Implantable Sensors for Heart Failure

CHU-PAK LAU, DAVID CW SIU, HUNG-FAT TSE

From Division of Cardiology, Department of Medicine, The University of Hong Kong, Queen Mary Hospital, Hong Kong

Why Heart Failure Monitoring

About 5 million Americans suffer from heart failure, carrying significant morbidity and mortality. It is estimated that 550,000 new cases occur each year, and the estimated cost of treatment reaches $33.2 billion, most of the cost were incurred during hospitalization for acute decompensation heart failure (ADHF).[1]

ADHF refers to a clinical condition of worsening heart failure with dyspnoea and often with evidence of fluid overload.[2] This is often triggered by one of the four main factors: atrial fibrillation, anemia, hypertension and medication/dietary indiscretion.

In the 1991-1994 Connecticut Medicare beneficiaries review,[3] ADHF that results in hospitalization carries an 8% in-hospital mortality. Importantly, of the 17,448 survivors, 44% will be re-admitted once, of which 18% were due to recurrent heart failure. Overall, 24% would die in 6 months after the first ADHF, and 53% either died or re-admitted over the same period. Thus prevention of ADHF can have significant prognostic impact for the patient, in addition to reducing the cost of heart failure management.

Address for reprints: Prof. Chu-Pak Lau, Honorary Clinical Professor Division of Cardiology, Department of Medicine, The University of Hong Kong, Queen Mary Hospital, Pokfulam, Hong Kong

Email: cplau@hkucc.hku.hk

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Limitations of Symptoms, Signs and Investigations

While dyspnea is the commonest presenting complaints for hospitalization in ADHF, it occurs relatively late in relation to hemodynamic and fluid status changes. Until the era of implantable devices, it is not possible to evaluate the hemodynamic changes leading to ADHF. Adamson et al[4] implanted a right ventricular (RV) sensor to measure RV systolic and diastolic pressure during heart failure exacerbation in 32 patients. They found that at a mean of 4±2 days before admission, RV systolic pressure started to increase in 9/12 heart failure event. As a group, there was an increase in RV systolic pressure by 25±4% and heart rate by 11±2% during ADHF. This study suggests that pressure changes is the initiating mechanism responsible for heart failure exacerbation. Likewise, using an implantable intrathoracic impedance sensor to assess pulmonary fluid, fluid overloading occurs at 18.3±10.1 days before dyspnea occurred.[5] Thus, dyspnea is a late event and does not allow neither the clinician nor the patient to have enough time for intervention to avert hospitalization.

The cardinal physical signs of congestive heart failure are: a third heart sound, pulmonary crackles, raised jugular venous pressure and pedal edema. However, these signs have poor sensitivity to detect heart failure. In a study[6] of 50 patients with raised pulmonary arterial wedge pressure (PAWP) ≥22 mm Hg, lung crackles were identified in 19% of patients, and a raised jugular venous pressure and peripheral edema were

present in only 50% and 20% of patients respectively. While a third heart sound was heard in most cases, it was also detected in those with a low PAWP. The combination of these signs have a sensitivity of 58% and specificity of 100% for congestive heart failure. Physical examination of jugular pressure is difficult and inaccurate.[7]

Body weight change is both a complaint or signs for ADHF. It has been suggested that this is an unreliable sign as body weight is not only reflective of body fluid, but may depend on amount of food/fluid intake and other causes of weight loss or weight gain. In a recent study,[8] 134 patients with heart failure hospitalization were compared with a case matched group without hospitalization. Body weight one week before hospitalization was associated with increasing risk of hospitalization (Relative risk: >2-5 lb=2.77; >5-10 lb= 4.46 and 5-10 lb=7.65). It is suggested that monitoring of body weight remains useful and identifies a high risk group for intervention.

Radiological evidence of ADHF tends to occur late. Brain natriuretic peptide (BNP) is proposed to improve heart failure management. In a randomized study on the N-terminal BNP to guide heart failure therapy (TIME-CHF) study,[9] 499 patients ≥60 years old with systolic heart failure were randomized. Titration to achieve a N-terminal BNP level of ≤2 times upper limit was compared to conventional management without BNP guidance. There was no difference in the survival rates free from all cause hospitalization between BNP-guided versus conventional therapy (41 vs 40%), and a similar degree of quality of life improvement. However, the secondary endpoint of heart failure hospitalization was significantly reduced (72 vs 62%), and outcomes were better in the 60-75 years old patients but not in those 75 years or older.

While vigilant monitoring of symptoms and signs (and BNP levels) are useful, they are not guarantee to accurately predict ADHF. On the other hand, frequent monitoring of some of these signs and symptoms, and the use of external physiological (and implantable) data are clearly superior to conventional care. In a meta-analysis of both cohort (2,354 patients) and randomized trials (6,258 patients),[10] with 6-12 months of follow up, there is a significantly lower rate of deaths and hospitalization compared to conventional management.

Taken together, frequent monitoring of physiological parameters are useful for clinical management of heart failure. As many patients with LV dysfunction requires implantable cardiac implantable electronic devices (CIED) either for arrhythmia prevent or therapy (ICD), or heart failure treatment (CRT or CRT-D), this opens the possibility to add implantable sensors for heart failure monitoring in these devices. The use of implantable sensors will allow continuous monitoring of physiological parameters without intensive manpower. Furthermore, the ability of these sensors to detect earlier physiological changes before ADHF may open a window for averting heart failure hospitalization. They can also measure hemodynamics at different body positions and on an ambulatory basis, and may obviate the need of invasive monitoring when the patient is admitted for heart failure therapy.

Monitoring of Pathophysiological Changes of Heart Failure

There are three possible pathophysiological areas for heart failure monitoring: monitoring of electrical remodeling, mechanical remodeling and neurohormonal changes that occur with heart failure (Table 1). Electrical remodeling in either the atrium or ventricle will result in changes in normal automaticity, conduction properties, and refractory period and predispose to atrial fibrillation (AF) and ventricular tachyarrhythmias. The occurrence of arrhythmias are routinely monitored and treated by CIED, both by pacing and defibrillation. Effective refractory period (ERP) can be monitored by physician activated electrical stimulation through a programmer.

Intra and inter-chamber conduction timing in heart failure are important, as they are either a result of, or the cause of electrical remodeling in heart failure. In a post mortem series of 34 patients with pre-morbid serial ECG, progressive PR and QRS duration prolongation occurred with worsening of heart failure. Cardiac mass index was significantly correlated with V1-V6 R-wave amplitude.[11] A wide LBBB QRS complex is associated with ventricular dyssynchrony

Table 1. Monitoring for heart failure pathophysiology

Electrical remodeling	**Examples**
Atrium	Rate, atrial ERP, atrial fibrillation
Ventricle	Rate, ventricular ERP, ventricular tachyarrhythmias
Conduction	Atrioventricular node conduction time and capacity, intra- and inter-atrial conduction, intra- and inter-ventricular conduction
Mechanical remodeling	**Examples**
Atrium	Size, function, structure
Ventricle	Size, function, structure
Pressure changes	End- diastolic pressure, pulmonary artery pressure (and wedge pressure), venous pressure
Neurohormonal changes	**Examples**
Sympathovagal invalence	Heart rate variability
Renina-angiotensina-aldosterona-system	BNP

BNP=B-type natriuretic peptide; ERP=effective refractory period

and impair left ventricular function. Optimal left side and atrio-ventricular (AV) and cross chamber sequencing are important for the proper systolic function of the heart . While relatively simple, these conduction parameters have not been examined as long term monitor of cardiac decompensation.

The initiating event of heart failure is most often systolic left ventricular dysfunction. This will affect the right and left ventricular size, and their systolic and diastolic function. There will also be an effect on the atria. Early recognition of these changes by monitoring may allow pharmacological or interventional approaches to reverse the changes before clinical heart failure develops. This opportunity may already present itself in a patient already implanted with a device such as a pacemaker in whom long term monitoring of heart failure may be possible.

However, the major immediate clinical consequence of heart failure is acute decompensated heart failure (ADHF). ADHF arises because of fluid overload (particularly in the lungs), and monitoring of pressure and volume status and appropriate therapy can prevent ADHF.

Finally, many neuro-hormonal changes result from the compensating mechanisms of heart failure. While not easily measurable directly, these changes may be reflected through heart rate variability and electrical repolarization such as the QT interval. This will be an interesting new area for monitoring and as a guide to therapy.

Sensors for Heart Failure

Sensors for rate adaptation can be classified according to the technical instrumentation. Table 2 summarizes the sensors that have been used for or proposed to monitor the events of heart failure. The paced QRS enables QT duration to be evaluated. In addition, the QRS width, measured as the ventricular depolarization gradient, had been proposed as a marker that is sensitive to catecholamines.[12] These sensors have long been used as surrogate markers of sympathetic level that increases with exercise, with a view to drive a rate augmentation. It is uncertain if they are also good markers of increase sympathetic tone that accompanies heart failure. These parameters are influenced by pacing rate, cardio-active medications and electrolytes that frequently occur in heart failure patients, making them unlikely to be robust sensors for heart failure. On the other hand, a high percentage of biventricular pacing is necessary to deliver a high dose of cardiac resynchronization therapy (CRT).[13] A low percentage of biventricular pacing may herald worsening of LV

Table 2. Sensor for monitoring heart failure

	Sensors	Parameters
Ventricular dysfunction or its triggers	Electrogram	Percentage of pacing ST segment AF Ventricular arrhythmias
	Intra-ventricular impedance	LV size and function
	Specialized lead	PEA to monitor LV function
Hemodynamic changes	Transthoracic impedance	Pulmonary edema
	Specialized leads	Minute ventilation PA pressures PA wedge pressures LA pressures
Clinical consequences	Electrogram	Paced QRS
	Piezoelectric	Paced QT Heart Rate variability Activity level

AF=atrial fibrillation; LA=left atrial; LV=left ventricle; PA=pulmonary artery; PEA=peak endocardial acceleration

function due to failure of adequate CRT, and is a good marker of heart failure decompensation. AF and ventricular tachyarrhythmias can either be a consequence or trigger event of heart failure that could be easily recognized and treated. Heart rate variability (HRV) can be measured in a non-pacing dependent patient, and is a well established prognostic marker of heart failure.[14] Reduction of heart rate variability antedates heart failure events. While percentage of biventricular pacing and HRV are rhythm diagnose rather than implantable sensors, they provide important indications of the prevailing heart failure status.

Piezoelectric crystals are used to monitor body motion. Decrease body activity is an intuitive consequence of heart failure exacerbation.

Impedance refers to low non-cardiac tissue stimulating alternating currents injected and recorded between pacing electrode pairs. When injected between a RV and LV leads, the lead configuration will encompass part of the LV, thus allowing intra-ventricular volumes and contractility to be measured. When injected between an intra-cardiac lead and the CIED casing, respiratory parameters such as respiratory rate and minute ventilation can be monitored, and these parameters are affected by dyspnea that occur in ADHF. This electrode configuration can also detect pulmonary fluid status, and may be a marker of pulmonary edema.

More direct measurements are now possible with pressure sensors instrumented in the RV, pulmonary artery (PA) or in the left atrium (LA). Worsening heart failure is associated with decreasing cardiac output, which the body compensates by increasing tissue oxygen uptake leading to a widening of arterio-venous oxygen difference. This is reflected by a reduction in the mixed venous oxygen saturation, which has been measured by implantable devices. As central hemodynamic changes are the precipitating events of ADHF, pressure sensors that measure LA, PA and RV pressures, have been studied and developed. Recent development and clinical applications of some of these sensors are summarized below.

Activity Monitoring

Kadhiresan et al[15] reported the use of externally attached accelerometers at the chest wall to monitor walking distance in heart failure patients. Using an acceleration

threshold of 50 mG, a walking speed of 2 mph (approximately=2.8 METS) can be detected in a group of 30 patients. The activity log index so defined was closely related to the walking distance of these patients, and was increased when patients were tested during CRT-on versus CRT-off phase. Similarly, time per day with physical activity greater than a threshold of 70 steps/minute was detected in an implanted accelerometer sensor,[16] and the activity level trended similarly to HRV trend during ADHF, and correlates with the NYHA class at baseline. While a crude index, activity sensing is a good reflection of general well being of a heart failure patient. It is a readily available sensor in most CIEDs, and uses minimal battery energy. In addition, the absence of activity usually signifies the patient is at rest, and allows other measurements such as respiratory parameters to be determined. The use of accelerometer rather than piezoelectric crystal avoids some of the external vibration interference on measuring body activity. An activity sensor is used in conjunction with other sensors for heart failure monitoring.

Heart Rate Variability

In patients with heart failure, neurohormonal activity predicts cardiovascular outcome. HRV is an indirect measure of autonomic tone, and predicts both sudden and non-sudden cardiac death.[17,18] HRV has been proposed not only to prognosticate heart failure severity, but also as a guide to treatment and perhaps predict ADHF.

In a randomized study of 50 patients with an implanted CRT,[19] HRV was measured in the atrial sensing mode (VDD at 30 bpm) in either the CRT-on or CRT-off mode. HRV, measured as the SD of atrial cycle length of all atrial sensed beats, was significantly higher in the CRT-on versus the CRT-off arm (25% higher) and when the patients were receiving betablocker (27% higher). There was no difference in the level of catecholamines measured in the study. The authors concluded that time-domain HRV was improved with CRT, likely reflecting changes in both sympathetic and parasympathetic activities with heart failure improvement.

In the Boston Scientific device, HRV is measured by the so-called SDANN. SD of the intrinsic intervals in the 288 five-minute segments of a day is measured, and averaged over a week. If the percentage of intrinsic beats is <67% for 24 hours, the data for that day is discarded. Using the SDANN in a cohort study of 113 heart failure patients with CRT, CRT resulted in a reduction in the ventricular heart rate, mean heart rate and an increase in SDANN (from 69±23 ms to 93±27 ms) after three months. Furthermore, lack of HRV improvement predicts non-responders to CRT.[20]

The HRV can be plotted at each heart rate over a twenty four hours period, resulting in a so-called "foot-print" in the Boston Scientific CRT devices (Figure 1).[21] The normalized size of the foot-print is termed the foot-print number, and the graph and number give an easy understanding of the level of HRV: "the larger the better". In another cohort study,[22] HRV using either the SDANN or foot-print predicts mortality in 842 patients implanted with CRT during a 11.8 months follow-up. A clinical score was derived based on a 2-week post implant diagnostic data: SDANN <43 ms, mean heart rate >74/bpm, foot-print number <29 and activity percent <5% from a 436 patient cohort in the CRT RENEWAL study.[23] Using this scoring system, patients could be triaged to a low, moderate and high risk group. When applied to a separate group of CRT recipients in the HF-HRV cohorts, this scoring system accurately predicted the level of mortality risk (low 2.8%, moderate 10.1% and high 13.4%) depending on tertiles of their score.

In the Medtronic device, a long term measure of HRV, the SD of a 5-minute median AS-AS interval (SDAAM) is used. The algorithm averages the 24-hour SD of intrinsic atrial cycle length, and will exclude the day's data if the percentage of atrial pacing exceed 80% or an atrial high rate episode (AHRE) are detected. The change in SDAAM is compared to a rolling average of the preceding 6 months. The SDAAM, night time heart rate and activity level were used to predict outcome and to detect HF hospitalization in a 397 patients cohort.[24] A SDAAM <50 ms predicts overall mortality, and the absolute value of SDAAM remains low in those who were either hospitalized or died. SDAAM declines from 76±27 ms to 64±26 ms at the time of hospitalization,

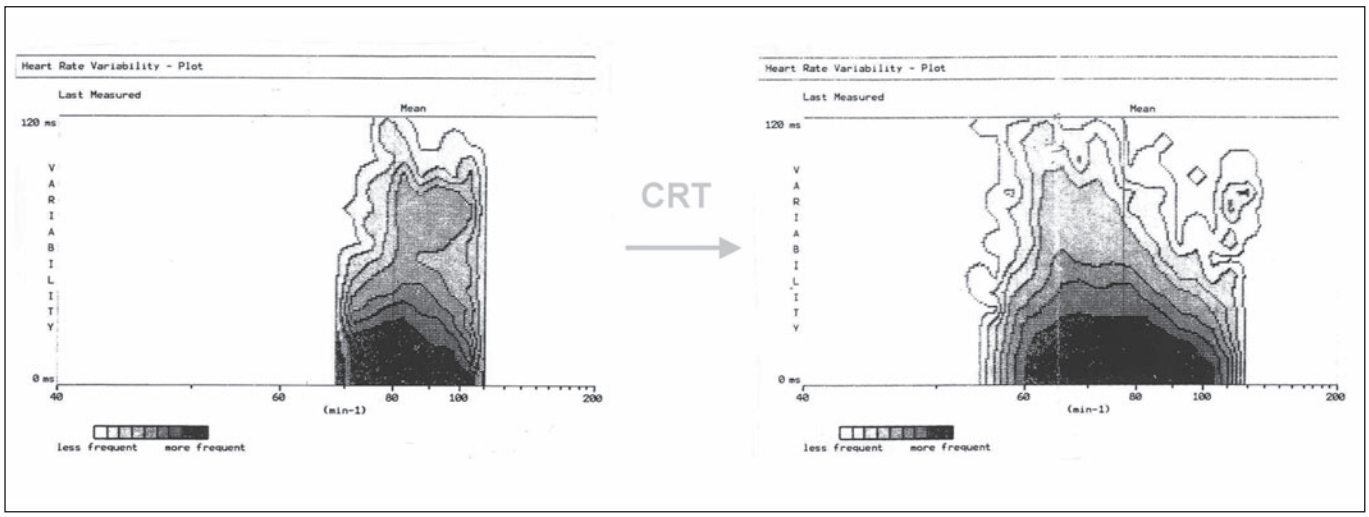

Figure 1. *Heart Rate Variability represented by "foot-print". In this patient, improvement of heart failure concurred with an increase in size of the foot-print after initiation of cardiac resynchronization therapy (CRT).*

and the change was apparent up to 3 weeks before the event. An algorithm was developed to use SDAAM to predict hospitalization. At a threshold of 200 ms days, a sensitivity rate of 70% was associated with 2.4 false-positive events per patient year of follow up, at a median of 16 days before the event. The sensitivity is not affected by the use of beta blockade. The SDAAM is significantly better than the night time heart rate and activity level change for predicting heart failure. These date suggest that autonomic surveillance such as the use of HRV is a good way to monitor both HF prognosis and to predict ADHF. HRV is limited when these are high percentage of atrial pacing and during atrial tachyarrhythmias, and medications may affect HRV measurements.

Percentage Biventricular Pacing

When CRT is used to treat patients with heart failure with a widened QRS complex on the ECG, it is expected that an adequate percentage of biventricular pacing will be needed to maximize the "dose" of resynchronization. In a cohort retrospective analysis of 2 heart failure trials involving CRT-D's (1,812 patients), Koplan et al[13] analyzed the relationship between the percentage of biventricular pacing and the outcome of death and heart failure hospitalization. The mean age of the patients was 72±11 years, 72% were men and 67% had ischemic cardiomyopathy. When subjects were divided into quartiles, there was a lower event rate with an increasing percentage of biventricular pacing. In particular, there was a 44% reduction in event rates in those paced 100% of the time versus those paced less than 92%, and even subjects paced 93-97% had a higher event rate compared to those paced between 98-99% (22% higher mortality). The main reason for an inadequate percentage of pacing was atrial arrhythmias. Thus a high percentage of biventricular pacing of ≥98% is an important goal to achieve in patients with CRT (Figure 2).

A low percentage of biventricular pacing is particular the problem in those with AF, especially when permanent. Because of frequent intrinsic conduction and fusion beats in AF, a high percentage of biventricular pacing may still not reflect the percentage of true mechanically synchronized beats. In one study on 19 patients with permanent AF with diagnostic counters showing >90% biventricular pacing,[25] 12 lead Holter System was used to monitor 'true' complete biventricular capture using a template matching system. Only 9/19 (47%) had adequate complete biventricular pacing, the remaining had either fusion or pseudo-fusion beats. Patients with 86.4±17.1% full capture had ≥1 NYHA Class

improvement than those fully captured at 66.8±19.1% of the time. This study suggests careful evaluation of the percentage of biventricular pacing using multiple surface ECG lead will be needed in those with AF and conducted response, and sensor to detect full biventricular capture will be an interesting development.

Right Ventricular Pressure

PA pressure and PAWP monitoring have been shown to be effective for tailored therapy in patients admitted with advanced heart failure.[26] Early attempts have been made to continuously record PA pressure on an ambulatory basis.[27,28] An implantable sensor that measures pressure has been incorporated into a pacing electrode with an initial application for rate adaptive pacing.[29] This sensor is a hermetically sealed piezoelectric crystal with a diaphragm facing the blood stream. Early experiences have shown the ability to continuously record RV pressure by connecting this electrode to an implanted hemodynamic monitor.[30,31]

The Medtronic Chronicle IHM (Model 9520) is a non-pacing implantable pulse generator capable of

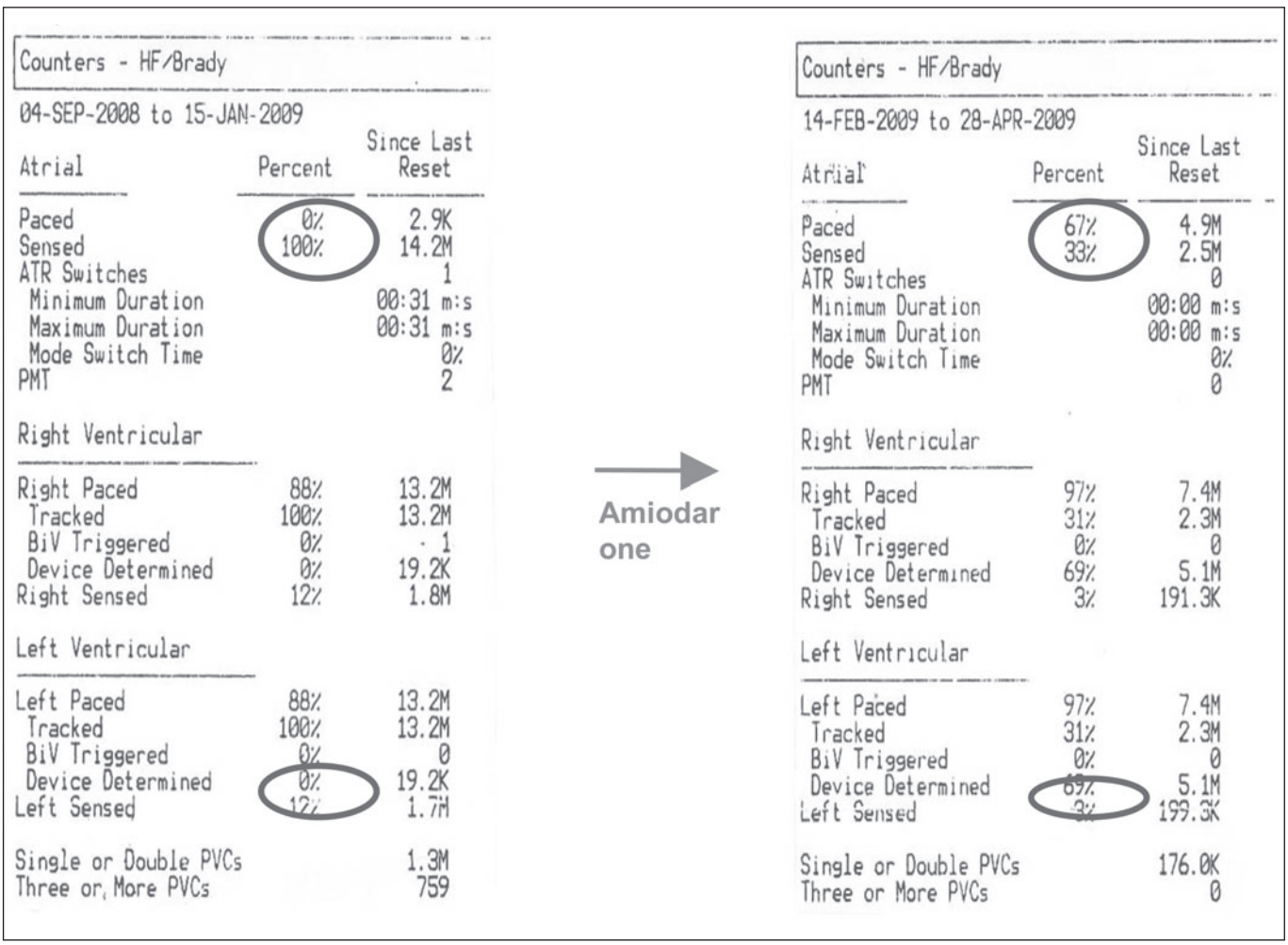

Figure 2. *Optimization of Biventricular pacing. This patient had an initial response to cardiac resynchronization therapy (CRT), but developed heart failure associated with a reduction of left ventricular pacing to 88%. This was found to be due to frequent ventricular ectopics interfering with CRT. Prescription of amiodarone suppresses ectopics, and resulted in a 97% biventricular pacing (and 67% atrial pacing) and significant clinical improvement.*

external radiofrequency connection and integration in a web-based system. It has a 128 kb of RAM for continuous storage of sensor data. Piezoelectric activity from a passively fixed lead in the RV outflow tract is sampled up to once every 2 seconds, timed to the sensed unipolar RV electrogram. The sensor frequency is linear up to 100 Hz, and a 60 Hz high pass filter is used. The frequency and timing of RV systolic pressure sampling are programmable, and often at early morning when the subject is likely to be supine and rested. In addition, high resolution recording can be made using an external triggering device. RV pressures (systolic, diastolic and dp/dt) were recorded, and RVSP reflects PA systolic pressure. A prior work[32] has assessed the ability to estimate PA diastolic pressure which occurs at the time of pulmonic valve opening. This is estimated at the time of the maximum positive RV dp/dt. Pre-implant calibration pressure is required to allow absolute pressure measurement. An external barometric pressure measurement device provides external pressure reference against which sensor data can be subtracted.

Feasibility Study

The long term stability of the pressure sensor has been previously reported. In one study,[33] serial Swan-Ganz catheterizations at 3, 6 and 12 months post implant showed a small baseline error at 12 months of <1 mm Hg from the time of implantation. Furthermore, the accuracy of pressure measured is not affected by body posture. Adamson et al[4] studied 32 patients with heart failure who received a Chronicle IHM. They found that long term RV pressure was stable in most patients. However, in certain subjects, it showed significant variability despite measurements were taken at 4 am with no activity level registered. During a total of 36 volume-overloaded events, RV systolic pressure increased by 25±4%, heart rate by 11±2% and estimated PA diastolic pressure rose 26±4%. In all events, pressures were increased one day before the required clinical intervention. In patients with heart failure hospitalization, increases in one of the pressures occurred in 9/12 events, whereas this occurred in 9/24 patients during a non-hospitalized episode. During a volume depleted state in 7 patients, RV pressure parameters were reduced. All patients returned to baseline levels after therapeutic intervention. The authors further proposed a sustained increase in one of the pressures (>20% from baseline) may occur in patients subsequently admitted, at a mean of 4.2 days before admission. When the device data were available to the monitoring physician, a reduction in heart failure hospitalization was subsequently observed. This important study also documents the time sequence of RV pressure changes that occurred before heart failure exacerbation, suggesting that pressures (and very possibly also volume) build up may occur for several days and reduce the patient's "tolerable reserve", before the final increase in pressures that lead to clinical heart failure exacerbation. In a further study, Zile et al[34] compared the ongoing RV hemodynamics between systolic and diastolic heart failure patients during heart failure events. They found RV diastolic pressure to be elevated in both conditions, although there was a trend for more rapid RV diastolic pressure elevation to occur in diastolic heart failure with less compliable ventricle than during systolic heart failure. Thus quite aside from monitoring heart failure for intervention, the implantable pressure device enables an understanding of heart failure pathophysiology that was not possible before.

Clinical Outcome Study

The COMPASS – HF (Chronicle Offers Management to Patients with Advanced Signs and Symptoms of Heart Failure) Study[35] prospectively randomized 274 NYHA Class III or IV heart failure patients into conventional care group or therapy guided in addition by Chronicle derived RV pressure parameters. The two safety endpoints documented no pressure sensor failure and 8% implanted system complications. During a follow up of 6 months, there was a statistically insignificant trend for reduction of either heart failure hospitalization or the need of intravenous diuretics (primary endpoint) by 21%. A post-hoc analysis showed a 36% prolongation in time to the final heart failure-related hospitalization in the Chronicle-guided treatment group.

As suggested by the authors, the lack of significance observed in the primary efficacy endpoint may be due to the lower than expected number of heart failure events (predicted 1.2/6 patient-month; actual

0.85/6 patient-month), thus decreasing the power of the study. The lower event rate may be due to enrollment in highly specialized centres in which there was high compliance of evidence based heart failure treatment. Importantly, Chronicle guided therapy resulted in 54% more adjustment in diuretic doses, without an increase risk in hypovolemic related heart failure events. At the time of study, patient transmitted Chronicle data at least once per week. It is arguable if a more frequent transmission such as in a remote patient monitoring system may further contribute to reduction in ADHF. As mentioned above, the study also includes 70/274 patients with diastolic heart failure patients, A subgroup analysis[36] found a 20% non-significant reduction in heart failure events when diastolic heart failure patients were managed occurred with Chronicle-guided information. This will be of interest in future larger trials to prevent heart failure in diastolic heart failure which has few proven therapies.

Other Pressure Sensors

Left Atrial Sensor

PA diastolic pressure is an indirect assessment of the filling LV pressure, and measurement of LA pressure may reflect an earlier pressure change that triggers pulmonary congestion. This may allow a longer time window for physician intervention to avert ADHF.

The HeartPOD LA pressure monitoring device (St Jude Medical Inc) comprises an implantable sensor lead that is attached to a coil antenna for telemetry of sensor signals. The sensor is a pressure sensor with a titanium pressure sensing membrane of 3 x 7 mm. It is capable of high fidelity pressure, temperature and electrogram measurement. An external patient advisory module (PAM) sends a 125 KHz radiofrequency transmission to the antenna, which then captures a 20 second sensor data. The PAM has a 13 Mb of memory, and can store about 3 months' data of 6 recordings per day.

In a feasibility study in a single centre,[37] 8 patients received the LA pressure device using a transeptal approach from the femoral vein. Venous entry at 1 cm above the inguinal ligament was achieved guided by a guide wire introduced in the conventional manner in the femoral vein below the inguinal ligament. After standard transeptal puncture, an II F sheath was placed in the LA, and the sensor was deployed until the distal set of anchor was on the left side of the atrial system. The sheath was then removed, and the sensor membrane was positioned 1-2 mm on the left atrial septum. All patients received dual antiplatelet therapy for 6 months (aspirin 160 mg and clopidogrel 75 mg per day). The device was calibrated overtime using a Valsalva maneuver technique during which the expiratory pressure as measured by the PAM will equate to the LA pressure. Over a period of 6 months, the net drift was 0.2±1.9 mmHg per month, although in 1 patient the drift was much more. The authors commented on the need to maintain the sensor orthogonal to the septum to avoid distortion of LA pressure waveform.

The Hemodynamically Guided Home Self-Therapy in Severe Heart Failure Patient (HOMEOSTASIS) trial enrolled 40 patients with Class III to IV HF.[38] All patients received LA pressure device successfully, although sensor failure occurred in 4 patients, which was subsequently replaced in 3. The study started after a 3 months run in period in which heart failure hospitalization and related events, and medication dosages were documented. Thereafter, LA pressure data were disclosed to the patients, who in conjunction with the physician, adjust the dosages of diuretics. Survival without heart failure events occurred in 61% at 3 years. Mean daily LA pressure therapy resulted in a fall of LA pressure (17.6 mmHg to 14.8 mmHg), reduction in elevated LA pressure frequency (events >25 mmHg by 67%), and better NYHA Class, LVEF, and more frequent up-titration of angiotensin converting enzyme inhibitors and reduction in diuretic dosages. This titration was effected by the patients themselves using a regimen advised by the digital assistant machine that interrogate the device on a daily basis.

The HOMEOSTASIS trial is an interesting observational study in which LA pressure parameter is treated similarly to blood glucose parameters in a diabetic patient, in which self adjustment of dosages of diuretics may maintain an euvolemic state. Thus the possibility of reduced clinical events may be due to up-

titration of angiotensin converting enzyme inhibition by reducing the dose of diuretics if LA pressure is low. Conversely, when LA pressure increases, increasing the dose of diuretics would enable a larger dose of beta blockers to be given. As a result the target doses of both drugs were achieved in 54% of patients compared to only 27% at baseline.

The LA pressure sensor is an interesting concept and will require to be confirmed in prospective randomized trials. At present, there remains the issue of sensor stability, ease of implant (subclavian implant tools are now available), and the risk of thromboembolism (which is probably low similar to occluder for closing atrial septal defect).

Pulmonary Arterial Pressure Sensors

A PA pressure transducer (Champion, CardioMENS, Atlanta, GA USA) has been developed.[39] The preliminary results of a 550 Class III heart failure trial has been recently reported. Patients were either randomized to PA pressure guided therapy versus conventional care, and a 30% relative risk reduction was observed. The trial has not reported any significant safety issues.

Intrathoracic Impedance for Pulmonary Fluid Status

Dyspnea is the commonest presenting symptoms for ADHF, and congestion or edema are the main underlying mechanisms for dyspnea. Increase in fluid in the lungs will decrease the transthoracic impedance which can now be measured with an implantable device.

Device Description

The concept of impedance to monitor pulmonary congestion is based on a canine experiment by Wang et al.[40] The Medtronic Optivol™ fluid management system uses transthoracic impedance to measure pulmonary fluid. Low voltage, non-stimulating currents are injected between RV ICD electrode (e.g. InSyn Sentry) or RV bipolar electrode (e.g. Advisa) to the ICD or pacemaker casing between noon and 5 pm, at a time when the subject is presumably ambulant and upright. A sampling over every 20 patients is made and averaged. The moving average of the impedance used to establish a baseline impedance level against which any change can be compared. The algorithm is inactive for the first 34 days after device implantation to allow time for post-implant pocket healing and electrode stabilization. When pulmonary fluid has accumulated beyond a programmable threshold, an alarm will be used to alert the patient (or the physician via remote monitoring). (Figure 3)

Feasibility Studies

The feasibility of using intrathoracic impedance to monitor fluid status has been tested in 34 patients with NYHA Class III or IV heart failure in the MID-Heft Study.[5] A defibrillation lead in the RV apex is connected to a special pacemaker capable of injecting and sourcing impedance. Three impedance current vectors were tested: RV lead ring to device case and sampled from coil to device case; RV coil to device case and sampled from RV coil to device case; RV ring electrode to device case and sampled from RV tip electrode to device case. The electrode pairs that use RV coil to device case has been found to be most suitable. An initial decrease in impedance followed by an increase to steady state is observed during pocket healing, which peaks by about 4 weeks.

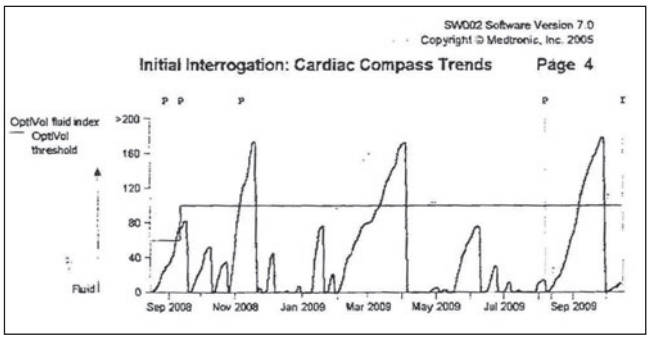

Figure 3. *Recurrent heart failure episodes in a patient with dilated cardiomyopathy, as documented by impedance recoding of pulmonary fluid index (Medtronic Optivol). A threshold of 60 Ω. day was found to be unspecific to detect fluid overload. Fluid index exceeding 100 Ω. day was used and correctly identified clinical (and BNP confirmed) heart failure episodes.*

During a follow up of 20±8.4 months, 25 adjudicated heart failure hospitalization occurred in 10 patients. Intrathoracic impedance started to decrease before worsening symptoms at 15.3±10.6 days, whereas dyspnea was only reported at the earliest 3 days before hospitalization. During 17 hospitalizations, pulmonary capillary wedge pressure was found to significantly correlated with impedance ($r=-0.61$, $p<0.001$), and impedance increased as fluid removal occurred with dieresis.

An algorithm for heart failure detection was derived from 6.2 patient-years of monitoring from 10 patients, and tested in the remaining cohort. Depending on the set threshold for impedance crossing, a receiver operator curve was constructed. Lower detection thresholds lead to higher sensitivity to detect ADHF but also a higher false positive rate of detection. Conversely, a higher threshold will be more specific but may under-detect some ADHF events. A 60 Ω. day was suggested to give a sensitivity of 76.9% at the expense of 1.5 false-positives per patient-year of monitoring. Early warning occurred at 13.4±6.2 days of heart failure hospitalization event. This landmark study shows that intrathoracic impedance is correlated with pulmonary congestion, and changes in a predicted way as dieresis occurs, allowing its use for acute monitoring. Furthermore, the impedance changes days before ADHF and suggests its role to monitor heart failure on an ambulatory basis.

Clinical Outcome Studies

The impact of automatic Optivol alert to guide therapy was observed in 532 heart failure patients in the Italian Optivol Study.[41] With the Optivol heart failure alert on, a 67% detection of heart failure that required either hospitalization or therapy adjustment were detected. Interestingly, of the remaining patients in whom Optivol alert was inactivated, heart failure hospitalization was significantly higher (20% vs 7%). The study also showed a false positive detection rate of 0.5 per patient-year of follow up.

While impedance monitoring from RV coil to device case monitors lung edema, measurement of RV and LV lead vectors (for lead integrity) may be able to assess LV volumes better. In an interesting study on 170 patients, with 43 being replacements, Maines et al[42] showed that a 12-week maturation period was required for the pocket and the leads occurred in the de-novo implants. However, a similar, albeit stabilizing earlier, adaptation was still required for replacement group, suggesting the adaptation is in part due to the leads or algorithm itself. Interestingly, using the RV-LV impedance vectors, this study suggests that there are significantly difference in impedance measured in the volume responder versus non-responder groups, with a higher biventricularly measured impedance in the responders This suggests the role of impedance to tract responders to CRT.

The ability of Optivol to reflect heart failure outcome has been examined in several cohort studies. In a multi-centre studies of 558 heart failure with In Sync Sentry from 34 Italian centres, device recorded Optivol fluid index above 60 Ω. day was associated with a 36% increased risk heart failure hospitalization over a 326±216 days of follow up.[43] Multivariate analysis showed that in addition to Optivol level, a higher percentage of days with low activity, low HRV and increased night time heart rate were independent predictions of hospitalization. In 62 patients with Optivol algorithm, prospective observational measurements of NT-pro BNP, clinical heart failure status were collected over 27±2 weeks.[44] There was a significant but weak relationship in all pooled change in impedance and change in NT-Pro-BNP level over all the visits ($r=0.30$, $p<0.001$). However, NT-Pro-BNP level increased significantly when an Optivol alert is associated with clinical signs of ADHF (89±25% increase) versus an insignificant increase in those without signs (25% increase). In patients with an alert, NT-Pro-BNP increase by >10% in most incidents. By the time of patient medical visit, impedance continued to fall suggesting worsening heart failure status. In 42% of cases, a device alert was not related to clinical signs of heart failure, although BNP on the whole increased significantly by 25% in these patients. Several explanations are proposed, including improvement of medication/dietary compliance by the patients due to the alert, signs of heart failure may be less sensitive than objective monitoring, or true false detection by the Optivol. Nevertheless, the higher BNP level related to Optivol alert means that heart failure prognosis will be

affected when Optivol threshold crossing occurred.

The usefulness of Optivol to prevent heart failure was reported in a single centre case control study in which 27 patients with Insyn Sentry was compared to clinically similar group of 27 patients with CRT-D without Optivol.[45] 12/27 patients had Optivol alerts, resulting in intervention. Hospitalization occurred in only 1/27 over a year of follow up. In contrast, 7/27 patients had heart failure hospitalization in the controlled patients treated with conventional CRT-D without the Optivol algorithm. When coupled with remote patient monitoring (Medtronic Carelink), 20/28 (71%) Optivol alerts in 67 patients can be remotely managed.[46] The temporal relationship between arrhythmias and Optivol measured fluid level has been reported. In one study,[47] Optivol threshold crossing >60 Ω. day was related to a higher risk of occurrence of AF. AT occurred in 43% before or 29% after Optivol level crossing. This relationship was not observed in another study.[48] However, the latter study showed a higher prevalence of VT/VF at lower level of Optivol 15-45 Ω. day, suggest VT/VF occurred at a time of fluid index crossing. The ability of fluid index to predict arrhythmias required further study.

Algorithm Considerations

Small et al[49] examined in a prospective cohort of 326 patients with InSyn Sentry followed up for nearly a year. In the first 4 months (observational period), threshold crossing at the nominal 60 Ω. day occurred in 17 patients (22 ADHF episodes). The occurrence of threshold crossing predicted a 35% increase in hospitalization in the subsequent period. Furthermore, the following are predictive of hospitalization: >3 threshold crossing per year or >30 days threshold crossing per year. When a multivariate analysis was applied, only night time heart rate remained predictive of ADHF in addition to Optivol threshold crossing. Thus not only the threshold crossing but the duration in which Optivol threshold above the programmed threshold are predictive of heart failure hospitalization.

The threshold for Optivol alert has also been tested in 115 patients implanted with Medtronic InSyn Sentry CRT-D.[50] During a follow up of 9±5 months, 45 Optivol alerts occurred in 30 patients. Fifteen alerts (33%) were correlated with clinical signs and symptoms of heart failure, and the authors suggested an increase of threshold to 90 Ω. day may increase the specificity to 73%. The authors did not find any causes for false positive alerts, but patients with heart failure had significantly higher Optivol level versus those without. On the other hand, in the European InSyn Sentry Observational Study on 373 subjects,[51] the level of 60 Ω. day was associated with a 60% sensitivity and 60% positive prediction of ADHF. This study documented 9/53 (17%) events were not associated with an Optivol alert, and in an additional 11 events, an increase in Optivol level occurred but did not exceed the programmed detection threshold. These studies confirm the usefulness of intrathoracic impedance to monitor ADHF, but pointed out the need of fine tuning of detection algorithm and/or individual programming of Optivol detection level.

The SENSE-HF study is a prospective trial to assess the sensitivity and positive predictive value of implantable intrathoracic impedance to predict heart failure hospitalization.[52] The study is of 3 phases. Phase I is a double blind phase in which retrospective analysis of Optivol algorithm in predicting ADHF is evaluated. In Phase II which takes place after 6 months in Phase I, the device alarm is used to identify ADHF. When this happens, the patients enter Phase III in which the utilization of Optivol level is assessed prospectively in averting ADHF and hospital resource utilization. The recruitment has been completed in 2008.

Advantages and Limitations

Intrathoracic impedance to monitor heart failure is one of the most extensively used sensors for monitoring heart failure. The advantages of this sensor is the relative ease of instrumentation, requiring no additional leads or complexity of implantation. The battery energy expenditure is low. It has been relatively well characterized in acute setting and for long term monitoring. While sensitive, its specificity may be limited as impedance in the vector used may be liable to be affected by a number of clinical events that do not indicate pulmonary congestion, such as the occurrence of pleural effusion (Table 3).[53] However, some of the Optivol alert without clinical evidence of heart failure

might represent clinical resolution of heart failure due to delayed presentation, subclinical congestion in addition to being false positive. Nevertheless, when combined with other sensors, intrathoracic impedance is useful for long term and acute monitoring of heart failure (see below).

Intracardiac Impedance

Impedance signal derived from fully intracardiac electrodes gives better reflection of volume changes of the heart than transthoracic impedance. Indeed, Salo et al[54] reported the use of a tripolar RV lead to measure RV volume changes during cardiac cycle, from which RV volume and contractility can be derived for rate adaptive pacing. With the addition of a LV lead in CRT, more accurate measurement of LV volume is now possible for heart failure monitoring.

Unipolar Impedance from Right Ventricle

Unipolar impedance injected from the RV apex to the CIED casing samples a small region in the cardiac apex. This results in a signal that has been termed closed loop stimulation (CLS) sensor (see above). As the majority of the current is lost over a distance of about 1 cm from the apex, the signal reflects regional contractility of the ventricle rather than reflecting a change in stroke volume. Likewise, during acute induction of ventricular fibrillation, the fall in unipolar RV impedance reflects the fall in arterial pressure. However, the sensitivity is not enough to discriminate between hemodynamically stable ventricular tachycardia and supraventricular tachycardia.[55] These results suggest that unipolar impedance reflects LV contractility only when the changes are significantly gross, and may not be able to detect small changes in cardiac contractility as in heart failure monitoring.

Table 3. Possible causes of increase in optivol fluid index in the absence of pulmonary congestions

Mechanism	Examples
Blood viscosity	Anemia
Extra-pulmonary changes	Pleural effusion Pneumothoracic
Right sided heart failure	Peripheral edema not detected
Pulmonary changes	Pneumonia

Multipolar Impedance

Several groups and manufacturers have investigated on the optimal electrode arrangement for detecting ventricular volumes. With currents flowing between intracardiac electrodes (RV, LV and RA) and to the CIED casing, enlargement in ventricular volumes will decrease impedance as more of the heart is encompassed. Four intrathoracic and 2 intracardiac vectors were examined in 16 dogs and 5 sheep.[56] Cardiac function was monitored by biweekly cardiac catheterization and echocardiography, and LA pressure by an implantable LA pressure monitor. After several weeks of high rate pacing to induce heart failure, there was significant fall in ejection fraction (52 to 34%), increase in LV end diastolic volume (65 to 97 ml), RV end diastolic volume (7 to 16 mmHg) and LA pressure (7 to 26 mmHg). Impedance value measured by all vectors decreased with the onset of heart failure, with the maximum decrease occurring with LV-Can and LV-RV. Importantly, LV-Can impedance changes more with heart failure than vectors involving the right heart electrodes (RA-Can, RV-Can and RV Coil-Can), and RV-LV and LV-RA changes were intermediate. LA pressure correlated best with LV-Can impedance (r^2=0.73) than RV-Can (r^2=0.43) and RV Coil-Can (r^2=0.52). Circadian variation in impedance also decreased in heart failure (5±2 to 2±1%). Thus in these animals models, incorporation of a LV vector significantly improve the detection of LV volume increase that occurred in heart failure.

Biventricularly by measured impedance has been measured using a quadripolar electrode arrangement.[57,58] In 9 mini-pigs with pacing induced heart failure,[58] biphasic pulses (15 μs pulse width, 600 μA constant current amplitude) were injected between the RV ring and tip electrode, and impedance was sourced using the LV ring and tip electrode. The impedance signal (measured as voltage divided by 600 μA current) was

recorded using a resolution of 8 bits, and the mean impedance was calculated over the entire cardiac cycle. "Stroke impedance" was calculated by the difference between impedance values during systole and diastole. Systolic impedance was defined as the highest impedance 50-500 ms after the R-wave, whereas diastolic impedance was measured by a 20 ms window within the R-wave. After 20 days of heart failure induction by rapid pacing in these animals, the increase in LV end diastolic pressure was found to be significantly correlated with the end diastolic impedance, which decreased by 30% ($r=-0.81$, $p<0.001$). End-diastolic volume also trended in the same direction as the impedance value which decreased by 20%. The corresponding measured intrathoracic impedance decreased by 8%, which had a poorer correlation with the end diastolic pressure. The less striking change of intrathoracic impedance versus biventricularly measured impedance might be attributed to countering effect of lead device casing maturation which did not occur with biventricular impedance, and the fact that pulmonary fluid collection was relatively less in the mild heart failure model studied.

These animal experiments suggest that biventricular impedance can be used to monitor LV size and pressure changes that occur with heart failure. The theoretical advantage over transthoracic impedance are that there will not be significant time lag for lead / pocket maturation, and no influence of changes in pulmonary condition such as pleural effusion and pneumonia. As elevation of LV end diastolic pressure occurs earlier than pulmonary edema, this sensor can be used to detect deterioration of early heart failure which has not resulted in significant pulmonary fluid accumulation, and indeed used for monitoring LV function. The limitations include the need of an LV lead (which restricts its use in a CRT device), dependence on the relative position of RV-LV leads (only relative changes rather than absolute value can be detected), and significant diurnal (and possible postural) changes that need to be accounted for in an implantable system.

Clinical Studies

An acute study on biventricularly measured impedance in 14 heart failure patients during implantation of CRT devices was reported.[59] The authors also tested the effect of different LV lead locations on biventricular impedance measurements, changes in stroke volume were induced with overdrive pacing. During a study of 20 overdrive pacing episodes and 6 different lead locations, the pooled data showed good correlation between measured stroke impedance with stroke volume ($r=0.82\pm0.10$) and pulse pressure ($r=0.81\pm0.16$). the authors reported no significant effect of LV lead positions but the accuracy and signal sizes tend to be the best in the mid-ventricular region compared to either the basal and apical regions. There was one outlier in the study, and lack of lead fixation was suggested.

At present, there is lack of data on long term implant. The relative merits and limitations of intrathoracic and intracardiac impedance are summarized in Table 4. In patients with a suitable device (i.e. with an LV lead), it is very likely that a combined transthoracic and biventricular impedance can be used.

Minute Ventilation

Dual sensor pacemakers encompassing activity and minute ventilation have been available for rate adaptive pacing. Heart failure leads to compensatory hyperventilation especially in the resting state. An expert system has been tested to examine the combined activity and minute ventilation (MV) to predict heart failure.[60] The algorithm includes:- (1) mean daily resting and MV during activity; (2) mean daily activity level. A stable MV and activity level will suggest stable clinical heart failure, whereas an increase in MV especially at rest and combined with decrease in activity suggests deteriorating heart failure. Conversely, a stable MV level with increase in activity indicates recovery from heart failure. Nineteen patients with no history of heart failure receiving Talert™ (Sorin-ELA, Italy), were compared with 48 patients with Talent CRT with heart failure. Wide inter-individual and intra-individual variability occurred, and a fast Fourier transformed data allowed 7-day periodicity to be accounted for. While mean activity was similar, the resting and activity MV levels were higher in the CRT group. Overall, it was reported that the expert system allowed a sensitivity of 88%, specificity of 94.7%, positive predictive value of 71%

Table 4. Relative merits of intrathoracic versus biventricular impedance to monitoring pulmonary edema

	Intrathoracic impedance	Biventricular impedance
Heart failure parameters	Pulmonary edema	LV volume
Electrode arrangement	RV lead or coil to casing (tripolar)	RV-LV bipoles (Quadripolar)
Lead/casing maturation	Takes up to 1 month	Less
Influence of lung disease	Yes	Less
Influence of lead location	Less	Significant
Circadian & postural effect	Yes	Yes
Sensitivity & specificity	~70% (depends on threshold)	N/A
Applicability	Pacemakers and ICD	CRT-P or CRT-D
Clinical evaluations	Relatively extensive	Limited

and negative predictive value of 98.2% for heart failure.

ST-Segment Shift

ST segment deviation either heralds ischemia or myocardial injury. Myocardial ischemia requires medical therapy or revascularisation, especially in symptomatic individuals. Myocardial injury, on the other, is a medical emergency that calls for emergency reperfusion. Prompt treatment of a myocardial infarction will significantly reduce mortality. Delay in recognition by the patient of chest pain due to infarct (and in some instances silent infarct) is a significant contribution to delay presentation of myocardial infarction.[61] As long term external ambulatory ECG recording is unlikely to be practical, intracardiac electrograms have been tested and proposed to reflect infarct and ischemia in an animal model.[62] When incorporated into a CIED with patient alert and remote monitoring, ST segment monitoring becomes a possibility.

The Angel Med Guardian (now under St Jude Medical) is a single chamber device with a RV apical lead. An intracardiac electrogram (ICEG) was derived from RV apex to the device casing. The device records a 10s ICEG data once every 90s for normal sinus beat within 50 - 90 bpm. Data are amplified with a gain of 62.5 - 625 times and band passed between 0.25 to 45 Hz, followed by A/D conversion at 200 Hz. ST segment level is compared to the corresponding PQ segment level, and a baseline ST segment level is calculated as a rolling 24-hour average which are acquired hourly. The extent of the deviation is normalized by the average R-wave voltage. The "normalcy" of ST segment deviation at different heart rates is further tested during an exercise, as ST shifts tend to occur at different heart rates in the absence of ischemia. A rate adjusted spontaneous ST deviation will then be considered as an ischemic events and an alert will be triggered.

A limited number of devices have been implanted in humans.[63] During angioplasty with temporary coronary artery occlusions, ST segment deviations occurred, with a negative shift during left anterior descending artery occlusion, and a positive shift in other arteries. Ten abnormal alerts occurred in 6 patients, leading to coronary artery interventions. During stress testing, the ICEG showed much cleaner signal and bigger shift than the corresponding surface ECG. Typically a 40% ST depression in ICEG corresponds to -0.8 mV on the surface ECG. As the ICEG is recorded at the RV apex closed to the left anterior descending territory, ischemia in this artery leads to ST depression, whereas ischemia in other territories results in a reciprocal ST elevation. Further work will be required to explore the ability of ST segment sensor to detect the culprit artery.

The ST segment sensor is an interesting sensor for ischemia. In addition to ischemic detection, the relationship of ST deviation and occurrence of arrhythmia such as ventricular tachycardia may shed

light on the ischemic cause of arrhythmia. Quite aside from the logistic implication of ST segment monitoring [which requires urgent intervention], ST segment monitor will be possible only for non-pacemaker dependent patient. The influence of medications, electrolytes and heart rate on ST segment needs further evaluation.

Peak Endocardial Acceleration

Peak Endocardial Acceleration (PEA) sensor has been used for rate adaptation. The PEA signal measures the closure sound of the mitral valve, and reflects cardiac contractility. A minimal PEA signal occurs during optimal AV interval in DDD devices,[64] and reflects the optimal AV interval in most patients. A new CRT-P (The New Living™ CHF, Sorin-Ela, Italy) is now available to monitor heart function and to program AV interval in CRT device. The PEA is contributed by both the contractility and LV filling and an index known as PEA area is derived by measuring the PEA values at different AV interval scanning at each VV interval. The maximum PEA area will define the optimal VV and AV interval for the patient.

In 15 patients implanted with CRT with PEA sensor, cardiac catheterization with LV dp/dt was measured with PEA area determined.[65] AV interval was scanned between 60 and 220 ms. The authors found a responder rate to CRT (defined by 10% increase in dp/dt) in 75% of patients. Concordance of PEA area versus dp/dt methods occurred in 8/12 patients. These data are interesting, although the role of AV interval programming on the long term is uncertain, and the ability of the sensor to monitor LV function remains to be tested.

Combined Heart Failure Diagnostics

The PARTNERS HF (Program to Access and Review Trending Information and Evaluate Correlation to Symptoms in Patients with Heart Failure) study is an observational study on the use of diagnostics to predict heart failure.[66] 100 sites in the US prospectively recruited 694 CRT-D patients and followed them for 11.7+2 months. Table 5 shows the diagnostic data considered important in an algorithm to predict ADHF. A positive algorithm was defined as the occurrence of

Table 5. Eight heart failure device diagnostic parameters and algorithms used to predict heart failure in the COMPASS-HF study

HF device diagnostic parameter	Algorithm
AF duration	AF ≥6 hours on at least 1 day in patients without persistent AF (7 consecutive days with ≥23 hours AF)
Ventricular rate during AF	AF ≥24 hours and the average ventricular rate during AF ≥90 beats/min on at least 1 day
Fluid index (OptiVol)	High fluid index on at least 1 day; thresholds included ≥60, ≥80, and ≥100 Ω. day
Patient activity	Mean patient activity <1 hour over 1 week
Night heart rate	Mean night heart time rate >85 beats/min for 7 consecutive days
HRV	HRV <60 ms everyday for 1 week (minimum 5 measured days)
% of biventricular pacing	Ventricular pacing ≤90% for 5 of 7 days
ICD shock for potentially lethal VT/VF	≥1 shocks during the evaluation period

AF=atrial fibrillation; AT/AF=atrial tachycardia/atrial fibrillation; CRT=cardiac resynchronization therapy; HF=heart failure; HRV=heart rate variability; ICD=implantable cardioverter-defibrillator; VT/VF=ventricular tachycardia/ ventricular fibrillation.

22/8 variables during a 1-month period that include: Long AF duration, rapid AF rate, increase Optivol fluid index, low patient activity, abnormal automonic tone, or device therapy. A very high Optivol fluid level (>100) is considered ADHF.

Ninety patients had 141 adjudicated heart failure events, occurring after 60 days of implantation. A positive combined diagnostic set predicts a 5.5 fold risk of hospitalization in the next month, even after adjusting for the clinical variables. The main diagnostic parameters are Optivol ≥60 Ω. day, low activity and HRV. When additional Optivol ≥100 (28% of patients), it is also predictive of ADHF. Further sub-group analysis suggests that the specificity of ADHF is improved with setting a higher level of fluid index, and using more non-fluid related indices at the expense of loss of specificity. Interestingly, in patients with a prior history of heart failure, diagnostic parameters are no longer predictive. There is an improvement of diagnostic accuracy if sampling is performed every 15 days versus less frequently. Whether closer monitoring with the use of remote web based system can further reduce ADHF remains to be tested. Using externally measured parameters such as Weight Monitoring in Heart Failure[67] and/or blood pressure (SPAW CHF II),[68] benefit of monitoring was not observed in the former but occurred in the later study. In the first study, patients were recruited right after a heart failure hospitalization. The authors suggest that the role of diagnostic data in repeat heart failure hospitalization may be less than inpatients without prior hospitalization.

The PARTNERS HF is an important study suggesting the role of combined heart failure diagnostics to predict ADHF. While the sensitivity and specificity of the algorithm needs to be tested in prospective randomized trials, the occurrence of positive diagnostic criteria are predictive of a group of high risk heart failure patient. Conversely, the absence of diagnostic alerts predict a stable heart failure group. This risk stratification is over and above the conventional clinical risk factors.

Conclusion

Sensors have been introduced to optimize pacing rate in patients with chronotropic incompetence. The art has now matured such that sensor driven rate adaptive pacing is a programmable parameter of almost all CIEDs. With the increasing use of CIED to treat and monitor heart failure, sensors have now metaphored to optimize programming of CRT devices, and to monitor heart failure progression.

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