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
Why N-Tidal?
Transforming the Management of Respiratory Diseases
Cambridge Respiratory Innovations Limited
The function of the lungs is to take oxygen to and carbon dioxide (CO₂) from the bloodstream.

The measurement of CO₂ 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 CO₂ 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

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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 CO₂ 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
Cambridge Respiratory Innovations Limited
30 COPD patients used the N-Tidal C for six weeks
  – Dr Ravi Mahadeva, Addenbrookes Cambridge
  – Funded by SBRI Healthcare
2,600 75-second TBCO₂ records
74% completed the study without any feedback
84% of the target respiratory records
95% acceptance of the technology
TBCO$_2$ Data Analysis Programme
Transforming the Management of Respiratory Diseases
Cambridge Respiratory Innovations Limited
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
- Female age 60 – COPD steady state
- Male age 6 – healthy
- Male age 30 – asthma
Phase 3 Waveform Consistency

- Demonstrated consistent TBCO$_2$ waveform at any specific time
  - Capno Data Program
    - Auto Breath De-Composition
Demonstrated consistent TBCO₂ shapes with changing respiratory condition

- Capno Data Program
  - Auto Breath De-Composition

Key parameters in the TBCO₂ 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

- Developed an algorithm to model the TBCO\textsubscript{2} waveform
  - Exhalation
  - Inhalation
  - The result is 7 parameters
- Created a **Single TBCO\textsubscript{2} Waveform** for each breathing record
  - 3,750 data points condensed into 7 parameters

Enabled Longitudinal Data Analysis and Visualisation
Longitudinal Data Visualisation

![Graph of Stable COPD Patient 021]

Stable COPD Patient 021

![Graph of Exacerbating COPD Patient 008]

Exacerbating COPD Patient 008
Predictors of Chest Infection

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 TBCO₂ Waveform Parameterisation including low level CO₂

- Waveform parameters for individual breaths
  - ~ 50 Simple
  - Compound
  - Temporal

Previous Basic Waveform Descriptors

Previously poorly defined due to inaccuracy of earlier CO₂ sensors
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
Next Steps
Transforming the Management of Respiratory Diseases
Cambridge Respiratory Innovations Limited
COPD Exacerbations

- Characterisation of COPD breathing records during exacerbations
- Statistically valid study 100% funded by a 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\textsubscript{2} respiratory records
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
Low-Cost Self-Care Asthma Monitor

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 TBCO₂ 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
## Funded Clinical Studies

<table>
<thead>
<tr>
<th>Condition</th>
<th>Investigator</th>
<th>Patients</th>
<th>TBCO$_2$ records</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asthma Adults</td>
<td>Prof Chauhan, Portsmouth</td>
<td>20</td>
<td>11,500</td>
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<tr>
<td>Asthma CYP</td>
<td>Prof Smyth, Nottingham</td>
<td>15</td>
<td>350</td>
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<tr>
<td>Asthma Challenge</td>
<td>Dr Shaw, Nottingham</td>
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<td>60</td>
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<tr>
<td>Cystic Fibrosis CYP</td>
<td>Prof Smyth, Nottingham</td>
<td>10</td>
<td>850</td>
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<tr>
<td>Congestive Heart Failure</td>
<td>Dr Paul Kalra, Portsmouth</td>
<td>20</td>
<td>11,500</td>
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<tr>
<td>COPD</td>
<td>Dr Mahadeva, Addenbrookes</td>
<td>50</td>
<td>28,750</td>
</tr>
<tr>
<td>COPD MRI Lung Imaging</td>
<td>Prof Hall, Nottingham</td>
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<td>150</td>
</tr>
<tr>
<td>Pneumonia/LRTI</td>
<td>Prof Chauhan, Portsmouth</td>
<td>10</td>
<td>5,750</td>
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<tr>
<td>Dysfunctional Breathing</td>
<td>Prof Chauhan, Portsmouth</td>
<td>10</td>
<td>5,750</td>
</tr>
<tr>
<td>Pre-NIV MND</td>
<td>Dr Smith, Papworth</td>
<td>30</td>
<td>17,250</td>
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<tr>
<td>NIV MND</td>
<td>Dr Adeniji, Portsmouth</td>
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<tr>
<td>Healthy</td>
<td>Prof Chauhan, Portsmouth</td>
<td>10</td>
<td>5,750</td>
</tr>
</tbody>
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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

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Path to 2020 Launch

Next Steps

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