The Highly Focalized Thermotherapy in the Treatment of Solid Tumors: Temperature Monitoring Using Thermography

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SUMMARY

The use of hyperthermia in the tumor treatment is based on the well-established concept that heat has selective lethal effects on tumor tissues. A new hyperthermia technique, the Highly Focalized Thermotherapy (HFT), was developed in an attempt to localize the heat in the tumor. The aim of the present study was to evaluate the capability of monitoring the temperature variation by using the HFT in a melanoma mice model, through thermography. B16F10 melanoma mice (C56BL6) were injected with a Ferrimagnetic Cement and exposed to a high frequency magnetic field to generate heat within the tumor. The animal body temperature was monitored through a thermal camera FLIR A325, after removing the fur in the area of the tumor. Through thermography, the skin temperature was assessed and logged its maximum value. The HFT application in the melanoma mice model resulted in a temperature increase in the tumor. Comparing the initial tumor temperature with the tumor treatment temperature, there was an increase of 5-6 ºC in the first 5-10 minutes, whereas the body temperature showed only a limited increase (2-3 ºC). In this superficial melanoma model, the animal's temperature can be monitored using a thermographic camera. It is possible to measure the temperature variation, simultaneously, in the whole body and in the tumor, during the treatment, preventing unwanted heat effects in other tissues.

1. INTRODUCTION

THyperthermia, in the tumour treatment, is based on the well-established concept that heat has selective lethal effects on tumour tissues (2). Nowadays, many techniques are available to produce hyperthermia, but they are generally limited by the in-ability to selective target the tumour cells, with subsequent risk of affecting adjacent healthy tissues (2, 4, 5). In an attempt to solve this limitation, a new hyperthermia technique was developed, the Highly Focalized Thermotherapy (HFT). This new methodology is based on the concept of the Magnetically Mediated Hyperthermia (MMH) (6). The technique consists in the direct injection of an experimental material, the Ferrimagnetic Cement (FC) within the tumour and then the exposition to a high frequency magnetic field (HFMF). The aim is to increase the tumour tempera-ture, based on the principle that a magnetic particle can generate heat, under a HFMF. Heat is than dissi-pated throughout the tumour tissues. With this ap-proach we pretend to localize the heat in the tumour region, to the intended temperature (4 to 10 ºC upper them the initial temperature), without damaging nor-mal tissue.

The temperature monitoring during the treatment is crucial, because at Higher temperatures, up to 56 ºC, will produce the unwanted "thermo-ablation", yield-ing widespread necrosis, coagulation or carbonization (3).

In superficial tumors such as the melanoma, the tumor temperature variation can probably be moni-tored through a termographic camera that will be a non invasive method for the temperature monitoring during the HFT treatment.

The aim of the present study was to evaluate the capability of thermography to monitor the temperature variation in a melanoma mice model during the HFT treatment.

2. METHODS

2.1 Tumor induction

The experimental tumours were induced by subcu-taneous inoculation of B16F10 melanoma cells (2 x 10^5 cells/80µl culture medium) in the C57BL6

animals dorsal lumbosacral region. Tumours grew freely until they reached approximately 10 mm in diameter (corresponding to ≈ 520 mm^3 in volume), which was observed 15 days after inoculation.

2.2 HFT treatment

FC is a calcium silicate cement that, with a determined powder/water ratio, a paste can be obtained (7). The FC paste was injected in the tumor and, 48h latter, animals were exposed to the HFMF (frequency 10 kHz) created by a vertical coil (diameter 110 mm, 12 turns), using the induction system High Frequency Electronic Furnace K10/RV (CALAMARI and Milan, Italy).

2.3 Temperature monitoring

The animal body temperature was monitored through a thermal camera, FLIR A325, and analyzed using the software ThermaCAM™ Researcher Professional 2.9. The control of the HFMF strength was manually adjusted, so that the desired temperature of the tumor was kept constant. To allow a more accu-rate body temperature measurement using thermography, the fur that covers the animal's body was removed in the tumors area. The camera color pallet range was set from 19.5 to 43 ºC, and the area to be evaluated, defined as a circle within the software, logged the maximum value.

3. RESULTS

The HFT application in the melanoma mice model resulted in a temperature increase in the tumor. It was observed, through the thermographic image that the initial tumour temperature varies between 30 and 35 ºC and the animal's body temperature showed values between 27 and 31 ºC, depending on the animal (Figs. 1A and 3A). It is important to note that the animal all body fur was not removed and this certainly interferes with temperature lecture, due to the fur isolation of the temperature and to the different emissivity, and this is the major explication for the temperature discrepancy between the tumor and the animal's body. However, comparing the initial tumor temperature with the tumor treatment temperature, there was an increase of 5-6 ºC in the first 5-10 minutes, whereas the body temperature showed only a limited increase (2-3 ºC). When the desired temperature was reached, it was maintained during all the treatment period, by controlling the magnetic field intensity (Fig. 2).
The temperature increase during the HFMF exposition is confirmed in all animals, independent of its initial temperature, as seen in figs. 1B and 3B. It was also evaluated the capacity to increase the initial tumor temperature, more than the 6 ºC, and it was possible by the augmentation of the HFMF intensity in 2-3minutes (Fig. 3C). It is possible to increase the tumor temperature 9-10ºC above the initial temperature.

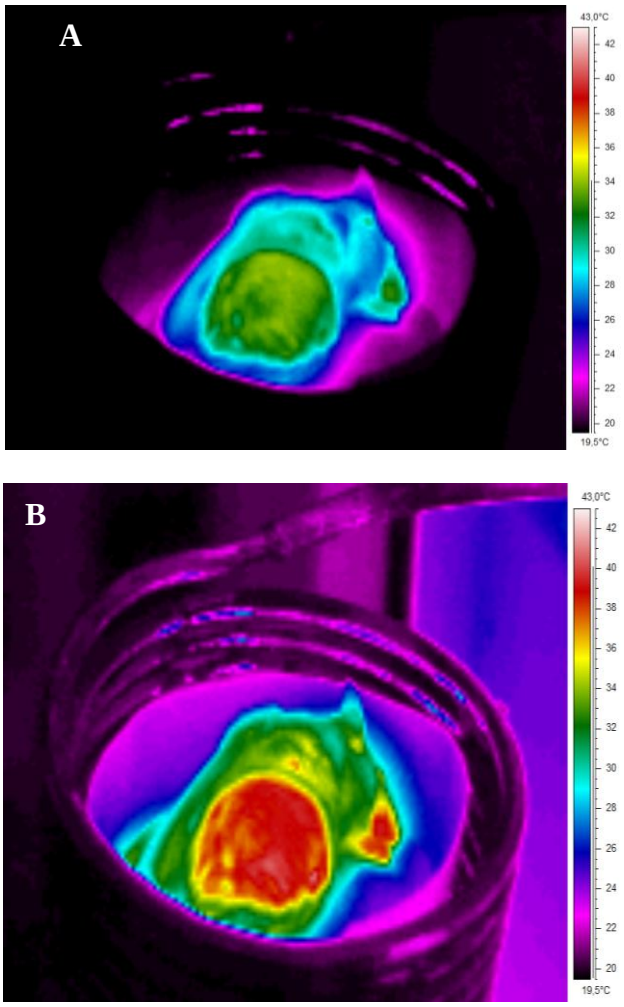

Fig. 1 - Animal thermographic image. A) Initial state temperature - before the HFMF exposure. B) During the treatment - 30 minutes of exposure to the HFMF.

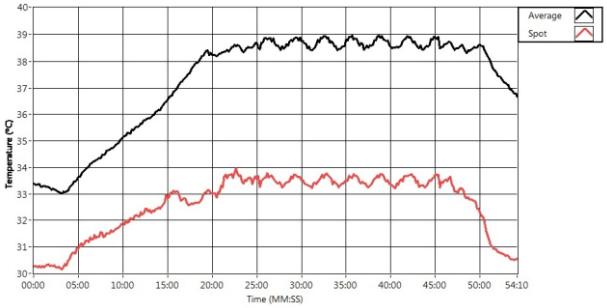

Fig. 2 - Time/temperature monitoring during the animal's HFMF exposition. Tumor area and the point (spot) in the animal's body far from the tumor.

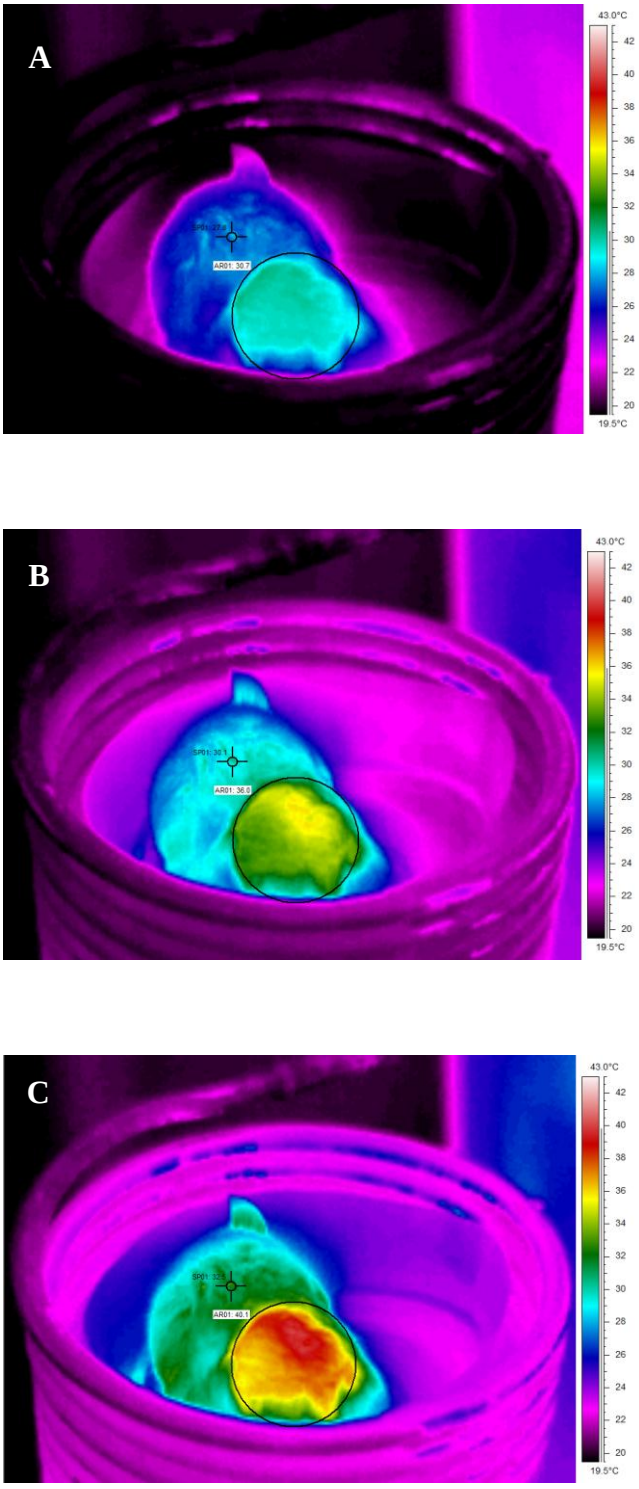

Fig. 3 - Animal thermographic image. The software used with the thermographic camera allows the determination of defined temperature points (spot) or areas.
A) Initial - area 30.7 ºC, spot 27.8 ºC.
B) During the treatment - area 36 ºC, spot 30.1 ºC.
C) It is possible to increase the tumor temperature through the augmentation of the magnetic field intensity. Area 40.1 ºC and spot 32.5 ºC.

4. CONCLUSIONS

In this superficial melanoma model, the animal's temperature can be monitored using a thermographic camera. With this methodology, it is possible to measure the temperature variation, simultaneously, in the whole body and in the tumor, during the treatment. Since energy deposition in tissues as well as cooling by blood flow are difficult to model, a good thermometry control is always needed in clinical practice. With the thermographic camera used in this study, it is possible to determine the temperature distribution in the tumor, the tumors average temperature, selected points in the image field and the temperature evolution along the time, just throughout the surface observations. This is essential to control the tumor temperature during the treatment period. In some studies it was used an optical temperature probe inserted intramuscularly near to the tumor, or within the tumor, near to the injection site of the magnetic particles. The disadvantages are that the temperature measured doesn't correspond to the real tumor temperature, is necessary skin opening and the leakage caused in the gelatinous melanoma tumor parenchyma increases the variability in tumor volumes (Saito 2008). The only limitations of the thermographic camera, is the tumor location. In the melanoma model and in a mammary tumor model (1), superficial tumors, this methodology has a great potential as a thermometry control method. In deeper location tumors, is necessary to use thermometry probes, which are invasive and give us just a temperature point and not the real temperature of the entire tumor.

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