Detection of Right Ventricular Volume Changes by Intracardiac Impedance

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Summary

The purpose of this study was to investigate whether changes in the right ventricular end-diastolic and end-systolic volume, and consequently of the stroke volume, can be detected by a DC-coupled intracardiac impedance signal. Measurements were conducted in 13 patients with an implanted Inos pacemaker, testing various measurement configurations. Volume changes were induced by incremental overpacing and by postural changes. The pulse contour systolic integral from the peripheral blood pressure was used as a marker of stroke volume changes. Four out of seven patients with quadrupolar impedance measurement configurations showed a good correlation between the stroke impedance and the pulse contour systolic integral (r^2: 0.51 – 1.0) with the expected slope sign. All six patients tested with different tri-, bi-, or unipolar configurations had a good correlation (r^2: 0.73 –0.96) with a correct slope. Similar results were obtained for the Starling regression, stroke impedance vs. end-diastolic impedance. Three out of seven patients with quadrupolar measurement configurations showed good correlation coefficients (r^2: 0.53 – 0.96) and a correct slope sign. All six patients with tri-, bi-, or unipolar configurations showed the correct Starling behavior (r^2: 0.87 – 0.99). It follows that DC-coupled intracardiac impedance can detect right ventricular end-diastolic and end-systolic volume changes. With the Inos measurement system, the quadrupolar configurations offer better amplitude resolution, but the tripolar and intraventricular bipolar configurations are better hemodynamic markers.

Key Words

Hemodynamics, stroke volume, end-diastolic volume, intracardiac impedance, sensor

Introduction

Ventricular end-diastolic volume (EDV) and end-systolic volume (ESV) are important parameters for assessing the hemodynamic state of the circulatory system. The stroke volume (SV) and the ejection fraction (EF) can be derived from EDV and ESV measurements. Based on these quantities it is possible to monitor the pumping functionality of the patient's heart (preload and contractility), observe the progression of certain heart diseases, e.g., congestive heart failure, or detect and discriminate tachyarrhythmias. Furthermore, certain parameters of implanted devices (pacemakers or implantable cardioverter-defibrillators) such as pacing rate, AV delay, VV delay for biventricular pacing, and others can be individually adjusted for optimization of cardiac output.

Ideally, the implanted device should be able to measure ventricular volume changes in order to automatically and continuously self-adjust. Hence, the goal is to find a hemodynamic sensor that can be easily integrated into an implantable device. Such a sensor needs to be reliable, robust, accurate, provide long-term stability, and should be powered with as little energy as possible. A promising approach for a hemodynamic sensor principle that might fulfill these requirements is the measurement of intracardiac impedance. With this method a constant sub-threshold electrical current is injected into the ventricular cavity and the resulting voltage is measured between two electrodes. The voltage is directly proportional to the impedance of the cavity. Because the conductivity of blood is higher than that of the surrounding myocardium [1-3], the measured impedance depends largely on the ventricular blood volume. During the cardiac cycle the course of the intracardiac impedance mirrors the prevailing volume of the ventricle, both during systole (emptying) and diastole (filling). The physical and technical aspects of the impedance method are described by Hochgraf and Irnich [4,5] in detail.

The impedance method was successfully established by Baan et al. [6,7]. A multipolar catheter was used to determine the absolute volume of the left ventricle. This method was not acceptable for implants, but it is frequently used during electrophysiologic examinations. Subsequently, Chirife et al. introduced a method of determining the relative volume, i.e., volume changes, of the right ventricle using standard bipolar pacemaker leads without additional electrodes or hardware [8]. Khoury et al. used intracardiac impedance for detection and discrimination of stable and unstable ventricular tachycardia [9]. Arthur [10] gives a detailed review of several clinical applications of the impedance method.

The goal of this study was to investigate the impedance method for determining right ventricular volume changes using standard pacemaker leads and a pacemaker with an integrated impedance sensor. It was hypothesized that the EDV correlates with the minimum value and the ESV with the maximum amplitude of the impedance signal within a certain timeframe during systole. The impedance was determined using various measurement configurations. Several tests were conducted to modify the preload and the SV of the study patients.

Materials and Methods

Impedance measurements were performed on ten patients with previously implanted Inos^2 or Inos^{2+} pacemakers (Biotronik, Germany), and on three patients with external devices temporarily connected to pacemaker leads. For the duration of the study the devices were programmed to a mode where – in addition to normal DDD or VVI pacing – the intracardiac impedance was continuously recorded and the data were transmitted online via a programming coil to the programmer device. The impedance was filtered with a 40 Hz lowpass filter. No highpass filter was used in order to preserve the DC component of the impedance, which contained the information about EDV and ESV. In addition to the impedance, the surface ECG (PMS1000, Biotronik), the continuous peripheral blood pressure (Colin7000, USA), and the respiratory chest movements (Pneumotrace (R), UFI, USA) were recorded. The data were sampled and digitized with a four-channel data acquisition system. Figure 1 gives an example of the recorded data. Additionally, for several of the patients the velocity-time-integral (VTI) of the aortic flow was determined by echo-Doppler cardiography (CFM700, Vingmed, Sweden); see Figure 2.

Thirteen patients were enrolled in the study (five male, eight female, mean age 71.5 ± 14.6 years). Ten of the

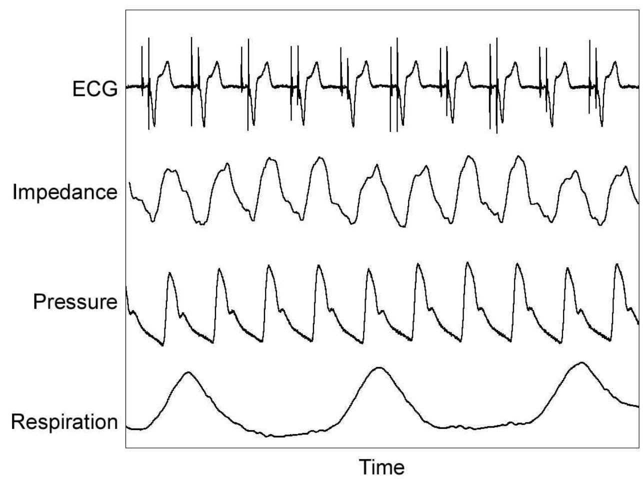


Figure 1. Sample of the recorded data.

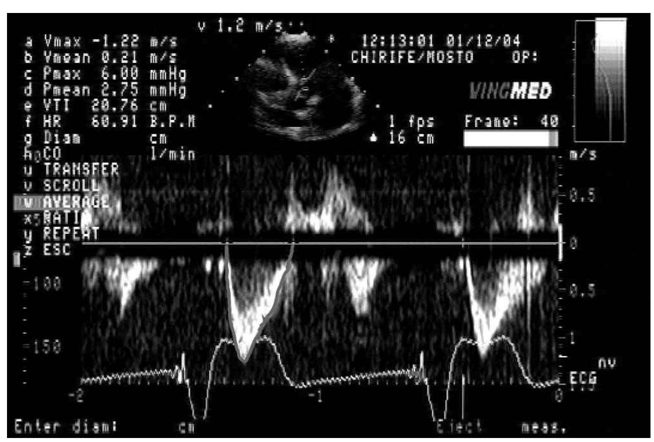


Figure 2. Determination of the aortic velocity-time-integral (VTI) from the Doppler echocardiography.

patients had an implanted Inos^2 or Inos^{2+} pacemaker. Three patients were investigated during an implantation procedure using an external Inos^2 for the measurements. Peripheral blood pressure and respiration were not measured during the implantation procedures. Three patients had only a ventricular lead, while the remainder had bipolar leads in the right atrium and ventricle.

Initially, the intracardiac impedance was recorded with various measurement configurations for each patient. Quadrupolar, tripolar, bipolar, and unipolar electrode configurations were tested. Figure 3 depicts the various impedance measurement configurations. The most promising configuration – a compromise between signal resolution and morphology – was selected for the consecutive tests for each individual patient. Subsequently, the following tests were performed in order to modulate the hemodynamic state: overpacing, AV delay variation, postural changes, handgrip exercises, isoproterenol stress, and treadmill ergometry. Not all of the tests could be conducted for all patients.

In this report only the pacing and postural test results are described, since they are challenges of preload (EDV). In order to decrease the EDV, and therefore the SV, the pacing rate was increased in four steps during the pacing test. The pacemakers were programmed to:

- pacing rate = sinus rate + 10 ppm,
- pacing rate = 80 ppm, 100 ppm, and 120 ppm

for 1 min each while the impedance was recorded. For the postural tests the body position was altered for 1 min each as follows: supine, sitting, recumbent left side, recumbent right side, supine, deep breathing, upright, and deep breathing.

The minimum impedance value 0 to 100 ms after a ventricular event, i.e., the end-diastolic impedance (EDZ), and the maximum value, 100 to 400 ms after a ventricular event, i.e., the end-systolic impedance (ESZ) were determined. Various time frame within these ranges were tested. The "stroke impedance" SZ = ESZ – EDZ was computed. Figure 4 shows the evaluation of the impedance data. The blood pressure

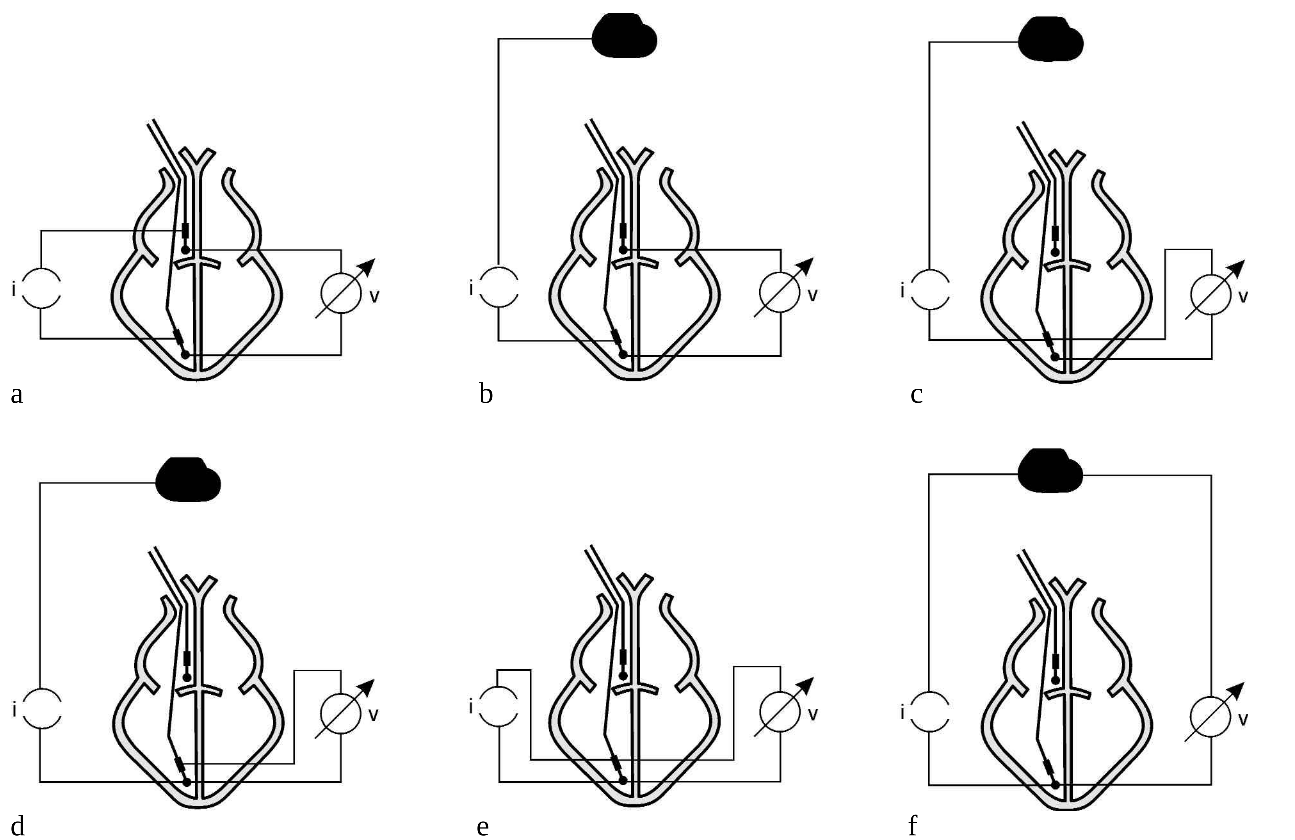


Figure 3. Impedance measurement configurations. i = injected current, v = sensed voltage, a) quadrupolar without case (QP), b) quadrupolar with case (QP_C), c) tripolar with common ventricular ring (TP_{VR}), d) tripolar with common ventricular tip (TP_{VT}), e) bipolar (BP), f) unipolar (UP).

signal was used as a reference for determining the SV changes. The signal was analyzed using a pulse contour analysis method published by Wesseling et al. [11]. The basic Wesseling correction formula for heart rate, age, and mean pressure correction was applied. Since no inter-individual comparison was performed, no normalization to a measured cardiac output value was done. The pulse contour systolic integral (PCSI) was calculated according to the following formula, which is proportional to the true SV of the ventricles in an individual patient:

$$PCSI := \int_{t_{\min}}^{t_{incisura}} \left(P(t) - P_{\min}\right) dt \cdot C\left(HR, A, P_{mean}\right)$$

$$C\left(HR, A, P_{mean}\right) = 0.66 + 0.005 \cdot HR - 0.01 \cdot A \cdot \left(0.014 \cdot P_{mean} - 0.8\right)$$

PCSI:	pulse contour systolic integral (assumed to be SV-proportional within an individual patient)
C(HR, A, P_{mean}):	correction factor
P(t):	arterial pressure
P_{min}:	minimum arterial pressure during a heart cycle
P_{mean}:	mean arterial pressure in mmHg
t_{min}:	time of minimum pressure
$t_{incisur}$:	time of pressure incisura-like feature
HR:	heart rate in bpm
A:	age of patient in years

The integral was computed from the time of the minimum pressure in each heart cycle to the time of the first local minimum after the maximum of the curve (similar to the incisura); see Figure 5.

Linear regression analysis between heart rate (HR), posture, EDZ, SZ, and PCSI was performed for various evaluation windows. The time window with the best correlation was taken for each patient to create a summary of the results. The measurement results were assessed based on these correlation factors. The correlation analysis was performed with averaged data, i.e., the EDZ, ESZ, and PCSI value were each averaged for a certain test condition. For the postural tests arbitrary numbers were assigned to the different body positions that are believed to reflect the SV during that test. Table 1 lists the classification of the patient positions. In addition to the correlation, it also was evaluated

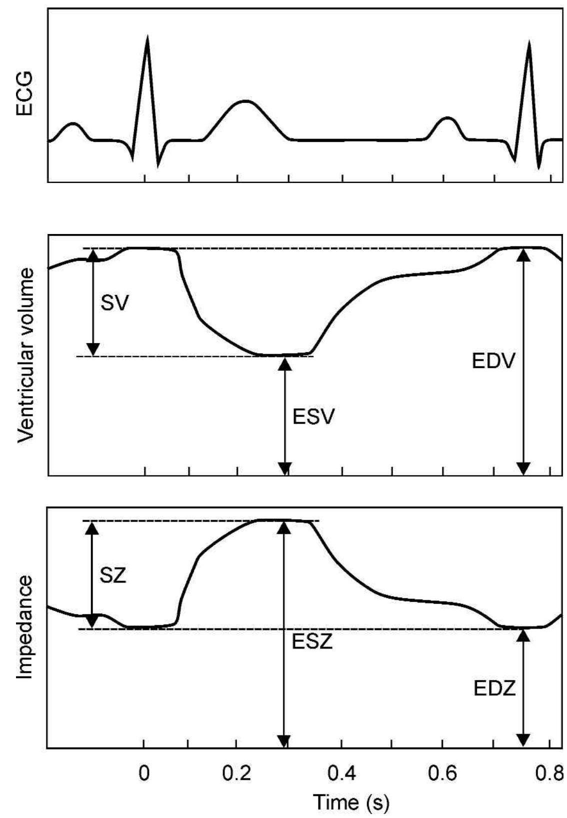


Figure 4. Time course and evaluation of the impedance signal in relation to the ECG and the ventricular volume. Volume and impedance display reverse behavior.

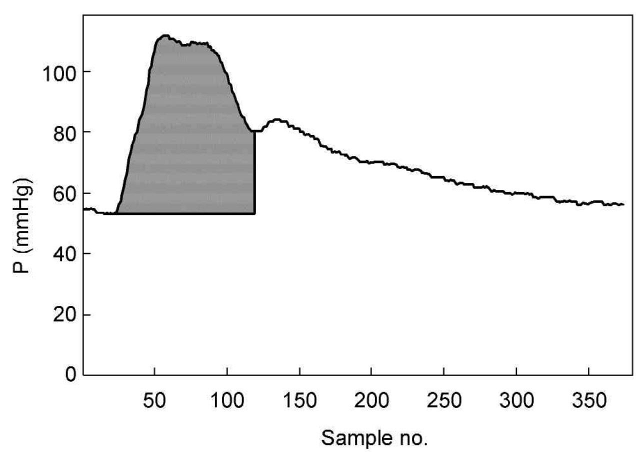


Figure 5. PCSI computation from the blood pressure curve. The shaded area is the integral used as an indicator for the stroke volume.

whether the slope of the regression had the correct sign, i.e., whether it exhibited the expected physiologic behavior. The correlation between SZ and EDZ, i.e., between SV and EDV, has a special physiologic mean-

Position, condition	Posture value
Supine	0.0
Supine, deep breathing	0.1
Recumbent, right side	0.2
Recumbent, left side	0.3
Sitting	8.0
Standing	10.0
Standing, deep breathing	10.1

Table 1. Definition of the assigned postural values. Increasing numbers mean decreasing stroke volume.

ing. It is called the "Starling regression," as it marks the well-known Starling curve [12].

Results

Impedance Curve Morphology

Different measurement configurations resulted in different impedance curve morphologies for the same patient. Figure 6 shows four different average impedance waves for the same patient. The signal resolution also varies as the DC component of the impedance varies with the measurement configuration.

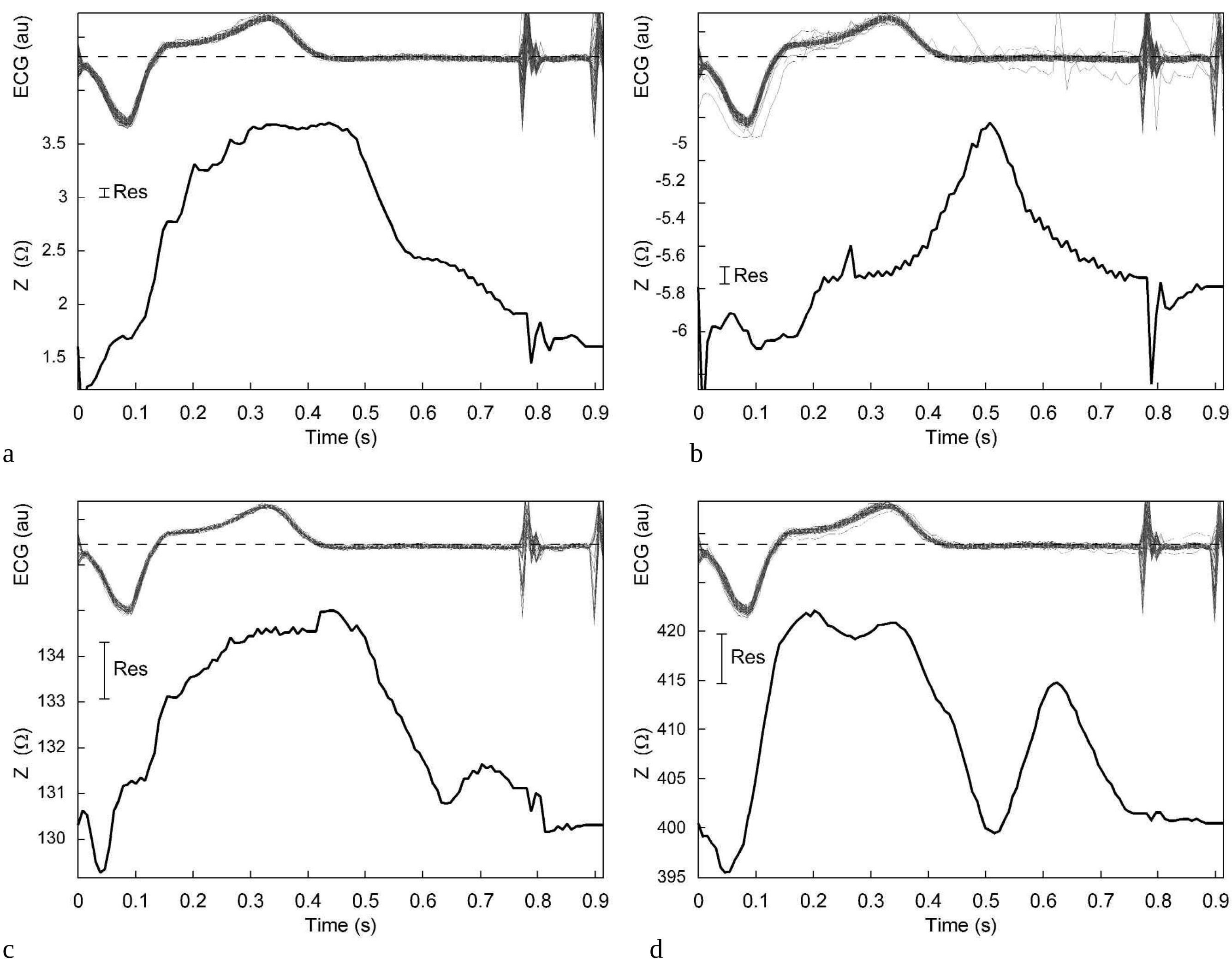


Figure 6. Example of four impedance curve morphologies for patient #8. Pacing mode DDD, pacing rate 65 ppm. The ECG is displayed in the upper part of the graphs as a bundle plot. The small bar indicates the signal resolution for each configuration. au = arbitrary units; Res = resolution.
Panel a) quadrupolar measurement configuration (QP).
Panel b) quadrupolar measurement configuration (QP_C).
Panel c) tripolar measurement configuration current injection: $V_{Ring} – A_{Ring}$ voltage measurement: $V_{Ring} – A_{Tip}$.
Panel d) bipolar measurement configuration (BP).

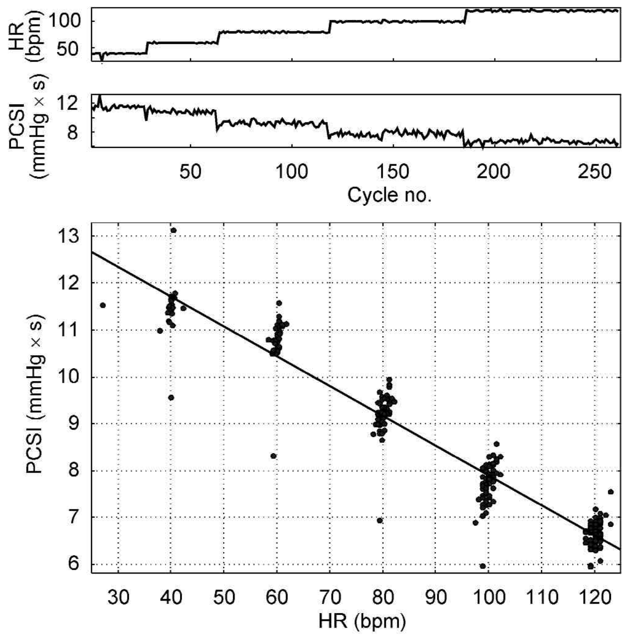


Figure 7. Beat-to-beat correlation between PCSI and heart rate (HR) for the pacing test, patient #2, r^2 = 0.93.

Patient ID	PCSI vs. HR r^2	slope sign	PCSI vs. posture r^2	slope sign
1	0.90	-		
1	0.99	-		
2	0.99	-		
2	0.90	-	1.00	-
3	0.96	-	0.40	+
3	0.86	-		
5	0.96	-	0.96	-
5	0.96	-		
5	0.96	-		
5	0.92	-		
6	0.84	-	1.00	-
6	0.95	-		
7	0.77	-		
8	0.98	-	0.88	-
8	0.96	-		
8	0.86	-		

Table 2. Correlation results PCSI versus heart rate (HR) and PCSI versus posture.

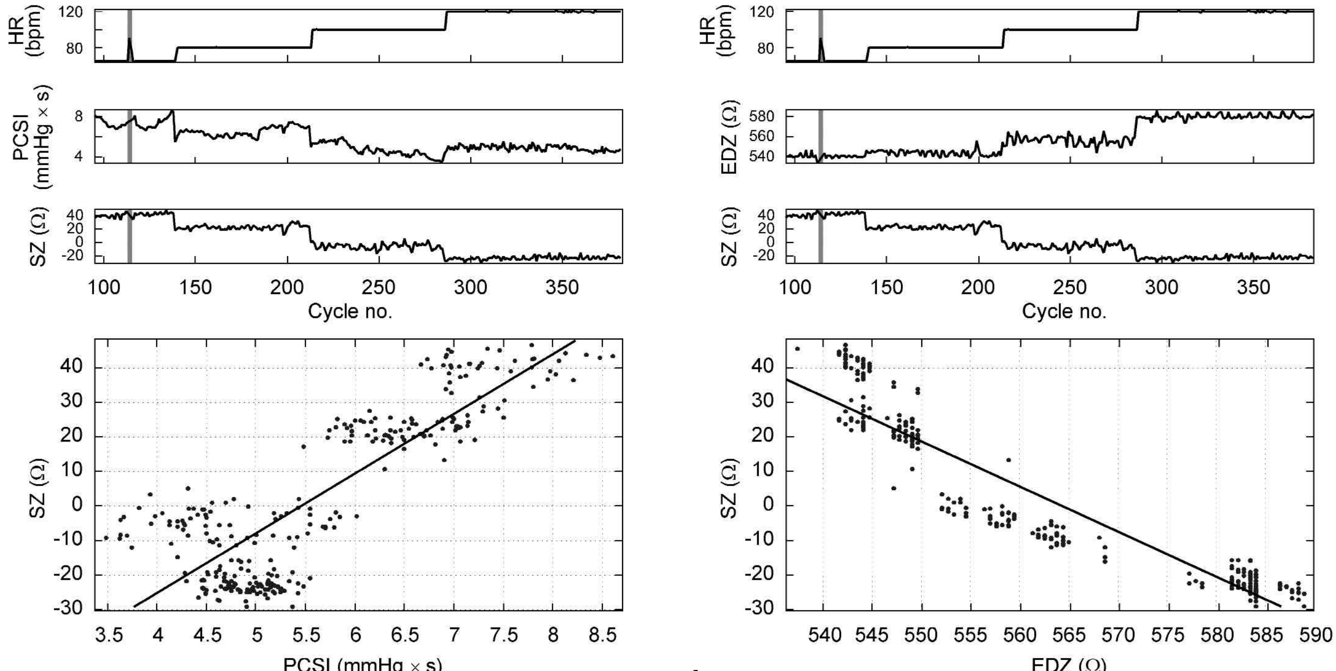
PCSI Reference

The normalized pressure integral PCSI was used as a reference method to assess the true SV. To verify this method, the PCSI was correlated with the heart rate

Meas. config.	Pt. ID	Position	SZ vs. PCSI r^2	slope sign	SZ vs. EDZ r^2	slope sign
QP	1	Supine	0.45	+	1.00	-
QP	1	Sitting	0.96	+	0.00	o
QP	3	Supine	1.00	+	0.02	o
QP	3	Supine	0.90*	+	0.93	-
QP	8	Supine	0.28	+	0.57	-
QP	8	Supine	0.01*	o	0.16	-
QP	10	Supine	0.90*	-	0.95	-
QP_C	2	Supine	0.86	+	0.94	-
QP_C	2	Sitting	0.67	+	0.91	-
QP_C	2	Supine	0.38	-	0.53	-
QP_C	5	Supine	0.92	+	0.90	-
QP_C	5	Sitting	0.59	+	0.83	-
TP_{VR}	12	Supine	0.79*	-	0.99	-
TP_{VT}	6	Supine	0.90	+	0.87	-
TP_{VT}	6	Sitting	0.94	+	0.99	-
TP_{VT}	6	Supine	0.81*	-	0.97	-
BP	3	Supine	0.73	+	0.99	-
BP	8	Supine	0.96	+	0.99	-
BP	8	Supine	0.90	+	0.88	-
UP	7	Supine	0.96	+	0.95	-

*Table 3. Correlation results for the pacing tests with various measurement configurations. * = correlation with heart rate (HR) instead of PCSI. See text for abbrevations.*

during the pacing tests and with the body position during the postural tests. Figure 7 shows a correlation plot for one of the patients. Table 2 summarizes the results for the correlation between PCSI and HR or posture, respectively. The pacing test was repeated in a different body position or with a different impedance measurement configuration for several patients. No peripheral pressure was measured during implantations. The pressure was not determined for other reasons in some patients. Since SV should decrease with an increased pacing rate, the slope of the PCSI-HR correlation should be negative. According to the definition in Table 1, the slope of the PCSI-posture regression should also be negative. An incorrect sign was observed for the correlation between PCSI and posture in one patient. In summary, it is concluded that the pulse contour systolic integral PCSI is a good method for assessing true SV. Therefore, it can be used as a reference method for evaluating impedance data.



a b

Figure 8. Example of the correlations SZ-PCSI and SZ-EDZ (Starling regression) for the pacing test, patient #6, pacing mode: VVI. The gray bar marks one beat that was excluded from the analysis. The negative SZ results from an EDZ that is greater than ESZ. Panel a) SZ versus PCSI, r^2 (beat-to-beat) = 0.72, r^2 (averaged) = 0.90.
Panel b) SZ versus EDZ, r^2 (beat-to-beat) = 0.87, r^2 (averaged) = 0.87. See text for abbrevations.

Pacing Test

Table 3 shows the correlation factors of the pacing tests that were conducted. For the correlation of SZ and PCSI, the slope sign is expected to be positive, as PCSI is believed to correlate with SV. Stroke impedance was correlated with HR for several tests because no pressure measurements were available. In these cases, the slope should be negative, since the SV decreases with increased rate. A negative slope is expected for the Starling regression, i.e., the SZ vs. EDZ correlation. With increasing EDZ (i.e., decreasing EDV), the SZ, and hence the SV, decrease. Figure 8 shows a sample plot of the evaluation of a pacing test result. An incorrect slope sign was observed in three of the tests, with one of the cases exhibiting a high correlation (patient 3, correlation SZ vs. HR). In Figure 9, the aortic VTI and the SZ are plotted versus the pacing rate for one patient. The SZ shows the same course as the VTI.

Posture Test

Table 4 shows the correlation results of the postural tests. Due to the posture classification in Table 1 a negative slope sign is expected for the SZ vs. posture correlation. The slope of the Starling regression should also be negative. In two of the cases the slope of the SZ vs. posture regression was not as expected. In two other cases the slope of the Starling regression was not as expected.

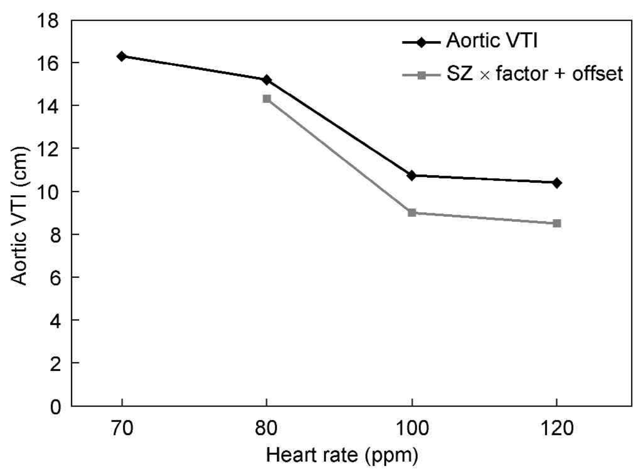


Figure 9. Aortic VTI and SZ during the pacing test for patient #6. Tripolar measurement configuration (tvt). The SZ course is scaled to fit into the same plot with the VTI. See text for abbrevations.

Meas. config.	Pt. ID	Pacing rate	SZ vs. PCSI r^2	SZ vs. PCSI slope sign	SZ vs. EDZ r^2	SZ vs. EDZ slope sign
QP	3	70 ppm	0.70	+	0.99	-
QP	8	65 ppm	0.85	-	1.00	-
QP_C	2	60 ppm	0.00	o	0.28	+
QP_C	5	60 ppm	0.27	-	0.40	+
TP_{VT}	6	65 ppm	0.30	-	0.70	-

Table 4. Correlation results for the postural tests with various measurement configurations.

Measurement configuration	No. of patients	No. of passed patients	Passed r^2 range (SZ-PCSI)
QP	4	2	0.90 – 1.00
QP_C	3	2	0.51 – 0.92
TP_{VR}	1	1	0.79*
TP_{VT}	1	1	0.90 – 0.94**
BP	3	3	0.73 – 0.96
UP	1	1	0.96

*Table 5. Summary of passed/failed tests from the pacing and postural challenges. * = correlation with heart rate instead of PCSI ** = repeated tests for one patient.*

No correlation with the PCSI was performed for the postural tests, as the peripheral blood pressure could not be reliably determined for the postural transitions.

Signal Resolution

Due to the different electrical field distributions with the various measurement configurations, the DC component of the impedance signal varies strongly depending on the measurement method. With a higher DC offset the gain of the voltage measurement had to be decreased to prevent signal clipping. Hence, the resolution of the alternating signal component became smaller for these cases, i.e., the resolution was decreased. Essentially, it was observed that the resolution was highest with quadrupolar configurations and smaller with tri- and bipolar ones. This corresponds to theoretical investigations.

Summary

Table 5 summarizes the results of the measurement configurations and assesses them using a pass/fail criterion. A patient with a certain measurement configuration is classified as having passed if the coefficient r^2 for the SZ-PCSI correlation is greater than or equal to 0.5, the slope sign of the SZ-PCSI correlation is as expected, and the slope sign of the SZ-posture correlation is as expected. For those tests where no pressure measurements were performed, the slope of the SZ-HR correlation was assessed. It was observed that three out of seven patients with quadrupolar impedance measurement configurations failed the criteria, whereas all the patients with tri-, bi-, and unipolar configurations passed. Table 6 summarizes the results of the Starling regressions. Here, a test is classified as passed if the correlation coefficient is greater than or equal to 0.5 and the slope sign is as expected.

Discussion

The results of this study demonstrate that the intracardiac impedance with the described measurement settings essentially reflects volume changes of the right ventricle. The best signal resolution was observed with quadrupolar measurement configurations. For this rea-

Measurement configuration	Pacing test: No. of patients	Pacing test: No. of passed patients	Pacing test: Passed r^2 range	Posture test: No. of patients	Posture test: No. of passed patients	Posture test: Passed r^2 range
QP	4	1	0.95	3	3	0.99 – 1.00
QP_C	3	2	0.53 – 0.96	2	0	-
TP_{VR}	1	1	0.99	0	-	-
TP_{VT}	1	1	0.87 – 0.99**	1	1	0.70
BP	3	3	0.88 – 0.99	1	1	1.0#
UP	1	1	0.95	0	-	-

*Table 6. Summary of Starling regressions SZ vs. EDZ for the pacing and postural tests. ** = repeated tests for one patient # = correlation 1.0 due to only two data samples.*

son, most of the tests were conducted using a quadrupolar configuration. Furthermore, theoretical investigations have shown that information about the complete ventricular volume can be obtained with a quadrupolar measurement. The signal from tri- and bipolar configurations is dominated by the geometry in the vicinity of those electrodes that serve both for current injection and voltage measurement. On the other hand, quadrupolar measurements are distorted by artifacts, which explains the failed tests. Two independent pacing leads, one located in the right atrium, the other in the ventricle, were used for the measurement. The atrial lead moves during atrial contraction and relaxation. This movement (relative to the ventricular lead) alters the impedance signal. Thus, the quadrupolar impedance signal is not a reliable volume indicator if the electrodes are located on two leads. Better results were observed with those measurement configurations where the electrodes were located on one lead, i.e., tri- or bipolar measurements, because there is no atrial motion artifact with these configurations. Although the signal might not mirror the full volume, it correlates well with the ventricular volume. It follows that better results would be obtained if four electrodes were placed on the same lead, preferably all within the ventricle.

Conclusion

- DC-coupled intracardiac impedance can detect right ventricular end-diastolic and end-systolic volume changes.
- With the Inos measurement system, the quadrupolar configuration offers better amplitude resolution, but the tripolar and intraventricular bipolar configurations are better hemodynamic markers.

It shall be emphasized, that completely different quantities are monitored by the impedance technique using other measurement settings and evaluation methods, e.g., different filters and electrode configurations, that were not used in this study. Examples are detection of contractility [13] for Closed Loop Stimulation (CLS, Biotronik) and minute ventilation [14].

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