Gel phantom study of a cryosurgical probe with a thermosiphon effect and liquid nitrogen-cooled aluminum thermal storage blocks

Haruo Isoda1, 2, MD, PhD; Yasuo Takehara3, MD, DMSc; Hitoshi Fujino4, Kazuya Sone4, Takeshi Suzuki5, Yoshinari Tsuzaki6, Kouji Miyazaki6, Michio Fujie7, PhD; Harumi Sakahara8, MD, PhD and Yasuaki Maekawa9, 10

1Brain & Mind Research Center, Nagoya University, Nagoya, Japan
2Department of Radiological and Medical Laboratory Sciences, Nagoya University Graduate School of Medicine, Nagoya, Japan
3Department of Radiology, Hamamatsu University Hospital, Hamamatsu, Japan
4Twinbird Corporation, Tsubame, Japan
5Zeon Medical Inc., Tokyo, Japan
6Zeon Corporation, Tokyo, Japan
7Research Equipment Center, Hamamatsu University School of Medicine, Hamamatsu, Japan
8Department of Radiology, Hamamatsu University School of Medicine, Hamamatsu, Japan
9JST Innovation Satellite Shizuoka, Japan Science and Technology Agency, Hamamatsu, Japan
10Strategic Innovation Division, Hamamatsu Agency for Innovation, Hamamatsu, Japan

ABSTRACT

Cryosurgery is a minimally invasive treatment for certain types of cancers. Argon-based cryosurgical devices are available at present, however a large compressed gas cylinder with the pressure of 300 atmospheres is needed. To overcome these drawbacks, we developed a new cryosurgical probe measuring about 50 cm in length with separate lumens inside for liquid and gaseous ethylene to be used as a thermosiphon and liquid nitrogen-cooled aluminum thermal storage blocks. The probe needle was 8 cm in length and 3 mm in outer diameter. To investigate the freezing capabilities of our new cryosurgical system we inserted the needle 5cm into a poly-acrylamide gel phantom warmed to 36.5 °C. Thermal storage blocks made of aluminum, cooled at –196 °C in liquid nitrogen, were attached to the condenser of the probe and replaced with thermal storage blocks every 4 to 5 minutes to compensate for warming. We took digital camera images of the ice ball at the needle and measured the temperature in certain locations of the cryoprobe. Ice ball formation started at one minute after cooling. The sizes (longest diameter × minimum diameter) at 10, 20 and 30 minutes after the start of the procedure were 4.5×2.1, 4.5×3.1 and 4.6×3.7 cm, respectively. During the procedure the minimum temperature of the condenser was –85 °C and the needle was –65 °C. This newly developed compact cryosurgical probe with thermosiphon effect and cooled thermal storage blocks created an ice ball that can be used for cryosurgery within 20 minutes.

Key Words: cryoablation, cryosurgery, cryotherapy, thermosiphon, phantom study

INTRODUCTION

Cryosurgery is a minimally invasive treatment to kill cancer cells with extreme cold. During
cryoablation, a cryoprobe is inserted through the skin to the tumor. A ball of ice (“ice ball”) is formed around the tip of the cryoprobe and causes necrosis in the tumor. Cryosurgery can be used for certain types of cancers such as renal cell cancer, prostate cancer, breast cancer, lung tumors, hepatoma and bone tumors. Rapid freezing with slow thawing and temperatures from –20 to –40 °C are necessary for effective cryo-treatment. According to an animal experiment and MR-guided cryosurgery cryonecrosis occurs up to 5 mm from the ice ball surface. Therefore the size and location of the ice ball are important for effective treatment.

Argon-based cryosurgical devices are presently available for cryoablation but they need large compressed argon and helium gas cylinders with a pressure of 300 atmospheres and are expensive. An exclusive room is also necessary for these cylinders. A compact, easy-to-use and low-cost cryosurgical system would overcome these drawbacks.

A paper regarding cryosurgical equipment using thermosiphon and free piston Stirling cooler was published recently. A thermosiphon system uses natural convection for heat exchange and therefore does not need a mechanical pump. In the previous study, the cryoprobe with thermosiphon effect was able to create an ice ball at the needle of the cryoprobe; however, the probe needle diameter of 5 mm was somewhat large. The needle temperature of –33 to –44 °C and the time required for ice ball formation were also not considered adequate for cryosurgery. To alleviate these problems, we developed a new cryosurgical probe with a needle diameter of 3 mm and an inner pipe to accelerate the thermosiphon effect. We used aluminum blocks cooled in liquid nitrogen (–196 °C) for cooling. The result was a new cryosurgical system that combines a cryosurgical probe with a thermosiphon effect and liquid nitrogen-cooled aluminum thermal storage blocks.

The purpose of our study was to investigate the freezing capabilities of our new cryosurgical system with the aid of a poly-acrylamide gel phantom warmed to 36.5 °C.

**MATERIALS AND METHODS**

**Cryoprobe**

Our cryoprobe was 500 mm in length and 169 g (Fig. 1). The needle was 80 mm long with an outer diameter of 3 mm, the body was 190 mm with an outer diameter of 8 mm and the condenser was 230 mm with an outer diameter of 6.35 mm (Fig. 1). The needle was made of stainless steel (SUS316L). The body and condenser were made of copper. There was an inner pipe from the body to the needle (Fig. 1). The cryoprobe was filled with 0.99 g of ethylene. We covered the body of the cryoprobe with a 12-mm-diameter stainless steel sheath leaving a small air gap between them (Fig. 1). The probe did not have any heat insulating structure due to its prototypical nature.

The condenser was placed at a higher position than the needle during cryosurgical procedure. The gaseous ethylene condensed to liquid ethylene at the condenser, which was cooled by thermal storage blocks, and went down through the inner pipe to the needle of the cryoprobe. We surmised, but could not verify, that the condensed ethylene liquid would flow down along the inner surface of the condenser and not into the gas conduits located on the outer part of the inner pipe because the conduits were angled slightly inward (Fig. 1). An ice ball was created around the needle. Ethylene evaporated at the needle because of high temperature around the needle. Gaseous ethylene went up to the condenser through the outer part of the inner pipe and the gas conduit. The separate lumens were designed to enhance the thermosiphon effect of this cryoprobe. Therefore, convection of ethylene occurred and heat transferred from the needle to the thermal storage blocks. As a result the ice ball increased in size. Removal of aluminum
blocks from the condenser or attachment of warmer blocks to the condenser would rewarm the cryoprobe and thaw the ice ball.

**Thermal storage blocks**

We used three sets of thermal storage blocks consisting of two aluminum semicircular columns (diameter, 35mm; height, 45 mm; a total of weight, 416 g) combined with hinge braces (Fig. 2). We clipped the aluminum blocks to the cryoprobe condenser (Fig. 2).

**Phantom experiment**

We performed the following gel phantom study (Fig. 3).

We circulated warmed water with the aid of a low temperature bath (NCB-2500, Tokyo Rikakikai Co., LTD., Tokyo, Japan) in an acrylic container measuring 40 × 20 × 12 cm (Fig. 3g). A coil-type heat exchanger (JC-S1 1-8978-01, Asone, Osaka, Japan) (Fig. 3f) with an external temperature sensor (STP-300, Tokyo Rikakikai Co., LTD., Tokyo, Japan) was used to keep the temperature of the warmed water to around 36.5 °C. We made 3% weight concentration polyacrylamide gel, with density and specific heat similar to human tissue, in a 10 ×10 × 10 cm acrylic container (Fig. 3d). The gel consisted of 35.04 g acrylamide (011-08015, Wako Pure Chemical Industries, Ltd., Osaka, Japan), 0.96 g N,N'-Methylene-bis-acrylamide (138-06032, Wako Pure Chemical Industries, Ltd., Osaka, Japan), 1.2 g ammonium persulfate (0168-08021, Wako Pure Chemical Industries, Ltd., Osaka, Japan), 480 μl N,N,N',N'-Tetramethyl-ethylenediamine (205-06313, Wako Pure Chemical Industries, Ltd., Osaka, Japan) and 10.8 g NaCl in 1,200 ml pure water. This container (Fig. 3d) was placed in the 40 × 20 × 12 cm-container (Fig. 3g) for eight hours and warmed to around 36.5 °C. We inserted the needle of the cryoprobe (Fig. 3a) 5 cm into the poly-acrylamide gel phantom (Fig. 3d) at around a 30-degree angle from the vertical
Fig. 2 Thermal storage block.
The upper figure shows one set of unfolded thermal storage blocks consisting of two aluminum semicircular columns (a) combined by hinge braces (arrowhead). Lower figure indicates another set of unfolded thermal storage blocks touching the medial side of the condenser (left) and another set of attached thermal storage block fixed by a set of clips (arrow) at the lateral side of the condenser (right).

a, aluminum block; b, the body of the cryoprobe; c, the condenser of the cryoprobe; arrowhead, hinge brace; arrow, clip

Fig. 3 Experimental devices used in this study.
a, cryoprobe; b, thermal storage block; c, probe holder; d, poly-acrylamide gel phantom; e, ice ball; f, warm water circulation system; g, container filled with warmed water; h, stopwatch; i, digital camera; j, ruler
Cryoprobe with a thermosiphon effect

We immersed three sets of aluminum thermal storage blocks in a container of liquid nitrogen and cooled them at −196 °C. We started the cryosurgical procedure by attaching one thermal storage block, removed from the container, to the lateral side of the condenser of the probe. After 5 minutes from the beginning of the procedure we moved the previously attached thermal storage block to the medial side of the condenser and then attached a new thermal storage block removed from liquid nitrogen to the lateral side of the condenser. After that we removed the thermal storage block at the medial side of the condenser, moved the thermal storage block at the lateral side to the medial side of the condenser and attached a new thermal storage block to the lateral side of the condenser every 4 to 5 minutes to compensate for warming over 30 minutes from the beginning of the procedure.

We measured the temperature of the needle, the condenser and the thermal storage block with a thermocouples and recorder (TR-V, KEYENCE, Osaka, Japan). We took digital camera images of the ice ball at the needle (Fig. 3e) every 30 seconds. A ruler (Fig. 3j) and a stopwatch (Fig. 3h) were also visible in the camera images.

**RESULTS**

Ice ball formation started from the middle portion of the needle around the orifice of the inner pipe (Fig. 4b arrowhead) at one minute after cooling (Fig. 4b). The sizes (longest diameter × minimum diameter) at 5, 10, 15, 20, 25 and 30 minutes after cooling were 4.4×1.4, 4.5×2.1, 4.5×2.7, 4.5×3.1, 4.5×3.5 and 4.6×3.7 cm, respectively (Fig. 4).

During the first 5 minutes after the start of the procedure the temperature of the condenser reached −43 °C, the needle portion outside of the warmed gel (Fig. 5d) reached −38 °C and the
middle portion of the needle (Fig. 5b) where the ice ball was formed reached –33 °C. Twenty minutes after the start of the procedure the condenser reached –85 °C, the needle portion outside of the warmed gel reached –78 °C and middle portion (around the orifice of the inner pipe) of the needle reached –65 °C 20 minutes after the start of freezing. During replacement of the liquid nitrogen-cooled aluminum thermal storage blocks every 4 or 5 minutes the needle and condenser become warmer. In the graph, the letters “a” to “e” correspond to the needle portions in legend symbol at the top of the figure.

DISCUSSION

Our cryoprobe needle temperature reached –65 °C and a 4.5×3×3 cm ice ball was created 20 minutes after the start of the procedure in the gel phantom warmed at 36.5 °C. According to an animal experiment9) and MR-guided cryosurgery10-12) cryonecrosis occurs up to 5 mm from the ice ball surface. Therefore, we expected a cryonecrotic area of 3.5×2.0×2.0 cm in our system within 20 minutes.

The freezing capability of the device used in this study was superior to that of the cryosurgical device using a thermosiphon cryoprobe and a free piston Stirling cooler in the previously reported paper.18) This was because our newly developed cryoprobe had an inner pipe that enhanced the thermosiphon effect, refrigerant gas was ethylene instead of carbon dioxide, and temperature...
of the liquid nitrogen-cooled aluminum thermal storage blocks, –196 °C, was lower than the previous study.

The external probe temperature of the middle portion of our current needle was –65 °C at 20 minutes from freezing, whereas those temperatures are reported to be around –125 °C at 1 minute from freezing for argon-based cryosurgical devices and –165 °C at 3 minutes from the freezing for liquid nitrogen cryosurgical devices. Therefore our freezing capability was lower than present cryosurgical devices.

Our current system using a cryoprobe with a 3 mm diameter created an ice ball with a minimum diameter of 14 mm after 5 minutes, 21 mm after 10 minutes, 27 mm after 15 minutes, 31 mm after 20 minutes, 35 mm after 25 minutes and 37 mm after 30 minutes. Hewitt and his colleagues reported maximum diameters of ice balls in warm water (42 °C) of around 11.5mm at 5 minutes, 12mm at 10 minutes and 12.5mm at 15 minutes after freezing. They used three different types of cryoprobes (3 mm in diameter) with an argon-based and liquid nitrogen cryosurgical systems. Although we could not compare our results and their results directly because of the difference of the temperature of the phantoms, the freezing capability of our system was not considered to be inferior to those of cryosurgical systems. Sprenkle and his colleagues reported that an argon-based cryosurgical device with mean argon gas pressure and with a needle size of 1.47 mm created ice balls with a mean diameter of 30.8 mm at 8 minutes after freezing in a gelatin phantom (25 °C). Our system needed 20 minutes to create a similar sized ice ball. Littrup et al. showed in their paper that an argon–based cryosurgical device with a needle size of 2.4 mm created a 34 mm ice ball in an agar phantom (39 °C) 15 minutes after freezing. Our current system needed 25 minutes to create a similar sized ice ball. Therefore, our current cryosurgical system was thought to need double or triple freezing time for cryoablation as compared with the state-of-the-art cryosurgical systems.

Our compact cryosurgical system did not need large compressed argon and helium gas cylinders. In this study, we used liquid nitrogen and needed a liquid nitrogen tank. When we can use an efficient and compact freezer using a free piston Stirling cooler operated by normal electric power to prepare and store enough cooled (–150 to –200 °C) aluminum thermal storage blocks for two freeze-thaw cycles cryosurgery, our system will be reduced in size and easy to handle.

There were several deficits in our system. The condenser must be placed at a higher position than the needle of the thermosiphon cryoprobe because the thermosiphon effect utilizes gravity. Cooled aluminum thermal storage blocks should be exchanged several times to keep the probe condenser cooled. During replacement of thermal storage blocks the temperatures of the needle and condenser increased. The interval of exchanging aluminum blocks might change with improvements of the probe in the future. Standardization of this procedure is necessary to achieve consistent results. A more efficient exchange procedure for thermal storage blocks may prevent warming and increase ice ball formation. Our prototype cryoprobe did not have any heat insulation structure in this current study. A cryoprobe with insulation structure in this current study. A cryoprobe with insulation structure would increase its freezing capability and prevent normal tissue from freezing. Because the size of ice ball created by the cryoprobe was limited, multi-probe operation is necessary for large tumors. However, our current system did not permit placing cryoprobes in close proximity due to the sizes of the aluminum blocks, which made a multi-probe operation impractical. Our current cryoprobe was not able to generate an ice ball around the tip of the needle and this might cause post cryosurgery complications around the tissue in an untreated area. We should modify the structure of the needle to create an ice ball that covers the tip of the needle.
CONCLUSION

This newly developed compact thermosiphon cryoprobe with liquid nitrogen-cooled aluminum thermal storage blocks created an ice ball that can be used for cryosurgery within 20 minutes.

CONFLICT OF INTEREST

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