NOTE

Cooled water-irrigated intraesophageal balloon to prevent thermal injury during cardiac ablation: Experimental study based on an agar phantom

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Abstract

A great deal of current research is directed to finding a way to minimize thermal injury in the esophagus during radiofrequency (RF) catheter ablation of the atrium. A recent clinical study employing a cooling intraesophageal balloon reported a reduction of the temperature in the esophageal lumen. However, it could not be determined whether the deeper muscular layer of the esophagus was cooled enough to prevent injury. We built a model based on an agar phantom in order to experimentally study the thermal behavior of this balloon by measuring the temperature not only on the balloon, but also at a hypothetical point between the esophageal lumen and myocardium (2 mm distant). Controlled temperature (55ºC) ablations were conducted for 120 s. The results showed that: 1) The cooling balloon provides a reduction in the final temperature reached, both on the balloon surface and at a distance of 2 mm; 2) Coolant temperature has a significant effect on the temperature measured at 2 mm from the esophageal lumen (it has less effect on the temperature measured on the balloon surface); and 3) The pre-cooling period has a significant effect on the temperature measured on the balloon surface (the effect on the temperature measured 2 mm away is small). The results were in good agreement with those obtained in a previous clinical study. The study suggests that that the cooling balloon gives thermal protection to the esophagus when a minimum pre-cooling period of 2 minutes is programmed at a coolant temperature of 5ºC or less.

Keywords: agar model, atrial fibrillation, cooling balloon, computer modeling, esophagus, finite element method, radiofrequency ablation

1. Introduction

Much current research is focused on finding a way to minimize thermal injury in the esophagus during radiofrequency (RF) catheter ablation of the left atrium [Aupperle et al. 2005, Marrouche et al. 2007, Ren et al. 2006, Sherzer et al. 2007]. In a previous report [Berjano et al. 2005a], we proposed a device to minimize esophageal damage during RF ablation, which consisted of a balloon with internal cooling situated in the esophageal lumen next to the atrial lesion. The theoretical feasibility of this proposal was studied by means of computer modeling. Tsuchiya *et al* (2007) subsequently conducted a pilot clinical study using this type of device and their results suggested that it provides a reduction of the temperature measured in the esophageal lumen [Tsuchiya et al. 2007]. However, due to the fact that they only measured the luminal temperature, no information was obtained on whether the deeper muscular layer of the esophagus was cooled enough to prevent injury (i.e. it was impossible to know the effect of the esophageal cooling on the temperature reached at deeper levels of esophageal tissue). This question is essential, since two recent experimental studies demonstrated severe cases of thermal injury in the esophagus muscular layer during RF cardiac ablation [Aupperle et al. 2005, Marrouche et al. 2007].

With the foregoing in mind, we built a model based on an agar phantom in order to experimentally study the thermal behavior of a cooled water-irrigated intraesophageal balloon identical to that used by Tsuchiya *et al* (2007). Ablations were conducted by measuring the temperature not only on the cooling balloon, but also at a hypothetical point distant from the cooling balloon (i.e. between the esophageal lumen and myocardium). We also studied the effect of coolant temperature and the pre-cooling period on temperature measured at the two locations.

2. Materials and methods

2.1. Experimental model

Agar was used as tissue-equivalent material. This technique facilitates the precise positioning of very small temperature sensors (e.g. thermocouples), and achieves reproducible conditions between ablations. Figure 1 shows a schematic view of the experimental set-up in general, and of the phantom in particular. General details of the phantom construction can be found in [Rodriguez et al. 2007]. In this study, the phantom included a transversal hole (10 mm diameter) to locate a cooled water-irrigated intraesophageal balloon (RPC-9 Abdominal Pressure Catheter 9F, Life-Tech Inc., Stafford, TX, USA). The phantom also included two T-type IT-21 0.4 mm diameter thermocouples (Physitemp Instruments, Clifton, NJ, USA) which were fixed at different levels on the catheter axis (see Fig. 1). A thermocouple was placed on the cooling balloon, i.e. at a distance of 6.5 mm from the electrode-agar interface. This distance value coincides with the human anatomic distances previously reported [Ho et al. 1999, Sanchez-Quintana et al. 2005] . The another thermocouple was located at 2 mm from the first (i.e. at 4.5 mm from the electrode-agar interface). The temperature measured by the first thermocouple ($T_{0\text{-mm}}$) would mimic the temperature on the inner surface of the esophagus in firm contact with the cooling balloon. The temperature measured by the second thermocouple ($T_{2\text{-mm}}$) would mimic the temperature at an intermediate point (e.g. the muscular layer of the esophagus), according to the relative thickness of the different tissues and layers between endocardium and esophageal epithelium. The signals provided from the thermocouples were monitored by a multimeter 2945 BK Precision (Dynascan, Chicago, IL, USA) and recorded at 30 s intervals.

The phantom was submerged in a bath (25×20×18 cm) containing 12 L of 0.5%

NaCl in deionized water as blood-equivalent solution [Cao et al. 2000] maintained at 37ºC with an immersion thermostat. The experimental set-up included two hydraulic circuits. The first circuit (A in Fig. 1) was set up to simulate blood flow, and consequently removed heat from tissue and electrode surface during ablation. This circuit employed a Stöckert Shiley roller pump (Shiley Inc., Irvine, CA, USA) which re-circulated the saline solution from the bath at a rate of 1 L/min, and irrigated the phantom surface and the ablation electrode by means of an 18 mm diameter tube located 25 mm from the ablation catheter [Rodriguez et al. 2007]. The second circuit was set up to cool the inside of the cooling balloon and employed two pumps: a Flodos Liquiport NF 100 KT.18S membrane pump (KNF Flodos AG, Sursee, Switzerland) with a variable flow rate of 0.4 to 1.2 L/min operating at 1 L/min (C in Fig. 1) and a Gilson's peristaltic pump (Minipuls 3 Pump, Viliers Le Bel, France) at 25 mL/min (B in Fig. 1). Coolant temperature was controlled by a Frigiterm S-282 external cold bath (JP Selecta, Abrera, Barcelona, Spain). Coolant temperatures were considered for four values : 37, 23, 15 and 5ºC. Two standard K-type thermocouples were placed at the inlet and outlet of the cooling circuit, and as near as possible to the phantom, in order to assess coolant temperatures as accurately as possible (T_{in} and T_{out} in Fig. 1). Two pressure transducers (DLP60000, Grand Rapids, MI, USA) were located at the same points (P_{in} and P_{out} in Fig. 1) to ensure stability and reproducibility of the hydraulic cooling circuit. The control case corresponded to ablations with a coolant temperature of 37ºC and a coolant flow rate of zero.

2.2. Radiofrequency ablation

The ablations were conducted using a Blazer II 7Fr/4 mm ablation catheter (Boston

Scientific, Natiok, MA, USA). A methacrylate scaffold was used in order to place the catheter axis precisely on the symmetry axis of the phantom. The scaffold allowed the ablation electrode to apply a constant pressure, ensuring good reproducibility throughout the experiments. An ablation generator EPT-1000XP (EP Technologies, Sunnyvale, CA, USA) was utilized to deliver RF power between the ablation electrode and a 20×20 cm metallic plate located on the bottom of the bath. The ablations were conducted by programming a constant temperature of 55ºC at the electrode tip, while limiting output power to 50 W. The duration of the ablations was 120 s in all the experiments. At the end of each ablation, the values of mean power delivered for the ablation period were recorded.

2.3. Statistical analysis

Ten ablations were conducted for each group of the study and the analyzed variable was the temperature recorded at 30 s intervals. We first checked that population distributions were approximately normal and then calculated the sample mean and constructed 95% confidence intervals for each variable, in order to compare the different groups graphically. In the figures presenting the results, symbols represent the mean, and the bars show the 95% confidence intervals. This allows a straight statistical comparison between variables. The statistical analyses were performed with SPSS version 12.0 software (SPSS, Chicago, IL, USA).

3. Results

We analysed the normality of the data by means of Shapiro-Wilk test. We found that all groups had a normal distribution, and hence no non-parametric test were required.

3.1. Pre-cooling

All the recorded variables showed normal distributions. Figures 2, 3 and 4 show the progress of the temperature measured at $T_{0\text{-mm}}$ and $T_{2\text{-mm}}$, for temperatures of 5, 15 and 23ºC, respectively. The control and 37ºC coolant temperature cases are also shown. In addition, each figure shows three cases of pre-cooling (2, 4 and 8 minutes) along with control case.

During pre-cooling, the decrease in temperature was higher for the lower coolant temperatures. This decrease was more marked in the first 2 minutes (ranging from 6 to 10ºC on the balloon), being almost negligible for longer times (a drop of ≈1ºC). This was probably the reason why the temperature prior to ablation was similar (differences were lower than 3ºC) for the different coolant temperatures. The difference between $T_{0\text{-mm}}$ and $T_{2\text{-mm}}$ prior to ablation was at ≈4ºC for the different coolant temperatures. In other words, the pre-cooling process is more or less predictable and independent of coolant temperature.

3.2. Behavior during ablation and assessment of final temperature

Figure 5 shows the final temperature measured at $T_{0\text{-mm}}$ and $T_{2\text{-mm}}$ for the three coolant temperature (5, 15 and 23ºC) and for the no pre-cooling and pre-cooling (2, 4 and 8 minutes) cases. The control is also shown. We observed that the use of the cooling balloon provides a reduction of the final temperature (both on the balloon and 2 mm away) compared to the non-cooled balloon case. In addition, the progress of $T_{0\text{-mm}}$ and $T_{2\text{-mm}}$ was similar and was in no way affected by the value of the pre-cooling period.

Regarding the final temperature reached at a distance of 2 mm ($T_{2\text{-mm}}$), this value was significantly lower when the coolant temperature was lower. The pre-cooling period had no influence on temperature at this location. These results suggest that the use of pre-cooling together with a 5ºC coolant temperature keep the temperature in the external esophagus (i.e. at 2 mm from the lumen) below 50ºC, which could be considered a safe limit.

Coolant temperature also had a significant effect on the final temperature reached on the cooling balloon ($T_{0\text{-mm}}$). The use of pre-cooling did however have a significant influence on the final temperature at this location (a decrease of ≈3-4ºC). In this case, the final temperatures in the esophagus lumen could be kept below 40-44ºC, which could also be considered safe. The temperature measured at the inlet and outlet of the cooling circuit (T_{in} and T_{out} in Fig. 1) were 4.9 ± 0.3ºC and 13.6 ± 0.3ºC respectively. The hydraulic pressure measured at the same points (P_{in} and P_{out} in Fig. 1) were 114.1 ± 6.7 mmHg and 18.4 ± 1.4 mmHg respectively.

3.3. Comparison to previous studies

Finally, Figure 6 compares the results obtained with our experimental model and those obtained by Tsuchiya et al (2007). Temperatures are given at the beginning of ablation and at 30 seconds, measured on the cooled balloon when using 2 minutes pre-cooling and a 5ºC coolant temperature. Dispersion of Tsuchiya's clinical results was considerably higher than in our experimental results, which makes it impossible to find significant differences between cases. This dispersion could be due to the fact that in their clinical study, ablation was not finished at 30 seconds, but when esophageal temperature reached > 41ºC. However, there was a slight tendency towards higher values in our experimental study regarding the temperature reached after 30 seconds of ablation. This could be due to their using an intraesophageal temperature probe, which can underestimate esophageal temperature [Rodriguez et al. 2007].

4. Discussion

The objective of our experimental study was to assess the feasibility and the thermal behavior of a cooling balloon to avoid thermal injury to the esophagus during RF catheter ablation. The balloon under test was identical to that employed in a previous clinical study (Tsuchiya *et al* 2007). By using an agar phantom model, we had the advantage of being able to measure the temperature not only on the cooling balloon, but also at a distant point (i.e. in the deep esophagus layer). We also assessed the effect of coolant temperature and the pre-cooling period on the final temperature reached at the two above-mentioned points.

In general, our experimental results suggest that the use of a cooling balloon with a coolant temperature of 5ºC and a pre-cooling period of 2 minutes, such as that employed in clinical practice (Tsuchiya *et al* 2007) could be a suitable option for achieving the objective, since the temperatures reached around the esophagus were significantly lower than those reached when the cooling balloon was not employed. In fact, if we consider the following three levels of thermal damage to the esophagus (50ºC is the irreversible injury threshold):

1) Totally transmural esophageal lesion: both $T_{0\text{-mm}}$ and $T_{2\text{-mm}}$ are higher than 50ºC.
2) Partially transmural esophageal lesion: $T_{0\text{-mm}} < 50$ºC but $T_{2\text{-mm}} > 50$ºC.
3) Non esophageal lesion: both $T_{0\text{-mm}}$ and $T_{2\text{-mm}}$ are kept lower than 50ºC.

Our results suggest that:

1) Ablation without the use of a cooling balloon could cause a totally transmural esophageal lesion.

2) Cooling balloon with coolant temperature > 5ºC (with or without pre-cooling), or cooling balloon with coolant temperature of 5ºC without pre-cooling, could cause a partially transmural esophageal lesion.

3) Cooling balloon with coolant temperature ≤ 5ºC and pre-cooling ≥ 2 minutes could avoid esophageal lesion.

Our results also suggest that it is not necessary to pre-cool for more than 3-4 minutes.

Our experimental study involves certain limitations, which should be taken into consideration. Since it was based on an agar phantom, all the tissues were homogenously modeled, and hence no allowance was made for the different layers of the esophagus connective and cardiac tissues. However, the thermal and electrical characteristics of these tissue are very similar, and in fact, our results are found to be in agreement with those found clinically by Tsuchiya *et al* (2007).

We are, nevertheless, aware that other factors (not considered in this study) could significantly influence the potential of the cooling balloon to minimize esophageal temperature. Future studies should be conducted to investigate all the factors which are known to influence tissue temperature during RF ablation, such as the angle between the electrode and cardiac surface [Panescu et al. 1995], distance between electrode and cooling balloon [Berjano et al. 2005b], pressure of the electrode on the cardiac surface (i.e. insertion depth of the electrode into the tissue) [Tungjitkusolmun et al. 2001], and blood flow on electrode and cardiac surface [Cao et al. 2001]. The effect of different electrode designs [Marrouche et al. 2007] or even different energy sources [Aupperle et al. 2005] could also be considered.

5. Conclusions

Our experimental results (which are in close agreement with those obtained in a previous clinical study) suggest that it is possible to thermally protect the esophagus during an RF cardiac ablation (even up to a distance of 2 mm away) by means of a cooling balloon placed in the esophageal lumen and by programming a minimum pre-cooling period of 2 minutes with a coolant temperature of 5ºC or less.

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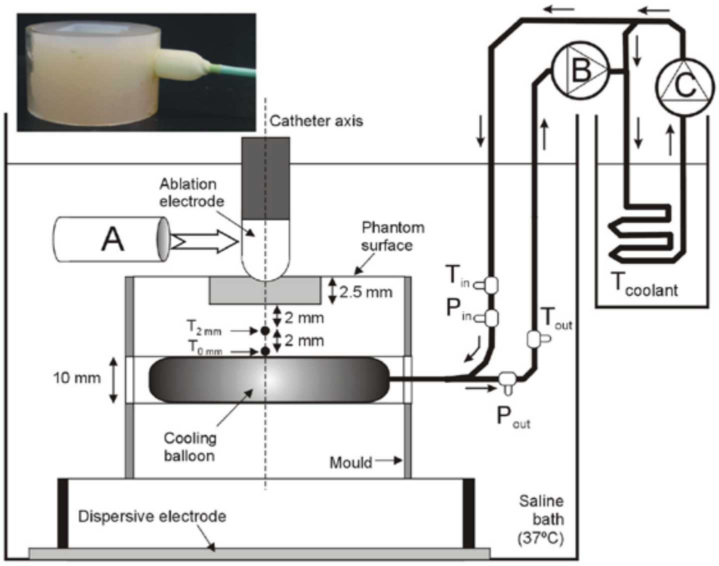

Figure 1 Schematic side view (out of scale) of experimental set-up. The phantom was constructed by utilizing a mould formed by a circular methacrylate tube (50 mm external diameter) (see photo). The agar phantom contained a cavity (10 mm diameter) to contain the cooling balloon, temperature sensors on the balloon ($T_{0\text{-mm}}$) and at a distance of 2 mm ($T_{2\text{-mm}}$), and ablation electrode. The phantom also included a compartment of 20×20 mm and 2.5 mm thick placed at top center in the phantom, in which agar fragments of equal dimensions (black rectangle) were replaced after each ablation (since the agar zone closest to the RF electrode often melted during ablation). The cooling balloon was located 6.5 mm from the surface of the phantom and perpendicular to the symmetry axis (this distance coincides with the human anatomic distances previously

reported [Ho et al. 1999, Sanchez-Quintana et al. 2005]). The phantom was submerged in a saline bath maintained at 37ºC. Two hydraulic circuits were used in the experimental set-up: 1) a circuit simulating blood flow inside the atrium (A), and 2) a circuit for the cooling balloon employing two pumps (B and C). At the balloon inlet, and as near as possible to the phantom, we placed transducers to measured hydraulic pressure.

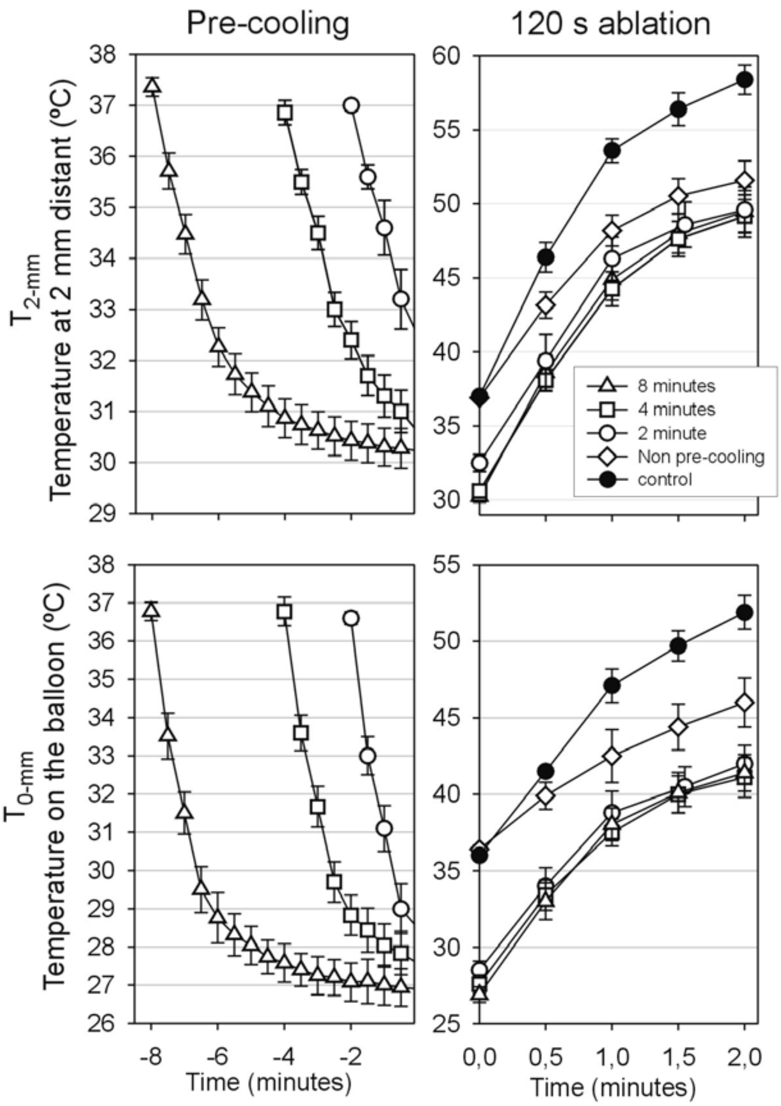

Figure 2 Time progress of the temperatures measured at 2 mm from the surface of the cooling probe (up) and on the cooling probe (down) for a coolant temperature of 5ºC during an ablation of 120 s (55ºC target temperature), and for four conditions of pre-cooling: non pre-cooling, 2, 4, and 8 minutes. The control case (i.e. no cooling) is also shown. Symbols show the mean and the bars the 95% confidence interval.

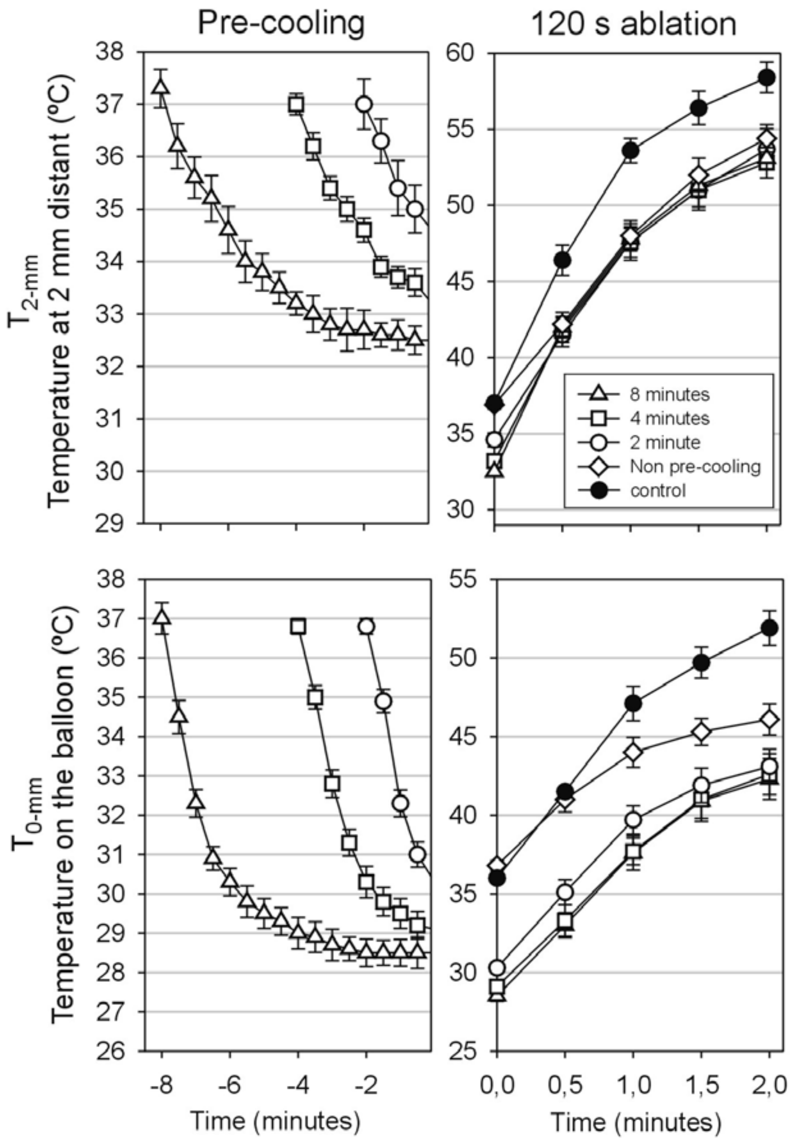

Figure 3 Time progress of the temperatures measured at 2 mm from the surface of the cooling probe (up) and on the cooling probe (down) for a coolant temperature of 15ºC during an ablation of 120 s (55ºC target temperature), and for four conditions of pre-cooling: non pre-cooling, 2, 4, and 8 minutes. The control case (i.e. no cooling) is also shown. Symbols show the mean and the bars the 95% confidence interval.

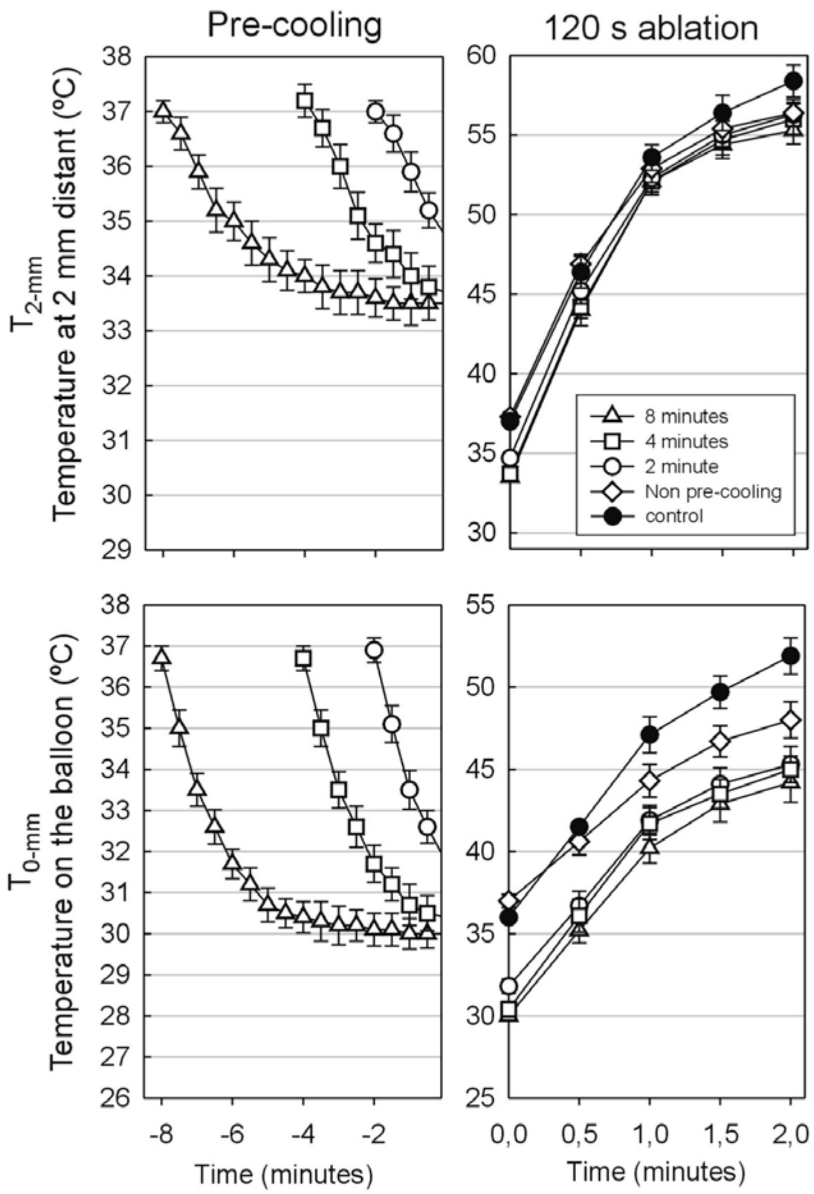

Figure 4 Time progress of the temperatures measured at 2 mm from the surface of the cooling probe (up) and on the cooling probe (down) for a coolant temperature of 23ºC during an ablation of 120 s (55ºC target temperature), and for four conditions of pre-cooling: non pre-cooling, 2, 4, and 8 minutes. The control case (i.e. no cooling) is also shown. Symbols show the mean and the bars the 95% confidence interval.

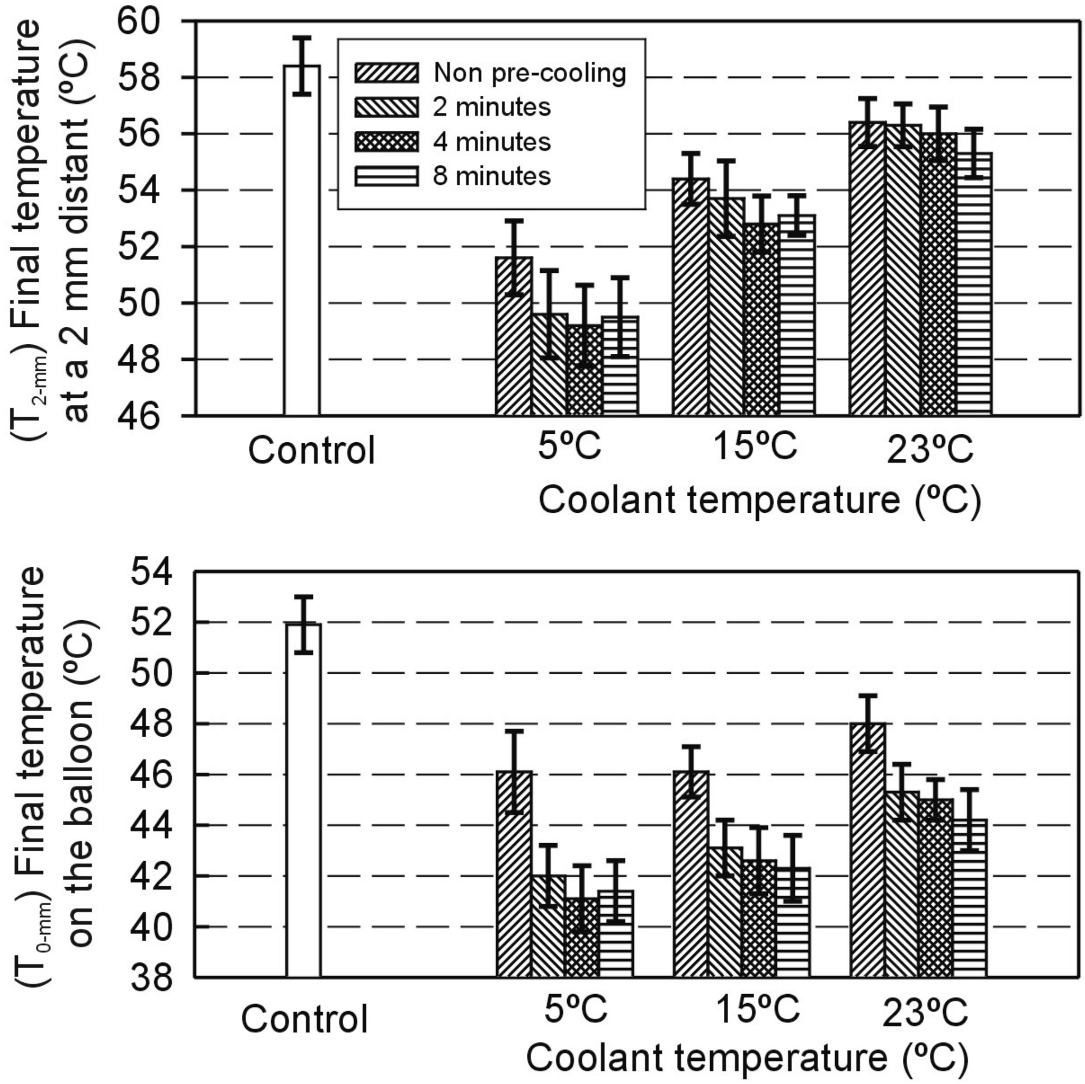

Figure 5 Final temperature measured at 2 mm from the surface of the cooling probe (up) and on the cooling probe (down) for the three coolant temperature (5, 15 and 23ºC) and for the cases of non pre-cooling and pre-cooling (2, 4 and 8 minutes). The control case is also shown.

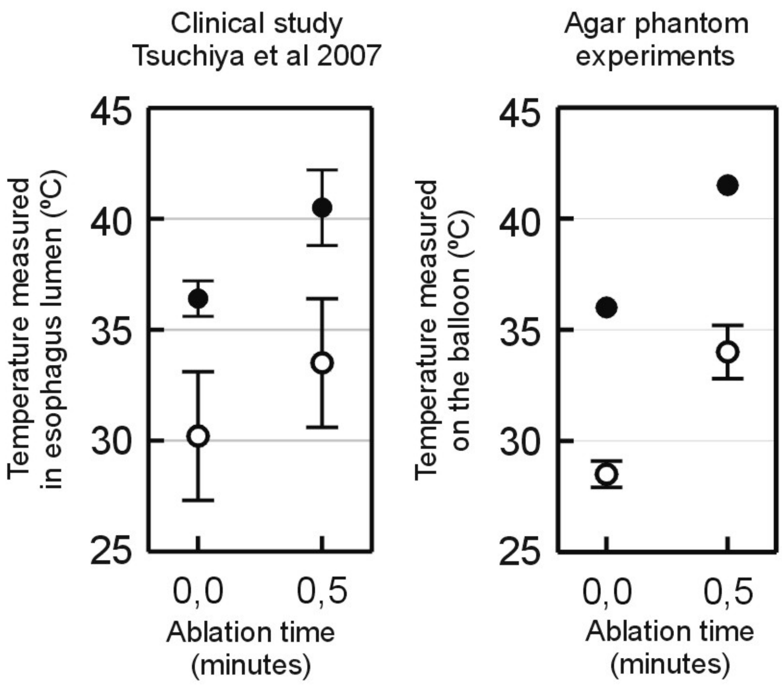

Figure 6 Comparison between the temperature measured in the esophagus lumen during a previous clinical study (Tsuchiya et al 2007) and the temperature measured on the cooling balloon in the present experimental study. Both studies employed identical cooling balloons. The temperatures were measured at the beginning of the ablation (i.e. after 120 minutes of pre-cooling using a coolant temperature of 5ºC) and after 30 s of ablation time.