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# Optimisation and regulation of breathing in heart failure

| Submission date | Recruitment status | [_] Prospectively registered |
|---|---|---|
| 05/05/2010 | No longer recruiting | [_] Protocol |
| **Registration date** | **Overall study status** | [_] Statistical analysis plan |
| 06/05/2010 | Completed | [X] Results |
| **Last Edited** | **Condition category** | [_] Individual participant data |
| 29/12/2020 | Circulatory System | |

**Plain English summary of protocol**
Not provided at time of registration

## Contact information

**Type(s)**
Scientific

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## Additional identifiers

**Protocol serial number**
7352

## Study information

**Scientific Title**
Optimisation and regulation of breathing in heart failure: a randomised interventional treatment trial

**Acronym**
DRN 370 (SRF Optimisation)

## Study objectives

Evaluation of beat-by-beat continuous noninvasive blood pressure measurement by digital photoplethysmography to optimise haemodynamics in patients with an atriobiventricular pacemaker for chronic heart failure:
1. Changes in atrioventricular and interventricular delays, within the range of settings typically used in clinical practice, will cause reproducible and significant changes in arterial pressure as measured by digital photoplethysmography (Finapres)
2. At higher heart rates, changes in atrioventricular and interventricular delay will have a more pronounced effect on arterial pressure than they do at lower heart rates
3. If echocardiographic measurement of stroke volume is able to identify an optimal setting for maximal stroke volume, that setting will correspond to a maximal or near-maximal systolic arterial pressure
4. Patients clinically considered non-responders will have a smaller increment in systolic arterial pressure than will the responders, when the device is switched from off to on
5. Dependency of haemodynamics on pacemaker settings will be similar, whether measured at rest or during exercise (low-level, steady state)

Immediate effects of higher-rate pacing or altered AV delay on periodic breathing:
6. Increasing heart rate through pacing significantly stabilises breathing pattern and reduces oxygen desaturation in awake patients with chronic heart failure and can also be used as a model of periodic breathing
7. The effect is prompt in effect, with a substantial stabilisation in the early few minutes after a change in heart rate
8. The effect is reversible, on a similarly rapid timescale, including with dynamic CO2 administration
9. The stabilising effects are paralleled by a rise in cardiac output and fall in chemoreflex delay time, and the destabilising effects are paralleled by a fall in cardiac output and prolongation of chemoreflex delay time
10. Carefully-timed dynamic variation in rate or AV delay can achieve greater stability of breathing control than constant-rate pacing with the same mean rate

Dynamic therapy with inhaled carbon dioxide as a novel form of "pacing" to stabilise cardiorespiratory control in patients with chronic heart failure and periodic breathing:
11. In patients whose usual pattern of respiration is steady (i.e. non-periodic), alternating between CO2 supplementation and normal inspired air for 30 second periods will generate a pattern resembling periodic breathing, which can be used as a model of periodic breathing
12. In patients with periodic breathing, dynamic intervention with alternation between CO2 supplementation and normal air (with CO2 given in the 30 seconds of the periodic breathing cycle with the lowest respiration) will worsen cardiorespiratory instability
13. In patients whose usual pattern of respiration is periodic, dynamic intervention with alternation between CO2 supplementation and normal air (with CO2 given in the 30 s with the highest respiration) will significantly stabilise cardiorespiratory control
14. Once the most effective timing strategy for dynamic therapy with CO2 is determined by this study, application of this strategy achieves more stabilisation of cardiorespiratory control than is obtained by delivering the same average dose of CO2 as a continuous stream
15. An automated algorithm, using respiratory excursion and/or end-tidal CO2 data, can control the timing of delivery of CO2 to improve cardiorespiratory control stability in a pacemaker model of periodic breathing

## Ethics approval required

Old ethics approval format

## Ethics approval(s)
Royal Brompton Hospital Research Ethics Committee approved (ref: 05/Q0404/018)

## Study design
Single centre randomised interventional treatment trial

## Primary study design
Interventional

## Study type(s)
Treatment

## Health condition(s) or problem(s) studied
Topic: Diabetes Research Network; Subtopic: Type 2; Disease: Cardiovascular disease

## Interventions
All the sub-studies described below will be one-off visits for each patient with no long-term follow-up required.

Experimental design  Study A (digital photoplethysmography to optimise haemodynamics in patients with atriobiventricular pacemaker):
Protocol for AV delay experiment: The experiment will be carried out at 4 heart rates: resting, 90, 110 and 130 bpm. At each rate, a series of AV delays will be trialled: 40 ms, 80 ms, 100 ms, 120 ms, 140 ms, 160 ms, 200 ms and 240 ms (if native AV conduction occurs at long AV delays, longer AV delay values will be omitted). A trial of an AV delay involves recording of a series of alternations of the pacemaker programming between that AV delay and a default values (120 ms). At each rate, a series of delays between ventricular activation (VV delays) will also be trialled (LV-RV delays of -40 ms, -20 ms, 4 ms [or nearest available value to 0], 20 ms, 40 ms) in a corresponding fashion. These will be performed with AV delay set to the value found to give the highest BP. The study will be repeated at 110 bpm (only).

Study B (Immediate effects of higher-rate pacing on periodic breathing in patients with chronic heart failure):
Protocol: With the patient positioned as indicated above, a pacemaker programmer telemetry head will be secured over the pacemaker pulse The programmed rate of the pacemaker in 16 periods of 10 minutes. This will comprise 4 cycles of 4 ten-minute periods, with each period consisting of resting rate, followed by 20 bpm above resting, followed by resting rate again, and then 40 bpm above resting. This protocol gives 80 minutes of resting rate, 40 minutes of 20 bpm above resting, and 40 minutes of 40 bpm above resting. It gives several onset and offset events, to allow time course of effect (if any) to be detected. It spreads out all like transitions over time, minimising the opportunity for secular changes in stability status to confound results. Dynamic CO2 will thewn be applied to the induced oscillations.

Study C (Dynamic therapy with inhaled carbon dioxide as a novel form of "pacing"):
Protocol: Patients will be monitored as above. In addition, a loose-fitting, non-occlusive face-mask will be applied. A fine-bore catheter will be held in position by the mask, directing toward the left nostril a potential flow of humidified gas (3% CO2, 21% O2, balance nitrogen). The flow will be controlled by an electrical actuator and can change position in less than 0.5 s. Directed towards the right nostril will be an aspiration catheter allowing the metabolic cart to monitor gas concentration, and a thermistor. The analogue O2 and CO2 signals produced by the cart's gas sensors will be read via our custom real-time data-monitoring system, which also receives

the signals from the respiratory strain gauge, earlobe oximeter and thermistor (and heart rate and blood pressure). A different module of the same software will control the electrical actuator that regulates delivery of CO2. Delivery of CO2 is programmable to be off, on at a constant level, alternating with a fixed period, or alternating in synchronisation to biosignal inputs. The regulatory algorithm can be programmed to utilise a combination of the inputs (including the system's knowledge of what therapy has been delivered) and to create independent cycling daemons that synchronise with and then track the rhythm of oscillation in the cardiorespiratory system, even when the externally-observable oscillations have been damped by therapy.

### Intervention Type
Other

### Phase
Not Applicable

### Primary outcome(s)
All parameters are measured continuously throughout the recordings:
Substudy 1: the effect on blood pressure of changes in AV and VV delay of a pacemaker
Substudy 2: the size of the change in end tidal carbon dioxide and ventilation achievable from a change in pacemaker setting and the application of dynamic CO2
Substudy 3: the size of the change in ventilation achievable from administration of CO2

### Key secondary outcome(s))
No secondary outcome measures

### Completion date
30/09/2010

## Eligibility

### Key inclusion criteria
1. Aged 18 - 80 years, either sex
2. Chronic systolic heart afilure confirmed by transthoracic echo

### Participant type(s)
Patient

### Healthy volunteers allowed
No

### Age group
Adult

### Lower age limit
18 years

### Sex
All

### Key exclusion criteria

1. Severe lung disease
2. Any condition that would preclude participants from lying comfortably on a couch for the duration of the study

**Date of first enrolment**
01/08/2005

**Date of final enrolment**
30/09/2010

# Locations

**Countries of recruitment**
United Kingdom

England

**Study participating centre**
**Imperial College London**
London
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# Sponsor information

**Organisation**
Imperial College London (UK)

**ROR**
https://ror.org/041kmwe10

# Funder(s)

**Funder type**
Charity

**Funder Name**
British Heart Foundation (BHF) (UK)

**Alternative Name(s)**
the_bhf, The British Heart Foundation, BHF

### Funding Body Type
Private sector organisation

### Funding Body Subtype
Trusts, charities, foundations (both public and private)

### Location
United Kingdom

# Results and Publications

### Individual participant data (IPD) sharing plan

### IPD sharing plan summary
Not provided at time of registration

### Study outputs

| Output type | Details | Date created | Date added | Peer reviewed? | Patient-facing? |
|---|---|---|---|---|---|
| Results article | dynamic CO2 therapy results | 12/08/2014 | 29/12/2020 | Yes | No |
| Participant information sheet | Participant information sheet | 11/11/2025 | 11/11/2025 | No | Yes |