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Nano-assisted radiofrequency ablation of clinically extracted irregularly-shaped liver tumors

Y.L. Shao[a], B. Arjun[b], H.L. Leo[c], K.J. Chua[a,*]

[a] Department of Mechanical Engineering, National University of Singapore, 9 Engineering Drive 1, Singapore 117576, Singapore
[b] Faculty of Engineering, Engineering Science Programme, National University of Singapore, 9 Engineering Drive 1, Singapore 117 576, Singapore
[c] Department of Biomedical Engineering, National University of Singapore, 9 Engineering Drive 1, Singapore 117576, Singapore

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ABSTRACT

Radiofrequency ablation (RFA) for liver tumors is a minimally invasive procedure that uses electrical energy and heat to destroy cancer cells. One of the critical factors that impedes its successful outcome is the use of inappropriate radiofrequency levels that will not completely destroy the target tumor tissues, resulting in therapy failure. Additionally, the surrounding healthy tissues may suffer from serious damage due to excessive ablation. To address these challenges, this work proposes the employment of injected nanoparticles to thermally promote the ablation efficacy of conventional RFA. A three-dimensional finite difference analysis is employed to simulate the RFA treatment. Based on the data acquired from measured experiments, the simulation results have demonstrated close agreement with experimental data with a maximum discrepancy of within ±8.7%. Several types of nanoparticles were selected to evaluate their influences on liver tissue's thermal and electrical properties. We analysed the effects of nanoparticles on liver RFA via a tumor rending process incorporating several clinically-extracted tumor profiles and vascular systems. Simulations were conducted to explore the temperature difference responses between conventional RFA treatment and one with the inclusion of assisted nanoparticles on several irregularly-shaped tumors. Results have indicated that applying selected nanoparticles with high thermal conductivity and electrical conductivity on the targeted tissue zone promotes heating rate while sustaining a similar ablation zone that experiences lower maximum temperature when compared with the conventional RFA treatment. In sum, incorporating thermally-enhancing nanoparticles promotes heat transfer during the RFA treatment, resulting in improved ablation efficiency.

1. Introduction

Radiofrequency ablation (RFA) is an effective treatment method for both primary and metastasized tumors. It has been widely applied to treat different cancer types of liver, lung and bone due to its fewer complications, minimally invasive advantages and low recurrence rate. The RFA electrodes and ablation system designs have been undergoing calibration and refinement to maximize the diameter of the tumor ablation zone. The major problem of percutaneous RF probe is the inability to produce a large ablation zone that envelopes large tumors. This is because the employment of larger RF power induces the undesirable tissue burns. To overcome the limitation of RFA, alternative ablation systems have emerged, including microwave ablation (Simon et al., 2005), cryosurgery (Ge et al., 2015) and laser-induced thermotherapy (Vogl et al., 2002).

To enhance RFA, the development of internally cooled probes has facilitated remarkable progress in obtaining larger ablation zones (Barauskas et al., 2008). Moreover, in many RFA therapies, large tumors have been ablated by sequentially overlapping single electrode (Dodd et al., 2001). Alternatively, multiple electrodes may be simultaneously applied to deal with large tumors where a single electrode is unable to independently ablate (Huang, 2015; Stoffner et al., 2012). In multiple-electrode RFA treatment, both bipolar and multipolar devices are simultaneously employed instead of monopolar systems (Mulier et al., 2015). From the above-mentioned literature studies, it is apparent that researchers are still focusing on the improvement of RFA probes' design. Thus far, little attention has been devoted to improving the thermal and electrical properties of the liver tumor in order to promote destruction of the cancer tissue during the RFA treatment. Additionally, considering the heat sink effect due to blood flow, a highly complex vascular system can also cause thermally instability during RFA of large-size tumors (Zhao and Chua, 2012).

Today, cancer-related nanotechnology and nano-medicine have attracted significant attention and are subjected to many clinical tests.

* Corresponding author.
E-mail address: mpeckje@nus.edu.sg (K.J. Chua).

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Nomenclature

TC1	position of Thermocouple 1
TC2	position of Thermocouple 2
V	electric potential at any point of a volume (V)
T	transition temperatures of tissue (K)
N	normality of physiological NaCl solution
c	tissue's specific heat (J/(kg·K))
k	thermal conductivity (W/(m·K))
Q_{met}	heat sources from metabolism (W/m^3)
Q_{ext}	heat sources from spatial heating (W/m^3)
t	time (s)
c_0	a constant specific heat at temperature below 63.5 ℃ (J/(kg·K))
L	length (nm)
A	frequency factor (s^{-1})
R	universal gas constant (J/mol ·K)
d	diameter (nm)
n	shape factor

Greek symbols

$\Omega(t)$	cumulative tissue damage
θ_d	fraction of necrotic tissue
ψ	particle sphericity
ρ	tissue density (kg m^{-3})
ω_b	blood perfusion rate (s^{-1})
σ	electric conductivity (S/m)
ω_{b0}	constant blood perfusion of tissue/tumor (s^{-1})
η	volume content

Subscripts

b	blood
T_{ref}	reference temperature
eff	effective value
t	liver tissue
p	loaded particle

The incorporation of nanotechnology to cryosurgery and radiofrequency-induced hyperthermia has gained much attention (Di et al., 2012; Li and Liu, 2010; Yan and Liu, 2008). From the recent works conducted by Di et al. (2012) and Yan and Liu (2008), magnetite (Fe_3O_4), MgO and diamond have proven to be effective in enhancing thermal ablation due to their good thermal properties and biological compatibilities. In RF nano-augmented therapy, gold (Au) nanoparticle and carbon nanotube (CNT) have been selected as suitable candidates because they not only promote RFA but also enable effective absorption of excessive RF radiation (Glazer and Curley, 2011; Lv et al., 2005). The newly explored nano-hyperthermia offers attractive possibilities in tumor therapy (Lee et al., 2011; Shenoi et al., 2011). The ability to treat cancer by utilizing the hyperthermia-introduced nanoparticles has demonstrated positive impacts on targeted tumor cell killing. In addition, the loading nanoparticles into liver tumors is deemed to be an effective method to enhance both electrical and thermal conductivities of targeted tissue. Thus far, there are few existing works that specifically investigate the performance of the nanoparticles when they are used in conjunction with a RFA procedure performed on a solid tumor.

In this study, we judiciously develop a computer simulation tool that predicts the tissue's temperature distributions as well as the corresponding degree of damaged tissue when a solid liver tumor undergoes RFA treatment. The findings from this study are expected to facilitate better understanding related to the influences of selected nanoparticles (Au, Fe_3O_4 and CNT) on RFA treatment of liver tumor surrounded by complex vascular networks.

2. In-vitro experiment

2.1. Materials

To validate the developed model, agarose phantom (composed of 1% of agarose (25 g) and 99% of water (2475 ml) by weight) was employed to simulate the biological tissue. To simulate the flow of blood vessels, several teflon tubes (4.5 mm ID with the thermal conductivity of 0.21 W/m K) were employed (Ge et al., 2017).

2.2. Experimental methods

In our experiment, the StarBurst XL Electrosurgical Device was inserted into an agar gel with an embedded pair of parallel counter-flow tube. The electrode was powered by a RF generator (RITA 1500X (Fig. 3), AngioDynamics Inc, Latham, NY). The RF generator has a maximum output power of 250 ± 2 W. The output frequency is 460 kHz ± 5%. Type T (copper-constantan) thermocouples were used to measure the tissue's transient temperature profiles. The measuring range spares −200 °C to +350 °C. The temperature reading of TC1 and TC2 were employed as a feedback sensor. The applied power and tip temperature data were utilized to valid our mathematical model.

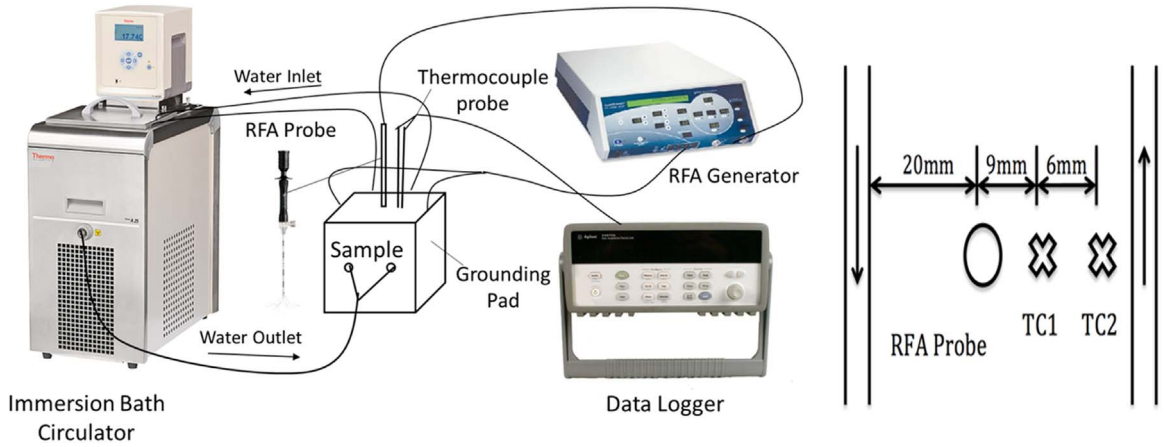

Fig. 1. The Radio-Frequency Ablation (RFA) experimental set-up and the layout of the temperature measuring thermocouples (TC1 is at a distance 9 mm and TC2 is at a distance 15 mm away from the RFA probe center, respectively).