Towards a non-invasive ultrasound method for the diagnosis of neonatal and infant meningitis

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Introduction
Lumbar Puncture (LP) is currently used to draw a sample of cerebrospinal fluid (CSF) and test for potentially lethal Bacterial Meningitis (BM) in infants (<1yr). Increased CSF cellularity is highly indicative of BM and triggers medication for the patient. In developed countries, 95% of LPs for BM in infants return negative. In developing countries, LPs are rarely available, with 50% of infants with BM dying from the disease.

Objective
To assess the capabilities of HFUS on a fontanel phantom involving mock CSF with varying leukocyte concentration and pig tissue.

Our solution
We propose using high-frequency ultrasounds (HFUS) to noninvasively determine CSF cell concentration through the fontanel.

Materials and methods

- 8 mock CSF samples with 0-100 leukocytes/µL
- 20MHz ultrasound (US) prototype from Cortex Technologies ApS
- Cell concentration quantified from the US cell echoes
- Agreement between backscatter measurements and cell concentration was measured ($R^2$)
- Pig tissue with variable thickness (0-2.2 mm, corresponding to 0-12 dB ultrasound attenuation) was used to mimic the fontanel tissue

Results
Echoes coming from individual leukocytes could be clearly identified in 2D ultrasound images at concentrations as low as 12 leukocytes/µL. The system was not sensitive to platelets as observed on separate experiments with platelet-only samples.

In the 0-50 cells/µL range, the coefficient of variation (CV=STD/AVG) in ultrasound measurements was below 18.3%, better than the CV=30-45% reported for the gold standard used in clinical settings, the Fuchs-Rosenthal chamber. Excellent linear agreement was observed between the theoretical leukocyte concentration and the ultrasound backscatter measurement.

Conclusions
HFUS can accurately measure leukocyte concentration in CSF-like medium in the diagnostic range for meningitis. The results involving tissue suggest this technology shows promise as a noninvasive method to measure CSF cell concentration and motivates further development of our prototype to show technical feasibility in a proof-of-concept study with patients.

References