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LIST OF ABREVIATIONS

AFP	Alpha fetoprotein
ASC	Asymptomatic carriers
CAH	Chronic active hepatitis
CEA	Carcinoembryonic antigen
CECT	Contrast enhanced CT
CH	Chronic hepatitis
CT	Computed tomography
CTAP	CT angioportography
CTHA	CT hepatic angiography
DC	Dentritic cells
FNH	Focal nodular hyperplasia
HAP	Hepatic arterial phase
HIFU	High intensity focused ultrasound
ILP	Interstitial laser photocoagulation
LC	Liver cirrhosis
LTAE	Lipiodol Transcatheter arterial embolization
MCT	Microwave coagulation therapy
MRI	Magnetic resonance imaging
PAI	Percutaneous acetic acid injection
PEI	Percutaneous ethanol injection
PEIT	Percutaneous ethanol injection therapy
PSI	Percutaneous saline injection
PVP	Portal venous phase
RFA	Radiofrequency ablation
TOCE	Transcatheter oily chemoembolization
TAE	Transcatheter arterial embolization
SAR	Specific absorption rate
3DUS	Three dimensional ultrasound

INTRODUCTION

The only potentially curative treatment of HCC is surgical resection including transplantation. Unfortunately, however most cases will fall within the category of being unresectable. The major reasons why patients cannot undergo conventional resectional surgery with a view to cure are the extent of the tumor, the implications of the associated cirrhosis, extrahepatic metastases, or unrelated co-morbidity. ***(O'Grady et al., 2000)***

Many other lines of treatment have been used in HCC such as systemic administration of combination of α-INF and cytotoxic drugs, tamoxifen administration, intra-arterial injection of cytotoxic drugs or radioisotopes, hepatic artery ligation or embolization, gene therapy and local ablative therapy (either percutaneous or intra-operative). ***(Shiina et al., 2002)***

Local ablative therapies include percutaneous ethanol injection, interstitial laser therapy, treatment with high-intensity focused ultrasound, cryoablation, percutaneous acetic acid injection, percutaneous boiling saline injection and percutaneous or laparoscopic radiofrequency thermal ablation. ***(Bascarini et al., 2001)***

Many clinical trials have been published confirming therapeutic effectiveness of RFA. ***Rossi et al., (1996)*** reported a survival of 94%,86%, 68% and 40% respectively to 1, 2, 3, and 5 years in patients with small HCC after RFA. ***Livraghi et al., (1999)*** comparing the results achieved with RFA versus percutaneous ethanol injection on 86 patients with HCC had shown that RFA has a greater percentage of complete necrosis and requires fewer sessions but has a higher incidence of major complications.

The first publications in RFA dated back to 1990, since then, many clinical studies using different devices (multipolar, bipolar, monopolar electrodes, cooled-tip electrodes, electrodes with expandable tip, multiple needle insertion-cluster) have been performed with the aim of increasing the zone of ablation. ***(Goldberg et al., 2000)***

Prior efforts at increasing local tumor control have been based on maximizing thermally mediated tissue coagulation by increasing the amount of thermal energy deposited during ablation. This has been accomplished largely by increasing generator output with electrode modifications (as cluster method) ***Goldberg et al., (1998)*** with the use of RFA by the cluster method, had confirmed a greater therapeutic effectiveness of this technique and the possibility to have 4 to 7 cm tissue necrosis with each application. Such strategies have met with some success, since coagulation diameters up to 7cm can be obtained. However, the application of high-current energy has not been without increased patient risk from complications, such as burns from the grounding pad. Therefore, other strategies with less complications have been searched for. ***(Goldberg et al., 2001)***

One potential strategy to increase the efficacy of RFA is to modulate the biologic environment of treated tissues. Along these lines, several investigators have demonstrated the possibility of increasing RFA heating by the combined intra-tumoral injection of ethanol ***(Goldberg et al.,2000)***, Doxorubicin ***(Goldberg et al.,2001)*** or saline ***(Goldberg et al., 2001).***

Using the combined RFA and intra-tumoral saline injection technique, ***Curly and Hamilton (1997)*** reported increasing the coagulation diameter from 1.4 to 2.6 cm. ***Livraghi et al. (1997)*** also reported increasing coagulation up to 4.1 cm in diameter.

Two mechanisms have been proposed to account for the improved tissue heating and increased RF-induced coagulation with simultaneous saline infusion :

a) NaCl alters tissue properties such as electrical conductivity to permit greater RF energy deposition, or

b) The infusion of fluid during RF application improves the thermal conduction within the tissues by more rapidly and effectively convecting heat over a large tissue volume. ***(Goldberg et al., 2001)***

AIM OF THE WORK

Comparison between radiofrequency ablation (RFA) alone and combined radiofrequency ablation with intra-tumoral sodium chloride injection in patients with hepatocellular carcinoma.

STUDY OF THE ENHANCING EFFECT OF SODIUM CHLORIDE INJECTION ON RADIOFREQUENCY ABLATION OF HEPATOCELLULAR CARCINOMA

Thesis

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HEPATOCELLULAR CARCINOMA

EPIDEMIOLOGY OF HEPATOCELLULAR CARCINOMA

While HCC is probably the most common solid human malignancy in the world, there is a pronounced geographic variation in its incidence. In general, the incidence of HCC increases with age and occurs most often between the third and fifth decades of life. Data on HCC incidence and mortality must be interpreted cautiously, since high and intermediate incidence areas for HCC are in developing countries without national cancer registries or adequate death certification mechanisms. In areas such as Southeast Asia and Africa, the methods of reporting HCC have improved gradually but may still lack adequate reliability. Nonetheless, due to the widely divergent rates of HCC worldwide, it is possible to identity high-, intermediate- and low-incidence areas. ***(Abeloff et al., 2000)***

High-incidence regions include Mozambique, Zimbabwe, Ethiopia, the southeastern coastline of China, Southeast Asia, Taiwan, Singapore, and Hong Kong. In areas of high HCC incidence with high-risk populations, defined as greater than 30 new cases per 100,000 popular on each year, HCC occurs in younger age groups. ***(Zuckerman, 1989)*** In Mozambique, the incidence of HCC begins to rise in late childhood and reaches exceedingly high levels in adults under 40 years of age: 103.8 cases per 100,000 people. ***(Cook-Mozaffai, 1985)*** In Mozambique, HCC accounts for 65.5 percent of all malignant diseases in men and 31 percent of malignant diseases in women. HCC rates in China and Southeast Asia are second only to rates in African countries. HCC is the third and fourth most common cancer in Chinese men and women, respectively. ***(Yeh et al., 1989)*** The incidence rate among men in one southeastern region of China is 120 per 100.000 with a male/to female ratio of 5:1. Males are affected by HCC at a much higher rate than females in all high- and intermediate-risk populations studied. In Ethiopia, HCC is the Second most common cancer in males (9.8 percent in incidence) and the 15th most common cancer in females (1.3 percent incidence). ***(Lindtjorn, 1987)*** In high-incidence regions, of the world, HCC is frequently a predominant cause of mortality in males in the population. For example, in Taiwan, HCC is the leading cause of death for men over 40 years of age. ***(Lanier et al., 1987)***

Intermediate incidence rates are found in Central and southern Europe; northern Africa; Japan; Swaziland; and in Eskimos, Indians, and Aleuts in Alaska. Japan was thought to be an intermediate-incidence country, but must now be considered a high-