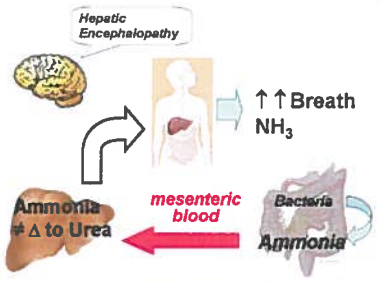
Real Time, Ultra-fast, Breath Ammonia Determination

Timothy B. Schwartz[1], Steven F. Solga[1,2], Lisa Spacek[2], Rafal Lewicki[3], Frank Tittel[3], and Terence Risby[2]
[1] St. Luke's Hospital, Bethlehem, PA, 18015, USA
[2] Johns Hopkins University, Baltimore, MD, 21205, USA
[3] Rice University, Houston, TX, 77251, USA
email: timbschwartz@gmail.com

A Major Opportunity



NH_3 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 NH_3 will be a robust biomarker for the study of whole body NH_3.

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[1] to determine exhaled breath NH_3 in participants without signs of liver and kidney disease.

[1]Lewicki, R et al "Real time ammonia detection in exhaled human breath using a distributed feedback quantum cascade laser based sensor", submitted to SPIE 2011 Photonics West Proceedings.

Methods

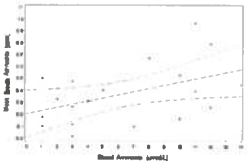
- Participants provided fasting breath (x3) and blood (x1) samples.
- Pressure and carbon dioxide were measured to ensure careful sampling.
- Blood NH_3 was measured by a standard clinical assay.
- Blood and breath NH_3 levels for each participant were compared.

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

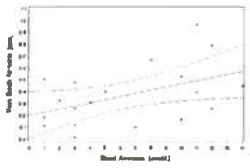
Results

- 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 NH3 and treatment intervention studies to evaluate the performance of breath NH3 over a broader range of values and clinical scenarios.
- Ultimately, "success" could be measured by ↓'d Office visits, Emergency Room visits, hospitalizations, death
- Saved $$:
  - Medicare spends ~$28B/yr for dialysis;
  - Chronic liver disease costs ~$1-5B/yr
- ↑'d Quality of Life for millions

Acknowledgements

- MIRTHE
- Hammamatsu
- Loccioni