No Nonthermal Effect Observed Under Microwave Irradiation of Spinal Cord

Jian Teng, Damien Carton de Tournai, Fabienne Duhamel, and André Vander Vorst, *Fellow, IEEE*

***Abstract*—The paper presents an in vivo experiment concerning cerebral evoked potentials in the presence and in the absence of microwaves irradiating the spinal cord. An electrical stimulus is applied on the peripheral nervous system of a rabbit while the impulse response (evoked potential) is measured by an electrode in the cortex. The spinal cord is irradiated at 4.2-GHz by an implanted micro-antenna. The purpose of the experiment is to distinguish between thermal and possible nonthermal effects. A statistical treatment of the recorded data shows that there is a microwave effect. Power deposition is calculated. The bioheat equation indicates that the microwave irradiation results in a temperature increase within the spinal cord. Nonthermal effects were not observed.**

I. Introduction

MICROWAVE thermal effects are well known. The possibility of nonthermal effects is an intriguing question and a number of experiments have been set up to demonstrate such an effect. It should be noted that there is a fundamental ambiguity about the distinction between the words thermal and nonthermal. According to Presman [1], intensities below 10 mW/cm^2 may be considered nonthermal for pulsed and CW microwaves in either whole-body or local irradiation. With intensities of 10 mW/cm^2 or less, conversion of microwave to thermal energy does not exceed the heat loss from 1 cm^2 of body surface under normal environmental conditions [1]. Since biological objects however are electrically heterogeneous and because microwave fields have a known selective thermal effect on various tissues and organs, a difference between a microwave effect and a neutral heat effect is not necessarily due to an unknown extrathermal factor, but might well be a function of an uneven distribution of heat in the organism that could exert its peculiar effect [2].

Discussions of the possible mechanisms of electromagnetic-neural tissue interaction are available. They can essentially be found in [2]. The reader is referred to Adey who discusses electromagnetic fields and the essence of living systems [3]. Some excellent general reviews are also available [4]. In vitro studies on neural effects took place already in 1975 and a number of investigations have been reported [5]. In vivo studies on the nervous system in experimental animals on the other hand are much less numerous. They mostly relate to rats fully exposed to microwaves. The study of "nonthermal" effects gradually occupied a central role in electrophysiological studies in the former Soviet Union. Reviews of the action of microwave fields on the nervous system have been published [6], as well as on the use of microwave acupuncture as a stimulus for the interaction between electromagnetic fields and the nervous system [7].

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The originality of the research reported here is that the nervous system is investigated in vivo as a system: an electrical stimulus is applied at the peripheral nervous system of a rabbit, and the impulse response is measured as the evoked potential in the cortex, in the presence and in the absence of microwave irradiation along the spinal cord. This experiment follows a behaviorial and a pharmacological experiment, which showed that applying microwaves to the peripheral nervous system (in some acupuncture points) induces analgesic effects: it increases the pain threshold and decreases the concentration of norepinephrine in the hypothalamic preoptic area [8].

The present experiment has in view the separation of thermal and possible nonthermal effects. The duration of irradiation is carefully controlled, since it affects the microwave thermal effects. The recorded data are statistically analyzed to detect microwave effects. The power deposition within the spinal cord is calculated, after calibration on experimental data, and the bioheat equation is solved in time domain to calculate the temperature increase. This yields a conclusion on the thermal or nonthermal character of the microwave effects.

II. Experimental Setup

In this in vivo experiment, the nervous system of a rabbit is investigated by observing the somatosensory evoked potentials (SEP) as a function of microwave irradiation of the spinal cord. The SEP, which measures the variation of the cerebral activity due to a somatosensory stimulation, is measured in the cortex with an electrode. The nerve impulse is generated on the superficial peroneal nerve of a back paw by an electric stimulation (Fig. 1). A microwave applicator is inserted into the spinal column, posterior to the spinal cord, at the level of the lumbar vertebrae. Responses under microwave irradiation form a group of data which are compared to a reference group, composed of responses without microwave irradiation.

The rabbits (New Zealand Albinos, about 3.5 kg) are anaesthetized (urethane 0.6 g/kg, intravenous injection) and placed on a stereotaxic instrument. The cranium is trephined and an active AgCl electrode is placed against the cortex, in the sensorial area 1 at a level corresponding to the back paws (left or right). The location for maximum response to the stimulations is determined experimentally. The reference

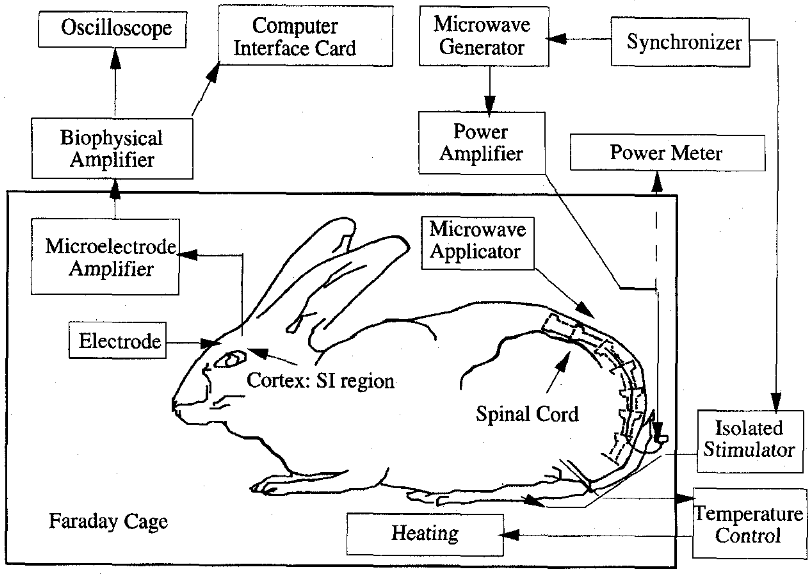

Fig. 1. Synoptic of the experiment.

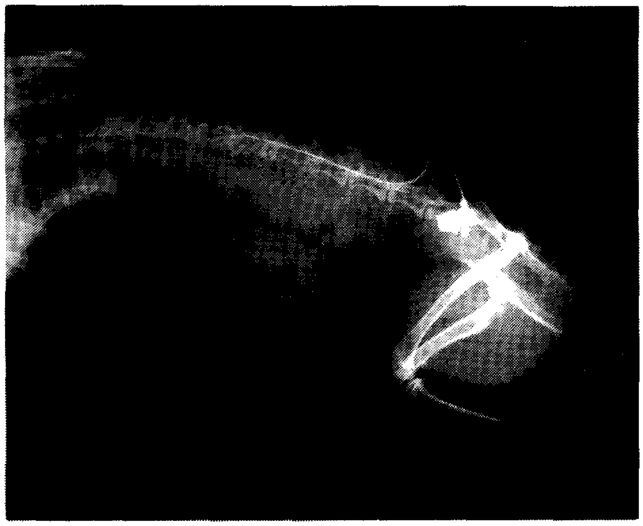

Fig. 2. Longitudinal radiography of antenna implanted along spinal cord.

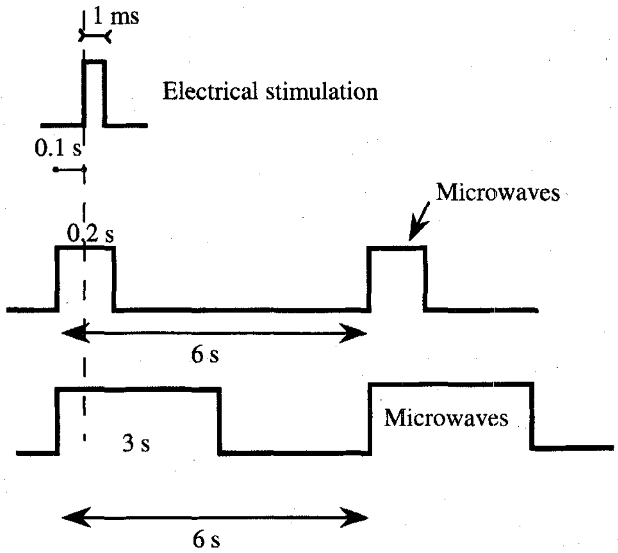

Fig. 3. Experimental sequences (1 ms electrical pulsed stimulation, 0.1 s aftermicrowave irradiation start; irradiation 0.2 s every 6 s, 3 s every 6 s, and continuous).

electrode is placed on the muscle, close to the trephined part. Start and duration of electric stimulation and of microwave irradiation are controlled. The measured potential is amplified, digitized, and stored. The electric stimulating pulses are about 15 V amplitude and 1 ms duration.

The microwave energy is radiated by an asymmetrical dipole. The coaxial-line applicator, about 1 mm in diameter, has a radiating gap in the outer conductor [9]. It is located in the extradural cavity reclining on the spinal cord (Fig. 2). A frequency of 4.2 GHz is chosen because it combines maximum power of the generator and good matching conditions. Microwave irradiation is applied in the following three modes (Fig. 3). 1) Pulsed irradiation: the width of the microwave pulse is 200 ms with a repetition period of 6 seconds, synchronized with the stimulation; 2) discontinuous irradiation: similar to the previous mode, except that the width of the microwave pulse is 3 seconds; and 3) continuous irradiation, respectively, for 30 s or 16 minutes.

III. Power Deposition Calculation

An electromagnetic model is established in which the spinal cord and extradural cavity are considered as a cylindrical dissipative medium characterized by a complex dielectric permittivity. The surrounding medium (vertebrae) has lower dielectric constant and conductivity. Because the insulated asymmetrical applicator is placed near the interface of these two media, parallel to the axis of the cylinder, near field and power deposition are influenced by reflection and coupling of the interface. The electromagnetic field is evaluated using King's formalism [10], extended by Zhang *et al.* [11] for an asymmetrical dipole antenna. They both consider however the dissipative media as homogeneous. To take into account the inhomogeneity, we have introduced a method of images [12] as well as a ray method. The steps are as follows:

1) For each point of the spinal cord where the power deposition is computed, we search for one or several reflection points on the cylindrical interface.
2) In each reflection point, the cylindrical interface is assumed to be the tangent plane to the cylinder, and the method of images is applied for each reflection, taking into account the reflection at the interface between bone and spinal cord, in amplitude and phase. This way, the single applicator near the interface in the inhomogeneous medium is replaced by a set of applicators in a homogeneous dissipative medium. The procedure has been validated on some simple configurations.

IV. The Bioheat Equation

From a macroscopic point of view, thermal effects resulting from the absorption of electromagnetic waves inside biological tissues are described in terms of the bioheat equation. A time domain modeling has been carried out in order to take into account pulsed microwave irradiation [13]. Because of the narrowness of the medium and imperfect knowledge of the power deposition in the nearby tissues of the spinal cord (bone, skin, and muscle) we have considered only the longitudinal bidimensional section of the spinal cord, assuming a homogeneous medium. The bioheat equation can therefore be written as

$$\rho(x,y)c(x,y)\frac{\partial T(x,y,t)}{\partial t} = k_t(x,y)\nabla^2 T(x,y,t) + v_s(x,y) \times [T_a - T(x,y,t)] + Q_m(x,y) + Q(x,y,t)$$

where

T	Is the temperature inside the medium at the considered point (°C).
ρ	Is the volumic mass of the tissues ($\rho = 1020$ kg/m^3).
c	Is the specific heat of the tissues ($c = 3500$ J/kg/°C).
k_t	Is the thermal conductivity of the tissues ($k_t =$ 0,6 W/m/°C).
v_s	Is the blood heat exchange coefficient ($v_s =$ 14 560 W/m^3/°C).
T_a	Is the arterial temperature (37°C).
Q_m	Is the heat generated by the metabolic activity (W/m^3).
Q	Is the heat generated by the absorption of the electromagnetic energy (W/m^3).
t	Is the time (s) and
$Q(x,y,t)$	is given by $Q(x,y,t) = \frac{1}{2}\sigma(x,y)\lvert E(x,y)\rvert^2 \cdot g(t)$ where
$g(t) = 1$	During the microwave irradiation.
$g(t) = 0$	Otherwise.

In the absence of adequate information about the thermal constants of the spinal cord, we have used the thermal constants of white matter [14]. The terms c, v_s, k_t, Q_m depend on the kind of tissues. They are assumed to be independent of temperature. We follow the usual practice by assuming that Q_m may be neglected when compared to Q. We assume that the spinal cord is evenly perfused.

The x, y parameters of the medium and the time t are discretized by using a finite difference scheme. It is used in conjunction with Crank–Nicholson's method [15], which is one of the classical three methods for solving the heat equation in time domain. For each value of t, the residual elliptic equation is solved using Choleski's method. The resulting equations form a complete set of partial differential equations with boundary conditions. Because of the narrowness of the spinal cord, the boundary conditions are applied far away from the energy source. The initial temperature is taken as the rabbit's body temperature, i.e., 37°C. Because of the approximations, the temperature increase is calculated only in the spinal cord.

V. Wilcoxon's Statistics

There are two possibilities to test if the SEP responses measured in the presence of microwave irradiation are different from those measured in the absence of microwave irradiation: either a parametric statistics based on the properties of the distribution function F of the investigated population, or a nonparametric statistics. In this last case, the analysis is based on less restrictive hypotheses, only assuming for instance that F is continuous and symmetrical. A nonparametric procedure is often more complicated and less powerful than a parametric one. Nevertheless it is especially useful when it is difficult to characterize the right hypothesis. Therefore we use here the nonparametric Wilcoxon's statistics [16], [17].

Let $X_1, \ldots, X_m, Y_1, \ldots, Y_n$ (X without microwave irradiation, Y with microwave irradiation) be the global sample of the responses, and $r(X_i)$ be the rank of X_i within the global sample arranged in ascending order. We define the following:

1) The null hypothesis (called H_0) $F_x = F_y$: the distribution functions are identical, and microwaves have no influence on measurements.
2) The alternate hypothesis (called H_1): amplitude and latency of the SEP responses decrease under microwave irradiation.

The principle of Wilcoxon's test is as follows: if H_0 is true, then the X_i are well mixed among the Y_j and therefore the ranks of the X_i can be considered as being m numbers randomly chosen among the $N = m + n$ numbers of the global sample. Hence we have

$$P(r(x_i) = k) = \frac{1}{N} \quad E(r(x_i)) = \frac{N+1}{2}$$

and

$$\mathrm{var}(r(x_i)) = \frac{N^2 - 1}{12}$$

with $i = 1, \ldots, m$ and $k = 1, \ldots, N$. We then consider the random variable T_x which is the rank summation of the X samples, given by

$$T_x = \sum_{i=1}^{m} r(x_i), \quad E(T_x) = m\frac{N+1}{2}$$

and

$$\mathrm{var}(T_x) = m \cdot n\frac{N+1}{12}$$

TABLE I
RESULTS OF WILCOXON'S STATISTICS (RABBIT NO. 5) (PW: PULSED; CW: CONTINUOUS) YES : H_0 IS REJECTED AND MICROWAVES DO INFLUENCE THE SEP. NO : H_0 IS NOT REJECTED, AND IT CANNOT BE CONCLUDED THAT MICROWAVES INFLUENCE THE SEP

Latency				Peak amplitude			
3 min, 2 W, PW200msec (m=30)				3 min, 2 W, PW200msec (m=30)			
	Tx	n	Conclusion		Tx	n	Conclusion
synchronous	-0.32	29	No	synchronous	1.64	29	No
after	-0.14	29	No	after	-0.23	29	No
15 min, 2 W, PW3s (m=29)				15 min, 2 W, PW3s (m=29)			
time	Tx	n	Conclusion	time	Tx	n	Conclusion
1'45	2.49	29	Yes	1'45	1.14	29	No
7'	4.59	30	Yes	7'	1.20	30	No
11'30	5.35	30	Yes	11'30	2.00	30	Yes
17'30	2.25	30	Yes	17'30	-0.52	30	No
16 min, 1 W, CW (m=30)				16 min, 1 W, CW (m=30)			
time	Tx	n	Conclusion	time	Tx	n	Conclusion
1'45	3.26	29	Yes	1'45	1.49	29	No
8'	5.28	29	Yes	8'	5.19	29	Yes
13'15	2.79	26	Yes	13'15	4.12	26	Yes
20'30	1.05	29	No	20'30	1.53	29	No

The null hypothesis H_0 is rejected if T_x is too high (the X distribution takes up the high ranks: the delay and/or the amplitude are too high). With a level of significance of 5%, H_0 will be rejected if one has

$$P(T_x = t_x \mid H_0) < 0.05$$

where t_x is the rank summation of the measured population X. The reduced random variable

$$T_{x\text{reduced}} = \frac{T_x - E(T_x)}{\sqrt{\text{var}(T_x)}}$$

reduces asymptotically to a normal distribution (0, 1) for large values of n and m, and H_0 is rejected if $t_{x\text{reduced}} > 1.65$.

VI. RESULTS

Fig. 4 illustrates typical evoked potentials as measured on a rabbit as a function of time. Peak amplitude is of the order of 0.3 mV. The duration of the potential response is of the order of 5 ms. The figure shows that the peak amplitude decreases with increasing irradiation duration, for 4 to 28 seconds, respectively. Variations of wave amplitude and peak latency as a function of the duration of continuous irradiation are shown in Fig. 5, respectively, for two rabbits. The least-squared linear approximations are also plotted. The incident power is 2 W. Amplitude and latency are extracted for each response.

Wilcoxon's statistics was applied to the SEP measurements on one rabbit, for a short-duration pulsed irradiation (0.2 s every 6 s), a longer-duration pulsed irradiation (3 s every 6 s), both with an incident power of 2 W, and for a continuous microwave irradiation with an incident power of 1 W. The obtained results are shown in Table I. Under short-duration pulsed irradiation (0.2 s), no influence of microwaves is observed either on the latency or on the wave amplitude: the null hypothesis is not rejected. On the other hand, when the pulsed irradiation is of a longer duration (3 s), changes appear both for the delay and the amplitude of the SEP response: H_0 is always rejected for latency and rejected after 11 min. 30 s irradiation for amplitude. Hence, in this case, microwaves have a significant influence. When the 3 s pulsed microwave irradiation is stopped for 2 min. 30 s, Wilcoxon's statistics shows that there remains an influence of microwaves on latency (rejection of H_0) and no influence on amplitude: the amplitude of the SEP before and after irradiation are identical. The same comments apply when the spinal cord is

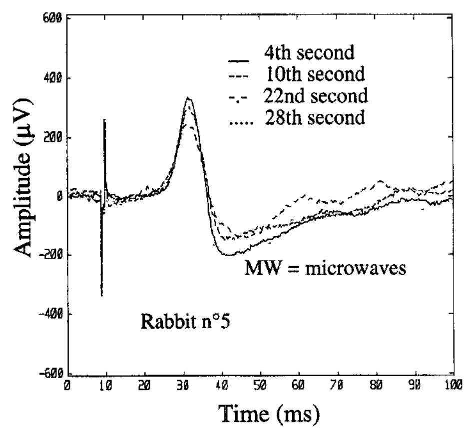

Fig. 4. Evolution of SEP as a function of time under CW microwave irradiation (incident power 2 W, irradiation for 30 s, average of 18 measurements).

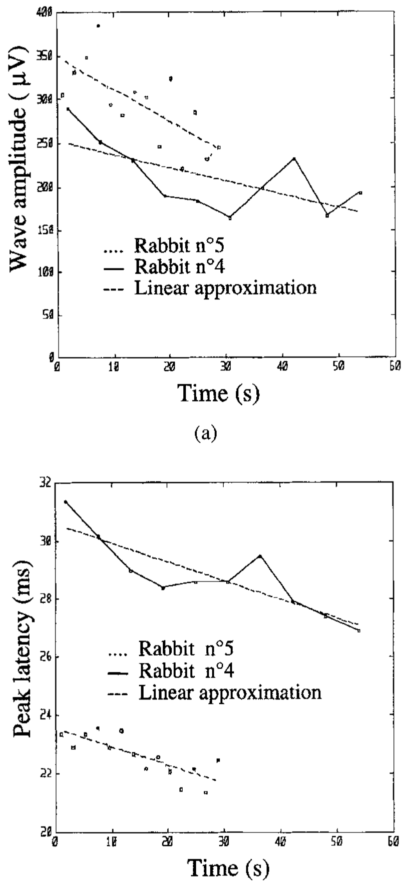

Fig. 5. Wave amplitude (a) and peak latency and (b) as a function of duration of a 2 W irradiation duration.

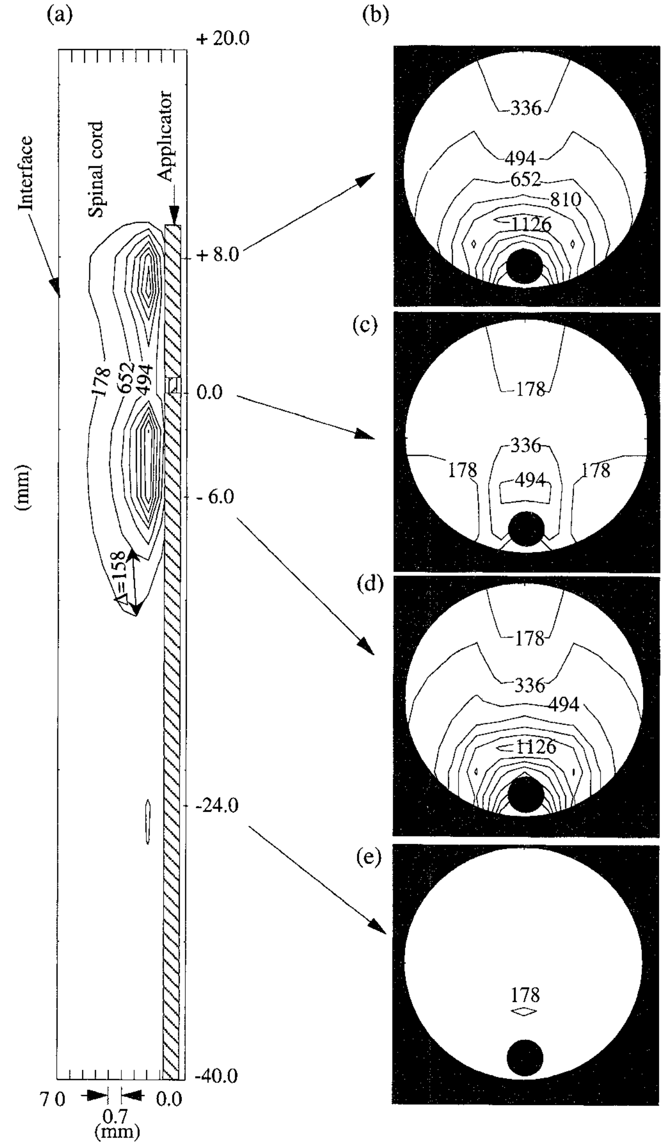

Fig. 6. Power deposition in mW/cm^3 for an absorbed power of 0.8 W (a) in the longitudinal plane, (b), (c), (d), (e) in transverse planes, respectively, at +8, 0, −6 and −24 mm of plane of gap).

continuously irradiated (with an incident power of 1 W): H_0 is rejected for latency whereas the rejection for amplitude only appears after 8 min. of microwave application. After a 16 min. irradiation, H_0 is rejected for both latency and amplitude.

To determine if the observed effects are due to a temperature increase, the power deposition is first calculated within the spinal cord, as a function of the transmitted power. For an incident power of 2 W , the measured absorbed power is 0.8 W [18]. The average diameter of the spinal cord is 7 mm. The longitudinal power deposition in a plane axial with the antenna is shown in Fig. 6(a). The power deposition in several transverse planes are shown in Fig. 7(b)–(e). Isopower lines are calibrated in mW/cm^3. (SAR can easily be obtained by dividing the power deposition by 1020 kg/m^3, the volumic mass of white matter [14]). It is apparent that the microwave power deposition is concentrated around two areas. This is due to the reflections at the interface between the spinal cord and the adjacent bone, and also to the very small distance between the observed points and the applicator.

Then the bioheat equation is solved at a distance of 1.4 mm from the antenna, where the absorbed power density is maximum (Fig. 7), under the following irradiation modes:

1) Pulsed (0.2 s every 6 s during 1 min.), transmitted power of 0.8 W—(a).
2) Pulsed (3 s every 6 s during 15 min.), transmitted power of 0.8 W—(b).
3) Continuous (30 s), transmitted power of 0.8 W—(c).
4) Continuous (16 min.), transmitted power of 0.4 W—(d).

The curves are calibrated in °C. It is observed that, except for the short-duration pulsed irradiation, there is a temperature increase of the spinal cord of at least 3°C. This exerts an influence on latency and amplitude of the SEP responses. It is already well known that a temperature increase makes the latency decrease [19]. Our results, however, also show an influence on the amplitude.

VII. Conclusion

From the experimental and theoretical work, we infer the following conclusions:

1) Statistical treatment shows that there is a microwave effect on the SEP response of the nervous system after a long period of irradiation and that these variations are reversible.

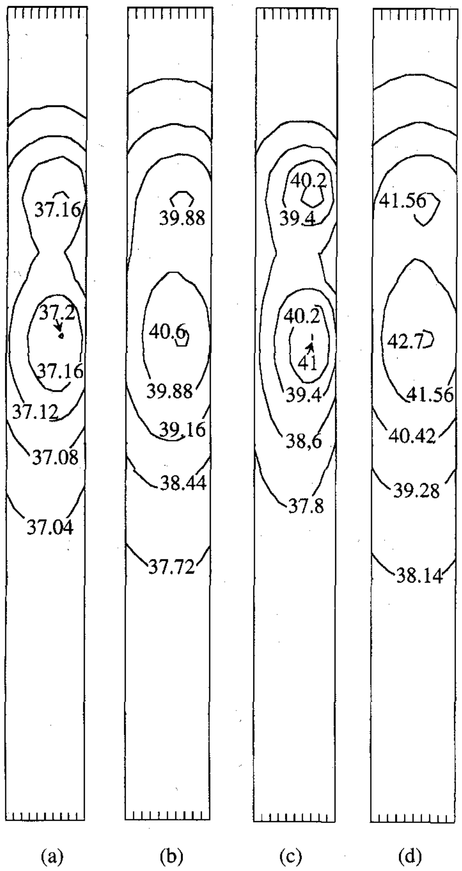

Fig. 7. Thermal mappings in °C (a) after 1 min. pulsed irradiation (0.2 s every 6 s), 0.8 W absorbed, (b) after 15 min. pulsed irradiation (3 s every 6 s), 0.8 W absorbed, (c) after 30 s continuous irradiation, 0.8 W absorbed, and (d) after 15 min. continuous irradiation, 0.4 W absorbed.

2) Computations of both power deposition and bioheat equation as a function of microwave irradiation duration point out a temperature increase of the spinal cord for long pulsed irradiation (3 s every 6 s) during 15 min. under an incident power of 2 W, continuous irradiation during 30 s under an incident power of 2 W, and continuous irradiation during 16 min. under an incident power of 1 W.

In these cases, there are variations of amplitude and latency of the SEP responses. Under a short-duration pulse irradiation (0.2 s every 6 s), neither significant variations of the SEP responses nor temperature increase are observed. The conclusion is that there is a definite microwave effect, which decreases the latency and amplitude of the SEP response, and that the effect is of a thermal origin.

Acknowledgment

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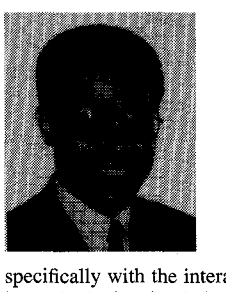

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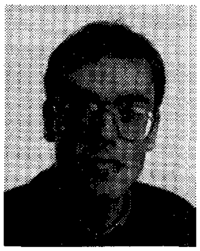

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Fabienne Duhamel, for a photograph and biography, see this issue, p. 1909.

André Vander Vorst (M'64-SM'68-F'86), for a photograph and biography, see this issue p. 1754.