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A Method of Controlled Local Hyperthermia

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Abstract: There are a lot of methods for high temperature cancer treatment in the world. Most of them use high frequency or ultrasound. These methods are harmful for patients and for medical staff too. Such devices can't provide high accuracy of temperature stabilization and have a lot of other serious shortcomings. In this paper a new method of controlled local hyperthermia is shown. It is based on using of direct current and eliminates all shortcomings of traditional hyperthermia methods. The method of controlled local hyperthermia can be used as the innovative method of cancer treatment not only in large special clinics and research centers but in small clinics and polyclinics too.

Key words: Local hyperthermia · Control system · Temperature stabilization · Oncology

INTRODUCTION

The using of hyperthermia in cancer treatment is known for thousands years. The first attempts to use high temperature were made by Hippocrates in 4th century BC [1]. He used red-hot iron to cauterize surface cancer tumors. Such long period of using of high temperature causes the large quantity of different methods of hyperthermia (Figure 1 for details) [2].

There are three groups of hyperthermia-total, regional and local. Total hyperthermia is heating the whole human body with cooling his head contemporaneously. It is very dangerous method for patient's life. Regional hyperthermia is the method of heating the whole body part such as leg, arm and so on. It is not such dangerous as total hyperthermia but it is impossible to have a strict control in temperature level.

Local hyperthermia is the most harmless method. It is method when only the tumor is heating. It is the most progressive method. This method doesn't damage health cells. There are a lot of different methods for local hyperthermia in the world. The base of these methods is the using of high frequency or ultrasound [3-5]. High frequency can cause a lot of different diseases in patients and in medical staff too. In addition, high frequency can heat only surface and subsurface tumors

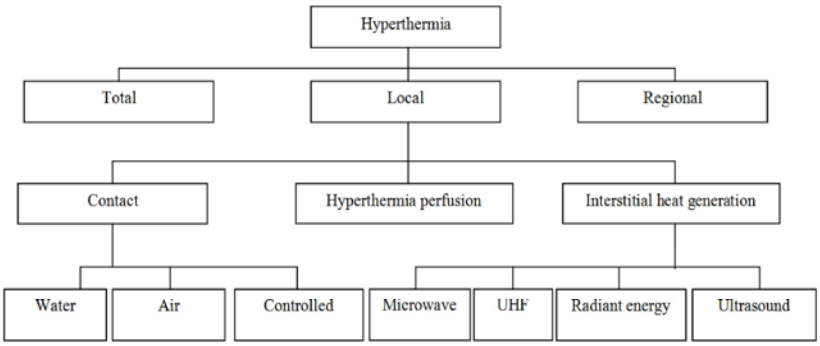

Fig. 1: Hyperthermia classification

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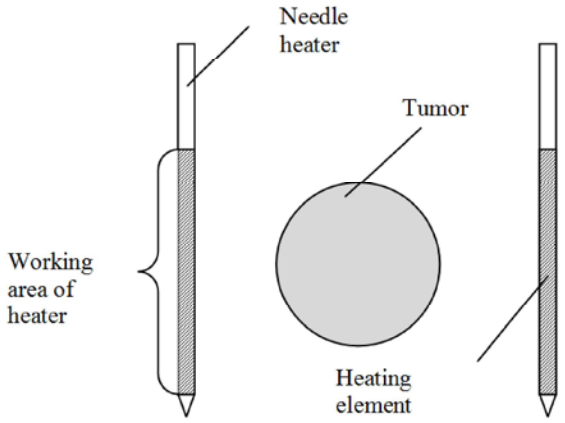


Fig. 2: The correlation of heaters length, the depth of the tumor and the working area

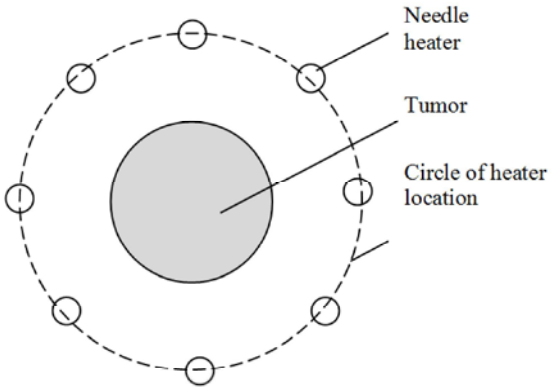


Fig. 3: The location of needle heaters around the tumor

(3-5 cm from the skin). The third shortcoming of them is impossibility of high precision control of temperature level. The fourth shortcoming is the necessity of using of temperature probes to know the current temperature. And, at last, high frequency local hyperthermia needs very large, high power and very expensive devices [6, 7].

So, the aim of work was to produce the method for controlled local hyperthermia that can eliminate all these shortcomings. The second aim was to make different experiments to know how the method treats tumors and to become sure that it prevailing over other known methods. To show the work of the method in this paper the results of experiments-both technical and medical are given.

The Method of Controlled Local Hyperthermia: First of all, before talking about the method of controlled local hyperthermia, it is necessary to show the base principles of local hyperthermia. The literature review and the consultations with Oncology research institute (Tomsk, Russia) gave a lot of requirements that must be performed to get the successful treatment:

- The temperature level must be 43-45 °C.
- The time of reaching of the desired temperature level must be 15-20 minutes or less. It is necessary to pass through the dangerous temperature zone (39-41°C) as soon as possible. Using temperature from this zone can stimulate the cancer growth.
- The duration of procedure must be for about 1 hour.
- It is necessary to repeat hyperthermia procedures every 3 or 4 days to provide a high probability of cancer cells death (all of them are in various stages of development so they do not all die equally well).
- First of all we must provide the heating of peripheral tumor region because most types of cancer have peripheral growth.
- It is necessary to provide the uniform temperature distribution.
- We must eliminate the burn of tissues in place of contact with heaters.
- It is necessary to provide the safeness of patients and medical staff.
- The heating area must be local and we must heat only tumor cells and the nearest healthy tissues.
- The hyperthermia procedure must completely eliminate the promotion of tumor growth and emergence of metastasis.

These principles are in the base of controlled local hyperthermia [2, 8]. This method lets to renounce the use of extra-high frequency and to eliminate all shortcomings of high-frequency hyperthermia. The method of controlled local hyperthermia is based on using of the direct current with special needle heaters. So, it gives the opportunity to treat tumors located on any depth in human body. The length of needle heaters is different and it must be individual to provide the uniform heating of tumor. The correlation of heaters length, the depth of the tumor and the working area of the heater you can see in the Figure 2.

You can see that it is necessary to take needle heaters with working area more than tumor's size in this duration (not less than 1 cm up and 1 cm down). It will help to avoid unheated or poorly heated areas of tumor tissues in the upper and lower sections. The focus of the heating in the tumor is provided by the special location of needle heaters (Figure 3 for details).

You can see that heaters are located around the tumor (in circle) as near as possible to avoid the damage of healthy tissues. So, the method doesn't require the introducing of the heaters in the tumor tissue and, of course, doesn't stimulate metastasis [9-10].

Table 1: The results of experiments for accuracy research

Calibration accuracy checking		Stabilization accuracy checking		
Calibration temperature, °C	Calibration temperature deviation, °C	Supply voltage, V	Temperature changing that causes the first signals, °C	Temperature changing that causes stabile signals, °C
47	± 0.1	5	0.02-0.03	0.04-0.05
		4.5	0.03-0.04	0.05-0.06

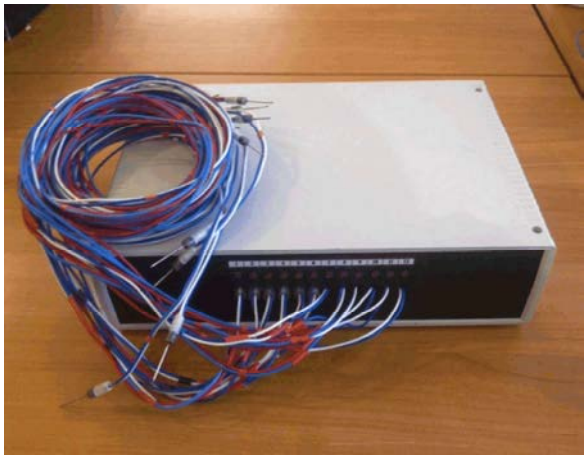


Fig. 4: The device for temperature stabilization

Such location of needle heaters lets to focus the heating at the tumor tissue. Needle heaters are look like cylinders with the very small diameter (negligibly small compared with their length). In this case the heat conduction is uniform in the borders of the circle. In addition, thermal waves in the circle will be superimposed on each other. So the method will give the uniform heat distribution in the tumor area and will guarantee that the temperature in the whole tumor will be on the desired level. The part of thermal waves that go out the circle will be drain by the blood flow. The blood flow inside the circle will not be able to reduce the temperature because of thermal wave superimposing and, in addition, the blood vessels in the tumor are already damaged. At the expense of these facts healthy tissues will be heat but will not be damage because of the less degree of heating compared with tumor.

So, the proposed method of controlled local hyperthermia consists in the fact that after the determining of tumor location by ultrasound or X-rays it is necessary to insert needle heaters in a circle around a tumor within healthy tissues to form the local heating area. After the insertion of heaters the special device gives the direct current to them and heats them to the desired level with high precision. And then it stabilizes temperature on this level during the whole procedure of local hyperthermia.

The Experimental Results: It was necessary to test the method of controlled local hyperthermia to test all it parameters and to know how does it works in live organism. So it was made a lot of different experiments. You can see the device for temperature stabilization at Figure 4. All experiments were produced using this device.

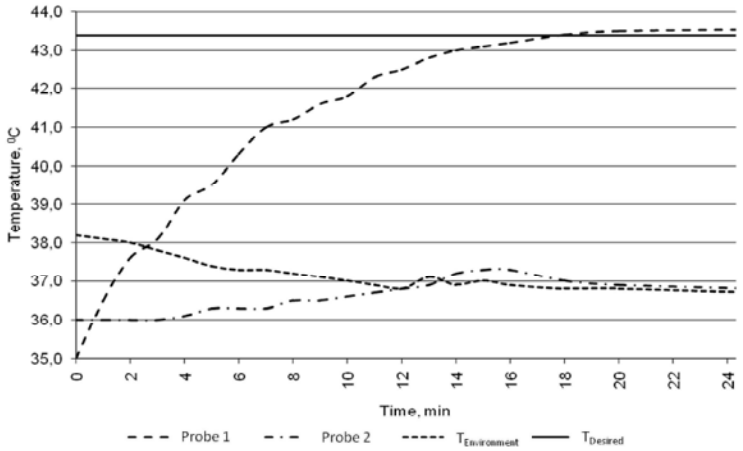
The accuracy of the device depends of two parameters. First of all, it is the accuracy of calibration. It means we must be sure that the temperature of calibration of needle heaters is absolutely correct. At second, it is the speed of system reaction at the situation when the temperature changes at the very small value-less than 0.1 °C.

The results of experiments that give us possibility to check both parameters are shown in Table 1.

You can see in Table 1 that both the first and stabile signals are detected when the temperature changed on less than 0.1 °C. And it is important that such accuracy of temperature stabilization took place both at nominal voltage (5 V) and at 10% less voltage (4.5 V). So, this table confirms that our device carrying the high precision stabilization of the temperature at the desired level.

To check the work of the temperature stabilization device in the biological tissues the special experiments (on meat) were done. During these experiments it was the task to provide the temperature stabilization at 43-44°C. In addition, we had to reach this temperature level in 15-20 minutes. Also it was necessary to establish that the device makes the minimal action at healthy cells. The results of these experiments are shown at Figure 3. You can see that temperature stabilization is at 43 – 43.5 °C and the time of reaching of this level is 16-18 minutes. Also you see that outside area (outside the circle of needle heaters) is practically not differs from environmental temperature (i.e. the living tissues temperature without heating).

There are some series of experiments were done to check and analyze the work of the device in living organism and to select the necessary parameters of procedure and to appraise the efficiency of the device applying. These experiments were done at laboratory animals (mice, rats and rabbits) in Oncology research institute (Tomsk, Russia). Each series takes for about 1



Probe 1-in the center of heating area, probe 2-28 mm from the center (outside the circle), $T_{Environment}$-environmental temperature (tissues far from heating area), $T_{Desired}$-desired level of temperature stabilization

Fig. 5: The results of experiments on the temperature stabilization (heating area-20 mm in diameter, heaters temperature-45 °C)

month (without the time of preparing to each of them). Each series had the special task-to check the method of needle heaters insertion, heater construction, to apprise the influence of local hyperthermia (by our device) at tumor and metastasis, cooperation with traditional chemotherapy and influence at chemical remedies doze.

All series of experiments were done using these technical parameters:

- The level of temperature stabilization-45 °C;
- The distance between two neighbor heaters-8-10 mm;
- The needle heaters diameter-0.8 mm;
- The time of reaching the level of temperature stabilization-10-15 minutes;
- The duration of each procedure of heating-30 minutes;
- The power of each heating element-1 W.

These experiments give the information that isolated local hyperthermia has not any advantages over traditional methods of treatment. However the cooperative using of local hyperthermia with chemotherapy let us to bring down (a few times) the doze of chemical remedies. It is possible because of the adjuvant (stimulating) influence of hyperthermia at chemotherapy. One of the most important marks of the efficiency of cancer treatment is the continuance of remission (the temporary decreasing of cancer activity). The results of analysis of remission are shown in Table 2.

This table shows that cooperative using of local hyperthermia and chemotherapy gives the decreasing of doze of chemical remedy (from 10 mg/kg to 5 mg/kg) with increasing of the remission continuance (from 4.4 to 9.3 days). In addition the doze 10 mg/kg is already less than usual treating doze.

Another important parameter is the damping of growth of metastasis (transfer cancer cells to distant organs). In Table 3 you can see that cooperative using of local hyperthermia and chemotherapy damps metastasis growth for 77.00% and isolated chemotherapy-only for 25.82%.

The third important mark of the efficiency of cancer treatment is the weight of the tumor node. In Table 4 it is shown that in cooperative using of local hyperthermia and chemotherapy the weight of tumor node is 8-10 grams and in isolated chemotherapy it is about 17 grams.

Table 2: The remission in different methods of cancer treatment

#	Method of treatment	The doze of chemical remedy	The remission continuance
1	Control group (without treatment)	None	None
2	Chemotherapy	10 mg/kg	4.4 days
3	Local hyperthermia	None	None
4	Chemotherapy + local hyperthermia	5 mg/kg	9.3 days

Table 3: The damping of metastasis growth in different methods of cancer treatment

#	Method of treatment	The doze of chemical remedy	The damping of metastasis growth
1	Control group (without treatment)	None	None
2	Chemotherapy	10 mg/kg	25.82%
3	Local hyperthermia	None	None
4	Chemotherapy + local hyperthermia	5 mg/kg	77.00%

Table 4: The Weight of Tumor Node in Differrent Methods of Cancer Treatment

#	Method of treatment	The doze of chemical remedy	The weight of tumor node
1	Control group (without treatment)	None	46.11 g
2	Chemotherapy	10 mg/kg	17.10 g
3	Local hyperthermia	None	24.14 g
4	Chemotherapy + local hyperthermia	5 mg/kg	10.75 g
5	Chemotherapy + local hyperthermia	8 mg/kg	8.62 g

Table 5: The lifetime in different methods of cancer treatment

#	Method of treatment	The doze of chemical remedy	The lifetime
1	Control group (without treatment)	None	100%
2	Chemotherapy	8 mg/kg	135%
3	Chemotherapy + local hyperthermia	8 mg/kg	146%

And, finally, the most important mark of the cancer treatment efficiency is lifetime. The comparison of lifetime in control group (without treatment) and in groups with isolated chemotherapy and with cooperative using of chemotherapy and local hyperthermia made with our device is shown in Table 5. You can see that if we shall take the lifetime in control group as 100% and then in group with isolated chemotherapy lifetime will be 135 % and in group with cooperative chemotherapy and local hyperthermia it will be 146%.

So, you can see that the new method of controlled local hyperthermia is very effective. It gives the possibility to decrease the doze of chemical remedies and contemporary to increase the result of treatment twice or even more.

CONCLUSION

The proposed method of controlled local hyperthermia is very effective in cancer treatment. The experiments in laboratory showed that cooperative using of chemotherapy and controlled local hyperthermia gives more chances to treat cancer. It means-there are a lot of people can realize there hopes to eliminate their tumors, to become healthy once more and to live for a long time.

Such parameters of the method as harmless direct current as the base of it, small size and low power and, in addition, cheapness (in compare with known devices) will give the possibility for small clinics and polyclinics (not only large research centers and special oncology clinics) to purchase the device for temperature stabilization and to treat more people than it is possible now.

Findings: So you can see in this paper that the new method of controlled local hyperthermia is very effective in accordance with other known methods. It shows good results in cancer treatment in animals.

Of course, the new method requires further experiments-cooperative treatment with radiotherapy and human experiments. Such experiments are planned to be done as soon as possible.

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