Model-based assessment of probe placement criteria in cancer therapy using RF ablation

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Abstract. Radiofrequency ablation has been developed as a minimally-invasive method for cancer therapy. Nevertheless, the unfeasibility of direct observation during ablation process sometimes becomes a challenge for practitioners, particularly those constrained by the absence of a proper monitoring system. Thus, aiming to develop a prudent cancer therapy planning, this research develops a 3D model that enable practitioners to predict the tissue damage resulted by a simulated ablation before a real ablation is executed. The model, developed using finite element method, is made to mimic real human liver tissue by simulating its physical properties as temperature-dependent functions. Three probe placement cases, representing three different approaches, are analysed to study the effect of probe placement configuration on tissue damage formed during a time-dependent ablation process. The three placement cases are surface-perpendicular placement, misaligned placement, and relatively accurate placement. It can be concluded that the accuracy of a probe placement configuration can be assessed by quantifying two major parameters: average tissue damage in the target domain and accumulated damage resulted in complementary tissue domain. Optimum ablation duration can also be determined by considering those parameters.

1. Introduction

Radiofrequency (RF) ablation is one of minimally invasive techniques that have been developed for various purposes including cancer therapy. In many cases, without the presence of proper monitoring system, Indonesian practitioners are faced with observation unfeasibility during ablation process. This condition may challenge the execution of an optimum ablation due to incomplete ablation process or inaccurate probe positioning. In addition to ineffectiveness, inaccuracy in probe placement planning could also lead to damage resulted in normal tissue surrounding the cancer.

This research applies numerical simulation method to develop a 3D model of bipolar RF ablation. It enables practitioners to predict damage formed in liver tissue before performing the actual therapy. As an outcome, practitioners can assess the effectiveness of each configuration and the corresponding time duration in order to eliminate cancer tissue with certain position, shape, and size. Thus, an ablative cancer therapy is planned quantitatively.

2. Theoretical backgrounds

Applied across the tissue, high-frequency AC electricity generates heat (Qheat) proportional to the product of current density and electric field produced in the tissue [1]. The generated heat is then substituted
into Pennes’ equation (1948), which has been modified by Yang et al. [2] by considering heat for tissue water evaporation process, to be

$$\rho_{ti} \left[ C_{ti} \frac{\partial T_{ti}}{\partial t} + \alpha \frac{\partial \rho_{water}}{\partial t} \right] = \nabla \cdot k_{ti} \nabla T_{ti} + \rho_{bl} C_{bl} W_{bl}(T_{bl} - T_{ti}) + Q_{heat} + Q_{meta}$$

Variables $\rho_{ti}$, $C_{ti}$, $T_{ti}$, and $k_{ti}$ are consecutively the density, specific heat, temperature, and thermal conductivity of liver tissue. Variables $\rho_{bl}$, $C_{bl}$, $W_{bl}$, and $T_{bl}$ are consecutively the density, specific heat, perfusion rate, and temperature of blood, while $\alpha$ and $\rho_{water}$ are water evaporation heat and tissue water density. $Q_{meta}$ represents the generated metabolic heat. The level of tissue damage resulted by the ablation can be approximated by the Arrhenius equation as

$$\Omega(t) = \ln \left[ \frac{c(0)}{c(t)} \right] = \int_{0}^{t} A \exp \left[ -\frac{\Delta E}{RT} \right] dt$$

$A$ is the frequency factor, $\Delta E$ is the activation energy and $R$ is the universal gas constant. Biological tissue is assumed to be dead (99% damage) when $\Omega(t)$ reaches 4.6 [3].

### 3. Model development

This model is developed using finite element method (FEM) in COMSOL Multiphysics 5.0. Multiphysical coupling is designed between Time-harmonic Electric Current and Time-dependent Bioheat Transfer modules. Bipolar RF ablation is modeled as in the prior research of Tanotogono et al. [4], yet only 280 kHz 121.8 Volt AC electricity is used in this paper. Targeted cancer tissue was modeled as a separated ellipsoid domain (figure 1) and the remaining tissue domain that is not covered by cancer domain is labeled as complementary domain.

![Geometry of ablation model with targeted cancer domain.](image)

Whilst the model developed in prior Tanotogono's model [4] are based on ex-vivo experiment, some improvements are added to this model to mimic tissue activities in in-vivo condition, such as blood perfusion phenomenon and metabolic heat generation, as well as setting the initial tissue temperature to 37°C. Blood perfusion rate, $W_{bl}$, is defined as a piecewise function of tissue damage fraction [5] as

$$W_{bl} = \begin{cases} \frac{(1 + 25\Omega - 260\Omega^2)W_{bl0}}{(1 - \Omega)W_{bl0}} & 0 < \Omega \leq 0.1 \\ 0.1 < \Omega \leq 1 \end{cases}$$

Density and heat capacity of the blood is assumed 1,060 kg m$^{-3}$ and 3840 J kg$^{-1}$K$^{-1}$ [1]. $W_{bl0}$, as the blood perfusion rate in fully active tissue, is approximated to be 1.583 x 10$^{-5}$ m$^3$kg$^{-1}$s$^{-1}$ [6]. On the other hand, metabolic heat generation [7] is defined as

$$Q_{meta} = \begin{cases} 33800(1 + 0.1(T - 37)) & 37 \leq T \leq 50 \\ 0 & T > 50 \end{cases}$$

In this model, the characteristic of cancer tissue is not differentiated from the surrounding normal tissue.

Probe placement configuration, shown in figure 2, is defined by six parameters that determine probe position and direction. Those six parameters are: $x$ and $y$, as 2-dimensional cartesian coordinates of probe insertion point at tissue surface; $\theta$ and $\phi$, as angles in spherical coordinates to determine the direction of insertion; $r$, as depth of insertion, which represents how far probe is moved along its axial; and $\alpha$, as probe rotation angle towards its own axial.
Three test configurations (table 1) were subjectively chosen for predictive assessment using the developed model. Configuration A represents a condition in which practitioners are able to locate the cancer position and insert the probe just in perpendicular to tissue surface. Next, Configuration B shows a condition of inaccurate probe placement. Lastly, parameters in Configuration C were carefully determined by considering the position, direction, and size of the target domain to ensure relatively effective therapy.

| Parameters | Configuration A | Configuration B | Configuration C |
|------------|-----------------|-----------------|-----------------|
| x          | 36.5 mm         | 42.5 mm         | 40.5 mm         |
| y          | 36.5 mm         | 40 mm           | 40.5 mm         |
| θ          | 0°              | 30°             | 20°             |
| φ          | 0°              | 30°             | 42.5°           |
| α          | -50°            | 90°             | 90°             |
| r          | 22.5 mm         | 25 mm           | 23 mm           |

4. Result and analysis

Images in figure 3 show isosurface representations of tissue damage resulted by the three probe configurations after 60 and 120 seconds of ablation. From the three configurations, Configuration B, shown in figure 3(b), depicts how the least ideal result can be yielded by inaccurate probe placement. It is clear that ablation in Configuration B keeps some of the target domain active and destroys a sizeable volume of normal surrounding tissue instead. Thus, placement in Configuration B can be said as not optimum.

At overall, Configuration A in figure 3(a) is more optimal than Configuration B. Nevertheless, in addition to the fact that a part of the target domain still remains, a sizeable amount of complementary
tissue is affected by the damage. Finally, figure 3(c) shows that Configuration C is the most effective probe placement since the shape and position of damage are almost identical to the target domain. Therefore, the damage of complementary tissue around the target is minimized and cancer is eliminated effectively.

Spatially averaged tissue damage ratio in target domain could serve as a parameter to analyze the level of completion during the ablation. It exposes the ratio of cancer cell damaged by the ongoing ablation. Graphic on figure 4 below shows a range of value between 0 and 1 along y-axis since it represents the ratio of killed cancer cells \((c(0)-c(t))\) over initial cancer cells \(c(0)\) spatially averaged over the target domain. Ideally, an optimum probe configuration should bring this value up to 1 in the shortest duration possible. We can see from the plot that Configuration B is not able to reach total cancer killing even after 120 seconds of ablation. This shows that inaccurate probe positioning is not effective in killing cancer. On the other hand, Configuration C is the most effective ablation, followed by Configuration A.

![Figure 4. The average fraction of tissue damage in target domain.](image1)

![Figure 5. Integral fraction of the tissue damage in complementary domain.](image2)

Measuring the effectiveness of probe placement configuration should also consider the damage of normal surrounding tissue as a constraint. In figure 5, the complementary domain is being taken into concern by calculating the integral of tissue damage ratio all over the domain. This exposes how much damage on complementary tissue already generated by an ablation process over time. It is clearly visible
that at all time, more complementary tissue damage is produced by Configuration B, compared to those resulted by Configuration A and C. This gives idea that inaccurate probe placement, in addition to its ineffectiveness in killing target domain, could lead to the damage of normal surrounding tissue. Configuration C, on the other hand, has the lowest impact on complementary domain, followed by Configuration A.

By first glimpse at figure 4, Configuration A and C appear to have nearly the same effectiveness, yet whether or not they are all optimum is still questionable. Let us assume that target domain will be dead when the spatial average of tissue damage is 0.99. Configuration C only needs 95 seconds of ablation to reach a spatial average of 0.99 ($\Omega = 4.6$) in target domain. Nevertheless, Configuration A can only reach that level of completion no earlier than 110 seconds. This 15-second difference definitely brings substantial impact on complementary tissue damage. At figure 5, it is shown that complementary damage resulted by Configuration A after 110 seconds is 19.7% bigger than that resulted after 95 seconds of ablation using Configuration C. It can be inferred that Configuration A damages 19.7% more non-targeted tissue compared to Configuration C. Conclusively, despite the similar effectiveness, converting from surface-perpendicular insertion to a more careful placement could prevent more surrounding tissue from being damaged.

5. Conclusion
Optimum RFA ablation probe placement and duration for cancer therapy could be planned by conducting model-based assessment. The accuracy of a probe placement configuration can be tested by quantifying two major parameters: average tissue damage in target domain and accumulated damage resulted in surrounding tissue. In this research, Configuration C, which is carefully determined by considering cancer position, direction, and size, is the most optimum ablation: yielding maximum tissue damage spread in target domain while producing minimum damage in complementary domain. Configuration C optimally eliminates target after 95 seconds. Due to shorter required duration compared to surface-perpendicular insertion, Configuration C generates 19.7% less damage in surrounding tissue compared to Configuration A.

6. References
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