It has a short duration of radio frequency pulses tuned to the resonance frequency of fat, which is applied before starting the MRI sequence. In Fat-Sat, these chemically selective pulses cause the signal from fat to be saturated while the water signal is relatively unaffected (Elster, 2014).

2.3 Gradient echo sequence

In this research, Spoiled Gradient Recalled Echo (SPGR), merge three-dimensional (M3D) and Volume Image Breast Assessment (VIBRANT) techniques were used to acquire T_1WI. The selection of these techniques was based on routine clinical breast MRI imaging techniques in Radiology Unit. SPGR is a fat suppression technique in high resolution as

well as VIBRANT for simultaneous bilateral breast imaging in axial and sagittal scan planes which improved breast imaging screening. Measurements of the SPGR signal intensity (S_{SPGR}) is simply stated from a work published by Bluml *et al.* (1993) for the following equation:

$$S_{SPGR} = \frac{M_0\,(1-e^{-\frac{TR}{T_1}})\sin(\alpha)}{1-e^{-\frac{TR}{T_1}}\cos(\alpha)} \qquad \text{(Eq. 8)}$$

T_1 = longitudinal relaxation time

TR = time of repetition

α = flip angle

M_0 = equilibrium longitudinal magnetisation

The signal intensity in SPGR is maximised by Ernst Angle:

$$\alpha_E = \cos^{-1}(e^{-\frac{TR}{T_1}}) \qquad \text{(Eq. 9)}$$

A curve characterised by T_1 is generated by using a constant T_R with increasing flip angle, α. Bluml *et al*. (1993) demonstrated that these data can be represented in the linear form, Y = mX + b as:

$$\frac{S_{SPGR}}{\sin(\alpha)} = e^{-\frac{TR}{T_1}}\left(\frac{S_{SPGR}}{\tan(\alpha)}\right) + M_0\left(1-e^{-\frac{TR}{T_1}}\right) \qquad \text{(Eq. 10)}$$

Whereby the slope, *m* and the Y-intercept, *b* can be estimated by linear regression, allowing T_1 and M_0 to be extracted:

$$T_1 = \frac{-TR}{\ln(m)} \quad \text{(Eq. 11)}$$

$$M_0 = \frac{b}{(1-m)} \quad \text{(Eq. 12)}$$

2.4 Spin echo sequence

In T_2-weighted, a routine clinical breast imaging protocol was used to acquire the T_2 relaxation time for every sample. Fast Spin Echo-Extra Large (FSE-XL) technique was used to enhance the fast spin echo (FSE) sequence by using RF pulses with higher amplitude but a shorter duration that allowed to longer echo train length (ETL). ETL is a number of echoes selected by the researcher in FSE sequence to reduce blurring and echo spacing when scanning, thus increased the Signal-to-Noise Ratio (SNR) (GE Medical Systems Training in Partnership, n. d.). The spin echo sequence equation is:

$$S_{SE} = \left(1 - e^{-\frac{TR}{T_1}}\right) e^{-\frac{TE}{T_2}} \quad \text{(Eq. 13)}$$

T_2 = transverse relaxation time

TE = time of echo

Whereby T_1 factor is $1 - e^{-\frac{TR}{T_1}}$ and T_2 factor is $e^{-\frac{TE}{T_2}}$.

2.5 Magnetic Resonance Imaging (MRI) parameter

2.5.1 Spin echo

Spin echo (SE) pulse sequence produces standard T_1WI, T_2WI and proton density-weighted images (PDWI). T_1WI emphasize differences in the T_1 relaxation times between tissues and usually provide the anatomic detail and identifying fat and subacute haemorrhage. T_2WI emphasize differences in the T_2 relaxation times of tissues and usually provide the detection of pathological lesions. PDWI accentuate proton density differences in tissues and most useful in brain imaging. Two major components of MRI machine settings for SE sequences are namely the time of repetition (TR) and the time of echo (TE). TR is the time for the protons to align with the magnetic field or the time between administrated RF pulses. TE is the time provided for radio wave energy to be released and detected by the magnetic field.

2.5.2 Slice location

Slice location is determined by application of a slice selection gradient of gradually in increasing intensity along the z-axis. The small energy pulses released by tissue protons are further localized by frequency-encoding in the x-axis and phase-encoding in the y-axis. Images can be obtained in any anatomical plane by adjusting the orientation of the x-axis, y-axis and z-axis of the magnetic field gradients.

2.6 Breast Composition

Breast tissues are mostly made up by fibroglandular tissue and adipose tissue without a muscle tissue. The composition of breast is different in every person due to the proportions of fibroglandular and adipose tissues. According to a study performed by Nelson *et al.* (2008), the composition of breast was best characterised as being a 30% of fibroglandular tissue and 70% of adipose tissue.

2.7 Previous studies

A study performed by Mustafi *et al.* (2009) in making agar phantoms for the breast MRI as shown in Figure 2.2, that mimic human tissue in terms of their pathways, including T_1, T_2, T_2* and other magnetic interactions. In this study, different concentrations of agar (0-3%) and Omniscan (0-1 mM) solutions were used. A heterogeneous air bubble free phantom which is a better model for human tissue has been developed. The heterogeneous mixtures were produced by the suspension of other materials in the agar so that the phantom is more accurately mimicking the breast. There are two types of phantoms for two different applications specifically for quality assurance and clinical protocol. The quality assurance phantom was designed for overall scanner function evaluation and the clinical phantom was designed for attachment to the breast or other areas of the body during scanning in the clinical protocol.

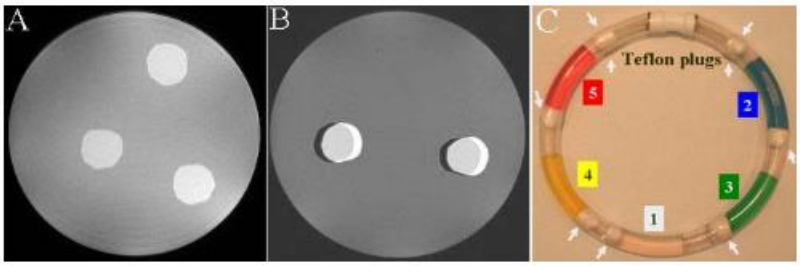

Figure 2.2: Panel A - MR image of agar with 3 different OMNISCAN solutions (0.2-0.5 mM); Panel B - MR image of agar with 100% fully saturated fat; Panel C - Standard agar phantom with different concentrations of OMNISCAN (0-1 mM) [Adapted from: Mustafi *et al.*, 2009]

Furthermore, a development of breast MRI phantom for quality control (QC) has been done by Tuong & Gardiner (2013) as shown in Figure 2.3. A dual-cavity breast phantom was designed for this purpose. The inner cavity of phantom contained a saline solution and the outer cavity of phantom contained a mineral oil to mimic fat in the human breast. The phantom has a resolution plate inside with various shapes and ranging in size from 1 to 20 mm. In this study, three tests were performed which are STIR, T_1-weighted fat-suppressed and T_2-weighted sequences tests. The fat has a longer T_2 relaxation time than in the breast tissue, thus the composition of mineral oil may have to be altered to be more accurately reflected physiologic breast fat. Meanwhile, the T_1 relaxation time for fat cannot be measured because only a VIBRANT sequence was performed in this study. However, the phantom has created signal characteristics which are reproducible and reliable.

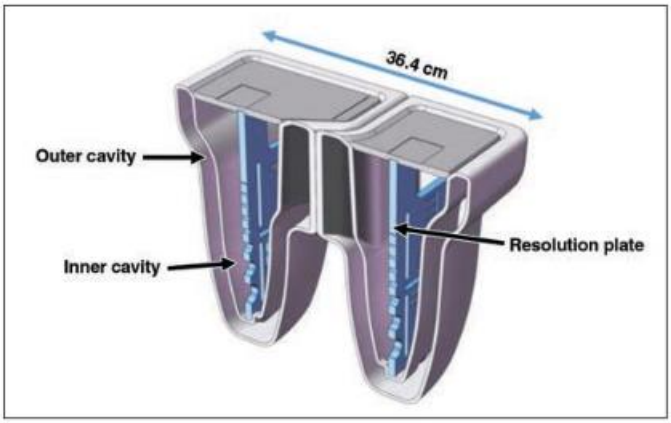

Figure 2.3: Dual-cavity breast phantom [Adapted from: Tuong & Gardiner, 2013]

Besides, Hellerbach *et al.* (2013) performed a study to find the alternative material instead of agar to design the MRI phantom. In this research, six types of gelling agents were evaluated to determine which material could be potentially used as an ideal MRI phantom. The chosen materials are sodium alginate, xanthan gum, FAVOR-PAC-300, PNC-400, Carbomer-980 and Carbopol-974P. These types of gelling agents were chosen based on their common usage in the pharmaceutical, cosmetic and food industries. From the result, Carbomer-980 and Carbopol-947P are suitable materials to replace an agar due to their characteristics which are non-hazardous, inexpensive, readily available and easy to handle. Furthermore, these gelling agents did not require thermal treatment. However, these materials are pH dependent which means that the concentration of these materials may have to be altered to get a similar T_2 relaxation time in the human breast tissue.

Additionally, a development and characterization of dynamic lesions for Dynamic Contrast-Enhanced MRI (DCE-MRI) breast phantom for quantitative evaluation also have

been performed in previous studies (Freed *et al.*, 2011). In this study, a dynamic lesion phantom which can produce physiological kinetic curves was developed to represent human DCE-MRI data. The phantom was consisted of a hollow plastic mould with inlet and outlet tubes. These tubes allowed the contrast agent solution to flow through the lesion over time. Two types of phantoms were designed by using a lesion mould production method. The lesion mould with smooth and spherical border shape was represented as a benign and the lesion mould with lobulations was represented as malignant. Four different flow rates (0.25, 0.5, 1.0 and 1.5 ml/s) were determined by using x-ray images of the lesion for evaluation of resultant kinetic curve shape and homogeneity of the contrast agent distribution in the dynamic lesion.

In a comparative study of fat suppression Short T_1 Inversion Recovery (STIR), Spectral Presaturation with Inversion Recovery (SPIR) and Spectral Attenuation Inversion Recovery (SPAIR) techniques in breast MRI, Ribeiro *et al.* (2013) used seven samples with different components as the materials of the breast phantom. The mixture of agarose and gelatine were used to represent human breast tissue, turkey breast to represent the breast parenchyma and pork fat to represent the breast adipose tissue in the breast. The main objective of this study is to find a solution to eliminate fat signal for a better image quality. This is because of the difficulty to diagnose between benign and malignant lesions in the breast MRI examinations due to the amount of fat in the breast tissue. Based on the results, the agarose and gelatine provided sufficient strength and time for T_1 and T_2 values to mimic human breast tissue. However, this study has its limitations. The breast phantom did not simulate any lesions due to its similar response pattern. In addition, this limitation probably occurred due to the calibration procedures and quality check programme of the equipment.

At 1.5 T, the T_1 values for adipose tissue and fibroglandular tissues are about 250 ms and 700 ms respectively in the normal breast. Meanwhile, the T_1 value for most lesions and cancers is about 800 ms to 1 s. In the meantime, the T_1 value for cystic fluids is about 3s. In addition, the T_2 values for fat and fibroglandular tissues are around 60 to 80 ms in the normal breast tissue. Most breast lesions and cancers have slightly longer T_2 values around 80 to 100 ms and the T_2 value for cystic fluids is more than 100 ms (Hendrick, 2008).

CHAPTER 3

MATERIALS AND METHODOLOGY

This chapter discusses the breast mimicking materials and methods that were used to fabricate the agarose breast phantom. It introduces the materials and methodology involved in this study and explains the MRI study protocols that were used in obtaining the Spoiled Gradient Recalled Echo (SPGR) T_1 and T_2 relaxation times.

In this research, the agarose gel samples were prepared throughout the research to get a suitable agarose concentration to mimic breast tissue. Figure 3.1 shows the overall of the research flowchart. Next, the breast mimicking samples were prepared and undergone MRI scan. The procedure of the data collection needs to be considered to make sure the data collection was satisfied and simple analysis was done on the samples.

The methodology section describes the breast mimicking sample fabrication and MRI study protocols. Meanwhile, data acquisition and data analysis section presents the techniques and software used to analyse the results.

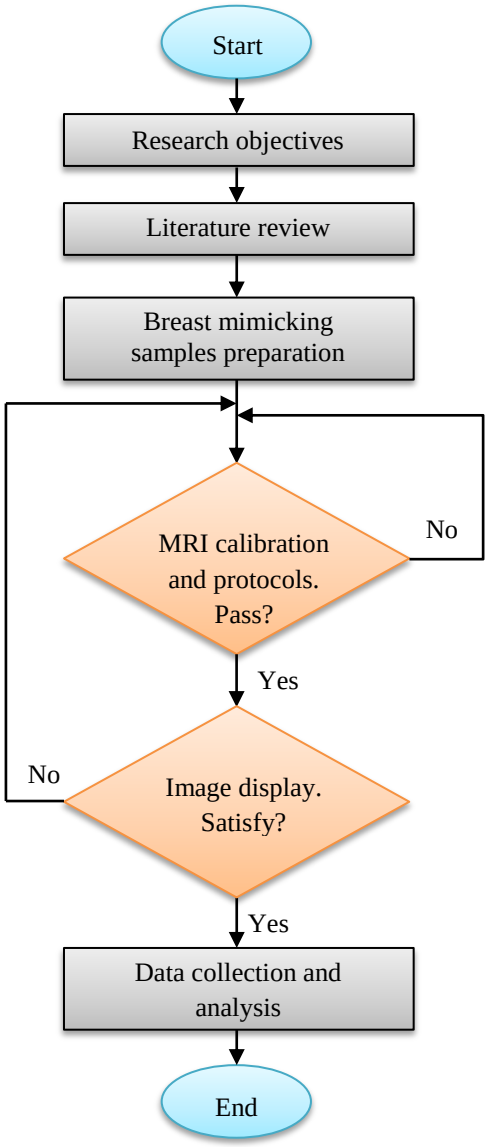

Figure 3.1: Research flowchart

3.1 Breast mimicking materials

The breast mimicking materials consisted of agarose and gelatine mixture as the background material, which mimics the breast tissue. In this study, the agarose solution acts as a glandular fibrous and gelatine acts as a fat in the breast. The composition of breast tissue was best characterised as being 30% of glandular fibrous and 70% of fat (Nelson *et al.,* 2008). Therefore, each sample consisted of 30% of agarose solution and 70% of gelatine solution. The agarose concentration used in this study was 0.5%, 1.0%, 1.5%, 2.0%, 2.5%, 3.0% and 3.5%. Meanwhile, the concentration of gelatine needed depending on agarose concentration that was used for that solution.

Besides, there are different types of materials that were used to mimic an abnormal tissue in the sample such as polyacrylamide crystal soil (PCS) and eggshells. PCSs were used to imitate cysts. Polyacrylamide has a capability to absorb and hold water inside before it dry. Calcifications have various patterns which can be either benign or malignant. One of the calcification patterns that are typically detected in clinical is eggshell-like calcifications (Nalawade, 2009). Eggshells were used to imitate calcifications by which crushed eggshells (CrE) imitate microcalcifications and irregular shapes of eggshells imitate calcification in the sample. Eggshell is a semipermeable membrane which is made from almost entirely calcium carbonate ($CaCO_3$) crystals. The type of tissue mimicking materials needed for preparing the samples was shown in Table 3.1.

Table 3.1: Tissue mimicking material specification

Tissue mimicking material	Material	Volume (ml)	Diameter (cm)	Shape
Breast tissue	Agarose and gelatine	60	4.2	Cylinder
Fibrocystic	Polyacrylamide crystal soil (PCS)	-	1.0	Round
Microcalcifications	Crushed eggshells (CrE)	-	-	-
Calcifications	Eggshells	-	10.0, 20.0, 30.0	Irregular

3.2 Method of breast mimicking materials production

The composition of the tissue mimicking materials is given in Table 3.2. The breast mimicking materials contains agarose (NORGEN BIOTEK CORP, Canada), sodium chloride (NaCl) (Sodium Chloride, 58.44 g/mol, R&M Marketing, Essex, UK), bovine gelatine (Halagel Gelatin, Halagel Products Sdn. Bhd., Malaysia) and distilled water. The concentration of NaCl was constant 0.7%.

Table 3.2: Composition of tissue mimicking materials of human breast

Material Concentration (%)	
Agarose	**Gelatine**
0.50	1.17
1.00	2.33
1.50	3.50
2.00	4.67
2.50	5.83
3.00	7.00
3.50	8.17