001 UNBIASED ASSESSMENT OF SYMPTOMATIC "RESPONSE RATE" TO CARDIAC RESYNCHRONISATION THERAPY BY SYSTEMATIC REVIEW OF RANDOMISED CONTROLLED TRIALS (REVERSE, MIRACLE, MIRACLE ICD, MIRACLE ICD II, CARE-HF, COMPANION, CONTAK-CD, AND MUSTIC)

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Background Varied rates of individual symptomatic response are cited for cardiac resynchronisation therapy (CRT) but have never been systematically evaluated together. Nor has spontaneous recovery rate been routinely subtracted, to clearly identify rate of symptomatic response genuinely attributable to CRT.

Method and Results First, we systematically reviewed the last 92 papers on PubMed about CRT. 74% referred to responder rates but only 18% recognised the existence of "response to doing nothing". Second, we examined symptomatic response rates in the randomised CRT trials CARE-HF, COMPANION, CONTAK-CD, MIRACLE, MIRACLE-ICD, MIRACLE-ICD II, MUSTIC, and REVERSE, totalling 3904 patients. The weighted average symptomatic response rate, assessed using the clinical composite score was 54% for those randomised to CRT vs 40% for those randomised to no CRT. Using NYHA score, these values were 51% and 35% respectively. When symptomatic response rate was measured using 6-min walk distance and Minnesota Living with Heart Failure Quality of Life Score, a much larger spontaneous improvement was seen in the control arm of the blinded studies (device implanted but turned off in the control arm) compared to the open studies (no device implanted in the control arm). Spontaneous improvement was almost twice as high in the control arms of the blinded studies vs the open studies. With 6-min walk distances, 55% of the improvement in distance walked in the CRT arm was seen in the control arm for the blinded studies, vs 25% in the open. These values were 56% and 23% respectively with the Minnesota Living with Heart Failure Quality of Life Score.

Conclusions Quoting CRT responder rates in isolation, without recognising spontaneous responders, is common but invalid. Response rate with CRT, at 54%, is not the response rate attributable to CRT, which is only 14% of implanted patients. Three-quarters of those who "responded" with CRT would have done so even without CRT. Subjective quantitative markers seem to show an additional placebo effect and the placebo effect is more pronounced in the blinded studies than open studies. CRT definitely prevents death and reduces symptoms, but commonly-quoted "responder rates" are exaggerated, and are dependent on the measure used, and the blinding methodology used in the trial referenced.

002 A RANDOMISED STUDY OF TEMPORARY EPICARDIAL CARDIAC RESYNCHRONISATION VS CONVENTIONAL RIGHT VENTRICULAR PACING IN CARDIAC SURGICAL PATIENTS

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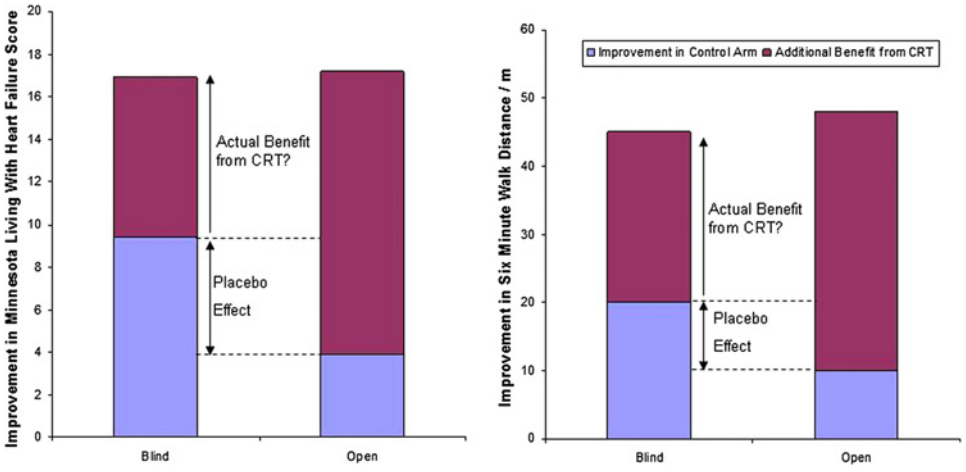
Introduction Left ventricular (LV) function is an important indicator of morbidity and mortality after cardiac surgery. Therefore, interventions to optimise peri-operative LV function may improve surgical outcomes. Biventricular (BiV) pacing has been shown to improve haemodynamic function in heart failure patients and temporary BiV pacing is feasible after cardiac surgery. Therefore, temporary BiV pacing may be beneficial to heart failure patients after cardiac surgery.

Aim The aim of this trial was to investigate the clinical utility of temporary BiV pacing delivered via epicardial wires attached to the right atrium (RA), right ventricle (RV) and left ventricle (LV) after cardiac surgery.

Methods 55 subjects undergoing elective cardiac surgery (coronary artery bypass grafting and/or valve surgery) were recruited from two cardiac centres, over an 18-month period commencing January 2010. 38 subjects completed the protocol. Nine subjects were removed at the operators request including: "off pump" bypass surgery, patient referred for alternative mode of revascularisation or surgical "turn down". 19 subjects were randomly assigned to receive temporary (BiV) pacing using a dedicated triple chamber temporary pacing box with the capacity to programme the atrio-ventricular (AV) and inter-ventricular (VV) intervals. 19 received "standard pacing" after cardiac surgery. The duration of level 3 care was measured for each subject. In brief, this is the requirement for either invasive ventilation, multi-organ support or haemodynamic support with more than one inotrope/vasocontrictor or intra-aortic balloon pump. The trial was powered to compare the primary endpoint of transition from level 3 to level 2 care in the two groups. Secondary endpoints included acute haemodynamic performance in different pacing modes: immediately after the operation, 6 h, 18 h and 24 h after admission to cardiac intensive care. The pacing modes assessed



Abstract 001 Figure 1 Weighted average improvement in 6-min walk distance and Minnesota living with heart failure score in control and therapeutic arms of CRT trails.

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included: atrial inhibited (AAI); ventricular inhibited (VVI-RV); dual chamber (DDD-RV); biventricular (DDD-BiV) and left ventricular pacing (DDD-LV). Base rate for pacing was set at 86/min and continued for the duration of level 3 care. The haemodynamic data were measured using a pulmonary arterial catheter using either thermodilution or continuous cardiac output measurements.

Results The baseline demographics are illustrated in Abstract 002 table 1. The acute haemodynamic measurements at 18 h, Abstract 002 table 2.

Abstract 002 Table 1

Demographic	Biventricular pacing	Standard pacing	p Value
Age/years (SD)	69.2 (9.3)	65.5 (12.7)	0.32
Male gender/%	79	79	1.0
NYHA score pre-operation (SD)	2.5 (0.7)	2.4 (0.9)	0.69
Euroscore/additive (SD)	8.3 (3.1)	7 (2.8)	0.18
QRS duration/ms (SD)	113.3 (29.3)	115.2 (24.4)	0.84
CABG only/%	63	58	0.63
Ejection fraction (pre-op)/% (SD)	26.1 (5.4)	28.0 (7.3)	0.34
Cardiopulmonary bypass time/min (SD)	127.1 (41.1)	144 (45.9)	0.25
Duration of Level 3 Care/hours (SD)	44.5 (36.8)	57.1 (73.0)	0.56

Abstract 002 Table 2

Pacing mode	Cardiac output l/min/(SD)	p Value (paired student t test vs AAI)
AAI	5.4 (1.1)	
VVI	4.3 (1.7)	<0.001
DDD-RV	5.3 (1.1)	0.77
DDD-BIV	5.8 (1.2)	0.02
DDD-LV	5.4 (0.7)	0.73

Conclusions BiV pacing significantly improved haemodynamics in the early part of the post-operative period compared to standard AAI pacing at 18 h. There is a suggestion that the improvement in haemodynamic function may translate into clinical benefit. The duration of level 3 care was 57.1 h in the standard pacing group compared to 44.5 h in the BiV group. However, the 22% reduction in level 3 care in the BiV group compared to the standard pacing group did not reach statistical significance.

003 VALIDATING MARKERS OF MECHANICAL DYSSYNCHRONY BY EXPERIMENTAL MANIPULATION OF INTERVENTRICULAR TIMINGS: WHAT IS NEEDED TO MAKE THEM A REASONABLE PROSPECT FOR CARDIAC RESYNCHRONISATION THERAPY SELECTION?

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Background Any dyssynchrony marker proposed for selection of patients for cardiac resynchronisation therapy (CRT) should be stable between heartbeats but change markedly when interventricular delay is experimentally manipulated; the marker should also minimise at some "optimal" interventricular delay.

Methods and Results We performed 3264 echocardiographic measurements in 13 patients with CRT: separate, replicate measurements at interventricular delays from RV-first 40 ms to LV-first 60 ms, in 20-ms intervals of (1) 3D systolic dyssynchrony index (SDI), (2) Tissue Doppler imaging (TDI), (3) aortic pre-ejection time, (4) interventricular mechanical delay (IVMD), (5) LVOT VTI and (6) QRS duration. In each patient, we identified with blinding on several successive repetitions, an apparently-optimal (minimally-dyssynchronous) interventricular delay for each variable. Agreement between successive optimisations was low: κ values of 0.24 for SDI, 0.02 for TDI, 0.36 for aortic pre-ejection time, 0.14 for IVMD, 0.40 for LVOT VTI and 0.47 for QRS duration. Intraclass correlation coefficient, indicating measurement reproducibility, was low when single measurements were taken (ranging across methods from 0.32 to 0.63), but improved when pairs of measurements were averaged (0.51 to 0.74, p=0.0008). Using averages of pairs of measurements reduced the disagreement between replicate optimisations p=0.007.

Conclusions Under blinded conditions these mechanical dyssynchrony markers cannot reliably discriminate even large changes in interventricular delay, and can be quickly rejected as candidates for predicting clinical benefit from CRT. It would save time and expense if markers considered for clinical trialling under formal scientific conditions first underwent screening for plausibility by such a stage of inexpensive, active experimentation.

004 SIMULTANEOUS INVASIVE PRESSURE AND FLOW MEASUREMENTS DURING ATRIOVENTRICULAR DELAY IMPROVEMENT REVEAL A COMPENSATORY PERIPHERAL VASODILATOR RESPONSE WHICH ATTENUATES THE INITIAL BLOOD PRESSURE INCREMENT: IMPLICATIONS FOR THE DESIGN OF OPTIMISATION PROTOCOLS

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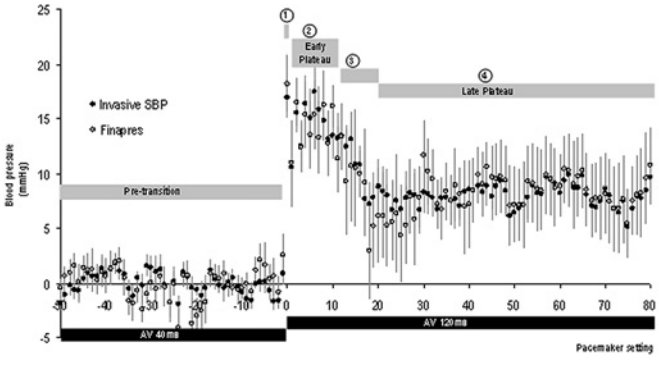
Introduction With synchrony of ventricular contraction already restored by cardiac resynchronisation therapy (CRT), optimisation of atrioventricular (AV) delay relies on improving filling. Although when AV delay is improved blood pressure immediately rises, there is a subsequent partial decline. Is this secondary decline because (1) non-invasive measurements are unreliable, (2) cardiac function increment is short-lived or (3) peripheral vasodilatation occurs? We conducted invasive experiments to distinguish between these hypotheses.

Methods Nine patients with heart failure and CRT underwent changes in programmed AV delay from 40 ms to 120 ms. We simultaneously measured beat-by-beat invasive aortic pressure and flow, and non-invasive pressure (Finometer). Triplicate sets of experiments were performed and averaged to minimise the impact of noise.

Results There was an immediate increment in invasive blood pressure of +14.7±2.0 mm Hg (p=0.0001), but after ~10 beats there



Abstract 004 Figure 1

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