Design and Mathematical Simulation of Portable Radiofrequency Heating Device by Long-Term Mild-Hyperthermia

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Abstract. In the present day, cancer remains one of the main cause of death, normal therapeutic treatment for superficial cancer enhance the life of patient. However it lows the quality of patient life. A novel design of portal radiofrequency heating device is present to inhibit the growth of tumor. The results numerical simulation of heat transfer in tumor by RF heating device show that heat generated by heating device is powerful enough to suppress tumor, however large vessel and fat in tissue will play an important role in the treatment effect.

Keywords: numerical simulation, quality of patient life, radiofrequency heating device, superficial tumor

1. Introduction

Cancer is a major public health problem all over the world. Based on the cancer statistics from the American cancer society, cancer is the second of leading course of death in United State, 23% of deaths is due to cancer in 2014 [1]. The cancer invasion and recurrence is the main reason for death of patient [2, 3]. Surgery, radiotherapy, chemotherapy are the main treatments for cancer patient. Though the death rate of is decreasing, the number of people die from cancer is still enormous [1].

It is found that the surgical removal of primary tumor may result in the rapid growth of metastases. Kevin also found the use of radiation to eradicate a primary Lewis lung carcinoma results in the growth of the growth of previously dormant lung metastases [4]. And the production of angiogenesis inhibitor by the primary tumor is one mechanism for the inhibition of metastatic tumor [5].

In the 1990s, some scientists found whole body hyperthermia at a relatively lower temperature (about 40.0±0.1°C) for long duration (LL-WBH) had greater antitumor effect than that with a higher temperature (41.5±0.1 °C) for a short time (SH-WBH) [6, 7]. In their experiments, 6,8,10 and 12h LL-
WBH significantly increase the tumor growth delay compared with the SH-WBH, 2h LL-WBH and 4h LL-WBH. Furthermore, LL-WBH reduced the incidence of axillary lymph node metastasis at 14 days post-treatment.

It has been proved long-term mild hyperthermia reduces the microvessel density, which plays an important role in tumor growth and metastasis [8]. The microvessel density of experiment group (heating temperature maintained at 40.0 °C for 12h each day) descends from day 3 to day 14, and the microvessel density is much lower than that of control group [9]. It also has been found that long-term mild hyperthermia alters metabolism pathway of tumor cell [10]. Metabonomics is induced to analysis abundance of long chain fatty acids and acyl glycerol. The results show that long chain fatty acids and acyl glycerol increases from day 3 to day 14 in the experiment group, while those decrease in the control group. As long chain fatty acids is the basic material of phospholipid bilayer, which is necessary for cell proliferation, and acyl glycerol is the energy supply of tumor cell, the abundance increasing reflect the slowing down of tumor cell activity [11].

These experimental results have shown that under long term hyperthermia treatment, the growth of primary tumor can be suppressed and the distal metastasis foci inhibited. It is a promising conservative tumor treatment method for patients who prefers better living quality than taking a painful conventional treatment.

In this paper, a portable radiofrequency based long term hyperthermia device for breast/ melanoma cancer suppression is designed. Radiofrequency is one of the most popular heating technique. As a volume heating technique, it has the ability of killing tumor which is about 3~5cm away from the electrode probe [12, 13]. It has been used for ablation of tumors with temperature higher than 50°C [14]. A lot of studies have focused on short-time, high-temperature (>50°C), which aims to erase tumor tissue. Therefore most of studies focus on the temperature and heating time to predict the therapy effect of radiofrequency ablation by numerical study [15].

However, unlike the high temperature ablation treatment, in this newly proposed treatment process, temperature should be well controlled in the mild heating range while sparing any possible damage to normal tissues as a long duration of heating is necessary. Thus, control and planning of the energy of the radiofrequency is very important. And the existing of fat (has very low electro conductance) [16, 17] and large blood vessel (large convection effect) [18, 19] in the tissue are two major parameters influencing the control of the system.

Thus, a mathematical model is also established to evaluate the function of the designed device by simulating the temperature distribution of the tissue. The influence of fat and large blood vessel in the treatment process is also studied. An optimization method is proposed for better planning and control of the heating process.

2. Device design
The portable radiofrequency heating device consists of RF electrode probe, control circuit module, and power supply module. The schematic diagram is showed in figure 1. The RF electrode probe concluded positive electrode and ground pad. In order to lower the contact temperature of RF electrode and skin, the electrode was immersed in water which was forced circulating around the electrode by fan inside the device. The electrode probe was placed right above the superficial tumor, while the ground pad is placed opposite of the body. The power supply module had two separated battery group, one for control system, and the other for RF electrode which contained 126000 J energy for continuous heating of 12 h. The main function of the control circuit module was to transfer DC to AC of 460 KHz, which was suitable for RF heating with no side effect for nerve and muscle. It was also used to monitor the temperature of skin to avoid overheating and protect patients.
3. Modeling
To test the function of the device designed and evaluate the influence of fat and big blood vessels existence, a model is established. The geometric sketch of the model is illustrated in Figure 2. The normal tissue is simplified to be a cylinder with a radius of 35 mm and a length 60 mm long. The electrode is attached on the surface as shown in figure 2. The contact surface of electrode and tissue is a circle with a diameter of 5 mm. The bottom surface of tissue is attached to the ground pad. The tumor is assumed to be a sphere with a diameter of 8 mm, and located 10 mm below the contact surface.

3.1. Heat transfer
The Pennes’ equation [20] was used to describe the heat transfer in the tissue.

$$\rho_t c_t \frac{\partial T_t}{\partial t} = \nabla \cdot (k_t \nabla T_t) + \rho_b \omega_b (T_b - T_t) + Q_{meta} + Q_{SAR}$$

(1)

Where $\rho_t$, $c_t$, $k_t$, $T_t$ represented the density, heat capacity, heat conductivity and temperature of tissue; $\rho_b$, $T_b$, $\omega_b$ represented density, temperature, and blood perfusion of tissue. And $Q_{SAR}$, $Q_{meta}$ are the volumetric heating rate of the Radiofrequency and tissue metabolic heating rate.

The outer surface of the tissue, electrode and ground pad were surrounded by air or cooling water in which heat exchange occurred via heat convection.

$$k \nabla T|_{boundary} = h_s (T_{air} - T_t)$$

(2)
Where $h_s$ was the natural heat convection coefficient of passive flow air, and $T_{air}$ was the temperature of air.

### 3.2. RF electrode field

The RF frequency used in this model is 460 kHz, which is much lower than 1 MHz, thus the quasi-static approximation of the electrical field in the tissue can be applied [21].

$$\nabla \sigma_t \nabla V = 0$$  \hspace{1cm} (3)

Where $V$ and $\sigma_t$ presented the electric potential and electric conductivity of tissue.

The heat generated by RF could be calculated by the electric potential gradient and electric conductivity of tissue.

$$Q_{SAR} = \sigma_t (\nabla V)^2$$  \hspace{1cm} (4)

The outer surface is surrounded by air, whose electric conductivity is $10^{-15}\text{S/m}$. Therefore, the outer surface could be considered as insulation.

$$\nabla V = 0$$  \hspace{1cm} (5)

With the temperature rising, blood vessel lost the ability of blood perfusion because the intima and media smooth muscle cell underwent irreversible coagulative necrosis and block the vessel while temperature was above 50°C.

$$\omega_b = \begin{cases} 
\omega_b & T < 50^\circ\text{C} \\
0 & T \geq 50^\circ\text{C}
\end{cases}$$  \hspace{1cm} (6)

Also, the cells was dead because of protein inactivation above 50°C, and the metabolic rate of cells was assumed to be zero.

$$Q_{meta} = \begin{cases} 
Q_{meta0}[1 + 10\%(T_t - T_0)] & T < 50^\circ\text{C} \\
0 & T \geq 50^\circ\text{C}
\end{cases}$$  \hspace{1cm} (7)

Where $T_0$ was the normal temperature of core body.

The rising temperature would also cause the corresponding change of electric and heat conductivity of tissue [22]. The relationships had been obtained by experiments [23] [24].

$$k(T) = k_0 [1 + 0.003(T - T_0)]$$  \hspace{1cm} (8)

$$\sigma(T) = \sigma_0 [1 + 0.016(T - T_0)]$$  \hspace{1cm} (9)

Where $\sigma_0$ and $k_0$ were the electric and heat conductivity at $T_0$, respectively.

The fat in human body had the similar phenomena [17]

$$\sigma_f = \sigma_{f0} [1 + 0.002(T - T_0)]$$  \hspace{1cm} (10)

$$k_f = k_{f0} [1 + 0.017(T - T_0)]$$  \hspace{1cm} (11)

The larger vessel inside the body would affect the temperature distribution of RF heating and then affect the result of therapy, especially when it was close to tumor [18]. The blood vessel wall was assumed to be thin enough that thermal resistance of the vascular wall was neglected, and heat was dissipated by heat convection. The vessel was assumed long enough that the blood flow reached thermodynamic equilibrium. The coefficient of heat conductivity of blood was:
\[ h_v = \frac{Nu k_B}{D} \]  

(12)

Where \( Nu \) was Nusselt number, which could be calculated by,

\[ Nu = 4 + 0.48624 \ln \frac{Re Pr D}{18 lv} \]  

(13)

Where \( Re \) was Reynolds number, \( Pr \) was Prandtl number, \( D \) was the diameter of blood vessel, and \( lv \) was the length of blood vessel.

\[ Re = \frac{\rho b v_b D}{\mu} \]  

(14)

Where \( \rho_b, v_b, \mu \) represented density, flow rate, and viscosity of blood vessel respectively.

In order to keep the temperature of skin maintained around 37~40 °C under cooling condition, the potential voltage of RF electrode was control by PID algorithm. The central point of contact surface was set as the monitor point. Proportional and integral were induced

\[ V = V_0 [0.04(T - T_{set}) + 0.01 \int (T - T_{set}) dt] \]  

(15)

Where \( T_{set} \) was the setting temperature of monitor point.

Table 1. Parameters used in the model

| Parameters                  | Symbol | Value          | Reference |
|-----------------------------|--------|----------------|-----------|
| Temperature of blood        | \( T_b \) | 37°C           |           |
| Temperature of air          | \( T_{air} \) | 20°C           |           |
| Metabolic rate              | \( Q_{meta} \) | 33800 W/m³    | [25]      |
| Electric conductivity       | \( \sigma_b \) | 0.336 S/m     | [21, 26]  |
| Blood perfusion             | \( w_b \) | 0.008 s⁻¹     | [21]      |
| Electric potential of electrode | \( V \) | 15V           |           |
| Density of blood            | \( \rho_b \) | 1050 kg/m³    | [27]      |
| Electric conductivity of blood | \( \sigma_b \) | 0.22 S/m     | [28]      |
| Heat conductivity of blood  | \( k_b \) | 0.5 W/(m·K)   | [29]      |
| Flow rate of blood          | \( v_b \) | 22.9 cm/s     | [30]      |
| Viscosity of blood          | \( \mu \) | 0.0032 Pa·s   | [31]      |
| Prandtl number              | \( Pr \) | 25            | [32]      |
| Vascular length             | \( lv \) | 60 mm         |           |
| Vascular diameter           | \( D \) | 8 mm          | [33]      |
| Desity of fat               | \( \rho_f \) | 960 kg/m³    | [34]      |
| Heat capacity of fat        | \( C_f \) | 2600 J/(kg·K) | [34]      |
| Electric conductivity of fat | \( \sigma_f \) | 0.02 S/m   | [34, 35]  |
| Heat conductivity of fat    | \( k_f \) | 0.17 W/(m·K) | [34]      |

4. Results and Discussion

The theoretical model was solved by COMSOL. Tissue was assumed to be constituted of muscle. With natural cooling, the temperature of tissue trended to balance after 1000s. The result was shown in 0. The highest temperature was 48°C and appeared on the contact surface, while the lowest temperature of tumor was 38.9 °C, which appeared at the bottom of tumor. Thus the lowest temperature of tumor was above 39 °C, which was efficient to suppress the tumor growth. However, the skin temperature was 5 °C higher than threshold of tissue burn damage.
In order to lower the temperature of the contact surface, forced air flow was used to cool down the contact surface. The coefficient of heat convection was $100\text{W/(m}^2\cdot\text{K})$, and the temperature of air was $20^\circ\text{C}$. The result was shown in Figure 4. After treatment with 1000s of RF heating, the highest temperature of tissue was $42.6^\circ\text{C}$, which was lower than $43^\circ\text{C}$. And the temperature range of tumor was from $38.5^\circ\text{C}$ to $42.5^\circ\text{C}$, which was almost enough to suppress the tumor growth and protect the normal tissue.

Thus, with passive cooling, the temperature of tumor was high enough to slow down the tumor growth, however it would also cause damage to normal tissue. With forced air cooling, RF heating was efficient to suppress the tumor growth and protect the skin. From these results, it is implied that cooling unit in RF electrode module was necessary.

4.1. Influence of blood vessel
The blood vessel was assumed to be located right under the tumor. The distance of upper vascular wall and the bottom of tumor was set to be 2mm and 4mm as shown in Figure 5. In this simulation, the RF probe with cooling unit was applied. The simulation results were shown in Figure 6. The temperature of tumor tissue ranged from $37.62^\circ\text{C}$ and $42.43^\circ\text{C}$. Compared with the tumor without large blood vessel, the highest temperature had dropped $0.15^\circ\text{C}$, and the lowest temperature obtained at the bottom of tumor, had dropped $1.1^\circ\text{C}$. 

![Figure 3](image3.png)

**Figure 3.** Temperature distribution of tissue under RF heating for 1000s under passive cooling.

![Figure 4](image4.png)

**Figure 4.** Temperature distribution of tissue under RF heating for 1000s under forced air flow.
Figure 5. The blood vessel position and the meshing of the tissue.

From the results, it showed that the blood vessel had little effect on the region of tumor away from blood vessel, but had obvious effect on the region of tumor close to it while the minimal distance of tumor and blood vessel was set to 2mm. The lowest temperature was not high enough to exceed the threshold of the mild hyperthermia.

Figure 6. The influence of blood vessel located just below the tumor on the temperature distribution inside tumor, while the RF electrode is cooled by forced air flow.

If the minimal distance of tumor and vascular was 4mm, the temperature distribution of tumor tissue had little change compared with the non-vascular model. Thus, the influencing effects of vascular was determined by the distance of blood vessel and tumor. And the region close to the larger blood vessel dropped dramatically while the distance between vascular wall and bottom of tumor was 2mm. Thus the suppression effect of long-term mild-hyperthermia treatment would be weaken by the large blood vessel.

4.2. Influence of fat
Under the skin in normal human body was a fat layer, which was a material with low electric and heat conductivity. In this paper, two different fat distribution had been assumed: (a) the bottom half of tumor is packed in the fat layer; (b) the upper half was packed in the fat layer.
Figure 7. Distribution of fat layer in the tissue. The purple area represents the fat.

In this model, the RF probe with cooling unit was applied. And the convection coefficient on the probe surface was 100W/(m²·K) as same with the previous simulation. The simulation results was showed in Figure 8. In the two distribution, the highest temperature of tissue were below 43 °C, especially in (a) distribution the highest temperature is only 39.39 °C which is under the threshold of tissue damage. In (a) distribution, the temperature is almost uniform at about 39 °C. However, when the fat layer was above the tumor, the bottom of tumor is only 37.95 °C which couldn’t satisfy the mild hyperthermia condition.

Figure 8. Influence of different locations of fat layer on the temperature distribution in the tumor.

From the results, due to low conductivity of fat layer, the temperature distribution had changed a lot compared to the tissue without fat layer. On a whole, the temperature of tissue is lower. As for different distribution, when the bottom half of tumor was packed in the fat layer, the tumor would be heated uniformly, and the temperature distribution could satisfy the mild hyperthermia requirement. However when the top half of tumor was packed in the fat layer, the bottom region of tumor is lower than mild hyperthermia threshold. Thus, for different patient, determine the fat layer location was necessary in the mild hyperthermia treatment.

5. Conclusion
In this paper, a long term mild hyperthermia device was designed. Furthermore in order to evaluate the feasibility of the device, some simulations were performed. Firstly, by the comparison between the RF probe with cooling unit and without it, the former one was more appropriate due to the protection of normal tissue. Besides, the location of large blood vessel around the tumor was also a vital factor, the blood vessel could lower the temperature of tumor dramatically, but when the distance between blood vessel and tumor is longer than 4mm, the cooling effect of large blood vessel could be neglected. Lastly,
fat layer around the tumor could play a significant role in the RF heating. To be specific, when the top half of tumor was above the fat layer, the temperature in the tumor would be uniform and satisfy the requirement of mild hyperthermia. Whereas the temperature of the bottom region was lower than the threshold of mild hyperthermia when the top half of tumor was packed in the fat layer. On a whole, this device could implement long term mild hyperthermia treatment on superficial tumor. Before the treatment, the component in the tissue around the tumor should be checked, especially the large blood vessel and fat layer.

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