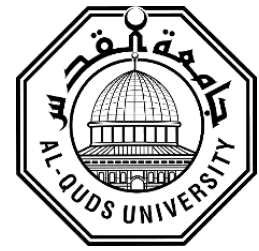


**Deanship of Graduate Studies
Al-Quds University**



**“Evaluation of Multimodal Liver Phantom efficacy and
Detectability of Hepatocellular Carcinoma”**

Osama Mahmoud Shehadeh Makhamreh

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Detectability of Hepatocellular Carcinoma”**

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the Degree of Master of Medical Imaging Technology/Graduated
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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

الإهداء

إِلَى نَبْعِ الْحَنَانِ وَمَلَائِكَةِ الْحَارِسِ إِلَيْنِكَ يَا بَلَسَمَ الشِّفَاءِ .. أُمِّي الْعَالِيَةِ

إِلَى مُنِيرِ دَرْبِي وَمُلْهِمِ مَسِيرَتِي إِلَيْنِكَ أَيُّهَا الْقَلْبُ الْكَبِيرُ .. أَبِي الْعَالِي

إِلَى نِصْفِي الثَّانِي وَمَلَأْذِ رُوحِي إِلَيْنِكَ يَا نَبْضَ الْقَلْبِ .. زَوْجَتِي الْعَالِيَةِ

إِلَى الْقُلُوبِ الطَّاهِرَةِ وَالنُّفُوسِ الْبَرِيئَةِ ... إِلَيْكُمْ يَا رِيَّاحِينَ حَيَاتِي .. أَوْلَادِي الْأَعْرَاءِ

إِلَى مَنْ كَانُوا سَنَدِي وَعَوْنِي إِلَيْكُمْ يَا كُلَّ آمَالِي .. أُخْتِي الْعَزِيْزَةَ وَ إِخْوَتِي الْأَعْرَاءِ

إِلَى مُشْرِفِي الْعَالِي ... إِلَيْنِكَ يَا مُعَلِّمِي .. دُكْتُورَ مُحَمَّدٍ حُجُوج

إِلَى جَامِعَتِي الْعَرَّاءِ ... إِلَيْنِكَ يَا صَرْحَ الْعِلْمِ وَالْعُلَمَاءِ .. جَامِعَةَ الْقَدْسِ

إِلَى دَكَاتِرَتِي الْأَفَاضِلِ .. أَسَاتِدَتِي الرَّائِعِينَ

إِلَى أَصْدِقَائِي الَّذِينَ لَمْ يَبْخُلُوا عَلَيَّ بِالنُّصْحِ وَالْإِرْشَادِ

إِلَى كُلِّ مَنْ سَانَدَنِي حَتَّى أَصِلَ إِلَى هَذِهِ الْمَرْحَلَةِ

إِلَى وَطَنِي الْمَكْلُومِ .. إِلَى فِلَسْطِينِ الْحَبِيبَةِ

أَهْدِيكُمْ جَمِيعاً هَذَا الْعَمَلَ الْمُتَوَاضِعَ ...

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:

A handwritten signature in blue ink, consisting of several overlapping horizontal strokes with a small loop at the end.

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. ويعتبر 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 الأمراض 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 أنواع 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 الأسواق العالمية. ولكن تم تطوير معظم هذه المجسمات لاستخدامها في البحث في تطبيقات التصوير بالموجات فوق الصوتية والتصوير الطبقي المقطعي. و تم تطوير بعض المجسمات لتناسب 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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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.

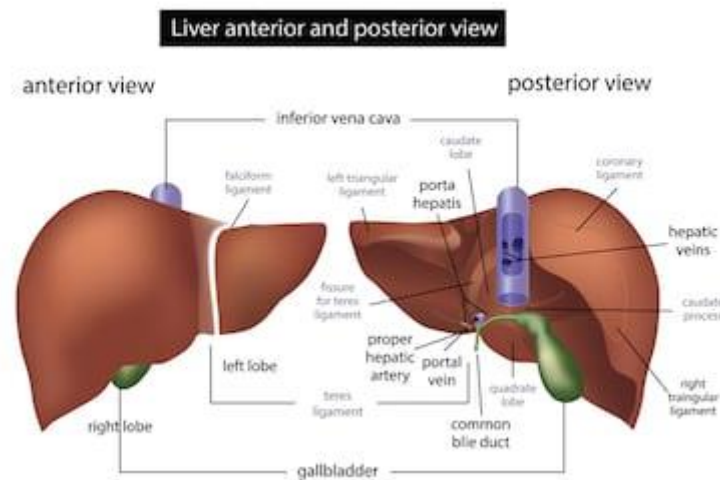


Figure 1 : Anterior and Posterior Views of the Liver.

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