

Role of High Intensity Focused Ultrasound in the Treatment of Hepatocellular Carcinoma

Essay

*Submitted for partial fulfillment of the Master Degree
in Radiodiagnosis*

Presented by

Ali Elsaeed Abdel Rahman Ali

M.B., B.Ch
Ain Shams University

Under Supervision of

Prof. Dr. Sameh Mohamed Abdel Wahab

*Professor of Radiodiagnosis
Faculty of Medicine - Ain Shams University*

Dr. Mohamed Elgharib Abou Elmaaty

*Assistant Professor of Radiodiagnosis
Faculty of Medicine - Ain Shams University*

Faculty of Medicine
Ain Shams University
2011

List of Contents

Title	Page
♦ Introduction	1
♦ Aim of the Work	2
♦ Chapter I:	
▪ Anatomy of the liver	3
♦ Chapter II:	
▪ Clinical, pathological features & management of HCC	20
♦ Chapter III:	
▪ Physical principles and technique of HIFU	67
♦ Chapter IV:	
▪ Role of High intensity focused ultrasound (HIFU) in HCC	92
♦ Summary and Conclusion	127
♦ References	129
♦ Arabic Summary	--

List of Figures

Fig. No	Title	Page
Figure (1):	Gross anatomy of liver	6
Figure (2):	Caudate lobe of the liver	8
Figure (3):	segmental anatomy of the liver, along with the pattern of hepatic venous drainage,.....	10
Figure (4):	Segmental anatomy according to couinoud.....	11
Figure (5):	H.Bismuth's functional classification of the liver.....	12
Figure (6):	Transverse segmental anatomy of liver LEFT: above the level of left portal vein. RIGHT: at the level of the left portal vein.....	14
Figure (7):	Transverse segmental anatomy of liver LEFT: at the level of right portal vein. RIGHT: at the level of splenic vein	14
Figure (8):	Vascular supply of the liver	17
Figure (9):	Biliary system anatomy	19
Figure (10):	Trabecular hepatocellular carcinoma	24
Figure (11):	Acinar hepatocellular carcinoma	24
Figure (12):	Undifferentiated hepatocellular carcinoma	25
Figure (13):	Fibrolamellar hepatocellular carcinoma	26
Figure (14):	Small hepatocellular carcinoma, deeply located in segment VIII Conventional Gray-scale U/S study shows a hypoechoic nodular lesion	38
Figure (15):	Small, overt hepatocellular carcinoma.....	41

List of Figures (Cont.)

Fig. No	Title	Page
Figure (16):	Small, encapsulated hepatocellular carcinoma.....	42
Figure (17):	Early-stage, hypovascular hepatocellular carcinoma	43
Figure (18):	Multifocal HCC	44
Figure (19):	Small, poorly demarcated hepatocellular carcinoma	45
Figure (20):	Hepatocellular carcinoma with internal mosaic architecture, intra-tumoural septa and areas of necrosis	46
Figure (21):	Infiltrative type hepatocellular carcinoma.....	47
Figure (22):	Diffuse type hepatocellular carcinoma.....	48
Figure (23):	Hepatocellular carcinoma with satellite lesions	49
Figure (24):	Well-differentiated hepatocellular carcinoma.....	51
Figure (25):	Poorly differentiated hepatocellular carcinoma.....	52
Figure (26):	Small hepatocellular carcinoma	53
Figure (27):	Celiac arteriogram shows grade IV vascular staining in the tumor (arrows).....	55
Figure (28):	Graph demonstrates ultrasound guided RF.....	59
Figure (29):	RF ablation of HCC performed after fluid instillation in a 74-year-old woman.....	61
Figure (30):	Digital subtraction angiogram, shows arteries draped around the large tumor.....	63-64

List of Figures (Cont.)

Fig. No	Title	Page
Figure (31):	Digital subtraction angiogram of the celiac arterial trunk demonstrates right hepatic arterial supply to the HCC (arrow)	65
Figure (32):	Diagram of an ultrasound therapy transducer	68
Figure (33):	Block diagram of basic components of an ultrasound therapy system.....	70
Figure (34):	Axial Ultrasound intensity distribution from a planar transducer.....	71
Figure (35):	diagram of spherically curved ultrasound transducer	73
Figure (36):	Diagram of a phased array	75
Figure (37):	Diagram shows the temperature time relationship of thermally induced tissue necrosis	81
Figure (38):	Diagram shows how focused ultrasound beams reach the patient.....	84
Figure (39):	Patient positioning during the treatment process..	88
Figure (40):	Schematic diagram shows the therapeutic plan for HIFU therapy.....	89
Figure (41):	Hyperechoic changes during HIFU denoting Successful treatment of a small HCC	93
Figure (42):	Real-time ultrasound image: grey-scale changes during HIFU treatment	94
Figure (43):	MRI guided HIFU system.....	95
Figure (44):	Gray-scale changes of large high intensity focused ultrasound (HIFU) obtained on real-time ultrasound (US) images during HIFU procedure.....	96

List of Figures (Cont.)

Fig. No	Title	Page
Figure (45):	A 35-year-old patient with hepatitis C. This is a postcontrast dynamic arterial phase fat saturated echo image	97-98
Figure (46):	Axial T1WI series MRI images, 1 min post IV gadolinium contrast.....	100
Figure (47):	Magnetic resonance imaging (MRI) on T1-weighted images showing improvement in hepatocellular carcinoma (HCC) in a typical case (male, aged 58 years) after high intensity focused ultrasound (HIFU)	102
Figure (48):	CT evaluation of the therapeutic response in a patient who had one-session high intensity focused ultrasound (HIFU) treatment alone for hepatocellular carcinoma	104
Figure (49):	Transverse contrast agent-enhanced MRI scan of a 64-year-old patient with HCC.....	105
Figure (50):	Transverse contrast agent-enhanced MRI scan of a patient with HCC	106
Figure (51):	Enhanced magnetic resonance scans of patient 62 years of age with hepatocellular carcinoma who received the combination of transcatheter arterial chemoembolization (TACE) and one-session high intensity focused ultrasound (HIFU).....	107
Figure (52):	Cumulative survival curves for 55 patients following HIFU treatment of HCC according to tumor, node and metastasis stage	108

List of Figures (Cont.)

Fig. No	Title	Page
Figure (53):	Bar graph shows median rates of reduction in tumor size during the follow up period from 3 to 12 months for patients treated with either TACE alone or TACE and ultrasound ablation	109
Figure (54):	A 74-year-old patient with hepatocellular carcinoma CT before and after TACE and HIFU	110
Figure (55):	A 42-year-old man with hepatocellular carcinoma MR before and after TACE and HIFU	111
Figure (56):	Enhanced computed tomography scans obtained in a patient 56 years of age who received one-session high intensity focused ultrasound (HIFU) treatment alone for advanced-stage HCC	112
Figure (57):	Kaplan–Meier curve shows overall survival rates for patients who received TACE–HIFU combination therapy	113
Figure (58):	Transverse contrast-enhanced CT images (nonhelical) obtained in a 58-year-old patient who underwent one course of TACE and one session of ultrasound ablation for HCC	114
Figure (59):	Kaplan–Meier curve shows disease-free survival rates for patients who received TACE–HIFU combination therapy	115
Figure (60):	Illustration shows HIFU ablation of a hepatic tumor with the tissues out of focus kept undamaged	116
Figure (61):	Transverse contrast agent-enhanced CT and MRI of a patient with HCC	117
Figure (62):	A contrast agent-enhanced MR images of a 68-year-old patient with HCC	118

List of Figures (Cont.)

Fig. No	Title	Page
Figure (63):	Transverse contrast agent-enhanced CT and MRI of a patient with HCC treated sequentially with RFA and then HIFU	119
Figure (64):	Grade 1 skin toxicity following intercostal HIFU treatment to a liver metastasis. With Close-up of lesion showing scale	124

List of Tables

Tab. No	Title	Page
Table (1):	Groups at whom HCC screening and surveillance is recommended	30
Table (2):	Benefits and limitation of HIFU	123

Acknowledgement

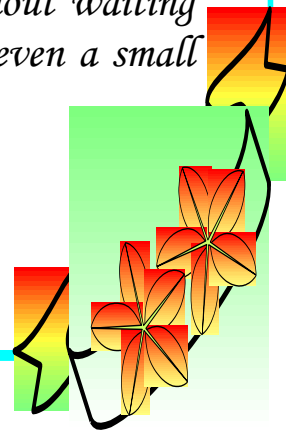
First of all, all gratitude is due to **God** almighty for blessing this work, until it has reached its end, as a part of his generous help, throughout my life.

Really I can hardly find the words to express my gratitude to **Prof. Dr. Sameh Mohamed Abdel Wahab**, Professor of Radiodiagnosis, Faculty of Medicine, Ain Shams University, for his supervision, continuous help, encouragement throughout this work and tremendous effort he has done in the meticulous revision of the whole work. It is a great honor to work under his guidance and supervision.

I am also indebted to **Dr. Mohamed Elgharib Abou Elmaaty**, Assistant Professor of Radiodiagnosis, Faculty of Medicine, Ain Shams University, for his guidance, continuous assistance and sincere supervision of this work.

Finally, I dedicate this work to my parents who have done and still doing a lot for me without waiting for anything in return and hope I can pay even a small part of my debt to them.

Ali Elsaeed Abdel Rahman Ali



List of Abbreviations

Abbrev.

AFP	Alpha fetoprotein
AJCC	American joint Committee of Cancer
ALP	Alkaline Phosphatase
ALT	Alanin transaminase
AST	Aspartate trasaminase
BCLC	Barcelona Clinic Liver Cancer
CLIP	Cancer Liver Italian Program
CT.....	Computed tomography
CTAP.....	CT arterial portography
CTHA	CT of hepatic arteriography
CUPI	Chinese University Prognostic Index
d	Diameter of transducer element
DN	Degeneration nodule
F	French
Gy.....	Gray
HCC	Hepatocellular carcinoma
HIFU	High Intensity Focused Ultrasound
IVC	Inferior vena cava
KPS.....	Kafrnofsky performance status
LDH	Lactate Dehydrogenase
LLS	Left lobe side
MHz	Mega hertz
MR.....	Magnetic resonance
mRNA	Messenger Ribonuclic acid

List of Abbreviations (Cont.)

Abbrev.

NRS	Numerical rating scales
OLV	One lung ventilation method
PEI.....	Percutaneous ethanol injection
PV	Portal vein
QOL	Quality of life
R.....	Radius of curvature
RF.....	Radiofrequency
RFA.....	Radiofrequency ablation
RN.....	Regeneration nodule
SMA.....	Superior mesenteric artery
SMV.....	Superior mesenteric vein
TACE	transcatheter arterial chemoembolization
TNM.....	Tumor, Node, Metastasis classification
UK	United kingdom
US.....	Ultrasound
Z	Acoustic impedance

Introduction

Hepatocellular carcinoma (HCC) is the fifth most frequent cancer in the world and the third common cause of cancer related mortality in the world (*Verslype et al.,2009*).

Hepatocellular carcinoma is also one of the most difficult types of cancer to treat. Surgical resection can change the natural course of HCC at early stages. Unfortunately, because of tumor multifocality, portal venous tumor invasion, and underlying advanced liver cirrhosis, surgical resection can be performed in only 20 % of patients.

Therefore, non surgical treatment is the only available option for the majority of patients with HCC (*Feng et al., 2005*).

Several minimally invasive techniques have been used for the local ablation of liver lesions including laser, microwave, radiofrequency, cryo and ethanol ablation. Trans catheter arterial chemoembolization (TACE) is a widely used treatment for the patients with large volume HCC (*Feng et al., 2005*).

Aim of the Work

The aim of this work is to review the role of the high intensity focused ultrasound (HIFU) technology in the treatment of hepatocellular carcinoma being a completely non invasive ablative technique.

Anatomy of the Liver

The shape of an organ is studied before its function except for the liver whose function has been studied at first and studying progress during three millenniums led to the modern knowledge (*Bonnichon et al., 2006*)..

Embryologically, the pancreas and liver being as epithelium of the foregut grows out from the digestive tract and into the dorsal and ventral mesenteries, respectively. The *liver* (liver epithelial cords) and *biliary tree* appear late in the third week or early in the fourth week as the hepatic diverticulum, an outgrowth of the ventral wall of the distal foregut (duodenum) (*Neas, 2003*).

Gross morphology:

The anatomy of the liver can be detailed based on the external appearance of the organ (external or descriptive anatomy) or based on its vascular and biliary architecture (vascular or functional anatomy).

As regarding the *descriptive external anatomy* of the liver, it is the largest organ in the body. It is situated in the upper and right quadrants of the abdominal cavity, occupying almost the