MR Guided Pulsed High Intensity Focused Ultrasound Enhancement of Docetaxel Combined with Radiotherapy for Prostate Cancer Treatment

Lili Chen Ph.D (PI)
Radiation Oncology Department, Fox Chase Cancer Center, Philadelphia, PA 19111, USA

Introduction

In this 6-month progress report, we report on the research accomplishments associated with aim 1: to determine if HIFU increases the cellular uptake of ^{3}H-docetaxel in vivo. We will provide detailed information below for the results between July, 2008 and Dec 2008.

Study of ultrasound output parameters

Pilot experiments were performed on an MRgFU system with an acoustic phantom provided by InSightec. The purpose of this study was to determine the ultrasound output including frequency, acoustic power and pulse width that are adequate for the enhancement of chemotherapy therapy in mice, without damage to normal tissues. The MR proton resonance frequency shift sequence was used for temperature mapping during the treatment. We assumed that tissue would not be damaged below 42°C in temperature. Our results from the phantom study suggested that with the acoustic power of < 5 W, the temperature elevation was < 4°C. Our results were also showed that with a given acoustic power of 4W. The 4°C temperature elevation was maintained with the ultrasonic exposure time from 10seconds to 45 seconds due to thermal equilibrium. These phantom measurements provided basic ultrasonic parameters for the *in vivo* studies (see below).

Effect of HIFU on the cellular uptake of ^{3}H-docetaxel in vivo

All animal studies in this research proposal were carried out in compliance with the FCCC animal facility protocol (02-7). LNCaP 10^{5}, were grown orthotopically in the prostates of mice. The animal was treated with pulsed ultrasound using 1 MHz; 4 W of acoustic power and the 81 mode setting (5 Hz frequency with 0.1s power on, 0.1s power off) for 60 seconds. During the MRgFU treatment, phase MR images were used for measurement of the temperature in the focal spot. It was found that the temperature elevation was below 4 °C for the ultrasonic parameters used. ^{3}H-docetaxel (1.25 µci/25 g mouse weight) was injected by tail vein injection immediately after HIFU. Animals were sacrificed 30 minutes post treatment and treated tumor was prepared for measurement of the ^{3}H-docetaxel quantitatively (cpm counts) using a Liquid Scintillation Counter. Figure 1 compares the uptake of 3H Docetaxel in mice with and without HIFU treatment by measuring cpm. It is clear that in the HIFU treated group the cpm counts are significantly increased compared to the group without HIFU treatment and the control group. This preliminary result has been presented in the International Symposium on MRgFUS 2008.

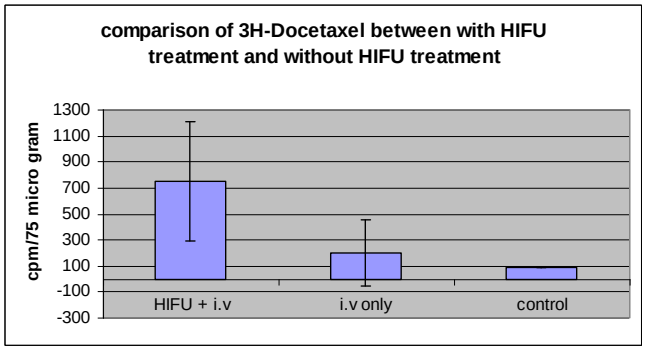

Figure 1 shows the comparison of ^{3}H-docetaxel between with HIFU and without HIFU treatment. One standard deviation of the mean was also provided.

Summary

We have performed a feasibility study on enhancing ^{3}H-docetaxel uptake in implanted prostate tumor with MRgHIFU *in vivo.* Future studies will be carried out on the efficacy of docetaxel combined with radiotherapy (RT) to inhibit prostate cancer growth in vivo.