Received: 14 June 2022 | Revised: 15 September 2022 | Accepted: 31 October 2022

DOI: 10.1111/pace.14618

PACE WILEY

DEVICES

Laser Doppler flow for the hemodynamic differentiation of tachycardia

Emilia Stegemann MD[1,2] | **Mia Weidmann MD**[3] | **Alejandra A Miyazawa MD**[4] | **Matthew J Shun-Shin MD**[4] | **Francisco Leyva MD**[5,6] | **Abbasin Zegard MD**[5,6] | **Berthold Stegemann MD**[4,5,6]

[1]Clinic for Internal Medicine & Angiology, Agaplesion Diakonie Kliniken Kassel, Kassel, Germany

[2]Klinik für Kardiologie und Angiologie, Medizinische Fakultät der Philipps-Universität Marburg, Marburg, Germany

[3]Medizinische Klinik II, Klinikum Kassel, Kassel, Germany

[4]National Heart and Lung Institute, Imperial College London, Hammersmith Hospital, United Kingdom

[5]Aston Medical School, Aston University, Birmingham, United Kingdom

[6]Queen Elizabeth Hospital, Birmingham, United Kingdom

Correspondence
Emilia Stegemann, MD, Clinic for Internal Medicine & Angiology, Agaplesion Diakonie Kliniken Kassel, Herkulesstr. 34, 34119 Kassel, Germany.
Email: emilia.stegemann@t-online.de

Abstract

Background: Implantable cardioverter defibrillators (ICDs) offer effective therapy for the prevention of sudden cardiac death (SCD) due to ventricular arrhythmias. However, inappropriate shocks have detrimental effects on survival and quality of life. The addition of hemodynamic monitoring may be useful in discriminating clinically important ventricular arrhythmias.

Objective: In this study, we assess the ability of laser Doppler flowmetry to assess the hemodynamic effect of paced atrial and ventricular arrhythmias using mean arterial blood pressure as the reference.

Methods: In this acute human study in patients undergoing an elective electrophysiological study, laser Doppler flowmetry, arterial blood pressure, and surface ECG were acquired during high-rate atrial and ventricular pacing to simulate supraventricular and ventricular tachycardias.

Results: Arterial blood pressure and laser Doppler flow signals correlated well during atrial and ventricular pacing (rho = 0.694, $p < .001$). The hemodynamic impairment detected by both methods was greater during ventricular pacing than atrial pacing (–1.0% vs. 19.0%, $p < .001$). Laser Doppler flowmetry performed better than rate alone to identify hemodynamic impairments.

Conclusion: In this acute study, laser Doppler flowmetry tissue perfusion served as a good surrogate measure for arterial pressure, which could be incorporated into future ICDs.

KEYWORDS
hemodynamic sensor, implantable cardioverter defibrillator, inappropriate shock, LDF, sudden cardiac death

Abbreviations: ASCII, American Standard Code for Information Interchange; ATP, antitachycardia pacing; AUC, area under the curve; AV, atrioventricular; AVNRT, atrio-ventricular nodal re-entrant tachycardia; ECG, electrocardiogram; EGM, electrogram; EP, electrophysiology; ICD, implantable cardioverter defibrillator; LDF, laser Doppler flowmetry; MAP, mean arterial pressure; SCD, sudden cardiac death.

1 | INTRODUCTION

Sudden cardiac death (SCD) is a major healthcare problem, affecting about 5 million[1] people worldwide each year. Implantable cardioverter defibrillators (ICDs) can effectively treat ventricular arrhythmias and prevent SCD.[2–4] However, patients may receive inappropriate therapies if a device falsely detects a ventricular arrhythmia, or unnecessary therapies, if the ventricular arrhythmia may have spontaneously terminated without intervention and/or is hemodynamically tolerated. Such inappropriate or unnecessary shocks are harmful, as they reduce the quality of life and increase mortality.[5–9] Even anti-tachycardia pacing (ATP) is not benign and may accelerate arrhythmias.[10]

Currently, arrhythmia detection by ICDs relies solely on electrical signals of atrial or ventricular origin from their device leads. Whilst various algorithms and enhanced device programming have improved the detection of ventricular arrhythmias and reduced inappropriate therapies,[11–16] inappropriate shocks still occur. Prominent among the causes of inappropriate shocks are rapidly conducted atrial fibrillation and T-wave over-sensing.[17–20]

As current devices are unable to determine a patient's hemodynamic status during an arrhythmia, ICD programming guidelines rely primarily on heart rate. The addition of an accurate hemodynamic assessment to ICDs would enable these devices to provide hemodynamic-guided therapies. This would mean that in the presence of a hemodynamically tolerated arrhythmia, therapies would be deferred, and in hemodynamically compromising arrhythmias (whether ventricular or supraventricular), therapies would be delivered to reduce the duration of hypoperfusion.

Laser Doppler flowmetry (LDF) is a well-established technology to measure tissue perfusion. LDF is based on the principle of interference of tissue incident laser light reflected from static tissue structure and moving blood cells. The relative amount of Doppler-shifted photons, and their mean Doppler shift, are directly related to the concentration and velocity of red blood cells. The frequency analysis of the temporal speckle pattern created by the time-varying interference provides an estimate of blood flow and flow velocities.[21] Laser Doppler has been applied to assess blood flow and perfusion in several manifestations of microvascular disease such as diabetes, peripheral arterial occlusive disease, systemic autoimmune disease, etc.[22–24] It has been found to discriminate hemodynamically stable from unstable ventricular arrhythmias in animal models.[25–27] Recently, Keene et al. tested an electrogram (EGM)-gated algorithm for the quantification of electromechanical coupling using laser Doppler flow measurements during ICD defibrillation threshold testing. This method was 100% reliable in distinguishing loss of perfusion during ventricular fibrillation from sinus tachycardia, T-wave oversensing, and right ventricular lead fractures.[28] In the past, LDF was restricted to external equipment due to its size and energy requirements. Advances in microelectronics in the past decade have reduced these, and with the simultaneous increase in computational power, LDF can now be considered for implantable cardiac devices.[29,30] LDF sensors can be integrated into the can or the header of an ICD. Integration of the LDF sensor into the can requires the addition of an optical window into the ICD can, while in the header the sensor can be embedded into the epoxy directly. In both cases the LDF sensor will optically measure the perfusion of the vasculature in the fibrous capsule surrounding the device.

We, therefore, assessed the ability of LDF to reliably discriminate hemodynamically tolerated arrhythmias from hemodynamically compromising arrhythmias.

2 | METHODS

2.1 | Patients

This was a single-center, acute hemodynamic study assessing the feasibility of hemodynamic monitoring during simulated supraventricular and ventricular tachycardias using a novel laser Doppler perfusion monitor. The study was approved by the local medical ethics committee and the local regulatory body at the University Clinic Aachen. All patients gave written informed consent. The study complied with the Declaration of Helsinki.

Patients referred for a clinical electrophysiological study were recruited. Inclusion criteria were an indication for an electrophysiological study, and the patient's willing to sign informed consent.

2.2 | Monitoring

LDF perfusion monitoring, arterial blood pressure, surface electrocardiogram (ECG), and intracardiac electrograms (EGMs) obtained from the electrophysiology (EP) catheters were monitored and recorded throughout the study procedure.

Transcutaneous laser Doppler flow perfusion monitoring was performed using a commercial system equipped with two channels (PF5000, Perimed AB, Sweden). Two fiber optic probes were used in the experiment to measure the tissue perfusion signal. The LDF sensors were attached to the skin on the left forearm and/or on the left high chest using double-sided adhesive tapes. The sensor position was individually tailored to each patient to achieve good, stable, and artifact-free perfusion signals.

The arterial pressure was measured from a femoral site using a three French sheath (Abbott, USA). The pressure signal was appropriately zeroed prior to the start of the data acquisition.

The analog perfusion signal, in addition to the arterial pressure and surface and intra-cardiac EGMs were connected to the Prucka EP-lab recording system (General Electrics, Boston, USA).

2.3 | Pacing protocol

Supraventricular and ventricular tachycardias were simulated using pacing. This was delivered by a Micropace stimulator (General Electrics, Boston, USA) via a standard EP catheter at rates of 120, 140, 160, 180, and 200 bpm (if tolerated) to the high right atrium and right ventricular apex. The pacing was preceded by one minute of baseline

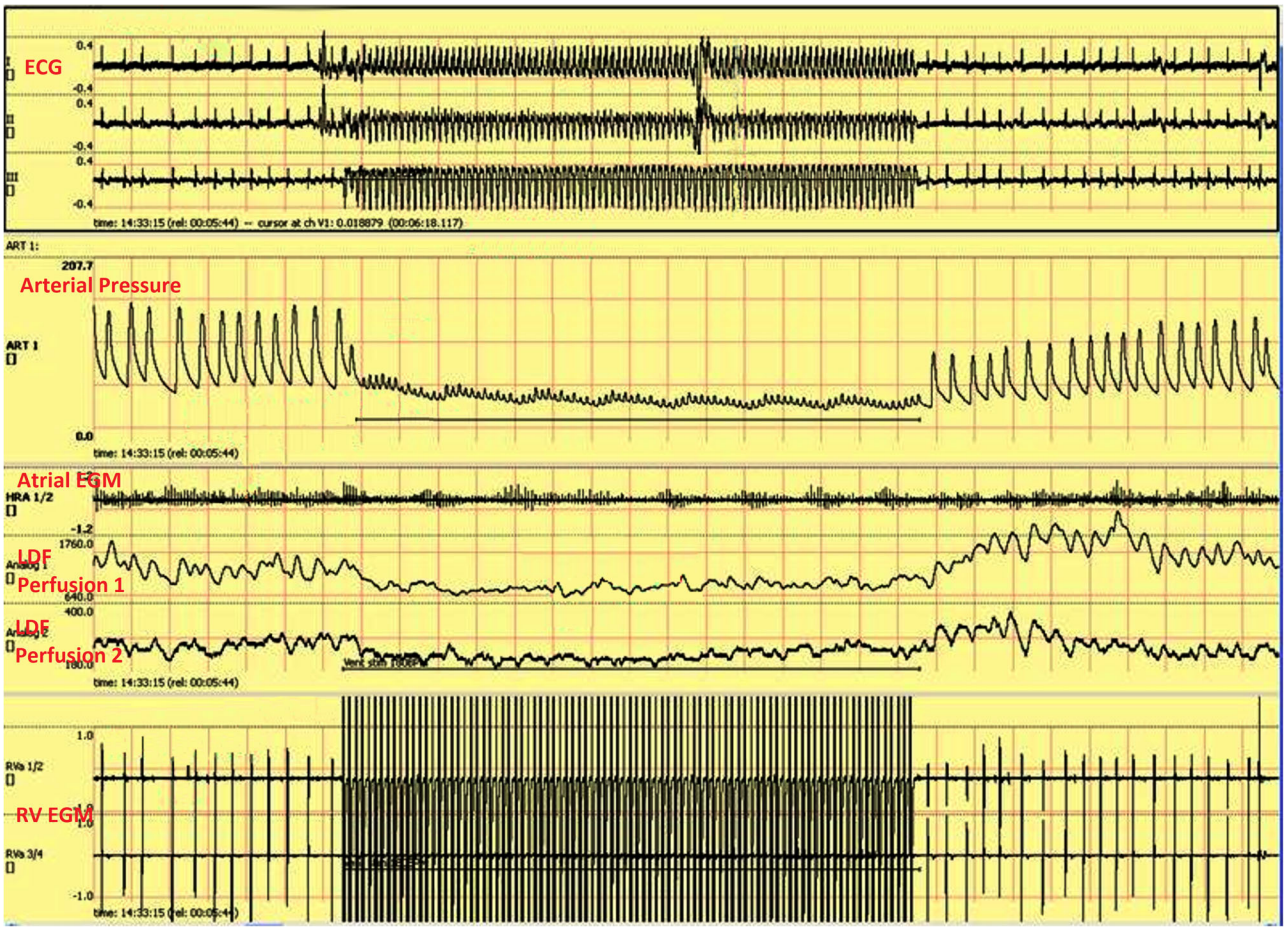


FIGURE 1 Experimental recording for ventricular stimulation at 180 bpm. Arterial blood pressure and laser Doppler perfusion signal show an immediate decline following the start of the pacing intervention. For analysis of hemodynamic data, tissue perfusion signal, and arterial blood pressure were averaged for the last 5 s before (baseline) and for the first 5 s from the onset of the pacing intervention. [Color figure can be viewed at wileyonlinelibrary.com]

recording at the intrinsic heart rate. High-rate pacing was delivered for 10–15 s during the ventricular stimulation protocol, and for 20–30 s during the atrial stimulation protocol. Each pacing experiment was followed by a 1-min recovery period.

2.4 | Data processing

All recorded data were exported in ASCII text format from the EP laboratory system after the completion of the acute study. Prior to data analysis, the exported data were visualized, visually checked, and annotated by one of the researchers for all pacing interventions using the libRASCH software.[31] The annotated physiological signals were then extracted and processed using customized software using Matlab (Mathworks Inc; Natick, Massachusetts, USA).

Arterial blood pressure and LDF tissue perfusion signals were averaged over 5 s intervals. The last 5 s before the start of any pacing intervention were considered baseline (Figure 1). We expected that patients during the pacing intervention would demonstrate an initial immediate change of arterial pressure and tissue perfusion, before a baroreflex response would reduce or neutralize the pressure and tissue perfusion effects.[32] We therefore calculated and analyzed the mean change in arterial pressure and tissue perfusion for the first 5 s following the start of the pacing intervention (Figure 1).

Signals from the surface ECG, endocardial EGM, arterial blood pressure, and laser Doppler perfusion were recorded on the Prucka EP-lab recording system throughout the study. All physiological signals were displayed on the main lab monitor and were visible to the investigator.

Mean arterial pressure (MAP) change and mean perfusion change was calculated as the difference between the respective baseline value and the value averaged for the first 5 s from the onset of the pacing intervention. Relative changes were calculated and analyzed to account for differences between individual patients.

2.4.1 | Statistical analysis

Patient characterization and hemodynamic data presentation are descriptive. Continuous variables are presented as median ± standard deviation. For normally distributed data, the two-sided t-test was

TABLE 1 Patient characteristics

Characteristic	N = 15
Male	10 (66.7%)
Height	179.3 ± 9.1
Weight	88.9 ± 17.0
LVEF	51.8 ± 9.1
LV end diastolic diameter	50.0 ± 5.5
LA diameter	35.0 ± 1.4
Indications for EP Study	
Ventricular arrhythmia	6 (40.9%)
AVNRT	4 (26.7%)
WPW	1 (7%)
SVT	4 (26.7%)

used, otherwise, the Mann–Whitney test was applied. All tests were two-sided. Proportions were compared using the Fisher test.

MAP and tissue perfusion were analyzed as a percentage change from the intrinsic rate for each patient. For correlation analysis of MAP and LDF perfusion, a linear regression model with and without offset was used, with no further covariates added, and all data points were equally weighted. Regression data are visualized as "scatter plots" and Bland–Altman plots. A p-value of $p \leq .05$ was considered statistically significant. Analysis and visualizations were performed using the statistical environment "R" Version 4.0.[33]

3 | RESULTS

Fifteen patients were enrolled into this study, and all completed the study protocol, without any adverse event. Patients were referred for: ventricular arrhythmia,[7] atrio-ventricular nodal re-entrant tachycardia (AVNRT),[4] Wolff-Parkinson-White,[1] and supra-ventricular tachycardias.[4] The mean left ventricular ejection fraction was 52 ± 9.1 %. Three patients had a reduced systolic function and were NYHA class II with a mean ejection fraction of 37 ± 1.5 %. Baseline characteristics are summarized in Table 1.

3.1 | Hemodynamic results

Of the 15 patients studied, two data sets could not be used for the following reasons: one data set was corrupted on the recording system, and the second data set had no pressure information recorded. The analysis performed and presented here is therefore based on 13 complete data sets.

High-rate atrial stimulation with proper AV conduction was obtained in 11 patients at 120 bpm, 10 patients at 140 bpm, eight patients at 160 bpm, six patients at 180 bpm, and finally, two patients at 200 bpm. Pacing-induced AV nodal block limited the measurements performed at higher atrial pacing rates. High-rate ventricular stimulation was obtained in all 13 patients up to 180 bpm, and only nine patients at 200 bpm due to hemodynamic intolerance in the remaining four.

3.2 | Correlation %LDF vs. %MAP

There was a significant correlation (rho = 0.694, $p < .001$) between the percentage change in LDF (%ΔLDF) and the percentage change in MAP (%ΔMAP). The regression coefficient was 1.12 ± 0.08 ($p < .001$), that is, the relative change in LDF perfusion was numerically similar to the relative change in MAP. Individually, both the atrial and ventricular stimulation showed a significant correlation (Figure 2) between %ΔLDF and %ΔMAP (atrial: rho = 0.644, $p < .001$; ventricular: rho = 0.642, $p < .001$). The individual regression coefficients were atrial: 0.99 ± 0.13, $p < .001$ and ventricular: 1.21 ± 0.13, $p < .001$. Overall, regression for ventricular stimulation was steeper, suggesting %ΔLDF to be more sensitive to %ΔMAP.

Bland–Altman plots confirmed the linear relationship between %ΔLDF and %ΔMAP. There was no significant bias (0.54 ± 1.47 $p < .001$, Figure 3).

3.3 | Relationship between %ΔLDF and %ΔMAP against pacing rate

Overall, there was a significant correlation between both the %ΔLDF and %ΔMAP with a change in heart rate (Figure 4). %ΔLDF decreased 4.81 ± 0.95 % per 10 bpm rate increase ($p < .001$), and %ΔMAP decreased 3.29 ± 0.48% ($p < .001$).

For atrial stimulation, %ΔLDF decreased by 4.86 ± 1.30 % per 10 bpm rate increase ($p < .001$) and %ΔMAP decreased by 3.81 ± 0.73 % per 10 bpm rate increase ($p < .001$). For ventricular stimulation, %ΔLDF decreased by 4.33 ± 1.29 % per 10 bpm rate increase ($p = .001$) and %ΔMAP decreased by 2.36 ± 0.48 % per 10 bpm rate increase ($p < .001$)

In contrast to the ventricular stimulation experiments, atrial stimulation showed an initial improvement of hemodynamics at 120 and 140 bpm, before declining at higher rates.

We assessed the ability of heart rate and LDF perfusion to predict hemodynamic deteriorations for both atrial and ventricular pacing. At predefined levels of arterial pressure drops, we calculated the area under the curve (AUC) for heart rate and LDF to be able to detect hemodynamic compromise (Figure 5). LDF perfusion was superior to heart rate to predict hemodynamic deterioration for atrial and ventricular pacing.

4 | DISCUSSION

We found that changes in MAP, induced by atrial and ventricular pacing, are reflected by changes in LDF tissue perfusion. Relative LDF changes can therefore serve as a valid surrogate parameter for blood pressure and can be compared to a stored value during normal rhythm. The LDF sensor can be miniaturized and incorporated into future ICDs to be used in conjunction with current arrhythmia detection

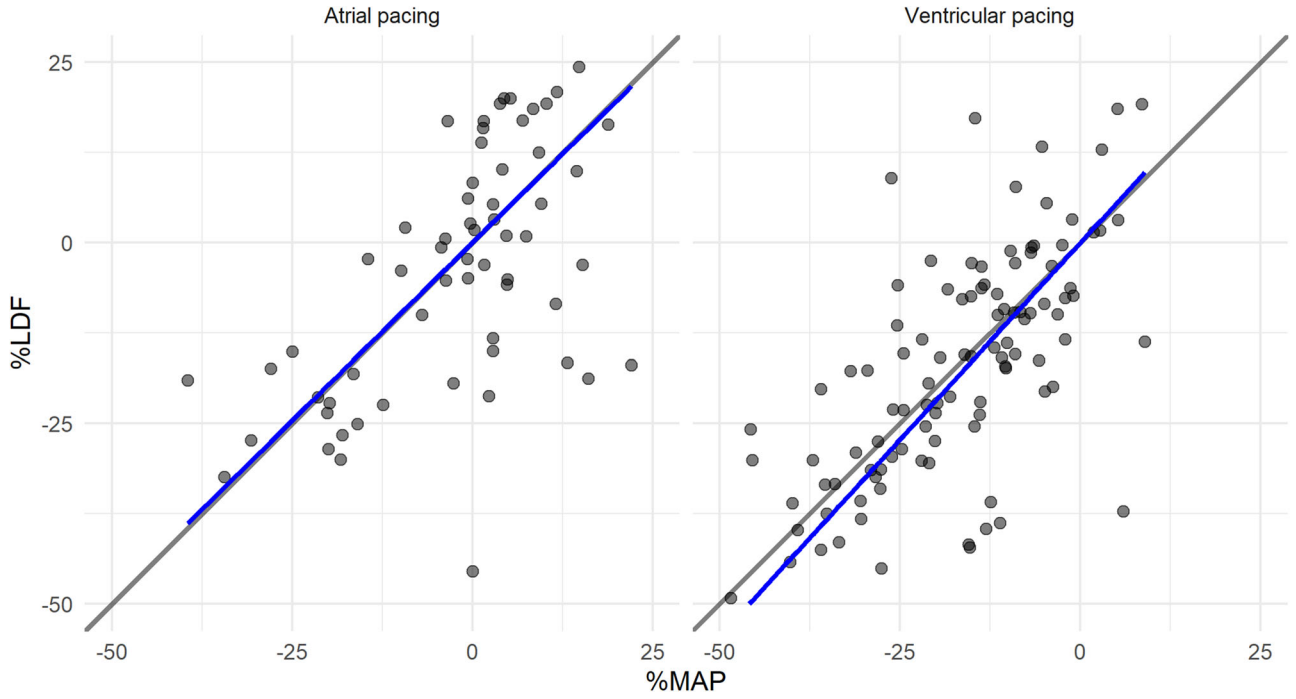


FIGURE 2 Correlation of tissue perfusion and arterial pressure for atrial and ventricular stimulation experiments. Data are displayed for all patients and all pacing frequencies. [Color figure can be viewed at wileyonlinelibrary.com]

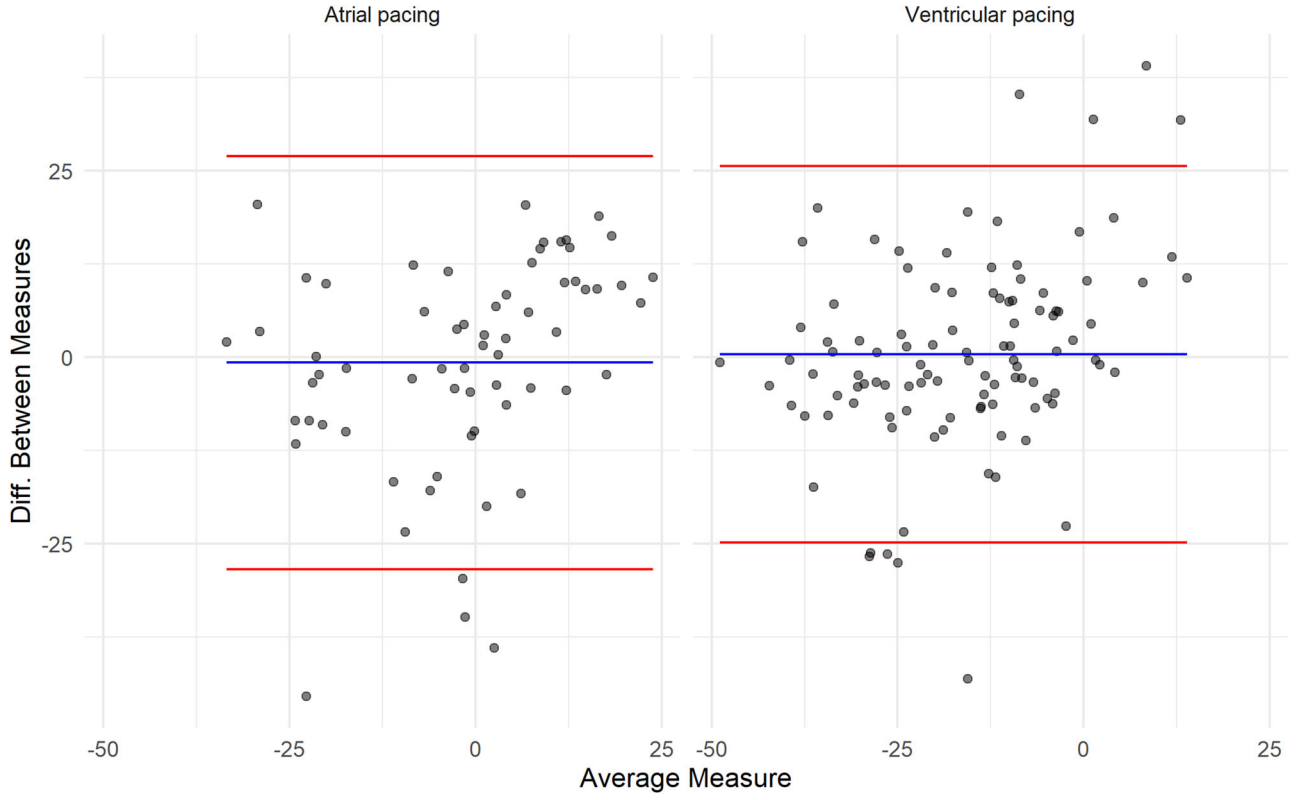


FIGURE 3 Bland–Altman Plot for atrial and ventricular simulation experiments. Data are displayed for all patients and all pacing frequencies. [Color figure can be viewed at wileyonlinelibrary.com]

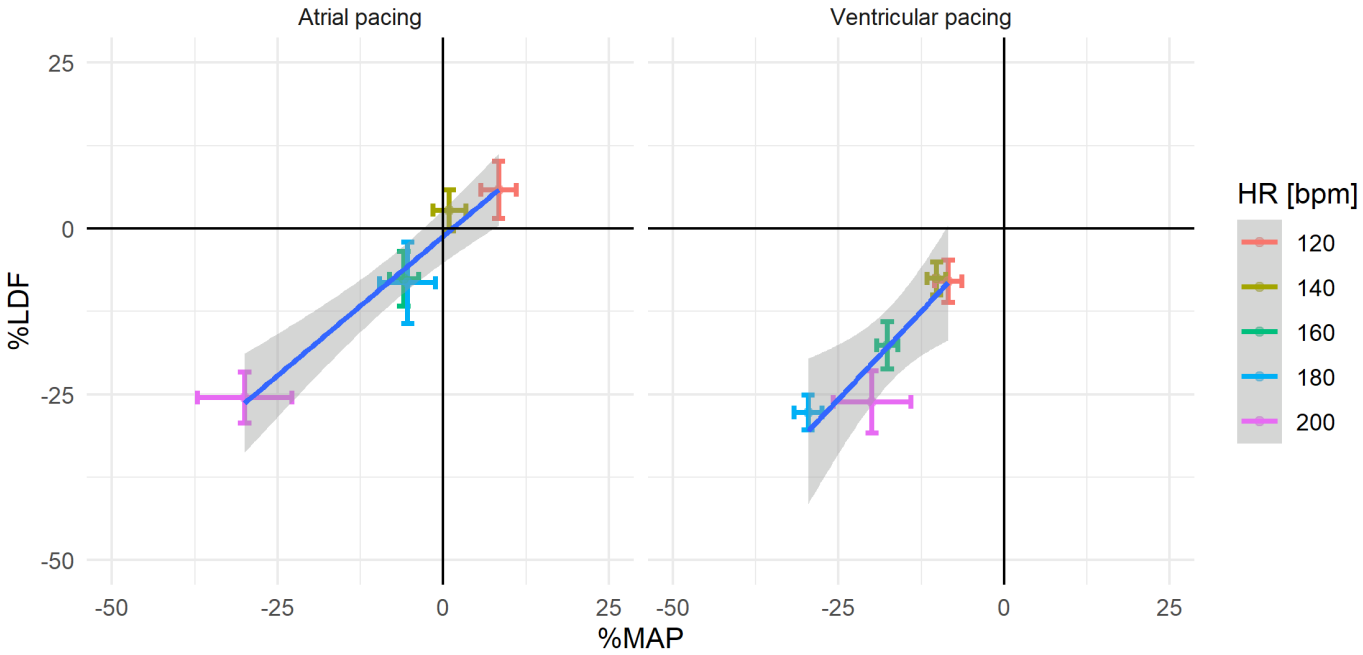


FIGURE 4 Correlation of tissue perfusion and mean arterial pressure and the effect of heart rate for atrial and ventricular stimulation. Tissue perfusion and mean arterial pressure data are aggregated per heart rate. [Color figure can be viewed at wileyonlinelibrary.com]

algorithms. This would potentially allow hemodynamically tolerated tachyarrhythmias to be monitored for longer, without the need for aggressive therapies.

We found good agreement between changes in tissue perfusion and blood pressure: the fall of the MAP is immediately followed by a reduction in tissue perfusion. To compensate for the sudden drop in central blood pressure and prevent collapse, there is an immediate physiological response of arteriolar vasoconstriction, resulting in reduced perfusion pressure. The vasoconstriction may amplify the direct blood pressure-related effects on tissue perfusion.

The hemodynamic decrement at faster pacing rates was similar for tissue perfusion and MAP. This is because, at faster rates, vasoconstriction cannot sufficiently compensate for the impaired cardiac output that results from the unphysiological contraction pattern during ventricular tachycardia.[34] Our data correlate well with clinical findings that ventricular tachycardia up to 140 bpm is usually well tolerated, and in many cases, not noticed by patients. Trying to keep the rate of ventricular tachycardia low is one of the objectives of antiarrhythmic medication, along with avoiding syncope and increasing the likelihood of successful ATP termination.

To demonstrate that LDF was not simply responding to heart rate changes, we performed two further experiments. First, we examined the effects of higher-rate atrial pacing on blood pressure and LDF perfusion. Then, we assessed the ability of heart rate and LDF to predict the relative change in blood pressure.

During higher-rate atrial pacing, blood pressure on average increased by 10.3% at 120 bpm. This was reflected by a similar relative increase in LDF perfusion. At even higher heart rates, both LDF and MAP similarly decreased. The hemodynamic decrement at elevated atrial pacing rates (perfusion/heart rate) was considerably less than during ventricular pacing. These results of atrial pacing represent the expected physiological reaction of sympathetically driven chronotropy. The increased heart rate and the associated increase in cardiac output initially cause an elevated MAP and increase in tissue perfusion. Further increasing the heart rate ultimately leads to a shortening of the diastolic phase, and consequently, a reduction in stroke volume. This explains the observed reduction in blood pressure at higher atrial rates.

When we compared the ability of LDF and heart rate to predict the relative changes in blood pressure, LDF outperformed heart rate.

In our study, tissue perfusion could detect the different hemodynamic effects of atrial and ventricular stimulation as reliably as MAP. In fact, LDF perfusion is better at detecting relevant changes in MAP than heart rate alone. Although ICD algorithms provide an estimate of the probability for the presence of ventricular tachycardias or supraventricular tachycardias based on rate, intra-cardiac conduction timing, and EGM patterns, none of these criteria reflect hemodynamic status. LDF tissue perfusion measurements appear to be a valid estimate of the hemodynamic state.

4.1 | Limitations

The clinical study was performed in a supine position at rest, and the length of the individual studies performed was short. Different activity levels, as well as autonomic control, will affect tissue perfusion, however, this could not be addressed in the current study. Most patients enrolled had a near-normal ejection fraction, and therefore, these results do not extend to an ICD population. Further research is required to confirm these findings in patients with a severe left

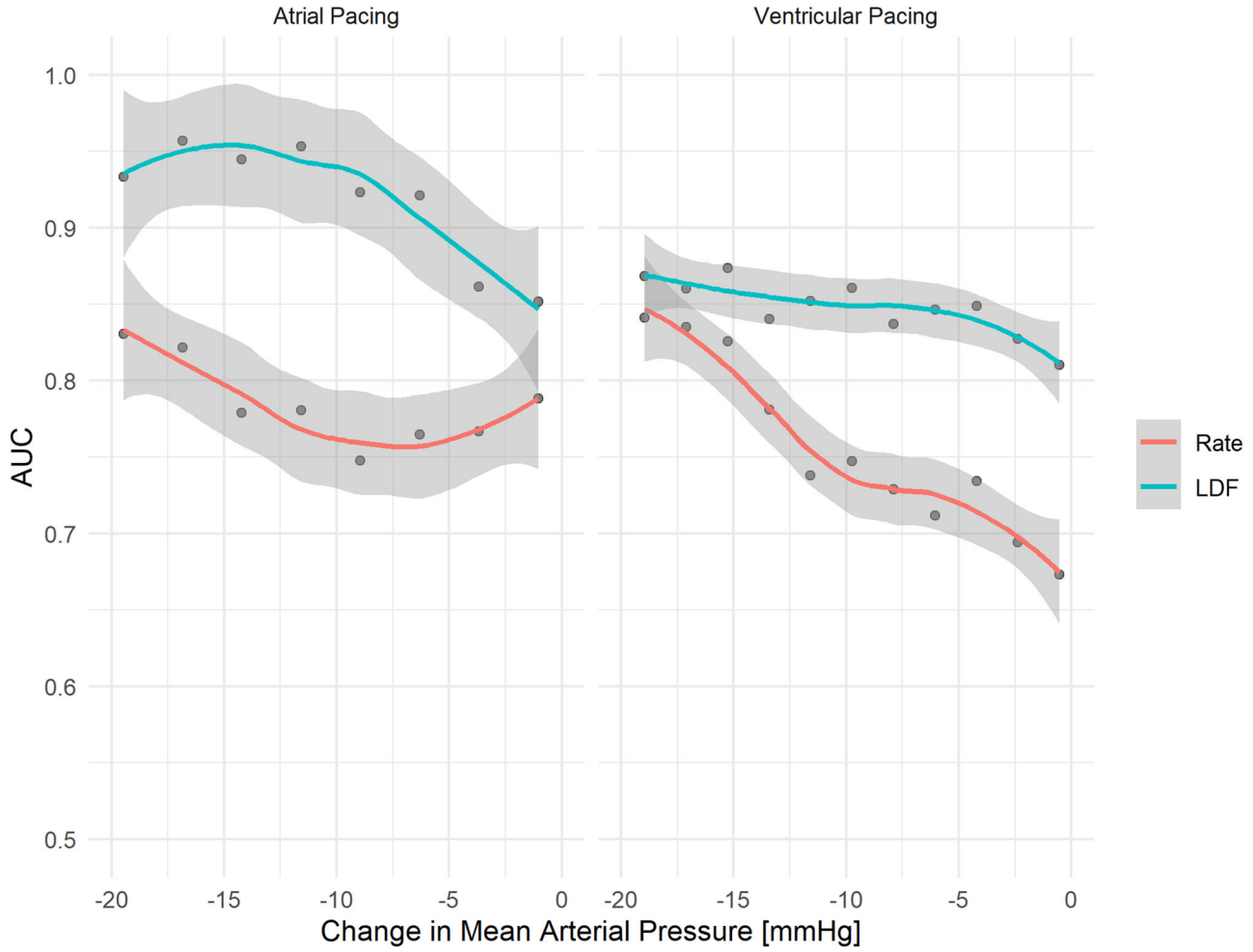


FIGURE 5 Accuracy for both atrial and ventricular stimulation experiments to detect drops in mean arterial pressure based on heart rate and LDF perfusion data. [Color figure can be viewed at wileyonlinelibrary.com]

ventricular systolic impairment that is more representative of an ICD target population.

In this study, we used tissue perfusion values just prior to the start of the pacing protocol as reference. For real-life applications, an appropriate reference value will need to be determined. Laser Doppler is also known to be sensitive to motion artifacts. As we performed measurements at rest, in a supine position, extra care was taken to minimize artifacts when applying the sensor. Therefore, advanced algorithms may be needed to obtain valid and robust measurements during motion, if incorporated into future ICDs. We also continuously monitored LDF tissue perfusion, which is impractical for its use in ICDs, due to its high-power consumption and drain on battery life.

5 | CONCLUSION

LDF perfusion measurements correlate with MAP during paced supraventricular and ventricular tachycardia. In our small dataset, LDF perfusion identified hemodynamic compromise better than the pacing rate alone. Incorporating an LDF sensor into ICDs may allow us to move away from classifying supraventricular tachycardias as inappropriate and incorporating them into necessary and unnecessary therapies based on hemodynamic status. These findings raise the possibility that future integration of LDF in ICDs may allow hemodynamic-guided therapies.

ACKNOWLEDGMENT

This work was supported by Medtronic PLC, Bakken Research Center, Maastricht, Netherlands.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

ORCID

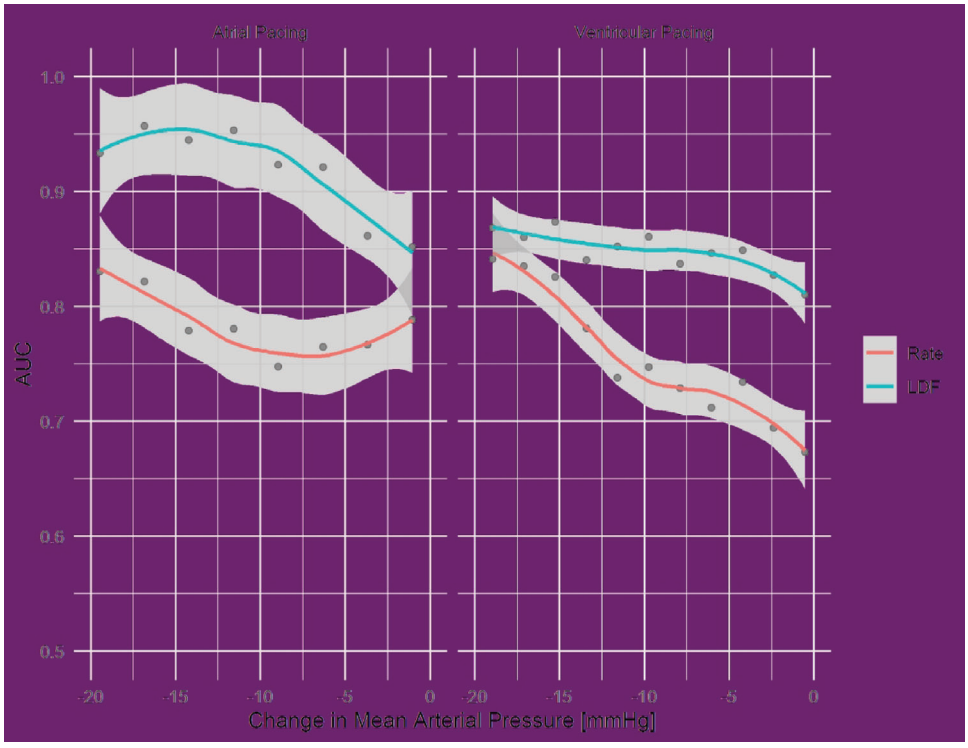
Emilia Stegemann MD https://orcid.org/0000-0003-2407-2837
Alejandra A Miyazawa MD https://orcid.org/0000-0003-1958-7027
Francisco Leyva MD https://orcid.org/0000-0002-2176-0223

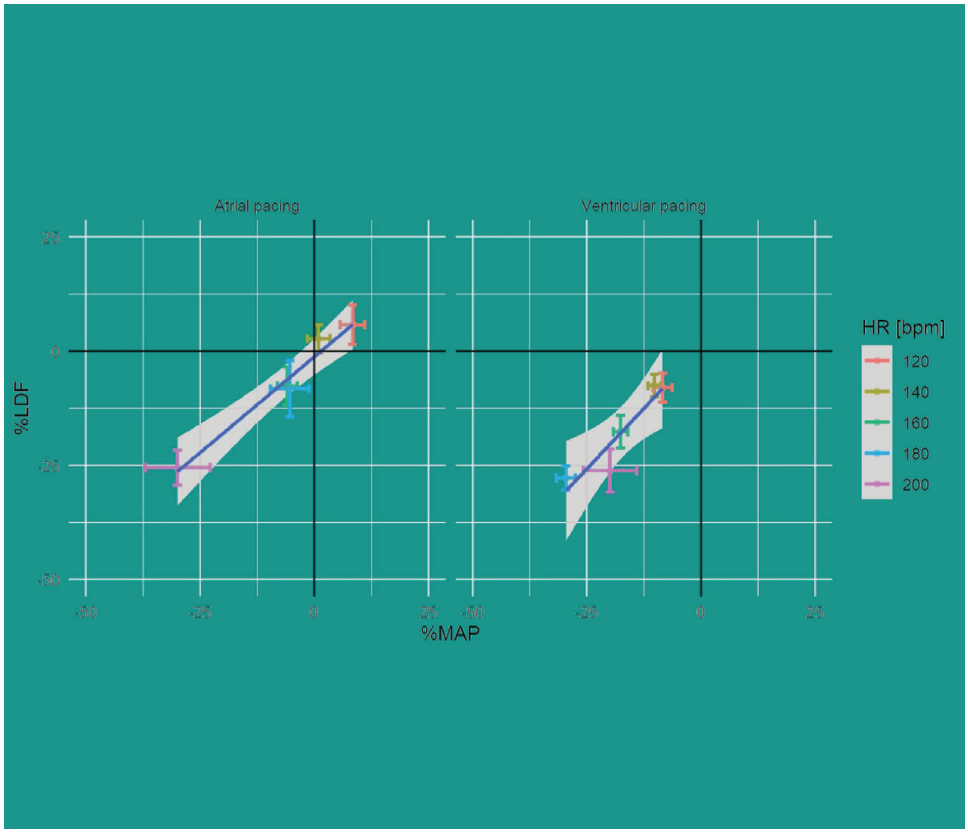
REFERENCES

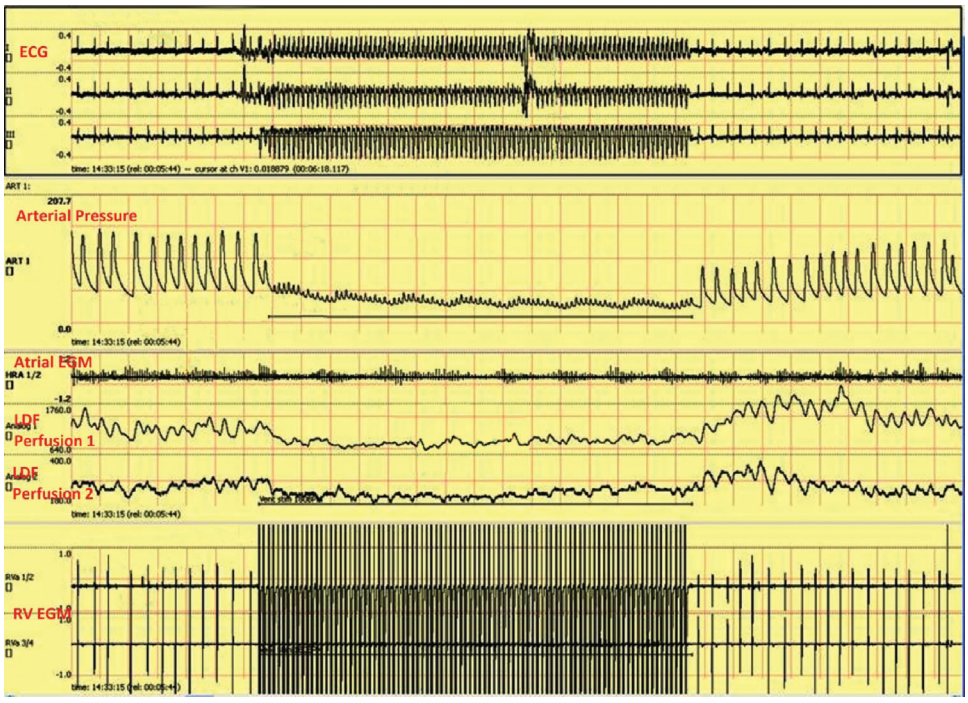
1. Primorac D, Odak L, Perić V, et al. Sudden cardiac death—a new insight into potentially fatal genetic markers. *Front Med*. 2021;8:647412.
2. Bardy GH, Lee KL, Mark DB, et al. Amiodarone or an implantable cardioverter-defibrillator for congestive heart failure. *New Engl J Med*. 2005;352(20):225-237.
3. Moss AJ, Hall WJ, Cannom DS, et al. Improved survival with an implanted defibrillator in patients with coronary disease at high risk for ventricular arrhythmia. Multicenter Automatic Defibrillator Implantation Trial Investigators. *N Engl J Med*. 1996;335(26):1933-1940.
4. Moss AJ, Zareba W, Hall WJ, et al. Prophylactic implantation of a defibrillator in patients with myocardial infarction and reduced ejection fraction. *N Engl J Med*. 2002;346(12):877-883. doi:10.1056/NEJMoa013474
5. Strickberger SA, Canby R, Cooper J, et al. Association of antitachycardia pacing or shocks with survival in 69,000 patients with an implantable defibrillator. *J Cardiovasc Electrophysiol*. 2017;28(4):416-422.
6. Sanders P, Connolly AT, Nabutovsky Y, Fischer A, Saeed M. Increased hospitalizations and overall healthcare utilization in patients receiving implantable cardioverter-defibrillator shocks compared with antitachycardia pacing. *JACC Clin Electrophysiol*. 2018;4(2):243-253.
7. Coleman CI, Giedrimiene D, Bhavnani S, Azeem M, Kluger J. Healthcare utilization and costs of treating patients experiencing inappropriate implantable cardioverter defibrillator shocks. *J Am Coll Cardiol*. 2013;61(10):E1580-E1580.
8. Hocevar A, Rotar Z, Jese R, et al. Do early diagnosis and glucocorticoid treatment decrease the risk of permanent visual loss and early relapses in giant cell arteritis. *Med (United States)*. 2016;95(14):e3210.
9. Powell BD, Saxon LA, Boehmer JP, et al. Survival after shock therapy in implantable cardioverter-defibrillator and cardiac resynchronization therapy-defibrillator recipients according to rhythm shocked: the altitude survival by rhythm study. *J Am Coll Cardiol*. 2013;62(18):1674-1679. doi:10.1016/j.jacc.2013.04.083
10. Fang Y, Gu K, Yang B, et al. What factors lead to the acceleration of ventricular tachycardia during antitachycardia pacing?—results from over 1000 episodes. *J Arrhythmia*. 2018;34(1):36-45.
11. Wollmann CG, Lawo T, Kühlkamp V, et al. Implantable defibrillators with enhanced detection algorithms: Detection performance and safety results from the painfree SST study. *PACE - Pacing Clin Electrophysiol*. 2014;37(9):1198-1209.
12. Auricchio A, Meijer A, Kurita T, et al. Safety, efficacy, and performance of new discrimination algorithms to reduce inappropriate and unnecessary shocks: The PainFree SST clinical study design. *Europace*. 2011;13(10):1484-1493.
13. Moss AJ, Schuger C, Beck CA, et al. Reduction in inappropriate therapy and mortality through ICD programming. *N Engl J Med*. 2012;367(24):2275-2283. doi:10.1056/NEJMoa1211107
14. Gasparini M, Lunati MG, Proclemer A, et al. Long detection programming in single-chamber defibrillators reduces unnecessary therapies and mortality: the ADVANCE III trial. *JACC Clin Electrophysiol*. 2017;3(11):1275-1282.
15. Schwab JO. Optimizing ICD programming for shock reduction. *Fundam Clin Pharmacol*. 2009;24(5):653-659.
16. Gasparini M. Avoiding unnecessary aggressive ICD programming after MADIT-RIT and ADVANCE III trials. *J Am Coll Cardiol*. 2014;63(2):189-190. doi:10.1016/j.jacc.2013.07.105.7
17. Ricci RP, Pignalberi C, Landolina M, et al. Ventricular rate monitoring as a tool to predict and prevent atrial fibrillation-related inappropriate shocks in heart failure patients treated with cardiac resynchronisation therapy defibrillators. *Heart*. 2014;100(11):848-854.
18. Auricchio A, Schloss EJ, Kurita T, et al. Low inappropriate shock rates in patients with single- and dual/triple-chamber implantable cardioverter-defibrillators using a novel suite of detection algorithms: PainFree SST trial primary results. *Hear Rhythm*. 2015;12(5):926-936. doi:10.1016/j.hrthm.2015.01.017
19. Larbig R, Motloch LJ, Bettin M, et al. Device updates successfully reduce T-wave oversensing and inappropriate shocks in subcutaneous ICD patients. *Netherlands Hear J*. 2018;26(12):606-611.
20. Powell BD, Asirvatham SJ, Perschbacher DL, et al. Noise, artifact, and oversensing related inappropriate ICD shock evaluation: ALTITUDE noise study. *Pacing Clin Electrophysiol*. 2012;35(7):863869.
21. Fredriksson I, Fors C, Johansson J. Laser Doppler Flowmetry - a Theoretical Framework, Department of Biomedical Engineering, Linköping University (2007), http://www.imt.liu.se/bit/ldf/ldf.pdf
22. Murray AK, Herrick AL, King TA. Laser doppler imaging: a developing technique for application in the rheumatic diseases. *Rheumatology*. 2004;43(10):1210-1218.
23. Stoyneva Z. Clinical application of laser doppler flowmetry in neurology. *Perspect Med*. 2012;1(1-12):89-93. doi:10.1016/j.permed.2012.03.009
24. Sohaib SMA, Whinnett ZI, Ellenbogen KA, et al. Cardiac resynchronisation therapy optimisation strategies: systematic classification, detailed analysis, minimum standards and a roadmap for development and testing. *Int J Cardiol*. 2013;170(2):118-131. doi:10.1016/j.ijcard.2013.10.069
25. Nabutovsky Y, Pavek T, Turcott R. Chronic performance of a subcutaneous hemodynamic sensor. *Pacing Clin Electrophysiol*. 2012;35(8):919-926.
26. Turcott RG, Pavek TJ. Identification of hemodynamically unstable arrhythmias using subcutaneous photoplethysmography. *J Cardiovasc Electrophysiol*. 2010;21(4):448-454.
27. Turcott RG, Pavek TJ. Hemodynamic sensing using subcutaneous photoplethysmography. *Am J Physiol Hear Circ Physiol*. 2008;295(6):2560-2572.
28. Keene D, Shun-Shin MJ, Arnold AD, et al. Quantification of electromechanical coupling to prevent inappropriate implantable cardioverter-defibrillator shocks. *JACC Clin Electrophysiol*. 2019;5(6):705-715.
29. Nieland J, Van Kranenburg H, Wallinga H, Serov A, Steenbergen W, De Mul FFM. 1999. Design of an integrated photo detector circuit for laser doppler blood flow monitoring. In ESSCIRC '99: proceedings of the 25th European Solid-State Circuits Conference, Duisburg, Germany, 21–23 September, 1999 (pp. 262–265). IEEE. https://ieeexplore.ieee.org/document/1471146
30. Serov AN, Nieland J, Oosterbaan S, et al. Integrated optoelectronic probe including a vertical cavity surface emitting laser for laser Doppler perfusion monitoring. *IEEE Trans Biomed Eng*. 2006;53(10):2067-2074.
31. Schneider R, Bauer A, Barthel P, Schmidt G. libRASCH: A programming framework for signal handling. *Comput Cardiol*. 2004;31:53-56.
32. Manisty CH, Al-Hussaini A, Unsworth B, et al. The acute effects of changes to AV delay on BP and stroke volume potential implications for design of pacemaker optimization protocols. *Circ Arrhythmia Electrophysiol*. 2012;5(1):122-130.
33. R Core Team (2021). R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria. https://www.R-project.org/
34. Wiggers CJ. The muscular reactions of the mammalian ventricles to artificial surface stimuli. *Am J Physiol Legacy Content*. 1925;73(2):346-378.

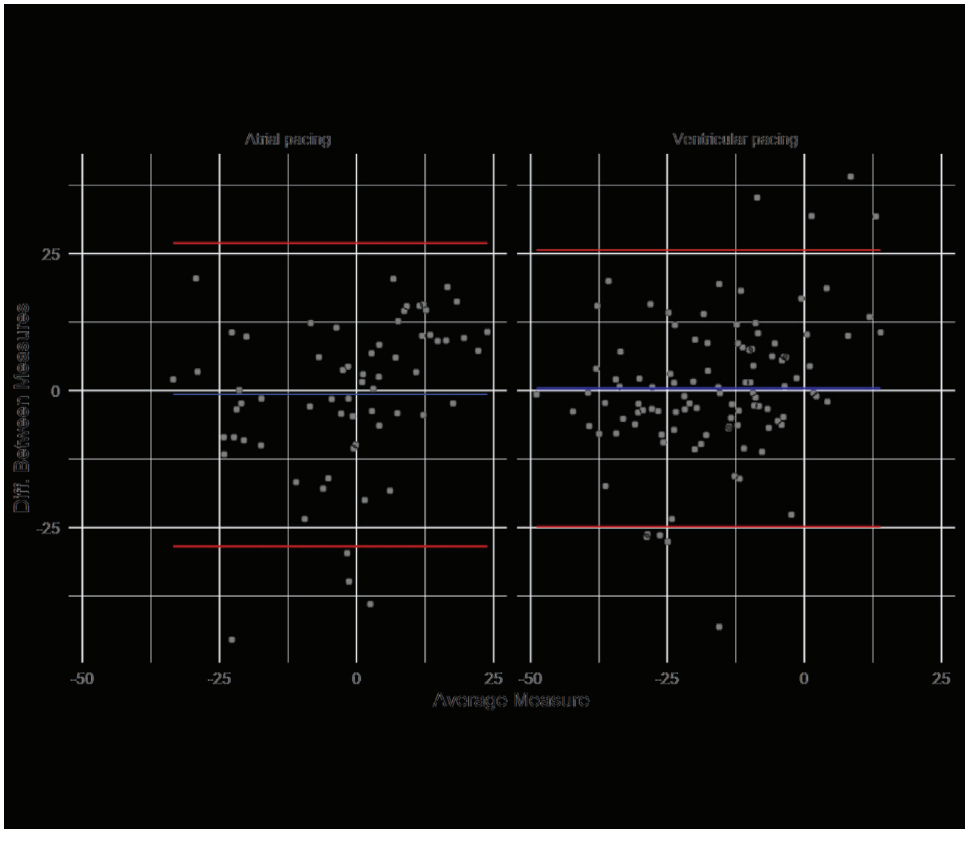
How to cite this article: Stegemann E, Weidmann M, Miyazawa AA, et al. Laser Doppler flow for the hemodynamic differentiation of tachycardia. *Pacing Clin Electrophysiol*. 2022;1-11. https://doi.org/10.1111/pace.14618

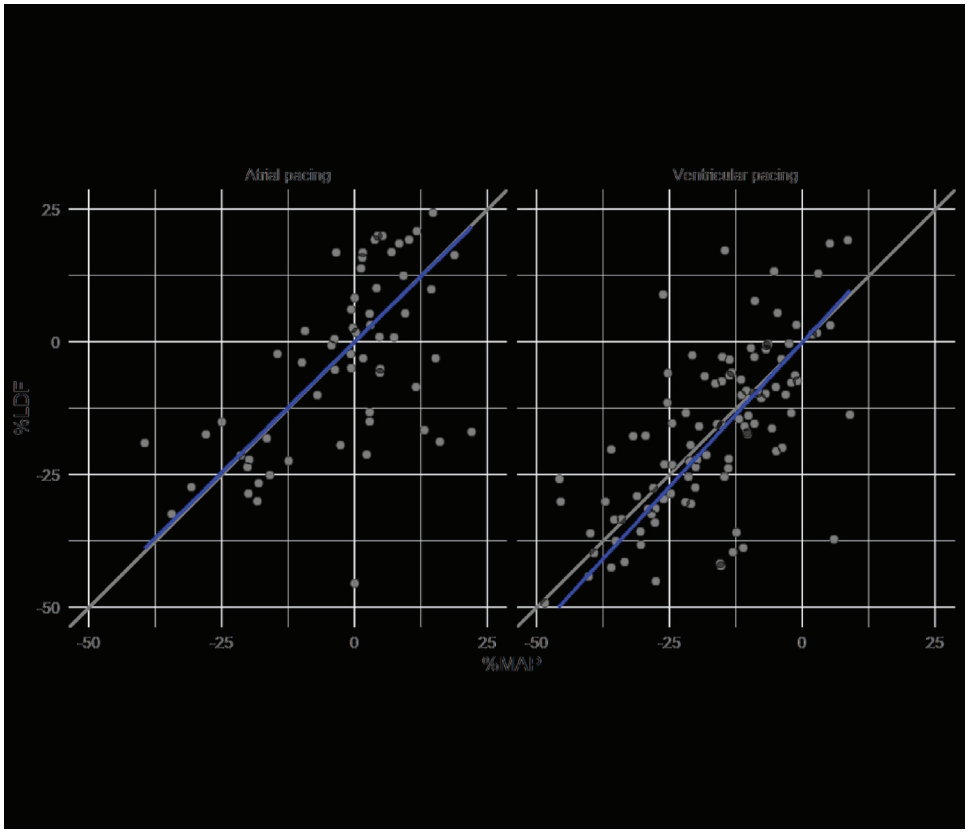
APPENDICES


Atrial Pacing
Ventricular Pacing
AUC
1.0
0.9
0.8
0.7
0.6
0.5
-20
-15
-10
-5
0
Change in Mean Arterial Pressure [mmHg]
Rate
LDF


Atrial pacing
Ventricular pacing
%LDF
25
0
-25
-50
%MAP
HR [bpm]
120
140
160
180
200


ECG
Arterial Pressure
Atrial EGM
LDF
Perfusion 1
LDF
Perfusion 2
RV EGM


Atrial pacing
Ventricular pacing
Diff. Between Measures
25
0
-25
-50
-25
0
25
Average Measure


Atrial pacing
Ventricular pacing
25
0
-25
-50
%LDF
-50
-25
0
25
%VAI