

# Implant and Long-Term Evaluation of Atrial Signal Amplification in a Single-Lead ICD

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**Background:** In patients without clinical indications for pacing the use of a single-lead implantable cardioverter defibrillator (ICD) implementing atrial sensing capability with proper signal amplification management may represent a useful therapeutic option, combining the positive features of both single and dual-chamber devices. The aim of the study was to evaluate the atrial signal amplification and its long-term stability in a single-lead ICD system adding atrial sensing to a standard single-chamber ICD.

**Methods:** P-wave amplitudes were collected and compared at implant both with a conventional external device ("unfiltered" P wave) and telemetrically with the implanted ICD ("filtered" P wave). Filtered/unfiltered P-wave ratio (amplification factor, AmF) was evaluated at implant and during follow-up.

**Results:** In 43 enrolled patients (38 men, age  $64 \pm 16$  years), the mean filtered P wave at implant was significantly higher than the unfiltered P wave ( $3.85 \pm 0.81$  mV vs  $2.0 \pm 1.49$  mV;  $P < 10^{-11}$ ), with a mean AmF value of  $2.77 \pm 1.62$ . In seven patients with atrial fibrillation at implant, the AmF was higher ( $4.62 \pm 1.94$ ) than in patients in sinus rhythm ( $2.41 \pm 1.30$ ;  $P < 0.001$ ). A significant linear correlation was found between the inverse of P wave and the AmF ( $R = 0.82$ ,  $P < 0.00001$ ). In 25 patients followed for  $384 \pm 244$  days, atrial undersensing was never documented and AmF did not change from implant ( $3.19 \pm 1.82$ ;  $P = 0.24$ ), also in different body position and breathing conditions.

**Conclusions:** The single-lead ICD system evaluated reliably amplified P-wave amplitudes by a factor of about three, maintaining this performance during the observed follow-up. (PACE 2012; 35:1119–1125)

**implantable cardioverter defibrillator, atrial signal, supraventricular tachyarrhythmia discrimination**

## Introduction

Implantable cardioverter defibrillators (ICDs) have definitely proven<sup>1–7</sup> their efficacy in primary and secondary prevention of sudden cardiac death, but device selection (single- or dual-chamber ICD), in patients without indication for pacing, is still a matter of discussion.

Currently, approximately 40–50% of the implanted ICDs<sup>8,9</sup> are single-chamber devices. Several considerations may suggest physicians to prefer a single-chamber ICD: a lower device cost, a reduced number of expected lead- or device-related complications,<sup>10–12</sup> and the not-relevant occurrence of sinus node dysfunction<sup>13</sup> requiring upgrading to a dual-chamber ICD system. Moreover, several trials have shown<sup>6,14–15</sup> that

in patients with a low ejection fraction, DDDR pacing is associated with higher rates of death and hospitalization for heart failure when compared with backup VVI pacing.

However, the main advantage of dual-chamber ICDs is a better discrimination between ventricular and supraventricular arrhythmias reducing occurrence of inappropriate therapies<sup>12–13,16</sup> and their negative consequences on patient stress,<sup>17</sup> ventricular arrhythmias induction,<sup>18</sup> and device longevity.

Therefore, in patients without clinical indications for pacing, the use of a single-lead ICD implementing atrial sensing capability with proper signal amplification management may represent a useful therapeutic option, combining the positive features of both single and dual-chamber devices.

The aim of this study was to assess the atrial sensing performance of a single-lead ICD system at implant and during follow-up, evaluating the P-wave amplification factor (AmF). AmF was defined as the ratio between P-wave amplitude measured at implant with a conventional external pacing and sensing analyzer (PSA) device (indicated

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**Table I.**  
Patient Clinical Characteristics

Enrolled Patients (n = 43)	
	Mean $\pm$ SD
Age (years)	64.0 $\pm$ 15.9
Male (%)	38 (88%)
Ejection fraction%	32.7 $\pm$ 9.4
<b>ICD implant indication</b>	<b>No. of patients (%)</b>
Primary	23 (53%)
Secondary	20 (47%)
<b>Structural heart disease</b>	<b>No. of patients (%)</b>
Hyschemic	33 (78%)
Cardiomyopathy	8 (19%)
Brugada syndrome	1 (2%)
None	1 (2%)
Prior atrial fibrillation	9 (21%)
Atrial fibrillation at implant	7 (16%)
Prior myocardial infarction	9 (21%)

in the following as *unfiltered P wave*) and the P-wave amplitude provided telemetrically by the ICD (*filtered P wave*).

## Methods

### Patient Population

From February 2008 to June 2010, we enrolled 43 patients (38 male, mean age 64  $\pm$  16 years). Primary prevention was the main indication for ICD implantation in 20 patients (53%), while ischemic cardiomyopathy was the most common etiology (78% of subjects). Seven patients were in atrial fibrillation (AF) at implant. Clinical characteristics of the population are reported with further details in Table I.

### ICD Single-Lead System

The ICD used in our study was the Lexos A+ model combined with the Kentrox A+ lead (Biotronik GmbH & Co, Berlin, Germany). The Kentrox A+ is a 9.3-F pentapolar defibrillation lead with passive fixation mechanism, two distal electrodes for true ventricular bipolar sensing/pacing, one coil for shock delivery, and a 15-mm-spaced floating atrial bipole mounted 15–17 cm from the lead tip. The ICD is equipped with a special atrial input stage to provide high-quality atrial sensing, progressively increasing atrial gain up to four times. High gains require efficient bandpass filters to exclude high-frequency noise, respiration artifacts, far-field QRS oversensing, myopotentials, etc. For this reason, the atrial input stage implements a special bandpass filter finely

tuned in the frequency component range of atrial signal (30–70 Hz). Moreover, the ICD is provided with the SMART algorithm for supraventricular tachyarrhythmia discrimination<sup>19</sup> implemented in the dual-chamber ICD of the same family. The atrial sensing function of this single-lead system also allows VDD pacing.

### Atrial Signal Measurements at Implant

ICD implant was performed following standard procedures. The atrial bipole position was radiographically determined and recorded. At implant, P-wave amplitude was always measured with a conventional PSA device (ERA 300 Model, Biotronik GmbH & Co); the average of at least 10 P-wave amplitudes was defined as the “unfiltered” P-wave value. After ICD connection, P-wave measurements were performed telemetrically by the programmer; the mean value of P-wave signals registered during automatic sensing test was defined as the “filtered” P-wave value. The AmF was defined as the filtered/unfiltered P-wave ratio.

### Atrial Signal Measurement at Follow-Up

At follow-up, standard atrial and ventricular sensing tests were performed under different patient conditions: supine or standing position and during normal or deep breathing. Filtered P-wave value at follow-up was measured telemetrically with the same procedure used at implant. AmF (the follow-up filtered/implant unfiltered P-wave ratio) was calculated in each condition and compared. The AmF in supine position and during normal breathing was then compared with the respective values obtained at implant.

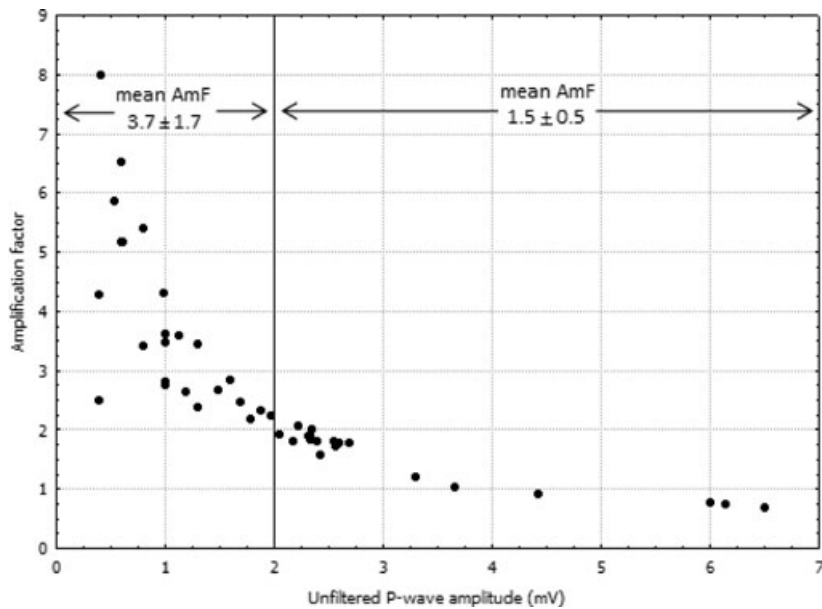
### Statistical Analysis

Continuous variables were expressed as mean  $\pm$  standard deviation (SD). Comparison between variables was performed with paired or unpaired Student's *t*-test. ANOVA was used to detect between more than two groups. A standard linear regression model was studied to correlate the AmF with inverse of input P-wave amplitudes. A 95% confidence interval (CI) for future prediction was obtained basing on this model. Two-sided statistical errors of 0.05 or less were considered statistically significant.

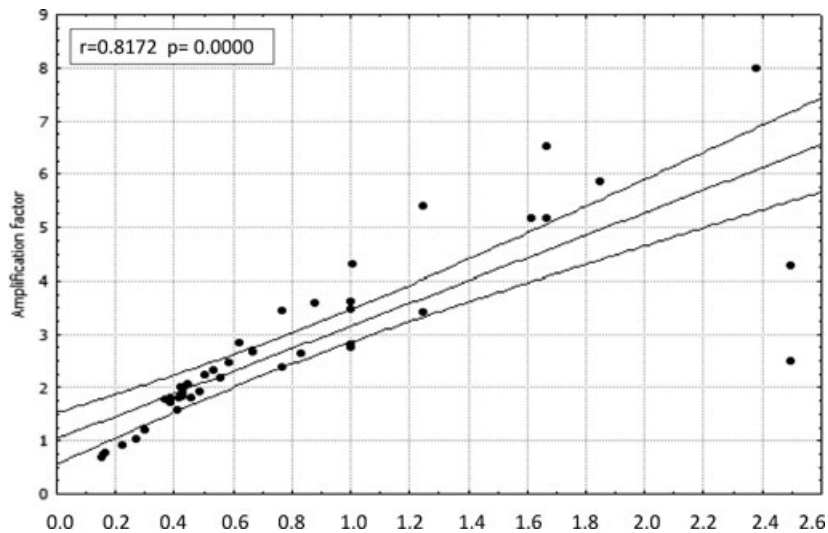
## Results

### Amplification Factor at Implant

At implant unfiltered and filtered P-wave values were 2.02  $\pm$  1.49 and 3.85  $\pm$  0.81 mV, respectively (*P* < 0.001). The mean AmF was 2.77  $\pm$  1.62. The AmF plot as a function of unfiltered P waves is reported in Figure 1 showing an evident inverse relationship (the smaller the



**Figure 1.** AmF trend as a function of unfiltered P wave (PSA measurements). The trend shows an inverse correlation between the AmF and the unfiltered P wave. Unfiltered P waves lower than 2 mV are associated to a mean amplification of about 3 whereas unfiltered P waves higher than 2 mV may be amplified by the device of about 1.5 factor.



**Figure 2.** Linear correlation between the AmF and the inverse of unfiltered P wave. The graph shows a strong correlation ( $R = 0.82$ ,  $p < 0.0001$ ).

unfiltered P wave, the greater the amplification factor, and vice versa). Arbitrarily assuming a threshold of 2 mV, patients with an unfiltered P wave below this limit had an AmF of  $3.7 \pm 1.7$ , significantly higher ( $P < 10^{-7}$ ) than the AmF of  $1.5 \pm 0.5$  observed in the other patients. A linear regression analysis was performed between the inverse of unfiltered P wave and the AmF in all

the patients (Fig. 2). The correlation found was highly significant with  $r = 0.82$  ( $P < 0.00001$ ). The correlation was even higher, excluding the seven patients with persistent AF at implant ( $r = 0.96$ ,  $P < 10^{-7}$ ). In the latter group of patients, the mean unfiltered and filtered atrial sensing amplitudes measured during AF were, respectively,  $0.65 \pm 0.28$  and  $2.84 \pm 1.14$  mV. For these patients, the

**Table II.**

Multiple Linear Regression Analysis Including AmF as the Dependent Variable and the Listed Variables as Covariates

	Regression Coefficient (SD)	P
Inverse of unfiltered P wave	2.38 (0.43)	<0.00001
Ongoing AF	0.79 (0.70)	0.27
Floating bipole position	-0.36 (0.30)	0.25
Ischemic etiology	0.19 (0.46)	0.52
Primary/Secondary ICD indication	0.26 (0.40)	0.68

AF = atrial fibrillation; SD = standard deviation.  $R^2 = 0.66$ ,  $P > 0.001$ .

AmF of  $4.62 \pm 1.94$  was almost twice than in patients in sinus rhythm ( $2.41 \pm 1.30$ ;  $P < 0.001$ ).

A multiple linear regression model was also studied, including the AmF as the dependent variable and the unfiltered P wave, the atrial bipole position (high, medium, low), AF ongoing at implant, ischemic etiology, and primary/secondary ICD indication as covariates. The results are listed in Table II: only the inverse of P-wave amplitude

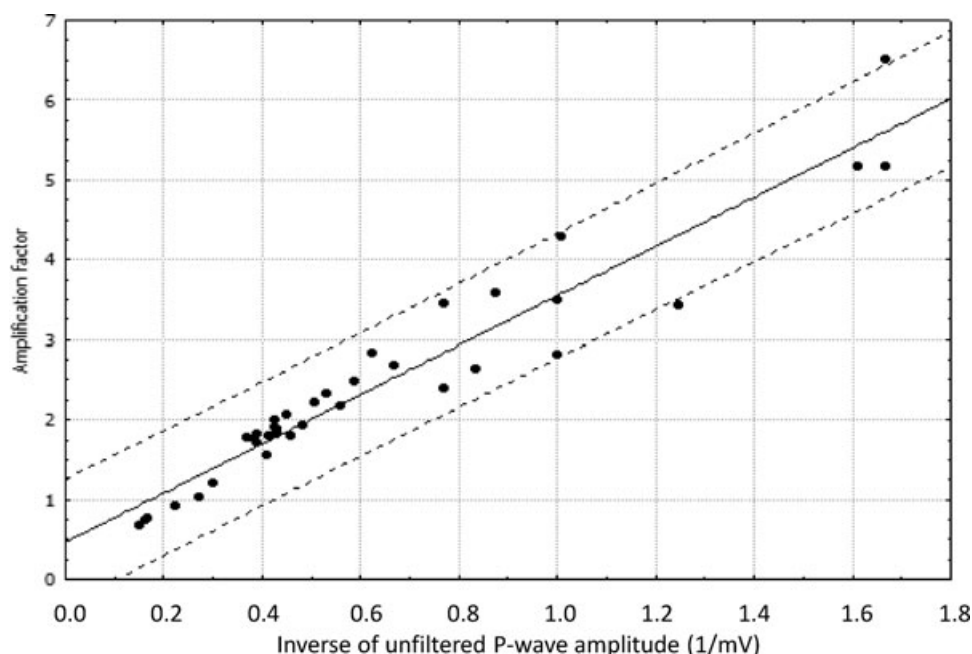
is significantly correlated with the AmF ( $P < 10^{-7}$ ) whereas the remaining covariates resulted largely uncorrelated.

### Amplification Factor to Predict Filtered P-Wave Amplitude

The previous univariate regression model correlating AmF with the inverse of unfiltered P waves was used to obtain a method predicting filtered P amplitudes as a function of the unfiltered P waves measured with the external PSA device during implant (Fig. 3). Table III shows a reference frame with several possible “input” unfiltered P wave and the corresponding intervals containing the P-wave amplitudes that will be obtained after ICD connection with a confidence of 95%. As an example, for an unfiltered “input” of 1 mV, the filtered P-wave amplitude will be between 3.4 and 3.7 mV with a probability of 95%. It is worth noting that in the range of the unfiltered P waves normally detected at implant (0.5–2 mV), the ICD will be able to amplify the unfiltered P waves for a factor of about 2 to 6.

### Amplification Factor and Episodes Detection at Follow-Up

Data from 25 patients were available after a mean follow-up of  $384 \pm 244$  days. In these subjects, atrial sensing was maintained in all the patients. Also, AmF was stable during that period



**Figure 3.** Linear regression analysis for prediction of filtered P-wave values (detected by ICD) according to the unfiltered P-wave measured at implant (PSA measurements).

**Table III.**

Predicted Values of Filtered P Wave at Implant

Unfiltered P Wave at Implant (mV)	Predicted Filtered P Wave Range (95% CI) (mV)
0.50	3.1–3.5
0.75	3.2–3.6
1.00	3.4–3.7
1.25	3.5–3.8
1.50	3.6–4.0
1.75	3.7–4.1
2.00	3.7–4.3

Predicted values of filtered P wave as a function of some unfiltered P-wave values: The filtered P wave obtained after the ICD connection will be within the reported ranges with a probability of 95%.

ICD = implantable cardioverter defibrillator; CI = confidence interval.

( $3.19 \pm 1.82$  at follow-up vs  $3.52 \pm 2.21$  at implant;  $P = 0.24$ ).

The filtered P-wave amplitudes at follow-up were collected and compared under four different conditions: supine position during normal or deep breathing and standing during normal or deep breathing (Fig. 4). No statistically significant difference was found (analysis of variance result:  $P = 0.48$ ).

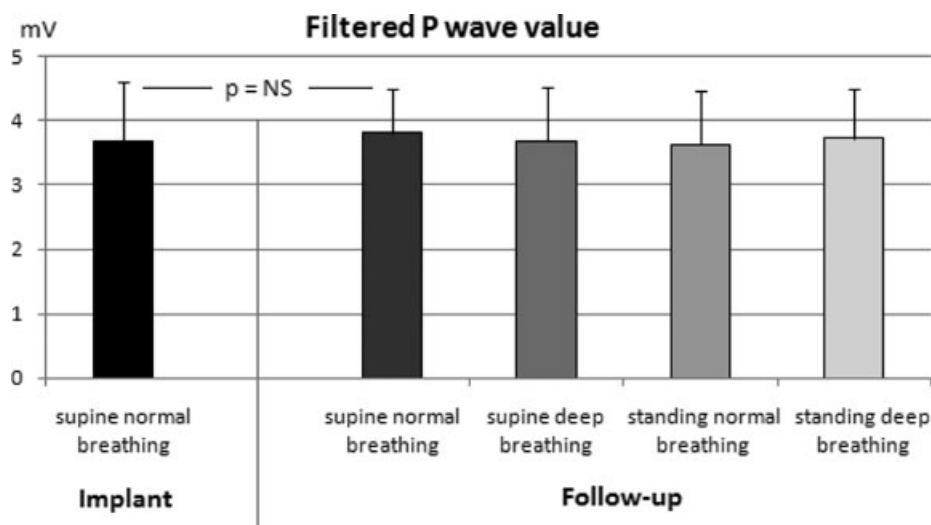
During follow-up, 30 appropriate ventricular tachycardia and/or ventricular fibrillation episode detections occurred in nine patients who re-

ceived 30 appropriate therapies. Two patients perceived inappropriate therapy deliveries due to an incorrect rhythm classification not related with atrial sensing detection as documented in the intracardiac electrogram recording of these episodes. No further inappropriate detection occurred after device reprogramming.

### Discussion

In our study, we have shown that the use of a single-lead ICD implemented with an atrial sensing capability provides a reliable acute and long-term atrial sensing. The good quality of the atrial sensing that we have obtained depends on the amplification of the spontaneous signal.

The main finding of our study is that the atrial signal amplification depends on the input P-wave amplitude. The correlation is well described by an inverse relationship between the AmF and the P-wave amplitude (the lower the P waves the higher the AmF). This feature appears very attractive in clinical practice where atrial sensing plays an essential role for correct discrimination between ventricular and supraventricular arrhythmias. As reported by Israel et al.,<sup>13</sup> atrial sensing mis-detection is present in 66% of detected episodes by dual-chamber ICD and atrial undersensing is the main reason of inappropriate therapies. In our experience, atrial sensing was reliable in all the patients at implant and was maintained during follow-up. The inappropriate therapies that occurred in two patients were not due to atrial undersensing and were effectively resolved by ICD reprogramming.



**Figure 4.** P-wave values detected by ICD at implant and at follow-up in different conditions: normal or deep breath, supine position or standing. Statistically significant differences were not found.



Undersensing of atrial signal has not been observed also in the seven patients with persistent AF although this arrhythmia induces a low and unstable atrial signal. The atrial amplification was higher (about 5:1) in these patients than in the subjects with sinus rhythm and always provided a correct arrhythmia classification.

The correlation between unfiltered P-wave and the AmF was strong enough to make out a simple model predicting the P-wave amplitudes that can be obtained after the lead-to-ICD connection basing on the unfiltered P-wave measured with a standard PSA. According to the model of Table III, also in the presence of poor P waves of 0.5 mV, one can be reasonably confident to get about a 3-mV signal after the ICD connection.

Our data confirm the results of the ADAMO registry<sup>20</sup> showing that a single-lead ICD with an atrial sensing feature is able to detect atrial electrical activity in all of the enrolled patients and this capability is maintained during a follow-up of about 1 year. As a rule of thumb, the single-lead ICD system amplified atrial input signals with a ratio of 3:1.

An issue frequently acknowledged in the literature about VDD pacemakers<sup>21</sup> is the instability of atrial sensing detected by a floating atrial electrode which may depend on body position and breathing. With this ICD system, as reported also in previous published results,<sup>22</sup> atrial sensing performances seem to not be affected by these conditions; in fact, we have not found any P-waves difference between supine or standing position and normal or deep breathing.

The high and selective gain of the atrial input channel and the neglectable influence of body position and breathing may result in a significant simplification of the entire implant procedure. No particular attention must be paid by the physician to the lead and atrial bipole positioning or to the unfiltered P-wave amplitude measured with the PSA.

### Study Limitations

This study, primarily aimed to evaluate and estimate the atrial signal amplification capability of a single-lead ICD system, was not focused on clinical benefits that could potentially derive especially from a more specific discrimination of supraventricular and ventricular episodes. Due to a relatively small sample size and the short follow-up, detailed data on specificity and sensitivity of this system could not be provided. The recently published ADRIA study<sup>23</sup> has, however, shown that this ICD is equivalent to a standard dual-chamber ICD with regard to the detection of ventricular tachyarrhythmias and supraventricular tachyarrhythmias.

### Conclusions

In conclusion, in our study a single-lead ICD was able to reliably amplify atrial P waves. This amplification proved to be stable during the follow-up and to be inversely dependent on input P-wave amplitudes. A simple model was provided correlating input P waves at implant with the P-wave amplitudes that can be obtained after ICD connection. This scheme may be helpful to simplify implant procedures.

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