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SmartCRT™

The Clinical Perspective

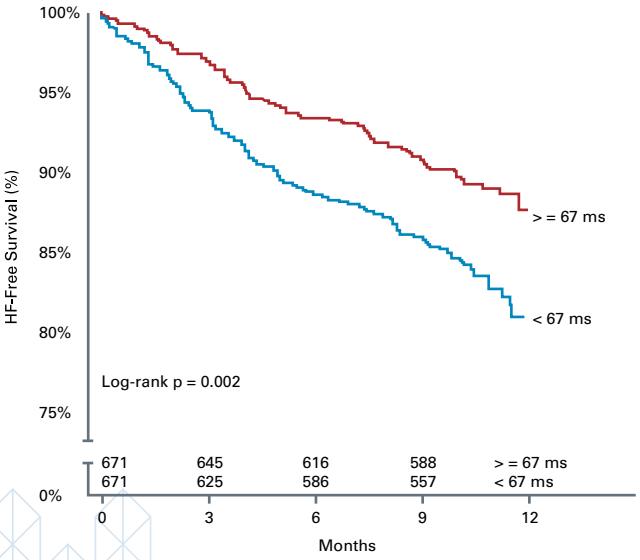
Where to pace

Gold et al. Poster @ HRS 2016 – full paper submitted

PEGASUS Sub-Analysis[1]

Evaluation of the relationship between RV-LV delay and HF hospitalisation and death

- n = 1342 enrolled in PEGASUS[2], multicentre, randomised, blinded endpoints
- Primary endpoint: composite score of hospitalisation and death
- What do we know?
  - Anatomic LV lead position has no significant impact on CRT response, except worsening in apex
  - Longer RV-LV delay results in greater reverse remodeling, reduced hospitalisation and death



Gold M. et al., ESC 2014 (n = 1342)[3]

30% **Reduction of risk of HF hospitalisation or death** associated with longer RVS-LVS delay.

Comparison	HR	P-value
RV-LV >= 67 ms vs. < 67 ms	0.70	0.030
Age (per 5 year increase)	1.04	0.308
Male vs. Female	1.39	0.068
Ischemic vs. Non-ischemic	1.31	0.093
NYHA (per 1 class increase)	1.77	0.017
QRS (per 10 ms increase)	0.96	0.102
LBBB vs. Non-LBBB	1.08	0.653
LVEF (per 5% increase)	0.99	0.912

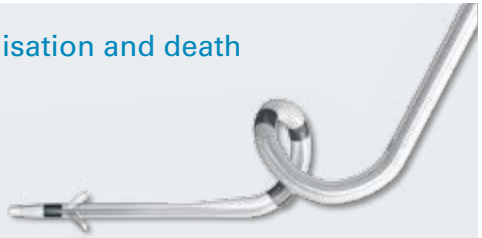
- Baseline RV-LV dyssynchrony predicted CRT response
  - Independent of QRS duration (> 130 ms) and morphology
- RV-LV pacing interval is a strong and independent predictor of clinical response for CRT
- Measuring RV-LV time at implantation may help to identify optimal pacing sites

Where to pace

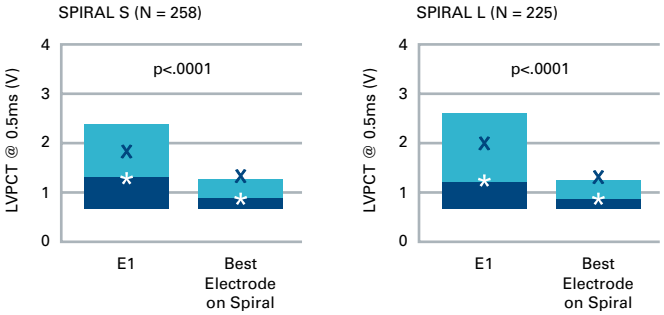
Mittal et al. 2016 J Cardiovasc Electrophysiol

NAVIGATE X4 Study[4]

Evaluation of the relationship between RV-LV delay and HF hospitalisation and death



- Prospective, single-arm, non-randomised, multicentre clinical trial
- Enrolment of 791 patients in 88 US centres
  - n = 520 (either Spiral L or S) / n = 218 (Straight lead)
- Primary endpoint: 6-month LV lead-related complication rates
- Three lead options – thus, greater opportunity for non-apical pacing
- Significant reduced number of complications (PNS and dislodgement) due to the lead design and 17 possible pacing vectors



- 99.1% dislodgement complication free rate
- 0.4% re-intervention rate for PNS
- 0.9V median pacing capture thresholds (PCT) for the best proximal electrode of the ACUITY X4 Spiral leads
- 97% implant success
- Low acute (i.e. dislodgement) and chronic complication rates
- Spiral lead: pacing threshold is lower from proximal electrodes
- Basal pacing reveals less PNS (PNS in 8% of patients)
- LV lead in apex: 2.4-fold risk of HF/death and 5-fold risk of death alone[5]
- Pacing from latest mechanical delay contributes to improved outcomes[5]

When to pace

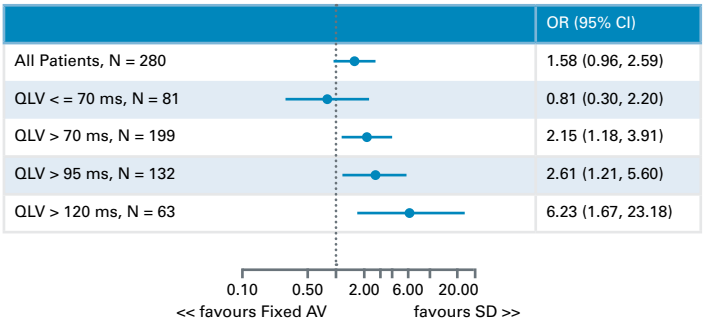
Gold et al. 2013 Heart Rhythm

Smart AV Sub-analysis[6]

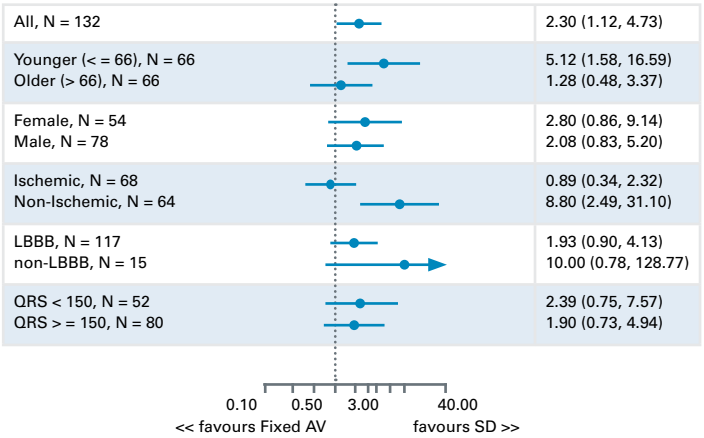
Evaluation:

- n = 280, 1:1 randomisation of AV delay based on SmartDelay™ vs. fixed 120 ms AV delay
- Primary endpoint: changes in LVESV
- Choose LV pacing sites with long electrical delay and optimizing AV timing to max electrical resynchronisation

Multivariate Logistic regression results adjusted for baseline
LVEF, LVESV, Ischemia, LBBB, Gender, NYHA, QRS



Univariate Logistic regression results
QLV > 95



- Electrical dyssynchrony, as measured by QLV, was strongly associated with LV volumetric changes with CRT.
- Benefit of SmartDelay optimisation was observed at the longest QLV interval.
- AVO is unlikely to be of benefit in the absence of long QLV intervals.
- Optimal fusion of intrinsic conduction down the right bundle branch with LV pacing maximises the hemodynamic response.
- The greater the electrical delay at the LV pacing site, the greater the electrical resynchronisation that can occur with an optimally timed stimulus.

SmartDelay™ is non-inferior to echo optimisation.

Zanon et al. 2016 Heart Rhythm

Long-Term Benefit of Optimised Multipoint CRT[7]

Evaluation of whether patients treated with MPP with optimised LV pacing location have better long-term clinical outcomes than patients treated with conventional CRT

- n = 110, single centre, non-randomised trial
- Primary endpoint: improvement of long-term clinical outcomes of patients with optimal lead position treated with MPP
- 3 non-randomised groups:
  - STD: standard group
  - OPT: group with optimised LV lead position
  - OPT + MPP: group with optimised LV lead position and MPP turned on
- LV lead in area of latest electrical delay may improve the response to CRT
- Positive correlations between between Q-LV and LVdP/dtmax and QRS narrowing
- Pacing at sites with longer Q-LV is linked to better long-term outcome

	STD (54) (%; 95% CI)	OPT (36) (%; 95% CI)	OPT + MPP (20) (%; 95% CI)	P
ESVi response	30 (55.6%; 42.4-68.0)	26 (72.2%; 56.0-84.2)	18 (90%; 69.9-97.2)	$X^2 = 0.015^{\dagger}$
				LT = 0.004
NYHA response	36 (66.7%; 53.4-77.8)	28 (77.8%; 61.9-88.3)	19 (95.0%; 76.4-99.1)	$X^2 = 0.039^{\dagger}$
				LT = 0.012
PACKER'S response	32 (59.3%; 46.0-71.3)	24 (66.7%; 50.3-79.8)	18 (90%; 69.9-97.2)	$X^2 = 0.043^{\dagger}$
				LT = 0.018

CI = confidence intervals; CRT = cardiac resynchronisation therapy; ESVi = end-systolic volume index; LT = linear trend; MPP = multipoint pacing; NYHA = New York Heart Association; OPT = optimised; STD = standard.
† X^2 = Pearson chi-square

- Long-term superiority of **LV site optimisation plus MPP** over conventional CRT
- Reversal of long-term progression of HF (non-sig. improvement of Packer score)
- Improvement of clinical outcomes (non-sig. improvement of NYHA class)
- Response rates of around 90%

SmartCRT™, Boston Scientific's approach to personalised CRT therapy, provides physicians with smart solutions to choose where, when and how to pace for optimal results.

1. Gold et al. The Role RV-LV Delay to Predict Time to First Heart Failure Hospitalization and Mortality with Cardiac Resynchronization Therapy. HRS 2016.
2. Martin et al. 2012 J Cardiovas Electrophys. Atrial Support Pacing in Heart Failure: Results from the Multicenter PEGASUS CRT Trial.
3. Gold et al. The relationship between RV-LV delay and left ventricular reverse remodeling with Cardiac Resynchronization Therapy. Eur Heart J. 2014; 35 (Suppl 1): Abstract P2962.
4. Mittal et al. 2016 J Cardiovas Electrophys. Performance of anatomically designed quadripolar left ventricular leads: Results from the NAVIGATE X4 clinical trial.
5. Moss et al. 2009 New Eng J Med. Cardiac-resynchronization therapy for the prevention of heart-failure events.
6. Gold et al. 2013 Heart Rhythm. The effect of left ventricular electrical delay on AV optimization for cardiac resynchronization therapy.
7. Zanon et al. 2015 Heart Rhythm. Multipoint pacing by a left ventricular quadripolar lead improves the acute hemodynamic response to CRT compared with conventional biventricular pacing at anysite.

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