Neonatal Necrotizing Enterocolitis Stool Tester (NeoNEST): Electronic Nose for NEC Diagnosis

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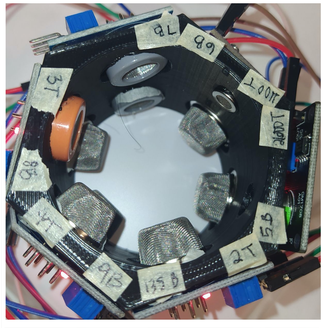
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Background

Necrotizing enterocolitis (NEC) is the leading cause of death among premature infants. There is no exact theory as to the pathogenesis and etiology of NEC. Many studies have hypothesized that the pathogenesis is multifactorial and often connected to gut dysbiosis, low birth weight, enteral feeding, and intestinal permeability. Currently, there is no bedside diagnostic device to diagnosis NEC. The purpose of the Neonatal Necrotizing Enterocolitis Stool Tester (NeoNEST) is to create an easily accessible bedside test to diagnose necrotizing enterocolitis prior to the onset of symptoms. This device could potentially add significant utility to the bedside diagnostic toolbox of neonatologists and pediatric surgeons.



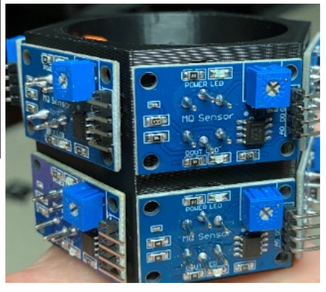


Figure 1. The current NeoNEST sensor array with twelve Metal Oxide Sensors (MOS) to detect volatile organic compounds (VOCs) from stool samples. Top view is shown by the picture on the right (top) and the side view is the picture on the right (bottom).

Description of Technology and Methods

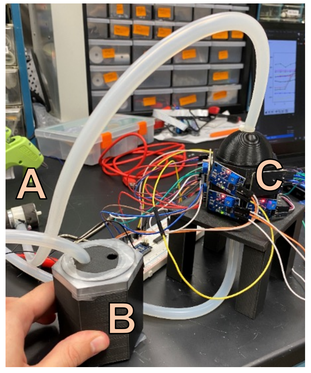


Figure 2. (Above) The current twelve sensor testing apparatus with:
A) Micro vacuum
B) Sample chamber
C) Sensor array

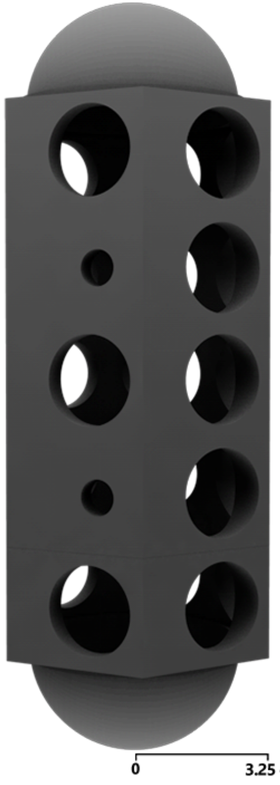
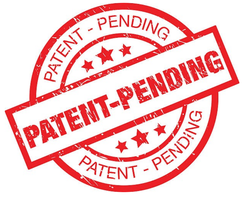


Figure 3. (Right) The complete 3D modeled sensor array chamber. The final sensor array will be comprised of approximately thirty sensors.



A novel method for clinically detecting necrotizing enterocolitis (NEC) is the analysis of volatile organic compounds (VOCs), organic gases emitted from certain solids or liquids of the human body. A prototype sensor array has been designed specifically to receive and analyze gases emitted from an inserted stool sample **(Fig 1-4)**. We plan to use machine learning to train the electronic nose sensor to detect gases present in stool from premature infants with or without NEC. The calibration of the device is performed by comparing common VOCs and the stool profile to gas chromatography.

The NeoNEST is an electronic nose made with a sensor array with thirty metal oxide semiconductor sensors. Each sensor has an affinity range for different target molecules. Our device will create VOC profiles that will be used as training data to identify healthy or NEC-probable stool samples. Our device consists of an actuator with two hollow-bore needles that pierce the stool sample container. A micro vacuum draws in any VOCs from the sample **(Fig 2A)**. As the sample goes through the 30-sensor array, a profile is created. The sample is filtered and sent out through the exhaust. The NeoNEST analysis package will become the first bedside stool analyzer to diagnose NEC.



Preliminary Results

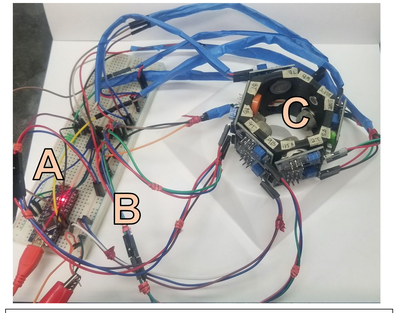


Figure 4. (Below) Our testing apparatus:
A) Arduino nano collecting sensor data
B) Connection cord to stream data
C) Sensor array

Sensor Model #	Primary Targets	P-Value
MQ2	Methane, Butane, LPG, smoke	0.02105
MQ6	LPG: isobutane, propane, methane	0.0172
MQ7	H2 gas, carbon monoxide	0.01585
TGS2602	Air pollutants (VOCs, ammonia, hydrogen sulfide)	0.01045

Table 1. (Above) Sensor information and the primary targets during preliminary tests.

In preliminary studies, we tested stool from healthy preterm infants and preterm infants with NEC. Frozen stools were warmed and emitted VOCs were analyzed by our sensor array. After a series of t-tests, five of our sensors with sensors showed statistically significant differences between the healthy and NEC preterm infant stool samples.

Four of the sensors had no statistically significant differences between the control healthy stool samples, but significant differences between the NEC samples and healthy stool samples. The MQ2, MQ6, MQ7, and TGS2602 had p-values < 0.03 between healthy and NEC stool samples (**Table 1**).

Two additional sensors will be recalibrated and retested. They had inconclusive results with no significant differences between the control samples tested, but minor differences between the healthy and NEC stool samples.

The remaining sensors had little to no statistical differences between any of the NEC and healthy stool samples. These serve as controls.

Conclusions

Based on the preliminary results, we are confident that our analysis package will be able to detect NEC in a patient based on a stool sample. Five of our original sensors can be used as control samples while the MQ2, MQ6, MQ7, and TGS2602 sensors had the most promise to differentiate between NEC stool and healthy stool. We believe further work on calibrating the MQ135 and MS1100 sensors we believe may yield statistically significant data going forward.

This NeoNEST will be a non-invasive, bedside stool test for early diagnosis of NEC. With earlier intervention and treatment, it is possible to reduce the morbidity and mortality in infants with NEC.

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