Real Time, Ultra-fast, Breath Ammonia Determination

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NH₃ and Hepatic Encephalopathy

- Management "imprecise": hindered by the lack of a reliable, rapid, and inexpensive monitoring: Blood NH₃ determination is inherently problematic (it is unreliable in real world situations, and only measured episodically).
- Treatments "suboptimal": unpleasant→ serious side effects, unpredictable dose-response.

Benefits of Breath Analysis

- Non-invasive
- Real-time measurements
- Portable
- We hypothesize that breath NH₃ will be a robust biomarker for the study of whole body NH₃.

If successful, this achievement could lead to breakthroughs in the study and management of patients with encephalopathy.

Ammonia Sensor

We used a distributed feedback quantum cascade laser based sensor to determine exhaled breath NH₃ in participants without signs of liver and kidney disease.

Methods

- Participants provided fasting breath (x3) and blood (x1) samples.
- Pressure and carbon dioxide were measured to ensure careful sampling.
- Blood NH₃ was measured by a standard clinical assay.
- Blood and breath NH₃ levels for each participant were compared.
**Statistical Analysis**

- Paired data are compared by linear regression, including slope, intercept, and correlation coefficient.
- Mean breath NH$_3$ determined by finding mean of 3 breath samples.
- Analyses performed using SAS version 9.1.3

**Results**

- N=24
- 4 M, 15 F
- Mean age = 29.3
- Mean weight = 146.2 lbs
- Mean BMI = 23.0
- Mean breath NH$_3$ = 0.387 ppm
  - SD = 0.290
  - Range = 0.014-1.089
- Mean blood NH$_3$ = 6.4 umol/l
  - SD = 4.4
  - Range = 1 - 14
- 5 participants had undetectable blood NH$_3$

**Results, cont.**

- Linear regression slope for remaining 19 paired data points was 0.03.
- Intercept was 0.20.
- Pearson correlation coefficient was 0.47 (p=0.042).
- R$^2$ was 0.22.
- Graph includes 95% confidence interval.

**Conclusions**

- Breath NH$_3$ correlates with the present standard NH$_3$ blood assay.
- This work creates a foundation of normative data among healthy subjects.

**Future Directions**

- Currently, we are conducting investigations of cirrhotic patients with elevated NH$_3$ and treatment intervention studies to evaluate the performance of breath NH$_3$ over a broader range of values and clinical scenarios.
- Ultimately, "success" could be measured by fewer Office visits, Emergency Room visits, hospitalizations, death
- Saved $$$:
  - Medicare spends ~$28B/yr for dialysis;
  - Chronic liver disease costs ~$1-5B/yr
  - 50% Quality of Life for millions

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