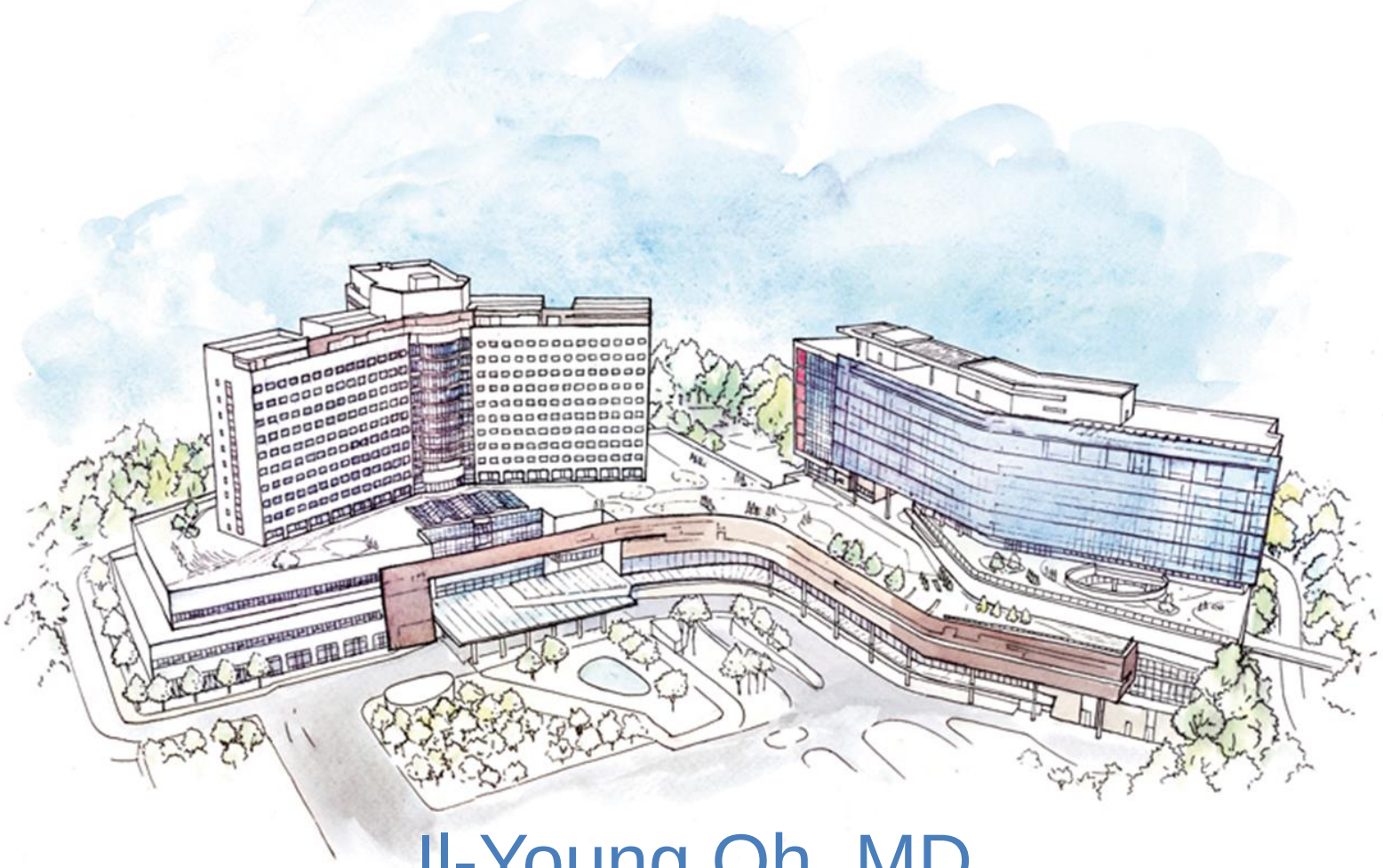
Neurostimulation for heart failure

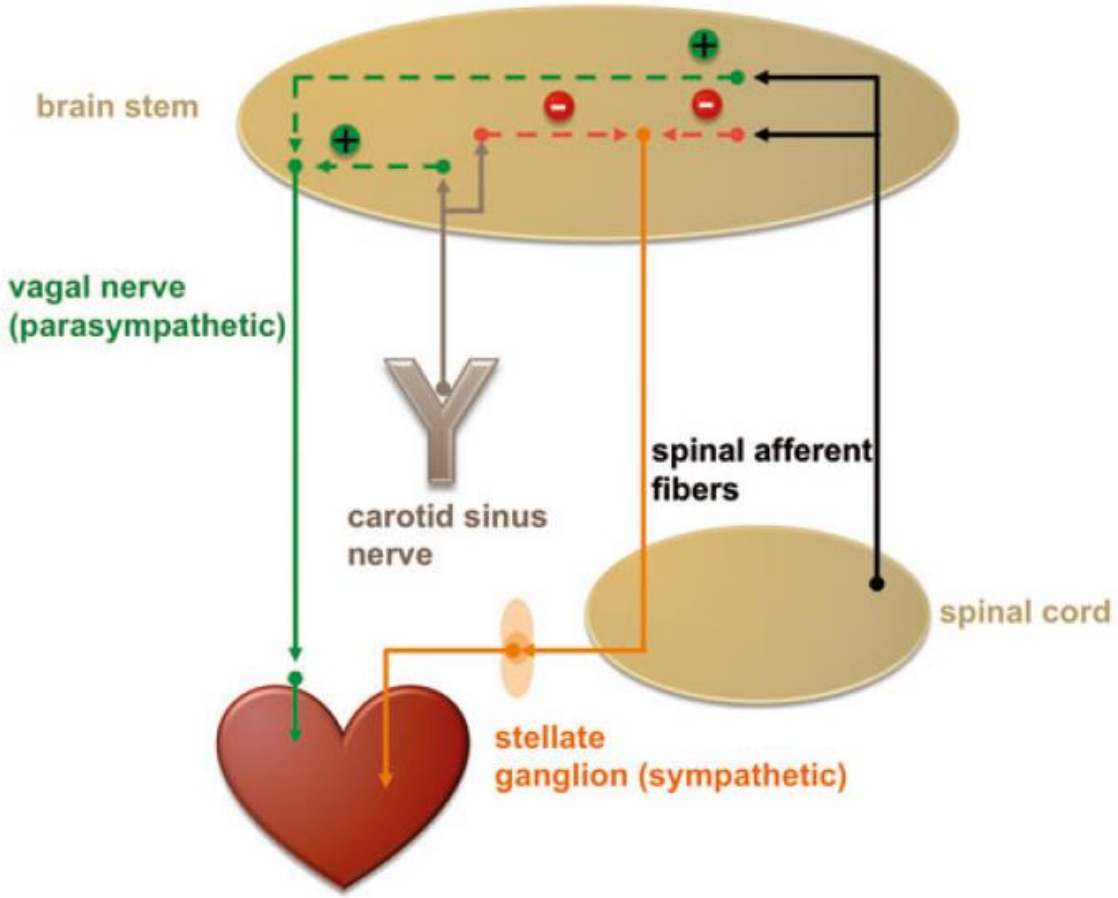


Il-Young Oh, MD

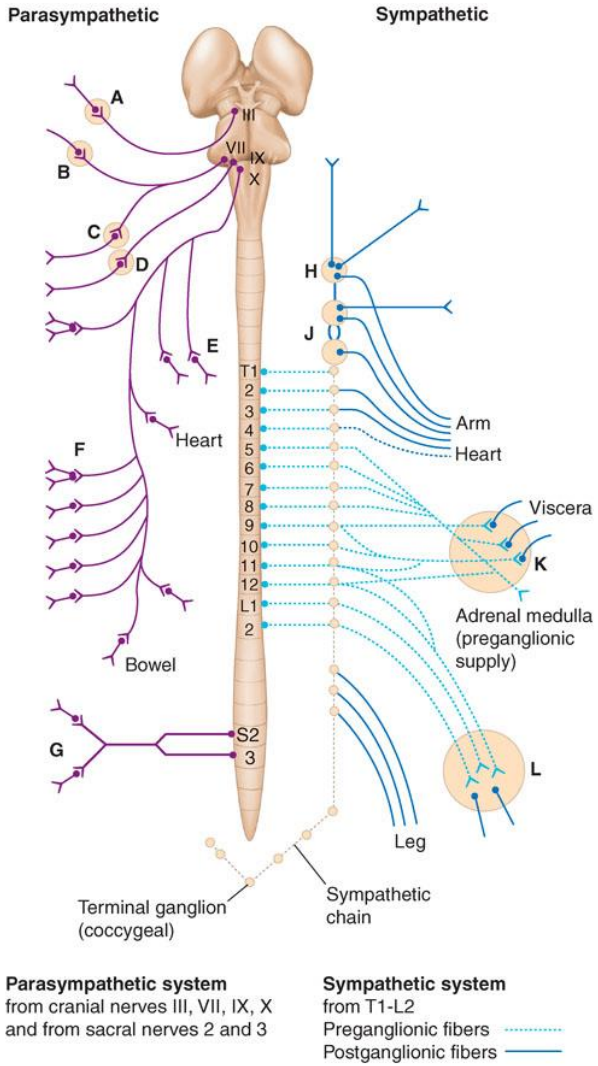
Contents

- Autonomic imbalance in HF
- Neuromodulation for heart failure
  - Spinal cord stimulation (SCS)
  - Carotid sinus nerve stimulation
  - Cervical vagal nerve stimulation
  - Intracardiac AV-nodal stimulation
- Unresolved issues in neurostimulation
- On going trials

Parasympathetic and sympathetic innervations of the heart



Europace. 2014;16:109-128



Clin Endocrinol Metab. 1977;6:77.

SPINAL CORD STIMULATION

History of SCS

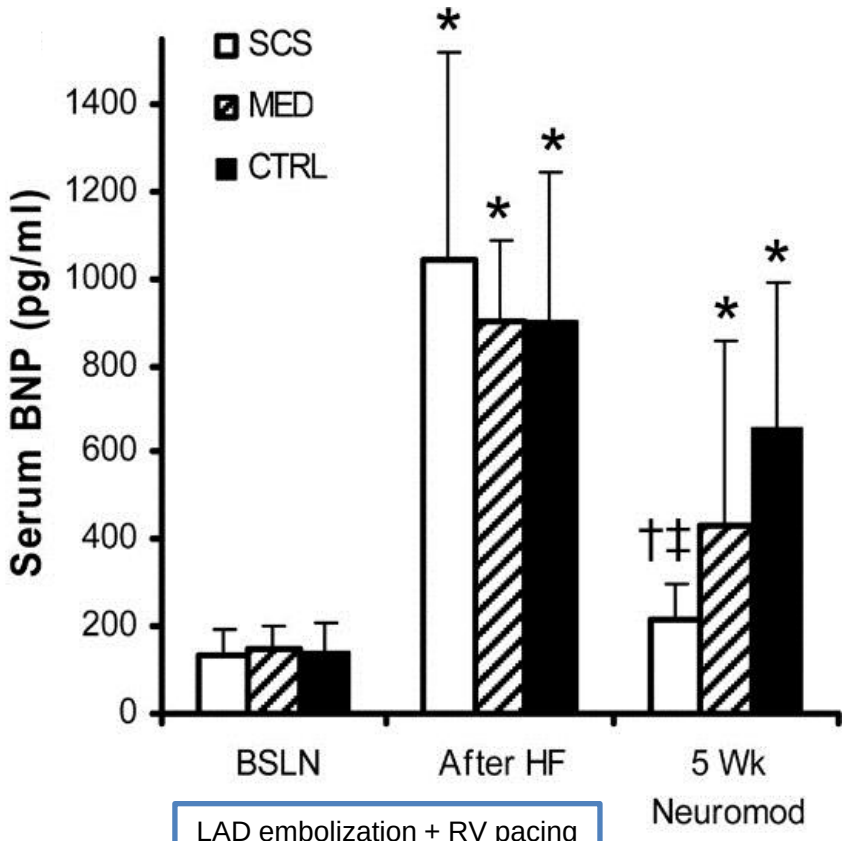
- Spinal cord stimulation has been used for over 40 years in the management of chronic intractable pain.

- According to the AANS, as many as 50,000 neurostimulators are implanted worldwide every year.

- In our fields
  - Refractory angina, syndrome X, critical leg ischemia, Raynaud's disease, etc.

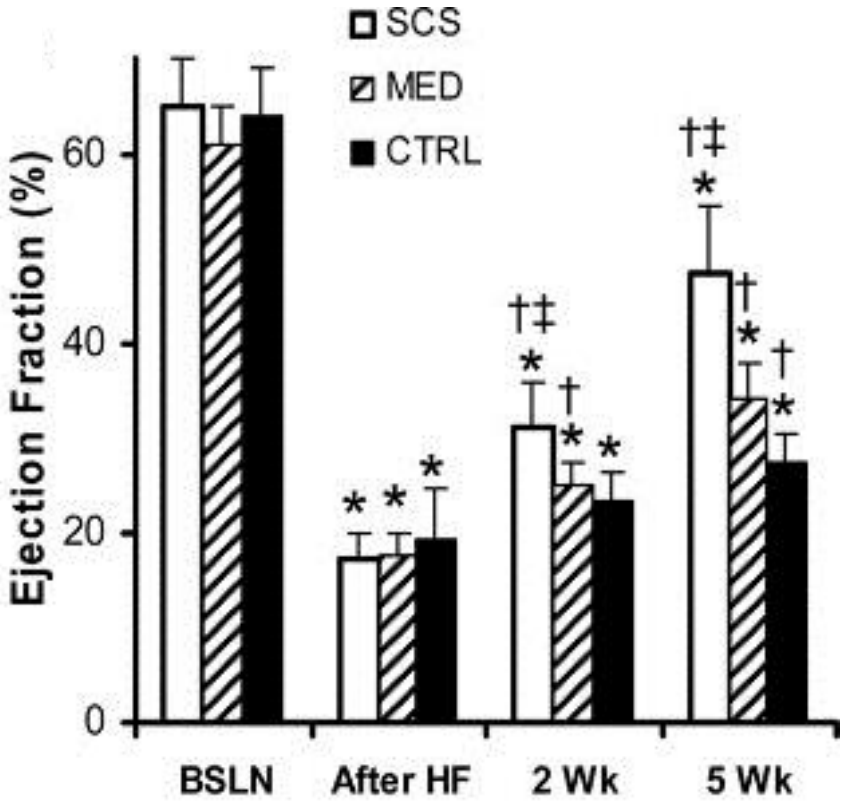
In a Canine Postinfarction HF Model

Clinical parameter – BNP



LAD embolization + RV pacing (240 ppm) for 3 weeks

Echocardiographic index



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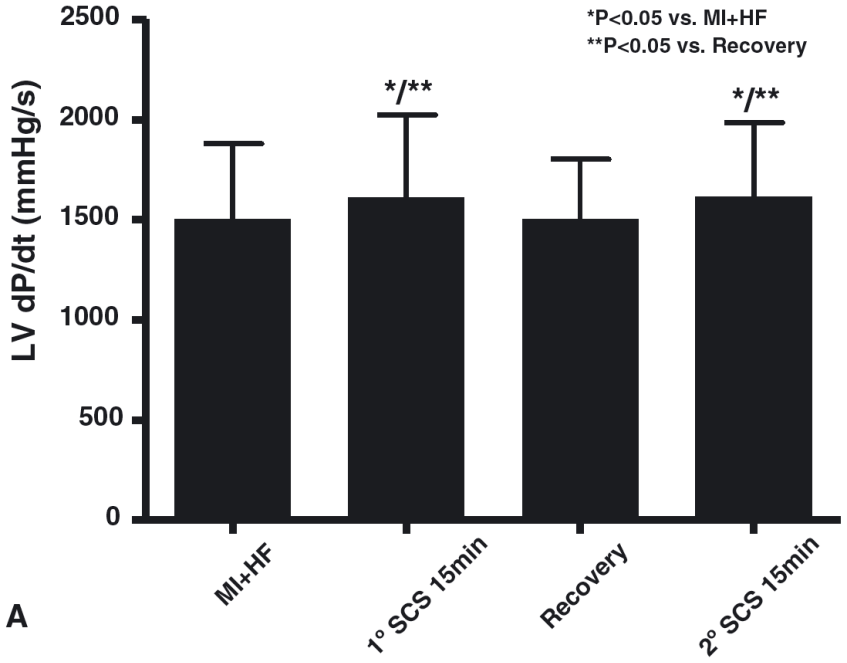
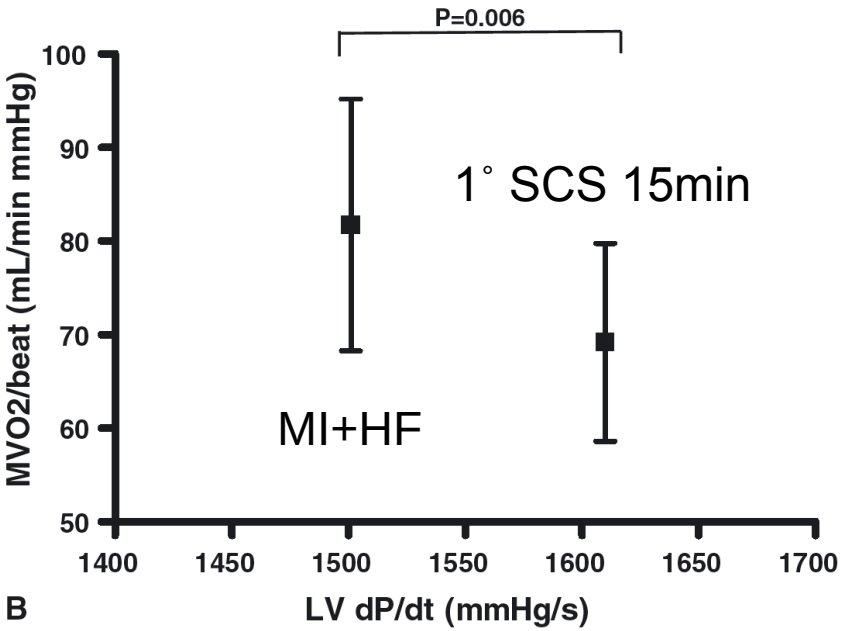
Circulation. 2009;120:286-294

In a porcine model of ischemic HF

Invasive hemodynamic assessment





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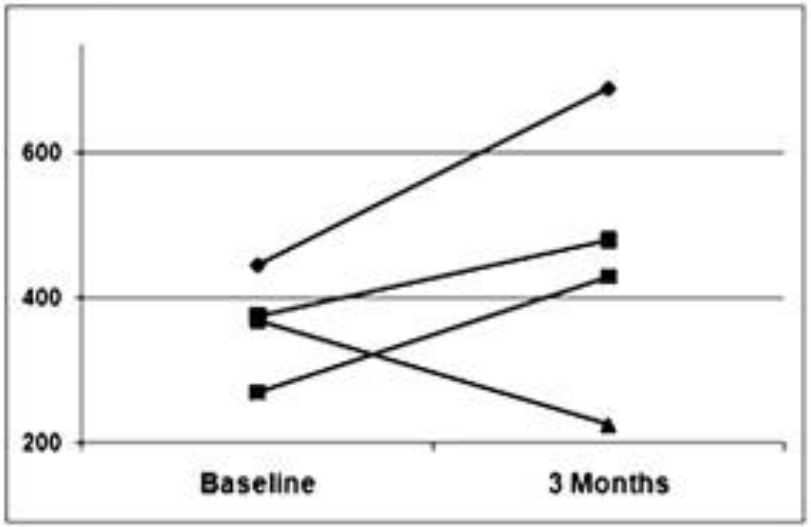
J Cardiovasc Electrophysiol. 2012;23:534-540

SCS for the Treatment of Advanced HF

A.1. Baseline Characteristics

Age/Sex	Diagnosis	LVEF (%)	LVED mm
52 y/o male	Ischemic	30	61
43 y/o male	Ischemic	18	65
18 y/o female	Non-Ischemic	10	77
77 y/o male	Ischemic	30	56

A.2. Exercise Duration (Meters)



- Two leads were implanted in each patient (T1-T3 and T9-T12).
- Stimulation frequency of 50 Hz, pulse width 200 msec with bipolar stimulation and output current amplitude set at 90% of initial parasthesias.
- Stimulation was programmed for 2hrs three times a day

Abstract. 2000. The 14th HFSA

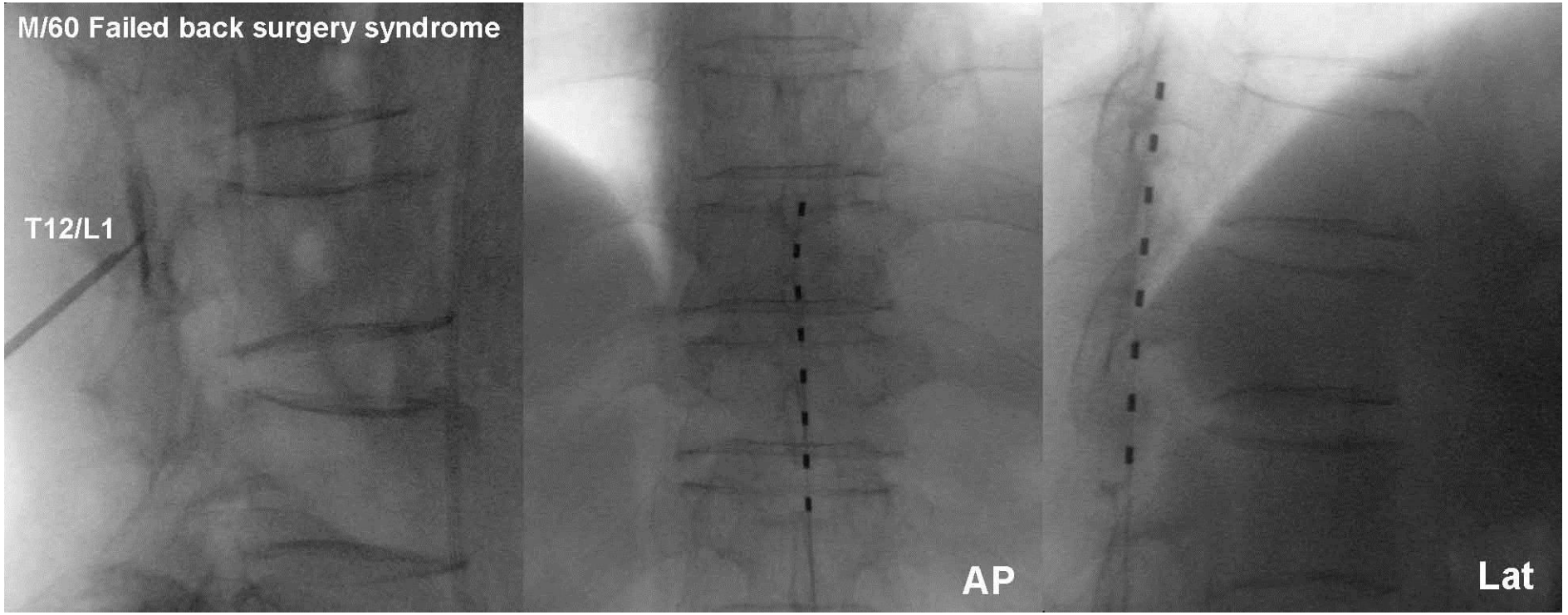
SCS results in a decrease in the TWA magnitude

Patient	SCS off	SCS on 2 h	SCS on 24 h
Patient 1	TWA rep: positive, Valt max: 6	TWA rep: positive, Valt max: 4	TWA rep: negative
Patient 2	TWA rep: positive, Valt max: 4	TWA rep: positive, Valt max: 2.5	TWA rep: negative
Patient 3	TWA rep: positive, Valt max: 8	TWA rep: positive, Valt max: 2.5	TWA rep: negative
Patient 1: after 2 months	TWA rep: positive, Valt max: 6.5	TWA rep: positive, Valt max: 2.5	TWA rep: negative
Patient 2: after 2 months	TWA rep: positive, Valt max: 6.5	TWA rep: positive, Valt max: 2.5	TWA rep: negative
Patient 3: after 2 months	TWA rep: positive, Valt max: 6	TWA rep: positive, Valt max: 3.8	TWA rep: negative

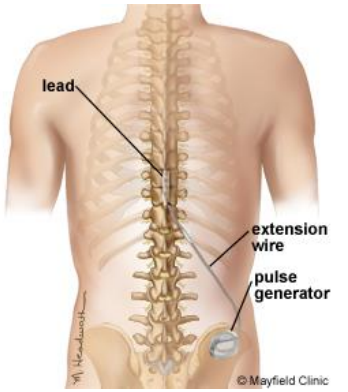
- T-wave alternans (TWA) has demonstrated to be a reliable non-invasive test for the stratification of the arrhythmic risk in both ischemic and non-ischemic cardiomyopathy.
- In all the three patients, we observed a significant reduction of TWA amplitude after 2 h stimulation.
- All the tests were classified as negative after 24 h stimulation with the nominal parameters.

Europace. 2008;10:506-508

Spinal cord stimulation: single-lead placement

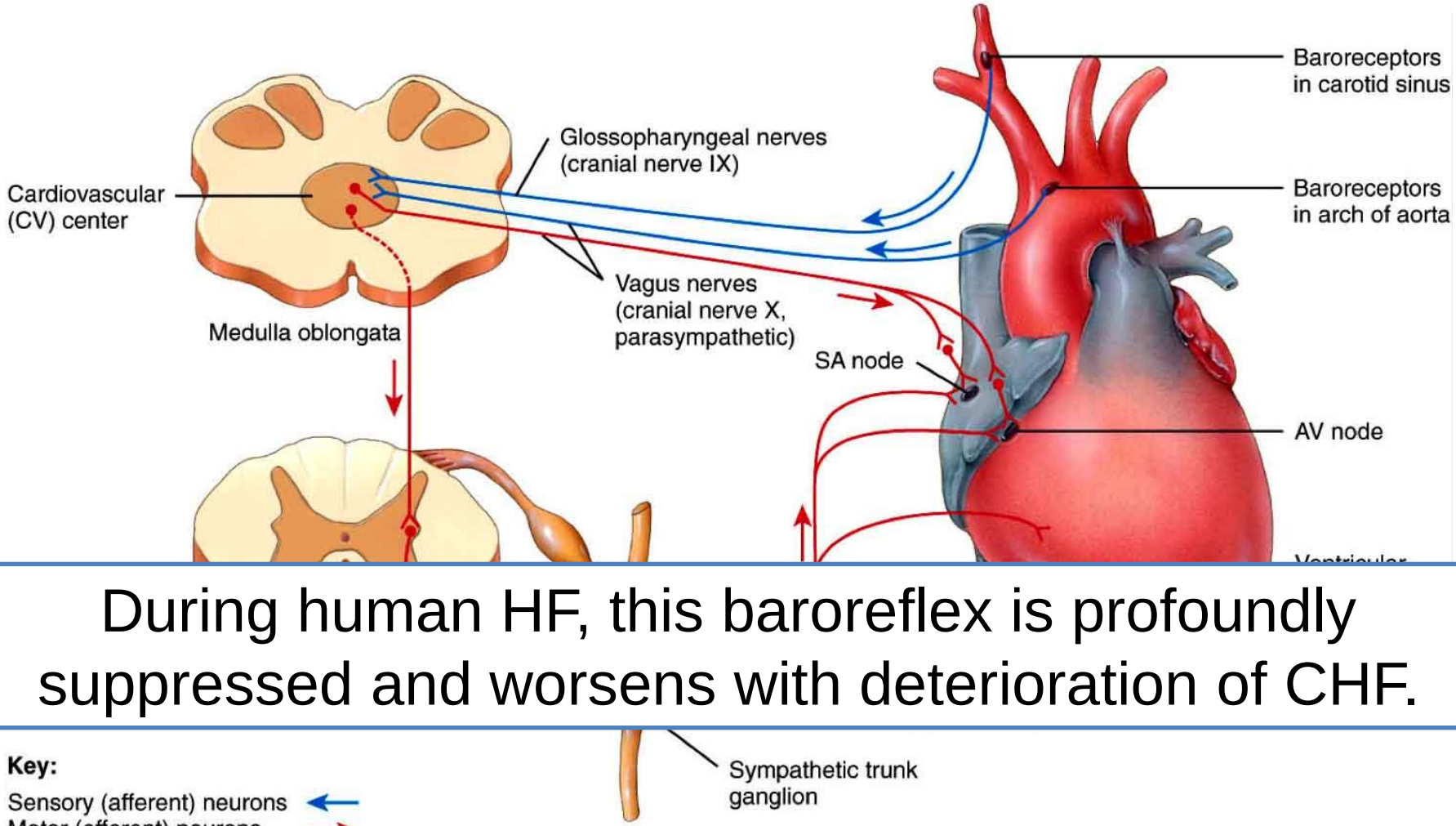


- The lead in the posterior epidural space in the mid-thoracic region at approx. T12/L1.
- The impulse generator is usually implanted subcutaneously in the low back or high buttock with tunnelling of the leads down to that region.



CAROTID SINUS NERVE STIMULATION

Baroreceptors

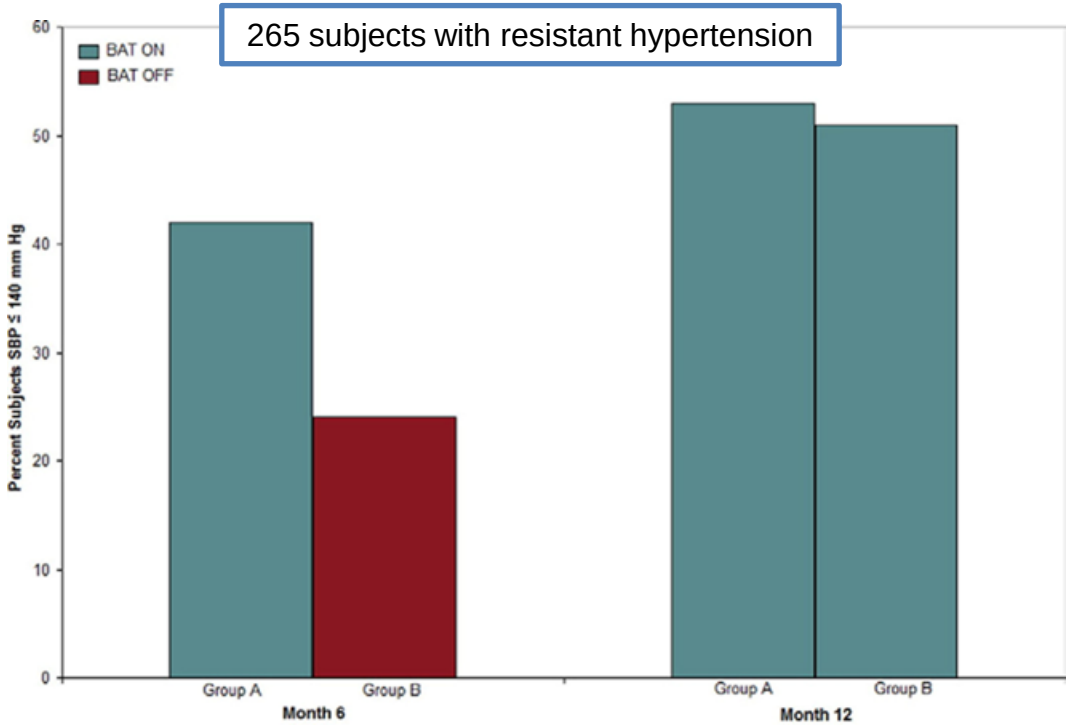


During human HF, this baroreflex is profoundly suppressed and worsens with deterioration of CHF.

Carotid sinus nerve stimulation

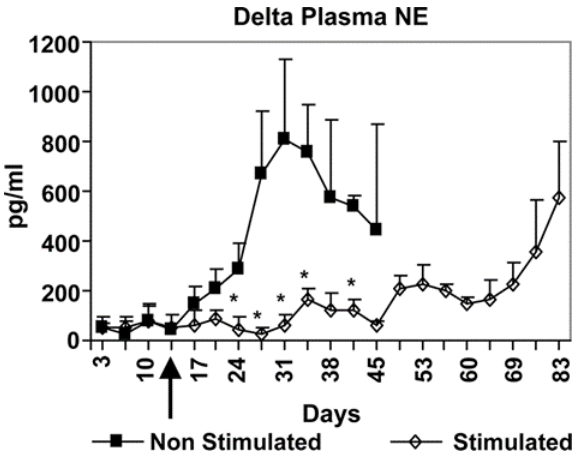
Proportion of Subjects That Achieved SBP <140 mm Hg

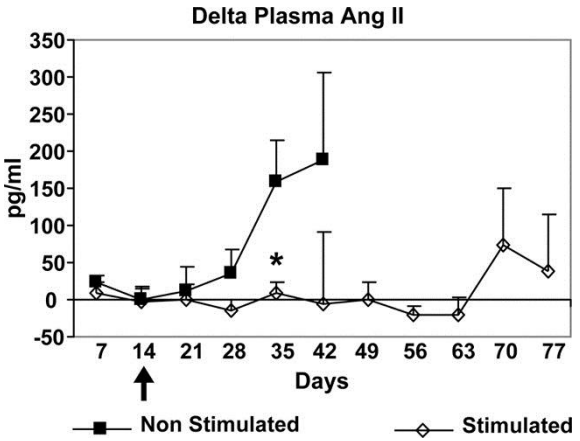
265 subjects with resistant hypertension



J Am Coll Cardiol. 2011;58(7):765-773.

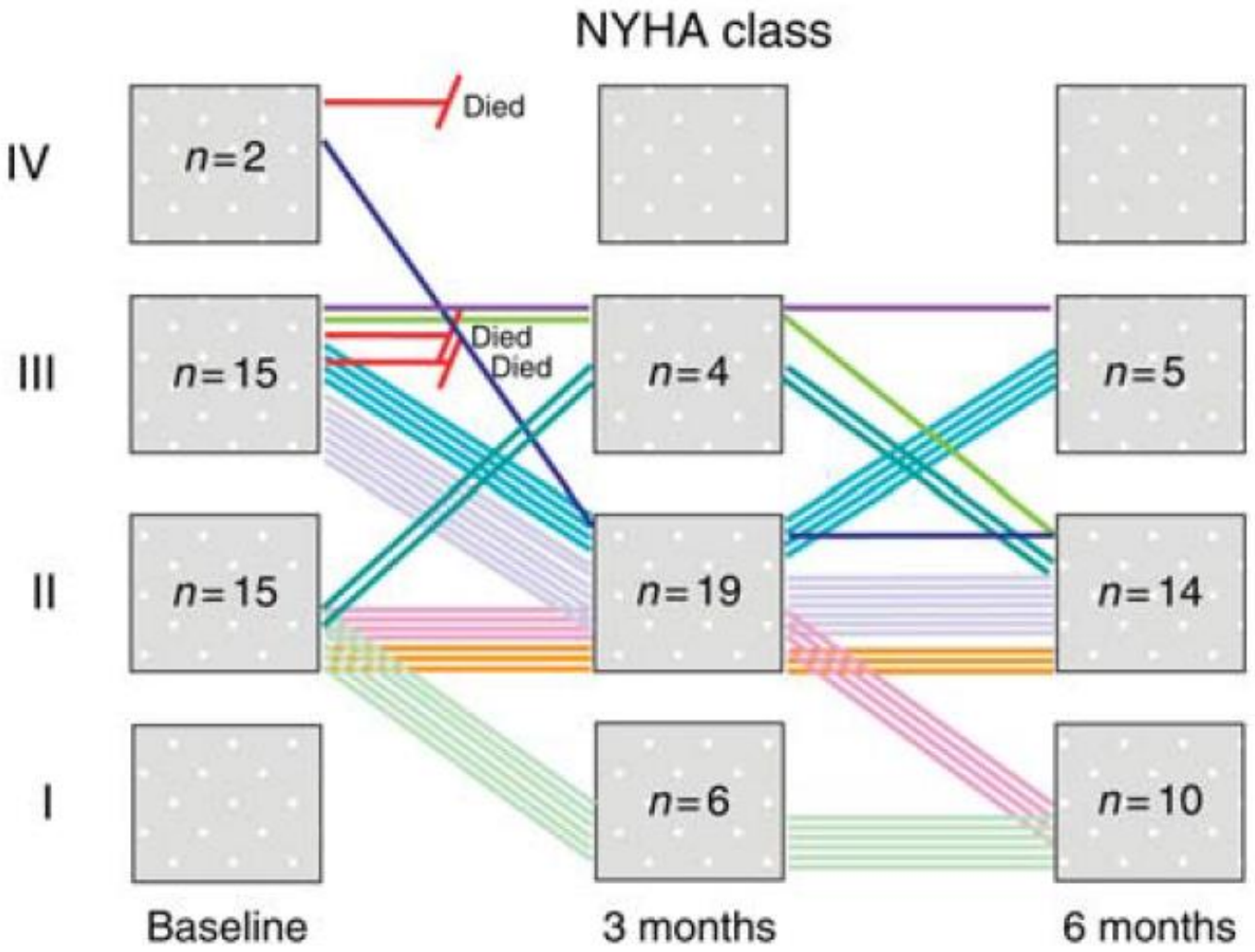
Chronic Baroreceptor Activation Enhances Survival in Dogs With Pacing-Induced HF





Hypertension. 2007;50(5):904-910.

Chronic vagus nerve stimulation



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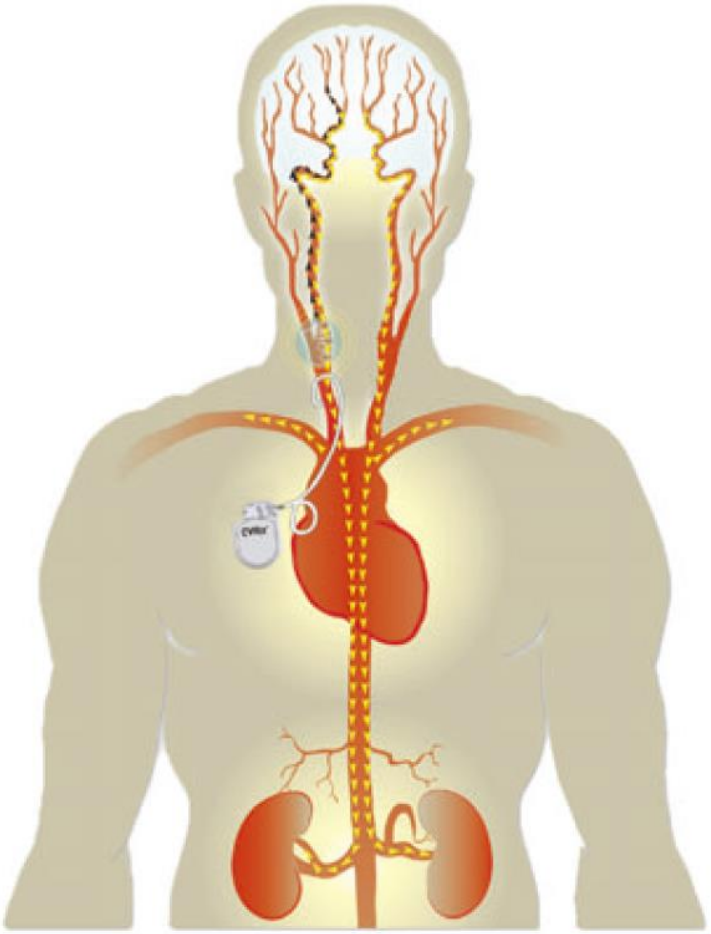
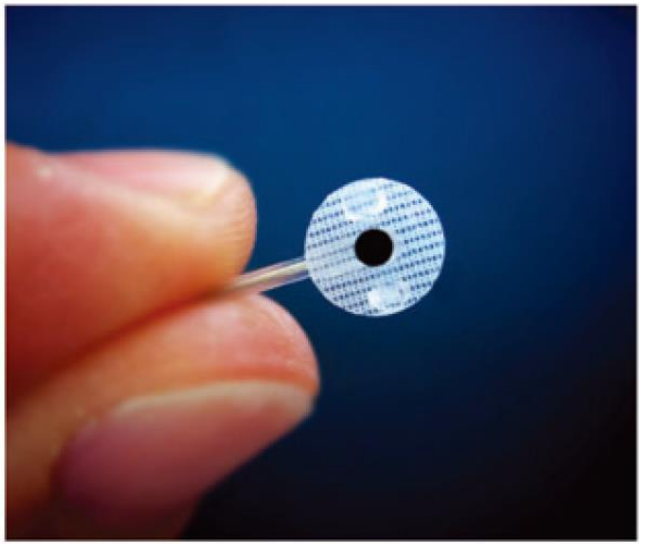
Eur Heart J. 2011;32:847-855

CVRx Neo system





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Europace. 2014;16:109-128

CERVICAL VAGAL NERVE STIMULATION

Parasympathetic system during CHF

- During CHF, the density of cardiac muscarinergic receptors is increased, which is most probably due to an adaptive upregulation secondary to a decreased efferent vagal input.

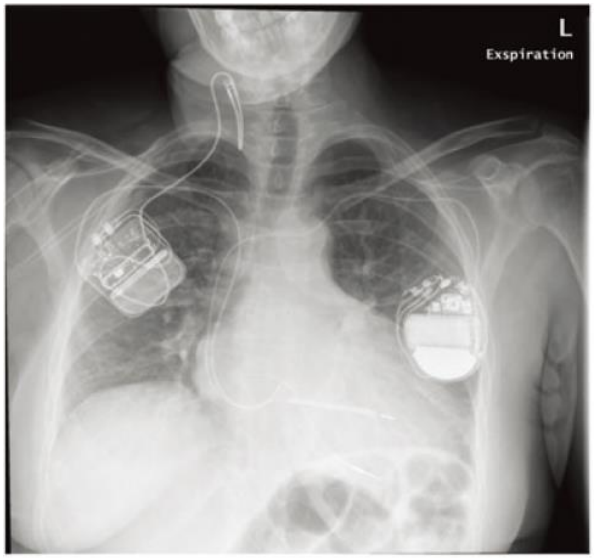
- The postganglionic vagal nerve transmission seems to be intact in HF.

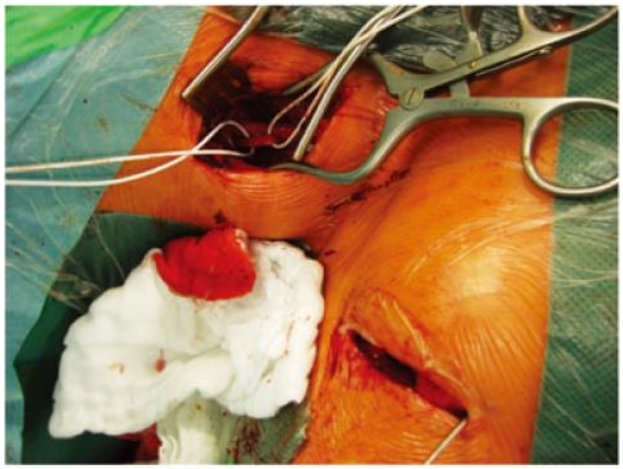
- Pre- to post-ganglionic parasympathetic efferent neurotransmission via nicotinergic acetylcholine receptors seems to be impaired during CHF.

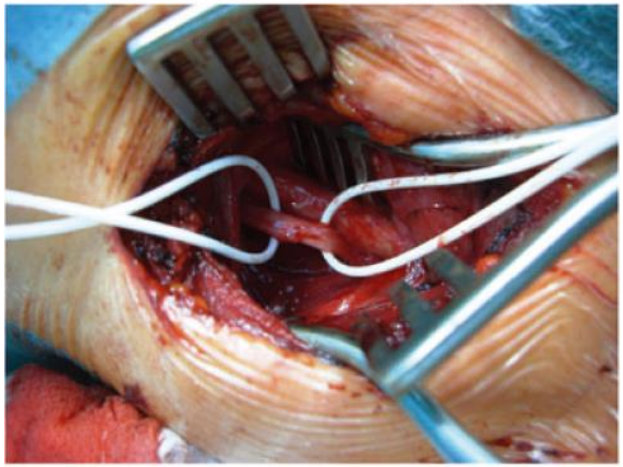
Mechanisms of action

- Antiarrhythmic effects – ↑Ventricular refractory period, ↑epicardial AP duration, ↓ventricular vulnerability to VF
- Rate slowing effects
- Antifibrotic effects
- Anti-inflammatory effects - ↓HF-associated increases of TNF-a, IL-6, and CRP
- Reverse remodelling

The CardioFit™ System







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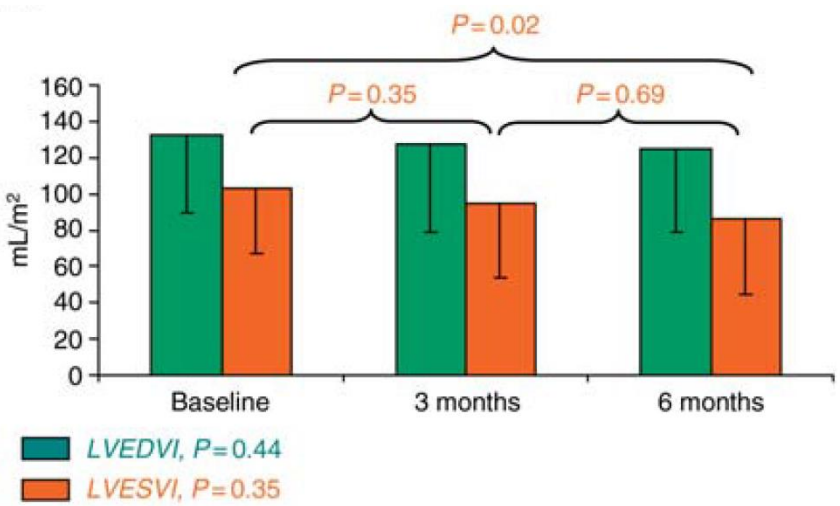
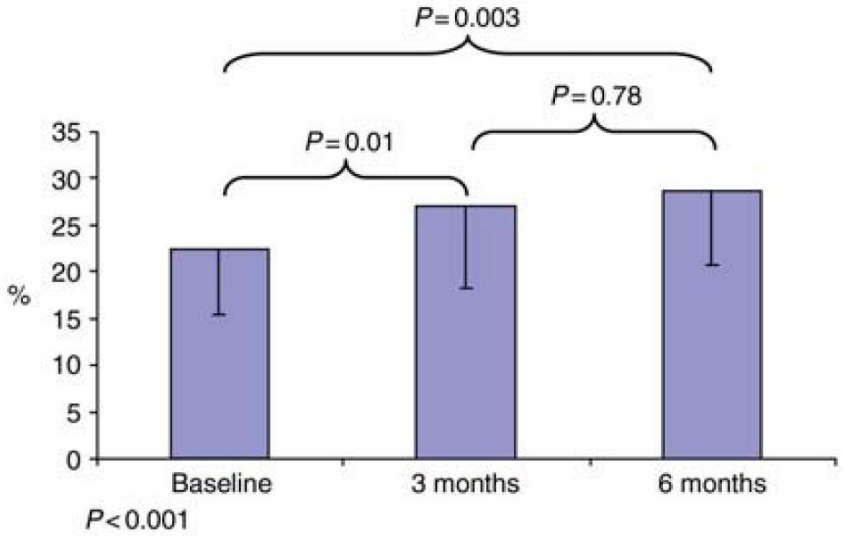
Europace. 2014;16:109-128

Echo evaluation after CVS

LV volume index (mL/m²)



LV EF (%)



32 NYHA class II–IV patients [56 ± 11 years, LVEF 23 ± 8%].

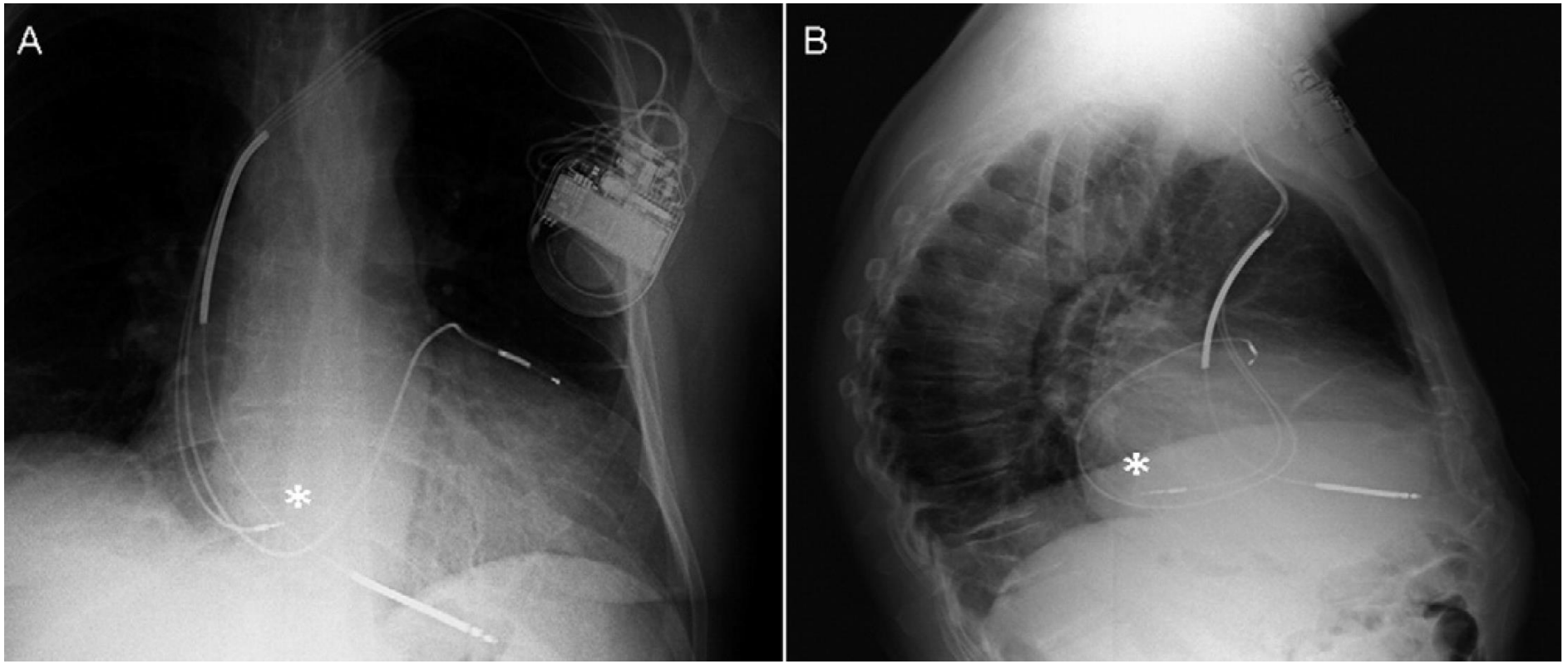
Eur Heart J. 2011;32:847-855

INTRACARDIAC AV NODAL VAGAL STIMULATION

Intracardiac AVN vagal stimulation

- 30-40% of patients with CHF eventually will develop AF.
- AF RVR may decrease the degree of LV resynchronization in patients with CRT and may ultimately lead to inappropriate shock delivery in up to 5% of ICD recipients.
- Long-term selective AVN vagal stimulation for ventricular rate control has been developed as potential adjunctive treatment modality for these patients.

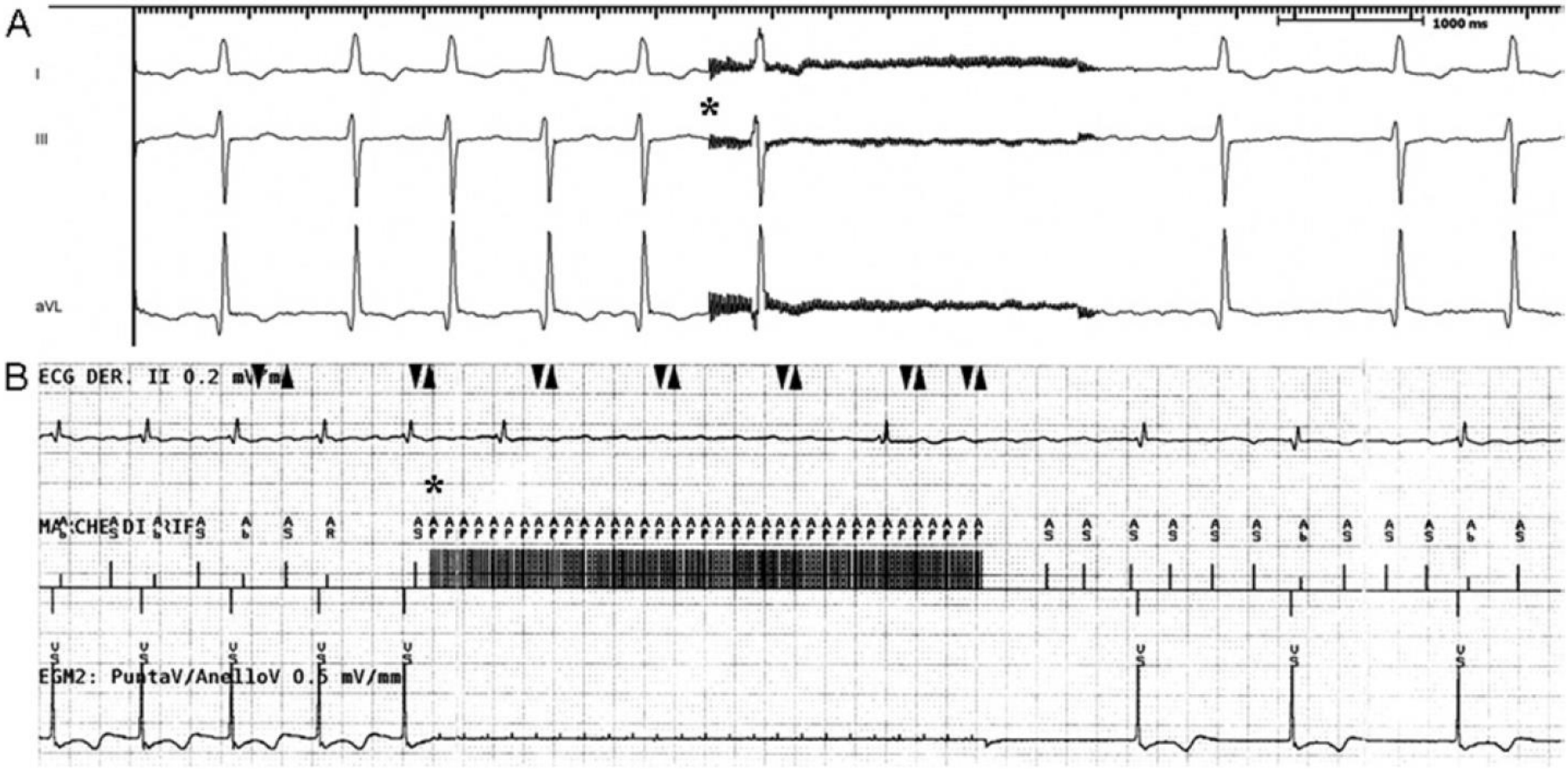
AVN vagal stimulation by transvenous permanent lead



Human parasympathetic nerves that control the AV node reside in an epicardial plexus (RIGP), which can be endocardially stimulated at the coronary sinus ostium and/or at the posteroseptal RA.

Heart Rhythm. 2009;6:1282-1286

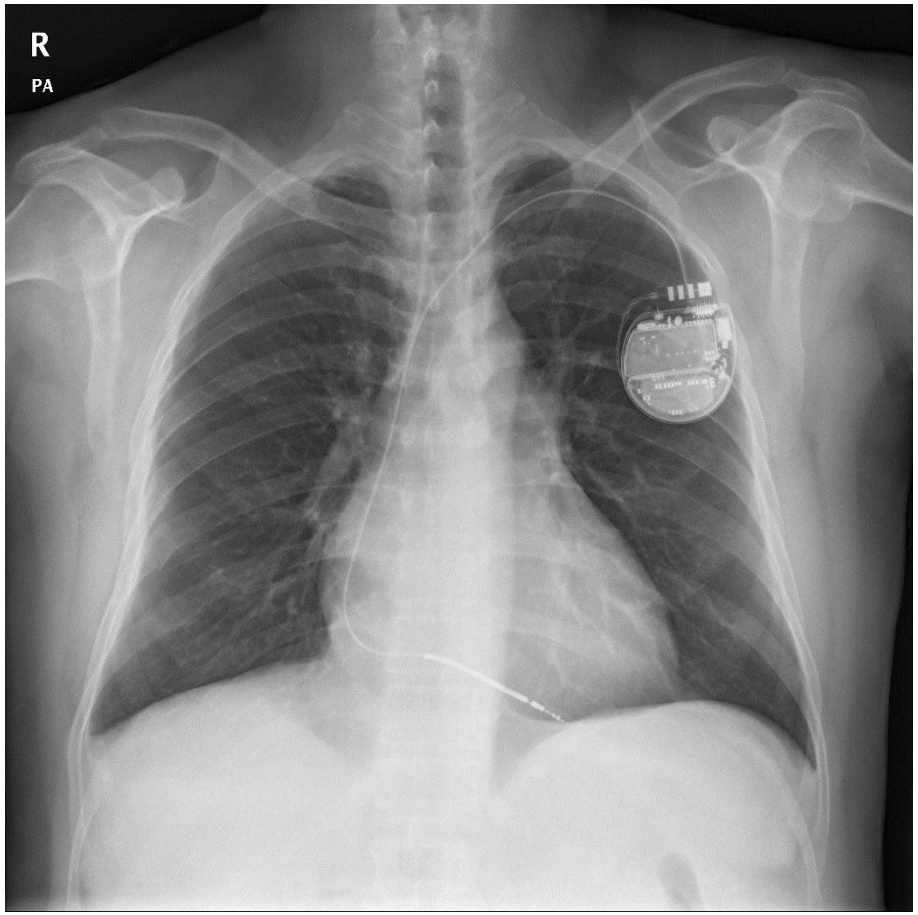
Effect of AVNVS



50-Hz atrial stimulation

Heart Rhythm. 2009;6:1282-1286

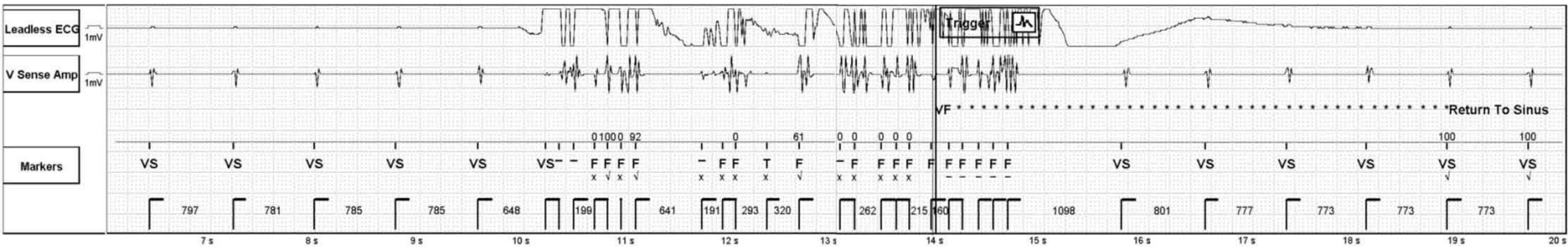
UNSOLVED ISSUES



M/50
ICD implanted for primary prevention of SCD

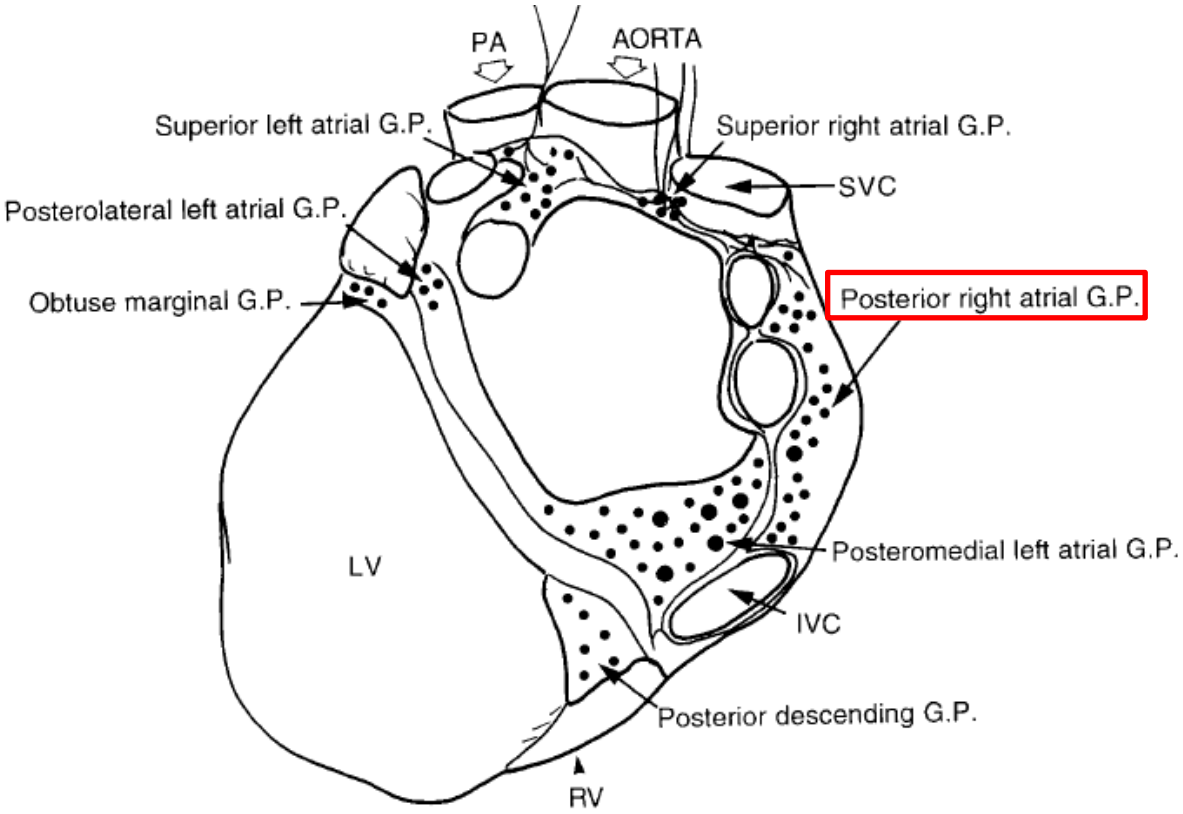
Inappropriate shock

Neuromodulation devices may have the potential for interfering with implantable cardioverter-defibrillator (ICD).

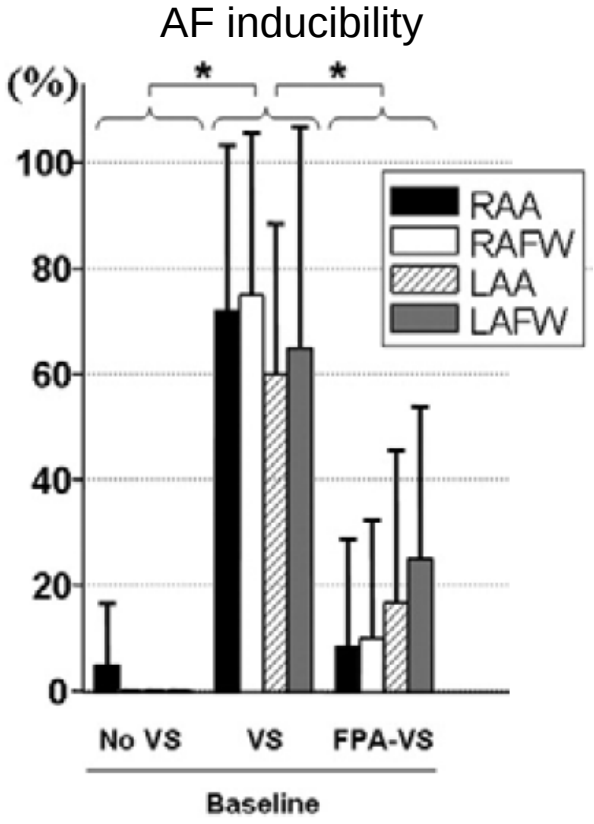


*Electrocautery devices resulted in oversensing, which led to false detection of ventricular tachyarrhythmia.

Induction of AF



Posterior atrial and ventricular GP



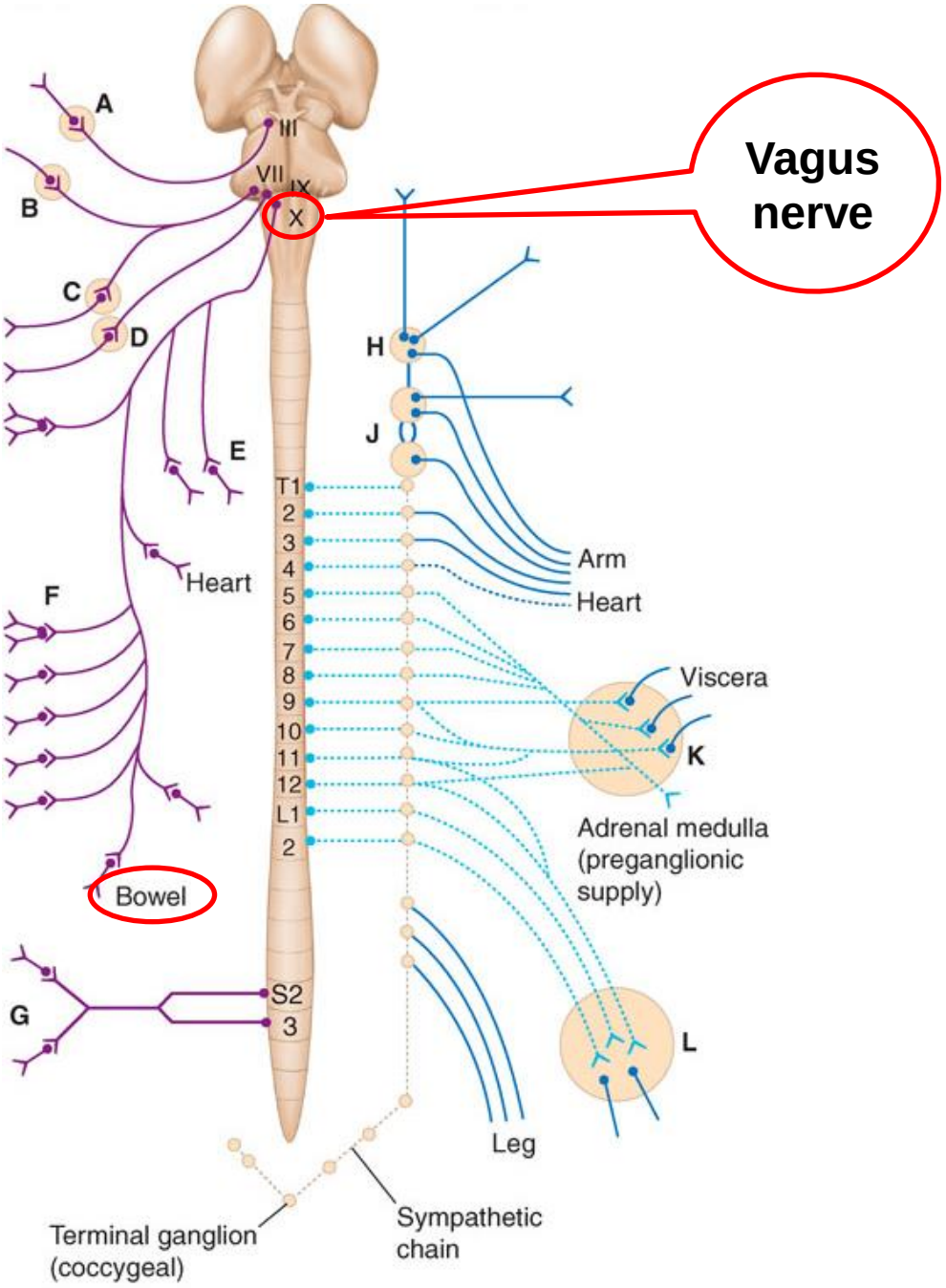
Seil Oh et al. *Heart Rhythm*. 2006

Vagal stimulation may facilitate spontaneous premature depolarizations in the atria, shorten the atrial and PV ERP, and increase heterogeneity of refractoriness.

Am J Physiol. 1996;271(1 Pt 2):H148-158.

Selectivity of neural stimulation

- The cervical vagal nerve contains efferent and afferent fibers coursing not only to the thoracic but also to or from the abdominal viscera.
- ↑Gastric acid secretion or intestinal motility?



On going trials

- Spinal cord stimulation
  - SCS-HEART (HF patients with ICD, non-random)
  - DEFEAT-HF (HF patients with ICD, on/off)
- Carotid sinus nerve stimulation
  - XR-1 heart failure study (HF patients, device vs. medical)
- Cervical vagal nerve stimulation
  - INOVATE-HF (HF patients, device vs. medical)
- Intracardiac AV nodal vagal stimulation
  - AV node stimulation study (HF patients with CRT-D)

Summaries

- HF is associated with significant perturbances of the autonomic balance with predominant sympathetic activation over the parasympathetic system.

- To therapeutically increase the cardiac parasympathetic tone
  - Spinal cord stimulation
  - Carotid sinus nerve stimulation
  - Cervical vagal nerve stimulation
  - Intracardiac AV nodal vagal stimulation

- However, many issues must be solved. Ongoing clinical trials will address the role and possible benefit.