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Research Paper

Effect of different breast density compositions on thermal damage of breast tumor during radiofrequency ablation

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HIGHLIGHTS

- Multi-layer breast models for different breast density compositions are developed.
- PID controller is used to perform temperature-controlled RFA of breast tumor.
- Effect of different breast density compositions on efficacy of RFA is studied.
- Thermal damage of breast tumor decreases with increase in fatty tissue during RFA.
- Provides *a priori* information to clinical practitioner in planning stage of RFA.

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ABSTRACT

The present study analyzes the efficacy of radiofrequency ablation (RFA) of breast tumor with different breast density levels {viz., extremely dense (ED), heterogeneously dense (HD), scattered fibroglandular (SF) and predominantly fatty (PF)}. A spherical tumor of 1.5 cm has been embedded at various locations in the heterogeneous three-dimensional numerical breast model to represent *in situ* early stage tumor. Temperature-controlled RFA has been performed by incorporating the proportional-integral-derivative (PID) controller. A thermo-electric analysis has been done to obtain the temperature distribution and the ablation volume by incorporating the coupled electric field distribution, the Pennes bioheat and the first-order Arrhenius rate equations. The effects of temperature-dependent changes in electrical and thermal conductivities of heterogeneous multi-layer breast models have been considered. The non-linear piecewise model of blood perfusion has been incorporated to achieve better correlation with the clinical RFA. The numerical results have been validated with the *in vitro* experimental results. The results revealed that, the breast density compositions significantly affect the treatment outcomes in terms of ablation volume and temperature distribution. It has been found that, the breast with lower fatty tissue requires significantly less time to attain complete tumor necrosis as compared to the breast with higher fat content.

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1. Introduction

Globally, breast cancer represents a significant personal, social and economic burden that affects women in the prime of their lives. In, 2012 breast cancer was by far the most common cancer diagnosed in women (25% of all new cases in women) and is the leading cause of women mortality worldwide [1]. Over the past few decades, the surgical management of breast cancer has evolved significantly from radical mastectomy (surgical removal of the breast) to breast-conserving surgery (surgical removal of the tumor and surrounding tissue). The breast-conserving therapy remains the gold standard for the treatment of localized breast cancer in spite of being a highly invasive procedure with poor cosmetic results [2]. In this context, non-surgical minimally invasive thermal ablation techniques have been explored by the scientists since the advent of modern imaging with the intention of achieving equivalent efficacy with improved cosmesis.

Among the different thermal ablative modalities available [3], RFA is the most extensively studied and widely applied technique in clinical practice due to low cost and ability to spare the surrounding healthy tissue with localized tumor damage [4]. RFA is a novel technique in which one or more radiofrequency electrodes are inserted into the tumor using various image guidance modalities [5]. Once positioned, a high frequency alternating current

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Nomenclature

A	frequency factor (s^{-1})
c	specific heat capacity (J/kg K)
d	tumor location from body core (cm)
e	error
E	electric field (V/m)
E_a	activation energy (J/mol)
J	current density (A/m^2)
k	thermal conductivity (W/m K)
K_d	derivative gain
K_i	integral gain
K_p	proportional gain
Q_m	metabolic heat generation (W/m^3)
Q_p	radiofrequency heat source (W/m^3)
R	universal gas constant
t	time (s)
T	temperature (°C)
V	electric potential (V)
x, y, z	position/coordinates

Greek symbols

ρ	density (kg/m^3)
σ	electrical conductivity (S/m)
ω_b	blood perfusion (s^{-1})
Ω	induced thermal damage

Subscripts

b	blood
0	initial value

Abbreviations

ED	extremely dense
FEM	finite element method
HD	heterogeneously dense
PID	proportional-integral-derivative
PF	predominantly fatty
RFA	radiofrequency ablation
SF	scattered fibroglandular

(450–550 kHz) is being delivered to the tissue by the electrode and returns back to the generator through an electrical ground pad placed at patient's back or thigh. The generated frictional (resistive) heating leads to the destruction of tumor cell within a few minutes above 50 °C and within seconds above 60 °C [6]. Importantly, the maximum temperature should be strictly below 100 °C to avoid tissue carbonization and water vaporization that can lead to abrupt drop in electrical and thermal conductivities along with poor image resolution [6].

RFA has already been proven to be an effective treatment modality for the treatment of hepatocellular carcinoma and colorectal metastasis of the liver along with gaining interest in treatment of other organs [7–9]. However, the application of RFA in breast cancer is still in its infancy phase of research with most of the initial studies limited only to assess its safety and feasibility [10]. Although, breast as an organ seems to be particularly suitable for RFA application because of its superficial location on the thorax and due to the absence of intervening organs. Also, as there are no large blood vessels located in the parenchyma of the breast, convectional heat loss is improbable to occur. Further, treating breast cancer using RFA technique would lead to better cosmesis and in turn could warrant psychological well-being and quality of life post therapy to the patient [11]. Unlike liver, breast is a heterogeneous tissue that comprises of varying concentrations of fat, glandular and muscular tissues [12]. In accordance with the Breast Imaging Reporting and Data System (BI-RADS) developed by American Cancer Research, different breast density levels for women can be classified into four main groups, viz., extremely dense (ED), heterogeneously dense (HD), scattered fibroglandular (SF) and predominantly fatty (PF) [13]. The extremely dense breast has a higher composition of glandular tissue as compared to the fatty tissue. Whereas, predominantly fatty breast contains higher fatty tissue composition as compared to the glandular tissue. The individual variation in the glandular and fatty tissues of breast may leads to a significant variation in the RFA outcome [14], which is the main motive to conduct the present study.

The mathematical models can play a vital role in providing *a priori* information to the clinical practitioners about the possible outcomes and risks involved before the onset of RFA application. Most of the computational studies available in the literature on mathematical modeling of RFA are mainly focused on liver cancer [15–19], and very limited studies are available on breast cancer [20–24]. Moreover, no study is available till date that takes into account the effects of different breast densities on the outcome of RFA due to the complexity in modeling realistic heterogeneous breast model with different breast density levels. Therefore, the present study is an initial effort in this direction and serves to investigate the effects of different breast density levels on the efficacy of RFA.

2. Materials and methods

2.1. Problem definition

The problem considers a three-dimensional multi-layer breast model (Fig. 1), comprising fat, glandular and muscular tissue layers [25]. A 1.5 cm diameter spherical tumor has been embedded in the breast model to represent *in situ* tumor for early stages at three different locations, viz., 2.6 cm, 3.6 cm and 4.6 cm from the body core to mimic deep rooted tumor (close to muscle), centrally located tumor and superficial tumor (close to skin), respectively. A minimum margin of 1 cm has been provided between the top extreme of the tumor and the overlying skin, and the bottom extreme of the tumor and the underlying pectoralis muscle, to avoid burns during RFA application [14]. Further, four different three-dimensional multi-layer breast models have been developed based on different breast densities, viz., ED, HD, SF and PF [13]. In Table 1, the dimen-

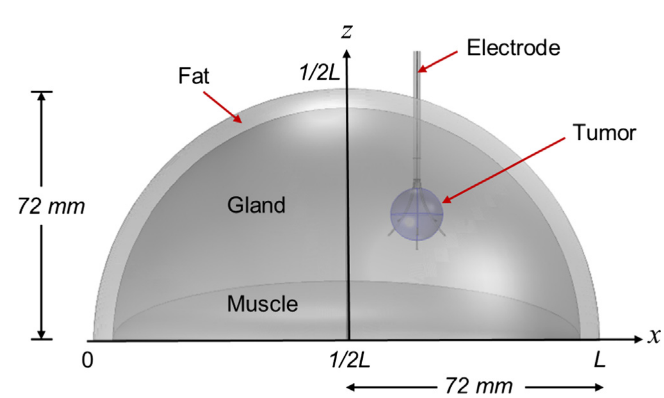

Fig. 1. Three dimensional computational domain of multi-layered breast model.

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