INTRODUCTION

The purpose of this study was to clinically validate a new, rapid version of the SeptiCyte® assay on a near-patient testing platform (Biocartis’ Idylla™ platform*) using samples collected as part of previously established retrospective studies [1,2]. SeptiCyte® LAB can differentiate between sepsis and systemic inflammatory response syndrome (SIRS) in critically ill patients. SeptiCyte® LAB is the first-in-class sepsis diagnostic to gain FDA-clearance but currently has a complex workflow and turnaround time (TaT) of ~ 6 hours [3]. The assay in Idylla™ cartridge format is called SeptiCyte® RAPID with a TaT of ~ 1 hour.

METHODS

SeptiCyte® LAB was translated to the Biocartis Idylla™ near-patient testing platform and analytically validated. Patients (N=195) were recruited from previously established cohorts in two Intensive Care Units (ICU) located in the USA and Europe. For this validation study, 0.9mL of peripheral blood (collected in PAXgene™ tubes) was pipetted directly into the cartridge and inserted into the Idylla™ instrument. SeptiCyte® RAPID results were reported as a SeptiScore® between 0 and 15 with higher scores representing higher probability of sepsis. Assay performance metrics included technician hands-on-time (HoT), assay TaT, repeatability, reproducibility and Area Under ROC Curve (AUC). The comparator was retrospective physician diagnosis (RPD) using a panel of three independent physicians.

RESULTS

For 195 cartridges run, the average technician HoT was 2 minutes, average TaT was 65 minutes, and coefficient of variation for a positive extraction control was 1.19% demonstrating repeatability. Correlation of SeptiScore® values between SeptiCyte® LAB and SeptiCyte® RAPID, based upon a subset of N= 100 samples run on both platforms, was very high (r2>0.94) (Figure 1). Figure 2A shows the SeptiCyte® RAPID ROC curve for differentiating sepsis and SIRS in the sample set (N=195) and a high AUC of 0.904. Figure 2B shows significant differentiation of sepsis and SIRS patients in box and whisker plot format with SeptiScore® on the Y-axis and RPD on the X-axis. Figure 3 shows test TaT comparison between SeptiCyte® LAB (FDA cleared, kit format) and SeptiCyte® RAPID cartridges on the Idylla™ platform. Preliminary precision studies conducted with three sample types (Low, Medium, High SeptiScore® pools), two lots of cartridges, three instruments and and across six days confirmed high reproducibility of the test (Figure 4). SeptiCyte® RAPID cartridges (Figure 5) are fully integrated and include sample nucleic acid extraction, RT-qPCR and reporting in ~ 1 hour on the Idylla™ platform.

Figure 1: SeptiCyte® LAB vs RAPID comparison

![Figure 1: SeptiCyte® LAB vs RAPID comparison](image)

Figure 2 - SeptiCyte® RAPID performance

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Figure 1
SeptiCyte® RAPID demonstrates high correlation (r² = 0.94) to the SeptiCyte® LAB (manual kit) for a cohort of clinical ICU patients (N = 100). In the case of SeptiCyte® LAB, all clinical PAXgene™ blood samples were extracted using the PAXgene™ Blood RNA Kit, IVD version (Qiagen Cat No./ID: 762164).

Figure 2
(A): Receiver operating characteristic curve for SeptiScore®, calculated for the clinical dataset (N = 195). (B): SeptiCyte® RAPID strongly discriminates sepsis (N=106) from SIRS (N=89) cases.

Figure 4
Test reproducibility was determined with three sample types (Low [gray], Medium [white], High [red] score pools), two lots of cartridges, and three Idylla™ instruments (INS). The study (N = 54) was conducted over six days (D), with three samples per instrument, per sample type, per day. Operator-to-operator variability was expected to be minimal and was not evaluated. The reproducibility of the SeptiCyte® RAPID test demonstrates minimal variation (SD < 0.3) for each sample pool when considering all sources of variation.

CONCLUSIONS
• This is the first demonstration of a validated, fully-integrated, rapid, repeatable, reproducible, near-patient, immune-response sepsis diagnostic, providing accurate results in ~ 1 hr to differentiate sepsis from SIRS.

• It is anticipated to improve patient management for critically ill patients to be admitted to ICU.

• Further validation of the performance of SeptiCyte® RAPID is underway in real-time studies across multiple US sites.

References
[1] MARS (Molecular Diagnosis and Risk Stratification of Sepsis) www.clinicaltrials.gov identifier NCT01905033
