



27 **INTRODUCTION**

28 Substrate-based catheter ablation is an effective, invasive treatment for recurrent episodes of  
29 scar-related ventricular tachycardias (VT), but the rate of recurrences remains still high. (1)  
30 Analyzing all the intracardiac electrograms requires acquiring a full electroanatomical map  
31 (EAM) of the area of interest, a process which is challenging and time-consuming. This  
32 increases the likelihood of having procedure-related complications.

33 One of the main objectives of VT substrate ablation procedures is to localize and ablate the site  
34 of origin (SOO, exit site) of the clinical VT, whose localization can be inferred from the VT  
35 morphology in the 12-lead ECG. (2) There are several algorithms that help localizing the SOO  
36 from ECG tracings, but they are solely based on visual inspection on the ECG, use nonstandard  
37 definitions for heart regions/areas and/or have applicability restrictions that prevent their use in  
38 all myocardial substrates. (3)

39 On the other hand, VT substrate ablation requires eliminating not only the clinical VT-SOO,  
40 but the whole arrhythmia substrate to abolish additional VT circuits. (4–6) Recent studies have  
41 showed that guiding the ablation with color-coded pixel signal intensity (PSI) maps delivered  
42 from pre-procedural late gadolinium enhancement cardiac magnetic resonance (LGE-CMR)  
43 imaging, results in more efficient procedures and improved VT recurrence-free survival. (7–9)  
44 We hypothesize that the identification of scar-related VT-SOO can be fully automated by  
45 combining the surface ECG and the LGE-CMR imaging data into a machine learning (ML)  
46 algorithm integrated into a commercially available post-processing software. This is a proof-  
47 of-concept study to evaluate the feasibility of the ML algorithm and usefulness of the new  
48 software.

49 **METHODS**

50 **Study populations**

51 *Training population*

52 To train the ML model, all patients with documented VTs in a 12-lead surface ECG who were  
53 referred for ablation from January 2015 until December 2019 were included in the study,  
54 irrespectively of the presence of structural heart disease (SHD). Patients with ventricular  
55 arrhythmias arising from the right ventricle were excluded.

56 *Validation population*

57 To test the ML model's accuracy, consecutive patients with scar-related (reentry mechanism)  
58 sustained VTs referred for ablation (i.e. invasive treatment of the arrhythmia) from December  
59 2019 until July 2020 were included.

60 The study complied with the Declaration of Helsinki, and the local ethics committee approved  
61 the study protocol.

62

63 **Study workflow and objectives**

64 The first step of the study was to develop and evaluate a complete pipeline that uses the surface  
65 ECG for predicting the SOO/SgO (site/segment of origin) of scar-related VTs (figure 1). A total  
66 of four ML models were used to predict/classify the location of the VT-SgO from the VT-ECG  
67 tracings, using the *American Heart Association* (AHA) 17-segment model.

68 The second step was to integrate this pipeline into current commercial software (ADAS 3D LV,  
69 ADAS3D Medical SL, Barcelona, Spain). This commercial software, with CE- and FDA-  
70 approval, identifies, from pre-procedural LGE-CMR imaging data, the border zone corridors  
71 (BZC) embedded within the myocardial scar structure. It also allows to export the PSI maps to  
72 the EAM navigation systems to guide ablation procedures.

73 The new version of the software is intended to predict the VT-SgO using multimodal, non-

74 invasive information: from pre-procedural 12-lead ECG and LGE-CMR. The primary objective  
75 of the study is to test the complete integration of the new software into the clinical practice,  
76 evaluating its accuracy in a prospective series of patients referred for VT substrate ablation.

77

#### 78 **Reference algorithm for VT-SOO/SgO detection**

79 A previously described visual ECG algorithm (3) was used as a reference to compare the  
80 sensitivity and specificity of the algorithm trained by ML with real anatomical reference. This  
81 visual algorithm can be used to predict the SgO of LV scar-related VT regardless of the  
82 underlying heart disease and the epicardial versus endocardial VT origin. Briefly, the method  
83 is based on QRS axis in the frontal plane and transition in V3/V4 precordial leads (figure 2);  
84 the SgO is referred using the AHA 17-segment model. (10)

85

#### 86 **Development of machine learning models for VT-SOO/SgO detection**

87 The development of the model consists in an annotation phase and a training phase. The  
88 annotation phase consists in retrieving the data to be processed. The model training, on its  
89 behalf, consists of the following steps (figure 1): data selection and preprocessing, data  
90 augmentation, feature extraction, feature selection and model training.

##### 91 *Annotation phase*

92 The data annotation phase was performed by extracting the VT-ECG morphologies and their  
93 respective associated SgO for the study population. For this purpose, both clinical VTs and  
94 paced QRS morphologies from the LV were included in the database. Clinical VTs were  
95 included whenever their SOO/SgO could be reliably identified from the EAM data during  
96 ablation procedures. For paced morphologies, the location of the catheter when stimulating was  
97 considered the SOO/SgO. The above identified locations in the EAM were subsequently  
98 projected into the PSI maps and were, in turn, used as classification targets for the identification

99 of the VT-SgO, by assigning the closest element in the AHA 17-segment model. In cases when  
100 the SOO occurred at the intersection of several segments, the most probable one was marked  
101 as valid and the remaining plausible segments were stored for further data augmentation. A  
102 secondary set of annotations, for completeness, was registered taking into account signal-based  
103 criteria for the identification of the SgO according to a clinical algorithm. (3) Once the SgO  
104 associated to the morphology was annotated, the QRS complex was manually delineated by a  
105 cardiac electrophysiologist, marking its onset and offset.

### 106 *Training phase*

- 107 • Data selection: The first step of the training phase is data selection, which consists in  
108 the division of the dataset into non-overlapping train and test sets, containing 50% of  
109 the data each, in a stratified manner. The training set was used for model development  
110 and tuning, whereas the test set was reserved for assessing the model's performance.  
111 Data preprocessing, whose focus is finding better data representations for increasing  
112 model robustness, was performed in two steps. Firstly, the QRS was manually  
113 delineated. Secondly, the selected QRS was cropped, zero-corrected, and scaled to the  
114 magnitude of the highest voltage lead within the beat. Data augmentation, on its behalf,  
115 consisted in the application of mix-up, an all-purpose data augmentation technique that  
116 creates synthetic datapoints from the existing database, allowing for a better  
117 identification of the inter- and intra-segment separation criteria.
- 118 • Feature extraction: The second step of the training phase was feature extraction, which  
119 was performed by retrieving a set of signal-based, wavelet-based and spectral-based  
120 features specifically tailored towards ECG processing. These features allow the  
121 description of the data to be analyzed in a more robust manner, by structuring the  
122 difficult-to-process raw ECG recording into a finite set values that have semantical  
123 meaning. These features comprise the computation of intra-lead (e.g. min/max

124 voltages/areas or aggregate of magnitudes of different frequential bands), inter-lead  
125 (e.g. does lead I have a higher magnitude than lead III?) and global (e.g. precordial  
126 transition location according to different means of computation) characteristics. A total  
127 of 357 markers of the QRS complex were extracted for characterizing its behavior.

128 • Model training: The extracted features were then employed for training a classification  
129 model, support vector machines (SVM). A forward feature selection step was also used  
130 to filter out features that were highly correlated or that did not enhance the model's  
131 accuracy. (11) The model was trained using 5-fold cross-validation for finding the most  
132 appropriate model configuration.

133 The model's performance was assessed by comparing the predicted and the true SgO on the  
134 held-out test set, and compared to its clinical counterpart. Given the probabilistic formulation  
135 of the model, a secondary measurement of performance was provided, consisting in the  
136 accumulated accuracy to the second and third most probable SgO within the prediction.

137

### 138 **Anatomic reconstruction of the heart and scar characterization using LGE-CMR**

139 The validation population consisted of 15 consecutive patients with scar-related (reentry  
140 mechanism) sustained VTs referred for ablation (i.e. invasive treatment of the arrhythmia). All  
141 of them underwent a LGE-CMR test prior the procedure using a 1.5-Tesla scanner (ACHIEVA,  
142 Philips Healthcare, Best, The Netherlands). Contrast-enhanced images were acquired 10  
143 minutes after bolus injection of 0.2 mmol/Kg Gadobutrol (Gadovist®, Bayer Hispania,  
144 Barcelona, Spain) using a commercially available, free-breathing, ECG-gated, navigator-gated,  
145 3D inversion-recovery, gradient-echo technique. Slice thickness was 1.4 mm, with no gap  
146 between slices. The field of view was set at 360 mm and matrix size was kept to 256 x 256  
147 pixels to yield an isotropic spatial resolution of 1.4 x 1.4 x 1.4 mm. In patients previously

148 implanted with an ICD, LGE-CMR was performed using a specific wideband sequence to avoid  
149 device artefacts.

150 All LGE-CMR images were analyzed using a previously described protocol. (12) A full left  
151 ventricular (LV) volume was reconstructed in the axial orientation, and the resulting images  
152 were processed with ADAS 3D LV software (ADAS3D Medical SL, Barcelona, Spain). Color-  
153 coded pixel signal intensity (PSI) maps based on LGE-CMR images were projected to 10  
154 myocardial shells (from endo- to epicardium), following a trilinear interpolation algorithm. The  
155 hyperenhanced area was characterized as core zone, border zone (BZ) or healthy tissue using  
156  $40 \pm 5\%$  and  $60 \pm 5\%$  of the maximum PSI as thresholds. (12) The total scar mass, BZ mass,  
157 and core mass in each shell were automatically measured using the ADAS 3D LV software.

158 Scar heterogeneity was defined as BZ percentage of the scar. BZ channels (BZCs) were defined  
159 as continuous corridors of BZ surrounded by scar core or an anatomical barrier (i.e. mitral  
160 annulus) connecting two areas of healthy tissue. The BZC mass was automatically computed  
161 using a full-automated tool embedded within the ADAS 3D LV software.

162

### 163 **Pipeline integration into ADAS 3D LV software**

164 The SVM classifier incorporated into the ADAS 3D LV software to enable identifying the  
165 location of the SgO from the VT-ECG tracings, using the American Heart Association (AHA)  
166 17-segment model. The new analysis allowed to import and visualize the ECG-signals from  
167 several polygraphs and includes a new user interface to select the QRS of the VT. Once the  
168 QRS is selected, the software executes the SVM for that particular QRS to obtain the SgO.  
169 Then, the probability of each AHA segment of being the VT-SgO was visualized in a table  
170 (figure 3). The software also includes a new visualization method to display the calculated SgO  
171 overlaid onto the LV visualization of the patient. This visualization allows the user to see  
172 together the post-infarction scar structure derived from the LGE-CMR and the VT-SgO

173 overlaid onto the LV. This further allows the user to even identify the heterogeneous tissue  
174 corridor that could be likely responsible for the reentry circuit causing the VT (figure 4).  
175 Finally, the user can export the results to the EAM navigation system in order to guide ablation  
176 procedures.

177

### 178 **Prospective validation during VT ablation procedures**

179 Unselected patients with documented scar-related VT, who were referred for VT substrate  
180 ablation, were consecutively enrolled to test the new ML-trained model of VT-SgO detection.  
181 The ablation procedures were performed according to a previously described protocol. (8)  
182 Briefly, the first step of the procedures was the acquisition of a fast anatomical map of the aorta,  
183 which was then used to integrate the anatomical heart reconstructions derived from a  
184 multidetector cardiac tomography and the LGE-CMR within the spatial reference coordinates  
185 of the CARTO3 (Biosense Webster, Diamond Bar, CA, USA) electroanatomic navigation  
186 system. The actual SgO of each VT was identified according to either one of the following  
187 criteria: i) Presence of presystolic local electrograms not earlier than 50 ms before the beginning  
188 of the QRS and termination of the VT during RF ablation or slow conducting channel exit site  
189 confirmed through entrainment maneuvers together with VT termination during RF ablation;  
190 or ii) achieving a 12/12 QRS morphology concordance with the 12-lead ECG of the VT during  
191 pacing from a site with no more than 50 ms delay between the stimulus artifact and the  
192 beginning of the QRS. The selection of the pacing sites was primarily based on the presence of  
193 BZC entrances identified by the pre-procedural CMR. Based in previous clinical experience,  
194 there is usually about one BZC entrance per AHA segment; that is, the identification of a VT-  
195 SgO usually identifies the BZC likely responsible of being the ‘critical isthmus’ of the VT  
196 reentry circuit (figure 5).



197 In order to test the accuracy of the new software for VT-SgO identification, once the actual  
198 SgO was recognized, it was compared with the SgO proposed by the software and the SgO  
199 predicted by the reference visual algorithm. The actual VT-SgO was identified according to  
200 data derived from the ablation procedures, anatomically referenced using either one of the  
201 following imaging datasets integrated during the interventions: electroanatomical maps, cardiac  
202 tomography, or LGE-CMR. Finally, a descriptive analysis of the presence of CMR-derived  
203 BZC at the predicted VT-SgO was performed, to estimate the potential ability of the software  
204 to predict the effective ablation target site. (8,13)

205

### 206 **Statistical analysis**

207 Continuous variables are given as mean  $\pm$  standard deviation or median (interquartile range),  
208 as appropriate. Confidence intervals (CI,  $\alpha = 0.05$ ) are provided for the model's performance  
209 metrics. Categorical variables are given as total number and percentages. To compare the means  
210 of 2 variables, the Student t-test or Wilcoxon test were used, as appropriate. Proportions were  
211 compared using the  $\chi^2$  or Fisher exact test, as appropriate.  $P < 0.05$  was considered of statistical  
212 significance. Statistical analysis was performed using IBM SPSS Statistics, version 26.0 (IBM  
213 Corp. Released 2019; Armonk, NY: IBM Corp.).

## 214 **RESULTS**

### 215 **Study populations**

216 For the training phase of the ML algorithm, a total of 209 VT morphologies corresponding to  
217 104 patients, recruited from 2015 until December 2019, were used. For the pilot validation of  
218 the ML model, 15 additional patients ('validation population') were prospectively recruited  
219 from January until July 2020. The baseline characteristics of these populations are shown in  
220 **table 1**. In the validation population, 15 clinical VT morphologies were analyzed with the ML  
221 model embedded in the ADAS software platform. Additionally, 62 non-clinical VT  
222 morphologies were induced by pacing the LV at different sites during the ablation procedures,  
223 locating the tip of the catheter at different BZC entrances previously identified with the LGE-  
224 CMR. Therefore, a total of 77 potential VT morphologies were used for final testing.

225

### 226 **ML model performance**

227 In the training phase (209 VT morphologies), the ML model provided a one-segment accuracy  
228 of 77%, (CI<sub>95%</sub> 71 – 83%) with respect to the real signal-based SgO, whereas if the second most  
229 probable SgO was considered its accuracy raised to 92% (CI<sub>95%</sub> 88 – 95%), and to 94% (CI<sub>95%</sub>  
230 90 – 97%) if the third most probable SgO was given as valid. The reference visual algorithm  
231 reached a score of 81%, (CI<sub>95%</sub> 72 – 89%) on the same dataset. The reference algorithm  
232 performed similarly when compared to the one-segment prediction of the ML model ( $p = 0.32$ ),  
233 but worse if taking as valid the best two or three SgO proposed by the model ( $p = 0.001$  and  $p$   
234  $= 0.0001$ , respectively).

235 For the validation population (77 VT morphologies), the ML provided a one-segment accuracy  
236 of 88% (CI<sub>95%</sub> 79 – 95%), 99% (CI<sub>95%</sub> 93 – 100%) when considering the second most probable  
237 VT-SgO, and 100% (CI<sub>95%</sub> 95 – 100%) when considering the third most probable VT-SgO. The  
238 reference visual algorithm reached a score of 91%, (CI<sub>95%</sub> 82 – 96%) on the same dataset. The

239 reference algorithm performed similarly when compared to the one-segment prediction of the  
240 ML model ( $p = 0.55$ ), but worse if taking as valid the best two or three SgO proposed by the  
241 model ( $p = 0.005$  and  $p = 0.002$ , respectively). Figure 6 shows an example of correlation  
242 between the VT-SgO predicted by the reference visual algorithm (operator-dependent) and the  
243 ML model, integrated with the LGE-CMR information and ready to be used with the ADAS  
244 3D LV customized software.

245

### 246 **Correlation between scar characteristics and predicted VT-SgO**

247 Main ablation results of the validation population are shown in table 2. All the patients had an  
248 inducible clinical VT; additionally, a mean of  $4.1 \pm 0.4$  potential VT morphologies per patient  
249 were simulated by pacing the LV at different CMR-derived BZC entrances (figure 5). The  
250 identified myocardial scars ( $n = 15$ ) occupied an area encompassing a median of 5 (4 – 6) AHA  
251 segments, thus representing a total of 74/255 (29%) scarred AHA segments. A total of 68 BZC  
252 entrances were identified, thus representing a median of 0.83 (0.8 – 1) BZC entrances per  
253 scarred segment. There were only 2/74 (3%) AHA segments showing more than one BZC  
254 entrance; one of them corresponded to a clinical VT-SgO, the other one to a paced VT  
255 morphology.

256 **DISCUSSION**

257 The main findings of the study are:

- 258 • This is the first clinical study to show the feasibility of training and integrating a ML  
259 model of non-invasive surface ECG data into the pipeline of a commercially available  
260 software (ADAS 3D LV) that allows to correlate ECG and anatomy by characterizing  
261 the myocardial scar from LGE-CMR studies. The clinical relevance comes from the fact  
262 that this pipeline may allow to standardize the invasive treatment (ablation) in patients  
263 that have suffered from life-threatening VTs.
- 264 • This study proves additional advantages of the use of ML when interpreting ECG  
265 tracings. When compared to a reference visual model, based on operator's expertise, (3)  
266 it shows a similar accuracy in terms of best predicted SgO, but it can further identify  
267 more SgO by suggesting up to 3 adjacent –and potential– SgO.
- 268 • There was a median of 0.83 (0.8 – 1) CMR-derived BZC entrances per scarred segment.  
269 These are considered ablation targets for invasive treatment of scar-related reentrant  
270 VTs. (8,13) Thus, the automatic identification of the VT-SgO using the proposed usable  
271 software-based pipeline almost equals the identification of the putative BZC being the  
272 critical isthmus of the reentry VT circuit.

273 With regards to the first and second points, the developed ML model has many advantages for  
274 the prediction of the VT-SgO location. On the first hand, it is flexible, facilitating the  
275 identification of non-linear relationships between the input data. Secondly, a probabilistic  
276 formulation is available, allowing for stratifying the prediction by returning a hierarchy of  
277 probabilities of adherence to a specific AHA segment instead of a single value. Reentrant VTs  
278 exit sites, which correspond to BZC entrances identifiable after post-processing a LGE-CMR,  
279 are not always found 'at the center' of a given AHA segment. On the contrary, BZC entrances  
280 can be found at any point of the LV anatomy, and, therefore, it is not uncommon to find them

281 close to the hypothetical boundary between 2 segments, or even more than 2. These localization  
282 differences represent mm or few cm of distance, but they can determine subtle changes in the  
283 morphological characteristics of the ECG. These distinctions may be incorporated when  
284 training a ML model, but they seem difficult to be merged into visual algorithms reliant on  
285 operator's knowledge.

286 The identification of the VT-SgO seems useful, since at this anatomical level it is possible to  
287 find at least one BZC entrance. BZC are, as already defined, corridors of heterogeneous (viable)  
288 myocardial tissue surrounded by dense scar and connecting two areas of healthy myocardium.  
289 It is an anatomical concept, based on what can be revealed when performing an LGE-CMR.  
290 This imaging technique is recognized as the gold standard to determine the location and extent  
291 of myocardial scar. (14) There is proven correlation between the anatomical findings of the  
292 CMR and functional electrophysiology: the CMR-defined scar has a good correlation with low-  
293 voltage areas in the electroanatomical maps (EAM), (15,16) and the presence of BZC is related  
294 to the presence of slow conducting channels within the scar. (15,17) Moreover, the size and  
295 heterogeneity of the post-MI scar, as evaluated with CMR, are variables that have been  
296 associated with VT inducibility, (18,19) arrhythmia events, and even mortality. (20–22)

297 Ventricular tachycardia (VT) substrate ablation is an effective treatment for patients that suffer  
298 from recurrent episodes of scar-dependent VTs. (23,24) However, different substrate-guided  
299 approaches have been proposed; targeting conducting channels based on timing of delayed  
300 electrogram components during sinus rhythm (scar dechanneling) has proven to be an effective  
301 approach. (6,13) Recently, CMR-guided VT ablation based on scar dechanneling has proven to  
302 halve the time required for the procedure, significantly reducing the need of fluoroscopy and  
303 radiofrequency delivery, and being associated with a a higher ventricular arrhythmia-free  
304 survival. (8)

305 All the aforementioned, the ability to automatically localize the BZC (and its entrance) from  
306 ECG and CMR data would permit to standardize ablation procedures, to shorten the time from  
307 the insertion of the catheter until abolition of the documented VT and, likely, to improve safety  
308 and reliability of these procedures.

309

### 310 **Study limitations**

311 An important limitation is the necessity of the actual pipeline to rely on manual identification  
312 of the QRS segment. The existing tools for delineation are often faced with poor performance  
313 on complex rhythms such as VT. The development of all-purpose, robust tools for wave  
314 delineation can fully automatize the developed pipeline. Finally, classical ML approaches are  
315 overtly reliant on the extraction of quality features for describing the data to be analyzed. More  
316 detailed spectral-, signal- or wavelet-based features could be applied for more adequate data  
317 representation.

318

### 319 **Future directions**

- 320 • The ability to import ECG tracings not only from specific electrophysiology recording  
321 systems in the cath lab, but also from ambulatory digital ECG recorders, or even paper  
322 (analogical) tracings would be a milestone on the path towards clinical applicability.  
323 Patients suffering from life-threatening VTs would have an ECG from the emergency  
324 department; this ECG could be automatically imported into ADAS 3D LV, and  
325 analyzed together with the LGE-CMR to plan the invasive treatment and select the best  
326 ablation target, all in a full automated way.
- 327 • Other ML approaches, such as directly using raw ECG data with deep learning  
328 algorithms, could also be explored. Deep learning typically yields an increased

329 performance, although these models require larger amounts of annotated data, besides  
330 producing black-box models that are difficult to interpret. (25)

331 • Some methodologies based on deep learning have shown promising results for  
332 automatic ECG delineation. Although the database employed for developing models for  
333 automatic ECG delineation do not perform adequately on complex morphologies such  
334 as sustained ventricular tachycardias, recent developments in the machine learning field  
335 could allow extending currently developed models to adapt to VT morphologies,  
336 enabling fully automated SgO identification.

337

### 338 **Conclusions**

339 The identification of scar-related VT-SgO and the putative BZC responsible for the reentry VT  
340 circuit can be fully automated by combining the surface ECG and the LGE-CMR imaging data  
341 into a machine learning (ML) algorithm integrated into a commercially available post-  
342 processing software. This could allow for standardization of ablation (i.e. treatment)  
343 interventions for these life-threatening arrhythmias.

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346

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430

431 **TABLES**

432 **Table 1.** Baseline characteristics of the ML training and validation populations. See text  
 433 for details.

	<b>Training population n = 104</b>	<b>Validation population n = 15</b>	<b>p</b>
<b>Age, y</b>	68 ± 9	65 ± 12	0.25
<b>Male, n (%)</b>	85 (82)	13 (89)	0.50
<b>HT, n (%)</b>	74 (71)	11 (75)	0.75
<b>DLP, n (%)</b>	52 (50)	9 (63)	0.35
<b>DM, n (%)</b>	28 (27)	4 (27)	1.0
<b>LVEF, %</b>	37 ± 15	39 ± 18	0.64
<b>LVEDD, mm</b>	63 ± 8	61 ± 12	0.40
<b>LVESD, mm</b>	45 ± 13	43 ± 11	0.57
<b>ICM, n (%)</b>	85 (82)	13 (89)	0.50
<b>Mean VT cycle length</b>	323 ± 135	341 ± 143	0.63
<b>ICD carriers before ablation [n (%)]</b>	94 (90)	13 (89)	0.90
<b>NYHA</b>			
• <b>I, n (%)</b>	29 (28)	5 (34)	0.77
• <b>II, n (%)</b>	60 (58)	8 (54)	
• <b>III, n (%)</b>	15 (14)	2 (14)	
• <b>IV, n (%)</b>	0	0	
<b>Approach</b>			
• <b>Endo, n (%)</b>	76 (73)	11 (75)	0.87
• <b>Endo/Epi, n (%)</b>	28 (27)	4 (25)	
<b>Indication</b>			
• <b>Incessant VT, n (%)</b>	7 (7)	2 (13)	0.42
• <b>Arrhythmic storm, n (%)</b>	10 (10)	1 (7)	

434 *CMR: cardiac magnetic resonance; DLP: dyslipidemia; DM: diabetes mellitus; HT:*  
 435 *hypertension; ICM: ischemic cardiomyopathy; LVEF: left ventricle ejection fraction;*  
 436 *LVEDD: left ventricle end-diastolic diameter; LVESD: left ventricle end-systolic*  
 437 *diameter; NYHA: New York Heart Association functional class; VT: ventricular*  
 438 *tachycardia.*  
 439

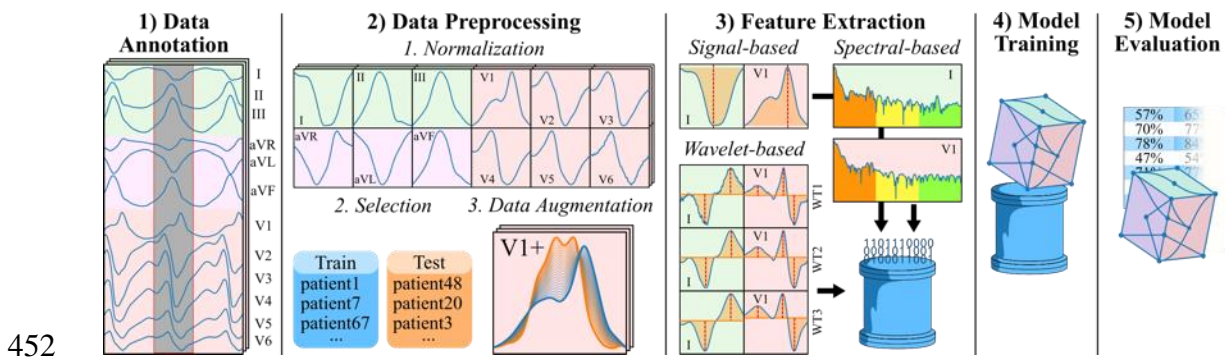
440 **Table 2.** Ablation results in the validation population (n = 15).

<b>Procedure time (min)</b>	103 ± 64
<b>RF time (min)</b>	12 ± 10
<b>RF applications (n)</b>	32 ± 23
<b>Fluoroscopy time (min)</b>	9 ± 5
<b>Residual VT after substrate ablation, n (%)</b>	5 (18)
<b>Induced VT morphologies</b>	1 (1 – 1)
<b>Complications (%)</b>	0
<b>Final procedure success (n, %)</b>	
• <b>Total</b>	13 (87)
• <b>Partial</b>	2 (13)
• <b>No</b>	0 (0)

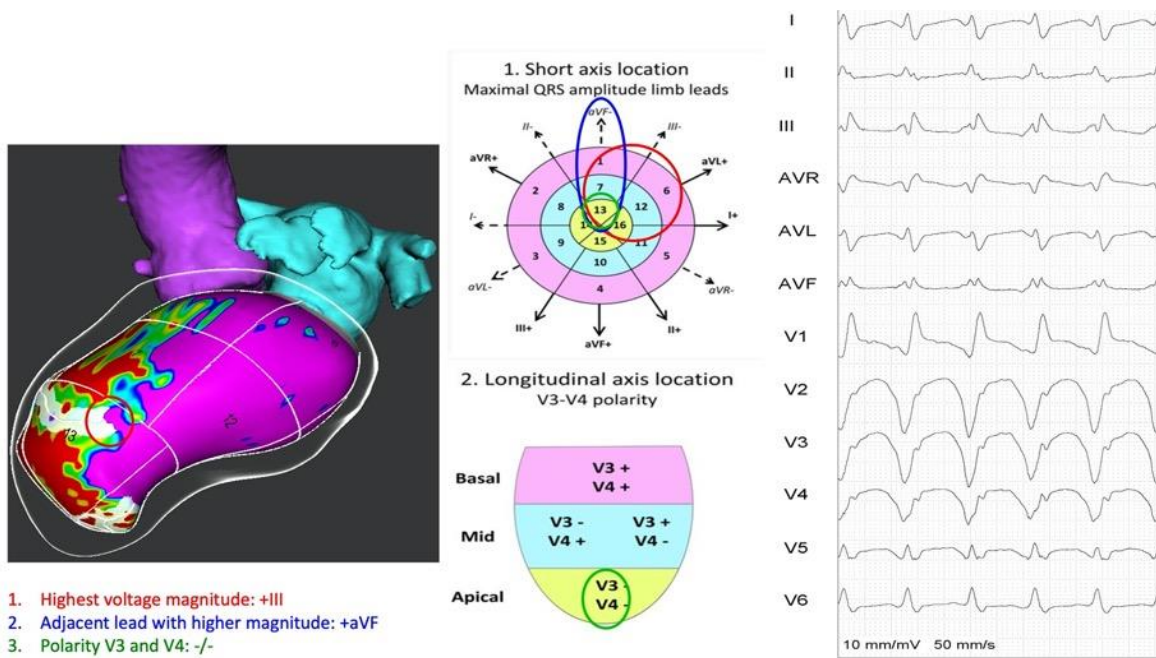
441 **RF:** radiofrequency; **VT:** ventricular tachycardia.

442 **FIGURES**

443 **Figure 1.** Employed machine learning (ML) pipeline. The first step consists in data  
 444 annotation, where the onset and offset were annotated for the ECGs in the study  
 445 population. The second step consists in data preprocessing, where the QRS' are isolated,  
 446 normalized, divided into training/testing sets for ML model tuning, and augmented. The  
 447 third step consists in the extraction of features for robust description of the input data;  
 448 signal-based, wavelet-based and spectral-based features were extracted for all recordings  
 449 in the train and test sets. The fourth step consists in model training from the extracted  
 450 features in the training set. Finally, the fifth step evaluates the performance of the model  
 451 in the features of the held-out test set.



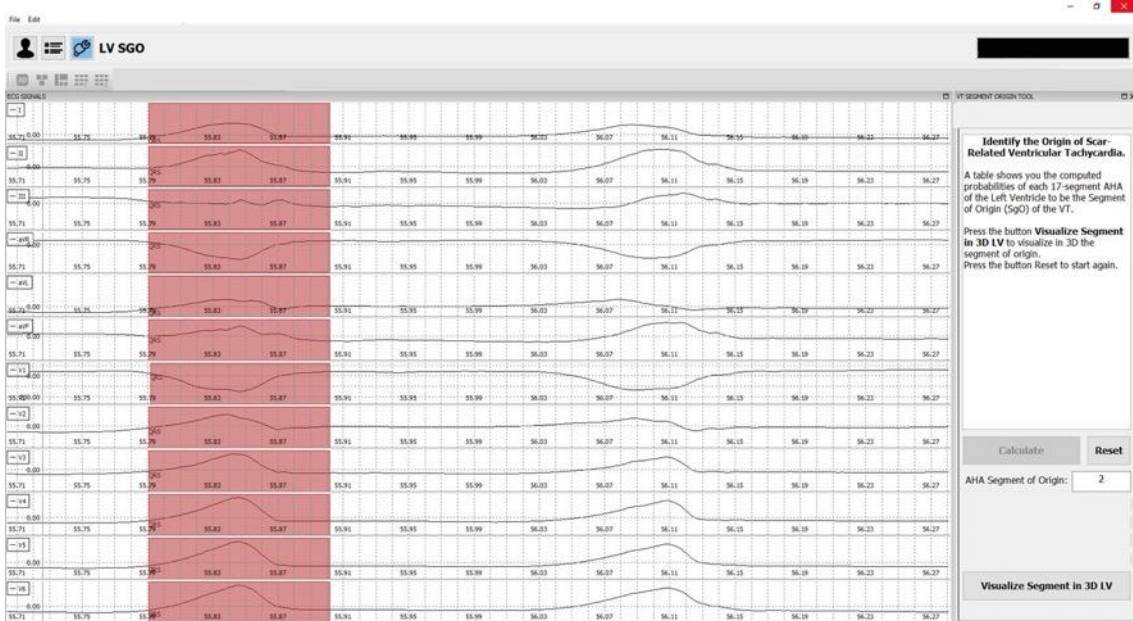
453 **Figure 2.** Example of application of the visual reference algorithm for identification of  
 454 VT-SgO. Patient with ischemic cardiomyopathy and anteroapical transmural scar. The  
 455 scar, visualized after CMR postprocessing using ADAS 3D LV (left panel), is  
 456 characterized as core (dense fibrosis) in *red*, border zone (intermediate fibrosis,  
 457 heterogeneous tissue) in *green*, and healthy myocardium in *pink*. The *red circle* marks  
 458 the site of the clinical VT exit, which corresponds to a BZC entrance (*white line*). The  
 459 12-lead ECG of the VT is shown in the right panel. Regarding the VT morphology, the  
 460 following considerations were made: Maximum absolute amplitude in ECG limbs: (+)  
 461 III. Adjacent leads to (+) III: (+) aVF. Segment group considered: 1 / 7 / 13. Polarity in  
 462 precordial leads: (-) V3 / (-) V4. Final Segment = 13 (apical anterior).



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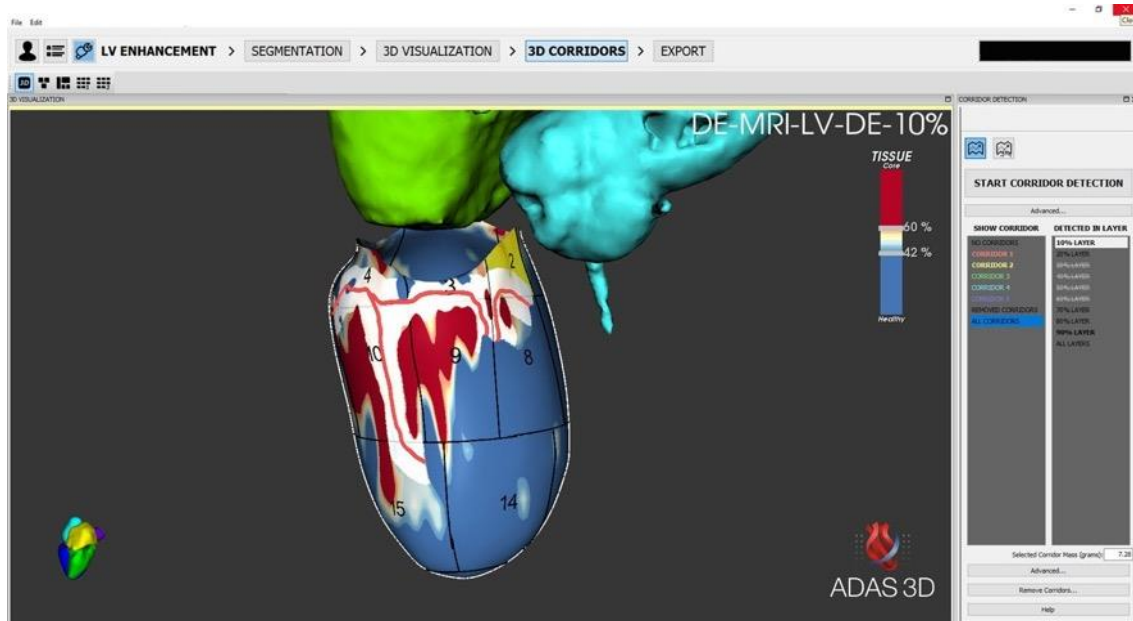


464 **Figure 3.** Example of the ADAS 3D LV interface showing a VT-ECG in a patient with  
 465 an anteroseptal myocardial infarction. The manually selected start and end times of the  
 466 QRS morphology are highlighted in the red box. After selecting the QRS, the SVM  
 467 classifier is executed to calculate the VT-SgO. This calculates the probability of each  
 468 AHA segment of being the VT-SgO. The software then displays the most probable  
 469 segment (in this case, segment 2, or basal anteroseptal) and then the user can press the  
 470 button ‘Visualize Segment in 3D LV’ which launches the screen of figure 4.



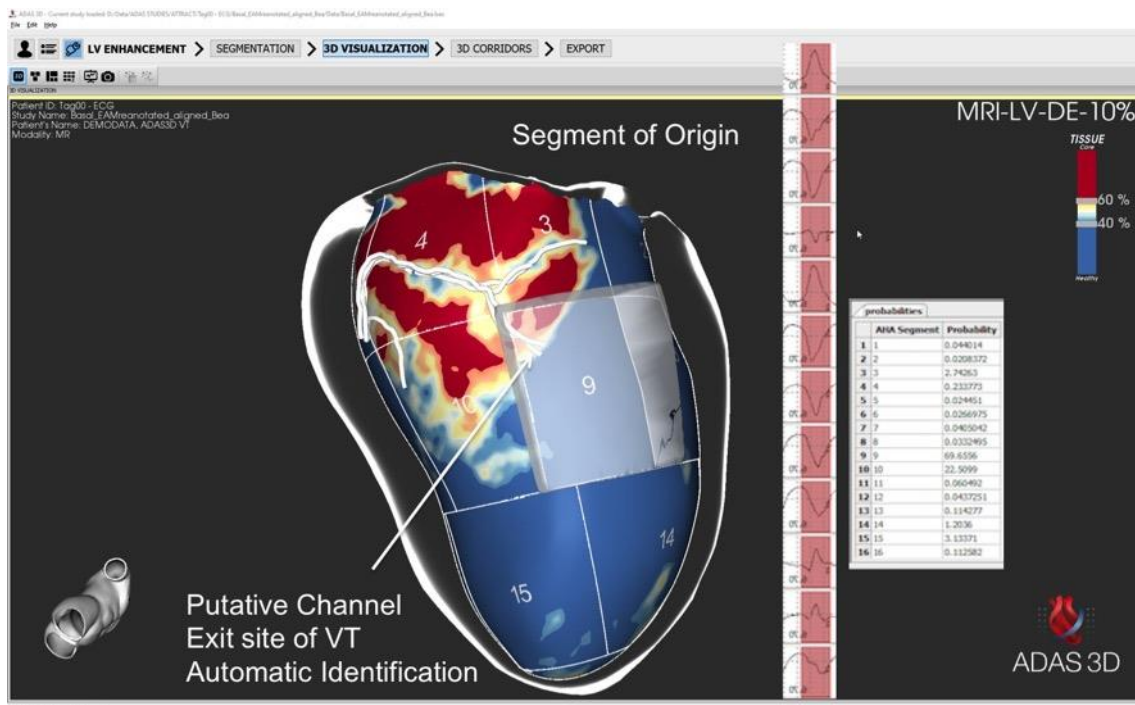
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472 **Figure 4.** Predicted VT-SgO (AHA segment 2, or basal anteroseptal) in a patient with an  
473 anteroseptal myocardial infarction. The scar, visualized after CMR postprocessing using  
474 ADAS 3D LV, is characterized as core (dense fibrosis) in *red*, border zone (intermediate  
475 fibrosis, heterogeneous tissue) in *yellow*, and healthy myocardium in *blue*. The red lines  
476 surrounded by *white* represent the heterogeneous tissue corridors (border zone channels)  
477 embedded within the scar and calculated automatically. The AHA segment 2 is  
478 highlighted in yellow and indicates the exit of the putative responsible channel for the  
479 reentry circuit causing the VT. Ablation treatment could be then first directed to this area.



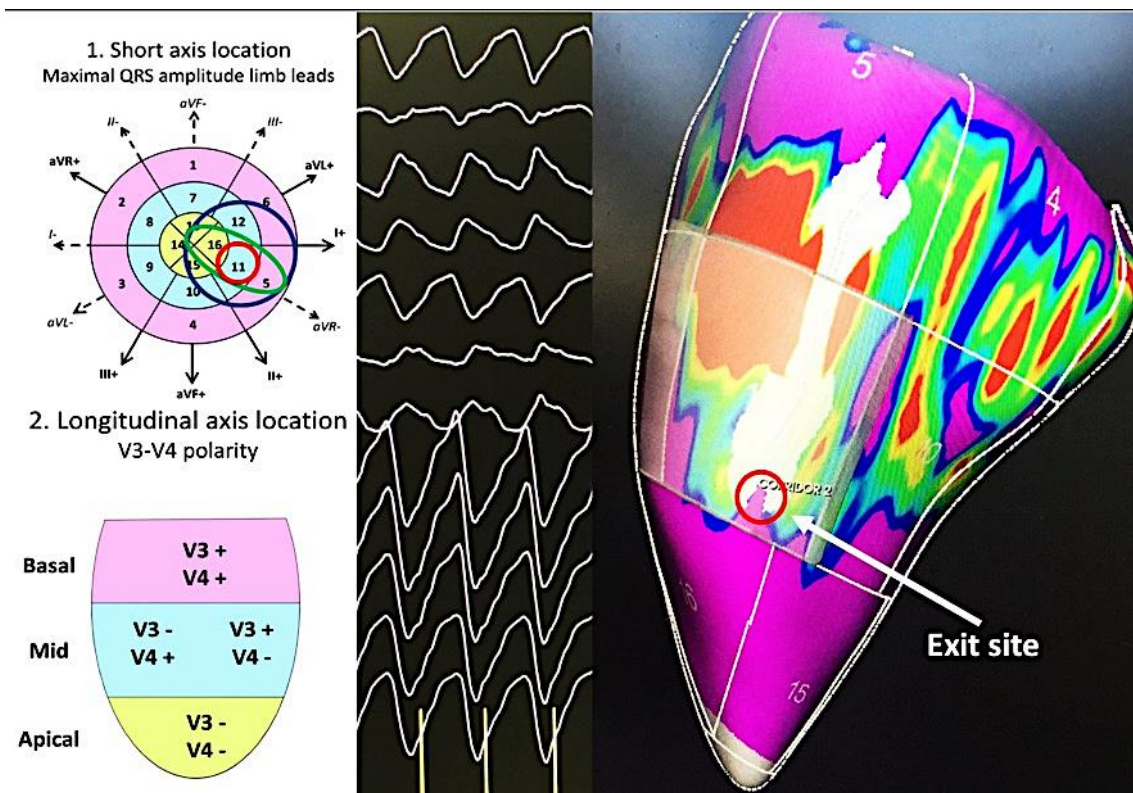
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483 **Figure 5.** Predicted VT-SgO (AHA segment 9, or mid inferoseptal) in a patient with an  
 484 inferior-inferoseptal myocardial infarction. The VT morphology was analyzed with the  
 485 ADAS 3D LV software, which detected segment 9 as the most probable VT-SgO  
 486 (segment 10 the second most probable). Using the same software, post-processing of the  
 487 LGE-CMR to characterize the myocardial scar permitted to detect a BZC entrance just  
 488 located in segment 9 (adjacent to segment 10). This BZC was considered responsible for  
 489 the VT reentry circuit; its entrance acting as the ‘exit site’ during VT. Radiofrequency  
 490 ablation of this BZC entrance rendered the VT non-inducible anymore.



491  
 492  
 493

494 **Figure 6.** Prediction of the VT-SgO using the reference algorithm (visual) versus a  
 495 complete automatic pipeline (ADAS 3D LV software with an integrated ML model to  
 496 predict the VT-SgO plus scar characterization from LGE-CMR data). Patient with an  
 497 inferolateral myocardial infarction referred for VT ablation. The VT morphology is  
 498 shown (*black panel*). The reference algorithm (*left panel*) allows to predict segment 11  
 499 as the VT-SgO, but it requires a high level of knowledge in recognizing ECG tracings.  
 500 The proposed pipeline using the new embedded tools in ADAS 3D LV software allows  
 501 to predict the same SgO in an automatic way, besides recognizing the BZC responsible  
 502 for the VT circuit and its entrance at the target SgO.



503