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Development and estimation of a novel cryoprobe utilizing the Peltier effect for precise and safe cryosurgery ☆

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ABSTRACT

We have developed a novel cryoprobe for skin cryosurgery utilizing the Peltier effect. The four most important parameters for necrotizing tissue efficiently are the cooling rate, end temperature, hold time and thawing rate. In cryosurgery for small skin diseases such as flecks or early carcinoma, it is also important to control the thickness of the frozen region precisely to prevent necrotizing healthy tissue. To satisfy these exacting conditions, we have developed a novel cryoprobe to which a Peltier module was attached. The cryoprobe makes it possible to control heat transfer to skin surface precisely using a proportional-integral-derivative (PID) controller, and because it uses the Peltier effect, the cryoprobe does not need to move during the operation. We also developed a numerical simulation method that allows us to predict the frozen region and the temperature profile during cryosurgery.

We tested the performance of our Peltier cryoprobe by cooling agar, and the results show that the cryoprobe has sufficient cooling performance for cryosurgery, because it can apply a cooling rate of more than 250 °C/min until the temperature reaches −40 °C. We also used a numerical simulation to reconstruct the supercooling phenomenon and examine the immediate progress of the frozen region with ice nucleation. The calculated frozen region was compared with the experimentally measured frozen region observed by an interferometer, and the calculation results showed good agreement. The results of numerical simulation confirmed that the frozen region could be predicted accurately with a margin of error as small as 150 μm during use of the cryoprobe in cryosurgery. The numerical simulation also showed that the cryoprobe can control freezing to a depth as shallow as 300 μm.

Introduction

Skin cryosurgery is commonly used in the treatment of verruca and initial carcinoma. In cryosurgery for skin, temperature history strongly affects the survival rate of the target tissue. The authors of two previous studies reported that object tissues must be cooled to −20 °C or −40 °C, respectively, to destroy them effectively [7,16]. Moreover, the cooling rate is a significant factor in destroying undesired tissues. Fig. 1 shows the destruction rate of single cells which were suspended in as it corresponds to the cooling rate [3]. The main cause of cell destruction is the formulation of an intracellular ice ball, which formulates at a cooling rate of about 50–200 °C/min. If the cooling rate becomes faster than 200 °C/min, the destruction rate decreases because of vitrification. In the cryosurgery of the living tissue, there are other factors to destroy cells such as vascular stasis; cell destruction rate of the tissue is much higher than that of single cells [16]. The thawing rate is considered to be another important factor that affects tissue injury during cryosurgery. During the thawing process, small ice crystals merge to form large crystals, which readily disrupt cellular membranes. This recrystallization may enhance the tissue destruction induced by the preceding freeze. Previous studies have shown that slow thawing is more destructive than rapid thawing [7,16]. For all these reasons, precise transient temperature control of the cooling surface is important in order to maximize cell destruction in cryosurgery. This is especially true in skin cryosurgery where most of the target tissues are thin and are in the vicinity of the skin surface.

The cooling methods used in cryosurgery have several problems. The method employed most often for cryosurgery of the skin is to use the phase change of a cryogen like liquid nitrogen or isoenthalpy expansion of a cryogen (known as the Joule–Thomson effect, or J–T effect). The basic cryosurgical techniques using the phase change utilize a dipstick soused in liquid nitrogen, a probe whose top is cooled by liquid nitrogen, or a spray of liquid nitrogen [8]. Cooling techniques using the J–T effect mainly utilize a

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Nomenclature

c	specific heat, J/kg °C
e	system deviation, °C
g	liquid fraction
H	enthalpy, J/m^3
i	electric current density, A/m^2
I	electric current, A
K_P	proportional gain
L	latent heat, J/kg
r	position of radial direction, m
t	time, s
t_D	derivative time, s
t_I	integral time, s
T	temperature, °C
T_{fs}	supercooling point, °C
x	position of axial direction, m
α	seebeck coefficient, V/°C
φ	coefficient for Kirchhoff transformation, W/m
λ	thermal conductivity, W/m °C
ρ	density, kg/m^3

Subscripts

l	liquid phase
s	solid phase

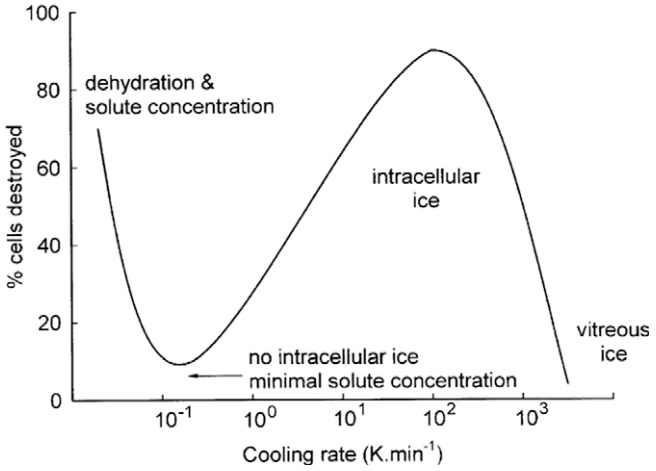

Fig. 1. Cell damage vs. cooling rate [6].

needle-shaped probe, and argon or chlorofluorocarbon (CFC) is employed as the cryogen [14,1]. However, the cooling performance of these methods strongly depends on the thermophysical properties of cryogen, so the cooling rate or thawing rate cannot be controlled by these methods. Moreover, with these methods it is difficult to control the cooled area and frozen region, so the surrounding healthy cells can be damaged. With these commercial cooling methods utilizing liquid nitrogen it is difficult to conduct repetition cooling and heating without moving the cryoprobe, because they can perform only cooling. Although cryoprobes utilizing the J–T effect can conduct a cooling and heating sequence, there is insufficient controllability of the cooling and heating rate.

Currently, there is an urgent need in cryosurgical research to develop tools and methods that can maximize the cell death rate within a tumor yet maintain high cell survivability in the periphery of the cryolesion. If cryosurgery is to be applied to diseases of the skin, such as areas of discoloration, clinicians must be able to target extremely small regions, in some cases less than 1.0 mm in diameter. To achieve this purpose, a cryoprobe that makes it possible to control heat transfer actively and precisely must be developed. Rabin et al. developed a cryoprobe that combined cooling of liquid nitrogen and the use of an electric heater to control the cooling rate [15]. However, this method needs a huge amount of energy to control the cooling rate, and lots of liquid nitrogen is wasted to counterbalance the heating energy from the electric heater. Cryoprobes utilizing the Peltier effect to control the cooling sequence with electric current have been developed [6,9,5]. Holman et al. designed a cryoprobe using the Peltier effect and coolant which was cooled by a fan [9]. Deng et al. developed a cooling device utilizing a multi-stage Peltier module [6]. Although these cryoprobes are able to control the cooling sequence, they have little use in cryosurgery because the cooling performance is not sufficient and/or Peltier modules are impractically large. Unless large Peltier modules are used, the cooling power of a Peltier module alone is insufficient for cryosurgery.

Maruyama et al. used Peltier elements, which are usually used to control temperature in steady state, to transiently control heat flux and developed a cooling system capable of both rapid cooling and heat transfer control. In that system, the heat sink attached to the hot junction is cooled to cryogenic temperature, so rapid cooling can be achieved as a result of the large temperature gradient across the Peltier element. [11,12]. Using this cooling system, Takeda et al. developed a prototype cryoprobe with a Peltier module that can cool and heat skin tissues actively and precisely compared to the conventional cryoprobes [19]. Maruyama et al. also developed a cryoprobe utilizing the Peltier effect with a flexible thin tube for treating inner parts of the body such as the stomach or bowels [13]. These cryoprobes can attain various cooling rates by adjusting electric current applied to the Peltier module without moving any part of the cryoprobe. Although many cooling methods without Peltier module do not have a mechanism to heat tissues after cooling, this cryoprobe can conduct active heating when the appropriate electric current is applied. Also, the cooling system of these cryoprobes is remarkably different from the other cryoprobes utilizing Peltier effect; the dominant factor in cooling is heat conduction rather than the Peltier effect which is utilized only to control the magnitude of the heat flux. However, the cooling performance of these cryoprobes was not sufficient with a maximum cooling rate of about 20 °C/min at −40 °C. In addition, constant values of electric current were applied during cooling and heating, so the cooling or heating rate varied depending on the cooling time and the temperature of the skin surface.

For precise and safe cryosurgery, it is also important to predict the temperature profile or determine the frozen region by numerical simulation. There are methods for calculating the phase change utilizing the effective heat capacity or enthalpy method, but these methods involve some error depending on the time step and grid size. To counter this, Swaminathan and Voller [18,20] developed a calculation method in which both temperature and enthalpy are calculated, compared, and modified in relation to one another.

The goal of this study is to perform cryosurgery of the skin and control the size of the frozen region to within one micrometer by utilizing the cooling system with the Peltier effect and liquid nitrogen as coolant, in order to treat diseases such as maculae or early carcinomas. In this study, we have modified the structure of previous cryoprobe to achieve sufficient cooling performance and developed a novel cryoprobe, which is available for real cryosurgery of the skin. We used a proportional-integral-derivative (PID) control-