Role of High Intensity Focused Ultrasound in Treatment of Hepatocellular Carcinoma

Essay

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By

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INTRODUCTION

Hepatocellular carcinoma (HCC) is one of the most common types of malignancy in humans and 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. Transcatheter arterial chemoembolization (TACE) is a widely used treatment for patients with large-volume HCC. It is almost impossible to achieve complete necrosis of HCC with embolization of the hepatic artery alone. Viable tumor cells still remaining after TACE may cause local recurrence and distant metastasis. For this reason, TACE has recently been used with other ablative therapies to ablate residual tumor cells ***(Feng et al., 2005).***

High-intensity focused ultrasound (HIFU) is a noninvasive method for the treatment of liver tumors **.**This procedure is an extracorporeal technology for the thermal ablation of tumors. An ultrasound beam can be focused using an extracorporeal transducer to thermally ablate a large tumor without requiring insertion of instruments into the lesion ***(Feng et al., 2004).***

There is a great difference between the acoustic intensities used with HIFU and those of the diagnostic ultrasound. HIFU has significantly higher intensities in the focal region of the ultrasound transducer. While typical diagnostic ultrasound transducers deliver ultrasound with intensities of approximately 0.1–100 W/cm^2, HIFU transducers deliver ultrasound with intensities in the range of 100–10,000 W/cm^2 to the focal region ***(Dubinsky et al., 2008).***

The major effect of high acoustic intensities in tissue is heat generation due to absorption of the acoustic energy. The heat raises the temperature rapidly to 60˚C or higher in the tissue, causing coagulation necrosis within a few seconds**.** Other mechanical phenomena including cavitation, microstreaming and radiation forces are associated with HIFU ***(Dubinsky et al., 2008).***

HIFU can be also used in combination with other treatment modalities for treatment of advanced HCC. TACE followed by HIFU ablation would be better than TACE alone in the treatment of patients with advanced HCC ***(Feng et al., 2005).***

HIFU can be used as an effective modality in patients with advanced HCC, even in those who have failed a prior therapy ***(Feng et al., 2004).***

Aim of Work:

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

LIST OF ABREVIATIONS

AASLD…….. American Association for the Study of Liver Disease.
AFP…………Alpha Feto Protein.
ALP…………Alkaline Phosphatase.
ALT…………Alanine Transaminase.
AST……….. Aspartate Transaminase.
BCLC………Barcelona Clinic Liver Cancer.
CHD……….. Common Hepatic Duct.
CLIP……….. Cancer of the Liver Italian Program.
CR…………. Complete Response.
CT…………. Computed Tomography.
DN…………. Dysplastic Nodule.
FDG……….. Fluoro Deoxy Glucose .
FLR ………..Future Liver Remnant
GB…………. Gall Bladder.
HCC……….. Hepatocellular Carcinoma.
HBV……….. Hepatitis B Virus.
HCV……….. Hepatitis C Virus.
HIFU………. High Intensity Focused Ultrasound.
IVC…………Inferior Vena Cava.
KPS……….. Karnofsky Performance Status.
LDH……….. Lactate Dehyderogenase.
LITT……….. Laser Induced Thermotherapy.
MRI………... Magnetic Resonance Imaging.
MW………... Micro Wave.
NR…………. No Response.
NCR……….. National Cancer Registry.
OLV……….. One Lung Ventilation.
PR…………. Partial Response.
PEI............. Percutaneous Ethanol Injection.
PET……….. Positron Emission Tomography.
PVA……….. Polyvinyl Alcohol.
PVE………. Portal Vein Embolization
PVTT……… Portal Vein Tumor Thrombus
QOL………. Quality Of Life.
RES………. Reticulo Endothelial system.
RF…………Radiofrequency.
RFA………. Radiofrequency Ablation.
RN…………Regeneration Nodule.
SIRT……... Selective Internal Radio Therapy.

SPIO………Superb paramagnetic iron oxide.
TACE…….. Trans Arterial Chemo Embolization.
TNM………Tumour-Node-Metastasis.
US………... Ultrasound.

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ANATOMY OF THE LIVER

Gross Anatomy of The Liver:

The anatomy of the liver according to its external appearance identifies a superior or diaphragmatic surface and an inferior or ventral surface. On the superior aspect of the liver the falciform ligament separates the liver into a larger right lobe and a smaller left lobe **(Fig. 1)** ***(Majno et al., 2005)***.

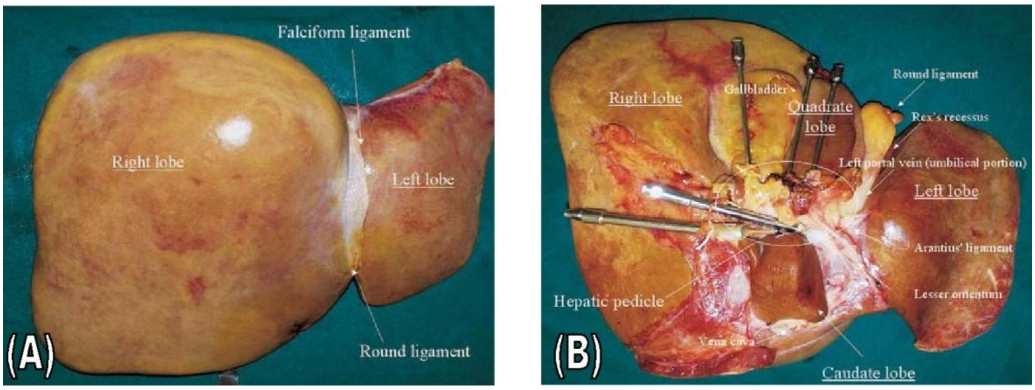

Fig. 1: Illustrated photographs show the anatomy of the liver.(A) Superior surface of the liver, (B) Inferior surface *(Majno et al., 2005)*.

Two further lobes are described. The caudate lobe posteroinferiorly between the IVC and fissure for ligamentum venosum and the quadrate lobe anteroinferiorly between the gall bladder and the fissure for ligamentum teres. These lobes are part of the right lobe

(Ryan & McNicholas, 1994).

The ”hepatic pedicle” containing the portal vein, the hepatic artery and the bile duct spreads out, near the liver, in a space called the”porta hepatis or hepatic hilum” (defined by the bifurcation of the portal vein) and divides into a shorter right pedicle and a longer left pedicle ***(Majno et al., 2005)***.

Hepatic Circulation:

The liver receives a dual blood supply from both the portal vein and the hepatic artery **(Fig. 2)**. Although the portal vein carries incompletely oxygenated (80 %) venous blood from the intestine and spleen, it supplies up to half the oxygen requirements of the hepatocytes because of its greater flow. This dual blood supply explains the low incidence of hepatic infarction ***(Majno et al., 2005).***

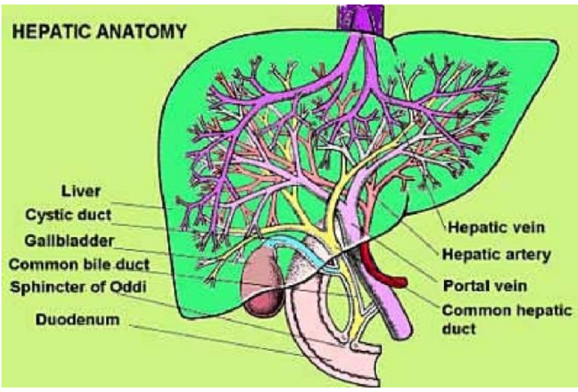

Fig. 2: Diagram shows the intra hepatic vascular and duct systems *(Ryan & McNicholas, 1994).*

Portal Vein:

The portal vein results from confluence of the superior mesenteric and splenic veins posterior to the neck of the pancreas. The portal vein passes in the free edge of the lesser omentum posterior to the bile duct and the hepatic artery to the porta hepatis, where it divides into the right and left branches to the morphological right and left lobes. The portal system is much less prone to anatomical variation than the hepatic artery ***(Ryan & McNicholas, 1994).***

The portal venous system comprises all of the veins draining the abdominal part of the digestive tract, including the lower esophagus but excluding the lower anal canal. The portal vein conveys blood from viscera and ramifies like an artery at the liver, ending at the sinusoids. Tributaries of the portal vein, which make up the portal venous system are the splenic,superior mesenteric, left gastric, right gastric, paraumblical, and cystic veins. The portal triad contains a branch of the portal vein, hepatic artery and bile duct. These are contained within a connective tissue sheath that gives the portal vein an echogenic wall on sonography and allows for its distinction from the hepatic veins, which have an almost imperceptible wall. The main portal vein divides into right and left branches **(Fig. 3)** ***(Gallego et al., 2002).***

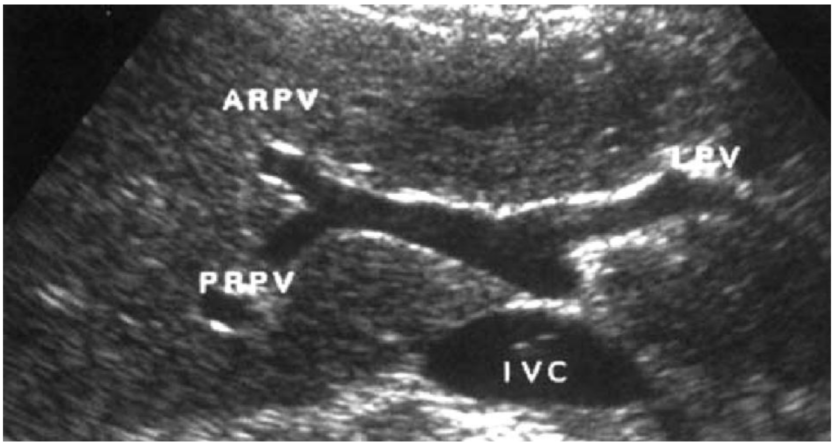

Fig. 3: U.S appearance of the main divisions of the Portal vein at the porta hepatis.
ARPV*: anterior right portal vein, *PRPV*: posterior right portal vein, *LPV*: left portal vein *(Rumack et al., 1998).

The right portal divides into anterior and posterior branches supplying the right hepatic lobe while the left portal vein divides into ascending and descending branches supplying the left lobe (***Gallego et al., 2002).***

Arterial Supply of The Liver:

The hepatic artery, one of the three branches of the coeliac trunk, supplies the right gastric, gastro duodenal arteries before approaching the liver in the free edge of the lesser omentum, anterior to the portal vein and medial to the bile duct. It divides into right and left hepatic arteries before entering the liver at the porta hepatis. The right hepatic artery usually supplies the cystic artery to the gall bladder. Within the liver, the left hepatic artery supplies the anatomical left lobe, the quadrate lobe and most of the caudate lobe and the right artery supplies the remainder of the right lobe and a variable small amount of the caudate lobe ***(Ryan & McNicholas, 1994).***

Venous Drainage of The Liver:

Blood perfuses the liver parenchyma through the sinusoids and then enters the terminal hepatic venules. These terminal branches unite to form sequentially larger veins. The hepatic veins vary in number and position. In the general population, there are three major veins: the right, middle and left hepatic veins. All drain into the inferior vena cava and like the portal veins without valves. The right hepatic vein is usually single and runs in the right intersegmental fissure. The middle hepatic vein courses in the main lobar fissure, and forms a common trunk with the left hepatic vein in 65-85 % of cases. The right, middle and left hepatic veins enter the retro hepatic inferior vena cava just before it traverses the diaphragm, approximately 2 cm caudal to the right atrium. Although the liver has a dual blood supply, the hepatic veins providethe sole route for blood exiting the liver ***(Ryan & McNicholas,1994).***

Lymphatic Supply:

There are few or no lymphatic vessels going to the liver, but there is a rich lymphatic drainage from the liver. Minor lymphatic drainage is along the falciform ligament to the para-aortic, and the para oesophageal lymph nodes. It follows the phrenic lymphatics from the capsular surface of the liver. The majority of the lymphatic drainage from the liver parenchyma is retrograde along the porta hepatis into the hepatic, celiac, and superior mesenteric lymph nodes. From here, the drainage is upward into the thoracic duct ***(Tompkins et al., 1989).***

Nerve Supply:

Nerve supply of the liver is derived from both the sympathetic and vagus nerves. Pain in the GB and liver capsule is referred to the right shoulder via the third and fourth cervical nerve ***(McMinn, 1994).***