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On the dependence of HIFU temperature on size and concentration of silicon microparticles

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***Abstract*— For a decade, silicon microparticles have attracted the attention of the scientific community. Currently, a large number of scientific advances are based on the use of microparticles as acting surfaces, vehicles, information systems, new materials or in biomedicine. This report focuses on increasing the efficiency of the High Intensity Focused Ultrasound technique (HIFU) by using silicon microparticles, which are characterized by their good biocompatibility, the easy obtention in different sizes and shapes, as well as the easy functionalization.**

***Keywords*—HIFU, ultrasounds, silicon microparticles, temperature**

I. Introduction

Cancer is one of the principal causes of death in advanced societies, in particular, in Spain 210.000 people are diagnosed with cancer every year [1]. Almost 50 % of deaths in middle-aged people are caused by this pathology [2]. These facts justifiy the importance of research on this field.

Technological advances have made possible the developement of new devices , techniques and medical procedures, establishing as a group of therapies called minimmally invasive or interventionists, allowing in some cases to replace complex surgical interventions and to complement pharmacological treatments with non aggressive procedures for the patient, increasing the efficiency of the treatment.

In this group of minimmally invasive techniques are High Intensity Focussed Ultrsound (HIFU), which allow tumor ablation without a surgical intervention.

At this moment, the most developed HIFU applications are the treatment for solid benign tumors such as the benign prostate hyperplasia and benign tumors of uterus and breasts. Between the oncological applications, treatments for primary and secundary cancerous tumors of liver, breasts, kidney, pancreas, soft tissue and bone sarcoma and retroperitoneal tumours are found [3,4].

HIFU treatment consists in focussing a high frequency ultrasound beam in a small tissue volume (figure 1).

Ultrasound passes safely through soft tissue, with enough energy to locally destroy the tissue in which its beam is focussed. The two mechanisim of ablation are the direct increasemnet due to energy accumulation in the focal point and cavitation. The first one inmediately induces coagulative necrosis in the tissue, when exposed to temperatures between 60 and 100 degrees for a second. The temperature increase depends on the tissue absortion coefficient, shape and the temperature sensitivity of the affected area. Biological changes depends on the time and level of exposure. A thermal dose that exceedes a certain threshold causes tissue coagulation and conducts an irreversible cell damage [4], as shown in figure 2.

The other physical phenomenon is cavitation, produced when intracellular microbubbles resonate with the high intensity ultrasound waves, destroying the tumor.

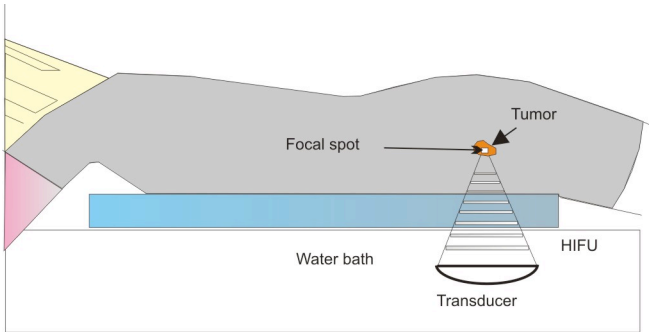

Figure 1: HIFU technique for tumor ablation

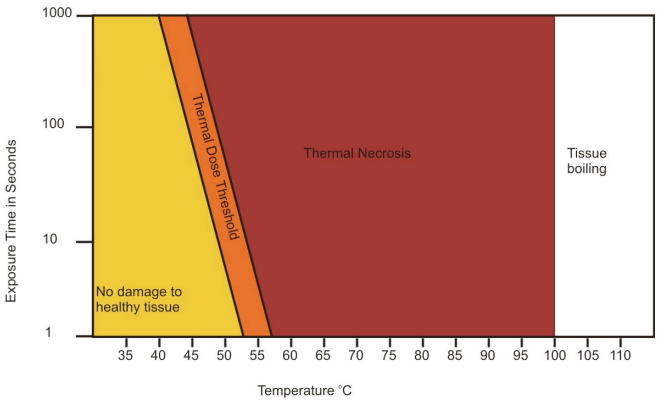

Figure 2: Tissue damage

This paper studies the influence of silicon microparticles in the increase of temperature.

II. Experimental Setup

Two types of mesures have been takes upon agar samples with different sizes and concentrations of silicon microparticles. The agar samples were obtained heating 500 ml of distilled water with 30 ml of agar (6% solution).

The used microparticles were obtained from different manufactures: the 2 μm diameter come from ECUTEC, the 75 μm from SILGRAIN, and the 100 μm from FA.

In a typical procedure, 400 mg of Agar-agar (Algamar) were delayed in 30 ml of distillated water in a beaker equipped with a stirring bar, and the mixture was heated to 100ºC with a hot plate and degas for 10 min. Silicon microparticles were mixed with 10mL of distillated water and 10 ml of surfactant (Triton X 100, Panreac), and sonicated for 10 min in an ultrasonic bath. Silicon microparticles suspension was

poured into the Agar-agar solution and the mixture was heated on the magnetic stirring plate for 5 min.

The beaker was then removed from the hot plate and was maintained under stirring until the mixture has cooled to a warm temperature. Then the solution of silicon microparticles in Agar-agar was transferred into a 50ml bottle containing a both sides open PVC pipe of 2 cm of diameter, with 2 holes previously drilled for sensor temperature. The bottle was immediately plunged into liquid nitrogen for 10s, and left at 4ºC for 2-4h for complete solidification. Agar-agar/Silicon composite was removed from the bottle and the sample casted into PVC pipe was employed for ultrasound experiments. The figure 3 shows the silicon microparticles used.

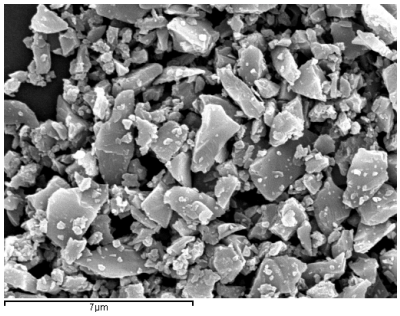

Figure 3: TEM image of Si microparticles.

The studied concentrations were 8g/l (2 grams of Si in 250ml of agar) and 40 g/l (10 grams of Si in 250 ml of agar). In order to calculate the ultrasound propagation speed in the samples, a Panametrics 5072PR Pulser-Receiver was used as the ultrasound source, two Olympus 3.5 MHz transducers and a Tektronix TDS1002B osciloscope was used to represent the signals.
Direct transmission measures were made trough an 11mm diameter cylinder 34.3 mm long, obtaining for each case the resulting 3.5 MHz pulse, and calculating the ultrasound speech as the divison of the distance of the transducers and the pulse's time of flight.
Besides, temperature measures have been taken using a K termocouple, with the Cobra 4 acquisition system (figure 4).

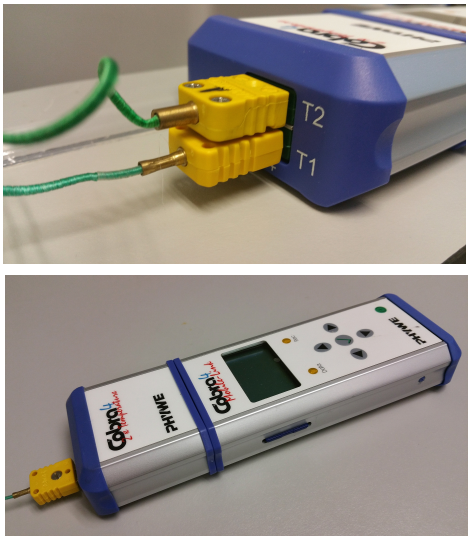

Figure 4: (a) Type K thermocouple, (b) Acquisition system Cobra 4

In order to measure the temperature, 23 mm diameter cylindrical samples 30 mm long contained in PVC holder were used as shown in figure 5. A type K thermocouple was introduced in the focal region, which then registers temperature rise due to the sonicaction of high intensity ultrasound produced by the 3.5 MHz SU-102 Sonic Concepts's transducer. Data was recorded for 60 seconds, in which the transducer was acting for 30 seconds.

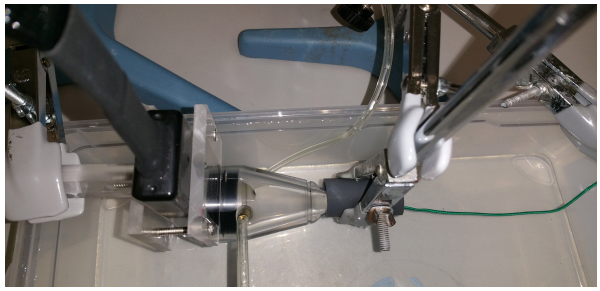
Figure 5: Experimental setup.

III. Results and discussion

In the first place, the agar samples were characterized without the presence of microparticles and a 1429.13 m/s propagation speed was measured. When the silicon microparticles were added to the samples, a decrease in the ultrasound propagation speed was observed, depending on the size and concentration of the particles. The results are shown in the following tale:

	Microparticles diameter (µm)		
(g/l)	***2***	***75***	***100***
8	v=1395,44 m/s	v=1401,14 m/s	v=1426,78 m/s
40	v=1387,54 m/s	v=1363,27 m/s	v=1408,5 m/s

According to the values of the table, the ultrasound propagation speed in every agar solution with microparticles is lower than the speed obtained with no particles. Besides, as the particles concentration increases, the temperature decreases. Therefore, the sound wave remains longer in the tissue, contributing to the temperature rise.
In the figure 6, the graphic results of temperature for different concentrations are shown. It can be observed that when 40 g/l concentration are used, higher temperature are reached in less time than when 8 g/l are used, independently of the size of the silicon microparticle.

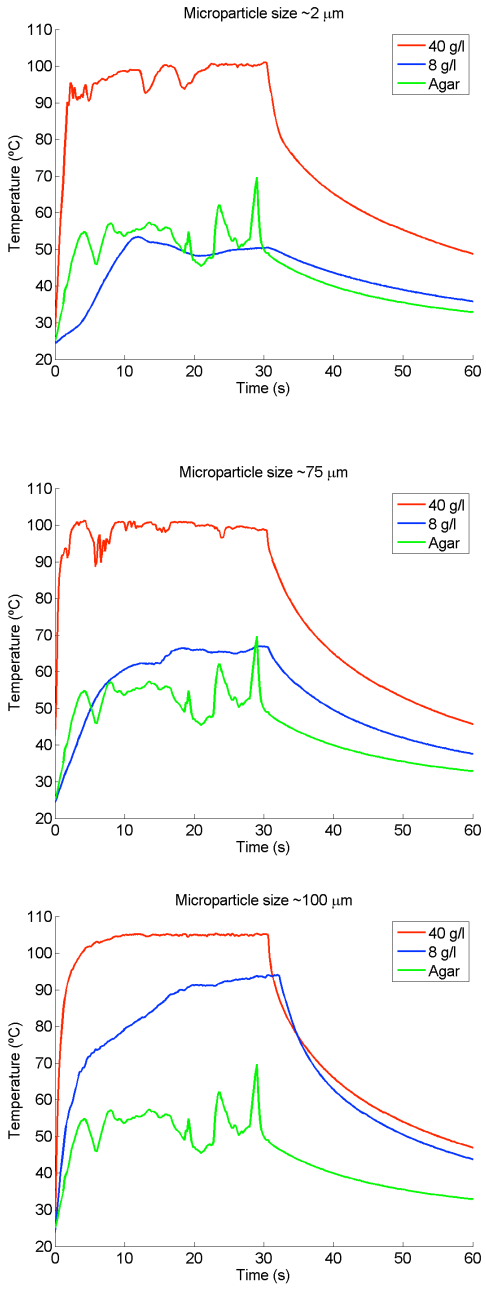

Figure 6: Temperature rise for (a) 2 μm particles, (b) 75 μm particles, (c) 100 μm particles.

In the figure 7 we can see the temperature rise for the two concentrations. Independently of the particle size, for a 40 g/l concentration temperatures higher than 95 ºC are reched in less than 2.5 seconds, whilst for a 8 g/l concentration, the higher temperature reached is 59 ºC for the 100 μm diameter particles and just 28 ºC for the 2 μm diameter particles.

For a 40 g/l concentration, the maximum reached temperature is around 100 ºC for all sizes, whilst for a 8 g/l concentration, the particle size is an influential factor, as for the 100 μm diameter particles temperatures of 94 º C are reached, while in the case of 2 μm diameter particles, the maximum reached temperatured is of 53 ºC.

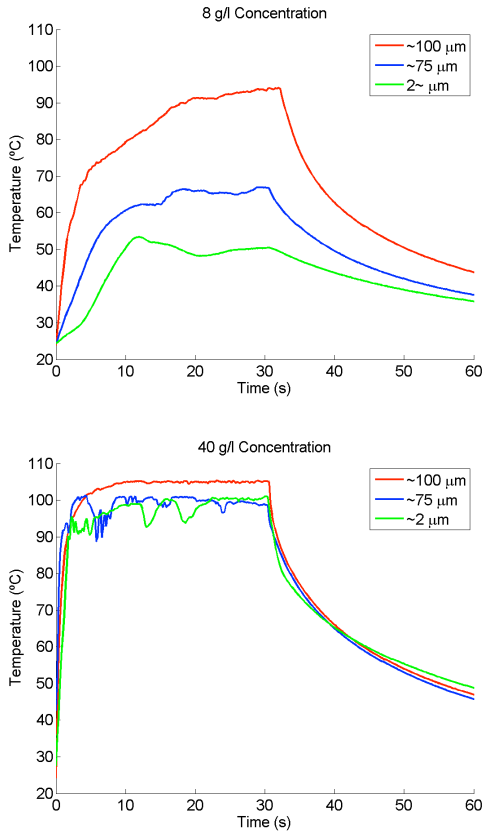

Figure 7: Temperature rise for (a) 8 g/l concentration, (b) 40 g/l concentration

As for the radiological images, there are clear differences between the samples with and wihout silicon microparticles (Figure 8).

Silicon microparticles increase the echogenicity of the sample, independently of the size and concentration of the microparticles. Because of its echogenicity, it is possible to distinguish the variations of the concentration of microparticles in the sample, as shown in figure 8.

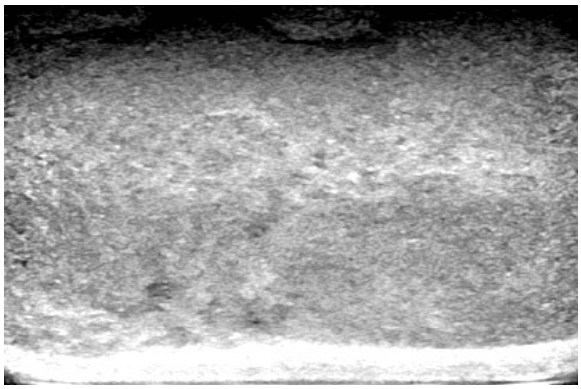

Figure 8: Ultrasound image with a 15 MHz probe. Sample with 40 g/L concentration of 100 μm particles.

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IV. Conclusions

The previous results suggest that, despite the fact that when adding silicon particles to an agar solution the ultrasound propagation speech decreases, and the energy remains more time inside the sample contributing to increase its temperature, this is not the principal cause. In that case, there would be a direct relation between the propagation speed and the reached temperature. In this paper, and due to the possibility of bubble formation within the preparation of the samples, it is possible that other mechanism such as cavitation are actively contributing to the heating.

It has been confirmed that for high enough concentrations, independently the size of the particles used, the temperature reaches 95 ºC, which is much greater than the 55 ºC reached in agar. It should also be pointed out that in presence of silicon microparticles, the maximum temperature is reached within three seconds.

In this paper, it has been demonstrated that it is possible to reach high temperatures with 2 µm particles when applying the right dose, so it would be of interest to study the behaviour of silicon nanoparticles as well.

Acknowledgment

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