FIRST CLINICAL RESULTS OF APPLICATION OF HYPERTHERMIA IN ORTHOPEDICS

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Interest in microwave applications in medicine has increased in recent years.
In this paper we report the results of a first experiment in microwave hyperthermia applied in the field of orthopedics, with special reference to the problem of bone insertion tendinitis.
After a short preliminary explanation of the principles which are the bases for oncological and orthopedic hyperthermia, the structure of the system for orthopedic hyperthermia designed and developed by the ENEA Division of Physics and Biomedical Sciences (Italy) and the SMA Research Center (Italy) is described.
The number of patients who have been treated, classified according to type of disorder, has provided significant statistical analysis.
The satisfactory results of the experiment suggest that hyperthermia should be used as elective therapy for bone insertion tendinitis and that this therapy should be extended to other types of pathology, vertebral arthrosis in particular.

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1. INTRODUCTION

Medical applications of microwaves (MW) and radiofrequencies are increasingly common. The MW utilized in therapy are based on mechanisms of interaction between electromagnetic energy and biological tissues. The energy deposited in the treated part induces a rise in body temperature. Some therapies have now become routine after being used for years to treat lesions and inflammatory processes involving the muscular and skeletal systems [1,2]. Still in the experimental stage instead is oncological hyperthermia, which utilizes the cytotoxic effect of high temperatures (41-45°C) and the sensitizing effect of other tumour therapies, such as ionizing radiation or antiblastic drugs, on neoplastic cells.

While the non-thermal effects of microwaves are still being investigated, as regards both epidemiological aspects and cellular and molecular problems, the thermal effects have been known for some years now. In vitro experimentation has confirmed that many cell lines are activated in a manner dependent on both the time-temperature relationship and the cell cycle phase. Moreover, it has been seen that the response of cells to heat is strongly influenced by the metabolic and nutritional state of the cells themselves and by the intra- and inter-cellular environment. Experimentation has shown that heat acts mainly on the nuclear and cytoplasmatic proteins, favouring their denaturation, while it has no direct effect on the DNA molecule. Thus it causes alterations in cellular metabolism, in the synthesis of macromolecules and the transport of precursors (tRNA), in the structure of the cytoskeleton; provokes conformation alterations in the structure of the membranes (interference in the flow of cations and metabolites which transmit information between cells, Ca++, H+, cAMP, and alteration in the redox state of the cell) as well as release of hydrolysis [3]. On a more macroscopic level, the major physiological and functional effect of heat on the part of the body undergoing treatment is an increase in the velocity of vascular flow, providing a greater supply of metabolites, i.e., those cellular substances which are useful in repair processes. In this way, heat exerts a positive effect on the evolution of the inflammatory process, since phlogistic disorders depend not only on the nature and mode of action of the triggering chemical-physical agent but also on the patient's capacity for defense (and thus on his vascular reactivity as well). The role of blood perfusion can thus be demonstrated in the case of phlogosis resulting from fracture. After initial hemorrhaging and a phase of devascularization, the first repairing event consists of increased vascularization with neoformation of blood vessels, which is the basis for the regenerative and proliferative processes, followed by the formation of new

cartilaginous and bony structures with the deposition of Ca^{++} salts, and the neoformation of segments of bone tissue. The final reconstruction of the bone takes place in accordance with the load lines, influenced perhaps by electrical fields.
In oncology, the cytotoxic properties and the sensitizing effects of therapies utilizing ionizing radiations are the biological assumptions on which research with experimental animal models is based. Clinical protocols of stages 2-3 are now being developed [4]. These protocols are defined by variable physical parameters (such as number of applications, intervals between sessions and total time of treatment), taking into account some thermosensitization phenomena, characteristic of cell response to repeated heating and of the non-selectivity of the toxic effect of heat on normal and tumoral tissues [4,5].

Increased knowledge of the effects of heat and improvements in microwave technologies for administering it, deriving from oncological applications, have resulted in a rapid upgrading of quality in orthopedic applications as compared to conventional techniques (diathermy and radartherapy).
The first results of the application of MW hyperthermia in the orthopedic field for treating bone insertion tendinitis are reported here. This term is used to indicate a group of tendon pathologies involving the osteotendineaous junction. The main etiopathogenetic element is the mechanical factor: direct trauma or recurrent microtrauma. Also involved, however, are constitutional factors such as age and the reactivity of the tissues. This pathology is found mainly in normally active subjects of middle age or in young people who practice sports or do manual labour. Tendinitis of mechanical origin occurs more frequently in subjects who are engaging in a certain activity for the first time or who are returning to sports or to manual labour after a period of idleness.
In bone insertion tendinitis, from the pathological viewpoint, there exist on the level of the osteotendineous junction zones of hyaline degeneration with fragmentation and necrosis of the tendon tissue and microcystic formations, calcification, fragmentation of the bone insertion fibrocartilage with the formation of microcystic cavities containing necrotic matter, fibrocartilagenous metaplasia of tendon tissue in the vicinity of the joint, zones of inflammation secondary to degeneration and calcification, capillary and fibrous proliferation.
The heat induced by the MW increases the supply of blood and the oxygenation of the tissues (passive hyperemia) and thus tends to favour elimination of locally present toxic substances through the circulation, while simultaneously

exerting a toxic action on the inflammation cells, with an intrinsic analgesic effect.

2. Materials and Methods

2.1. Characteristics of the system

The system used for MW thermotherapy is a prototype designed and constructed by the researchers of the ENEA Division of Physics and Biomedical Sciences and the Research Department of SMA (Florence, Italy) working in collaboration. It has already been used in oncological hyperthermia in the initial stage of clinical experimentation [6]. The apparatus (Fig. 1) is composed of an Ailtech 125MA wide-band microwave generator with an applicator (antenna) of the "water-filled horn" type [7] for 434 MHz (Fig. 2), a thermostat with closed circuit of circulating distilled water and an Analog Devices thermometer with channel (for thermocouples). Through the antenna, which is equipped with an elastic membrane to contain the water circulating inside it with the function of "bolus", the generator radiates onto the area to be treated a microwave beam at the frequency of 434 MHz, which through the energy deposited heats the tissues undergoing treatment (Fig. 3 on dummy). With this system, the transmission of energy is optimized, allowing reduction in the power required (approx. 30 W). Moreover, the therapeutic action is focussed on the part where it is needed and, most important, without any overheating of the skin. By appropriately setting the temperature of the bolus according to the part of the body to be treated and measuring the surface temperature of the skin, it is possible to keep the zone involved within the correct temperature range for the therapy by controlling the emission of power. This is possible thanks to studies conducted on the distribution of temperatures deriving from heating induced by microwave beams in clinical oncology utilizing simulation techniques [8] through the application of electromagnetic and thermodynamic models (Fig. 4.).
To improve the quality of the therapy, information deriving from the quality control procedures used in oncological hyperthermia [9] has also been utilized to guarantee the technical quality and repeatability of the system. Due to the efficiency of the system, not only is there excellent selective and controlled heating, but the level of the electromagnetic field in the surrounding environment (Fig. 5) is far below the recommended precautionary levels [10], ensuring greater safety to operators in comparison with the apparatuses currently used for radartherapy and diathermia.

2.2 Application method

For the pathologies treated up to now, two 30-minute applications a week have been effected, for a time of 4 or 5 weeks. The applicator, adequately oriented, is placed in contact with the part of the body to be treated. The bolus has been thermostated at the temperature of 39°C, while the surface has been kept at a temperature of about 40-40.5°C with mean power of 20-30 Watts supplied by the generator.

2.3 Case histories

Forty patients affected by bone insertion tendinitis in various regions have been treated. Of these, 23 were men and 17 women. The minimum age was 18, the maximum 75, with a mean age of 45.5 years. Thirty-three of these patients had undergone previous treatments (physical therapy/kinesitherapy, infiltrations, etc.) without success. Nine patients were involved in regular sports activities (on both the amateur and the competitive levels) of various kinds, the remaining 31 in more or less sedentary activities. As regards the bone insertion tendinitis, hyperthermic treatment was applied to the following:

* scapulo-humeral periarthritis: 8 cases (3 women, 5 men)
* tendinitis of the long end of the brachial biceps: 3 cases (2 women, 1 man)
* epicondylites: 14 cases (9 women, 5 men)
* tendinitis of the adductors in the thigh: 1 case (man)
* quadriceps tendinitis: 4 cases (4 men)
* tendinitis of the rotula at the proximal insertion: 4 cases (2 women, 2 men)
* tendinitis of the femoral biceps at the proximal insertion: 1 case (1 woman)
* tendinitis of the Achilles tendon: 2 cases (2 men)
* tendinitis of the plantar aponeurosis: 3 cases (3 men)

The degree of pain was evaluated according to a scale of values ranging from 1 to 10. At the start of the therapy, the minimum value was 4 and the maximum 10, with a mean value of 7.9. The same criterion was used to evaluate functional impairment, which ranged from a minimum of 3 to a maximum of 9, with a mean of 7. The duration of the pathology ranged from a minimum of 3 months to a maximum of 3 years, with a mean of 9.3 months. The number of hyperthermia sessions averaged 7, with a maximum of 10 and a minimum of 5. Skin temperature, measured with the electronic thermometer, reached minimum values of 39.7°C, maximum 40.5°C, with a mean of 40.1°C per session. Only 6 patients underwent associated medical therapies (infiltration) or physical therapies (ultrasonics, ionotophoresis, magnetotherapy), given the severity of the subjective and objective symptomatology. None of the patients interrupted the treatment because of worsening of the clinical picture. All of the patients were advised to keep the affected limb at rest during the treatment period and for 30 days after the last application. The results obtained were classified as: excellent, good, fair, poor, on the basis of reduction or disappearance of the pain and of the functional impairment.

3. RESULTS AND CONCLUSIONS

Of the 40 patients treated, the results obtained were excellent in 24 (60%), good in 10 (25%), fair in 4 (10%) and poor in 2 (5%). The amount of pain at the end of the cycle of applications averaged 1.3 (min 0, max 7). As regards functional impairment, mean values of 1.5 (min 0, max 6) were obtained. Clinical results were obtained on the average within 30 days of the last MW application. In a follow-up carried out 12 months later, no worsening of these results was observed. None of the patients presented side effects on the cutaneous level during treatment. In 30% of the cases treated (pathology in acute inflammatory stage) there was a slight increase in the local algesic symptomatology during the first 2 applications, which had no effect however on the final clinical result. It is interesting to note that there was no difference between patients who practiced sports and those who did not, as far as results were concerned. In a few patients (6) who underwent associated therapy (physical therapy, infiltrations, etc.) the results were superimposable on those obtained with hyperthermia alone, indicating that combining other therapies probably does not improve the final result.
In the future, special attention should be dedicated to methods of administering treatment for patients affected by the pathology over a long period of time. In the two patients who showed poor results, with neither improvement nor worsening of the local clinical situation, the pathology had been present for over 18 months and had been refractory to all previous medical or physical therapy, while in the patients who showed only fair results (slight lessening of pain and temporary improvement in functional impairment), the pathology had been present for over 8 months. Analyzing the above results it is thus possible to suggest that MW hyperthermia should be considered the elective therapy for bone insertion tendinitis. In consideration of these positive results, the indication for hyperthermic treatment has been extended to other types of pathology and other anatomical districts,

vertebral arthrosis in particular. Initial results appear satisfactory.

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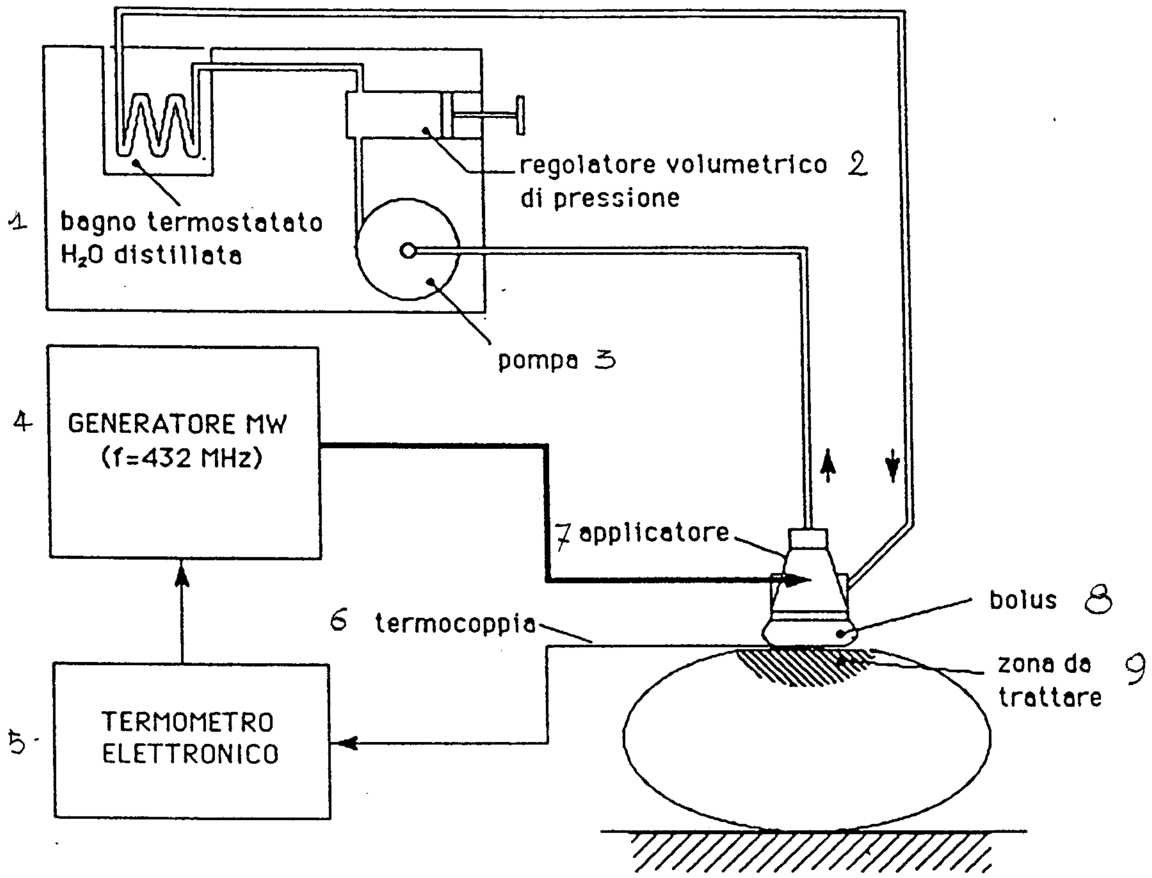


Fig. 1 - Diagram of experimental hyperthermia system

1 thermostated bath distilled H_2O

2 volumetric pressure regulator

3 pumps

4 MW GENERATOR (f=432 MHz)

5 ELECTRONIC THERMOMETER

6 thermocouple

7 applicator

8 bolus

9 zone to be treated

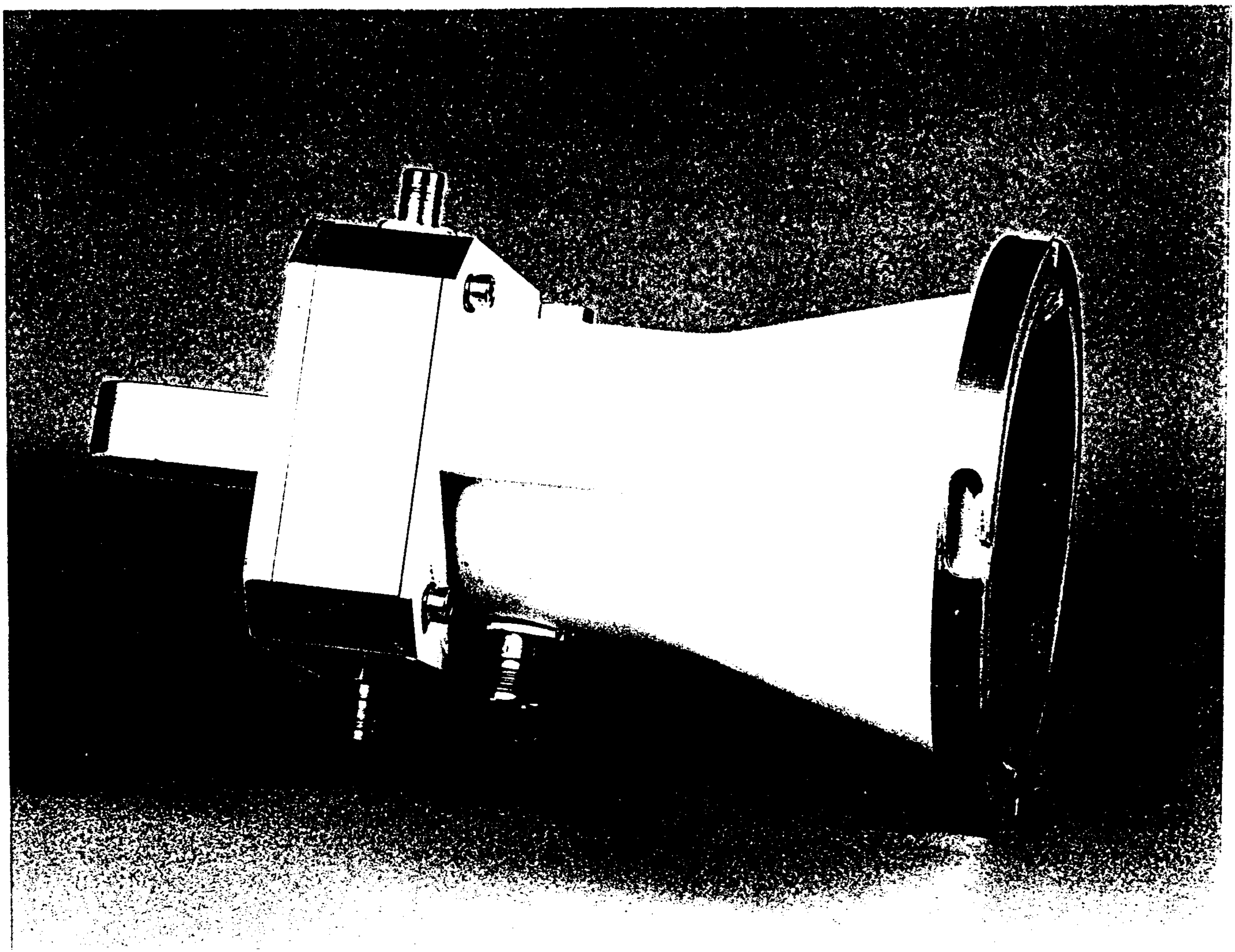


Fig. 2

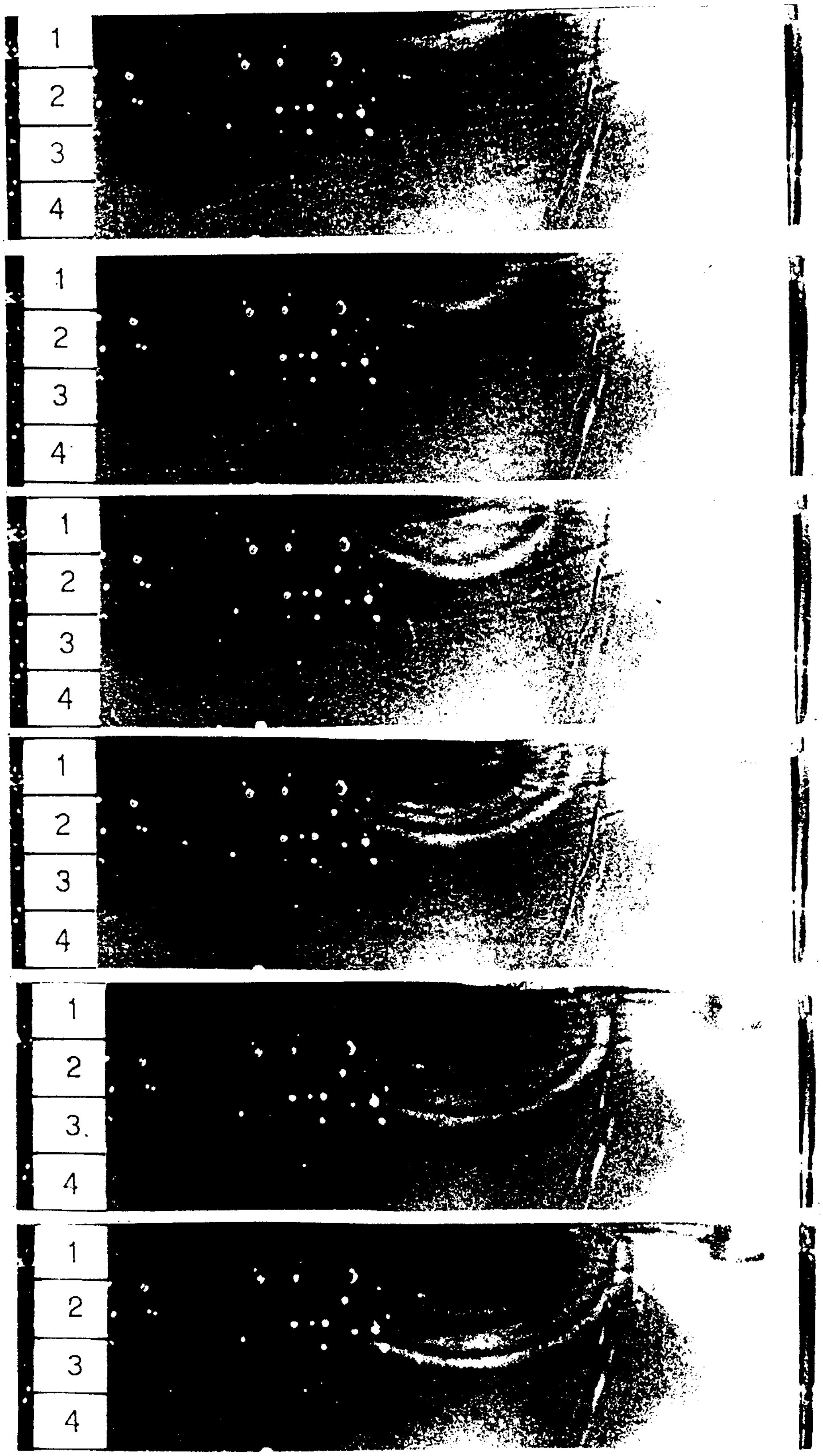


Fig. 3

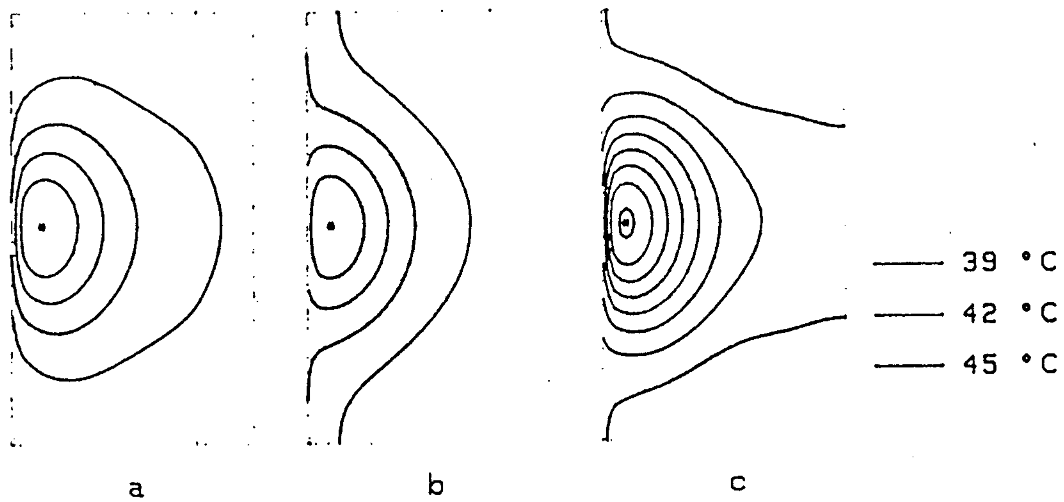
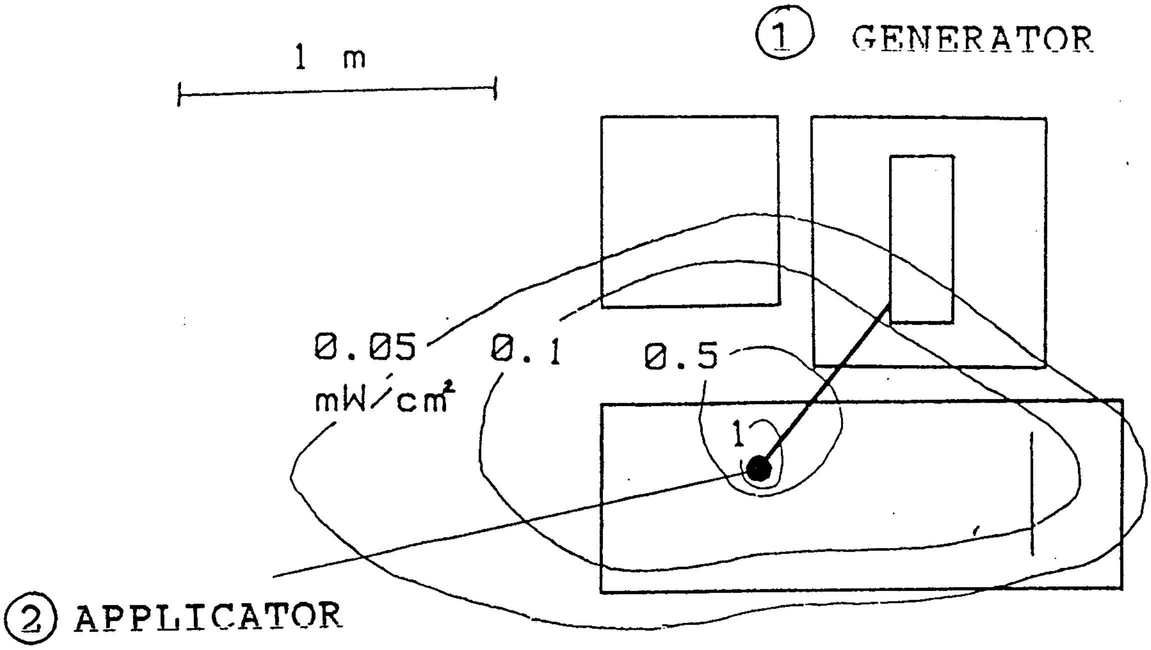


Fig. 4 - The three thermal maps have been produced by simulation of heating on a model of stratified tissues (from left to right on each map: 1 mm of skin, 4 mm of fat, 55 mm of muscle and 20 mm of bone tissue) with different conditions of bolus temperatures, surface temperatures and maximum temperatures: a) T_{bol} = 37°C, T_{sup} = 39.5°C, T_{max} = 42°C; b) T_{bol} = 39°C, T_{sup} = 40.5°C, T_{max} = 42°C; c) T_{bol} = 39°C, T_{sup} = 42.5°C, T_{max} = 46°C. Thus when T_{bol} and T_{sup} are known it is possible to know approximately the temperature distribution in the zone undergoing treatment. The applicator is considered to be in contact with the skin through the water-filled bolus (at left of each map).



f=433 MHz; P=150 W;

Fig. 5 - Map of levels of EM exposure in the environment surrounding the apparatus for a power of 150 W (3 times greater than the power used in therapy) at the frequency of 434 MHz. As the limit for professional exposure at this frequency is 1 mW/cm2, the safety of this apparatus for operators is obvious.