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THE USE OF MICROWAVE-INDUCED HYPERTHERMIA IN CONJUNCTION WITH AFTERLOADING IRRADIATION OF VAGINAL CARCINOMA

A preliminary report

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Abstract

Technically improved microwave antennas for clinical hyperthermia induction have made it possible to combine this treatment modality with external and intracavitary irradiation of vaginal and cervical carcinomas. A microwave applicator with a frequency of 915 MHz was used in tissue phantom measurements and inserted into perspex vaginal obturators for measurement of the specific absorption rate in different planes. A Lund Science Hyperthermia System 4010 with a 200 W generator and a separate thermometry system (ATS 100) was used in the patient treatments. Nine patients with vaginal squamous cell carcinomas have been treated with this applicator and obturator setup as an adjunct to intracavitary irradiation with high dose-rate afterloading technique. The treatments of two patients are described in this preliminary report.

Key words: Vagina, carcinoma, hyperthermia, afterloading irradiation.

Primary and secondary squamous cell carcinomas of the vagina have a poor prognosis regarding both local control rate and long-time survival rate (1), due to their spreading to paracolpic tissues and pelvic walls, and also due to local infiltration of the vaginal wall. The standard radiotherapy is usually similar as for cervical carcinoma with external beam therapy and intracavitary irradiation, using either mobile sources or afterloading technique. The rectal wall is the dose-limiting organ and the risk of complications, such as radiation proctitis and fistulas, is high (2).

One reason for the rather low local control rate is probably hypoxia, especially in bulky, necrotic and infected tumors (3). Together with hyperbaric oxygen therapy and various radiosensitizing agents (4), hyperthermia has become a method for trying to overcome the problem of reduced radiosensitivity associated with hypoxia.

Technical improvements, for example the possibility of using intracavitary antennas (5–10), have opened up new possibilities for combined intracavitary irradiation and hyperthermia in treatment of cervical (11) and vaginal carcinoma (12). The purpose of this study is to present results from phantom measurements of a new microwave antenna and to demonstrate its clinical application in conjunction with intracavitary irradiation of vaginal carcinoma.

Material and Methods

Hyperthermia. An applicator originally designed for hyperthermia treatment of cervical carcinoma (9) has been used. The length of the pen-shaped applicator is 190 mm and the diameter is 8 mm. The applicator was used at 915 MHz, which is the operating frequency of the hyperthermia system used for our patient treatments. Perspex vaginal obturators of 20 mm and 30 mm diameters and 180 mm lengths were designed, each having a central or peripheral canal for the insertion of the applicator. Measurements of the specific absorption rate (SAR) distribution in one longitudinal and one transverse plane of the obturator were performed using a muscle equivalent phantom material (13). A perspex box, 15 × 15 × 15 cm, was prepared in which thin teflon tubes (i.d. 1.2 mm,

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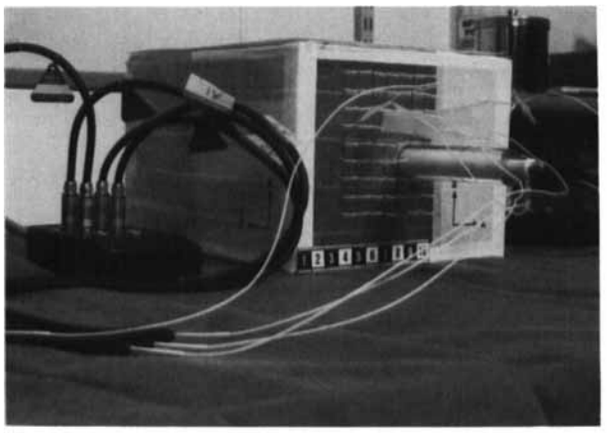

Fig. 1. The muscle tissue equivalent phantom used in the SAR measurements.

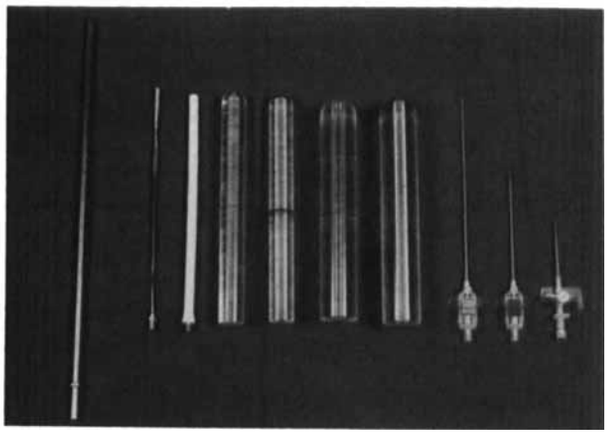

Fig. 2. A standard Cathetron treatment (steel) catheter, uncovered antenna, covered antenna and four perspex obturators.

o.d. 1.5 mm) were inserted parallel and in a grid configuration between two opposite box walls (Fig. 1). The obturator, including the applicator, was also inserted through one of the walls of the box parallel to the tubes and to a depth of 90 mm. The phantom material was then moulded into the box. All tubes were filled with 0.9% saline solution and non-perturbing temperature probes (BSD Medical Corp., Salt Lake City, Utah, USA) were inserted, each one in its own tube, to the measurement points. A microwave power generator (MCL Inc., Bolingbrook, Illinois, USA) was connected, together with power meters for measuring the forward and the reflected power levels, to the applicator. The microwave power was switched on and the temperature and time were immediately recorded. After a 20-s heating period the temperature and time were again recorded and the power was switched off. The temperature probes were repositioned to the next measurement points, and after a 20-min cooling time the heating and temperature/time recordings were repeated. In this way, a matrix of recorded temperature rise rate values was formed for one longitudinal and one transverse plane. The same applicators, obturators and thermistors were used for patient treatments (Fig. 2). Local anesthesia (Carbocain 10 mg/ml) was used when venflon needles were inserted into the vaginal walls through the vulva, but was not necessary for insertion into the upper half of the vaginal walls. Two hyperthermia treatment sessions (after the first and the last of the five intracavitary ^{60}Co irradiation treatments) were used for the patients treated so far. Treatment time was 60 min of at least 42.5°C measured by thermistors at the periphery of the tumor lesions. The delay time between irradiation and hyperthermia was 30–60 min.

Afterloading radiotherapy. The intravaginal irradiation was performed with remote afterloading equipment (Cathetron) loaded with high dose-rate ^{60}Co sources. Eight different source-trains with active lengths of 45 to 100 mm and activities of 100 to 370 GBq were used. A straight steel catheter of 6.3 mm diameter was inserted into the same type of perspex vaginal obturator, as has been described for the hyperthermia treatments. The irradiation dose was specified at 10 mm from the surface of the obturator. The dose-rate was approximately 1.0 Gy/min and the fraction dose 6.0 Gy. The number of fractions was five in combination with external beam therapy.

For primary treatment of vaginal carcinoma the external photon beam therapy (10 or 20 MV) was given to the pelvic tissue using a 'box-technique'. Dose fraction was 2.0 Gy, given five times a week, for 5 weeks up to a midplane dose of 50 Gy.

Case report No. 1. The first patient was a 75-year-old III-parous woman. Gynecologic examination revealed a 30 × 40 mm tumor infiltrate in the upper third of the vagina, expecially the posterior wall, and with a submucous spread into right and left lateral and anterior walls. Two more deposits (10 × 10 mm) were also palpated, in the midline of the posterior wall 25 mm from introitus and in the left side wall 20 mm from introitus. Cystoscopy was normal. Histopathology showed a poorly differentiated squamous cell carcinoma. External beam therapy was given to the pelvis with 50 Gy combined with 5 × 6 Gy intracavitary irradiation of the vagina. After the first and the last vaginal irradiation treatments (15 days apart) 60 min of hyperthermia treatment was added. A vaginal obturator of 20 mm diameter and with a central applicator position was used for both irradiation and hyperthermia. Thermistor probes were positioned into the tissue at the periphery of the tumor lesions and on the surface of the applicator. The whole treatment schedule could be carried out without complications. The vaginal mucosa did not show any signs of erythema or necrosis. The tumor lesions had regressed by more than 50% at the end of the treatment period and at the routine check-ups, one, three and six months later, the patient was clinically in complete remission.

Case report No. 2. The second patient was a 53-year-old I-parous woman. During September and October, 1986, she had received primary radiotherapy for cervical carcinoma stage IIIB (moderately well differentiated squamous cell carcinoma). External beam therapy was given to the pelvis with 60 Gy and three fractions of 6.0 Gy each were given, using afterloading technique, to the central part of the target volume. In April, 1987, a distal recurrence, 10 × 20 mm, in the left vaginal wall 10 mm from the vaginal introitus, was diagnosed. The recurrence was treated with 10 fractions, of 4.5 Gy each, encompassing the distal third of the

vagina. After two (the first and the last) of the irradiation treatments, 13 days apart, hyperthermia was added using a vaginal obturator of 30 mm diameter and a peripheral and asymmetric applicator position directed towards the tumor lesion in the vaginal wall. It was possible to perform the whole treatment series without interruption or any sign of unusual tissue reaction. A small necrotic area, 5 × 5 mm, at the surface of the tumor was noted at the end of therapy. The tumor volume was reduced by approximately 50% during the treatment period and one month later a minute residuum, 5 × 5 mm, with a small necrosis on its surface was noted. At the 6-month check-up the tumor was in complete remission.

Results

Phantom measurements. SAR-values for each measurement point were calculated as $SAR = c_{ph} \cdot dT/dt$ (W/kg), where $c_{ph} = 3\,000$ (Ws/kg°C) is the heat capacity of the phantom material (13) and dT is the recorded temperature rise during the time interval dt (20 s). The SAR-distribution in one transverse and one longitudinal plane of the 20 mm obturator, with a central position of the applicator, is shown in Fig. 3. In the transverse plane the 40% SAR contour line reaches a radial depth of 10 mm from the surface of the obturator. The longitudinal 40% SAR contour line reaches a depth of 55 mm from the phantom surface. The asymmetric applicator position, in the 30 mm obturator, produced a directed SAR-distribution in the transverse plane, as shown in Fig. 4. In the direction of the maximum SAR in the transverse plane, the 40% SAR contour reached a radial depth of 11 mm from the surface of the obturator. The longitudinal 40% contour (in the plane of maximum SAR) reached a depth of 70 mm from the phantom surface. The power delivered to the phantom material was 38.3 W for the 20 mm obturator and 21.6 W for the 30 mm obturator.

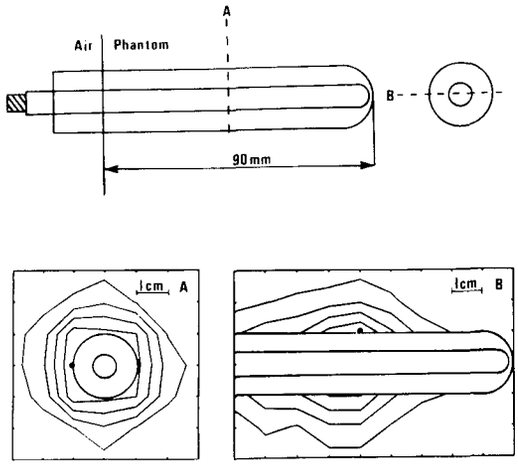

Fig. 3. Normalized SAR-distribution for the 20 mm obturator with a central applicator position. The maximum measured SAR-value (*) was 240 W/kg (100%) in both the transverse (A) and the longitudinal (B) plane. The contour lines, progressing inwards, are 20%, 40%, 60%, and 80% of the maximum SAR-value.

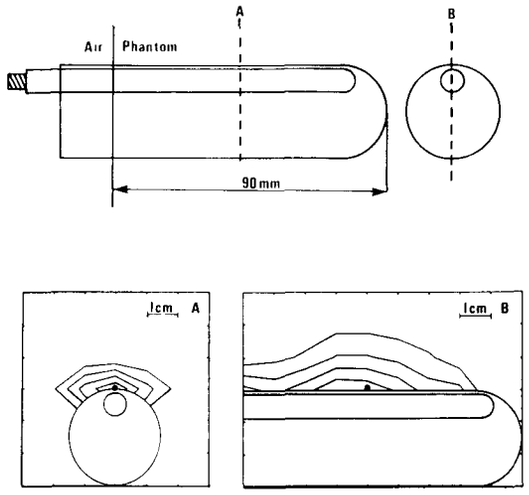

Fig. 4. Normalized SAR-distribution for the 30 mm obturator with a peripheral applicator position. The maximum measured SAR-value (*) was 345 W/kg (100%) in the transverse plane (A) and 390 W/kg (100%) in the longitudinal plane (B). The contour lines progressing inwards, are 50%, 60%, 70% and 80% (in A) and 20%, 40%, 60%, and 80% (in B) of the maximum measured SAR-value.

Patient treatment. During the first 10 min of hyperthermia the temperature rise was generally steep and smooth. During the next 5–10 min, a physiological counteraction from tissue circulation started and the power from the generator had to be increased up to 85 W to reach a measured minimum of 42.5°C at the tumor periphery after 20 min of treatment. During the following 60 min the temperature showed a continuous fluctuation of approximately ±1.0°C. During the treatment of patient No. 1 (first session) a mean temperature of 43.7 ± 2.0°C was reached at the periphery of the tumor. The corresponding thermal dose was 191.5 equivalent minutes at 43°C (14). For patient No. 2 (first session) the corresponding mean temperature and thermal dose were 44.1 ± 0.4°C and 143.0 equivalent minutes at 43°C. The two reported patients experienced only a slight, but not painful, sensation of heating in the vulva and vaginal region. No interruption of the treatment sessions was necessary. Measurements of microwave exposure to the staff in the treatment room showed that stray EM radiation levels were < 1 mW/cm^2 at distances of 10 cm or more from the microwave cable and the applicator.

Discussion

Antennas for microwave induced hyperthermia (5) present an interesting adjunct to intracavitary irradiation with high dose-rate afterloading technique. The shape and dimensions of the antennas (9) can be similar to the catheters and applicators which have long been used in radiotherapy.

The design of microwave antennas for hyperthermia

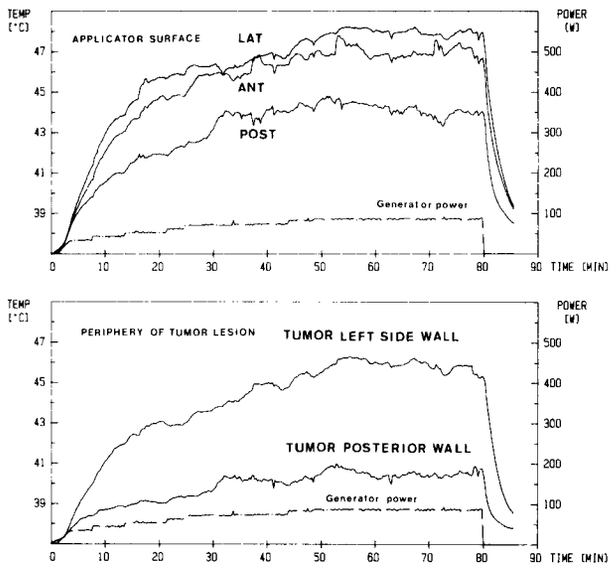

Fig. 5. Temperature curves from one of the vaginal treatments showing the difference in heat penetration in various directions.

involves careful temperature measurements to evaluate the SAR distribution. It is appropriate to use tissue equivalent phantom material for this purpose. It must be noted that the temperatures will change when a cooling blood circulation is in action. The output power from the generator has to be approximately 10 times higher in living tissues compared with phantom measurements.

Intracavitary hyperthermia reaches the central, and probably most hypoxic and necrotic, part of the tumor and may therefore increase local tumor control when combined with radiotherapy. The organs at risk, such as the bladder and the rectum, can be protected from excessively high temperatures, in contrast to the case of external hyperthermia to the pelvis (15).

Positioning of multiple thermistor probes at the surface of the applicator, at the margins of the tumor lesions and in the walls of the risk organs will make the measurements reliable and the treatment safe regarding adverse reactions.

The interstitial insertion of the thermistor probes into the paravaginal tissue may be a problem and local anesthesia is needed for the vulva and the distal part of the vagina. Our patients have not experienced any significant pain or discomfort during or after the treatment sessions nor have the radiation reactions from the bladder, intestine or vaginal mucosa so far been accentuated. The most sensitive parts for early reactions after intracavitary hyperthermia as well as after irradiation are the vulva, the introitus and the lower third of the vagina. A form of conically shaped spacer, adapted to the obturator surface at the vulvo-vaginal level, could reduce the risk of such reactions without interfering with the tumor heating, at least when the lesion is located well above this region. A water cooling system beneath the surface of the obturator would be another alternative.

When using obturators in a symmetrical applicator position, it seems to be easier to get good heat depth penetration anteriorly and laterally, compared with the posterior direction towards the rectum (Fig. 5). This is probably explained by the gas-filled lumen and the rich vascularization of the rectal wall. Our experience so far, from phantom measurements and 9 patient treatments, underlines the need for further technical development of the applicators, and future development will probably lead to separate applicators for vaginal, cervical and endometrial cancer treatments.

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