

Microwave Prostatic Hyperthermia: Interest of Urethral and Rectal Applicators Combination—Theoretical Study and Animal Experimental Results

David Despretz, Jean-Christophe Camart, Christophe Michel, Jean-Jacques Fabre, Bernard Prevost, Jean-Pierre Sozanski, and Maurice Chivé

Abstract—Microwave thermotherapy systems used for benign prostatic hyperplasia treatment generally operate with urethral or rectal applicator to deliver the microwave energy in the prostate. This technique does not allow an efficient heating of all the gland particularly in the case of large adenoma or when the treatment is limited to only one heating session. A solution to this problem is given by using simultaneously the rectal and urethral applicators [1]. A complete 915-MHz microwave thermotherapy system is presented with two applicators which can operate independently or simultaneously to deliver the microwave energy in the prostate. Electromagnetic and thermal modeling have been developed for the applicator antenna optimization, to calculate the specific absorption rate (SAR) and the thermal pattern in the prostate for each applicator alone and when they operate together in phase. Different canine experiments have been performed to prove the interest of using the two applicators simultaneously as compared when they operate alone. Histological examination cuts of the prostate gland after heating have been carried out.

I. INTRODUCTION

THE efficiency of microwave thermotherapy to treat benign prostatic hyperplasia has been demonstrated: many medical teams use this technique in clinical routine [2]–[5]. Nevertheless urologists still do not agree about the type of applicators. In order to increase the heating volume and above all to homogenize the temperature within the prostate (in the case of prostatic tumors) it is necessary to combine urethral and rectal heating.

The aim of this work is to make a thermoregulated focusing rectal applicator to be used simultaneously with an omnidirectional urethral applicator.

Radiation diagrams of urethral and rectal applicators are computed out by the finite-difference time-domain (FDTD) method, and determined by experimental measurements. The

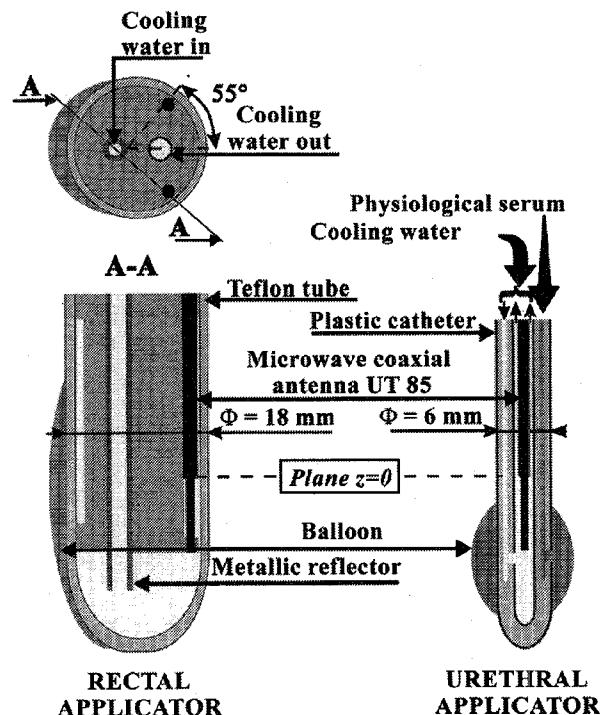


Fig. 1. Description of the rectal and urethral microwave applicators.

radiation diagram is also computed when the urethral and rectal applicator fed in phase, are used simultaneously too.

The solution of the bioheat transfer equation in the steady state gives the temperature field inside the volume of interest including the two applicators. During the heating, the temperature measurement by microwave radiometry allows to accurately determine parameters required to solve the bioheat transfer equation.

From the microwave power deposition, the measured radiometric temperature and the punctual temperature measurements (cooling water, rectum, and urethra surface), a software calculates thermal pattern in the plane $z = 0$ cm defined as shown on the Fig. 1 (highest temperature occurs in this plane).

Series of animal tests confirm theoretical results and prove the efficiency of rectal and urethral applicator combination.

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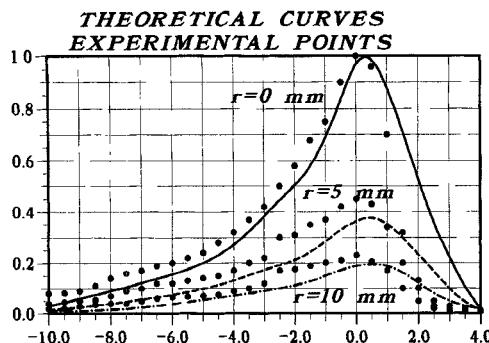


Fig. 2. Theoretical and experimental normalized power deposition of the urethral applicator versus the distance from the catheter in a longitudinal plane. The heating frequency is 915 MHz, the applicator is dipped in salt water 6 g/l.

II. MATERIALS AND METHODS

A. Description of System and Applicators

The rectal applicator is made of two coaxial antennas associated with a metallic reflector in order to focus microwave energy in the prostate (Fig. 1). These antennas are built from UT85 standard semi-rigid coaxial cable ($\varnothing = 2.2$ mm). The radiating zone of the antenna is obtained by removing the outside conductor of the coaxial cable on a length h . This allows a heating zone of about $2h$. Antennas and metallic reflector are put in a Teflon tube which includes a cooling system by water flowing in the tube as shown on the Fig. 1. Antennas are placed in the cooling flow. The external diameter of the Teflon tube is about 18 mm and its length 190 mm. An external inflatable balloon outside of the applicator and diametrically opposite to antennas allows an accurate positioning on the rectal wall. The water cooling temperature is adjustable. The flow is about 120 ml/min.

The urethral applicator is built from a Foley type plastic catheter. The short external diameter ($\varnothing = 6$ mm) of this applicator allows to insert it easily in the urethra (Fig. 1). A flexible coaxial cable ($\varnothing = 2.2$ mm), at the end of which the outer conductor is removed on a length h , is inserted in the catheter. To avoid hot spots at the applicator-urethra interface, a water cooling circulation is made in the catheter. The total length of this applicator is about 500 mm. The cooling water, which has a temperature adjustable from 10–25°C, flows under pressure inside the catheter (flow 50 ml/min) and allows a good thermoregulation of both the antenna and the urethral wall.

The system (prototype developed by U279 INSERM) to which the applicators are connected includes a heating generator operating at 915 MHz (with a maximum output power of 100 W) a 2–4 GHz frequency range radiometer, two water circulation systems connected respectively to each applicator, a thermoprobe system which is used to measure the temperatures on the rectal and urethral walls.

A central unit controls the system by operating an alternative heating-measuring sequence. This central unit records the different parameters of the HT session such as generated and reflected powers, radiometric, and thermoprobe temperatures. The radiometric temperature is used to adjust the generated power in order to obtain the required radiometer temperature

in the prostate which has been fixed at the beginning of the heating session. This temperature is determined from the numerous phantom and animals experiments which are always achieved before any patient treatment.

The radiometer used on this prototype has two internal temperature references [6] which allows to bypass cable and component imperfections and eliminates the need of calibration on an external water tank, a method which is characteristic for the previous generation of radiometer. Indeed the radiometric system contains an internal selfregulating module which calibrates the radiometer in less than one minute before the hyperthermia session.

B. Electromagnetic Applicator Modeling

The aim of the optimization is to develop a radiating antenna able to transfer during use at least 90% of the microwave energy to the surrounding media. The antenna is thus matched. Matching must be obtained not only at the heating frequency but also in a wide bandwidth around the central frequency of the radiometers used for temperature measurements and monitoring. In this case, because the noise power level emitted by the tissue is very low ($\sim 10^{-12}$ W in 1 GHz bandwidth) the antenna must be matched to pick up the maximum part of this power [7].

The quality of the matching is tested by measuring the power reflection coefficient (S_{11} parameter) at the coaxial cable entry as a function of the frequency with a network analyzer. Measurements are performed for the different applicators when they are inserted in a polyacrylamid phantom or in a saline water solution (6 g/l).

Once matching is achieved, the radiated microwave power which within the media where the applicator is inserted must be studied. Theoretically, the electromagnetic field is calculated with the FDTD method: the study consists of numerically solving the Maxwell's equations in which finite-difference approximations are employed for both time and space derivatives [8]. That method offers advantage of accurately taken into account the shape of the applicators and of the surrounding media.

The geometry of the urethral applicator allows to solve Maxwell's equations written in cylindrical coordinates system [9]. The coupling between applicator and surrounding tissues is assumed to be symmetrical allowing to solve these equations in a longitudinal plane. In the case of the rectal applicator, the two-dimensional theoretical study is made in the junction plane of antennas (this plane is perpendicular to antenna direction at the junction point ($z = 0$) in rectangular coordinates system. In fact, modeling shows that the maximum energy deposition occurs in this plane [10]. Moreover, the electromagnetic field is defined by one electric and two magnetic components [11]. From the electromagnetic field, the power deposition is then calculated at every point.

When this computation is applied to the radiometric frequency, it gives access to the contribution diagram of the power received by the antenna, i.e., the weight affected by the original thermal noise power coming from each point of the concerned volume and collected by the applicator operating as a radiometric antenna receiver (antenna reciprocity theory).

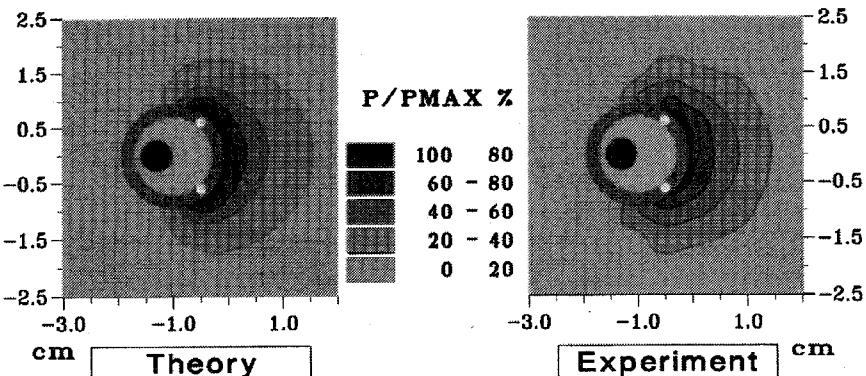


Fig. 3. Theoretical and experimental normalized power deposition of the rectal applicator in the cross section plane $z = 0$. The heating frequency is 915 MHz, the applicator is dipped in salt water 6 g/l.

To confirm the theoretical approach, two types of experiments have been carried out. First, the diagram of the deposited power is determined in a saline solution at the heating and radiometric frequencies with the electric field mapping system [12], and second, by the temperature increase measurement in a polyacrylamid phantom briefly heated (1 min). In this case, the conduction effects must be neglected, and this increase is assumed to be proportional to electromagnetic power deposition.

C. Thermal Applicator Modeling

The temperature pattern is obtained from the solution of the bioheat transfer equation in the steady state

$$k_t \times \nabla^2 T + v_s(T_a - T) + Q + Q_m = 0.$$

In this equation, T is the temperature, k_t the thermal conductivity ($\text{W} \cdot \text{m}^{-1} \cdot \text{C}^{-1}$), v_s the blood heat exchange coefficient ($\text{W} \cdot \text{m}^{-3} \cdot \text{C}^{-1}$), T_a the arterial temperature ($^{\circ}\text{C}$), Q the microwave power deposition, Q_m the power generated by metabolic process (Q_m is insignificant compared with Q).

For the solution of this equation, conditions must be respected. Particularly, the heat exchanges between the lossy medium and the external medium at temperature T_e (this medium may be a cooling system) are taken into account by means of the equation

$$k_t \times \frac{\partial T}{\partial x} = H \times (T - T_e)$$

where H is the heat exchange coefficient between applicator and external medium ($\text{W} \cdot \text{m}^{-2} \cdot \text{C}^{-1}$) and x is the perpendicular direction to the interface.

Except v_s , all these terms are, in a first approximation, not dependent on temperature and found in previous studies [13]. In fact, v_s is an effective exchange coefficient which characterizes heat exchange between blood flow and tissue; it is not measured or theoretically determined but numerically approached in order to obtain a good agreement between calculated and measured radiometric temperatures, that gives the most probable thermal pattern. The bioheat equation is numerically solved by the Choleski method [14].

D. Canine Experiment

The experimental studies were conducted using six anesthetized dogs weighing 20–25 kg in the experimental surgery

laboratory of the Centre Oscar Lambret according to the following protocol:

The applicators put into rectum and urethra are placed parallel and the junction points of their antennas are located in the same plane using a radiological verification. Distance between applicators is accurately measured. The thermal control for monitoring the heating generator [6] is achieved by microwave radiometry through the urethral applicator. The measurement of the thermal levels occurring during heating of the prostate gland has been made by optical fibers (ASE thermometer 1110 TAKAOKA) implanted after a laparotomy between the two applicators in the junction plane of the antennas (Fig. 5). This laparotomy incision was closed to avoid external cooling. After the hyperthermia session, the prostatic gland is removed for a histological examination, then the dogs are sacrificed immediately after the experiments.

III. RESULTS AND DISCUSSION

A. Power Deposition of Urethral and Rectal Applicators

The theoretical determination of the bare length (h) of the microwave coaxial cable, which assure a good matching at 915 MHz is equal to 36 mm for the urethral applicator and to 32 mm for the rectal one. These values were confirmed after measurement of the S_{11} parameter with a network analyzer. A correct matching (an average -10 dB) measured in a large frequency bandwidth around 3 GHz allows to use of the urethral applicator as an antenna receiver for radiometry in the 2–4 GHz band.

Urethral and rectal applicators have been characterized by their power deposition obtained at the heating frequency.

A comparison between theoretical and experimental power deposition at different depths in a longitudinal plane is presented in Fig. 2 for the urethral applicator. The applicator was dipped in a saline solution (6 g/l). The values were normalized to the maximum power value located on the applicator in the junction plane $z = 0$. Experimental points indicate a confirmation of the calculated curves. Forty percents of the deposited power are placed at five millimeters from the catheter in the junction plane.

For the rectal applicator computation and experiment have been performed in the cross section plane $z = 0$, where the deposited power is maximum. The results are presented in the Fig. 3. The left part of the figure gives the FDTD calculation,

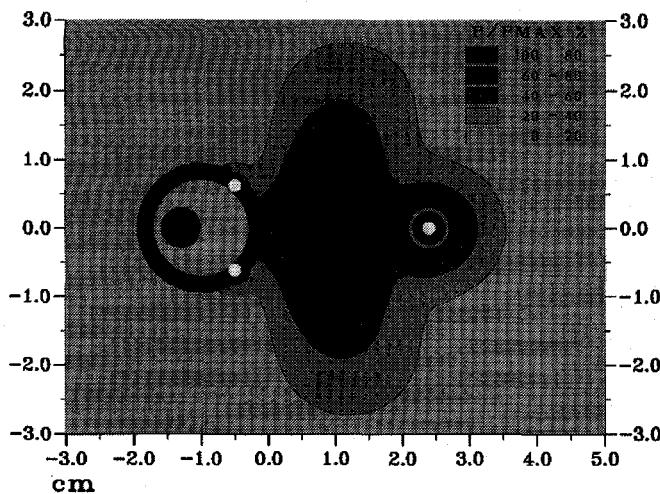


Fig. 4. Theoretical normalized power deposition in the antennas junction plane. Antennas are fed in phase at 915 MHz.

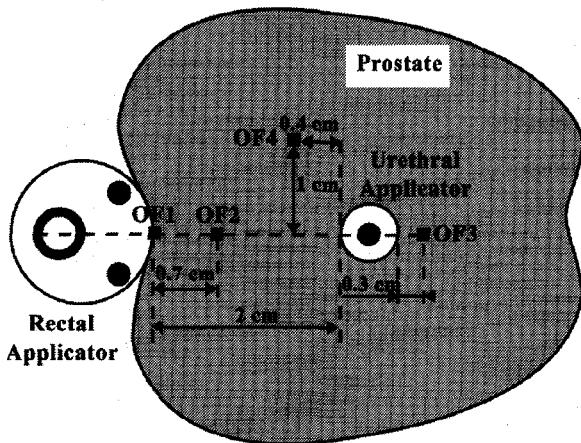


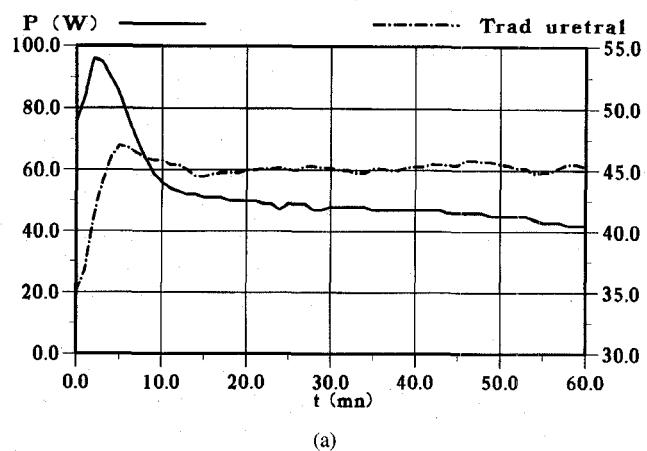
Fig. 5. Antennas and optical fibers positions in the dog prostate.

Results are normalized to the maximum deposited value on the applicator. The right part shows the experimental power deposition reconstructed from the measured values in the saline solution. The results show a good agreement between theory and experiment.

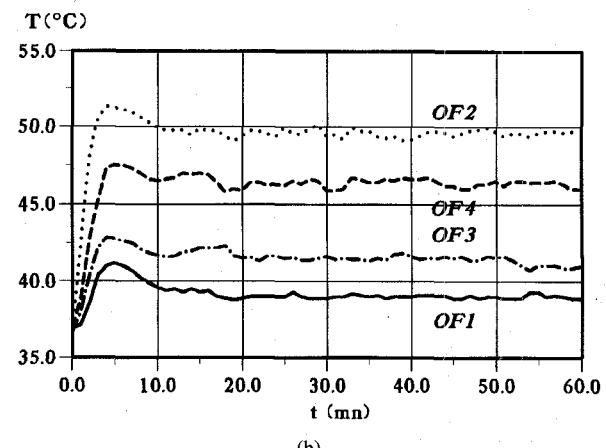
The power is focused in a half plane due to the metallic reflector. In this half plane, the heated zone limited by the isopower line 40% is extended to 8 mm from the catheter.

B. Combined Use of Urethral and Rectal Applicators

The urethral and rectal applicators are used in the same time to heat the prostate gland in order to obtain a larger heated zone. The applicators are assumed to be in the previously described conditions: they are at a distance of 20 mm. In that case, the three antennas of the two applicators are fed in phase. This parameter is controlled and adjusted with a network analyzer. Power deposition has been computed at every point of the cross section plane with the FDTD method. Due to the electric field composition, Fig. 4 shows that the heated zone is greater than previously obtained by applicators operating alone (about 200% with respect to the rectal applicator heated zone). The maximum of the normalized power deposition is now located in the middle axis of the two applicators.



(a)



(b)

Fig. 6. (a) Generated microwave power versus time controlled from the radiometric measurement. (b) Temperature profiles obtained from the four optical fibers during the canine experiment.



Fig. 7. Hystological cuts after an hyperthermia session.

C. Canine Experiment

Fig. 5 shows the applicators and optical fibers implantation into a dog prostate: Applicators are at a distance of 20 mm; antennas are fed in phase at 915 MHz heating frequency. The points of temperature measurement are noted:

- OF1: On the rectal applicator.
- OF2: In the zone where the temperature should be maximum.
- OF3-OF4: Other points.

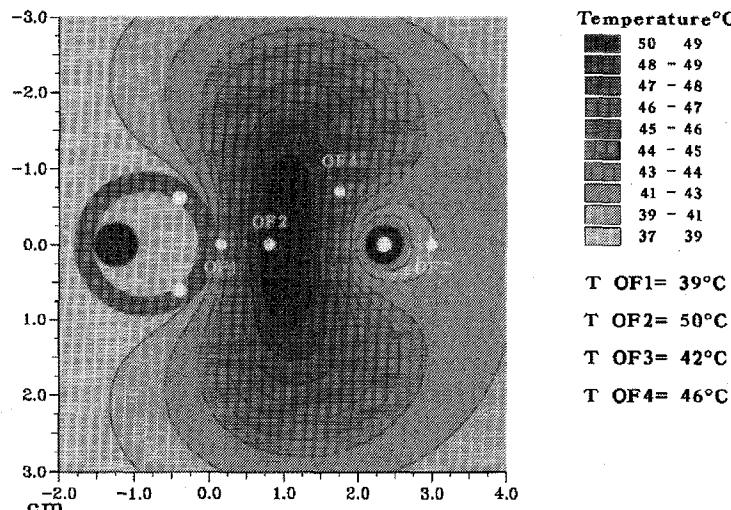


Fig. 8. Cross section plane thermal reconstructed pattern ($z = 0$) in the case of the dog session presented in Fig. 5, in the steady state.

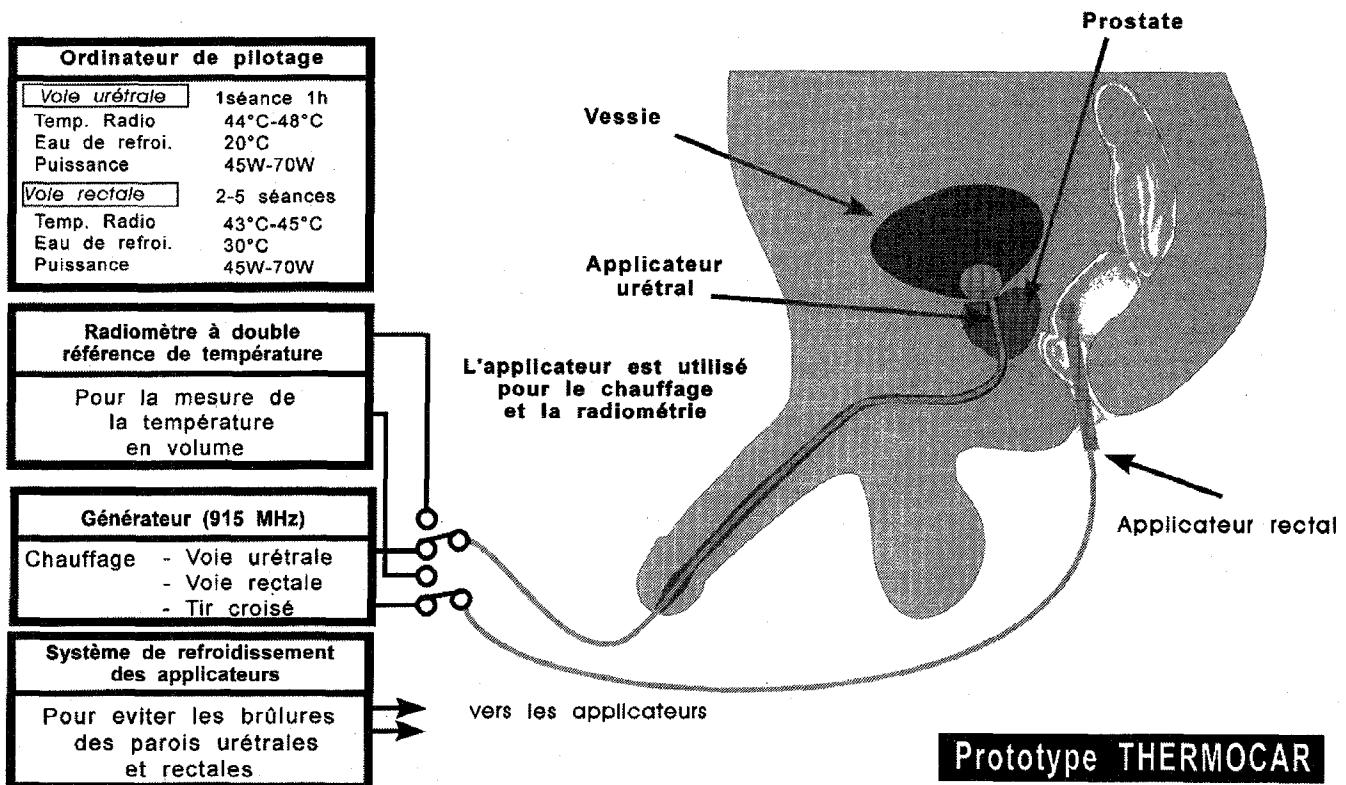


Fig. 9. Microwave thermotherapy system controlled by microwave radiometry for the treatment of the prostate.

The cooling water temperature is fixed to 25°C for the urethral applicator and to 30°C for the rectal one. These temperatures are estimated by computation. The heating power at the beginning of the session is equal to 76 W. This power is equally divided over the two applicators. The rectal power is again equally divided over each antenna (19 W/rectal antenna). The radiometric temperature level to be obtained is fixed to 45°C. After a sudden power increase, the thermal limit was obtained in 4 min and maintained during 60 min.

The Fig. 6(a) shows the control of the heating power from the radiometric measurements. In fact, a decrease of the

microwave power is necessary after 4 min of heating in order to obtain a steady state. The Fig. 6(b) shows the temperatures measurements. The maximum temperature (50°C) is obtained as expected on OF2. The lower temperature occurs on OF1 showing the efficiency of the cooling water system. After the session, the prostate is removed for a histological examination. In Fig. 7, histological cuts show necrosis reaching the prostate limit in the middle cross-section plane.

D. Reconstructed Thermal Pattern

The first computations confirm the validity of the hyperthermia session. From the power deposition computation,

using the transfer bioheat equation in the steady state and the radiometric temperature measurement, is determined the theoretical reconstructed thermal pattern in the cross section plane $z = 0$ cm induced by the two applicators. The data used in the software are the same as the ones during the canine session. In the bioheat equation, k_t the thermal conductivity is now equal to $0.38 \text{ W.m}^{-1} \cdot \text{C}^{-1}$, T_a is the arterial temperature (37°C), and H the heat exchange with the external medium is equal to $100 \text{ W.m}^{-2} \cdot \text{C}^{-1}$. These terms are constant and found in previous publications. v_s is adjusted from a comparison between calculated and measured radiometric temperature [7] and [15]. For this thermal pattern reconstruction v_s must be equal to $10000 \text{ W.m}^{-3} \cdot \text{C}^1$.

The reconstruction is presented in Fig. 8. The good agreement between the theoretical and experimental values validates the reconstruction of the temperature field. We can see that the cooling by the applicators and the electromagnetic field composition allows the penetration of the hottest point into the prostate. The volume where the temperature rise is considered efficient ($T > 45^\circ\text{C}$) extends over 3 cm in the junction plane. Those results are in agreement with the necrosis surface in hystological examination. By using the cooling system superficial burns on urethral and rectal walls are avoided.

IV. CONCLUSION

The development of microwave urethral and rectal applicators associated with an autonomous system allows a correct hyperthermia treatment of the prostate. From a theoretical approach we have shown the interest of two applicators combination. The slope of the temperature rise correlates well with the slope of the power rise. The efficiency of the temperature control by microwave radiometry, in the 2–4 GHz band, is proven by a good correlation between local measurements by optical fibers and reconstructed thermal pattern from radiometric temperature measurement.

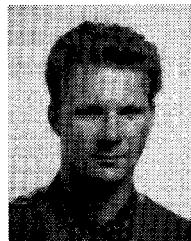
The temperature allowing prostate tissue necrosis is above 50°C . The thermoregulation of the antenna permits a cooling of the external wall of the applicators and also the maintenance of the urethral and rectal walls temperature below 44°C to preserve them. The cooling of the applicators and the electromagnetic field composition allows the penetration of the hottest point into the prostate: experimental results on dogs confirm this study. Due to its efficiency, different pathologies of the prostate (prostatic cancer or large adenoma) can be treated by our system (Fig. 9).

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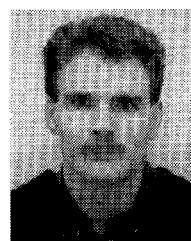
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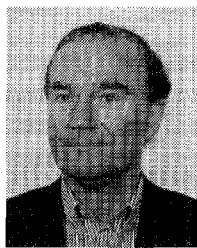
Jean-Christophe Camart, for a photograph and biography, see this issue, p. 1761.



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In 1976, he joined the Oscar Lambret Oncology Center of Lille (COL) as a radiotherapist. Since 1981, he has been working on medical applications of hyperthermia. He is now chief of the department (radiotherapy) at the COL.

Jean-Pierre Sozanski, for a photograph and biography, see this issue, p. 1761.

Maurice Chivé, for a biography, see this issue, p. 1761.