Spatial Thermodynamics of very High Power-Short Duration Catheter Ablation for Pulmonary Vein Isolation in an in-vivo model

Atsushi Suzuki[1], H. Immo Lehmann[2], Songyun Wang[2], Kay Parker[2], Kristi Monahan[2], Maryam Rettmann[2], and Douglas Packer[2]

[1]Mayo Clinic/St. Marys Hospital
[2]Mayo Clinic/St. Marys Campus

May 10, 2021

Abstract

Introduction: The spatial thermodynamics of very high power-short duration (vHPSD) radiofrequency (RF) application during pulmonary vein isolation (PVI) in in-vivo model has not been well characterized. This study was conducted to investigate the distance-temperature relationship during vHPSD-RF ablation. Methods: PVI was performed using the vHPSD catheter with the settings of 90W, RF time of 4 sec and 15mL/min irrigation in a canine model. Catheter contact force (CF) of 10-20g was defined as 'normal' and CF >20g as 'firm' CF. Tissue temperature was monitored using thermocouples implanted at the surface of the left atrial-pulmonary vein junction, left phrenic nerve, and the luminal esophagus. PVI using a standard contact-force sensing catheter (SCF) (settings of 35W, 30sec and 30mL/min irrigation) was performed for comparison. Results: A total of 334 TC profiles in 4 animals was investigated. Time to maximum tissue temperature (MTT) (6.0sec [vHPSD/normal CF] vs. 30.5 sec [SCF/normal CF], p<0.001; 8.0sec [vHPSD/firm CF] vs. 24.0sec [SCF/firm CF], p=0.022) was shorter with vHPSD than in SCF groups. MTT within 10mm from catheter-tip was lower in vHPSD ablation with normal CF than using SCF ablation (median 41.9°C [interquartile-range; 40.2-46.1] vs. 49.5°C [45.9-56.2], p=0.013). The distance margin to keep the MTT below 39ºC, 42ºC, and 50ºC were 4.9mm, 4.2mm, and 3.4mm, respectively in the vHPDS group. This margin was larger (8.0mm, 6.6mm, and 4.6mm) in the SCF group. Conclusion: Our study underscores that vHPSD creates greater resistive heating than conventional catheter ablation.

Spatial Thermodynamics of very High Power-Short Duration Catheter Ablation for Pulmonary Vein Isolation in an *in-vivo* model

Running title: Thermodynamics of high power-short duration ablation

Atsushi Suzuki, MD, PhD[1,2]; H. Immo Lehmann, MD[1,3,4]; Songyun Wang, MBBS[1,5]; Kay D. Parker, CVT[1]; Kristi H. Monahan, RN[1]; Maryam E. Rettmann, PhD[1]; and Douglas L. Packer, MD[1]

[1] Translational Interventional Electrophysiology Laboratory, Mayo Clinic/St. Marys Campus, Rochester, Minnesota, USA.[2] Department of Cardiology, Osaka Saiseikai Nakatsu Hospital, Osaka, Japan. [3] Department of Cardiology, Corrigan Minehan Heart Center, Massachusetts General Hospital, Boston, MA, USA. [4] Harvard Medical School, Boston, MA, USA. [5] Department of Cardiology, Renmin Hospital of Wuhan University, Wuhan, China.

Total word count: 4610words (20 pages, including title page, abstract, manuscript, references, tables and figures)

Sources of Funding: This study was funded by Biosense Webster Inc. Dr. Packer's work is funded in part by a Clinician Investigator Award from the Mayo Foundation.

Disclosures: Dr. Packer in the past 12 months has provided consulting services for Abbott, AtriFix, Biosense Webster Inc., Boston Scientific, CardioFocus, Johnson & Johnson, MediaSphere Medical, LLC, MedLumics, Medtronic, St. Jude Medical, Siemens, SigNum Preemptive Healthcare, Inc., and Thermedical. Dr Packer received no personal compensation for these consulting activities. Dr. Packer receives research funding from the Abbott, Biosense Webster, Boston Scientific/EPT, CardioInsight, CardioFocus, Endosense, German Heart Foundation, Hansen Medical, Medtronic, NIH, Robertson Foundation, St. Jude Medical, Siemens and Thermedical. Dr. Packer and Mayo Clinic jointly have equity in a privately held company, External Beam Ablation Medical Devices. Dr. Packer also receives royalties from Wiley & Sons, Oxford, and St. Jude Medical, outside the submitted work. The other authors report no potential conflicts of interest.

Correspondence:

Douglas L. Packer, MD

Heart Rhythm Services

Mayo Clinic, St. Marys Hospital

1216 2nd St SW, AL 2-416

Rochester, MN 55902

Tel: 507-255-6263

Fax: 507-255-3292

E-mail: *packer@mayo.edu*

May 7th, 2021

Abstract

Introduction: The spatial thermodynamics of very high power-short duration (vHPSD) radiofrequency (RF) application during pulmonary vein isolation (PVI) in *in-vivo* model has not been well characterized. This study was conducted to investigate the distance-temperature relationship during vHPSD-RF ablation.

Methods: PVI was performed using the vHPSD catheter with the settings of 90W, RF time of 4 sec and 15mL/min irrigation in a canine model. Catheter contact force (CF) of 10-20g was defined as 'normal' and CF >20g as 'firm' CF. Tissue temperature was monitored using thermocouples implanted at the surface of the left atrial-pulmonary vein junction, left phrenic nerve, and the luminal esophagus. PVI using a standard contact-force sensing catheter (SCF) (settings of 35W, 30sec and 30mL/min irrigation) was performed for comparison.

Results:A total of 334 TC profiles in 4 animals was investigated. Time to maximum tissue temperature (MTT) (6.0sec [vHPSD/normal CF] vs. 30.5 sec [SCF/normal CF], p<0.001; 8.0sec [vHPSD/firm CF] vs. 24.0sec [SCF/firm CF], p=0.022) was shorter with vHPSD than in SCF groups. MTT within 10mm from catheter-tip was lower in vHPSD ablation with normal CF than using SCF ablation (median 41.9°C [interquartile-range; 40.2-46.1] vs. 49.5°C [45.9-56.2], p=0.013). The distance margin to keep the MTT below 39^{o}C, 42^{o}C, and 50^{o}C were 4.9mm, 4.2mm, and 3.4mm, respectively in the vHPDS group. This margin was larger (8.0mm, 6.6mm, and 4.6mm) in the SCF group.

Conclusion: Our study underscores that vHPSD creates greater resistive heating than conventional catheter ablation.

Key words: Atrial fibrillation; Catheter ablation; Pulmonary vein isolation; Very high-power and short-duration ablation; Spatial thermodynamics.

Abbreviations: AF=atrial fibrillation, CF=contact force, ICE=intracardiac echocardiography, LA=left atrium, LIPV=left inferior pulmonary vein, LSPV=left superior pulmonary vein, PV=pulmonary vein, PVI=pulmonary vein isolation, RF=radiofrequency, RIPV=right inferior pulmonary vein, RSPV=right superior pulmonary vein, SCF=standard open-irrigation contact-force sensing catheter, vHPSD=very high power-short duration

Background

Catheter ablation with isolation of the pulmonary veins (PVI) has proven to be a successful treatment of atrial fibrillation (AF). However to date, it is marked by potential complications, as well as unsatisfactory success rates.[1]Ablation with higher power could facilitate shortening of ablation time, while reducing procedural time.[2-4]A novel, very high power-short duration (vHPSD) ablation catheter system has been developed for creation of continuous circumferential lesions for PVI. Several studies have reported lesion characteristics, efficacy and safety of vHPSD ablation in several*in-vivo*models.[5-7] Recently, PVI using this vHPSD RF catheter and its efficacy in a clinical case series has been reported.[8]However, spatial thermodynamics (relationship between tissue temperature and distance from the catheter) of vHPSD RF application in an *in-vivo* model have not been well described. Understanding of the thermodynamics of vHPSD catheter ablation is critical to achieve high PVI success rates without projected increments in procedural complications. This study aimed to investigate spatial thermodynamics during PV isolation using the vHPSD catheter in an *in-vivo* model. Secondly, it aimed to assess biophysics of lesion creation and collateral damage of very high-power ablation.

Methods

Animal Preparation: The experimental protocol was approved by Mayo Clinic's institutional animal care and use committee and performed in full compliance with the 'Guide for the Care and Use of Laboratory Animals'. Four adult mongrel dogs (30-40kg, three vHPSD ablation, one open-irrigated contact force 'SCF' ablation) were studied following methods previously reported.[9-11] The data, analytic methods, and study materials are available from the corresponding author to other researchers for the purposes of reproducing the results or replicating the procedure upon reasonable request.

The System of Very High Power-Short Duration Catheter: The vHPSD catheter (Qdot Micro, Thermocool Smart Touch SF-5D Catheter; Biosense Webster Inc.) has been described previously.[5-8] Briefly, it has 6 thermocouples embedded in its tip (3 proximal and 3 distal) with a distance of 75μm from the outer catheter tip surface. The RF generator (nGen RF generator, Biosense Webster Inc.) used in this study was modified to produce high-power RF energy and perform accurate and reliable temperature, impedance, and power measurements. It also entails a real-time 33msec feedback cycle with a 90W power ramp-up time of less than 0.5 sec.

Thermocouple Implantation and Distance Monitoring: Thermocouple (TC) implantation and distance monitoring: (Physitemp Instrument Inc., Clifton, NJ, USA) were implanted epicardially via a left-sided thoracotomy. Detailed tissue TC implantation and methods for measurement of distance from the ablation catheter electrode to thermocouples have been described in previous our reports.[9-11]

Vascular Access and Catheterization: Introducer sheaths were placed in the right or left external jugular vein and right femoral artery and vein. A 6-Fr decapolar catheter was advanced into the coronary sinus. Intracardiac echocardiography (ICE; Siemens Acuson, Mountain View, CA) with a 10Fr catheter (5.5-10 MHz) was used to measure LA size (superior-inferior, medial-lateral axis, perimeter, and area of LA), each PV antral diameter, and to guide the transseptal puncture. After transseptal puncture, the sheath was exchanged over a guidewire for an 8.5Fr steerable sheath (Agilis, St. Jude Medical, St. Paul, MN, USA).

Ablation Procedure ofIsolation of the Pulmonary Veins: In three animals, PVI was performed using the vHPSD catheter with application of 90W for 4 sec, and a temperature limit at 65ºC. Irrigation flow was set to 15mL/min with an average contact force (CF) of 10-20g (vHPSD with normal CF group) or >20g (vHPSD with firm CF group).[12] Full thickness temperature at the ablation site was monitored using epicardial thermocouples implanted at each site. Tissue temperature data of PVI using a conventional standard open-irrigated-tip CF catheter ('SCF', Thermocool Smart Touch) was obtained for comparison in one animal. Settings of 'SCF' ablation were 35W/30sec, irrigation flow rate of 30mL/min and CF of 10-20g

(SCF with normal CF group) or >20g (SCF with firm CF group). Tissue temperature during ablation was monitored in the same manner as in vHPSD ablation cases. Spatial thermodynamics were compared between vHPSD with 'normal' CF and SCF with 'normal' CF, vHPSD with 'firm' CF and SCF with 'firm' CF.

Gross and Microscopic Pathology: At the end of each procedure, 30mL of 1.0% triphenyltetrazolium-chloride was injected and animals and ventricular fibrillation was induced. Methods of gross and microscopic pathology have been described in our previous reports.[11] Each segment was stained with Hematoxylin–Eosin as well as Masson Trichrome stains and examined with light microscopy. PV lesions were measured using a digital caliper. Lesion circumferentiality (continuous transmural PV lesion length) of lesions was assessed.

Statistical Analysis: Continuous variables are expressed as mean±standard deviation or median with the quartiles (median [quartiles]), and compared by 2-sample student t tests, Welch's t tests or Mann–Whitney U tests, depending on distribution of variables. Categorical variables were compared using the chi-squared test or Fisher's exact test. Associations between continuous variables were assessed using Pearson's or Spearman's rank correlation tests. Receiver operating characteristic (ROC) curve and Youden index were used to determine the optimal distance margin from the catheter-tip to establish a tissue temperature of <39°C, <42°C and <50°C. Statistical analyses were performed using the SPSS statistical software (version 21.0, SPSS, Inc., Chicago, IL, USA). A two-sided p-value <0.05 was considered to indicate statistical significance.

Results

Baseline LA/PV dimensions: Four animals (33.1±1.2 kg) underwent assessment of LA/PV dimensions. LA diameter was 29.1±1.5 mm (mid-lateral), 31.2±1.8 mm (superior–inferior), and diameter of PV ostium was LSPV of 14.6±1.5 mm, RSPV of 14.8±1.8 mm, LIPV of 11.8±0.5 mm, and RIPV of 12.1±1.2 mm.

Isolation of the Pulmonary Veins (PVI) using vHPSD or a conventional standard open-irrigation contact force catheter (SCF):A total of 152 RF applications were performed using vHPSD (n=135) or SCF (n=17). Three right-inferior PVs (RIPVs) were ablated to assess internal esophageal temperature as monitored through the intraluminal temperature probe in 3 animals for vHPSD ablation. Six of 135 RF applications (sufficiently apart from each other, placed in the right-superior [RSPV] antrum in one of the 3 animals) were performed in order to compare individual PV lesions created by vHPSD catheter. Seventeen RF applications using the SCF were also evaluated in the left-superior PV[LSPV] and left-inferior PV [LIPV] in the remaining 1 animal. PVI data using vHPSD and SCF is summarized in Table 1. PVI was achieved in 7 of 8 PVs in the vHPSD, and 2 of 2 PVs in the SCF group (p=0.617).

During ablation, an audible steam pop occurred in 8 of 135 RF applications (5.9%) in the vHPSD group, and 2 of 17 (11.7%) in the SCF group (p=0.310). No pericardial effusions were observed in either group. Table 2 shows a comparison of ablation parameters between vHPSD ablations with and without steam pop occurrence. Maximum and average output, catheter tip temperature and contact force were not different between groups. Importantly, initial impedance was higher and impedance drop larger in ablations with steam pop compared to those without steam pop (Table 2).

Spatial Thermodynamics (Tissue Temperature-Distance Relationship): During 99 of 152 RF applications (82 RF applications using vHPSD catheter and 17 RF applications using SCF), a total of 334 tissue TC profiles: 222 at LA-PV junction, 81 at internal esophagus and 31 at phrenic nerve were analyzed. Figure 1A shows a representative case of time course changes of power, tissue impedance, catheter tip electrode temperature and tissue thermocouple temperature during vHPSD ablation. Spatial thermodynamics (data from all tissue thermocouples) are summarized in Table 3. Figure 1B shows a representative time course of temperature change during RF application using vHPSD and SCF. Tissue temperature time-course at the distance <10mm from the catheter tip (180 tissue TC profiles) is also summarized in Table 3. Maximum tissue temperature was lower in vHPSD ablation with normal CF than in SCF ablation with normal CF (median 41.9°C [interquartile-range; 40.2-46.1] vs. 49.5°C [45.9-56.2], p=0.013), in contrast, there was no significant difference between them with firm CF (44.4°C [39.8-52.1] vs. 47.5°C [41.7-49.0], p=0.696). However, time to maximum tissue temperature (6.0sec [vHPSD with normal CF] vs. 30.5sec [SCF with normal CF], p<0.001 and 8.0sec [vHPSD with firm CF] vs. 24.0sec [SCF with firm CF], p=0.022) were significantly shorter in the vHPSD groups compared to the SCF groups. Figure 2A shows the relationship between maximum tissue temperature and distance from catheter tip of each site. There was robust correlation between maximum tissue temperatures and minimum distance from the catheter in all groups (r=-0.672; p<0.001 in vHPSD with normal CF, r=-0.740; p<0.001 in SCF with normal CF, r=-0.759; p<0.001 in vHPSD with firm CF, r=-0.694; p<0.001 in SCF with standard CF). Figure 2B shows the results of a ROC analysis using maximum tissue temperature and distance data. The optimal distance margin to keep the tissue temperature below 39ºC, 42ºC, and 50ºC were 4.9mm, 4.2mm, and 3.4mm in the vHPDS, in comparison with 8.0mm, 6.6mm and 4.6mm in the SCF group.

Gross and Microscopic Pathology Outcomes: In gross pathology investigation, PV lesion circumferentially (continuous transmural PV lesion length/circumferential PV length) was 96.7±6.5% in the vHPSD and 89.7±14.6% in the SCF group (p=0.533). Comparison of lesion characteristics and collateral damages in surrounding organs between vHPSD and SCF ablation is summarized in Table 1. Figure 3A and 3B shows gross and microscopic pathology of transmural circumferential left superior PV lesions. Table 4 shows comparison of lesion characteristics created by vHPSD with normal and firm CF. Endo-/epicardial lesion size and transmurality were not different between normal and firm CF.

Eight of 135 lesions in vHPSD and 2 of 17 lesions in SCF group appeared with subendocardial hemorrhage consistent with audible steam pop during the ablation procedure. In the gross pathology investigation, no collateral lung and phrenic nerve injury was observed.

As for esophageal collateral damage in vHPSD ablation, 6 extraluminal esophageal lesions were observed in 11 RF applications, with gross and microscopic pathology (Figure 3C and 3D) showing that the deepest collateral lesion nearly reached the longitudinal muscular layer of the esophagus, and no evidence of an intraluminal esophageal lesion was found in any case. Average contact force of RF applications with extraluminal esophageal injury (25.3±2.8 [22 to 30g]) was not different from that without the extraluminal esophageal injury (22.8±7.1g [13 to 31g], p=0.437).

Discussion

Major findings: In this validation study using a vHPSD catheter, spatial thermodynamics and biophysics of ablation were largely similar to those of an SCF catheter. Heat propagation latency and distance appeared different between the two ablation catheters, however, maximum tissue temperature achieved within 10mm from the catheter was not different between the vHPSD and SCF group.

Efficacy of the vHPSD Catheter Ablation and Lesion Characterization: The present study showed the vHPSD catheter created transmural ablative lesions in the canine LA, achieving electrical PV isolation using one forth the RF application time than with SCF. This vHPSD catheter provided real time (33ms interval) feedback of catheter-tip electrode temperature and impedance monitoring even as high RF energy was applied. The feedback of impedance change was especially important to avoid steam pop occurrence. Focusing on a single lesion created by this vHPSD catheter, endocardial lesion diameter was 4 to 5mm with a transmurality of 74%. Therefore, this catheter provides durable PVI with recommended interlesion distance of less than 4-5mm.[13,14]

Spatial Thermodynamics and Safety of the vHPSD catheter: This study provided the data regarding *in-vivo* spatial thermodynamics for this vHPSD RF catheter compared with SCF RF ablation. Tissue temperature increase was steeper using vHPSD compared to SCF. The maximum tissue temperature of vHPSD ablation was lower than SCF ablation when catheter contact force was within a range of 10-20g, in contrast, no difference was present when contact force was greater than 20g. Additionally, the heat propagation distance (data from the ROC analysis) appeared shorted in vHPSD ablation compared with the SCF ablation. Tissue heating during RF energy delivery consists of "resistive" heating within 1-3mm of the tip with "conductive heating" beyond that point.[15] Our results show that tissue temperature changes beyond that point.

Incidence of steam pops, was similar between vHPSD and SCF ablation. In previous reports, applied contact force has been one of the major factors for steam pop occurrence.[16,17] However, there was no significant difference between ablations with, and without, steam pop occurrence; initial impedance and the impedance drop in the present study were mildly different, underscoring that impedance monitoring is a key factor also in using this new technology. Higher initial impedance may have resulted in more rapid increase of tissue temperature by resistive heating, leading to a more significant impedance drop compared to ablation using the standard settings.

Considering lesion characteristics and spatial thermodynamics, very high power-short duration (90W/4sec) RF ablation using vHPSD with a contact force of 10 to 20g appears reasonably more efficient compared to conventional RF catheter ablation using a SCF. Temperature latency with an SCF catheter was substantially longer raising a question regarding difference in SCF safety. Some of these findings are similar to those of other additional manuscripts, although with less rigorous review of the spatial hemodynamics and biophysics created lesions.

Limitations: There are limitations to this study that should be considered. First, the number of included samples, especially those created by the SCF was small. Second, this study was done in an *in vivo* canine model; dogs are an established animal model for catheter ablation studies, but cardiac anatomy and size are slightly different than that in humans. Therefore, catheter manipulation, tissue thermodynamics, lesion size, and efficacy might be different in humans. Third, TC implantation was performed using thoracotomy. Opening the chest with subsequent pericardiotomy affects the structural relationship and possibly impacted the change in temperature. Forth, the catheter tip contact force direction to the tissue TC was not investigated in this study. Tissue temperature-distance relationship was simply based on the spatial distance between the catheter-tip and tissue TC. Maximum tissue temperature was varied even at the similar catheter-TC distance, this may have been resulted from difference of the contact force direction. Lastly, this study included only acutely studied animals, no follow-up after catheter ablation was conducted, hence chronic durability of lesions as well as occurrence of chronic complications such as pulmonary vein stenosis was not evaluable.

Conclusion

This study of vHPSD ablation provided more robust data detailing the spatial thermodynamics and biophysics utilized to create rapid high output lesions, not acknowledged in several other studies in an *in-vivo* model for understanding the biophysics of very high-power ablation. There was an appreciable difference in heat propagation latency between the two ablation catheters present, reflecting the difference between resistive and conductive heating. Overall effects appeared equivalent to conventional catheter ablation, but the efficacy was greater driven by the imputed resistive heating.

References

1. January CT, Wann LS, Alpert JS, et al. 2014 AHA/ACC/HRS guideline for the management of patients with atrial fibrillation: executive summary: a report of the American College of Cardiology/American Heart Association Task Force on practice guidelines and the Heart Rhythm Society. *Circulation.*2014;130(23):2071-2104.

2. Nilsson B, Chen X, Pehrson S, Svendsen JH. The effectiveness of a high output/short duration radiofrequency current application technique in segmental pulmonary vein isolation for atrial fibrillation. *Europace.* 2006;8(11):962-965.

3. Bhaskaran A, Chik W, Pouliopoulos J, et al. Five seconds of 50-60 W radio frequency atrial ablations were transmural and safe: an in vitro mechanistic assessment and force-controlled in vivo validation. *Europace.*2017;19(5):874-880.

4. Di Biase L, Romero J. Power- Versus Temperature-Guided Radiofrequency Ablation: Have We Found the Perfect Catheter? *Journal of the American College of Cardiology.*2017;70(5):554-557.

5. Barkagan M, Contreras-Valdes FM, Leshem E, Buxton AE, Nakagawa H, Anter E. High-power and short-duration ablation for pulmonary vein isolation: Safety, efficacy, and long-term durability. *Journal of*

*cardiovascular electrophysiology.*2018;29(9):1287-1296.

6. Leshem E, Zilberman I, Tschabrunn CM, et al. High-Power and Short-Duration Ablation for Pulmonary Vein Isolation: Biophysical Characterization. *JACC Clinical electrophysiology.* 2018;4(4):467-479.

7. Rozen G, Ptaszek LM, Zilberman I, et al. Safety and efficacy of delivering high-power short-duration radiofrequency ablation lesions utilizing a novel temperature sensing technology. *Europace : European pacing, arrhythmias, and cardiac electrophysiology : journal of the working groups on cardiac pacing, arrhythmias, and cardiac cellular electrophysiology of the European Society of Cardiology.* 2018;20(FI_3):f444-f450.

8. Reddy VY, Grimaldi M, De Potter T, et al. Pulmonary Vein Isolation With Very High Power, Short Duration, Temperature-Controlled Lesions: The QDOT-FAST Trial. *JACC Clinical electrophysiology.* 2019;5(7):778-786.

9. Bunch TJ, Bruce GK, Johnson SB, Sarabanda A, Milton MA, Packer DL. Analysis of catheter-tip (8-mm) and actual tissue temperatures achieved during radiofrequency ablation at the orifice of the pulmonary vein. *Circulation.*2004;110(19):2988-2995.

10. Okumura Y, Kolasa MW, Johnson SB, et al. Mechanism of tissue heating during high intensity focused ultrasound pulmonary vein isolation: implications for atrial fibrillation ablation efficacy and phrenic nerve protection.*Journal of cardiovascular electrophysiology.* 2008;19(9):945-951.

11. Takami M, Misiri J, Lehmann HI, et al. Spatial and time-course thermodynamics during pulmonary vein isolation using the second-generation cryoballoon in a canine in vivo model. *Circulation Arrhythmia and electrophysiology.*2015;8(1):186-192.

12. Hoffmayer KS, Gerstenfeld EP. Contact force-sensing catheters. *Current opinion in cardiology.*2015;30(1):74-80.

13. Park CI, Lehrmann H, Keyl C, et al. Mechanisms of pulmonary vein reconnection after radiofrequency ablation of atrial fibrillation: the deterministic role of contact force and interlesion distance. *J Cardiovasc Electrophysiol.*2014;25(7):701-708.

14. El Haddad M, Taghji P, Phlips T, et al. Determinants of Acute and Late Pulmonary Vein Reconnection in Contact Force-Guided Pulmonary Vein Isolation: Identifying the Weakest Link in the Ablation Chain. *Circ Arrhythm Electrophysiol.*2017;10(4).

15. Bunch TJ, Day JD, Packer DL. Insights into energy delivery to myocardial tissue during radiofrequency ablation through application of the first law of thermodynamics. *J Cardiovasc Electrophysiol.* 2009;20(4):461-465.

16. Yokoyama K, Nakagawa H, Shah DC, et al. Novel contact force sensor incorporated in irrigated radiofrequency ablation catheter predicts lesion size and incidence of steam pop and thrombus. *Circ Arrhythm Electrophysiol.*2008;1(5):354-362.

17. Nakagawa H, Jackman WM. The Role Of Contact Force In Atrial Fibrillation Ablation. *J Atr Fibrillation.* 2014;7(1):1027.

Figure Legends

Figure 1. Change of tissue temperature. A: Exemplary case of time course of output, tissue impedance change, catheter tip electrode temperature and tissue TC temperature. Output, impedance and catheter tip electrode temperature from record of CARTO3 and RF generator.**B:** Change of tissue temperature during RF application using very high power-short duration (vHPSD) and standard contact-force sensing catheter (SCF). Numbers with mm indicate the distance between catheter and TC. CF=contact force, LA–PV=left atrium–pulmonary vein junction, RF=radiofrequency, TC=thermocouple.

Figure 2. Analysis of Spatial Thermodynamics. A: Relationship between maximum tissue temperature and distance catheter of each site. Each point represents the maximum tissue temperature and the distance

from the catheter. **B:** Heat propagation distance (the results of a ROC analysis using maximum tissue temperature and distance data). The abbreviations as in Figure 1.

Figure 3. Gross and microscopic pathology of transmural circumferential lesion. A: Gross pathology of transmural circumferential left superior PV (LSPV) lesion. Black arrow indicates RF lesion created by very high power-short duration (vHPSD) catheter.**B:** Microscopic pathology of transmural LSPV lesion. Black arrow indicates the area of thermal necrotic tissue which is well demarcated from normal atrial myocardium (black dotted arrow). Asterisk (*) indicates pericardial fat tissue. **C:** Extra-luminal esophageal lesion (white arrows in left panel) was consisted with the sites where right inferior PV lesions were observed epicardially (white dotted arrows in left panel). No evidence of intra-luminal esophageal lesion was observed (right panel). **D:** Upper panel shows the section of esophageal lesion. Upside of the section is luminal of the esophagus. Microscopic pathology showed that the deepest collateral lesion nearly reached to the longitudinal muscular layer of esophagus (lower panel). LA =left atria

Hosted file

`Table 1.pdf` available at https://authorea.com/users/412975/articles/521461-spatial-thermodynamics-of-very-high-power-short-duration-catheter-ablation-for-pulmonary-vein-isolation-in-an-in-vivo-model

Hosted file

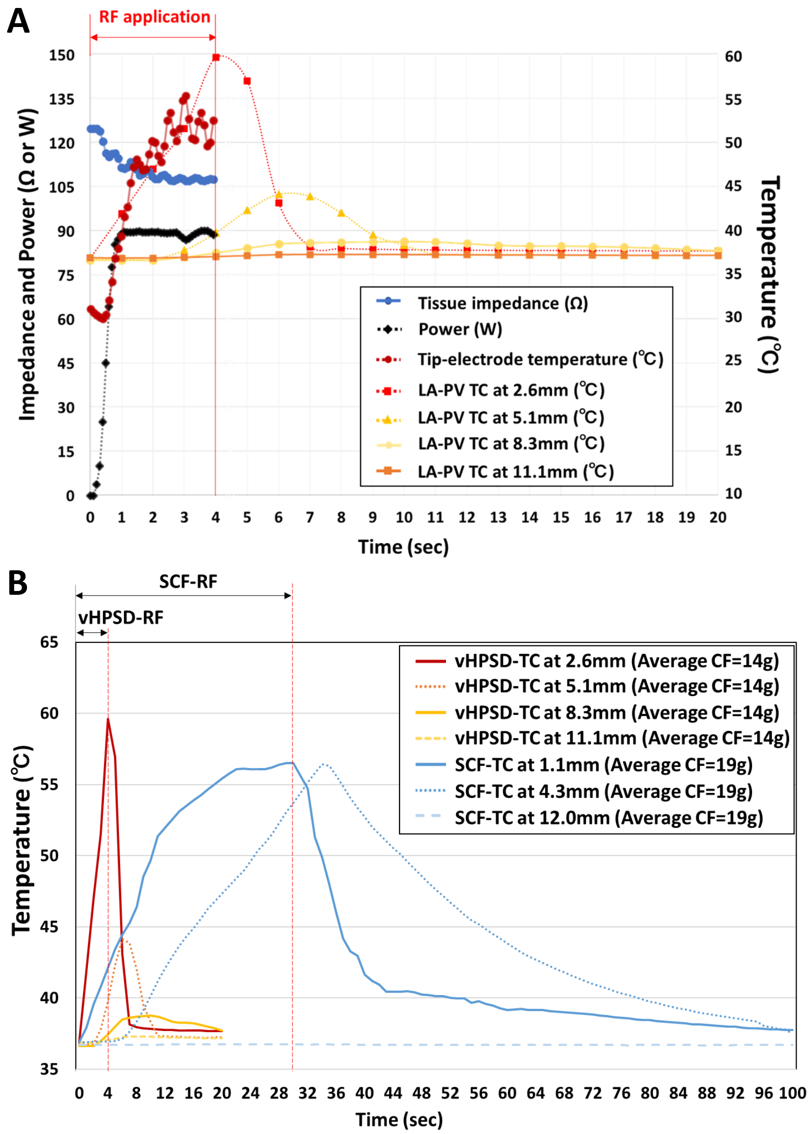
`Table 2.pdf` available at https://authorea.com/users/412975/articles/521461-spatial-thermodynamics-of-very-high-power-short-duration-catheter-ablation-for-pulmonary-vein-isolation-in-an-in-vivo-model

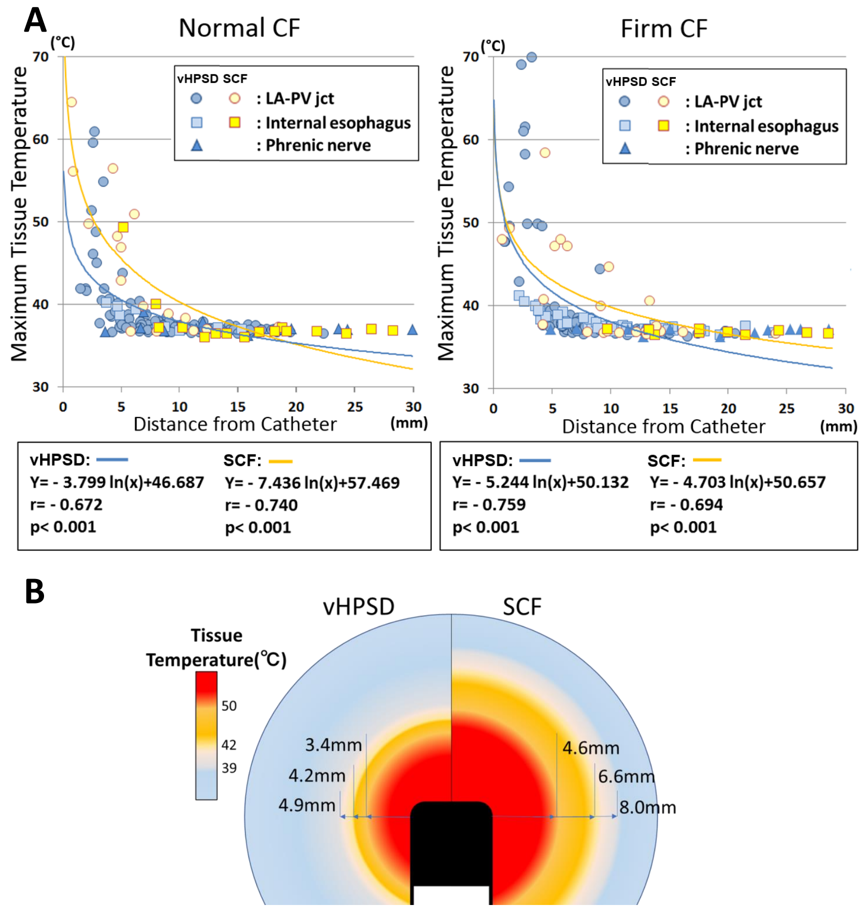
Hosted file

`Table 3.pdf` available at https://authorea.com/users/412975/articles/521461-spatial-thermodynamics-of-very-high-power-short-duration-catheter-ablation-for-pulmonary-vein-isolation-in-an-in-vivo-model

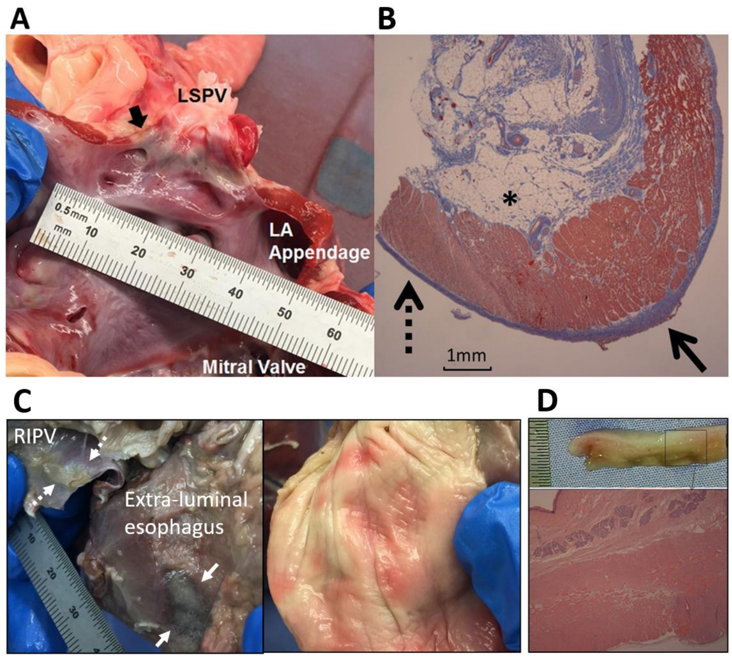
Hosted file

`Table 4.pdf` available at https://authorea.com/users/412975/articles/521461-spatial-thermodynamics-of-very-high-power-short-duration-catheter-ablation-for-pulmonary-vein-isolation-in-an-in-vivo-model


A
RF application
Impedance and Power (Ω or W)
Temperature (℃)
Time (sec)
Tissue impedance (Ω)
Power (W)
Tip-electrode temperature (℃)
LA-PV TC at 2.6mm (℃)
LA-PV TC at 5.1mm (℃)
LA-PV TC at 8.3mm (℃)
LA-PV TC at 11.1mm (℃)
B
SCF-RF
vHPSD-RF
Temperature (℃)
Time (sec)
vHPSD-TC at 2.6mm (Average CF=14g)
vHPSD-TC at 5.1mm (Average CF=14g)
vHPSD-TC at 8.3mm (Average CF=14g)
vHPSD-TC at 11.1mm (Average CF=14g)
SCF-TC at 1.1mm (Average CF=19g)
SCF-TC at 4.3mm (Average CF=19g)
SCF-TC at 12.0mm (Average CF=19g)



	Tissue temperature(℃)	AUC	P value	Distance from catheter Cut-off (mm)	Sensitivity	Specificity
vHPSD	<39	0.963	<0.001	4.9	0.937	0.830
	<42	0.953	<0.001	4.2	0.915	0.909
	<50	0.964	<0.001	3.4	0.946	0.900
SCF	<39	0.944	<0.001	8.0	0.955	0.857
	<42	0.955	<0.001	6.6	0.939	0.937
	<50	0.923	<0.001	4.6	0.917	0.800


A
B
LSPV
LA
Appendage
Mitral Valve
1mm
C
D
RIPV
Extra-luminal
esophagus