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Introduction:
Early, rapid diagnosis is integral to the efficient effective treatment of sepsis; however, there is no gold standard for diagnosis, and biochemical surrogates are of limited and controversial utility. The CytoVale system measures biophysical properties of cells by imaging thousands of single cells per second as they are hydrodynamically stretched in a microfluidic channel. This platform has been shown to measure dozens of mechanical, morphological, and cell surface biomarkers of WBC activation simultaneously [1,2]. In this study, we show the performance of the CytoVale system in measuring biophysical markers for sepsis detection in the emergency department (ED).

Methods:
We conducted an IRB-approved prospective cohort study of Emergency Department (ED) patients with 2+ SIRS criteria and evidence of organ dysfunction. 307 patients were included for analysis. Blood samples for the CytoVale assay were collected in the ED, and the diagnosis of sepsis was adjudicated by blinded clinician review of the medical record. Captured imaging data were analyzed using computer vision to quantify mechanical parameters per cell, and a logistic model was trained to discriminate patients who had sepsis from those who did not.

Results:
We found substantial biophysical differences between cells from septic and non-septic patients as observed at both the single cell level (Figure 1) and when looking at the overall leukocyte populations (Figure 2). A multiparameter classification algorithm to discriminate septic from non-septic patients based on biophysical markers currently yields a sensitivity of 88% with a negative predictive value of 95%.

Conclusion:
In patients presenting to the ED with 2 of 4 SIRS criteria and evidence of organ dysfunction, the CytoVale system provides a potentially viable means for the early diagnosis of sepsis via the quantification of biophysical properties of leukocytes.

References:
2. Crawford K et al. AJRCCM, under review, 2017
Mechanical phenotyping reveals new biophysical markers of WBC activation

Image 2:

Performance of two biophysical markers (diameter and aspect ratio) in discriminating non-septic and septic patients at the leukocyte population level.