

New devices in heart failure: a European Heart Rhythm Association report

Developed by the European Heart Rhythm Association;
Endorsed by the Heart Failure Association

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Need for position paper on new devices

- Several new techniques are under clinical evaluation or used in clinical practice.
- Most new techniques are not addressed in current guidelines.
- No data based on randomised trials or mortality data are available.
- Overview needed, particularly for NYHA class III and IV and narrow QRS complex: largest group in heart failure (HF).



Cardiac contractility modulation: rationale

- A significant proportion of patients are ineligible for or unresponsive to cardiac resynchronisation therapy (CRT).^{1,2}
- Cardiac contractility modulation (CCM) signals are non-excitatory electrical signals delivered during the absolute refractory period.
- Signals enhance left ventricular (LV) contraction, improve exercise tolerance and QoL in patients with HF.^{3,4}
- Effects are independent of QRS duration and additive to those of CRT.
- Signals consist of two biphasic +7 V pulses spanning a total duration of 20 ms.

1. Maggioni et al, Eur J Heart Fail 2010;12:1076–84

2. McMurray et al, Eur Heart J 2012;33:1787–847

3. Buckhoff et al, Am J Physiol Heart Circ Physiol 2005;288:H2550-6

4. Lawo et al, J Am Coll Cardiol 2005;46:2229–36

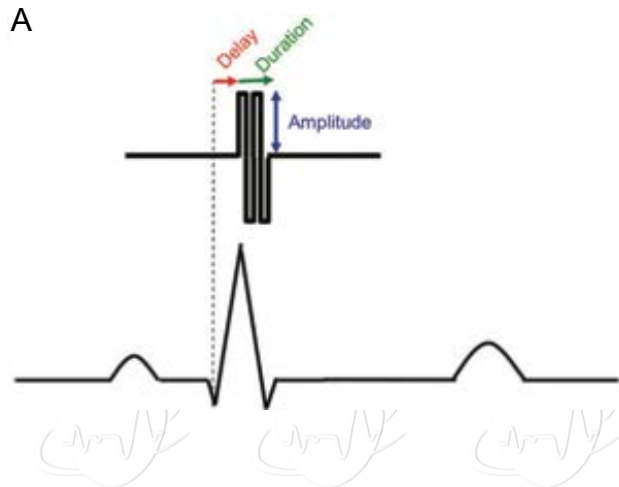


Implantation technique

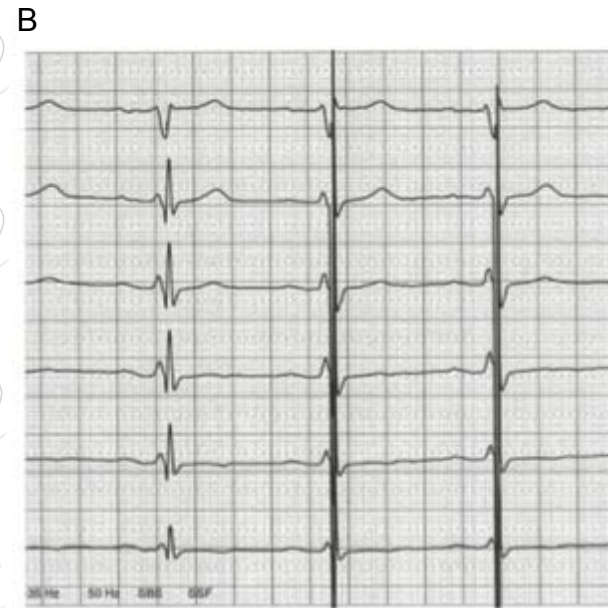
- Pacemaker-like impulse generator (OPTIMIZER IV, IMPULSE Dynamics) connects to the heart via two active-fixation leads placed endocardially on right ventricular (RV) septum.
- Additionally, a right atrial lead detects timing of atrial activation, allowing timing of signal delivery without risk of inducing ventricular arrhythmias.
- CCM pulses contain 50–100x the energy delivered in a pacemaker impulse and can be identified by body surface electrocardiography.
- Within minutes of acute CCM, a mild increase in ventricular contractile strength is detected as an increase in LV pressure (LVP).
- Haemodynamic responses are measured with a micromanometer catheter placed in the LV. Significant response = increase in max rate of LVP rise (dP/dt_{\max}) >5 %.



Cardiac contractility modulation signals

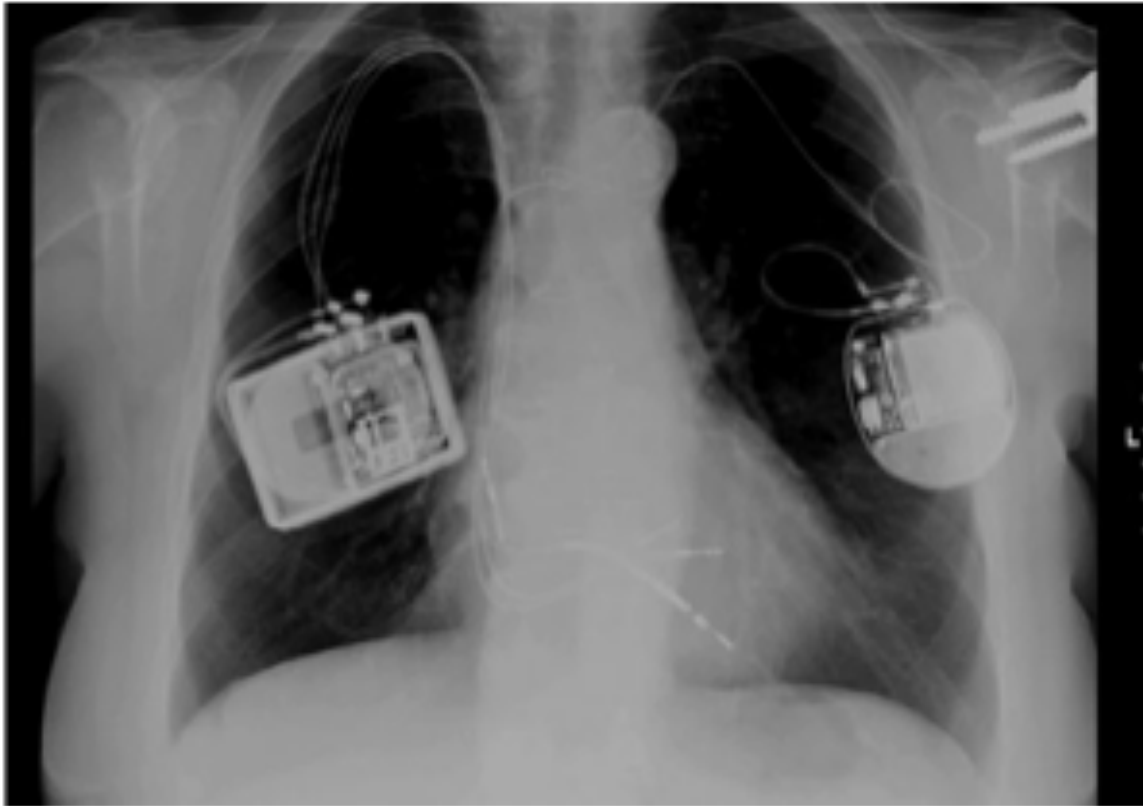


CCM signals are biphasic, delivered after defined delay.



Body surface ECG showing one beat prior to initiating CCM and first two beats of CCM application.

Implantation technique



Implanted CCM (right side) and one-chamber ICD (left side).

CCM comprises a can and three pace-sense electrodes: two fixed to the mid-septum, one to the right atrium.

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Effect of CCM on myocardial energetics

- Acute CCM was associated with an increase in dP/dt_{\max} from 630 to 800 mmHg/s (20 % increase). Despite acute increase in contractility, there was no detectible increase in myocardial O_2 consumption.¹
- Therefore, like CRT, acute increase in contractility achieved by CCM does not increase energy demands.
- Improvements in LV ejection fraction (LVEF) have been noted during CCM signal application.²
- CCM has the potential to achieve LV reverse remodelling.

1. Nelson et al, Circulation (Online) 2000;102:3053-9

2. Yu et al, JACC Cardiovasc Imaging 2009;2:1341-9



Mechanism of action

- Since CCM-induced increases in contractility are not associated with an increase in myocardial oxygen consumption (MVO_2), CCM may have direct impact on cellular physiology leading to short-term changes in gene expression.
- In animal studies, improvements in gene expression correlated with improvements in peak VO_2 and Minnesota Living with Heart Failure Questionnaire (MLWHFQ).¹
- CCM treatment reversed cardiac maladaptive foetal gene programme and normalised expression of key SR Ca^{2+} cycling and stretch response genes.

1. Butter et al, J Am Coll Cardiol 2008;51:1784–9

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Chronic CCM application in HF patients – FIX-HF4 trial

- Multicentre, randomised, double-blind, double crossover study, n = 164.
- Group 1: CCM for 3 months then sham 3 months; group 2 sham for 3 months then CCM 3 months.
- Similar increase in VO_{2peak} between 2 groups in first 3 months – placebo effect?
- During second 3 months, VO_{2peak} decreased in group 1 (20.86 ± 3.06 mL/kg/min) and increased in group 2 (0.16 ± 2.50 mL/kg/min).
- Net treatment effect on $VO_{2peak} = 0.52 \pm 1.39$ O₂/kg/min (p = 0.032).
- Significant improvement in QoL in group 2 in second 3 months (p = 0.03).
- No significant differences in adverse events between on and off phases.

Borggrefe et al, Eur Heart J 2008;29:1019–28

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Chronic CCM application in HF patients – FIX-HF5 trial

- Multicentre, randomised study, n = 428.¹
- CCM vs optimised medical therapy.
- VO_{2peak} 0.7 mL/kg/min greater (p = 0.024) in CCM group.
- Significant improvement in QoL in CCM group (p <0.0001).
- No differences between groups in VAT (primary endpoint).
- Safety endpoint met.
- Subgroup analysis showed that CCM significantly improves VO_{2peak} and VAT in a subgroup of patients characterised by normal QRS duration, NYHA functional class III symptoms and EF >25 %.²

1. Kadish et al, Am Heart J 2011;161:329–37

2. Abraham et al, J Card Fail 2011;17:710–7



Combining CCM with CRT

- CCM applied in acute setting to HF patients receiving CRT results in additive effects on LV contractility.¹
- Early studies show that combined CCM/CRT is feasible.²
- Prospective studies needed to confirm initial findings.

1. Pappone et al, Am J Cardiol 2002;90:1307–13

2. Nägele H et al, Europace 2008;10:1375–80



Clinical perspectives

- Two large-scale studies validated safety of and suggested efficacy of CCM.
- CCM improves exercise tolerance but no mortality benefit or reduction in hospital admission demonstrated, and no randomised data on remodelling.
- A subgroup of HF patients ($EF \geq 25\%$) is more likely to benefit.
- More studies required to determine the optimum pacing configuration: single/biphasic, optimum delay from pacing spike, optimal duration of each phase and optimal signal amplitude.
- No data yet on use of CCM in early stage HF.



Current limitations of CCM

- At present, CCM cannot be given in patients with AF or frequent ectopy as it relies on detection of a P-wave.
- Future device is planned that does not rely on P-wave detection.
- Development of a device combining CCM with ICD is desirable.
- Future studies should define whether CCM is additive to CRT pacemaker or CRT-D in patients with wide QRS.
- Single peri-implantation method to guide lead positioning is desirable.



Neuromodulation: rationale

- HF is associated with sympathetic nervous system activation over parasympathetic system.¹
- Indirect markers of cardiac vagal tone like heart rate variability are suppressed in CHF which in turn is predictive for a worse outcome of CHF.²
- Increase of cardiac vagal tone by β -receptor blockade has substantially improved functional status and survival of HF patients.³
- Cardiac vagal tone is controlled by pre-ganglionic parasympathetic cardiac neurons.
- Attempts to therapeutically increase the cardiac parasympathetic tone by electrical neural stimulation may operate at any part of this circuit.

1. Schwartz et al, Heart Fail Rev 2011;16:101–7

2. Cygankiewicz I et al, Heart Rhythm 2008;5:1095–102

3. Foody, JAMA 2002; 287:883–9

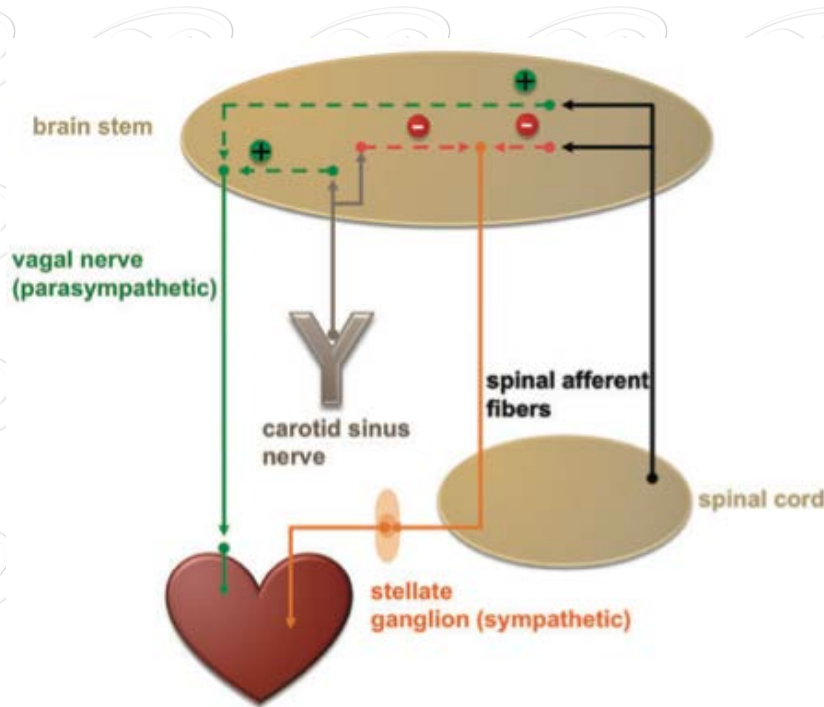


Neuromodulation: rationale

- Four neurostimulation approaches:
- Reflex activation of the parasympathetic tone and sympathetic inhibition via afferent fibre stimulation:
 - spinal cord stimulation (SCS)
 - carotid sinus nerve stimulation
- Efferent parasympathetic stimulation:
 - cervical vagal stimulation
 - intracardiac vagal stimulation



Parasympathetic and sympathetic innervation of the heart



Efferent pre-ganglionic vagal nerve (parasympathetic) fibres (green) course from brain stem to heart and connect with post-ganglionic cells in circumscript epicardial ganglionic plexus.

Sympathetic pre-ganglionic fibres (orange) switch to post-ganglionic fibres inside stellate ganglion.

Major afferent inputs to central autonomic centres: carotid sinus nerves (brown) and spinal cord afferents (black).

Spinal cord stimulation

- Long history of use in management of chronic pain.¹
- Benefits have been demonstrated in refractory angina.²
- Also beneficial effect in severe peripheral pain during atherosclerosis³ and Raynaud's disease⁴ and at the level of cerebral vasculature.

1. Long et al, Appl Neurophysiol 1981;44:207-17

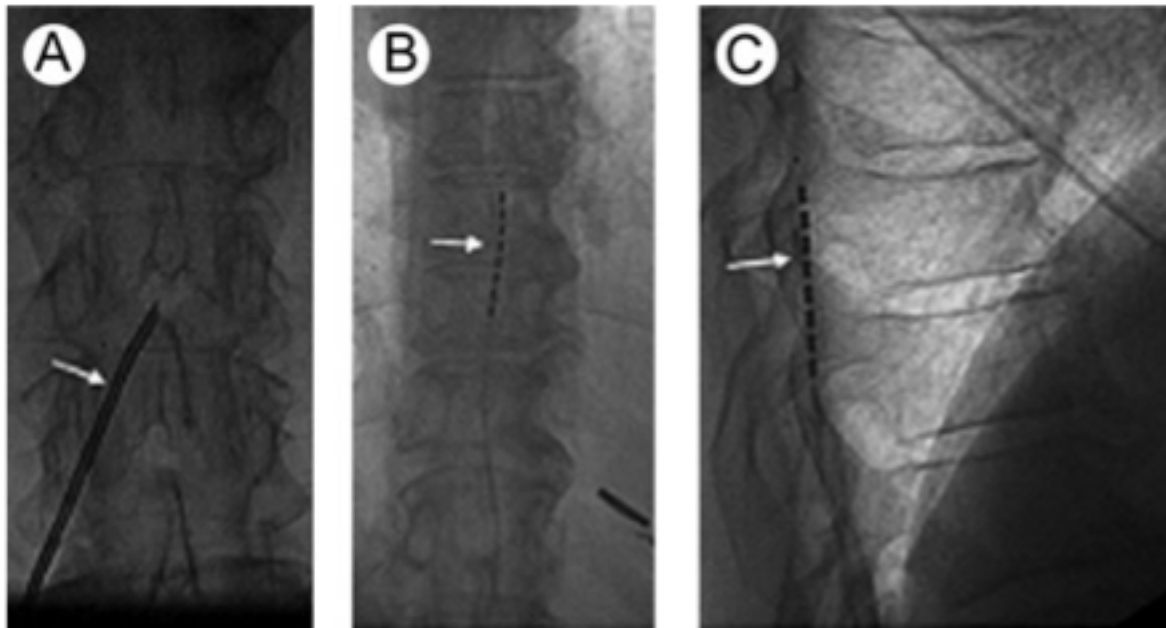
2. Mannheimer et al, Eur Heart J 2002;23:355-70

3. Ubbink et al, Cochrane Database Syst Rev 2005;CD004001

4. Sibell et al, Anesthesiology 2005;102:225-7



SCS: Mechanism of action



Single-lead placement (A).

Introducer (arrow) is directed into the epidural space (B and C, anterior and lateral views).

Lead is in mid-thoracic region at approximately T1 (arrows).

Mechanism of action

- Reflex activation of the vagus nerve and sympathetic system
- Limited impact on coronary blood flow in ischaemic patients.¹
- Affects balance between oxygen demand and supply.
- Establishes re-equilibrium of balance of sympathetic and parasympathetic system.
- Effects via cytokines and NO/NOS system.²
- Direct protective mechanisms on myocardium during ischaemia?³
- Effects on systolic function of LV.⁴

1. Diedrichs et al, Curr Control Trials Cardiovasc Med 2005;6:7

3. Southerland et al, Am J Physiol Heart Circ Physiol 2007;292:H311-7

2. Li et al, Heart Fail Rev 2011;16:137-45

4. Gersbach PA et al, Ann Thorac Surg 2001;72:S1100-04



Implant technique

- The North-American Neuromodulation Society (NANS) established guidelines.
- Performed under sedation on X-ray compatible table allowing antero-posterior and lateral views.
- Peridural space accessed at L1-L2 with needle.
- Leads advanced to position close to dorsal horn fibres under fluoroscopic guidelines.
- Impulse generator implanted s.c. in low back/high buttock.



Safety of SCS

- Acute complications observed in up to 38 % of patients.^{1,2}
- Longer term lead migration/breakage/other problem with impulse generator in 20–30 % of patients, mostly requiring surgical correction.^{1,2}
- Safe for use in patients with pacemakers or ICDs providing that the sensing of cardiac device is in bipolar mode, sensitivity set at 0.3 mV and SCS implanted contralaterally and at sufficient distance.³

1. Diedrichs et al, Curr Control Trials Cardiovasc Med 2005;6:7

3. Southerland et al, Am J Physiol Heart Circ Physiol 2007;292:H311–7

2. Li et al, Heart Fail Rev 2011;16:137–45

4. Gersbach PA et al, Ann Thorac Surg 2001;72:S1100–04



Clinical perspectives

- Appears promising in pre-clinical studies to improve systolic function of LV and to decrease ventricular arrhythmias:
 - Preliminary report on four HF patients who improved clinically with SCS.
 - Associated with smaller deterioration of LVEF due to adenosine administration in patients with multivessel CAD.
 - Associated with better invasive haemodynamic evaluation in patients with normal LV function.
- Associated with reduced risk of ventricular arrhythmias and LV function improvement in animal models of HF.



Clinical perspectives

- Ongoing clinical studies: SCS-HEART (non-randomised, n = 20), DEFEAT-HF (randomised, n = 250) and TAME-HF (non-randomised, n = 20).
- Data expected late 2014.

Until more data available, it is not possible to recognise SCS in HF patients outside of current recognised indications.



Carotid sinus nerve stimulation: rationale

- Baroreceptors in arterial walls respond to changes in arterial pressure and send signals to brainstem where they connect to efferent vagal neurons.¹
- Increased arterial BP elicits activates efferent vagal fibres, decreasing sinus heart rate.²
- This baroreflex is suppressed in HF³ and deteriorates with chronic HF.⁴
- Electrical stimulation of afferent carotid sinus nerves may therefore be a tool for increasing cardiac vagal tone in HF.

1. Czachurski J et al, Neurosci Lett 1982;28:133–7
3. Creager MA et al, J Am Coll Cardiol 1994;23:401–5

2. Andresen MC et al, Ann Rev Physiol 1994;56:93–116
4. Marin-Neto JA, Am J Cardiol 1991;67:604–10



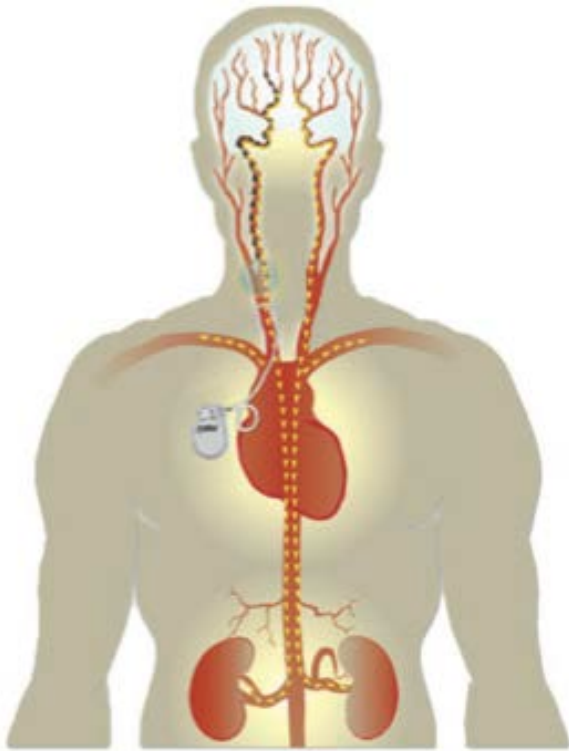
Mechanism of action

- Shifts autonomic balance towards higher parasympathetic tone.
- Direct or reflex decrease of the systemic sympathetic tone.
- In animal study, LV systolic and diastolic function improved due to reverse LV geometric remodeling.¹

1. Sabbah HN et al, Circ Heart Fail 2011;4:65–70.



Implant technique



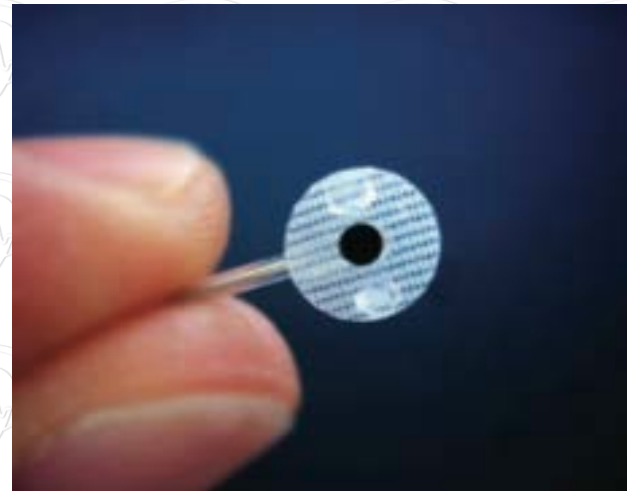
Device is implanted via the right side and is connected to a patch electrode fixed on the right-sided carotid sinus, under local anaesthesia and sedation.

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Carotid nerve stimulator

Device carries one electrode connected to the patch electrode, which is fixed to the carotid sinus nerve.



Longevity of battery: Rheos system 1 year; Neo system 3 years.

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Clinical data

- Rheos system evaluated in three multicentre studies in patients with resistant hypertension:
 - DEBuT-HT/DEBuT-HET in Europe¹
 - Rheos Feasibility Trial²
 - Rheos Pivotal Trial³
 - Sustained response to baroreceptor activation; 88 % responders after 12-month follow-up.
 - Met endpoints for short-term (6 months) and long-term (12 month) adverse events.
 - Did not meet endpoints for acute responders (54 vs. 46 % responders after 6-month follow-up) and procedural safety (event-free rate 74.8 %).
- No clinical data in HF.

1. Scheffers IJM et al, J Am Coll Cardiol 2010;56:1254–8

3. Bisognano JD et al, J Am Col Cardiol 2011;58:765–73

2. Illig et al, J Vasc Surg 2006;44:1213–8



Clinical perspective

- CVRx Neo system received the CE mark in 2011.
- Randomised XR-1 Heart Failure Study (n = 140) currently recruiting.
- Six-month follow-up for subjects treated with BAT (baroreflex activation therapy) versus standard of care:
 - Primary endpoint: change in LVEF.
 - Primary safety objective: rate of system and procedure-related complications.
- HOPE4HF study is planned: primary endpoint is effect of BAT on HF hospitalisations in patients with HF and preserved EF.¹

1. Georgakopoulos D et al, J Card Fail 2011;17:167-78



Cervical vagal nerve stimulation: rationale

- Efferent cardiac parasympathetic signaling chain comprises pre-ganglionic parasympathetic neurons, which connect to post-ganglionic neurons in the heart. These innervate cardiac target cells via muscarinergic acetylcholine receptors.
- Density of cardiac muscarinergic receptors is increased during CHF.¹
- Pre-to post-ganglionic parasympathetic efferent neurotransmission via nicotinic acetylcholine receptors is impaired in HF.²
- Chronic exposure to nicotinic agonist reestablishes neurotransmission.³
- Therefore electrical pre-ganglionic cervical vagal nerve stimulation (VNS) may reestablish diminished cardiac vagal tone in CHF.

1. Vatner et al, Circulation 1996;94:102–7

3. Bibeovski et al, Am J Physiol Heart Circ Physiol 2004;287:H1780–5

2. Bibeovski et al, Circulation 1999;99:2958–63



Mechanism of action

- Antiarrhythmic effects – increases ventricular refractory period.¹
- Rate slowing effects – elevated HR has worse prognosis in HF.²
- Antifibrotic effects – decreases ventricular replacement fibrosis and blunts the development of CHF-associated cellular hypertrophy.³
- Anti-inflammatory effects – attenuates increases in TNF- α , IL6 and CRP.³
- Reverse remodelling – improves LVEF.³

1. Prystowsky et al, Circ Res 1981;49:511–8

3. Sabbah, Cleve Clin J Med 2011;78(Suppl 1):S24–9

2. Böhm et al, Lancet 2010;376:886–94



Implant technique



Chest X-ray of an implanted cervical vagal nerve stimulator (CVS; right side) in a patient with severely reduced

LV systolic function.

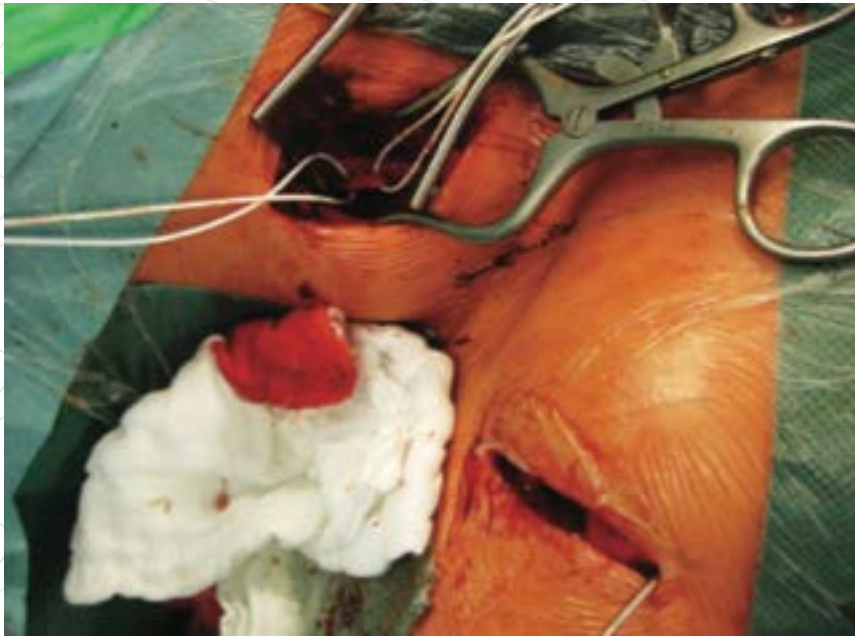
The device consists of a ventricular sensing lead and a cervical vagal nerve electrode. On the left side an ICD had been previously implanted.

Example of a cervical vagal stimulator



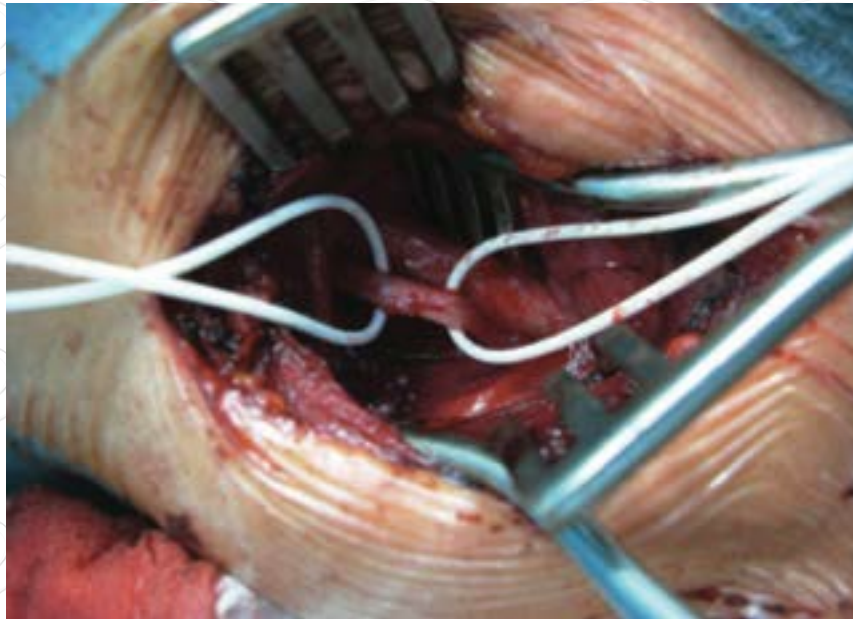
Device has two electrodes: one conventional RV screw-in pace/sense electrode monitors heart rate during VNS; the other cuff electrode is wrapped around the cervical vagal nerve.

Example of a cervical vagal stimulator



Two incisions: one for exposure of the cervical vagal nerve and a second for implanting the RV electrode. The vagal electrode is tunneled s.c. to the impulse generator, which is implanted below the collarbone.

Local implantation of the CVS



Exposed vagal nerve

Implant technique: important issues

1. Requires surgeon with knowledge and understanding of neck anatomy.
2. Surgical approach should favour exposure of vagus nerve rather than carotid artery, on dissection of carotid sheath.
3. Manipulation of nerve should be minimised.
4. Proper selection of cuff electrode size crucial: too tight might damage nerve, too loose does not allow stimulation currents concentration in the nerve, causing side-effects and decreasing effectiveness.
5. Fixation of stimulation lead should be via suture sleeves to stable fascia and not to muscles with wider range of motion.



Clinical data

Multicentre, open-label, phase II study (n = 32, NYHA Class II-III):

- VNS 2–4 weeks after implant, slowly raising intensity.
- Total of 26 serious adverse events in 13 patients including three deaths and two device-related adverse events.
- Non-serious device-related adverse events disappeared after stimulation intensity adjustment.
- Significant improvements in NYHA class, QoL, 6-minute walk distance (6MWD), LVEF and LV systolic volumes.

De Ferrari GM et al, Eur Heart J 2011;32:847–55

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Other clinical considerations

- Patients with mild-to-moderate HF can tolerate higher current amplitudes and other parameters vs. the parameters used for epilepsy.
- Side-effects include hoarseness, voice alteration and increased cough. Majority relate to underlying disease or comorbidities.
- In patients with both CVS and ICD, no interferences from vagal stimulation have been detected.
- CVS increases parasympathetic tone of subjects with HF.
- Vagal stimulation improved subjective, as well as objective clinically relevant parameters of NYHA class, QoL, sub-maximal exercise capacity, and cardiac structure and function in an early study.¹

1. Schwartz PJ et al, Heart Rhythm 2009;6(Suppl):S76–81

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Unresolved issues

- Atrial proarrhythmia – increased vagal tone shortens atrial refractory period.
- Selectivity of neural stimulation – central vagal nerve also has branches to abdominal viscera, therefore concomitant stimulation of GI tract may have consequences, e.g. increased gastric acid secretion or increased intestinal motility.

More data needed

1. Hart et al. Stroke 2012;43:1511-7

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Clinical perspectives

- No RCT data yet for CVS.
 - INOVATE-HF RCT investigating long-term safety and efficacy of vagus nerve stimulation with CardioFit™ ongoing; n = 650, EF <40 %, NYHA class III.
 - Planned study duration: 5.5 years.
 - Primary safety endpoints: freedom from procedure- and system-related events through 90 days post-implant and time to first event (all-cause mortality and complications requiring hospitalisation).
 - Primary safety endpoint: composite of all-cause mortality and unplanned HF hospitalisation using time to first event analysis.
- In patients whose baseline vagal tone is low and in whom parasympathetic tone is increased by VNS, clinical benefit may be observed.



Intracardiac atrioventricular nodal vagal stimulation: rationale

- 30–40 % of patients with CHF develop AF.
- Rapid ventricular rates during AF may further deteriorate HF or decrease the degree of LV resynchronisation in patients with ICDs and may cause inappropriate shock delivery in 5 %.¹
- Long-term AV nodal stimulation for ventricular rate control is a potential adjunctive treatment.
- Post-ganglionic cardiac vagal fibres, which supply the AV node reside at the postero-inferior interatrial septum, and are amenable to stimulation from endocardial surface.²

1. Koplán et al, J Am Coll Cardiol 2009;53:355–60

2. Schauerte et al, Circulation 2001;104:2430–5



Implant technique

- The inferior right ganglionated plexus (IRGP) is located at the epicardial surface of the heart between the ostium of the coronary sinus and the entrance of the inferior vena cava.
- For chronic electrostimulation, atrial pacing leads of current technology are screwed into the IRGP from the right atrial endocardial site at the postero-inferior interatrial septum either using specifically shaped guiding catheters or manually shaped conventional mandrins.



Clinical perspectives

- Feasibility has been shown in a series of chronic human implants in HF patients with AF.¹
- Prospective multicentre study (AVNS: AV node stimulation study) to investigate whether short-term probatory AV nodal vagal stimulation may avoid inappropriate shock delivery in patients with resynchronisation defibrillators is ongoing.
- Action potential of neurons is very short lasting: 10–20 ms. Electrical stimulation at higher frequencies may cause transmitter release and physiological effects.

1. Bianchi et al, Heart Rhythm 2009:1282–6.



Implantable haemodynamic monitoring devices

- Urgent unmet need to reduce acute decompensated heart failure (ADHF) and hospitalisation in ambulatory HF patients.
- A meta-analysis suggested that telemonitoring may provide better outcomes than usual care.¹ However, two RCTs found that telemonitoring did not significantly reduce HF hospitalisation.^{2,3}
- Parameters obtained from cardiac implantable devices (defibrillators, CRT) enable identification of patients at increased risk of ADHF but are not accurate enough to adjust treatment.⁴
- New implantable haemodynamic monitors are in development, e.g. RV, left atrial pressure and pulmonary artery pressure sensors.

1. Klersy et al, J Am Coll Cardiol 2009;54:1683–94

3. Chaudhry et al, NEJM 2010;363:2301–9

2. Kohler et al, Circulation 2010;122:2224 (abstract 21835)

4. Abraham, Europace 2013;15(Suppl 1):i40–i46



Right ventricular pressure monitoring

- Chronicle implantable haemodynamic monitor:
 - Specialised transvenous lead has sensor near the tip to measure intracardiac pressure.
 - Programmable device similar in size and shape to a pacemaker.
- Continuously monitors and telemeters:
 - RV systolic, diastolic and pulse pressure
 - RV dP/dt (positive and negative), pre-ejection interval and systolic time interval
 - Pulmonary artery diastolic pressure (ePAD)
 - Heart rate
 - Patient's activity
 - Core body temperature
 - Specific triggered events such as bradyarrhythmias, tachyarrhythmias or patient-activated episodes
- Implantation procedure is similar to that of a single-lead pacemaker.



Clinical data

- COMPASS-HF study:
 - Multicentre, single-blinded trial (n = 274, NYHA class III/IV), patients randomised to intervention arm in which device data used for patient management or control.¹
 - Safety endpoints met: system-related complications in only 8 % of cases.
 - Primary endpoint not met: device group had nonsignificant lower rate of HF-related events compared with control (p = 0.33), but lower than expected event rate.
 - Retrospective analysis showed 36 % reduction (p = 0.03) in RR of first HF-related hospitalisation.

1. Bourge et al, J Am Coll Cardiol 2008;51:1073-9

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Clinical perspective

- In 2007, the FDA Circulatory System Devices Panel voted against the approval of Chronicle because its use was not proved to significantly improve clinical outcomes in COMPASS-HF.
- Another trial, REDUCEhf was terminated early. Data analysis showed no benefit for haemodynamic monitoring.¹
- Many issues affect the ability to demonstrate clinical benefit:²
 - Degree of HF severity in the tested population.
 - Quality of comparative usual care.
 - Choice of primary endpoint: need for medical visits may increase due to earlier detection of worsening HF, but avoid subsequent hospitalisations.
 - Specific characteristics of the disease management programme.

1. Adamson et al, Congest Heart Fail 2011;17:248–54

2. Whellan et al, Prog Cardiovasc Dis 2011;54:107–14



Left atrial pressure monitoring

- Patients admitted for ADHF usually have elevated LAP. The rise is gradual and precedes symptoms.
- The HeartPOD comprises an implantable sensor lead that measures pressure, intracardiac electrograms and temperature, coupled to a coil antenna positioned in the subcutaneous tissue.
- The device is either standalone or coupled to a CRT-D unit.
- Powered by handheld patient advisory module (PAM) (no battery) using RF wireless transmission. PAM subtracts atmospheric pressure from pressure measured in the implant to obtain LAP.
- LAP and intracardiac electrograms are captured for periods of up to 20 s
- PAM can store 3 months of data with six daily interrogations.



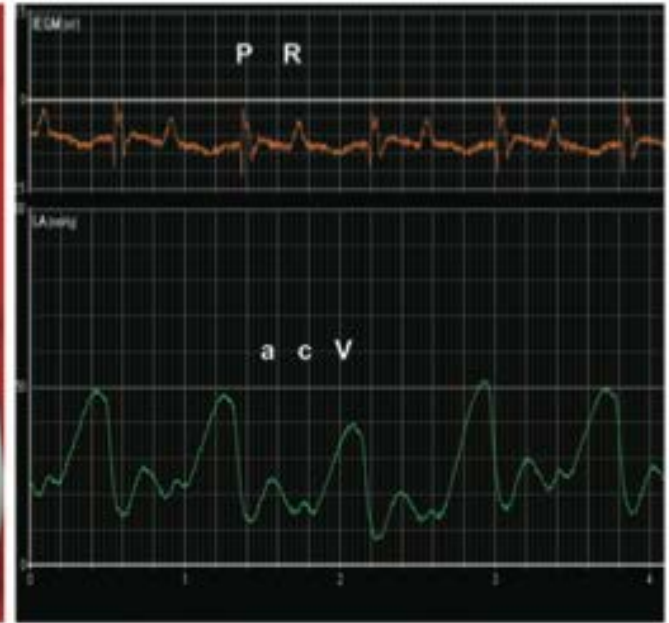
The HeartPOD



Standalone HeartPOD with communicator module attached to sensor lead



PAM



Electrograms and LAP waveforms recorded by HeartPOD

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Implantation

- The HeartPOD is implanted by cardiac catheterisation and transseptal puncture, and requires special training.
- Access may be:
 - entirely femoral, with implantation of the sensor module in a lower right abdominal pocket.
 - entirely superior with transseptal puncture performed by a deflectable sheath and a special puncture screw.
 - combined, with the transseptal puncture performed by femoral access and lead transfer to a superior access using a snare.
- Post-implantation, patients are maintained on dual antiplatelet therapy (DAPT) for ≥ 6 months.
- The bulk of foreign body material in the left atrium is less than with septal defect closure devices.



Autopsy 37 months after implantation of HeartPod



Fibrous tissue covers most of the pressure sensor, limiting thrombo-embolic risk

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Clinical data

- HOMEOSTASIS study (n = 84): prospective, multicentre, observational open-label registry in patients with NYHA III/IV HF, regardless of LVEF.¹
- Device was implanted successfully in 98 % of cases without major periprocedural adverse events.
- Correlation between simultaneous measurement of LAP and pulmonary artery wedge pressure was high at 3 months (r = 0.97) and 12 months (r = 0.99).
- Freedom from device failure was 95 % at 2 years and 88 % at 4 years.
- After 3-month observation, patients entered 3-month titration period: drug therapy was adjusted based upon the LAP readings, followed by a stability period ≥ 6 months.



Clinical data (continued)

- Compared with observation period, annual rate in death or HF events was significantly decreased during titration and stability periods (0.68 vs. 0.28 per year; $p = 0.041$). Improvements in NYHA class (20.7, $p < 0.001$) and LVEF (7 %, $p < 0.001$).¹
- LAPTOP-HF study: ongoing RCT recruiting up to 730 patients with maximally treated NYHA III HF (irrespective of LVEF) randomised 1 : 1 to receive a HeartPOD vs. a PAM only (for reminding drug therapy). Endpoint: reduction in worsening HF and hospitalisations.
- Successful extraction of the HeartPOD has been reported.¹

1. Troughton RW et al, J Cardiovasc Transplant Res 2011;4:3 –13

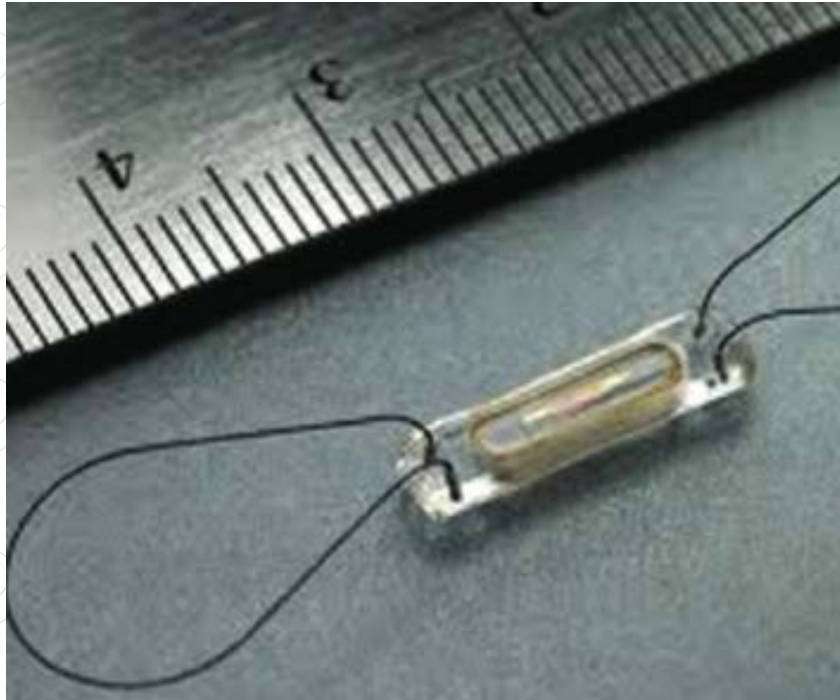


Clinical perspectives

- Self-titration of HF therapy by patients based upon LAP readings is a paradigm shift in HF management.
- Requires patient participation and compliance – may not be suitable for many individuals.
- Patients with diastolic HF are a therapeutic challenge: volume overload may rapidly cause pulmonary congestion. Analysis of LAPTOP-HF data in this patient subset will clarify whether titration of diuretics based upon LAP readings improves outcome.
- LAP data may be useful to optimise AV delay in CRT-HeartPOD devices
- Conclusions: appears promising but further experience and confirmation of early findings by LAPTOP-HF required.



Pulmonary artery pressure monitoring



CardioMEMS sensor: coil and pressure-sensitive capacitor in hermetically sealed silica capsule covered in medical-grade silicone. Two wired nitinol loops at the ends of the capsule act as anchors to prevent distal migration of the sensor.

CardioMEMS sensor

- Coil and capacitor form an electrical circuit that resonates at a specific frequency.
- Coil allows for electromagnetic coupling to the sensor by an external antenna, which is held against the patient's body.
- Antenna powers the implanted device, continuously measures resonant frequency, which is then converted to a pressure waveform.
- Interrogating device measures the atmospheric pressure, which is subtracted from the pressure measured by the implanted sensor.
- CardioMEMS sensor is designed to measure pulmonary artery pressure (PAP).



Implantation

Venous-femoral approach:

- Swan–Ganz catheter advanced into deployment site in pulmonary artery.
- After identification of the target artery, guidewire (0.018–0.025 inch) is placed through Swan–Ganz catheter to allow sensor delivery catheter system to be advanced.
- Delivery catheter advanced over the wire and the CardioMEMS sensor is released in the target vessel.
- After removal of delivery catheter, Swan–Ganz catheter is replaced into the pulmonary artery proximal to the sensor.
- Implanted sensor calibrated using PAPs from Swan–Ganz catheter.



Experimental data

- Animal and human studies found a good correlation between sensor based and invasive or echocardiographic measurements.¹
- No propensity for in situ thrombus.¹

1. Verdejo HE et al, J Am Coll Cardiol 2007;50:2375–82.
2. Castro PF et al, J Heart Lung Transplant 2007;26:85–8.

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Clinical data

- CHAMPION prospective, multicentre, randomised, single-blind trial: 550 patients implanted with CardioMEMS HF sensor but physicians blinded to daily PAP measurements in control group (n = 280).
- Safety endpoints met: freedom from device- or system-related complications (98.6 %) and overall freedom from pressure-sensor failures (100 %).
- Primary efficacy endpoint met: use of daily PAP measurements reduced rate of HF hospitalisations by 30 % (HR 0.70; $p < 0.001$).
- Rate of HF hospitalisations reduced by 39 % in treatment group. When admitted, hospital stays were shorter in treatment group (2.2 vs. 3.8 days, $p = 0.02$)

1. Abraham WT et al, Lancet 2011;377:658–66

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Clinical perspectives

- In 2011, the FDA Circulatory System Devices Panel voted against the approval of the CardioMEMS because its use was not proved to significantly improve clinical outcomes in the CHAMPION trial.
- Concern about trial's design: impossible to distinguish any treatment effect from the device itself in the single-blind trial.
- Physicians knew which patients had the device and specific treatment recommendations were made in the treatment group and not in the control group.
- After an extended open-access trial period the system was approved by the FDA on 28 May 2014. The pending issues with the Champion trial were resolved.



Summary and Conclusions

- Several new devices for the treatment of HF patients are being used in clinical practice or are under clinical evaluation in either observational and/or randomised clinical trials.
- Ambulatory HF patients are at high risk for hospital admission and there remains a need to reduce hospitalisations and re-admission rates for HF.
- New technologies for invasive haemodynamic monitoring show great promise as adjunctive tools in the management of HF patients.
- Future studies should evaluate the utility of combining impedance measurements by current cardiac devices with haemodynamic sensors.

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