

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.

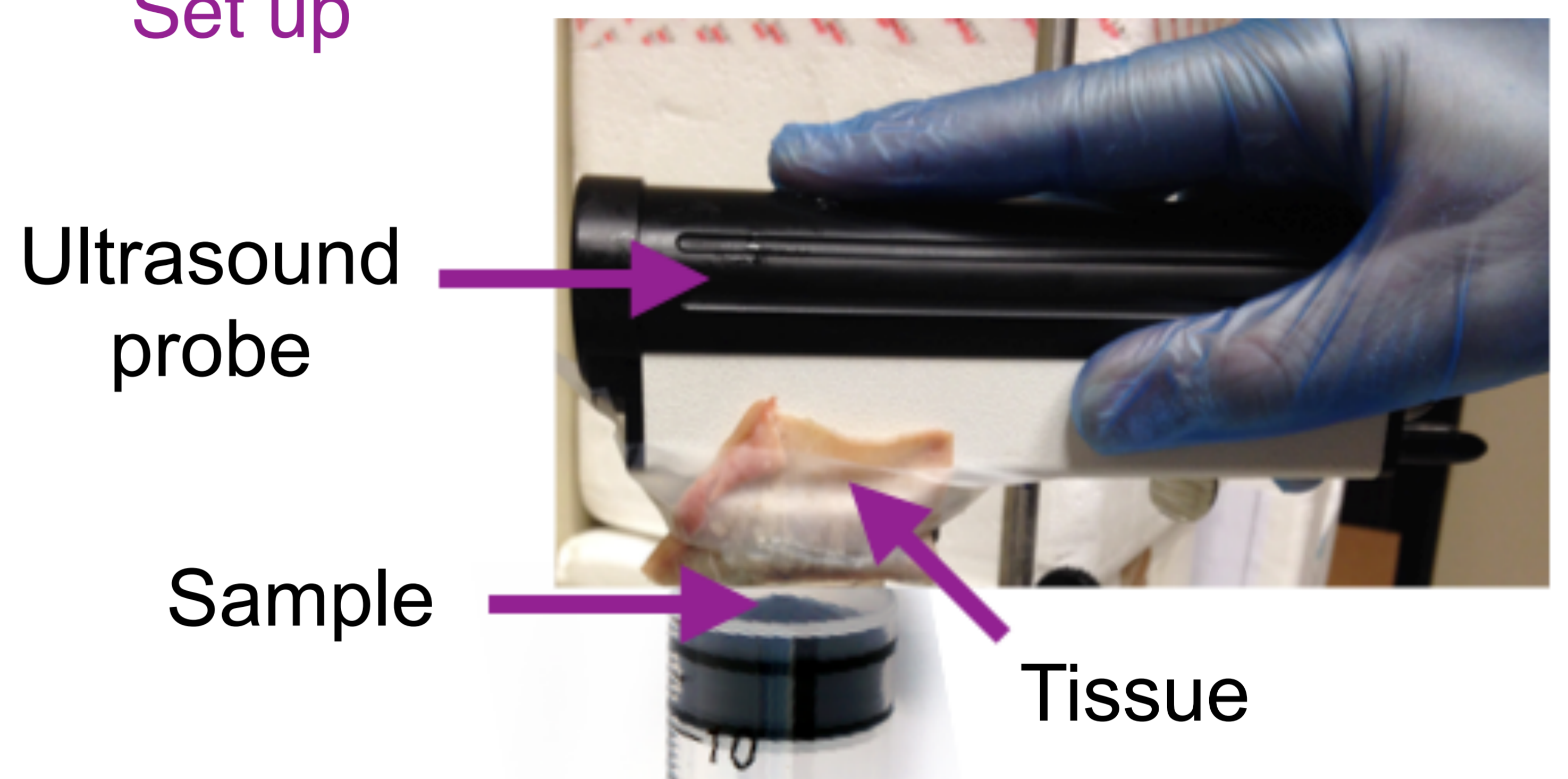


The NeoCounter

Materials and methods

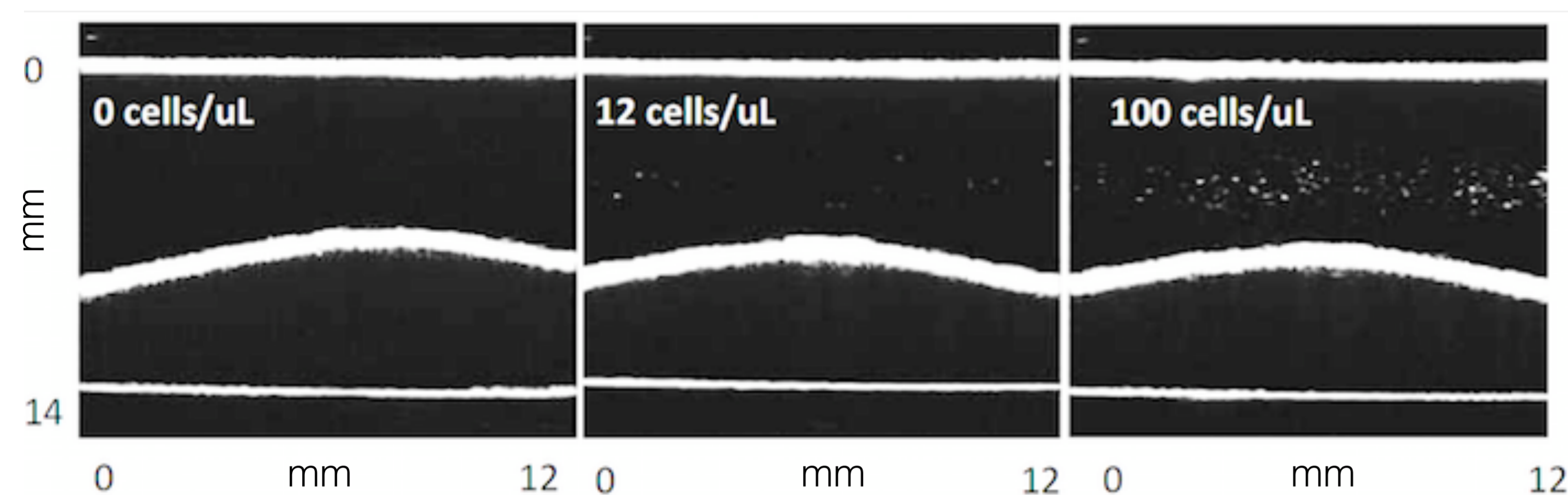
- 8 mock CSF samples with 0-100 leukocytes/ μ L
- 20MHz ultrasound (US) prototype from Cortex Technologies ApS
- Cell concentration quantified from the US cell echoes
- Agreement between backscatter measurements and cell concentration was measured (R^2)
- Pig tissue with variable thickness (0-2.2 mm,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

Set up



Results

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

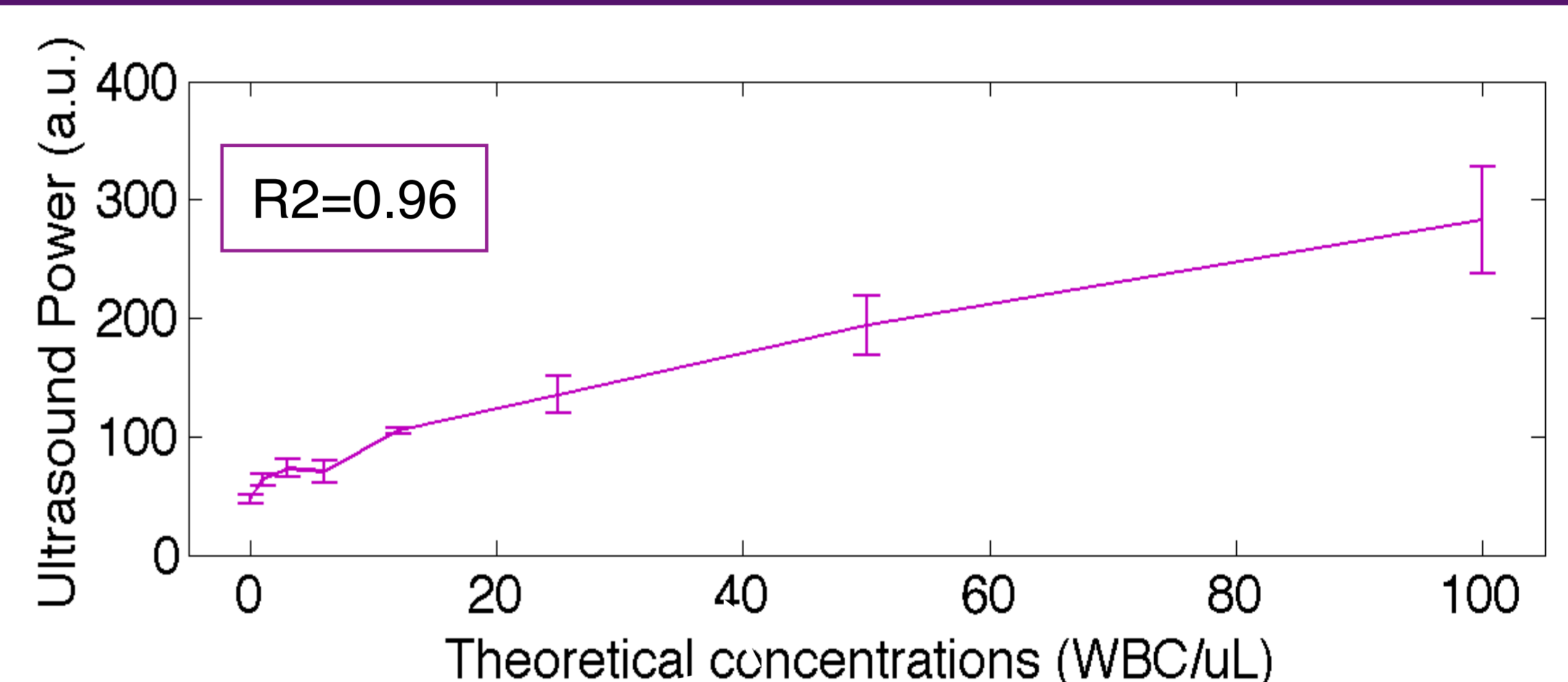


In the 0-50 cells/ μ L range, the coefficient of variation ($CV=STD/AVG$) in ultrasound measurements was below 18.3%, better than the $CV=30-45\%$ reported for the gold standard used in clinical settings, the Fuchs-Rosenthal chamber. Excellent linear agreement was observed between the theoretical leukocyte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

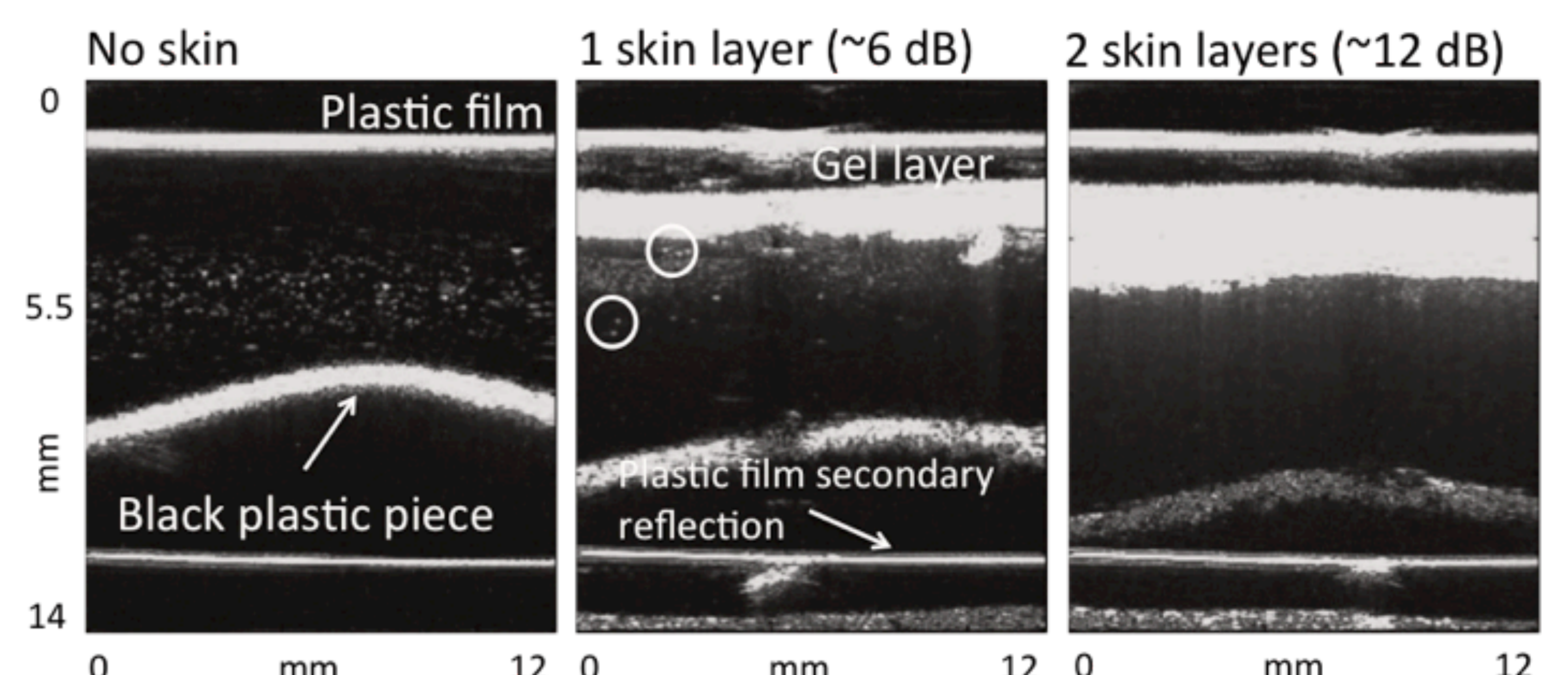
Conclusions

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.

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When imaging through tissue, echoes from individual cells could be visualized for attenuations not exceeding 6 dB, the low end of the expected fontanel attenuation range.



References

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