Diagnostic accuracy of OLM's *Cand*ID PCR kit for detection of candidaemia: a preliminary evaluation

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Background

Treatment for candidaemia is time critical, with delayed treatment associated with higher hospital mortality. Culture-based tests lack sensitivity and prolong turnaround times, minimizing clinical utility. In this context, non-culture-based methods for the identification of *Candida*, such as PCR, represent a promising approach to allow rapid diagnosis and species identification, allowing the rapid initiation of species-oriented therapy.
Our objective was to undertake an initial retrospective evaluation of the OLM Diagnostics *Cand*ID commercial PCR test for the diagnosis of invasive candida disease (IC).

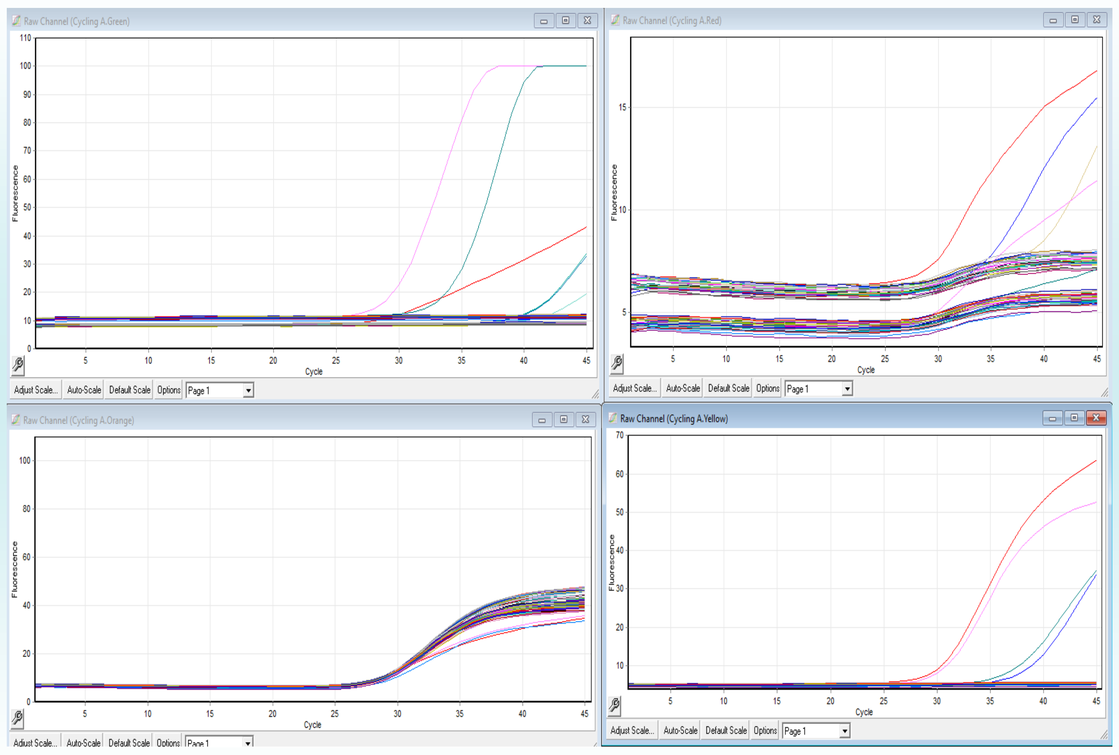
Materials/Methods

As part of routine testing across Wales, patients are prospectively screened for IC by Bruker Fungiplex *Candida* PCR and Fungitell (1-3)-β-D-Glucan (BDG). Samples from a 4-month period were retrospectively tested by the OLM *Cand*ID PCR assay. Initially, serum samples were selected based on a previous positive Fungiplex result, and required nucleic acid extraction of 0.5mL of serum (stored at -80ºC) on the BioMerieux eMAG platform. Additional *Cand*ID testing was performed on randomly selected DNA eluates, previously extracted during routine testing and stored at 4ºC prior to *Cand*ID testing performed on the Qiagen Rotorgene-Q , as per manufacturer's instructions.
Performance parameters (Sensitivity, specificity Positive/negative likelihood ratios) of the *Cand*ID were calculated, with IC defined as follows: Candidaemia (n=10) - *Candida* recovered by blood culture; Probable IC (n=12) - Clinical risk factor for invasive candidiasis (e.g. surgery, gut disruption, COVID-19), plus evidence of *Candida* colonization at ≥2 non-contiguous anatomical sites and a positive serum (1-3)-β-D-Glucan; or recovery of *Candida* from a central venous catheter or deep wound and a positive serum (1-3)-β-D-Glucan. A control population of 45 patients with no evidence of IC was included. *Candida* PCR testing played no role in defining IC.

Results

Nucleic Acid extraction through PCR amplification and result interpretation was completed in less than 4 hours.
74 serum samples were selected for testing (28 from 22 IC cases, 46 from 45 controls).
Positivity rate for samples from cases was 75% (21/28, 95% CI: 57-87), significantly greater than the false positivity rate (6.5%, 3/46, 95% CI: 2.2-17.5) for control samples.
Clinical performance is shown in the table.
False positive results were associated with an identification of *C. parapsilosis* (n=1) and *C. krusei* (n=2). Using a threshold of <37.5% cycles to define PCR positivity increased specificity to 100%, with a slight reduction in sensitivity (77%). Species identification with *Cand*ID kits was 100% concordant with that obtained through culture identification (*C. albicans* (n=13), *C. glabrata* (n=4), *C. tropicalis* (n=1), *C.krusei* (n=1)).
Two candidaemia cases falsely negative by PCR were also negative by BDG and routine PCR testing. One patient only had *Candida* recovered in 1/3 blood culture bottles, the other had received prior antifungal therapy.

C. albicans/tropicalis



C. dubliniensis/parapsilosis

Internal Control

C. glabrata/krusei

Population	Sensitivity (%)	Specificity (%)	LR+tive	LR-tive	DOR
Candidaemia (n=10) vs No IC (n=45)	**80 (49-94)**	**93 (82-98)**	**11.43**	**0.22**	**53.14**
Probable IC (n=12) vs No IC (n=45)	**92 (65-99)**	**93 (82-98)**	**13.14**	**0.09**	**152.79**
Combined IC (n=22) vs No IC (n=45)	**86 (67-95)**	**93 (82-98)**	**12.3**	**0.15**	**81.61**

Conclusions

*Cand*ID provides excellent performance and a rapid time-to-result, with accurate species identification that may prove beneficial in cases of suspected IC lacking candidaemia, by supporting clinical decision-making and avoiding treatment delay or inappropriate therapy choices for IC caused by non-*albicans* species. Retrospective data indicate the assay is useful for excluding but more so confirming IC. A prospective evaluation is required for confirmation.