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Studying the performance of bifurcate cryoprobes based on shape factor of cryoablative zones ☆

X. Zhao, K.J. Chua *

Department of Mechanical Engineering, National University of Singapore, 9 Engineering Drive 1, Singapore 117576, Singapore

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ABSTRACT

Conventional cryosurgical process employs extremely low temperatures to kill tumor cells within a closely defined region. However, its efficacy can be markedly compromised if the same treatment method is administrated for highly irregularly shaped tumors. Inadequate controls of freezing may induce tumor recurrence or undesirable over-freezing of surrounding healthy tissue. To address the cryosurgical complexity of irregularly shaped tumors, an analytical treatment on irregularly-shaped tumors has been performed and the degree of tumor irregularities is quantified. A novel cryoprobe coined the bifurcate cryoprobe with the capability to generate irregularly shaped cryo-lesions is proposed. The bifurcate cryoprobe, incorporating shape memory alloy functionality, enables the cryoprobe to regulate its physical configuration. To evaluate the probe's performance, a bioheat transfer model has been developed and validated with *in vitro* data. We compared the ablative cryo-lesions induced by different bifurcate cryoprobes with those produced by conventional cryoprobes. Key results have indicated that the proposed bifurcate cryoprobes were able to significantly promote targeted tissue destruction while catering to the shape profiles of solid tumors. This study forms an on-going framework to provide clinicians with alternative versatile devices for the treatment of complex tumors.

Introduction

In the treatment of benign or malignant tumors, one of the key considerations is to ablate the undesirable cancerous tissue and minimize the affection to the surrounding health tissue. Cryosurgery, also known as cryoablation or cryotherapy, has been used routinely to treat surface and internal malignancies. Advantages of this technique include reduced invasiveness, minimal bleeding, inexpensive and shorter hospital stay compared with conventional surgical excision methods [13,19]. Therefore, it has been widely applied to treat the cancerous tumors embedded in liver, lung, encephalon, prostate and bone [24,1,31,14,38,35].

Conventional cryoprobes are not effective in treating solid tumors that have irregular shape profiles as a large amount of nearby healthy tissue can be damaged due to excessive freezing. Several studies have been carried out to resolve this bottleneck [4,9,29]. Multiprobe cryo-therapy is a common surgical procedure to produce irregular ice balls for large tumors. However, the primary concern of this procedure is determining the probes' relative positions. Rossi et al. has utilized a bubble packing method to predict the actual experimental cryoprobe location [29]. Recently, Chua has introduced a piece-wise method whereby the placement of probes was estimated by superimposing ice contours obtained under discrete conditions [3]. These methods provide applicable results to improve the success of multi-probe cryo-therapies. However, the placement of the cryoprobes to yield optimal surgical outcome is still very much an art held by cryosurgeons. Prior to the surgical procedure, a well-developed plan would require careful consideration involving the employment of the correct number and position of the cryoprobes [25].

To treat solid tumors characterized by their boundary irregularities, it is essential to investigate the shape factor of solid tumors. Many theoretical and applied disciplines have expressed legitimate interests in shape analysis [2,17,12,6,22]. However, it is impossible to extend this unique methodology to a wide range of applications [2]. Golston et al. analyzed the border irregularity with an index termed "jaggedness" [12]. This method of detecting irregular border uses the ratio of the square of the perimeter of a given shape to its corresponding area in order to obtain a size-independent measurement on irregularity [12]. However, there are significant challenges associated with determining the perimeter and area

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* Corresponding author. Fax: +65 6779 1459.
E-mail address: mpeckje@nus.edu.sg (K.J. Chua).

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Nomenclature

CB	cryosurgery bulkiness
C	specific heat capacity (J m^{-3} K^{-1})
f_s	solid faction of the phase change
h	combined convection heat transfer coefficient (J)
h_L	latent heat (J kg^{-1})
I_{rr}	irregularity
k	thermal conductivity (W m^{-1} K^{-1})
$\hat{n}$	vector normal to the surface element
Q_m	metabolism heat generation (W m^{-3})
t	time scale (s)
T	temperature (K)
V_{iso}	volume of isothermal surface (m^3)
V_{equ}	volume of equivalent ellipsoid (m^3)

Greek symbols

β	angle between the primary and secondary probe (°)
Γ	computational volume in tissue unfrozen region
μ	dynamic viscosity (kg m^{-1} s^{-1})
Λ	computational volume in tissue mushy region
Π	computational volume in tissue frozen region
ρ	density (kg m^{-3})

Subscripts

a	tissue frozen region
b	tissue mushy region
c	tissue unfrozen region
t	tissue

values. Therefore, this method cannot be appropriately applied to solid tumors. In addition, results have highlighted that the border detection algorithm is only able to find a reasonably correct border from 60% of investigated cases [12]. Claridge et al. studied malignant skin tumors and expressed the shape of the lesion by a parameter known as the "bulkiness" [6]. They claimed that a figure may be perceived as irregular if either its overall shape is irregular or it has an irregular border [6]. While the shape factor parameter that they have proposed accounts for two-dimensional figures, it is unable to account for the invasive direction associated with cryosurgery. Other studies have also proposed shape descriptors such as the compactness index (CI) [7,34] or the fractal dimension (FD) [23] to quantify border irregularity. Unfortunately, both these parameters have limitations; CI is sensitive to the irrelevant border information while FD does not measure structural irregularities [17]. Combing through available literatures, it is evident that even though various studies have been carried out to investigate shape factor of figures, there exist little or no studies that effectively develop a three-dimensional parameter that comprehensively quantifies shape effects during irregular cryofreezing processes.

The shape factor in cryosurgical planning is more complex as it has to consider the surrounding biological environment. In addition, the size of the parent organ, the flow of large vessels, and the location of nearby bones in the tumor's vicinity affect the freezing path of the cryoprobe.

The complete ablation zone is a geographical region where all the cells are destroyed. It is defined to differentiate from the incomplete ablation zone where only partial cells are killed. Conventional cryosurgery techniques need better ablating protocols that account for the morphology of the complete ablation zone.

In this work, we propose a shape irregularity index that can be uniquely applied to the cryosurgery. The key objective of the present work is to investigate the irregularity index of a desired cryoablative zone. This index serves to promote freezing efficacy and minimize cryo-injury to the surrounding healthy tissue. Additionally, we proposed a unique cryoprobe that is specifically catered to the treatment of irregularly shaped solid tumors. Results realized in this work enable surgeons to analyze the efficacy of their treatment method specifically tailored for irregularly-shaped tumors.

Material and methods

Experimental setup

The freezing process during cryosurgery is characterized by the application of a cryoprobe and the propagation of the freezing interface from the surface of the probe to the interior of the tissue in the direction of the temperature gradients [30]. The schematic diagram of the experiment setup is portrayed in Fig. 1. The pressured liquid nitrogen was stored in the nitrogen cylinder and it was controlled by a needle valve. When the needle valve was open, the nitrogen flowed into the cryoprobe and vaporized at the tip of the cryoprobe. The outflow of the cryoprobe was directed through a temperature control bath (SAHARA S49, Thermo Fisher Inc., Waltham, MA) for a complete phase change to gas. Nitrogen gas was measured with a gas flow meter (MTF4130-D-01, Malema Sensor Inc., Boca Raton, FL) before the exhaustion to the atmosphere. The high resolution thermographic camera (VarioCAM) was used to map transient temperature contours. This infrared thermographic equipment has a temperature resolution better than 0.08 K at 303 K and is able to detect a temperature range of 233–393 K. Thermal images were acquired at every 10 s to an external computer and analyzed with software (IRBIS3 Professional). Three type-T copper-constantan thermocouples were also used to measure the tissue temperature with the essential labels marked. TC1–TC3 were allocated linearly with an adjacent distance of 5 mm. The distance between TC1 and cryoprobe center was 7 mm. The data was digitally logged with data acquisition (34970A, Agilent Inc., Santa Clara, CA) at the interval of every 10 s. The porcine livers, obtained from a local supermarket, were used as biological samples for experimentations. For each experiment, we judiciously selected liver samples with close proximity in terms of size and thickness. These samples were properly numbered. These numbers were used to differentiate the temperature readings during *in vitro* experiments. The *in vitro* experiments to acquire the data for model validation were repeated three times with the registered samples. The temperature readings of thermocouples at predetermined positions were recorded.

Bifurcate cryoprobe

Our proposed bifurcate cryoprobes employ similar freezing mechanism to that of conventional cryoprobes. Compared to conventional probe, it incorporates a supplementary secondary probe to develop irregularly-shaped freezing zones. Fig. 2 shows the main components and the perspective view of the bifurcate cryoprobe. The secondary probe has the capability to regulate its position and hence enables the bifurcate cryoprobe to change its overall shape profile. For example, the junction can be made of shape changing material such as shape memory alloy NiTi. The alloy changes from austenite (at 310 K) to martensite (from 208 K to 77 K) upon cooling [21].