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Numerical simulation of selective freezing of target biological tissues following injection of solutions with specific thermal properties ☆

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Abstract

Recently, we proposed a method for controlling the extent of freezing during cryosurgery by percutaneously injecting some solutions with particular thermal properties into the target tissues. In order to better understand the mechanism of the enhancement of freezing by these injections, a new numerical algorithm was developed to simulate the corresponding heat transfer process that is involved. The three-dimensional phase change processes in biological tissues subjected to cryoprobe freezing, with or without injection, were compared numerically. Two specific cases were investigated to illustrate the selective freezing method: the injection of solutions with high thermal conductivity; the injection of solutions with low latent heat. It was found that the localized injection of such solutions could significantly enhance the freezing effect and decrease the lowest temperature in the target tissues. The result also suggests that the injection of these solutions may be a feasible and flexible way to control the size of the ice ball and its direction of growth during cryosurgery, which will help to optimize the treatment process.

Keywords: Cryosurgery; Selective freezing; Phase change; Thermal properties; Tumor tissue; Numerical modeling; Minimally invasive injection

Since the mid-1960s, freezing tissue in situ has become a well-established method for the ablation of benign and malignant lesions [6]. This freezing technology is usually referred to as cryosurgery, and it offers some advantages over other traditional surgical procedures of cancer treatment: it is less invasive, involving only a small incision or

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insertion of a cryoprobe through the skin. Consequently, pain, bleeding, and other complications of surgery are minimized. Cryosurgery is less expensive than other treatments and requires a much shorter time for recovery and hospital stay. Sometimes cryosurgery can be carried out under local anesthesia [21]. Because of these merits, cryosurgery is becoming a fast-growing, minimally invasive surgical technique. In particular, recent improvements in imaging techniques, such as computerized tomography (CT), magnetic resonance imaging (MRI), and electrical impedance tomography (EIT), have further enhanced the popularity of cryosurgery [1]. However, it is widely accepted that indiscriminate freezing does not necessarily destroy all the target tissues and that tissue destruction depends on the thermal conditions during freezing [3,8,10,15,19]. Therefore, an important task for cryosurgical treatment is to enhance tissue destruction within the cryo-lesion while sparing the surrounding normal tissue from injury.

To improve the efficacy of cryosurgery, adjunctive therapy is needed to increase the rate and completeness of cell death in the periphery of the cryo-lesion. Several adjuvant therapies for cryosurgery have been investigated, including chemical adjuvants such as cancer chemo-therapeutic agents [3,13,17], antifreeze protein (AFP) [15,19], and salts [8]. The idea of using chemo-therapeutic drugs in association with cryosurgery was first tested by Ikekawa et al. [13]. In their study, two chemo-therapeutic agents, peplomycin and adriamycin, were introduced before and after cryosurgery, and an improved cryosurgical outcome was reported. Following this, Clarke et al. [3] reported that exposing a human prostate cancer cell line (PC-3) in vitro to the chemo-therapeutic agent, 5-fluorouracil, could enhance PC-3 cryoinjury by subsequent freezing. Mir and Rubinsky [17] investigated another chemo-therapeutic agent, bleomycin, and obtained a promising increase in cryoinjury to B16F0 melanoma cells. The clinical use of chemo-therapeutic drugs as an adjuvant to cryosurgery is now considered to be beneficial [6]. However, the optimal dose and timing of delivery is not well defined. The use of AFP is also an important adjuvant approach. AFPs have the ability to enhance freezing injury by modifying the ice crystals to a needle-like structure when present at high concentration while protecting cells from freezing injury at low concentrations by inhibiting ice formation [15,19]. Furthermore, Han and Bischof [8] investigated another effective method for increasing cell and tissue injury in cryosurgery by the use of eutectic freezing. These studies have demonstrated the feasibility of various chemicals as adjuvants to cryosurgery. However, the experience gained so far indicates that the possibilities for complete cryodestruction of sizable pathological lesions are limited. To overcome this barrier, recently we proposed a new approach which is to modify the status of the tissues and make them more sensitive to freezing by percutaneously injecting solutions with thermally important properties into the target tissues [23]. The experimental results of experiments on biological tissues in vitro have shown that the localized injection of such solutions could significantly enhance tumor killing, but the mechanisms and processes of the enhancement of freezing injury remains unclear.

The objectives of this article are: (1) To present a numerical solution for the multidimensional freezing problem of biological tissues injected in situ with these functional solutions, and to apply this model to improve cryosurgical results by percutaneously injecting appropriate solutions into the target tissues. (2) To quantitatively illustrate the enhancement of freezing by the injection of solutions. (3) To demonstrate the feasibility of controlling ice ball growth by the such injections.

Mathematical formulation

The solution presented in this study is a modification of one that was recently developed for combined cryosurgery and hyperthermia therapy [4]. To avoid complex iteration at the moving boundary, the effective heat capacity method is applied, and a unified equation that simultaneously describes frozen, partially frozen, and unfrozen tissues, is used. The mathematical formulation is established for the following assumptions: (1) The phase transition of biological tissue during freezing occurs over a temperature range $(T_{\mathrm{ml}}, T_{\mathrm{mu}})$, where T_{ml} and T_{mu} are, respectively,