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Scientific note

Multi-point feedback control system for scanned, focused ultrasound hyperthermia

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1. Introduction

In early hyperthermia heating systems, single-point temperature control (either manual or automatic) matched the capabilities of the available, geometrically fixed heating systems (one amplitude was used to control one temperature). However, in recent years a second generation of hyperthermia heating systems has been developed which are characterised by the ability to vary the geometric pattern of the power deposition. These include multi-element microwave surface applicators (Hand *et al* 1986), similar ultrasonic systems (Ogilvie *et al* 1986), mechanical scanning of a single external microwave (Lee *et al* 1986) or ultrasound applicator (ter Haar and Hopewell 1985), phased array surface applicators (Lin 1986), scanned focused ultrasound systems (Hynynen *et al* 1987, Lele and Parker 1982, Seppi *et al* 1985), phase and amplitude control of multiple antenna interstitial microwave systems (Trembly 1985, Trembly *et al* 1986) and multi-electrode localised current field systems (Doss 1985). These systems have significant potential for providing improved temperature distributions due to their flexibility in depositing power. However, concomitant with this ability are certain complexities and decisions, most importantly how to automatically control the power deposition pattern during treatments.

Previously reported multi-point controllers include the two-point controller of Knudsen and Heinzl (1986) and Knudsen and Overgaard (1986), a two-dimensional simulation of an interstitial radio-frequency controller by Doss (1985), a one-dimensional simulation of a proposed controller by Babbs *et al* (1986) for localised hyperthermia, and a two-dimensional simulation of an optimal temperature controller for a phased array RF hyperthermia system by Knudsen and Hartmann (1986). Nikawa *et al* (1986) present a controller which varies the applied power of a direct contact converging applicator and cooling water flow rate to vary the position of maximum temperature in tissue. With scanned, focused ultrasound the applied power can be varied as a function of position as proposed and clinically used by Dar and Lele (1984).

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2. Multipoint controller

The multi-point controller developed herein can be described as a set of separate single-point controllers operating sequentially to control a multi-input, multi-output distributed parameter system. The assumption that this distributed parameter system can be effectively controlled by a set of single-input, single-output controllers is valid if the coupling between the spatial regions controlled by each of these controllers is small. This would be true if the thermal energy transport between the regions is small, which should be the case if the controller is effective; that is, if the tissue on and inside the scan path is elevated uniformly to the set-point temperature, this will reduce coupling by thermal conduction and directed perfusion between the regions.

The controller is implemented on a scanned, focused ultrasound hyperthermia system in use at the University of Arizona (Hynynen *et al* 1987, Shimm *et al* 1988). This system consists of a five-degrees-of-freedom computer controlled, motorised mechanical gantry with four 1 MHz focused ultrasonic therapy transducers focused on a single point. The system is capable of varying power along an arbitrary scan path; however, an octagonal path has usually been employed in our clinical treatments (Shimm *et al* 1988). Two such (idealised) scan paths, thermocouple locations and control regions are shown in figure 1. During the hyperthermia treatment the scanning pattern is continuously scanned at the speed of 25 mm s^{-1}. The multi-point controller is divided into N single-point controllers, N being the number of control regions. The power applied in each region is controlled by the thermocouple in or nearest to that region. The single-point integral control law used for each of the regions is given by

$$P_j^{i+1} = P_j^i + \Delta P_j^i \quad \text{where} \quad \Delta P_j^i = G(T_j^s - T_j^i).$$

Here P_j^i is the power in the jth region at the ith time step, ΔP_j^i is the change in the jth region power at the ith time step, T_j^s is the jth region's set-point temperature, T_j^i

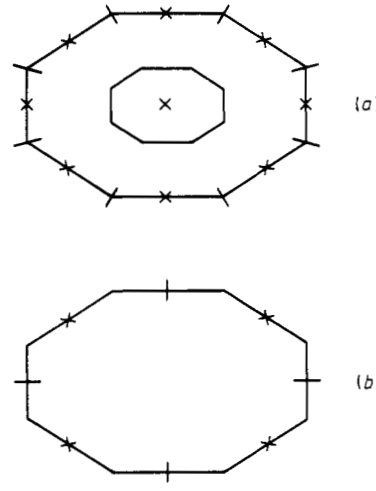

Figure 1. Idealised scanning patterns for (*a*) two concentric octagonal scans with a nine-point $N = 9$ controller and for (*b*) a single octagonal scan with a four-point $N = 4$ controller. The crosses indicate the controlling thermocouple locations, while the dashed lines indicate the boundaries of the regions controlled by the individual thermocouples. In (*a*) the central thermocouple controls the power for the complete inner octagon. In practice the thermocouple locations were not spaced so regularly.

is the jth region's temperature at the ith time step, and G is the controller gain. This form of the control law provides for small steady-state error with no offset and avoids overshoot due to control saturation.

3. Experimental results

The multi-point controller was tested using separate *in vitro* and *in vivo* canine kidney systems, and using *in vivo* canine thigh experiments. The *in vitro* experiments used the kidney preparation technique of Holmes *et al* (1984), with the single renal artery isolated and attached to an artificial perfusion apparatus. Thus, the perfusate flow, the ambient temperature and the thermocouple locations could be well controlled and measured (Zaerr 1989). The *in vitro* experiments demonstrated a number of important points, which are summarised here and discussed in more detail in Johnson (1986). First, the multi-point controller produced a temperature distribution close to that desired within this well defined environment. Second, there does exist an optimal gain setting that yields the best performance (best with respect to the classical dynamic response characteristics of minimising the rise time, overshoot and settling time in response to a step function input). Third, the major characteristics of the system response can be modelled and analysed with a simple first order model and its performance predicted (Johnson 1986, Kress *et al* 1990). The encouraging results of these tests prompted further *in vivo* tests.

In vivo kidney tests were performed in the kidney system developed by Kundrat *et al* (1986) and in dog thighs. The kidney system uses a vascular occluder and an ultrasonic Doppler velocity transducer on the isolated renal artery. The blood flow can be well controlled and measured; however, the ambient temperature and the thermocouple locations cannot be as well controlled as in the *in vitro* kidney system. Figure 2 shows the temperature responses for a step change in set-point temperature of 7 °C for a five-region, multi-point controller scanning a single octagonal path in one plane for the *in vivo* kidney system. The top figure shows the maximum and minimum temperatures of the five controlled thermocouples; i.e. the extrema control thermocouple temperatures, between which the three other control thermocouple temperatures fell. The middle figure shows the curves from the extrema thermocouples inside the scan region, i.e. from all of the thermocouples (both controlled and not controlled) inside and on the scan path. The bottom figure shows the temperatures of the two extrema thermocouples outside the scan region. These curves illustrate that, first, all the temperatures at locations on or inside the scan path were elevated to or above the set-point temperature. This is what one desires for a hyperthermia treatment so that the tumour receives the proper thermal dose. Second, the temperatures at locations outside of the scan path were kept below the set-point temperature. This is also desired so that healthy tissue is not damaged. Third, different control regions experience different responses to blood perfusion changes (which is logical because different control regions are located at different physical, and thus physiological, locations within the kidney). Finally, the controller remains robust even for large step changes in blood perfusion. This is important for hyperthermia treatments because of expected changes in blood perfusion during an actual treatment resulting from vasodilation and constriction.

Figure 3 highlights the differences in the temperature responses for manual against automatic control for a 5 °C step change in the control temperature in an *in vivo* canine thigh. The top figure shows the temperature against time response for the two extrema

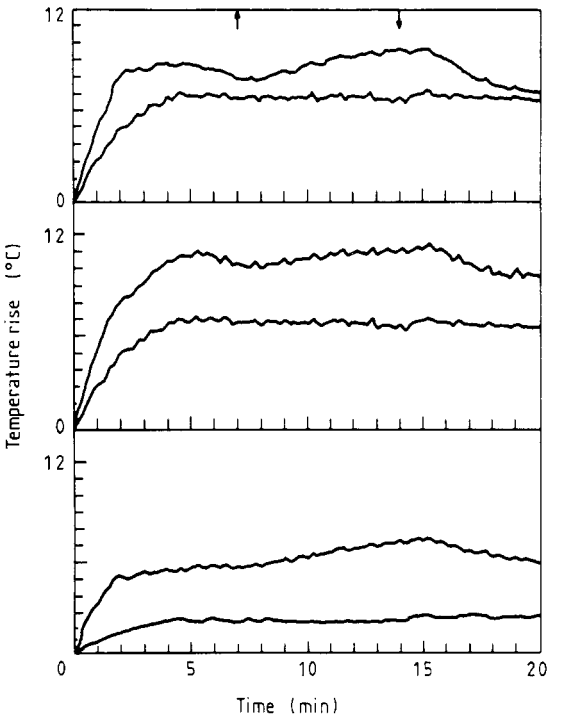

Figure 2. Five-point controller experimental results for a controlled temperature of 7 °C; (top) extrema of the controlled temperatures, (middle) extrema of all measured temperatures in the scanned volume and (bottom) the extrema of all measured temperatures outside the scanned volume, all for an *in vivo* dog kidney experiment in which the total blood flow to the kidney was changed from 28 ml min^{-1} to 52 ml min^{-1} at ↑ and returned to 28 ml min^{-1} at ↓.

control thermocouples when the single power amplitude is controlled manually. The bottom figure shows the responses when a nine region multi-point controller is used. The falling temperatures at around 10 minutes in the top figure is a result of thermally induced vasodilation. Clearly, the multi-point controller is doing a much more effective job of keeping the temperatures around the desired set-point temperature.

4. Conclusions

These results from the *in vitro* and *in vivo* kidney preparations with blood perfusion changes introduced purposely, and from *in vivo* canine thighs having blood perfusion changes resulting from thermally induced vasodilation demonstrate the following. First, a multi-input, multi-output, distributed parameter hyperthermia system can be controlled as a set of decoupled, single-input, single-output, non-distributed systems using the multi-point controller described in this paper. Second, that the multi-point controller appears to be quite robust, and can successfully compensate for both changes in reference temperature and blood perfusion, the two major variables in hyperthermia treatments. Third, the multi-point controller can successfully create a relatively uniform plateau of controlled therapeutic temperatures inside the scanned region, with a rapid temperature fall off outside that volume. While these are significant improvements over single point control, to become clinically practical, the two-dimensional (planar)

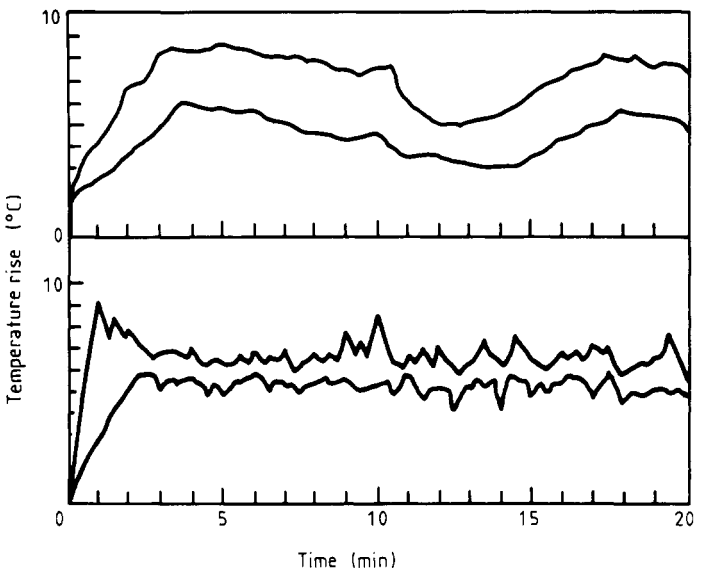

Figure 3. Temperature against time curves for an *in vivo* dog thigh experiment with a controlled temperature of 5 °C: the top figure is for manual control (note the thermally induced vasodilation at approximately 10 minutes); the bottom figure is for the nine-point control algorithm. The extrema of the controlled thermocouple temperature curves are shown. All other controlled temperatures fall between these two curves.

results of this study need to be extended to three dimensions. Other future improvements to be included are an improved single-point controller (Lin *et al* 1990) and the inclusion of adaptive control and parameter estimation (Kress 1988).

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