Lung Cancer Detection by Breath Analysis

American Lung Association Meeting
Lexington Kentucky
December 1, 2017

Michael Bousamra II
Director of Thoracic Surgery, Baptist Health Floyd
President & CEO, Breath Diagnostics, Inc.
The Lung Cancer Problem

Lung Cancer is the leading cause of cancer death in the United States
NCI statistics 2013: Deaths — 159,480

Early diagnosis is key to long term survival
Lung Cancer Screening Trial
CT Scanning reduces mortality by 20 %

Disadvantages
Expense — $3 billion per year in US
Exposure to repeated radiation
Low participation (15%)
False positive rate (96%)

patient CT scan
suspicious pulmonary nodule
Current Tools for Diagnosis of Lung Cancer

Post-CT Scan Procedures

- **Bronchoscopy**
  - COST = $7,000

- **Needle Biopsy**
  - COST = $7,000

- **Surgery**
  - COST = > $40,000

**Clinical niche:** A safe, non-invasive, reliable, and low cost tool for lung cancer diagnosis is needed.
Biomarker Strategy for Lung Cancer Detection & Diagnosis

- Blood-Proteinomics, Nucleosomes, imRNA
- Airway Genomics
- Cytologic Profiling
- Breath Analysis
  - Sensor Arrays
  - Colorometric Assays
  - Cloud Based Assays
Lung Cancer Detector

Specialized Canine Olfactory Receptors and CNS Processing

Artwork: Claus Lunau

Daisy Mae
The Complexity of Human Breath

The composition of breath ranges from hydrogen to more than 1000 volatile organic compounds.

Our Focus: Detect Lung Cancer

- Screening
- Monitoring after surgery
- Characterizing pulmonary nodules
Breath Diagnostics, Inc.

We quantify the carbonyl subset of breath VOCs

**Cancer Markers**

- 2-butanone
- 3-hydroxy-2-butanone
- 4-hydroxy-2-hexenal
- hydroxyacetaldehyde

Miekisch et al. *Inter. J. Cancer* 2010, 126, 2663
The Origin of Breath Diagnostics

Dr. Xiao-An Fu

Dr. Michael Nantz

Dr. Michael Bousamra
Silicon Microchip Design

2011: Analyst 136, 4662–4666
2012: Analytical Chemistry 84, 1288–1293
2013: Sensors and Actuators 180, 130–136
2015: Analytical Methods 7, 6027–6033; Lung Cancer, 89, In Press
Micropillars Capture Carbonyls

**US Patent No. 8,663,581**

ATM covalent adduct

ATM adducts in MeOH, analysis via direct injection into LC-MS

**US Patent No. 9,638,965**

<table>
<thead>
<tr>
<th>Healthy controls conc. (nmol/L)</th>
<th>0.208</th>
<th>1.38</th>
<th>0.085</th>
<th>0.001</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carboxylic acid</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ketone</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aldehyde</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fatty alcohol</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Quantitative Analysis of Exhaled Carbonyls

Clinical Mass Spectrometry
Collected Breath → MS Data → Diagnosis
Quantitative Analysis of Exhaled Carbonyls
Quantitative Analysis of Exhaled Carbonyls

Collected Breath → Breath Processing

Proprietary Silicon Microchip Technology
Clinical Chip Design

- Tube with connector (TBD) to exit from cassette back for connection to air bag
- Cassette bottom
- Cassette top
- Chip
- Chip potted with UV cured adhesive around all edges to ensure seal
Clinical Evacuation System

Evacuation System Design - Front

- Cassette Insertion
- Start / Stop Button
- Multi Character Display – provide time left to evacuate air bag
Elevated Cancer Markers (ECMs)
The Number of ECMs Differentiate Lung Cancer from Benign Disease

<table>
<thead>
<tr>
<th># Elevated Markers</th>
<th>4</th>
<th>3</th>
<th>2</th>
<th>1</th>
<th>0</th>
<th>Totals</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Stage 0, I, II</strong></td>
<td>14</td>
<td>21</td>
<td>17</td>
<td>7</td>
<td>5</td>
<td>64</td>
</tr>
<tr>
<td><strong>Stage III, IV</strong></td>
<td>16</td>
<td>21</td>
<td>5</td>
<td>1</td>
<td>0</td>
<td>43</td>
</tr>
<tr>
<td><strong>Benign Disease</strong></td>
<td>0</td>
<td>2</td>
<td>7</td>
<td>13</td>
<td>18</td>
<td>40</td>
</tr>
</tbody>
</table>

If criteria for positive result is **2 or more ECMs**, then the test captured: 98% of patients with stage III, IV (ID’d 42 of 43), 81% of patients with early stage lung cancer (ID’d 52 of 64) False positive = 9 of 40 = 23%

PET / ECM Comparison for Early Lung Cancer Detection

<table>
<thead>
<tr>
<th></th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>PET SUV ≥2.5</td>
<td>93%</td>
<td>39%</td>
</tr>
<tr>
<td>Breath: ECM ≥2</td>
<td>89%</td>
<td>75%</td>
</tr>
</tbody>
</table>

All tumors >2.5cm test breath positive (2-4 ECM)

M. Bousamra et.al AATS Presentation, April 2014
### Control vs. Lung Cancer

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<thead>
<tr>
<th></th>
<th>Sensitivity</th>
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<tbody>
<tr>
<td>All Cancer</td>
<td>94%</td>
<td>86%</td>
</tr>
<tr>
<td>Early Stage Lung Cancer</td>
<td>91%</td>
<td>86%</td>
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</table>

- $n = 202$ control, 156 cancer
- Positive Result selected as $\geq 1$ ECM

E. Schumer et.al AATS Presentation April, 2015
Post-Resection Data (n=38)
ECMs Correlate with Cancer

- Markers are not smoking related
- Concentration levels correlate to disease states
- Normalization of levels after surgery
FDA Preparation & Refinement

- Clean room microchip production and chemical coating
- Chip stability studies
  - shelf life & transport
- Limit of detection and limit of the blank
- Precision and reproducibility analyses
- Plans for a multicenter trial
# 2 Americas

There are 15,000,000 patients who qualify for screening in America, 1.5% annual risk of Lung Cancer

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### Assume 1/3rd undergo Breath Analysis:

- **5,000,000 screened**
- **68,000 cancers diagnosed**
- **94% sensitivity**

#### CT Scans:

- **15% will have a false positive breath test requiring a follow up CT scan:**
  - **750,000 CT Scans**
- **33% will be false positive**
- **250,000**
- **Assuming 2.5 scans per year: 625,000**

**Total CT scans: 1,625,000**

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Of the 250,000 patients with a positive CT scan a small proportion will undergo invasive and or expensive diagnostic testing beyond repeat CT scanning:[1] to determine if the pathology is actually cancer:

**Medicare Allowables**

<table>
<thead>
<tr>
<th>Workup of</th>
<th>Medicare Allowable</th>
</tr>
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<tr>
<td>Lung Cancers</td>
<td>$7,567 (3%)</td>
</tr>
<tr>
<td>Surgery</td>
<td>$40,000 (1%)</td>
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**5,000,000 Breath Diagnostics tests ($175/test)**

**Total CT scans: 1,625,000**

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### Assume 1/3rd scanned with CT:

- **5,000,000 screened with CT Scan**
- **69,000 cancers diagnosed**
- **95% sensitivity**

#### CT Scans:

- **21% will have a false positive* CT scan requiring a follow up CT scan:**
  - **1,050,000 CT Scans**
- **Each false positive will require a follow up CT scan: Assuming 2.5 total scans per yr: 2,625,000 scans**

**Total CT scans: 8,675,000 scans**

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Of the 1,050,000 patients with a positive CT scan a small proportion will undergo invasive and or expensive diagnostic testing beyond repeat CT scanning to determine if the pathology is actually cancer:

**Medicare Allowable**

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**8,675,000 CT scans ($300/scan)**

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## Cost of tests to discover 68,000 cancers:

<table>
<thead>
<tr>
<th>Test Type</th>
<th>Cost</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breath Tests</td>
<td>$875,000,000</td>
</tr>
<tr>
<td>CT Scans</td>
<td>$487,500,000</td>
</tr>
<tr>
<td>Workup of LC</td>
<td>$56,752,500</td>
</tr>
<tr>
<td>Surgery</td>
<td>$100,000,000</td>
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## Costs of tests to discover 69,000 cancers:

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<tbody>
<tr>
<td>CT Scans</td>
<td>$2,602,500,000</td>
</tr>
<tr>
<td>Workup of LC</td>
<td>$238,360,500</td>
</tr>
<tr>
<td>Surgery</td>
<td>$420,000,000</td>
</tr>
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## Total cost associated with the discovery of 68,000 cancers:

$1,519,252,500

*Using Breath Analysis to discover lung cancers costs 40% of the cost of using CT Scanning*

## Total cost associated with the discovery of 69,000 cancers:

$3,260,860,500

*CT Screening has a 21% false positive rate on first screen and 33% false positive rate on subsequent screening.*
China
National Cancer Institute
and
The Academy of Medical Sciences
The Mission

To Globally implement breath analysis technology to provide early cancer detection and to reduce patient exposure to costly and high risk medical procedures.
Thank You