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"Evaluation of Multimodal Liver Phantom efficacy and Detectability of Hepatocellular Carcinoma"

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"Evaluation of Multimodal Liver Phantom efficacy and Detectability of Hepatocellular Carcinoma"

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Thesis Approval

"Evaluation of Multimodal Liver Phantom efficacy and Detectability of Hepatocepllular Carcinoma"

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1441 - 2020

Dedication

I dedicate this dissertation to my beloved parents.

To my angel, my wife.

To my children; Belal, Baha' Alden and Mahmoud

To my sister and brothers.

To my country; Palestine.

Osama Mahmoud Shehadeh Makham

الإهْدَاء

إِلَى نَبْعِ الحَنَانِ وَمَلاكِي الحَارِس .... إِلَيْكِ يَا بَلْسَمَ الشِّفَاء .. أُمِّي الغَالِيَة

إِلَى مُنِيرِ دَرْبِي وَمُلْهِم مَسِيرَتِي .... إِلَيْكَ أَيُّهَا القَلْبُ الكَبِير .. أَبِي الغَالِي

إِلَى نِصْفِيَ الثَّانِي وَمَلاذَ رُوحِي .... إِلَيْكِ يَا نَبْضَ القَلْبِ .. زَوْجَتِي الغَالِيَة

إِلَى القُلوبِ الطَّاهِرَةِ وَالنُّفُوسِ البَرِيئَة ... إِلَيْكُمْ يَا رَيَاحِينَ حَيَاتِي .. أَوْلَادِي الأَعِزَّاء

إِلَى مَنْ كَانُوا سَنَدِي وَعَوْنِي .... إِلَيْكُمْ يَا كُلَّ آمَالِي .. أُخْتِي العَزِيزَة وَ إِخْوَتِي الأَعِزَّاء

إِلَى مُشْرِفِي الغَالِي ... إِلَيْكَ يَا مُعَلِّمِي .. دُكْتُور مُحَمَّد حجُوج

إِلَى جَامِعَتِي الغَرَّاء ... إِلَيْكِ يَا صَرْحَ العِلْمِ وَالعُلَمَاء .. جَامِعَةُ القُدْس

إِلَى دَكَاتِرْتِي الأَفَاضِل .. أَسَاتِذْتِي الرَّائِعِين

إِلَى أَصْدِقَائِي الذِينَ لَمْ يَبْخَلُوا عَلَيَّ بِالنُّصْحِ وَالإِرْشَاد

إِلَى كُلِّ مَنْ سَانَدَنِي حَتَّى أَصِلَ إِلَى هَذِهِ المَرْحَلَة

إِلَى وَطَنِي المَكْلُوم .. إِلَى فِلَسْطِينَ الحَبِيبَة

أُهْدِيكُمْ جَمِيعَاً هَذا العَمَلَ المُتَوَاضِع ...

Declaration

I certify that this thesis submitted for the degree of Master, is the result of my own research, except where otherwise acknowledged, and that this thesis has not been submitted for a higher degree to any other university or institution.

Signed: 

Osama Mahmoud Shehadeh Makhamreh

Date: 18/01/2020

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ABSTRACT

Medical imaging provides an image for internal parts of organ in non-invasive technique, it is one of the fastest areas developing in medicine specially for clinical and research settings. The aim of the current study is to mimic the HCC using the dynamic liver phantom displaying functional flow of contrast media through the HCC. The proposed phantom design consisted of three types of mimicked soft tissues; liver parenchyma; tumors; and vascular mold. The vascular mold consists of flow part (cylindrical medium) located inside the liver parenchyma and this part contains the tumor samples. The phantom are made of different ingredients; 4% weight of gelatin powder; 2.6% weight of hydroxyethylcellulose; 0.2% weight of benzalkonium chloride; 3.2% weight of propanediol; and 90% weight of water as a volume spreader. The tumor model was clearly demonstrated by imaging modalities CT, MRI, and ultrasound. The flow phantom or the dynamic part in phantom was well worked. Interestingly, this liver phantom enable the employment of the dynamic contrast studies and functional vasculature. In the conclusion, the multimodal liver phantom consisting HCC tumor models were produced in simple, low cost and quick method within short time. The principle of this technique can be used in different organs in the body.

تقييم فاعلية مجسم الكبد متعدد وسائط التصوير الطبي في الكشف عن سرطان الكبد

إعداد: أسامة محمود شحادة مخامرة

إشراف: د.محمد الحجوج

ملخص

يعتبر سرطان الكبد (*HCC*) أحد أكثر الأورام انتشارًا في العالم. و يعتبر الكشف المبكر عن هذا السرطان أفضل طريقة لتوفير العلاج وإنقاذ حياة المرضى. ولكن هناك العديد من التحديات التي تواجه العلماء والباحثين في دراسة بعض الأمراض هذه الأمراض للحصول على التشخيص المبكر وذلك بسبب عدم القدرة على دراسة هذه الأمراض في داخل جسم الإنسان. ومن هذه التحديات هي عدم وجود مجسم يحاكي الكبد الحقيقي مع وجود بعض الامراض فيه لإجراء الدراسات والبحوث عليه . لذلك تهدف هذه الدراسة إلى تطوير وتصنيع مجسم والذي يحاكي نسيج الكبد بحد ذاته وأيضاً يحاكي الأوعية الدموية الوظيفية وبعض الأمراض ، مثل سرطان الكبد *(HCC)*. بحيث يمكن استخدام هذا المجسم في جميع انواع التصوير الطبي ، مثل التصوير بالموجات فوق الصوتية (*U/S*) والتصوير الطبقي المقطعي (*CT*) والتصوير بالرنين المغناطيسي (*MRI*). يتكون هذا المجسم من ثلاثة أنواع رئيسية مختلفة من الأنسجة وهي نسيج الكبد والنسيج المرضي *(HCC)* والأوعية الدموية الرئيسية. إعداد هذا المجسم بسيط ومنخفض التكلفة ويمكن إعادة استخدامه ويستغرق حوالي 24 ساعة للتحضير. هناك بعض مجسمات الكبد المتاحة في الاسواق العالمية . ولكن تم تطوير معظم هذه المجسمات لاستخدامها في البحث في تطبيقات التصوير بالموجات فوق الصوتية والتصوير الطبقي المقطعي. و تم تطوير بعض المجسمات لتتناسب مع الرنين المغناطيسي. و لكن هذه المجسمات لا توفر خصائص تدفق الدم ولا يقدم دراسة ديناميكية للمادة الملونة بحيث يظهر تدفق الدم في الشرايين والاوردة. كانت النتائج في هذه الدراسة مرضية وقد حقق الباحثون أهداف الدراسة وتم عمل مجسم للكبد بحيث كانت خصائص هذا المجسم مشابهة لتلك الموجودة في الأنسجة الرخوة في الكبد الحقيقي . و هو ايضا قابل للتطبيق والاستخدام على جميع أنواع التصوير الطبي المتوفرة . وهذا المجسم الحالي يمكن أن تطبق الدراسات الديناميكية عليه ويظهر التدفق في الأوعية الدموية.

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LIST OF ABBREVIATIONS

AC : Attenuation Coefficient 4

AFP : α-fetoprotein 3

CEUS : Contrast Enhancement Ultrasound 3

CT : Computed Tomography iii

DCP : Des-Gamma-Carboxy Prothrombin 3

DMIP : Digital Medicine and Image Processing 2

FDG PET/CT : Fluorodeoxyglucose Positron Emission Tomography Hybrid with Computed Tomography 3

FTIR : Fourier Transform Infrared Spectroscopy 7

HBV : Hepatitis B 3

HCC : Hepatocellular Carcinoma iii

HCV : Hepatitis C-virus 3

HU : Hounsfield Unit 6

MRI : Magnetic Resonance Imaging iii

NAFLD : Non-Alcoholic Fatty Liver Disease 3

PAA : Polyacrylamide Gel 4

PAAG : Polysaccharide Gel 4

PEGDA : Polyethylene Glycol Diacrylate-based Hydrogel 4

RTV : Room-Temperature-Vulcanizing Silicone 4

US : Ultrasonography iii

Z : Acoustic Impedance 4

CHAPTER ONE

INTRODUCTION

1.1 Background

There are many diseases that affect the liver in the human body. Studying these diseases is very important. One of these disease is the hepatocellular carcinoma (HCC). Therefore, studying and understanding the anatomy and physiology of the liver are very important. In addition, studying liver diseases are also very important. But there are some difficult in studying some diseases inside the human body. So In order to study these diseases, it is necessary to have liver phantoms that mimic liver tissue with certain diseases and pathologies.

This study aims at developing a reusable, multimodal liver phantom, which applies functional vasculature and displays some pathologies, such as Hepatocellular Carcinoma (HCC). This phantom can be used with different modalities, such as Ultrasonography (US), Computed Tomography (CT), and Magnetic Resonance Imaging (MRI).

There are some liver phantoms available on the market, or described in the scientific literature, with tumor models and blood vessels structures. Most of these phantoms are developed to be used in the research for ultrasound and CT imaging applications. Some phantoms have been developed for MRI. But none of them provide blood flow functionality. To the best of our knowledge no known study's done in this field with a 3D-multimodal permanent liver phantom displaying functional vasculature and common pathologies.

The current phantom not only mimic the liver tissue with common pathology, but it also displaying functional vasculature with dynamic contrast applications and tri phasic studies (arterial, venous and delayed phases).

1.1.1 Liver anatomy and physiology

The liver is one of the largest organs in the human body and considered as the largest gland in the body with a wide variety of functions. Located in the right side of the abdomen. It is situated just above and to the left of the stomach and below the lungs. Weighing between 1.44 and 1.66 kilograms (kg), the liver is reddish-brown with a rubbery texture (1). There are four asymmetric lobes of the liver; right and left lobes in the front surface separates by falciform ligament, and quadrate and caudate lobe locates in the posterior surface(2). Figure 1 shows the anatomy of the liver.

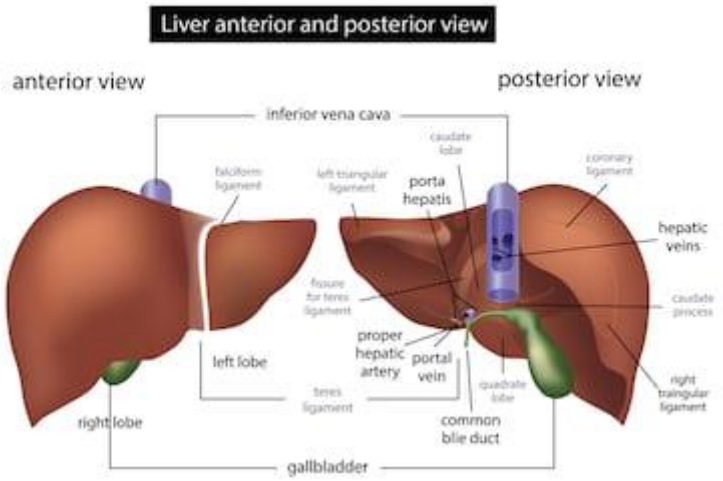

Figure 1 : Anterior and Posterior Views of the Liver.

1.1.2 Hepatocellular carcinoma (HCC)

The HCC is one of the most common diseases in the world. It is ranked as the third deadliest cancers in the human body (4). Early detection of liver cancer helps to save the patient by providing appropriate treatment. HCC occurs most often in people with chronic liver diseases, such as cirrhosis caused by hepatitis B or hepatitis C infection (5).

1.1.3 HCC diagnosis

One of the most important ways to diagnose HCC is the non-invasive imaging. The detection of HCC depend on the contrast enhancement in CT, MRI and other diagnostic modalities (4). These contrast enhancement studies basically have three phases of enhancement: arterial phase, venous phase and delayed phase. The HCC lesions take the blood directly from the hepatic artery while the parenchymal cells take blood from the portal vein. Because of that the HCC lesions appears hyper-vascularity in arterial phase and less bright in the venous phase. This HCC features in contrast enhancement is called classic features (2, 4).

HCC lesions which is more than 2cm can be easily detected by medical imaging modalities including US, CT and MRI. However, the optimal management for nodules less than 1 cm showing the typical HCC pattern has not yet been observed. (4). Regarding lesions between 1 and 2 cm there is a higher sensitivity for MRI ranging between 80 and 90 % compared to 60-75 % with CT. Besides the multimodal diagnostic criteria, MRI provides significant benefits with the use of hepatobiliary contrast.

1.2 Problem Statement

There are many diseases in the liver that must be studied, but there are many challenges facing scientists and researchers because of the limitations to study these diseases in the human body.

These challenges are the absence of an anthropomorphic 3D-multimodal permanent liver phantom to conduct studies and research on it. One example of these diseases is the HCC. Detection of liver cancer in its last stages (lesion greater than 2cm) is considered very easy. However, the detection of cancer in its early stages (< 1 cm) is very important to save the patient's life. The difficulty is finding the suitable technique to detect this size.

1.3 Justifications (Significance of the Work)

The new Phantom is important because it provides the researchers with a wide range of research experiments considering the 3Rs; in addition, it offers the opportunity to perform control quality to

different medical imaging modalities. This study aimed at developing a liver dynamic phantom, with HCC, so that it can be used for research. The phantom was applied on different medical imaging modalities, such as CT, MRI, and Ultrasound.

1.4 Study objectives

The objective of the study is:

- To develop and manufacture a 3D-multimodal permanent liver phantom displaying functional vasculature and common pathologies.
- To use this phantom for multimodal image applications (ultrasound (US), CT, and MRI). Producing realistic images in commonly used medical imaging modalities.

The phantom should be suitable for teaching, training, researching and liver imaging tri phasic applications.

1.5 Study Design (System Design)

This is an experimental study aims to manufacture a 3D-multimodal permanent liver phantom. Producing realistic images in commonly used medical imaging modalities. The phantom consists of three main components: liver parenchyma; pathology mold; and vascular mold.

CHAPTER TWO

THEORY AND LITRITURE RIVEWW

Literature studies are mentioned in the article that is included in this research.

CHAPTER THREE

MATERIALS AND METHODS

The presented anthropomorphic liver phantom consists of three main model components; liver parenchyma, blood vessels, and pathology mold. Different chemical materials with different concentration were used to produce the phantom with the three main components that have been mentioned above.

3.1 The liver Parenchyma

The liver parenchyma was produced by using different chemical materials with different concentrations. The polyvinyl chloride (PVC) human liver simulation mold with size 23x18x13cm and weight 0.62kg was used to form the liver shape. The liver parenchyma consists of different percentage of the following material: 4 % weight of gelatin powder, 2.6 % weight etherified hydroxyethylcellulose, 0.2 % weight benzalkonium chloride, 3.2 % weight propanediol and 90 % weight of water was used as a volume spreader.

3.2 HCC Samples

The HCC samples were made from two basic materials which are polyurethane combined with glycerol and placed in the cylinders inside the phantom. Our manufactured phantom was developed to contain three different sized cylinders. Hence, the tumor size can also be easily changed through the cylindrical medium.

3.3 Blood Vessels

Three input and output PVC tubes were used instead of vessel trees. The input and output tubes are connected by three different sized cylinders. The PVC tubes were connected between the input area and the output area, (the central area) which is composed with pathological mold, and it is located inside the phantom itself. Dynamic study was performed using these tubes, so there were three types of tubes that simulate the liver vessels: input tubes, output tubes and the cylindrical mediums which contain the pathologies and located inside the phantom itself, as shown in figure 2.

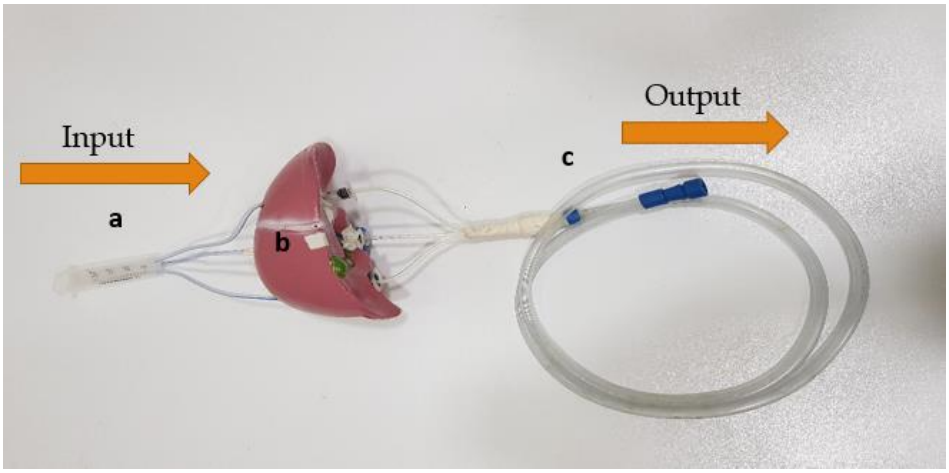

Figure 2 : Blood vessels components of the phantom; (a) input tubes; (b) the cylindrical medium; and (c) the output tubes.

As it is shown in figure 2, the input tubes are connected with the output tubes through a cylindrical medium that contains tumor samples. The input tubes are connected with contrast injector to achieve the dynamic application with tri phasic study. The output tubes are connected with a suction machine to wash out the contrast during the venous and delayed phases.

3.4 Phantom Formulation Process

The phantom has been manufactured by the following steps: First, hydroxyethylcellulose, benzalkonium chloride, and propanediol were added to the distillated water, mixed together. Then, the

mixture was heated to 90°C by using a hot plate magnetic stirrer with magnetic steering at the maximum speed of 250 rotations per minute until this mixture reaches the homogenous structure. In a different beaker, the gelatine powder is dissolved with distillate water and heated to 50°C. When the powder totally dissolved in water, this mixture was added to the first mixture and heated at the same temperature 90°C for 30 minutes to form a homogeneous composition

Finally, after all compounds were made, they were collected together in the liver mold. The input tubes are connected with the output tubes through a cylindrical medium, which contains tumor samples. Then the phantom was kept at a room temperature. The parenchyma materials should be kept inside the liver mold to reduce the erosion, which occurs later in time.

CHAPTER FOUR

RESULTS AND DISCUSSION

Results and discussion are mentioned in the article that is included in this research.

STUDY PUBLICATION

This study accepted and presented in 2019 International Conference on Digital Medicine and Image Processing (DMIP). The published article of our research study is listed below.

Evaluation of Liver Phantom for Testing of the Detectability Multimodal for Hepatocellular Carcinoma

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2.1 ABSTRACT

This study aims at developing a reusable, multimodal liver phantom, which applies functional vasculature and displays some pathologies, such as Hepatocellular Carcinoma (HCC). This phantom can be used with different modalities, such as Ultrasonography (US), Computed Tomography (CT), and Magnetic Resonance Imaging (MRI).

The current phantom consisted of different types of mimicked tissue; liver parenchyma; HCC and major input and output vessels. They are made of different ingredients; 4% weight of gelatin powder; 2.6% weight of hydroxyethylcellulose; 0.2% weight of benzalkonium chloride; 3.2% weight of propanediol; and 90% weight of water as a volume spreader. The selected materials mimicked liver tissue under MRI, CT and US.

The phantom preparation is simple, low cost, reusable, and takes about 24 hours for preparation. Additionally, comparison of ultrasound images, CT, and MRI of real patient's liver, the phantom's liver tissue with HCC and its structures are well simulated.

Using different steps to cast procedures, the researchers fabricated a multimodal liver phantom, with dynamic vascular channels, and models with different sized pathologies, which give a best procedure for training in different modalities. This technique can be applied to any organ in the body.

Keywords
"Liver phantom" "Dynamic contrast enhancement" "MRI" "CT"

2.2 INTRODUCTION

Hepatocellular carcinoma (HCC) is one of the most widespread cancers in the world. It is ranked as the third deadliest cancers in the human body [1]. Early detection of this cancer is considered as the best way to provide treatment and save patients' lives [2].The occurrence of this cancer is increased in patients with hepatic cirrhosis, chronic inflammations, such as Hepatitis B- (HBV), Hepatitis C-virus (HCV), alcohol consumption, aflatoxin exposure, non-alcoholic fatty liver disease (NAFLD), and autoimmunity cases [3].

The presence of this cancer is detected through its distinctive tumor biomarkers, which include α-fetoprotein (AFP), Des-Gamma-Carboxy Prothrombin (DCP), and other markers [4]. Additionally, modern techniques in medical imaging are among the most important methods of detecting this disease. These techniques include computed tomography (CT) [5], magnetic resonance imaging (MRI) [6], contrast enhancement ultrasound (CEUS) [7], and fluorodeoxyglucose positron emission tomography hybrid with computed tomography (FDG PET/CT) [8].

In the medical field, many phantoms have been developed to help in the assessment of medical imaging modalities and research experiments in many tasks, such as identifying image quality in diagnosis, assisting surgical navigation, helping students in their training to perform their tasks, and many other different applications. The anatomical phantom provides qualitative and quantitative estimates of the overall images as well as analysis of the clinical image processing systems [9]. By means of a phantom model, testing of clinical applications assistance systems is possible without the need of a real patient.

The phantom's properties should be similar to that of the real liver soft tissue. The surface should be soft enough like real liver. As for CT, the Hounsfield units should be the same of real liver; and they ought to have the same acoustic properties, such as velocity of sound, the attenuation coefficient (AC), acoustic impedance (Z) and backscatter coefficient in ultrasound. Finally, in MRI the relaxation times, T1 and T2 should be the same as the real liver. It is also important to mention that the materials used in the manufacturing of Phantoms are as inexpensive and available as possible.

Most of liver phantoms have been designed for CT imaging [10, 11, 12, 13], while fewer phantoms have been developed to be used in MRI [14, 15] and ultrasound [16, 17]. Some of these phantoms provide blood vascular while some others provide a realistic appearance. However, Multimodal liver phantoms are still uncommon [14, 18].

The liver phantoms, which was fabricated for the aims of this research have been prepared for CT imaging procedures, such as the (1) liver puncture test, which was developed for liver biopsy. Liver phantoms have used Flex Foam iT-III material because this material is elastic and amenable to needle puncture [19]. (2) The determination of the Iron Hepatic Accumulation using phantom was made of agar, which has the same attenuation coefficient to the liver parenchyma. It was immersed in six tubes with different iron concentration [20]. To assess the patient size effect onto the hypo vascular liver tumors detection, the phantom material that were used were water containers with different sizes [12]; however, to evaluate C-arm CT accuracy to detect liver lesions, the phantom was made by plastic foam to represent the patient's skin [21].

In previous studies, many substances with multi-techniques have been checked to achieve the liver phantom realization (Tissue Mimicking Material). The soft tissue mimicking materials were based on liquid substances, such as polyacrylamide (PAA) gel, carrageenan gel, polysaccharide gel (PAAG), agar gel, agarose gel, polyurethane gel, gelatin-alginate, silicone polymer, room-temperature-vulcanizing silicone (RTV), and polyethylene glycol diacrylate (PEGDA)-based hydrogel [22].

This study aimed at developing a liver dynamic phantom, with HCC, so that it can be used for research. The phantom was applied on different medical imaging modalities, such as CT, MRI, and Ultrasound. The new Phantom is important

because it provides the researchers with a wide range of research experiments considering the 3Rs; in addition, it offers the opportunity to perform control quality to different medical imaging modalities.

2.3 MATERIALS AND METHODS

Phantom Materials, Structure and Production:

Our Phantom consists of three main components: liver parenchyma; pathology mold; and vascular mold. The PVC liver mold with size 23x18x13cm and weight 0.62kg was used to form the liver shape. Figure () shows the liver mold used in the current study. The liver parenchyma was produced by using different chemical materials with different concentrations as appears in table 1. These materials were chosen to mimic the human liver, and at the same time to be suitable for different imaging modalities. In addition, these materials have a high elastic recovery without any decrease in their strength, and low modulus also have bacterial infection resistance.

The current study used 4 % weight of gelatin powder (Hefei TNJ Chemical Industry Co.,Ltd.); 2.6 % weight etherified hydroxyethylcellulose (Shin Etsu Tylose R HS 100000 YP2); 0.2 % weight benzalkonium chloride (StepanguatR 50 NF) was used as an antibacterial agent; 3.2 % weight propanediol (Dupont ZemeanTM) was used as a solvent; and 90 % weight of water was used as a volume spreader. The gelatin powder with hydroxyethylcellulose addition was used for gaining the necessary intensity, density, and echogenicity for MRI, CT, and Ultrasound imaging, respectively.

Figure 3: The liver mold; (a) is the inferior part of mold; (b) is the superior part.

Table 1: Material components of liver phantom

Gelatine powder	Hydroxyethylcellulose	Benzalkonium chloride	Propanediol	Water
4 wt %	2.6 wt %	0.2 wt %	3.2 wt %	90 wt%
HCC	5% agarose, 12% glycerol, 83%water.			

The tumors components consist of an agarose and glycerol for appearing hypo-intensity, hypodensity, and hypoechoic in the three modalities. The three input PVC tubes and three output PVC tubes were used instead of vessel trees. The input and output tubes are connected by the use of three different sized cylinders. Figure 4 shows the main phantom parts.

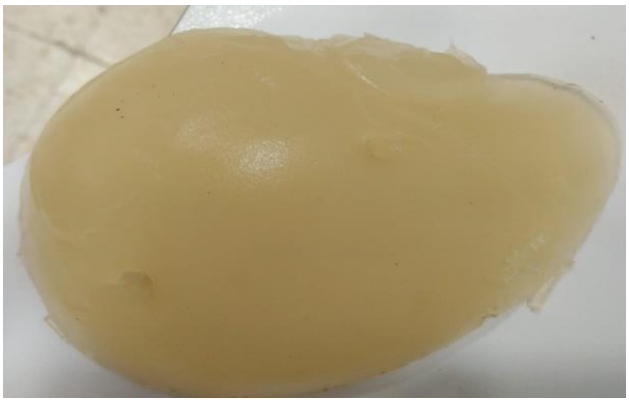

Figure 4: The liver phantom.

The steps for producing the phantom are as follows. First, hydroxyethylcellulose, benzalkonium chloride, and propanediol are added to the distillated water. They are mixed together, and heated to 90°C by using a hot plate magnetic stirrer with magnetic steering at the maximum speed of 250 rotations per minute, until this mixture reaches the homogenous structural.

In a different beaker, the gelatine powder is added to distillate water, and heated to 50°C. When the powder totally dissolves in water, this mixture is added to the first mixture and heated at the same temperature 90°C for 30 minutes. This time guarantees to make the mixture a homogeneous composition. Figure 5 shows all of these steps.

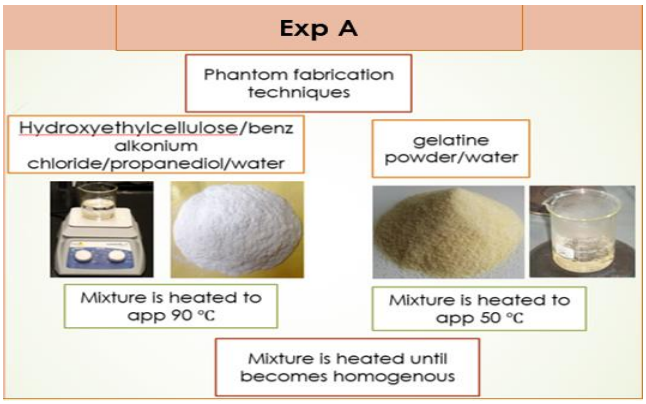

Figure 5: Phantom Formulation Process.

In case of the HCC model, agarose-glycerol mixture is used. It is produced by adding these components to the distillate water and heated to 80°C. Then, this compound is poured into silicon molds with different sizes; 0.5; 1; and 2cm. The new component is cooled in the refrigerator at a temperature 4°C for three hours.

Instead of vessels, PVL tubes were used. They were formed from the input area and the output area, the medium between them is composed with pathological mold, which is located inside the phantom itself (figure 6). Tubes are divided into three tubes input and three tubes output. Each tube is made of non-toxic PVC material with 10 cm in length and 14 FG in size, outer diameter of 2.0 ±0.05mm, and thickness ≥ 0.4mm. Input tubes are directly connected to the injector device by combining them to one syringe. The output tubes are also combined to one large tube, which is connected into a suction device.

The use of cylindrical medium was accurately modelled. It can investigate the actual transport processes in CT and MRI for specific organ or location of tumour. This part is the most important part in whole phantom. The main cylindrical design idea was taken and quoted from pervious articles [23] [24] [25] [26].

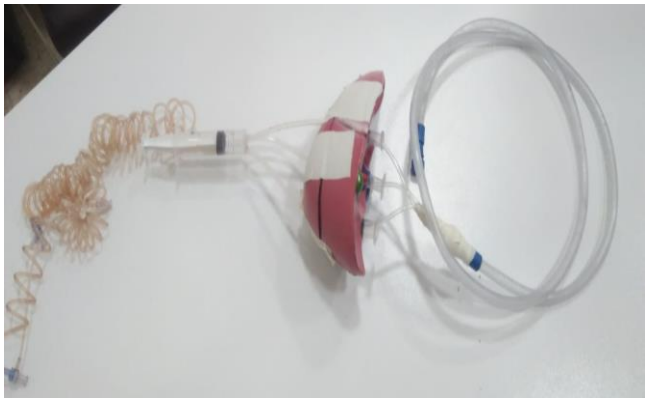

Figure 6: Input and output vessels mold.

After all compounds are made, they are collected together in the liver mold. The input tubes are connected with the output tubes through a cylindrical medium, which contains tumor samples. After these arrangements are made, the phantom was kept at a room temperature. The parenchyma materials should be kept inside the liver mold to reduce the erosion, which occurs later in time.

2.4 RESULTS

1.4.1 Phantom Image Appearance in Ultrasound

Ultrasound was used to scan the phantom. The ultrasonic properties were close to the real liver. In figure 7, an ultrasound image was obtained for the phantom parenchyma as well as the tumour inside the phantom. Compared with the normal liver parenchyma, the tumour is shown as a hypo-echoic signal. As shown in figure 8, the Doppler ultrasound was also obtained for the tumour mold.

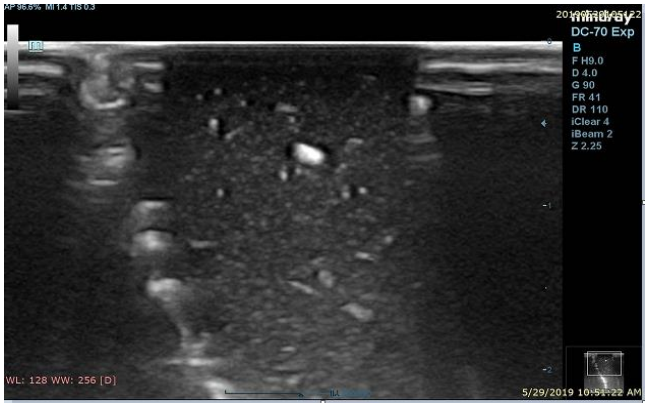

Figure 7: The ultrasound image shows the echogenicity of the liver parenchyma inside the phantom.

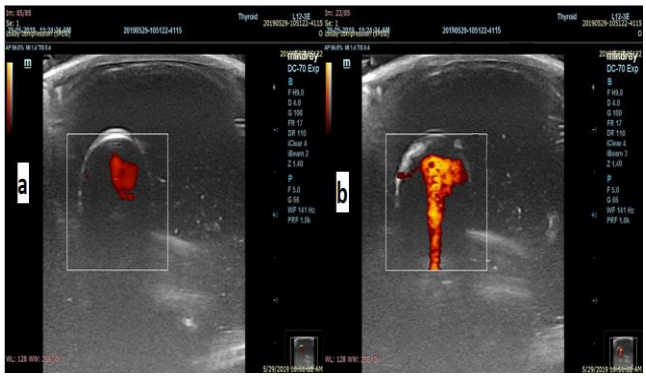

Figure 8: Doppler ultrasound imaging; (a) the signal from HCC in red color; (b) the fluid flow through the sample.

Figure 8 shows the Color Doppler ultrasound of internal vessels of the phantom with flow. The figure shows the Power Doppler ultrasound of a vessel structure next to a HCC model.

1.4.2 Phantom CT-Scan Image Appearance

The phantom was scanned by using Philips Brilliance 64 CT Scanner 64 slice. The protocol was obtained with a slice thickness of 0.6mm and pixel size 0.5*0.5 mm. The phantom parenchyma appeared with homogeneous texture, and the Hounsfield unit varied between 20-40 HU (see Figure 9).

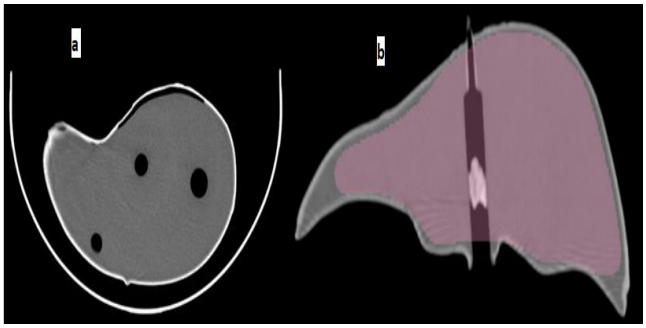

Figure 9: Phantom appearance in CT images; (a) axial cut showing the three cylindrical medium; (b) coronal section showing one HCC sample inside the cylinder.

Telebrix 30 Meglumine (300 mg I/ml) were used as a contrast media to check the HCC pattern through CT. The tumour models appeared with heterogeneous texture. The Hounsfield number for the HCC appeared between 80 to 90 HU in arterial phase after 22 seconds from injection, 40 to 50 HU in venous phase after 50 seconds from injection, and 20-30 HU for equilibrium phase after 180 seconds from injection. Figure 10 illustrates the result of contrast media enhancement through the sample in CT. The real liver parenchyma tissue without contrast media was approximately 50HU; however, with contrast media in arterial phase, it was around 90-125 HU. This means that phantom structures had the same appearances of the real liver.

Figure 10: CT axial images; (a) pre-contrast; (b) arterial phase after 22 sec (tumor is clearly bright); (c) venous phase after 50 sec (tumor is slightly bright); and (d) delayed phase after 180 sec (tumor clearly washout).

1.4.3 3D Reconstruction from phantom CT image and Model Registration A

The 3D planning model was obtained by using voxel size of phantom increased up to 1×1×1 mm. The 3D reconstruction was represented in figure 11.

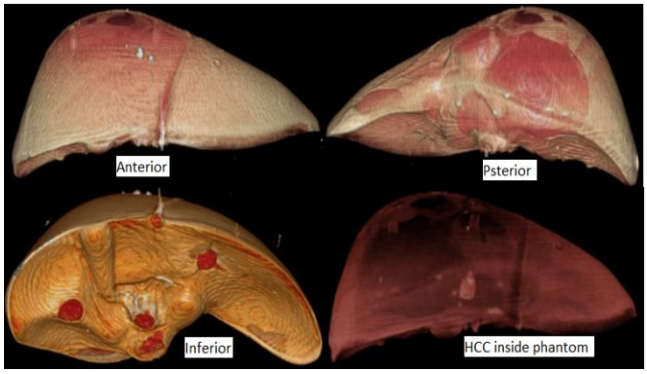

Figure 11: CT reconstruction images; (a) shows anterior surface; (b) shows posterior surface; (c) shows inferior surface; and (d) shows HCC inside the phantom.

1.4.4 Phantom MRI image Appearance

The phantom imaging was performed by using a 1.5-T MRI unit (MAGNETOM Aera, Siemens Healthcare, Erlangen) with a 48-radiofrequency channel system, which provided a maximum gradient strength of 45 mT/m and a peak slew rate of 200 mT/m/ msec. 72 images were recorded,

each with 512 × 512 pixels. The FOV reading was 380 mm, FOV phase was 81.3%, and the slice thickness was 3.0 mm. Figure 10 shows the images of the liver phantom depicted in Fig 12.

The figure 4.13 shows the study sample with a 2.5wt% concentration of gelatin after the sixth week. The figure shows one of the readings that were taken to calculate the signal intensity of the materials fabricated in the phantom, which was estimated at 181.

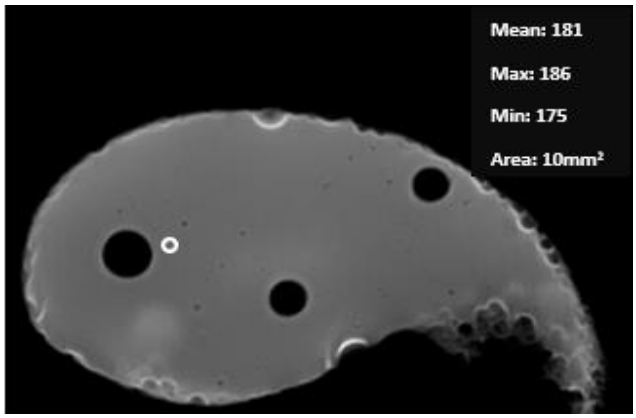

Figure 12: Liver phantom model; T1 maps of the phantom layer made of gelatin 2.5wt%; the phantom shows axial cross section of the three cylindrical, which contains the tumors sample.

1.5 DISCUSSION

The current method allows fabricating multimodal phantoms with reusable parts. The parenchyma can be reused to produce a new phantom. The phantom can easily release by removing the old liver only with effortless process. The hot water can be used to remove the liver parenchyma method. The gel-based liver parenchyma can be stocked in the closed counter at a room temperature.

Because the output orifice of cylindrical medium is located outside the phantom, the tumour size can also be easily changed through the cylindrical medium. It is easy to reuse it again with different pathological samples.

The limitations of current study consisted of the incorporation of exact representations of vessels as different types, e.g. portal and hepatic veins. Future work is needed to mimic the vessels with dynamic phantom and use different pathology models. The study can be used to perform typical HCC pattern. In addition of that, the chemical bonds between the phantom components of the phantom should be detected using some devices such as Fourier Transform Infrared Spectroscopy (FTIR) or Raman spectroscopy. Also, the temperature of the phantom should be adjusted at specific degree to check the actual effects of time on signal intensity.

The current phantom was designed to mimic the HCC and normal liver tissue characteristics including acoustic properties, Hounsfield unit, and signal intensity. Therefore, the phantom can support users with standardized environment in different medical modalities. The multimodal phantoms can be used for different purposes, such as research, image-designing system tests; quality control of imaging systems; the performance of comparison between imaging systems; establishing new protocols with different imaging systems; surgery action training for liver surgery; needle guided puncture of lesions; and assessment of 3D and reconstruction based on sizes and shapes knowledge.

1.6 CONCLUSION

The study has shown that the phantom mimics the real liver tissue with HCC sample. The phantom is efficient to be applied on possible training, scientific experiments, and for testing different purposes. The current phantom is a very suitable for different medical purposes such as training the operator, surgical guided and treatment monitoring by using different modalities including: CT, ultrasound, and MRI. The typical HCC pattern appearance in CT and MRI were already ascertained CONFLICT OF INTEREST

The authors declare that they have no conflict of interest. This article does not contain any studies with human participants performed by any of the authors.

1.7 ACKNOWLEDGMENT

The researchers would like to thank Ibn Rushd Radiology Centre for the giving us opportunity to use their Medical Imaging Modalities (CT, US, and MRI scanners) during this study.

CHAPTER FIVE

CONCLUSION AND RECOMMENDATIONS

This chapter include brief overview about, conclusion, future perspective, and appendices.

5.1 Conclusion

The current method allows fabricating multimodal phantom with dynamic contrast study, displaying functional vasculature and common pathologies with different size. The tumor size can also be easily changed through the cylindrical medium. The current phantom was designed to mimic the HCC and normal liver tissue characteristics including acoustic properties, Hounsfield unit, and signal intensity.

The study has shown that the phantom mimics the real liver tissue with HCC sample. It can be applied on possible training, scientific experiments, and for testing different purposes. The current phantom is a very suitable for different medical purposes such as training the operator and surgical guided by using different modalities including CT, ultrasound, and MRI.

This multimodal phantom can be used for different purposes, such as research, image-designing system tests, quality control of imaging systems, needle guided puncture of lesions, comparison between imaging systems, establishing new protocols with different imaging systems and surgery action training for liver surgery.

5.2 Future Perspectives

Future work is to mimic the vessels with dynamic phantom and use different pathology models for different organs with different pathologies.

The materials and methodology used in this study can be applied to different studies that mimic different organs and pathology.

Various studies can be conducted on the phantom in order to verify the chemical, physical, mechanical and electrical properties of the materials used in the manufacture of the phantom. Appendices.

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APPENDICES

APPENDIX 1 Notification of acceptance to DMIP

Unit Unit B, 6/F, Dragon Industrial Building, 93 King Lam Street, Lai Chi Kok, Kowloon, Hong Kong, Email: admin@cbees.org
Tel: +852-3500-0137(HK), +86-28-86528465(CN Branch), +1-206-456-6022 (USA)

Notification of Acceptance of the DMIP 2019

Shanghai, China, November 13-15, 2019

http://www.dmip.org/

Paper ID : S3004

Paper Title : Evaluation of Liver Phantom for Testing of the Detectability Multimodal for Hepatocellular Carcinoma

Dear Osama Makhamrah, Muntaser S. Ahmad and Mohammad Hjouj,

First of all, thank you for your concern. 2019 2nd International Conference on Digital Medicine and Image Processing (DMIP 2019) review procedure has been finished. We are delighted to inform you that your manuscript has been accepted for presentation at 2019 2nd International Conference on Digital Medicine and Image Processing (DMIP 2019), Shanghai, China. Your paper was tripling blind-reviewed and based on the evaluation. The reviewers' comments are enclosed.

The conference received submissions from different countries and regions during the submission period. And there are about 78 submissions accepted by our reviewers who are the international experts from all over the world. The selected papers could be published in the international conference proceedings with high quality. According to the recommendations from reviewers and technical program committees, we are glad to inform you that your paper identified above have been selected for publication and oral presentation. You are invited to present your paper and studies during our DMIP conference that would be held during November 13-15, 2019 in Shanghai China.

The DMIP 2019 is co-sponsored by Hong Kong Chemical, Biological & Environmental Engineering Society (HKCBEES) and Biology and Bioinformatics Society (BBS).

This paper of DMIP 2019 will be published in International Conference Proceedings, which will be indexed by Ei Compendex and Scopus, and submitted to be reviewed by Thomson Reuters Conference Proceedings Citation Index (ISI Web of Science).

(Important Steps for your registration): Please do finish all the 5 steps on time to guarantee the paper published in the proceeding successfully:

1. Revise your paper according to the Review Comments in the attachment carefully. (Five authors at most each paper)

- 1 -

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2. Format your paper according to the Template carefully.

http://www.dmip.org/Template.docx

3. Download and complete the Registration Form or register through the online system.

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Option B: http://confsys.iconf.org/register/dmip2019 (An account is needed for online registration.)

4. Finish the payment of Registration fee. (The information can be found in the Registration form or on the online system)

Option A: http://www.dmip.org/reg.doc (English)

Option B: http://confsys.iconf.org/register/dmip2019 (An account is needed for online registration.)

5. Send your final papers (both .doc and .pdf format), filled registration form (.doc format) and the scanned payment (in .jpg format) to us at dmip@cbees.net. (Before September 05, 2019) (Very important)

Note: Conference secretary will contact you later about the **copyright,** please pay attention to your e-mail box.

DMIP 2019 will check the format of all the registered papers first, so the authors don't need to upload the paper to the system. After the registration, we will send all qualified papers to the publish house and index organization for publishing directly.

We are looking forward to meet all the authors in our conference. But if you and your co-author(s) could not attend DMIP 2019 to present your paper for some reasons, please inform us. And we will send you the scanned version of official receipt of registration fee, electronic journals and/or other materials after DMIP 2019 free of charge.

Please strictly adhere to the format specified in the conference template while preparing your final paper. If you have any problem, please feel free to contact us via **dmip@cbees.net.** For the most updated information on the conference, please check the conference website at **http://www.dmip.org/.** The Conference Program will be available at the website in **late October, 2019**.

Again, congratulations. We are looking forward to seeing you in Shanghai, China.

Yours sincerely,

DMIP 2019 Organizing Committees

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APPENDIX 2 Certification of presenting in DMIP

Participation and Presentation Certificate

for

2019 2nd International Conference on Digital Medicine and Image Processing (DMIP 2019)
Shanghai, China, November 13-15, 2019

Paper title: Evaluation of Liver Phantom for Testing of the Detectability Multimodal for Hepatocellular Carcinoma

Presenter's name: Osama Makhamrah (S3004)

Presenter's affiliation: Quds University, Palestine

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