Document downloaded from:

http://hdl.handle.net/10251/202199

This paper must be cited as:

Segarra, I.; Cebrián Ferriols, AJ.; Ruiperez-Campillo, S.; Tormos Ferrando, Á.; Chorro, FJ.; Castells, F.; Alberola, A.... (2023). Mini Peltier Cell Array System for the Generation of Controlled Local Epicardial Heterogeneities. IEEE. 1-4. https://doi.org/10.1109/EMBC40787.2023.10340369

VNIVERSITAT POLITÈCNICA VALÈNCIA

The final publication is available at

https://doi.org/10.1109/EMBC40787.2023.10340369

Copyright IEEE

Additional Information

Mini Peltier Cell Array System for the Generation of Controlled Local Epicardial Heterogeneities*

Izan Segarra[1], Antonio Cebrián[1], Samuel Ruipérez-Campillo[1,2,6], *Student Member IEEE*, Álvaro Tormos[1], Francisco Javier Chorro[4,5], Francisco Castells[1], Antonio Alberola[3], Jose Millet[2,7]

Abstract— **The present study aims to design and fabricate a system capable of generating heterogeneities on the epicardial surface of an isolated rabbit heart perfused in a Langendorff system. The system consists of thermoelectric modules that can be independently controlled by the developed hardware, thereby allowing for the generation of temperature gradients on the epicardial surface, resulting in conduction slowing akin to heterogeneities of pathological origin. A comprehensive analysis of the system's viability was performed through modeling and thermal simulation, and its practicality was validated through preliminary tests conducted at the experimental cardiac electrophysiology laboratory of the University of Valencia. The design process involved the use of Fusion 360 for 3D designs, MATLAB/Simulink for algorithms and block diagrams, LTSpice and Altium Designer for schematic captures and PCB design, and the integration of specialized equipment for animal experimentation. The objective of the study was to efficiently capture epicardial recordings under varying conditions.**

Clinical relevance— **The proposed system aims to induce local epicardial heterogeneities to generate labeled correct signals that can serve as a golden standard for improving algorithms that identify and characterize fibrotic substrates. This improvement will enhance the efficacy of ablation processes and potentially reduce the ablated surface area.**

I. INTRODUCTION

The advent of multi-electrode catheters in array format for clinical use presents a challenge for electrophysiological exploration, aiming to improve the efficacy of cardiac ablation procedures. The Abbot Advisor HD Grid catheter features a grid distribution, enabling local exploration of myocardial tissue through 16 equidistant electrical recordings arranged in a 4x4 grid with a stable spatial position. This device allows high anatomical resolution recording without spatial limitations of conventional catheters, introducing a new paradigm in EGM recording with an additional modality known as omnipolar. Researchers from the LYRIC Institute explored the optimal threshold in two HD network catheter [1] configurations in a sheep infarction model, referencing the results obtained by MRI, and suggest a multicenter study to determine specific thresholds for high-density GRID electrodes [2].

The main purpose of this article is to induce localized and controlled heterogeneities in the electrophysiological characteristics of cardiac tissue, thus replicating a pro-arrhythmic substrate like that of fibrotic regions. One of the possible variables to achieve this purpose is temperature. The local temperature drop applied to the epicardium in experiments with perfused rabbit hearts showed a decreasing effect on the local dominant frequency of the fibrillatory recordings [3] without affecting the normothermic zones. It has been provided acceptable linear correlation between temperature and dominant frequency values, as well as decreased conduction velocity with hypothermia in sinus rhythm [7]. This model facilitates controlled and versatile localized modifications that can reproduce the effects of fibrotic areas on conduction, although its scope is limited to modifying the electrophysiological properties of healthy tissue. Furthermore, its design should be oriented to its simultaneous and integrated application with the Advisor HD Grid multielectrode.

II. MATERIALS & METHODS

A. Cooling System Design

To perform selective cooling of the epicardial substrate, a series of conditions are required: small size compatible with the Advisor™ HD Grid, no moving parts, a wide temperature range (from 37 ºC, which is the temperature of the Tyrode, to negative temperatures of the order of -5 or -10 ºC) and easy controllability by varying the voltage or current levels. The option that meets all the requirements is to use tiny Peltier cells and distribute them in an array compatible with the catheter gaps.

The distance between neighboring electrodes in the catheter is 3 mm, which reduces the number of possibilities available on the market. The CUI Devices CP0734-238 Peltier cell is a possibility, as it allows a temperature difference between its faces of up to 70 ºC and its cold side dimensions (1.8 x 3.4 mm) are compatible with the catheter. This allows the inclusion of the cooling system between the electrode columns as shown in Fig 1 A.

Finally, it should be noted that it is necessary to cool the hot side of the Peltier cell to avoid temperature saturation on the cold side and to be able to expel all the necessary heat. For this purpose, we use the Hydrus V2 liquid cooling system which allows for keeping the hot side of the CUI

---

*This work was supported by PID2019-109547RB-I00 (National Research Program, Ministerio de Ciencia e Innovación, Spanish Government) and CIacBERCV CB16/11/00486 (Instituto de Salud Carlos III).

[1] ITACA Institute, Universitat Politècnica de València, Valencia, Spain

[2] Swiss Federal Institute of Technology (ETH), Zürich, Zürich, Switzerland

[3] Departamento de Fisiología, Universitat de València, Valencia, Spain

[4] Departamento de Medicina, Universitat de València, Valencia, Spain

[5] Servicio de Cardiología, Hospital Clínic Universitari de València, Valencia, Spain

[6] School of Medicine, Stanford University, CA, United States of America

[7] Jose Millet is the corresponding author. `jmillet@eln.upv.es`

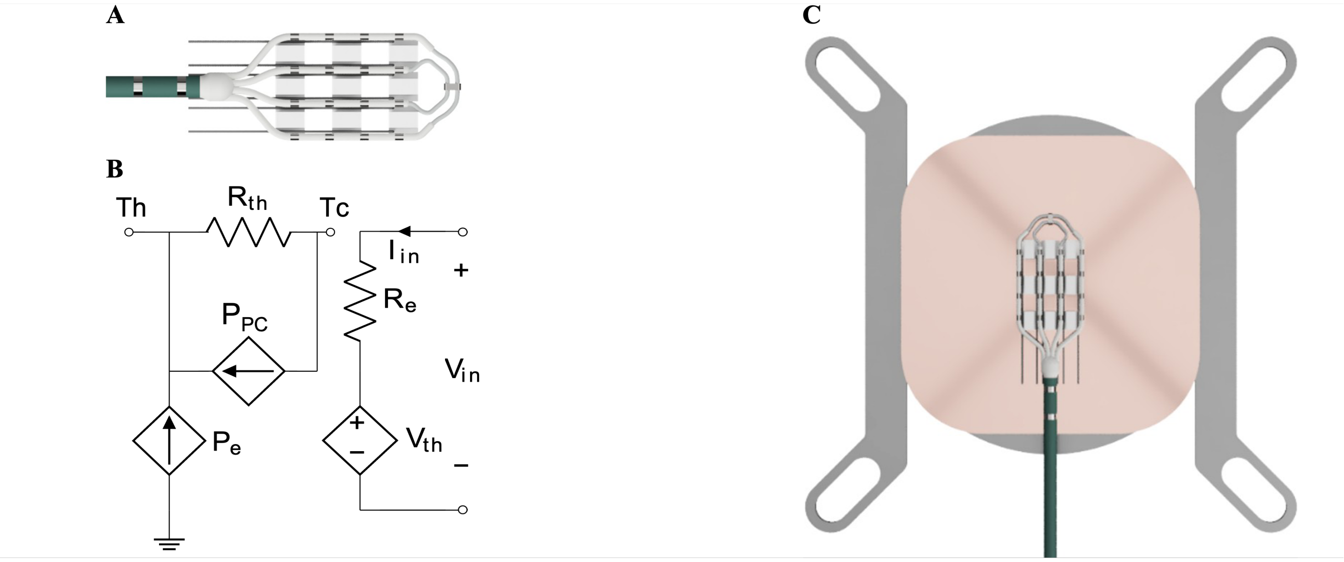

Fig. 1. A: Integration of the catheter in the cooling system.The matrix formed by Peltier cells (CUI CP0734-238). B: Equivalent circuit for the Peltier cell model. The left side represents the thermal behavior of the TEG using the electro-thermal equivalence while the right side represents the purely electrical behavior of the module. C: The Cooling element (Hydrus V2).

CP0734-238 at a constant temperature of approximately 25 ºC. As we can be seen in Fig 1 C.

B. Peltier Cell Modeling

The modeling of the behavior of Peltier cells or thermoelectric generator modules (TEG) is of vital importance to have an estimation of the response of the heterogeneity generation system and to have proof of its viability. Its operation is determined by the various physical effects involved: Seebeck, Peltier, Thomson, and Joule. All these effects are reversible, except the Joule effect [4]. They do not influence all equally, therefore, due to the temperature range with which the project is carried out (37 ºC to -10 ºC) we assume that the Thomson effect is negligible.

During the modeling, both steady state and transient state have been considered since the TEG materials have certain thermal inertia that can be modeled from the specific heat and mass to obtain the thermal capacity. Considering the thermal capacity provides accuracy to the simulations and allows us to see the system's time evolution, i.e., the transient state. The thermal inertia of the module is influenced by the thermal capacity of the ceramic substrate on both sides and by the semiconductor elements. From the device data sheet specifications [5], the volume of the substrate and the semiconductor is calculated. Multiplying the volume by the density of the material gives the mass. Finally, the product of the mass with the specific heat allows us to obtain the thermal capacity of the hot side, the cold side, and the semiconductor element [4] [6]. The complete circuit is shown in Fig 1 B, considering the effect of the thermal capacity of each component forming the Peltier cell and its equations (1), (2), and (3).

$$V_{in} = \alpha_{AB}\Delta T + I_{in}R_e = V_{th} + I_{in}R_e \tag{1}$$

$$P_e = V_{in}I_{in} = \alpha_{AB}\Delta T I_{in} + I_{in}^2 \tag{2}$$

$$P_{PH} = P_e + P_{PC} = P_e + \alpha_{AB}T_C I_{in} - I_{in}^2\frac{R_e}{2} - \frac{\Delta T}{R_{th}} \tag{3}$$

To verify that the simulation corresponds to reality, the response of a Peltier cell is simulated with the hot side over the cooling system and the cold side absorbing heat from the environment by convection. SIMULINK® is the MATLAB® environment that allows the behavior of different systems to be modeled by block diagram and their evolution over time to be studied. The modeling of the hot side environment consists of a 25 °C heat source in series with the refrigeration copper's thermal resistance and the same heat capacity. As for the cold side environment, it is modeled by the heat capacity of the laboratory air in which the tests will be performed, the ambient convection resistance of the alumina (Al2O3) that forms the cold side of the cell, and a heat source of 27 ºC. The simulation indicates that with the applied input voltage (0.58 V), it is possible to reach -5 ºC on the surface of the cold face of the thermoelectric module in approximately 1 minute.

C. Characterization of the thermoelectric module

The temperature measurement on the surface of the device is performed by a thin film platinum element (Pt-100). Sensor is placed on the surface of the cold side with a layer of highly conductive thermal paste to make the measurement as accurate as possible. The effect of the temperature decrease can be seen in Fig 2 A.

D. Control System

The Peltier cells are controlled by the variation of the voltage applied to their terminals, ranging from 0 V to 0.6 V. LT3081 is a 1.5 A low dropout linear regulator designed

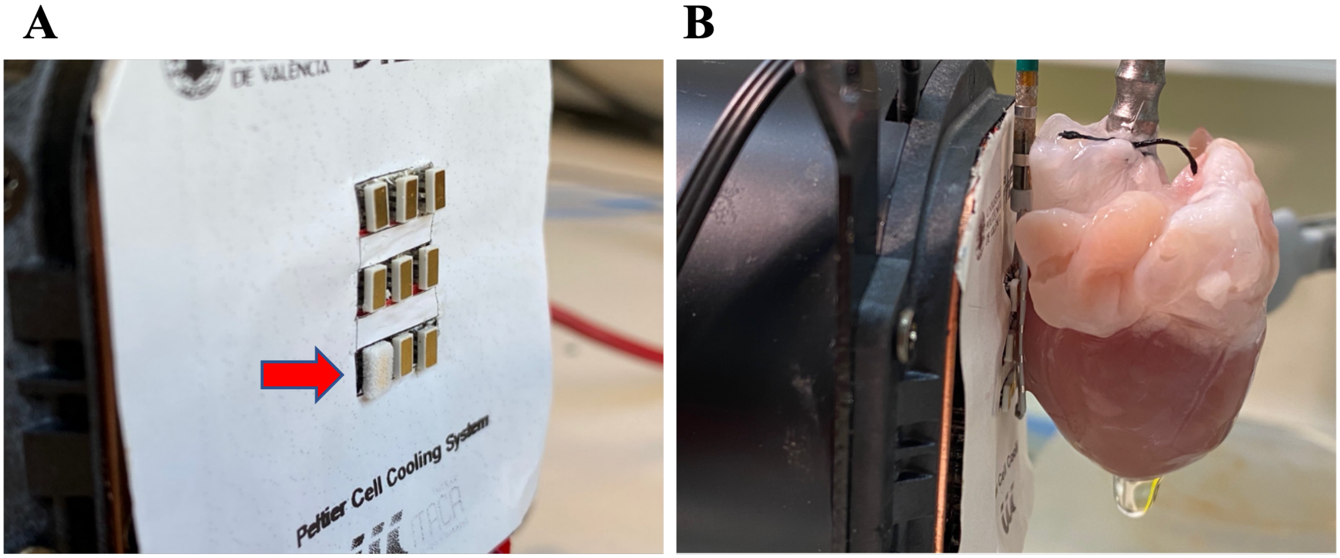

Fig. 2. A: Refrigeration system with one of the Peltier cells on freezing the ambient condensation. B: Array of TEG modules on the epicardial surface with the HD Grid attached in the recording position.

for rugged industrial applications. The main features are output current control, temperature control, and programmable current limit.

The LT3081's 50 μA reference current source allows a single resistor to program the output voltage to any level between 0 and 34.5 V. The current reference architecture makes load regulation independent of the output voltage. The LT3081 is stable with or without input and output capacitors. In addition, a single resistor sets the current limit. For all these reasons, we considered using this integrated for the control of the 9 Peltier cells distributed in a matrix format in the catheter holes.

E. Experiment

The Preliminary validation of the system was performed on three isolated perfused heart preparations from New Zealand breed rabbits (n=30). After anesthesia with ketamine (25 mg/kg, i.m.) and heparinization rabbits were euthanized by intravenous injection of sodium thiopental (60 mg/kg), the heart was removed and immersed in cold Tyrode (4 °C). Once the aorta is isolated, it is connected to a Langendorff system perfusing Tyrode's solution at a pressure of 60 mmHg and a temperature of 37 ± 0.5 ºC. Oxygenation is carried out with a mixture of 95% C02 and 5% C02.

Measurements are performed on the epicardial wall of the right ventricle since the thinner myocardial wall, in this case, is expected to facilitate the induction of thermal changes. The HD Grid catheter is integrated into the cooling system, avoiding touching to prevent short circuits or other problems derived from unwanted contacts. Once integrated, the catheter is brought close to the heart wall, trying to ensure maximum contact with all the electrodes (see Fig 2), checking this aspect without activating the cooling system. Next, a predefined series is performed, where first a single Peltier is activated each time, performing a sweep with all of them, then a grouping of two is performed, sweep, then 3 in triangle format, and 4 in cross format.

III. RESULTS

After the characterization of the TEG in the laboratory, Fig 3 A shows the superposition of the recorded data and the simulation of the thermal behavior of the device. The real data fits very well with the model made in SIMULINK® and its maximum absolute error is 5 ºC in the transient state. The discrepancies between a thermal model and empirical measurements in a Langendorff-perfused heart can be attributed to a number of factors. One of the key reasons for such disparities is the nonlinearity of the heat capacity resulting from the perfusion solution and tissue freezing [8]. The thermal model, on the other hand, utilizes a linearized heat capacity, which could potentially lead to slight variations of up to one degree Celsius under steady-state conditions. Additionally, minor discrepancies in measurement accuracy may arise due to measurement errors or voltage drops in cables. Despite these discrepancies, a nearly negligible error in the final temperature has been detected, signifying that the thermal model is a valuable instrument for examining the thermal dynamics of Langendorff-perfused hearts.

The results obtained provide evidence that the thermoelectric cell modeling is fully valid for estimating its behavior according to established requirements. In addition, our findings demonstrate that the designed cooling system does not have an adverse effect on epicardial recordings (see 3 B), which indicates that the catheter is capable of detecting possible changes in the signal.

During the experiments, the effects estimated and validated by simulation were obtained but only transiently. This effect was repeated in different batches and under different conditions. When certain Peltiers cells were activated, the amplitude of the unipolar recordings near the activated cells

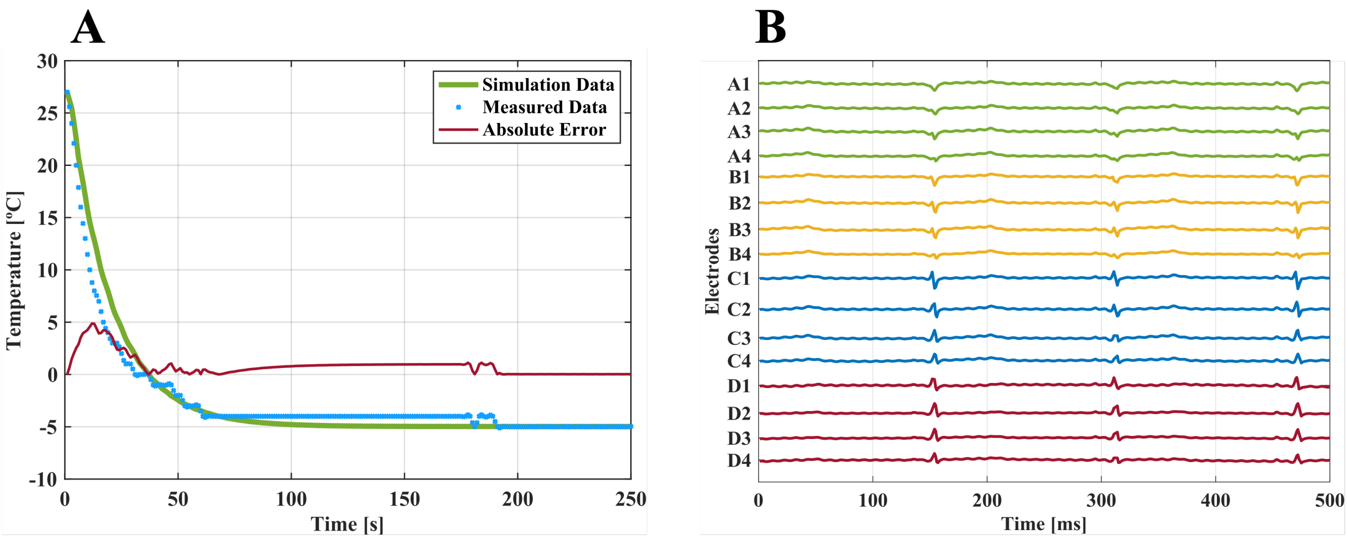

Fig. 3. A: Simulated Temperature vs Measured Temperature. B: Epicardical recordings.

TABLE I
COMPARATIVE RESULTS

Parameter	Simulated	Real	Error
Vin (V)	0.58	0.6	0.02
Temperature (ºC)	12.84	8	4.84

decreased significantly. They also slowed down, but only very briefly. After several tests, we corroborated that the cause of this effect was the Tyrode that oozed at 37 ºC, typical of the Langendorf System where the excess effluent accumulates in the right ventricle and is expelled through the pulmonary vein, oozing all over the epicardium. We were aware of this effect but its impact in previous experiments [3] and [7] had been minimal. In contrast to previous experiments that utilized a larger surface with screen-printed electrodes, our system uses tiny peltier cells arranged in an array with the HD Grid multi-electrode. However, the flow of Tyrode at 37°C sometimes accumulates between the slits, inhibiting the effect of the peltier. As future work, we aim to perform experiments with excess effluent recirculation and compensation mechanisms to mitigate these effects.

IV. CONCLUSION

A system based on a compatible peltier cell array configuration has been proposed with the objective of integrating it into an HD Grid catheter for experimentation in an isolated perfused heart. Simulation results using MATLAB/SIMULINK have corroborated the appropriate operating ranges based on the established requirements and a correct functioning of the control and triggering/activation system. Regarding the in situ operation in the animal experimentation laboratory, it was found that the integration between the selective cooling system and the HD Grid catheter has been feasible was correct, allowing quality recordings to be obtained at the same time as temperature changes were generated. However, due to the oozing of the effluent expelled through the pulmonary vein at 37 ºC, the expected effects could not be observed in a stationary manner.

ACKNOWLEDGMENT

We would like to thank the staff of the GRELCA group for their support in performing the experiments.

REFERENCES

[1] M. Takigawa, J. Relan, T. Kitamura, C. A. Martin, S. Kim, R. Martin, G. Cheniti, K. Vlachos, G. Massoullié, A. Frontera, N. Thompson, M. Wolf, F. Bourier, A. Lam, J. Duchateau, T. Pambrun, A. Denis, N. Derval, X. Pillois, J. Magat, J. Naulin, M. Merle, F. Collot, B. Quesson, H. Cochet, M. Hocini, M. Haïssaguerre, F. Sacher, and P. Jaïs, “Impact of spacing and orientation on the scar threshold with a high-density grid catheter,” Circulation: Arrhythmia and Electrophysiology, vol. 12, no. 9, 2019.

[2] F. Castells, S. Ruipérez-Campillo, I. Segarra, R. Cervigón, R. Casado-Arroyo, J. L. Merino, and J. Millet, “Performance assessment of electrode configurations for the estimation of omnipolar electrograms from high density arrays,” Computers in Biology and Medicine, vol. 154, p. 106604, 2023.

[3] A. Tormos, A. Guill, J. Millet, E. J. Roses, I. Trapero, L. Such-Miquel, and F. J. Chorro, “New epicardial mapping electrode with warming/cooling function for experimental electrophysiology studies,” Medical Engineering & Physics, vol. 33, no. 5, pp. 653–659, 2011.

[4] I. Segarra. ”Generación de heterogeneidades en la superficie epicárdica controlada mediante gradientes de temperatura, adaptado a un electrodo HD-GRID.” 2022.Antennas Propagat., to be publised.

[5] CUI DEVICES, “CUI DEVICES. CP07-M Series Datasheet - Single-Stage Peltier Modules.” CUI DEVICES, Tualatin, Oregon, 2020.

[6] J. A. Chavez, J. A. Ortega, J. Salazar, A. Turo, and M. J. Garcia, “Spice model of thermoelectric elements including thermal effects,” Proceedings of the 17th IEEE Instrumentation and Measurement Technology Conference [Cat. No. 00CH37066], 2000.

[7] A. Guill, Á. Tormos, J. Millet, E. J. Roses, A. Cebrián, L. Such-Miquel, L. Such, M. Zarzoso, A. Alberola, and F. J. Chorro, “QT interval heterogeneities induced through local epicardial warming/cooling. an experimental study,” Revista Española de Cardiología (English Edition), vol. 67, no. 12, pp. 993–998, 2014.

[8] G. Fischer, M. Handler, P. R. Johnston, and D. Baumgarten, “Impedance and conductivity of bovine myocardium during freezing and thawing at slow rates - implications for cardiac cryo–ablation,” Medical Engineering amp; Physics, vol. 74, pp. 89–98, 2019.