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DYNAMIC 'IN VIVO' PERFORMANCE OF TEMPERATURE CONTROLLED LOCAL MICROWAVE HYPERTHERMIA AT 2.45 GHz

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Abstract

A microwave system was constructed, suitable for local heating of animal tumours. The system basically consists of a 2.45 GHz generator, operating in a pulsed power mode, a micro-thermocouple temperature monitoring equipment and different applicators. Performance was tested on phantom tissue and by heating solid rat tumours, revealing differences in the heating response of the control-loop when both cases are compared. The system is capable of heating the tumours to a desired temperature level (eq. 43 °C) and maintains temperature within ± 0.1 °C during treatment.

1. Introduction

Hyperthermia is studied as an adjuvant to chemo-therapy or ionizing radiation in cancer therapy. Among the various heating techniques[1], electromagnetic (e.m.) radiation and ultrasonics are the two principal modalities potentially useful for local tissue heating. It is well known that the efficiency of hyperthermia depends on the temperature applied and the duration of treatment[2]. Therefore it is very important to produce a controlled heating of the tumour at a temperature tolerated by the surrounding normal tissue.

This paper describes the development of a temperature controlled 2.45 GHz microwave system suitable for controlled heating of small animal tumours. Dynamic heating properties using different applicators are studied at phantom tissue and at tumour tissue in situ.

2. Microwave apparatus

The system basically consists of a 2.45 GHz microwave generator (Philips MW 127) modified for external power control (fig. 1). The generator essentially includes a magnetron and can be operated at 25 W or 200 W maximum output power. In the later experiments, maximum power was 25 W. The control signal is gained from a set of micro-thermocouples (100 µm diam., Medtra phys.). The generator operates in a pulsed power mode, thus eliminating errors in the temperature reading due to direct heating of the thermocouples in the electromagnetic field. The temperature sample is taken at the end of the switched-off state, allowing the temperature of the probe to approach the ambient temperature. Temperature measurement was performed in a bridge arrangement, using the temperature of melting ice as a reference.

The PI-controller (PI = proportional-integral) was especially designed for the purpose of hyperthermia control. A fast heating transient to the stationary temperature was considered to be essential in order to define the dosis of applied radiation. To that respect, the control-loop may be operated in two modes. In a semi-automatic mode, a sequence of two prescribed output-powers can be programmed and applied for given time-intervals, until the final temperature-control is switched on. In an automatic mode, the integral portion of the control-loop is not switched on, until 80% of the stationary temperature are reached. Both modes allow a fast heating-up without excessive temperature-overshoot. If such an overshoot occurred, a safety threshold would be put into action, which switches off the power at a preselected temperature (0.2, 0.3, 0.5 °C above the chosen stationary temperature).

The amplification of the control-loop can be adjusted by means of the on-off-ratio of the power generator. In practise, it is matched to the efficiency of the microwave applicator, and to the (to some extent) incidental coupling between applicator and tumour. On-off-ratios between 2:1, 3:1 and 4:1 may be chosen, a variation that fits practical requirements.

The temperature outputs of four thermocouples including the signal, which is used for control, are stored on a recorder, together with a signal, proportional to the difference of the incident and reflected power at the applicator, i.e. the radiated power. The hyperthermia-controller incorporates a timer circuit, which turns the generator off after the treatment.

Three different applicators were tested during the experiments, which are adapted to a small tumour size comprising a commercially available non-contact spiral antenna (Bosch) with circularly polarized radiation (approx. 7 cm diam.), and a H_{10}-waveguide with J-band dimensions (cross section 16 x 34 mm) filled with a multilayer of Al_2O_3- and K25-ceramic, showing linear polarization. A crossfire arrangement with two of the waveguide applicators, driven in cophase from the same generator was also used.

3. Phantom tissue and tumours

The control-loop was tested first using jelly phantom materials similar to that used by [3]. Because of expected changes during hyperthermia treatment of the tumours, final adjustments were made in experiments with a solid rat tumour (rhabdomyosarcoma R1H). These are transplantable solid tumours, previously described in [4]. The rhabdomyosarcoma R1H appears to be a suitable object for studies on hyperthermia, since it is slowly growing, and, when transplanted in the flank of the animals, it can be easily treated by microwaves. The volume of the selected tumours was between 2 and 3 cm^3. For treatment, rats were anaesthetized. Under anaesthesia tumour and body temperature were lowered by more then 1 °C.

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In fig. 2, the heating of a rat tumour by the spiral antenna is shown. Three thermocouples are implanted into the tumour: the first subcutaneously, facing the applicator, the second intratumoral and the third subcutaneously under the tumour. A fourth thermocouple is inserted to monitor the rectal temperature of the rat. The rat is lying on isolating foam in order to eliminate cooling of the body by heat conduction.

With the system described the following experiments were performed:

1. The heating effect due to unwanted interference between thermocouples and electromagnetic fields was studied 'in vivo'.

2 The dynamics of the control system were evaluated on phantom tissue and on tumours. To this end, short hyperthermia sessions were performed on the rats with a duration of 15 min, and a stationary temperature of 43 °C at the tumour center or the subcutaneous site.

3. The different applicators and crossfire antennas were tested under the aspect of local heating.

3. Results and discussion

Fig. 3 shows the influence of e.m. fields on the temperature reading. The thermocouple was implanted subcutaneously, and temperature was 43 °C. A spiral antenna was used in the test. With such a device due to the circular polarization of radiation, decoupling of the e.m. fields and the thermocouples is not possible. In the case of a linearly polarized antenna, thermocouples and fields may be decoupled to a certain degree by orthogonal positioning. Hence, the case of a circularly polarized antenna is more critical. Fig. 3 shows, that the temperature-reading increases by 0.25 °C when 25 W of power are applied. If the power is turned off, the temperature decreases and approaches to the temperature of the tumour. In the case shown, temperature sampling at 1 sec after power turn-off causes less than 0.1 °C error in the recorded value. Therefore, the sampling circuit was adjusted to take its samples after a 1 sec interval.

Examination of the closed loop response on phantom tissue yielded the temperature response of fig. 4 (ceramic filled applicator). After 1 min heating time, the desired temperature of 43 °C at 10 mm below the surface is obtained. Then the irradiated power reduces. The dynamic behaviours of temperatures in 5 mm resp. 15 mm depth clearly reveal the superposition of the various temperatures from portions due to direct heating by e.m. fields and contributions caused by heat transport in the medium. The curves show that temperature decreases approximately exponentially with depth.

The 'in vivo' measurements (fig. 5) reflect a completely different situation. Although the spacing of the various thermocouples is similar (i.e. subcutaneous ≈ 5 mm, intratumoural ≈ 10 mm, below tumour ≈ 15 mm), heat distribution is completely different. The subcutaneous thermocouple served for temperature control in the case shown. Keeping the subcutaneous temperature at a desired value (43 °C) leads to a temperature maximum in the tumour center and to about the same temperature as at the subcutaneous site below the tumour. A kind of focusing effect is obtained without using a focusing antenna.

Differences to the phantom measurements may be explained by the different heat transport mechanisms. In the living system heat is transferred by blood flow from the skin and the tumour. It is well known, that heat modifies blood flow in the skin and the tumour in different ways.

In fig. 6, oscillations are shown which sometimes occurred and decayed in the temperature control-loop, although no environmental changes were involved, events which never took place in phantom measurements. Such changes could be attributed to thermal regulation mechanisms of the tumour itself or the animals. This phenomenon has to be further investigated.

Comparing the various applicators, it was found, that the ceramic-filled waveguide antennas exhibit a much better efficiency, i.e. a power coupling between tumour and antenna. A better localization of radiation is obtained, thus reducing the overheating-danger of unwanted regions. This is evidenced by the only weakly rising rectal temperature of the rat (fig. 5). Using the spiral antenna, care has to be taken, to aim the antenna beam to the tumour alone. The radiation efficiency is lower compared to the ceramic-filled applicator.

A final test was made with a crossfire arrangement of two ceramic-filled antennas, allowing for radiation application from below the tumour as an additional possibility (fig. 7). Both antennas act in cophase with the electrical vectors in parallel, giving rise to constructive interference of the fields inside the tumour. Features of such a scheme are an even better power concentration to the tumour, compared to the single antenna application. Less power per applicator is applied and faster heating to the final temperature is obtained.

4. Conclusions

With the described hyperthermia system, tumour-heating and stable temperature control due to microwave irradiation could be obtained. A fast heating to the desired temperature within 3 min was achieved. Significant differences for the 'in vivo' situation were observed compared to phantom measurements during both the transient and the stationary phase of temperature control. Thus evidencing the requirement to rely on 'in vivo' tests alone when investigating the control-loop. Microthermocouples may be used for temperature reading, when temperature sampling is performed at least 1 sec after power turn-off. Then the temperature error will be less than 30% of the temperature deviation during power irradiation. The misreading has to be minimized by proper orientation of the thermocouples. A ceramic-filled waveguide applicator shows a much better heating capability at small animal tumours compared to a commercially available non contact spiral antenna.

The heat distribution and the heating transient are optimum for a crossfire arrangement of applicators, although positioning of the rat is not as easy as for a single applicator. The amplification of the control-loop has to be matched to the kind of applicator chosen. The system is capable of heating the tumours to a desired temperature level (e.g. 43 °C) within 3 min and maintains temperature to ± 0.1 °C during treatment.

5. Acknowledgement

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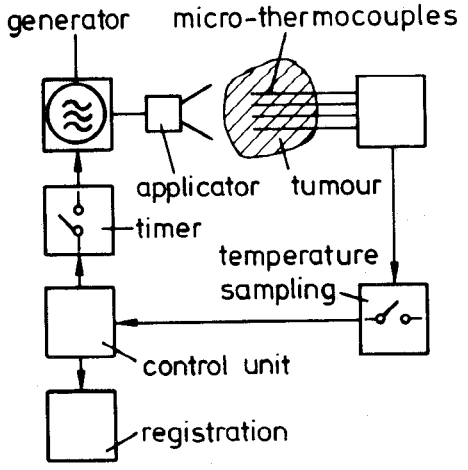

Fig. 1: Block diagram of the microwave hyperthermia system

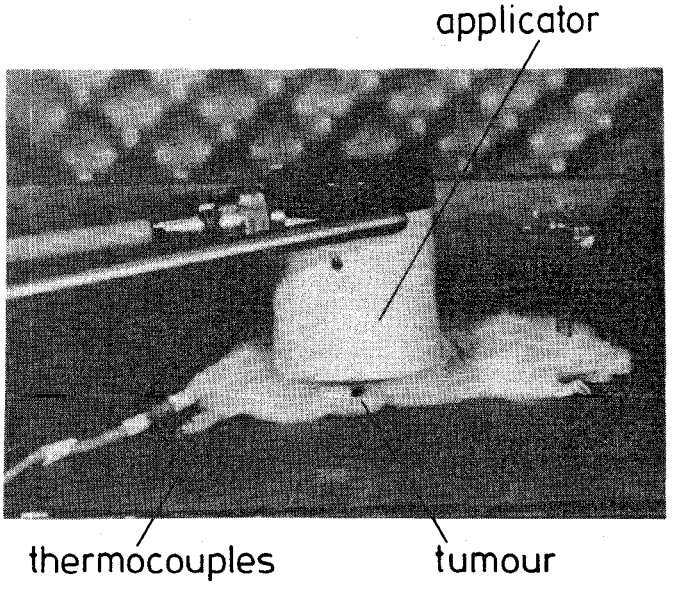

Fig. 2: Heating of rat tomour

References

1 Hand, J.W., ter Haar, Gail: 'Heating techniques in hyperthermia'. British Journal of Radiology, vol. 54, 1981, pp. 443-466.

2 Zywietz, F.: 'Effect of microwave heating on the radiation response of the rhabdomyosarcoma'. Proceedings of the 10th L.H. Gray Conference. British Journal of Cancer, Supplement V (in press).

3 Guy, A.W., Lehmann, J.F., Stonebridge, J.B.: 'Therapeutic applications of electromagnetic power'. Proc. IEEE, vol. 62, 1974, pp. 55-75.

4 Jung, H., Beck, H.P., Brammer, F., Zywietz, F.: 'Depopulation and repopulation of the R1H rhabdomyosarcoma of the rat after X-irradiation'. Europ. J. Cancer, vol. 17, 1981, pp. 375-386.

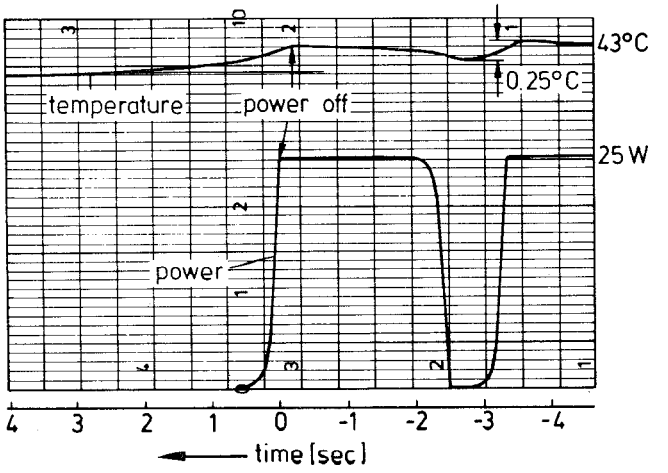

Fig. 3: Influence of microwave radiation on temperature reading

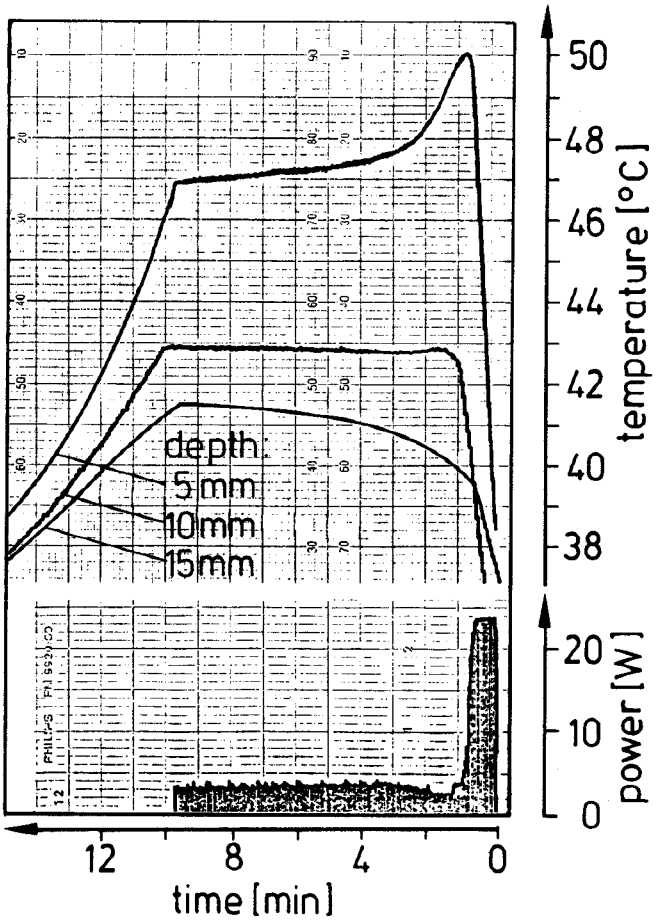

Fig. 4: Heating of phantom tissue: irradiated power and temperature distribution

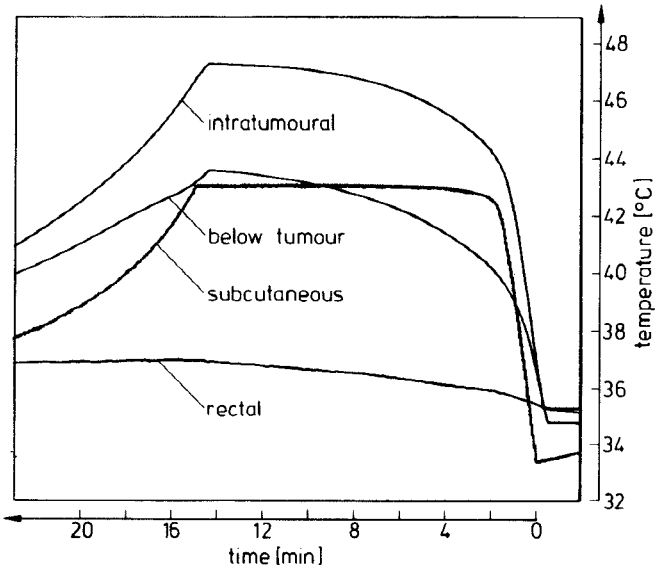

Fig. 5: Heating of a rat tumour in situ at 43 °C

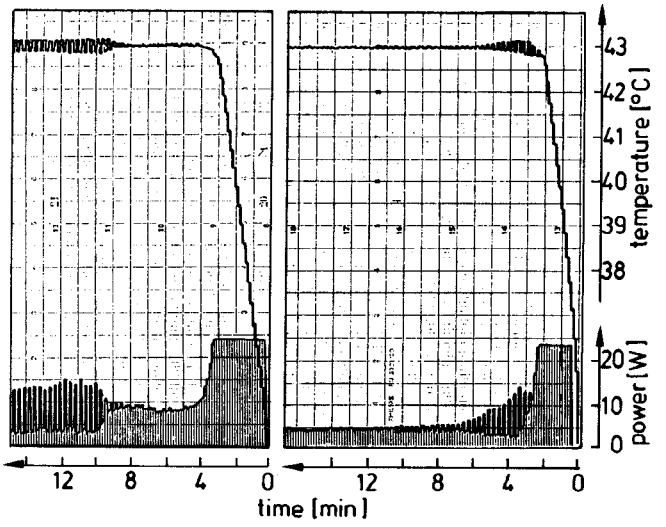

Fig. 6: Oscillations occuring in the control loop, measured in the 'in vivo' situation

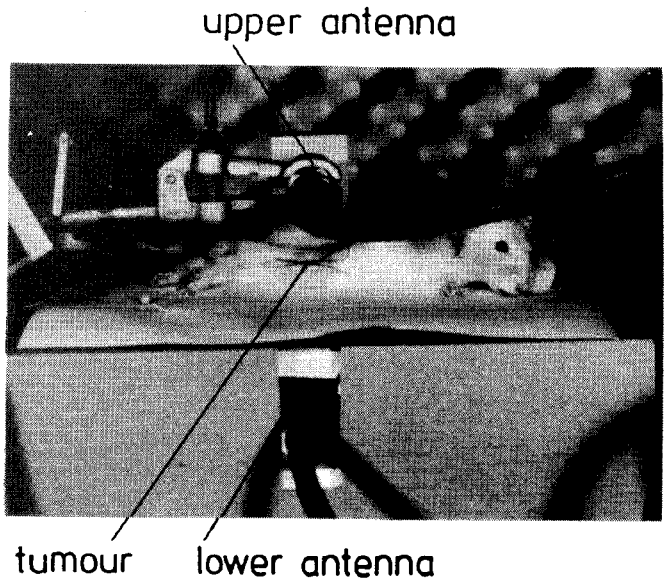

Fig. 7: Heating of a rat tumour in a cross-fire arrangement with two ceramic-filled waveguide applicators