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Breathtaking Technology

N-Tidal

Personal Respiratory Monitors

Jeremy Walsh, CEO - Cambridge Respiratory Innovations Limited

Overview

- Why N-Tidal?
- COPD Breathing Record Study
- Data Analysis
- Next Steps
- Panel Discussion

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Why N-Tidal?

Transforming the Management of Respiratory Diseases

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N-Tidal – The Basics

- The function of the lungs is to take oxygen to and carbon dioxide (CO_2) from the bloodstream
- The measurement of CO_2 in breath is a direct indicator of lung function
- CRiL makes low-cost medical devices that directly measure this respiratory performance
- Our devices improve Patient Activation Levels
- Our devices will provide a clear and unambiguous status of respiratory health
- Tidal Breathing CO_2 Waveform shape analysis

$TBCO_2$ Waveform Shape Analysis

- Established but Under-used Respiratory Biomarker
- First identified as a biomarker for asthma in early 1990s
- Demonstrated the effects of reliever medication
- Identified as a differentiator between COPD, CHF and healthy in 2014

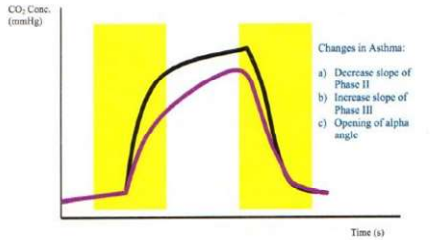


Figure 2. The capnographic waveform: changes in asthma.

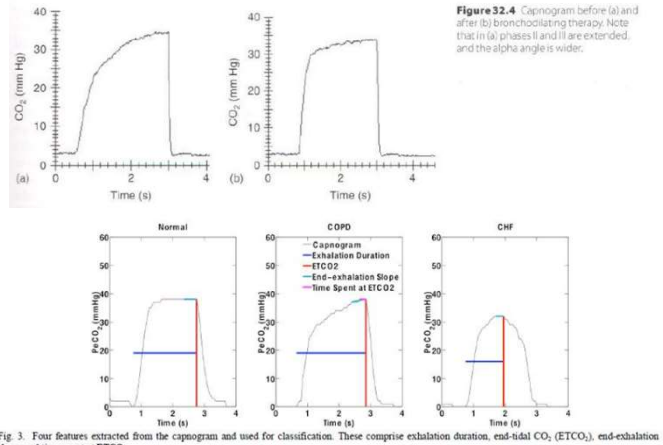
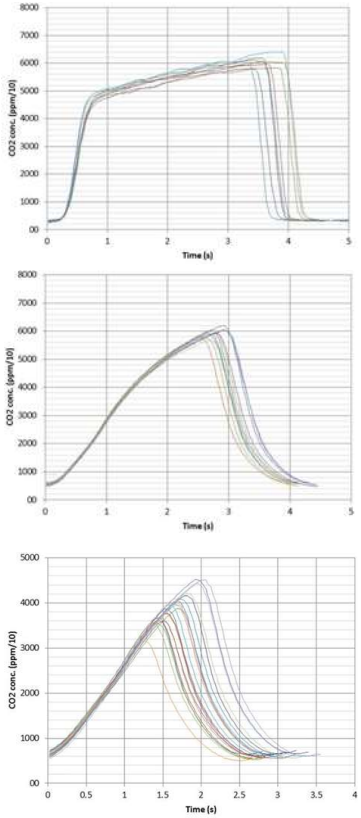


Fig. 3. Four features extracted from the capnogram and used for classification. These comprise exhalation duration, end-tidal CO_2 ($ETCO_2$), end-exhalation slope, and time spent at $ETCO_2$.

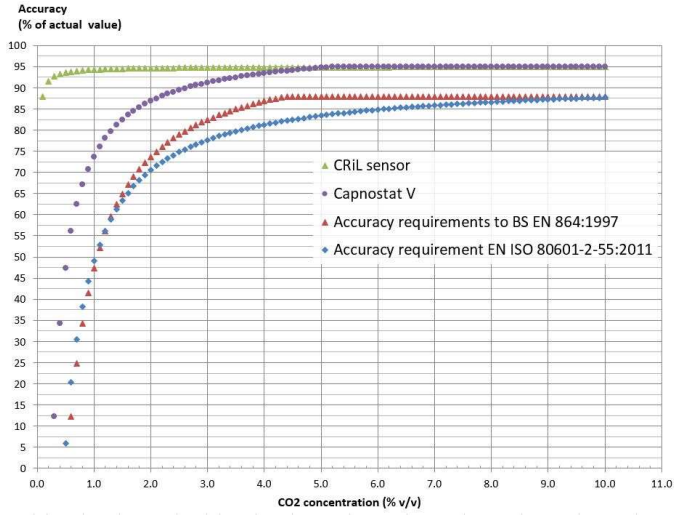
CRiL's 3 Development Hypotheses

- People breathe in a consistent manner at any specific time
- A respiratory condition alters the shape of the $TBCO_2$ waveform
- The state of the condition further changes the waveform



N-Tidal USPs

- Accurate at all CO_2 levels
- Consistent, repeatable data
- Measures close to the mouth
- Low cost and easy to use
- Personal respiratory monitors
- Predictive
- Reduce healthcare costs



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COPD Breathing Record Study

Transforming the Management of Respiratory Diseases

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COPD Breathing Record Study

- 30 COPD patients used the N-Tidal C for six weeks
  - Dr Ravi Mahadeva, Addenbrookes Cambridge
  - Funded by SBRI Healthcare
- 2,600 75-second $TBCO_2$ records
- 74% completed the study without any feedback
- 84% of the target respiratory records
- 95% acceptance of the technology

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$TBCO_2$ Data Analysis Programme

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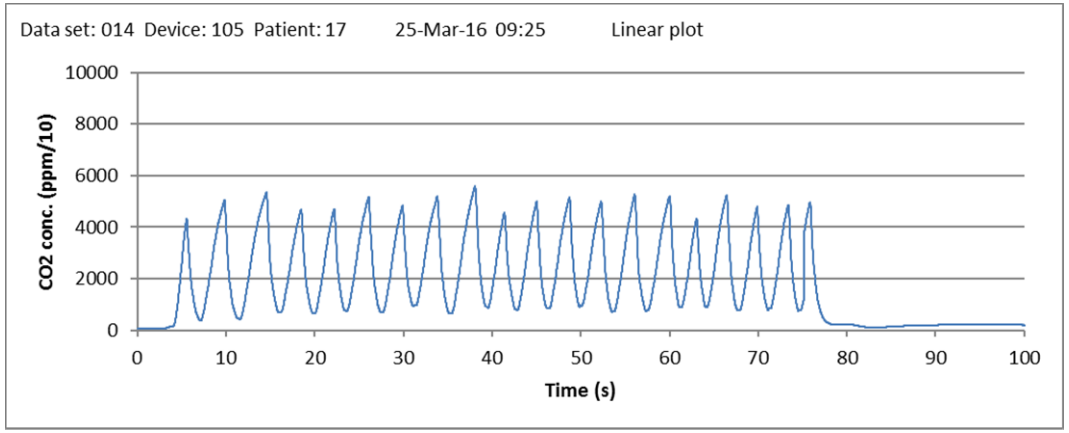
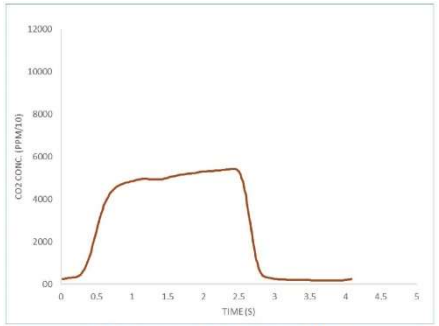
Phases 1 & 2 of Data Analysis

- Phase 1 – Data Validation
  - Professional Control Software
    - Device and data management
- Phase 2 – Visual Waveform Analysis
  - Capno Import program
    - Basic graphics
    - Data exclusion

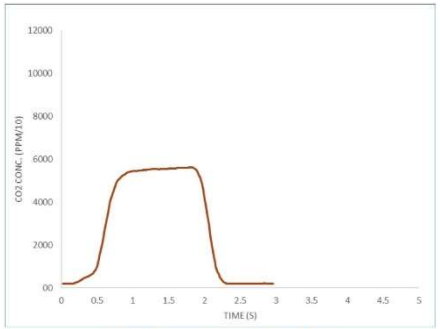


Phase 2 Waveforms Shapes

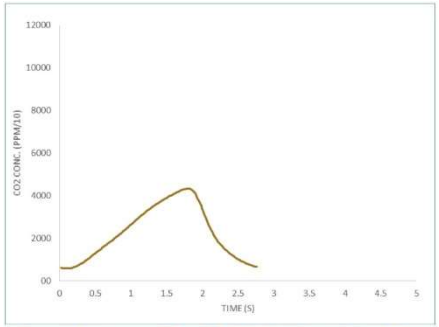
- Phase 2 Visual Waveform Analysis



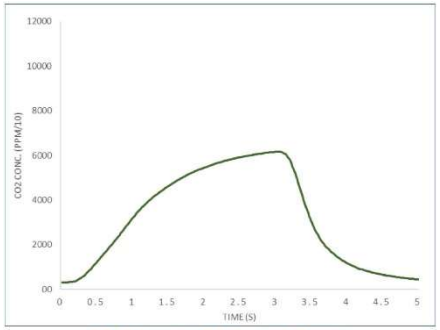
Male age 61 – healthy



Male age 6 – healthy



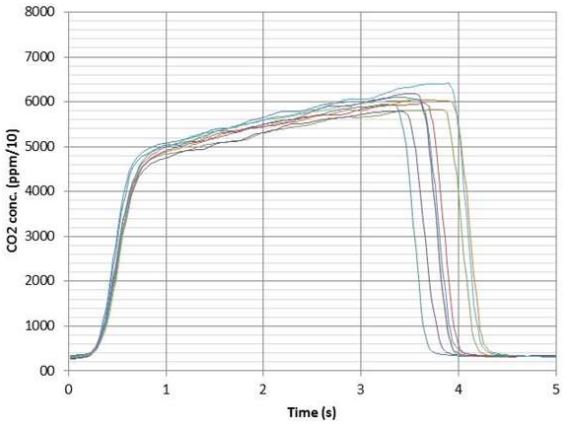
Female age 60 – COPD steady state

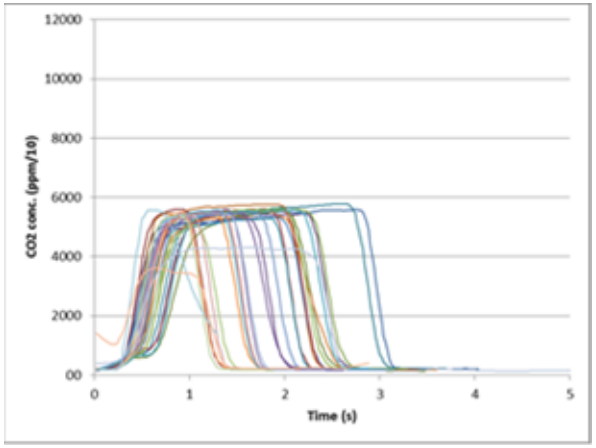


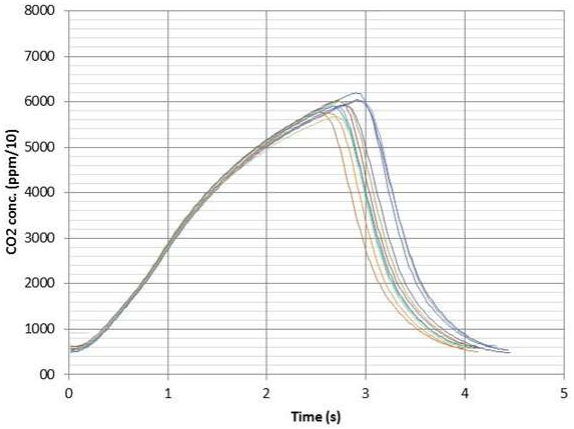
Male age 30 – asthma

Phase 3 Waveform Consistency

- Demonstrated consistent $TBCO_2$ waveform at any specific time
  - Capno Data Program
    - Auto Breath De-Composition

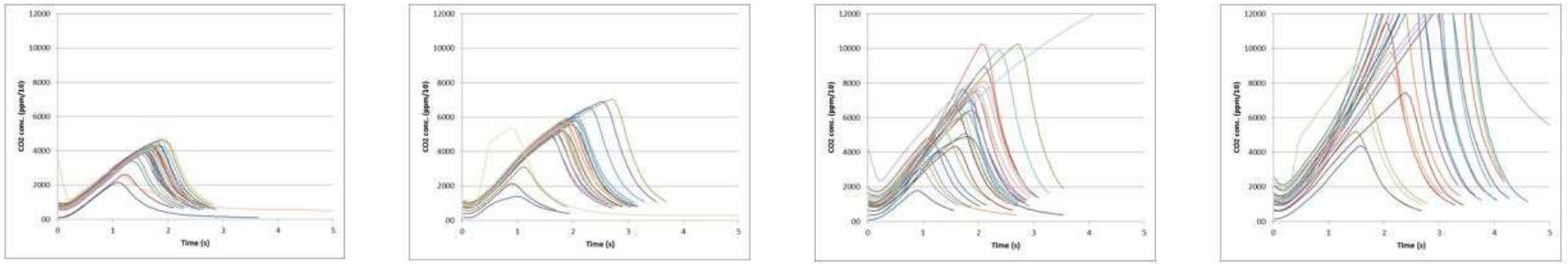






Phase 3 Waveform Consistency

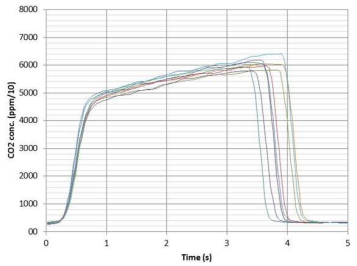
- Demonstrated consistent $TBCO_2$ shapes with changing respiratory condition
  - Capno Data Program
    - Auto Breath De-Composition

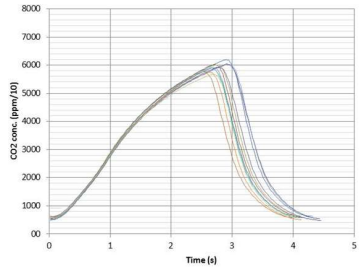


Key parameters in the $TBCO_2$ waveforms start changing more than 48 hours in advance of a COPD exacerbation, as demonstrated in these charts. (Source CRiL CBRS)

Phase 4 – Waveform Modelling

- Phase 4 – Waveform Modelling
  - Developed an algorithm to model the $TBCO_2$ waveform
    - Exhalation
    - Inhalation
    - The result is 7 parameters
  - Created a **Single $TBCO_2$ Waveform** for each breathing record
    - 3,750 data points condensed into 7 parameters
- Enabled Longitudinal Data Analysis and Visualisation





Longitudinal Data Visualisation

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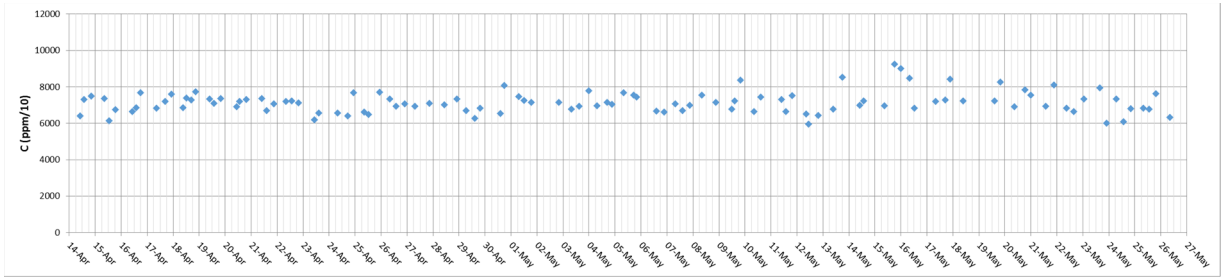
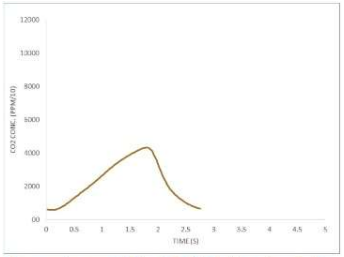
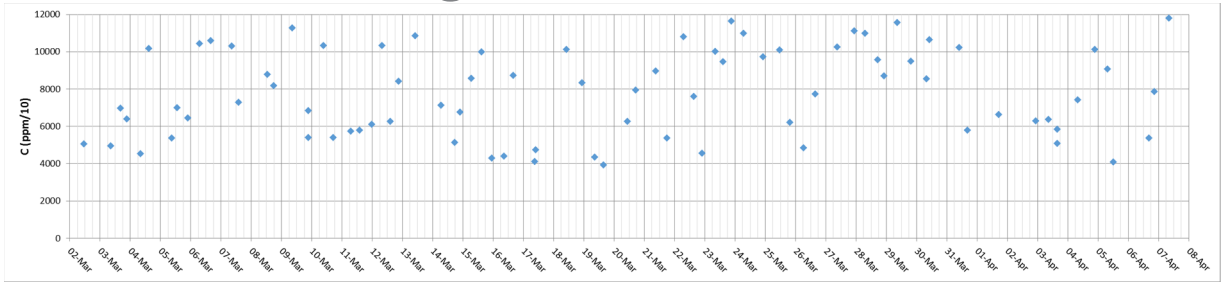
Stable COPD Patient 021

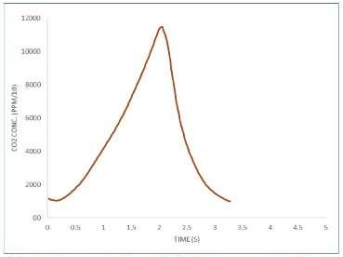




Female age 60 – COPD steady state

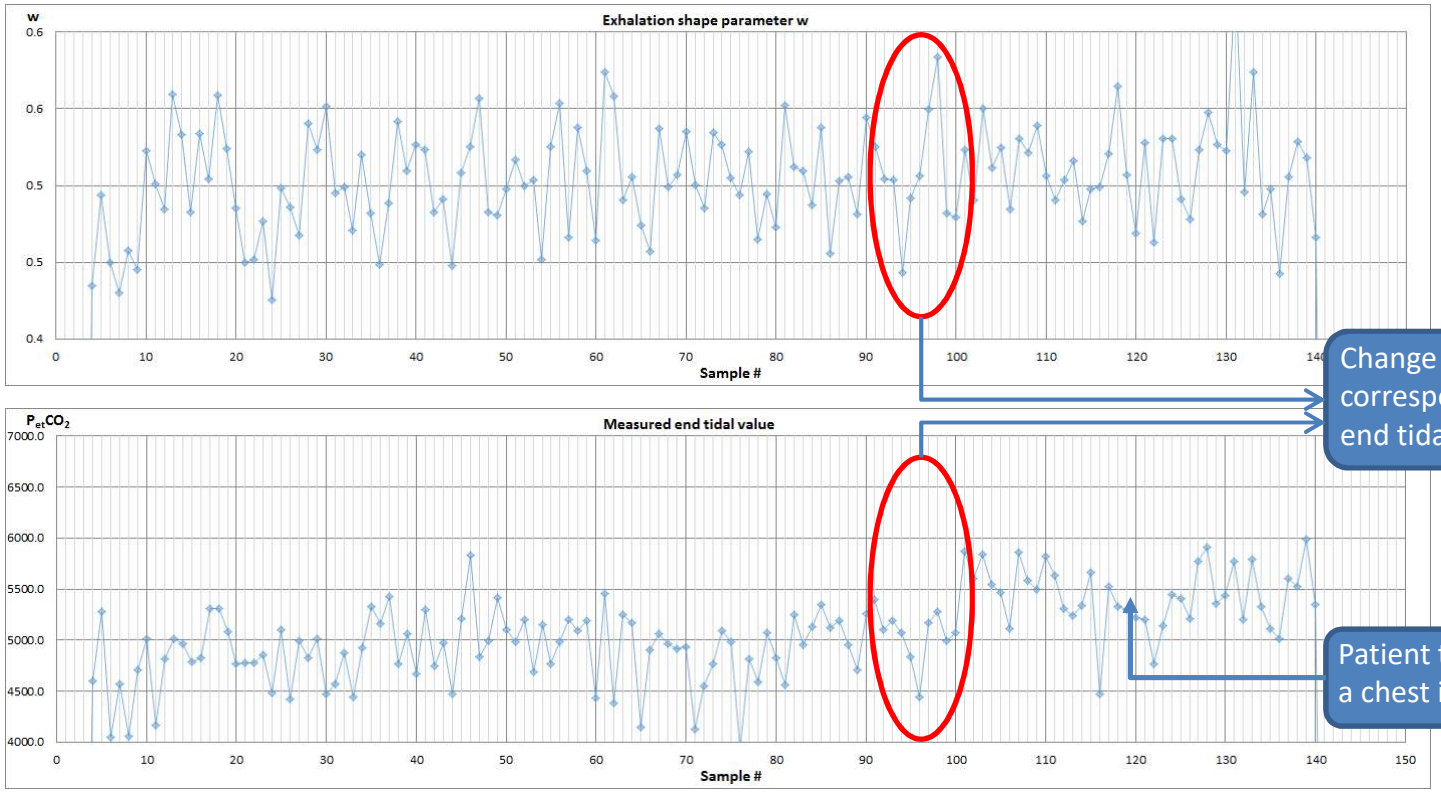
Exacerbating COPD Patient 008





Female age 60 – COPD exacerbation

Predictors of Chest Infection



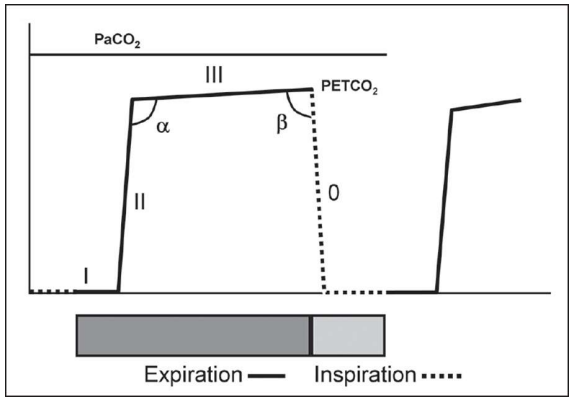
Patient 017

Change in shape parameter W corresponds to step change in end tidal value, $PetCO_2$

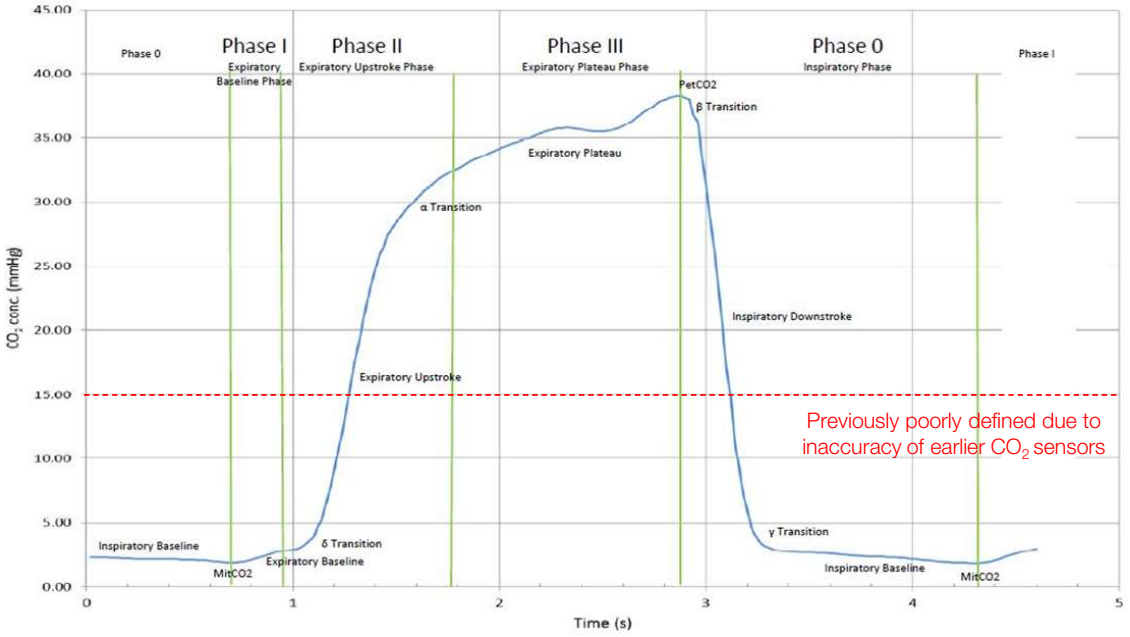
Patient treated for a chest infection

Phase 5 - Waveform Parameterisation

- First Detailed $TBCO_2$ Waveform Parameterisation including low level CO_2
  - Waveform parameters for individual breaths
    - ~ 50 Simple
    - Compound
    - Temporal

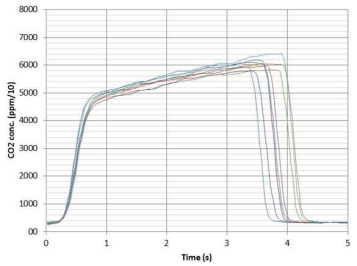


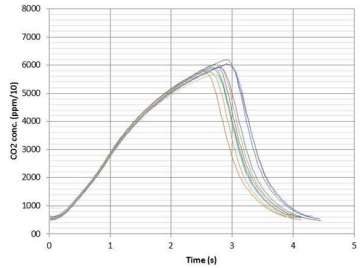
Previous Basic Waveform Descriptors



Phase 6 – Advanced Analytics

- Machine Learning
  - Supported by Cambridge University Machine Learning Group
  - We will use Bayesian and Discriminative techniques to **optimise the parameters that predict a deterioration** (exacerbation and chest infection)
  - Investigate each parameter (single, compound and temporal), singly and combined
  - For each of the 50,000 Individual Breaths





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Next Steps

Transforming the Management of Respiratory Diseases

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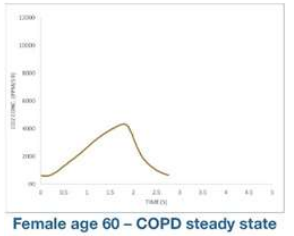
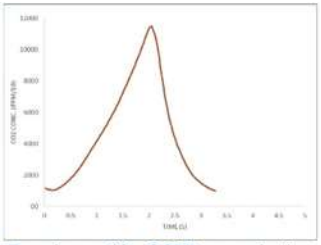
COPD Exacerbations

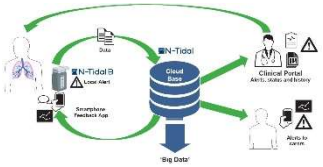
- Characterisation of COPD breathing records during exacerbations
- Statistically valid study 100% funded by an Pfizer Open Air grant
  - **CRiL supplying the N-Tidal Cs and analysis**
- Starts on 1 May 2017 at Addenbrookes under Dr Ravi Mahadeva
- 50 patients for six months
- Targeting 28,750 75-second $TBCO_2$ respiratory records



Female age 60 – COPD steady state

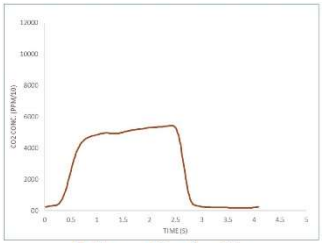


Female age 60 – COPD exacerbation

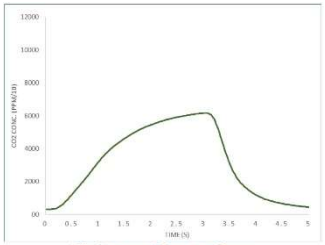


General Breathing Record Study

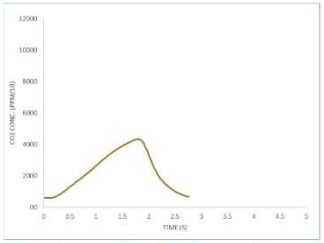
- 70% funded by Innovate UK
- Started on 1 March 2017 at Portsmouth (Queen Alexandra) and Nottingham (QMC)
- Exploring $TBCO_2$ waveforms from 90 participants:
  - Asthma
  - Congestive Heart Failure
  - Cystic Fibrosis
  - NIV – Motor Neurone Disease
  - Pneumonia/LRTI
  - Dysfunctional Breathing
  - Healthy



Male age 61 – healthy



Male age 30 – asthma



Female age 60 – COPD steady state

Low-Cost Self-Care Asthma Monitor

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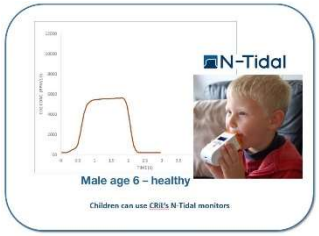
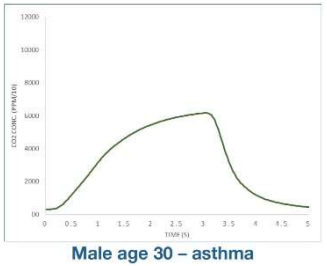
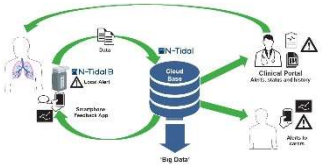
- Feasibility study 100% funded by an SBRI Healthcare (NHS England) contract
- Started on 15 March 2017 at Nottingham University / Queens Medical Centre
- Involves small proof-of-concept study
- Exploring $TBCO_2$ waveforms in children and young people with asthma or in bronchospasm
  - 15 patients

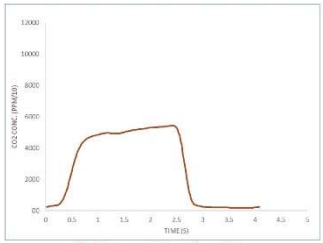




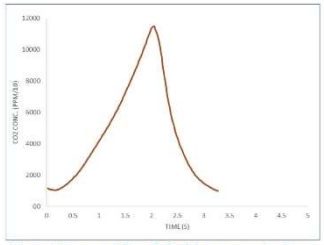


MRI Lung Imaging of COPD

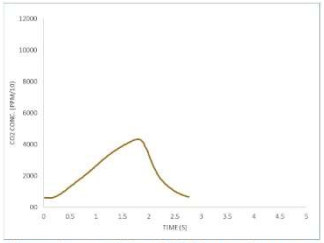
- 100% funded by James Tudor Foundation
- Starts on 1 July 2017 at Nottingham University / Queens Medical Centre
- Exploring $TBCO_2$ waveforms and their relationship to the high resolution MRI images of lungs
- 20 patients



Male age 61 – healthy



Female age 60 – COPD exacerbation

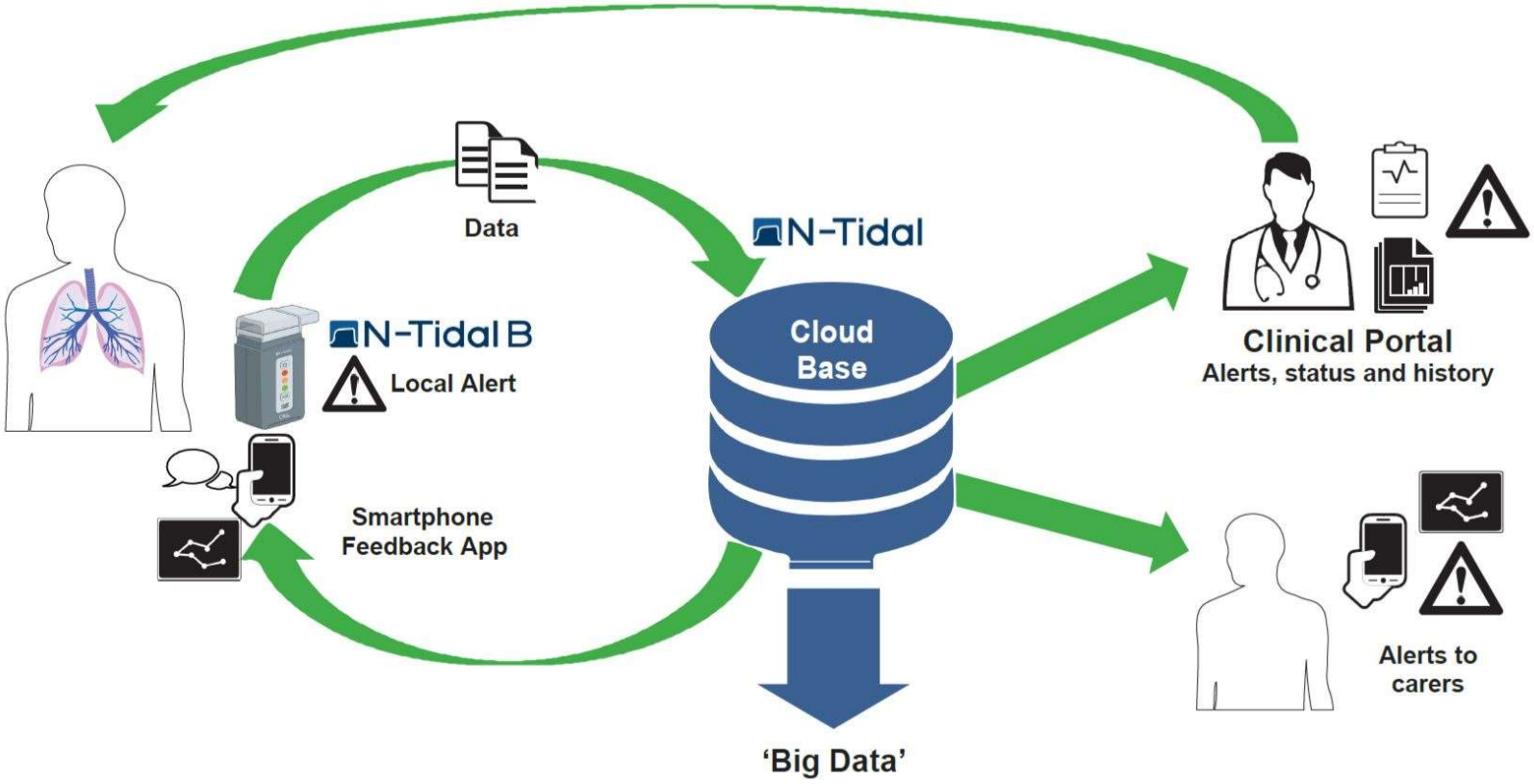


Female age 60 – COPD steady state

Funded Clinical Studies

Condition	Investigator	Patients	$TBCO_2$ records
Asthma Adults	Prof Chauhan, Portsmouth	20	11,500
Asthma CYP	Prof Smyth, Nottingham	15	350
Asthma Challenge	Dr Shaw, Nottingham	15	60
Cystic Fibrosis CYP	Prof Smyth, Nottingham	10	850
Congestive Heart Failure	Dr Paul Kalra, Portsmouth	20	11,500
COPD	Dr Mahadeva, Addenbrookes	50	28,750
COPD MRI Lung Imaging	Prof Hall, Nottingham	20	150
Pneumonia/LRTI	Prof Chauhan, Portsmouth	10	5,750
Dysfunctional Breathing	Prof Chauhan, Portsmouth	10	5,750
Pre-NIV MND	Dr Smith, Papworth	30	17,250
NIV MND	Dr Adeniji, Portsmouth	10	5,750
Healthy	Prof Chauhan, Portsmouth	10	5,750

The Future of N-Tidal



Redefining Respiration

N-Tidal - Innovation in Respiratory Digital Health

- Increase patient ownership
- Improve quality of life
- Optimise medication
- Predict exacerbations
- Avoid hospitalisation
- Reduce healthcare costs

Path to 2020 Launch

Next Steps

- Develop N-Tidal B
- 1st generation prediction algorithm
- Develop N3 data communications
- Complete licensing non-interventional COPD study
- 2nd generation prediction algorithm
- MHRA Class 2B license