Acta Oncologica Vol. 33, No. 4, pp. 451–455, 1994

DEEP HEATING USING A MOVABLE APPLICATOR PHASED ARRAY HYPERTHERMIA SYSTEM

A preclinical feasibility study

POVL RASKMARK, STEN N. HORNSLETH, LISBETH N. SALLING, JACOB C. LINDEGAARD and JENS OVERGAARD

A preclinical evaluation of the 'movable applicator phased array hyperthermia system' was performed. The system employs four coherent applicators enabling power steering by amplitude and phase control. This concept has already been used in other systems, but the combination with a compact applicator design and easy movement of applicators has not been used before. The paper contains a description of the system and a verification of its performance using quality assurance tests with scanned E-field measurements. A clinical simulation was performed in pig to address the clinical feasibility of the system. The target volume was the left kidney. Two heating sessions, with and without occluded blood-flow to the kidney, were performed. In the low-flow experiments a temperature of 48°C and 46°C was obtained in the upper and lower pole of the kidney respectively. For the high-flow experiment the temperature in the upper pole was 48°C.

Electromagnetic (EM) radiation at frequencies below 100 MHz seems to offer the best possibilities of achieving loco-regional deep heating (1). A number of deep heating systems which create some focusing of the electromagnetic power has been reported in the literature: the annular phased array (2), the four waveguide system (3), the coaxial TEM applicator (4), and the capacitive ring applicator (5).

All systems are designed to produce a circumferential, radiative field with the electric field lines parallel to the body axis of the patient, having the advantage of a low SAR level in the superficial fat layers and maximum SAR in the central part of the body. Differences exist in operating frequency, number of applicators and the ability to control. Thus the coaxial TEM and the ring applicator use patient position to steer power whereas the other systems use amplitude and phase control.

In order to improve the versatility and patient compliance a movable applicator phased array hyperthermia system (MAPAHS) was developed through a multi-institutional collaboration. In contrast to other systems the MAPAHS offers the possibility of individual applicator positioning, amplitude and phase control at the same time. In addition, the patients are less constrained and the applicators can easily be removed and their position changed. This is in agreement with Yuan et al. (6) who concluded that devices with movable apertures may play a useful role in clinical hyperthermia due to their flexibility and potential of increased comfort to the patient. The Danish developed MAPAHS is in principle finalized as regards its design, and a phase I–II trial is planned to start at the Department of Oncology in Bergen, Norway as a part of a Scandinavian collaborative project on hyperthermic oncology.

The aim of the present study was to investigate the clinical feasibility of the MAPAHS by performing a pre-

Accepted 30 March 1994.

From the Department of Communication Technology (P. Raskmark, S. N. Hornsleth), Aalborg University, Denmark, Department of Oncology and Radiation Physics (S. N. Hornsleth), Haukeland Sykehus, Bergen, Norway, and Danish Cancer Society, Department of Experimental Clinical Oncology (L. N. Salling, J. C. Lindegaard, J. Overgaard), Aarhus University Hospital, Denmark.

Correspondence to: Povl Raskmark, Aalborg University, Department of Communication Technology, Fredrik Bajers Vej 7, DK-9220 Aalborg, Denmark.

 ISSN 0284-186X

clinical simulation in vivo, with special attention to the influence of the blood flow on the heating ability.

The Movable Applicator Phased Array Hyperthermia System

Figs 1 and 2 show an overview of the MAPAHS. The system has four balanced coaxial applicators (BCA) (7) with integrated water bolus, balun (balanced to unbalanced network) and impedance transformer. The water bolus was made from 50 μm platilon U072, since this material has a very high elasticity, enabling the bolus to adapt easily to different contours, and to sustain cleaning with most antiseptics. The water bolus is mounted on the applicator using an O-ring and a clamp allowing the water bolus to be changed easily. The applicator is equipped with self shutting quick couplings and with a flow indicator to monitor the water flow through the bolus. The balun and impedance matching are made with transmission lines mounted on the back of the applicator. The applicators are mounted on arms controlled by a multi-function joystick which also controls the volume of water in the boluses. Each bolus has a separate, closed system maintaining a constant volume and flow in the bolus. The bolus water flows through a set of heat exchangers where cooling is achieved by running cold water from an external cooling unit through the heat exchangers. Heating is achieved by applying power to the heating elements inside the heat exchangers. The water bolus temperatures are individually controlled and monitored.

The power generator supplies 4 coherent channels with individual amplitude and phase control, with a phase resolution of 7° and an amplitude resolution of 0.1 dB. The generator can be tuned in the range of 65 to 75 MHz. The power amplifier is rigid, stable and with 350 W output power per channel (8). A set of directional couplers on the output of the power amplifiers allows the forward and reflected complex voltages on each channel to be measured automatically, using an HP 8405A Vector Voltmeter.

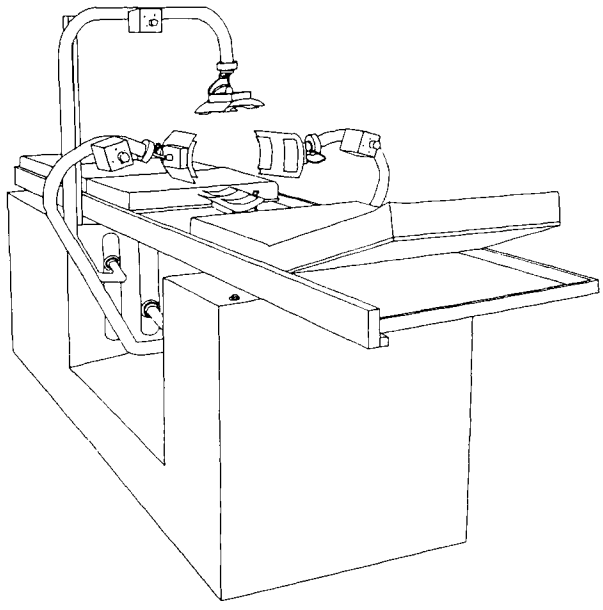

Fig. 2. Details of the movable applicator phased array hyperthermia system, showing the patient couch with the four applicators (without water bolus).

The thermometer is capable of measuring a maximum of 56 points, the probes are copper/constantan thermocouples from Bailey. The thermometer has a resolution of 0.05°C with an accuracy of 0.1°C in the range of 36°C–48.8°C. Because of the risk of self-heating the thermometer leads have been equipped with ferrite toroids. These toroids limit the high frequency currents running on the leads and thereby to some extent prevent self-heating. A duty-cycle is also used, so that power is switched off for 10 s before measuring the temperatures. Since the invasive probes used with the thermometer are conducting, care should be taken to avoid hazardous situations. This has been done by using batteries as power supply in the thermometer, and plastic optical fibres to connect the thermometer with the central computer. In this way the thermometer is completely isolated from ground and mains supply.

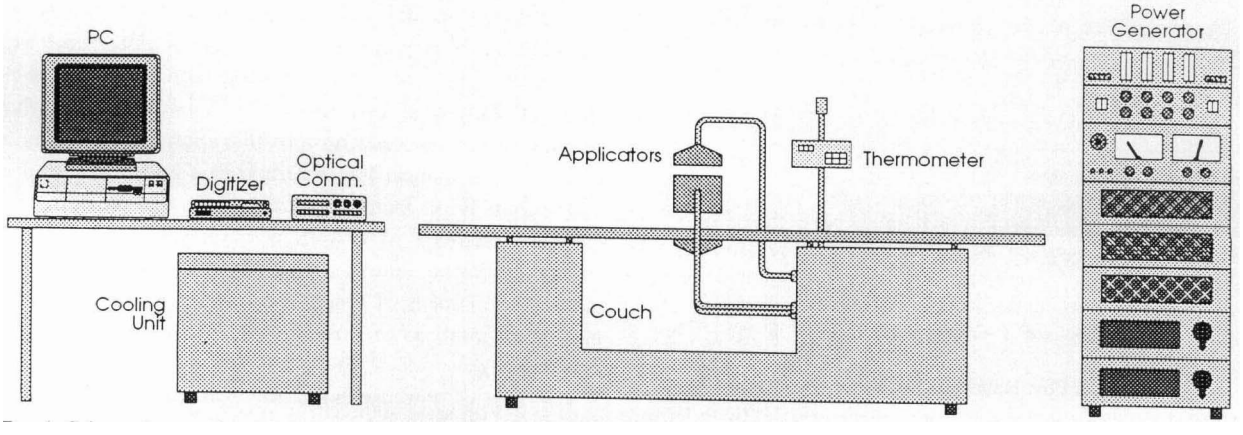

Fig. 1. Schematic overview of the movable applicator phased array hyperthermia system.

The central computer is a standard PC with a digitizing tablet. The PC is connected to the optical bus via a multiplexer. The software is built around a real-time kernel, enabling fixed sampling intervals and duty-cycle. The software features a window environment with scroll down curtains and pop-up menus and warning/alarm messages. The control software collects the following data from the subunits via the optical RS-232 bus or from the keyboard: forward/reflected amplitude and phase on all channels, water temperature in all boluses and in the cooling tank, all probe temperatures and all user inputs and warnings/alarms during treatment. With the digitizer a CT/MR scan of a cross-section of the treatment area can be entered and applicator and probe positions can be marked. This piece of information is stored together with the treatment data in the treatment file. The cross-section can also be displayed in a window during treatment and information on the current temperatures, amplitudes and phases will be shown as colours on the cross-section. The information can also be displayed in windows as standard x/t graphs.

Phantom measurements

To assure the performance of the system a series of phantom measurements were carried out, using a scanned E-field probe (9). The phantom was a standard CDRH (centre for devices and radiological health) elliptical phantom (10) (inside: 30 cm × 20 cm) with a 1 cm fat layer and filled with 3 g/l saline solution (11). The result of a measurement is shown in Fig. 3. Because of coupling and mismatches in the phased array system misalignment of the SAR focus may occur. A procedure to correct for these errors in the setup was thus used, based on scattering parameters and on-line measurements of forward and reflected complex voltages (12).

In vivo pre-clinical simulation

The simulation was performed on a female pig weighing 60 kg and measuring 80 cm around the abdomen. The animal was premedicated with Ketalar (Ketaminhydrochloid, Parke-Davis) and Dormicum (Midazolam, Roche) before intubation. Anaesthesia was obtained with Halothane. A midline incision extending from the sternum to a point about 20 cm below the umbilicus was performed and the left kidney was isolated.

Two experiments were performed. In the first experiment the renal artery and vein were ligated in situ to simulate a 'best case' tumour with a low blood flow. The blood flow was measured before and after the ligation and showed a decrease of approximately 60% (doppler technique). Eight temperature probes, each with 3 points were then inserted giving a total of 24 points measured. The probes were fixed with a suture in positions described in Table 1. Following the primary experiment the incision was re-opened and the renal blood flow was re-established by removing the ligature to simulate a 'worse case' tumour, characterized by ample vascularization. The position of the temperature probes was checked and the incision before the second heating session was initiated.

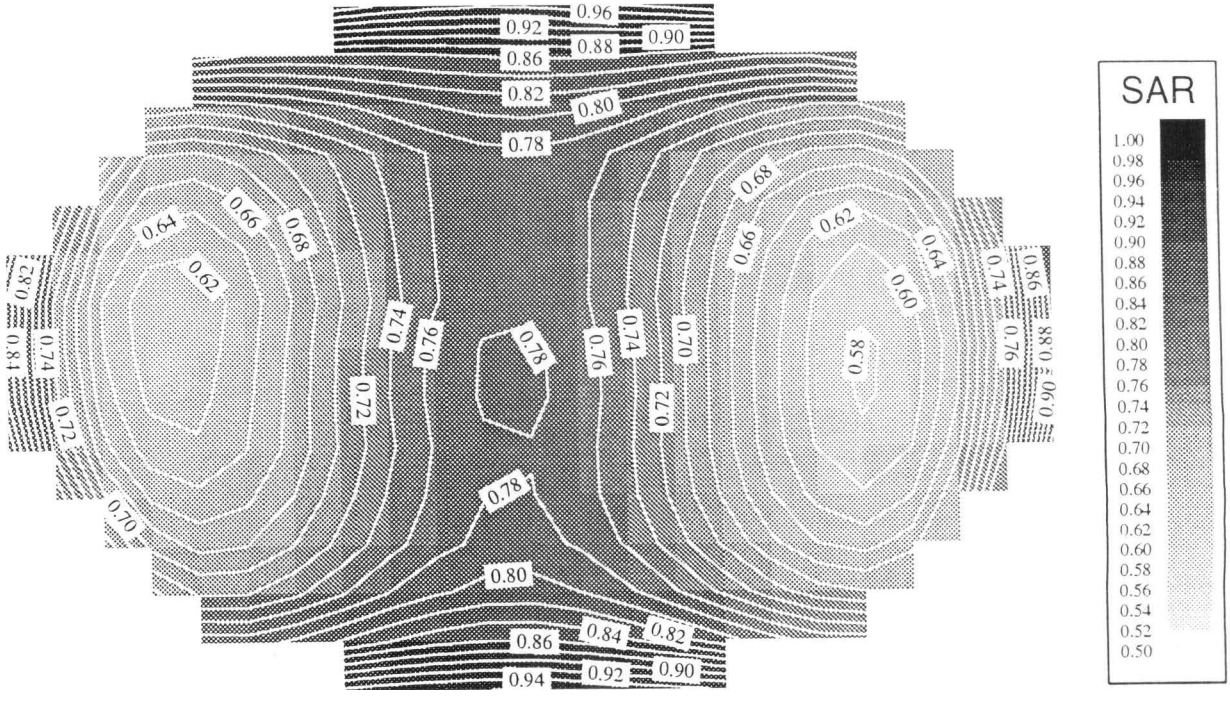

Fig. 3. Scanned E-field measurement showing central SAR. Intended excitation with same amplitude, top and bottom applicator with −45° phase-shift. Frequency 70 MHz.

Table 1

Temperature probe positions

Probe No.*	Position of probes
11–13	Kidney, entering laterally from the upper pole pointing towards the pelvis
21–23	Kidney, entering laterally from the lower pole pointing towards the pelvis
31–33	The perirenal fat ventrally to the renal vessels
41–43	Fixed to the abdominal wall laterally to the kidney
51–53	The fat dorsally to the perirenal vessels
61–63	Subcutaneous in the midline below the umbilicus
71–73	Peritoneal cavity
81–83	Rectal lumen

* The first digit refers to the probe number and the second digit is the point number with number 1 being at the tip of the probe, and the point interspacing being 15 mm.

Table 2

Applicator positions and steady stade excitation in the first pig experiment

Applicator position	Power (W)	Phase (degree)
Anterior (abdomen)	150	0°
Posterior (back)	200	−60°
Left side (near kidney)	200	−60°
Right side (opposite heated kidney)	150	0°

The setup of amplitude and phase (Table 2) was based on the experience gained through phantom experiments since no CT- or MR-scan could be obtained. The total power at 70 MHz applied at the start of the experiments was 1400 W. When high temperatures were obtained approx. 15 min later, the power was reduced to 800 W to stabilize the temperature in the kidney. The phase settings were also changed at the same time in order to lower the power deposition in the perirenal fat.

After the experiment the pig was sacrificed by infusion of hypertonic Kaliumchloride.

Results and Discussion

In both experiments, 24 temperature points were measured but only selected results will be shown. The selection was based on 'worst case', ie. in the kidney the point with the lowest temperature is displayed, and outside the kidney the point with the highest temperature is shown. Selected temperatures obtained in the first experiment are shown in Fig. 4. Steady state temperatures were reached within 10 min. In the upper pole of the kidney and adjacent abdominal wall steady state temperatures of approximately 48°C were obtained. The lower kidney pole and the perirenal fat dorsal to the kidney obtained steady state at

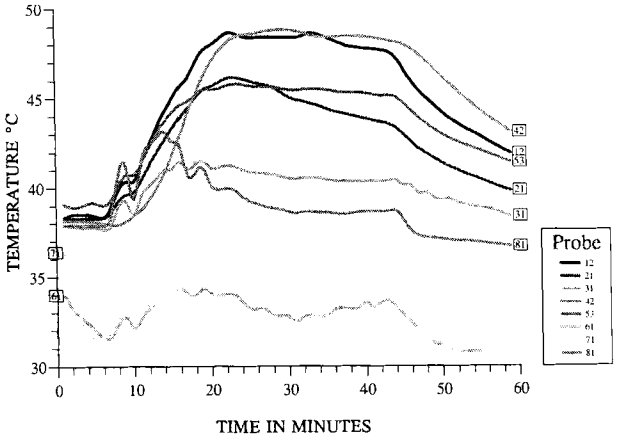

Fig. 4. Selected probe temperatures as a function of time in experiment 1. The probe localization is shown in Table 1.

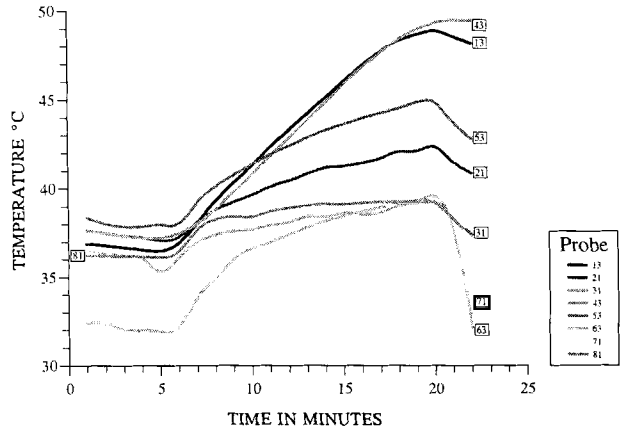

Fig. 5. Selected probe temperatures as a function of time in experiment 2. The probe localization is shown in Table 1.

45°C. In contrast, the subcutaneous fat and the ventrally located perirenal fat did not reach significant temperatures. In a few minutes in the beginning of the first heating session the systemic temperature (point 81) reached 43°C. This instance was caused by insufficient thermal contact and probe 8 was repositioned.

In the second experiment the blood supply to the kidney was reestablished, simulating a high-flow tumour. The time to reach steady state temperature was prolonged to approximately 15 min. The steady state temperatures reached in the upper kidney pole, the adjacent abdominal, and the perirenal fat dorsal to the kidney were on same magnitude as in the first experiment whereas the temperature in the lower kidney pole and in the perirenal fat ventral to the kidney were about 2°C lower than in the low-flow situation (Fig. 5). Thus, the effect of blood flow was primarily to narrow the high temperature volume. However, vascular damage induced during the first heating may also have contributed to the high temperatures achieved in the centre of the heated volume in the second experiment.

The experiments showed that the system is capable of heating in depth to clinical relevant temperatures even in a high-flow situation. The results cannot be transferred directly to the clinical situation, but the experiments gave realistic information on the performance of the system under treatment-like conditions. During the setup of the experiments the easy handling of the applicators was valuable, since this made it possible to perform the incision on the system couch, and simply slide the applicators in the desired positions using the joysticks. However, to take advantage of the many degrees of freedom in the system a full three-dimensional planning system has to be used. At the experiments the bolus temperatures were maintained at 19°C. The sampling of temperatures at 60-s intervals seemed adequate, and because of the ferrite toroids and a 10-s power off-time no serious self-heating of the probes was evident. It is clear though that 24 points are not sufficient to form a good picture of the temperatures, and it is hoped that the experiments can be made using non-invasive thermometry. The power generators proved stable and both control and data collection were performed without interruptions. The communication between the different units via the optical fibres worked without any interference problems from the high power RF-fields. During the treatments the stray radiation in the treatment room was measured using the Raham hazard meter with an isotropic field probe. High field levels (slightly above 10 mW/cm^2) were measured right at the snout of the pig only.

In conclusion, the experiments showed that the system is safe, easy to handle, and capable of heating in depth even in a high-flow situation. Whether or not the system can produce satisfactory clinical results still remains to be proved.

ACKNOWLEDGEMENTS

Supported by the Danish Cancer Society, and the Danish Hyperthermia Foundation. Presented in part at 6th International Congress on Hyperthermia Oncology, Tucson, Arizona, April, 1992.

REFERENCES

1. Raskmark P, Andersen JB. Electronically steered heating of a cylinder. In: Overgaard J, ed. Hyperthermic oncology 1984, Vol. 1. London: Taylor and Francis, 1984: 617–20.
2. Turner PF. Regional hyperthermia with an annular phased array. IEEE Transaction on Biomedical Engineering 1984; 31: 106–14.
3. van Dijk JDP, Gonzalez GD, Blake LECM. Deep local hyperthermia with a four aperture array system of large waveguide radiators. Results of simulation and clinical application. In: Sugahara T, Saito M, eds. Hyperthermic oncology 1988, Vol. 1. London: Taylor and Francis, 1989: 573–5.
4. De Leeuw AAC, Lagendijk JJW. Design of a clinical deep-body hyperthermia system based on the 'coaxial TEM' applicator. Int J Hyperthermia 1987; 3: 413–21.
5. van Rhoon GC, Visser AG, van den Berg PM, Reinhold HS. Evaluation of ring capacitor plates for regional deep heating. Int J Hyperthermia 1988; 4: 133–42.
6. Yuan X, Strohbehn JW, Lynch DR, Johnsen M. Theoretical investigations of a phased-array hyperthermia system with moveable apertures. Int J Hyperthermia 1990; 6: 227–40.
7. Andersen JB, Raskmark P. United States Patent No. 4,702,262. 1987.
8. Raskmark P. A power amplifier using quadrature hybrids, RF design 1994; (in press).
9. Gross E, Raskmark P. Phased array hyperthermia—An experimental investigation. In: Sugahara T, Saito M, eds. Hyperthermic oncology 1988, Vol. 1. London: Taylor and Francis, 1989: 724–5.
10. Allen S, Kantor G, Bassen H, Ruggera P. CDRH RF phantom for hyperthermia system evaluation. Int J Hyperthermia 1988; 4: 17–23.
11. Lagendijk JJ, Molls M. Summary on deep body QA. In: van Dijk J, ed. COMAC-BME Bulletin No. 5, 1991: 95.
12. Raskmark P, Larsen T, Hornsleth SN. Multi-applicator hyperthermia system description using scattering parameters. Int J Hyperthermia 1994; 10: 143–51.