Journal of Antimicrobial Stewardship, June 2017

T2 Magnetic Resonance assay improves timely management of candidemia

Wilson, N., Alangaden, G., Tibbetts, R., et al.

This multi-center trial at Henry Ford and Wayne State University, both of Detroit, Michigan, with 161 patients with probable or proven candidemia with a primary endpoint of time to appropriate antifungal therapy, time to candidemia detection, and patient outcomes were compared before and after T2MR demonstrated:

- The median time to appropriate antifungal therapy was reduced from 39 hours to 22 hours post-T2MR, P=0.003
- Among the subgroup of 37 patients detected by T2MR, the median time to appropriate therapy was 5 hours
- After adjusting for severe sepsis (adjusted OR 2.0, 95% CI [1.3-3.1], diagnosis by T2MR was independently associated with receipt of antifungal therapy within 12 hours (adjusted OR 5.8, 95% CI [2.5-13.6]); No significant differences in length of stay or mortality were detected
- This study suggests that T2MR is a valuable clinical tool to aid antifungal stewardship and to improve timely antifungal therapy for candidemia

Future Microbiology, April 2015

The economic impact of rapid *Candida* species identification by T2Candida among high-risk patients

Bilir, S.P., Ferrufino, C.P., Pfaller, M.A., and Munakata, J.

Published study on economic and clinical model for T2Candida Panel demonstrating that a 500 bed hospital could save $5.8 million annually and prevent 60% of *Candida*-related deaths.

Clinical Infectious Diseases, January 2015

T2 Magnetic Resonance assay for the rapid diagnosis of candidemia in whole blood: A clinical trial

Mylonakis, E., Clancy, C.J., Ostrosky-Zeichner, L., et al.

This multi-center prospective trial of 12 US institutions and 1801 hospitalized adult patients demonstrated:

- The overall sensitivity was found to be 91.1% (95% CI, 86.9%–94.2%) with a mean time of 4.4 ± 1.0 hours for detection and species identification
- T2MR demonstrated an overall specificity per assay of 99.4% (95% confidence interval [CI], 99.1%–99.6%) with a mean time to negative result of 4.2 ± 0.9 hours
- The limit of detection was as low as 1 CFU/mL
- T2MR represents a breakthrough shift into a new era of molecular diagnostics

Future Microbiology, September 2015

T2MR and T2Candida: Novel technology for the rapid diagnosis of candidemia and invasive candidiasis

Pfaller, M.A., Wolk, D,M., and Lowery, T.J.

T2 Magnetic Resonance (T2MR) is a miniaturized, magnetic resonance based diagnostic approach that measures how water molecules react in the presence of magnetic fields. The method is capable of detecting a variety of targets, including: molecular targets (e.g., DNA); and immunodiagnostics (e.g.,proteins).

Across multiple studies, T2Candida successfully detected 43 of 45 patients with confirmed candidemia (31/33) or candidiasis (12/12). When including patients with probable candidiasis, T2Candida detects 10 of 10 patients, totaling 53 of 55 cases detected for candidemia or candidiasis. In this aggregate population, BC only detected 33 of 55 patients.

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T2 Biosystems®

T2Direct Diagnostics™ Publication Summary

T2Bacteria® Panel

Annals of Internal Medicine, May 2019

Clinical performance of T2Bacteria among patients with bloodstream infections due to five common bacterial species

Nguyen, M.H., Pasculle, W., Pappas, P.G., et al.

This pivotal, clinical multi-center prospective trial was conducted in 11 U.S. Centers with 1427 subjects from presenting to the ICU or ED:

- Overall, the T2Bacteria Panel detected ~66% of BSIs, excluding common contaminants
- Mean time to BC positive: 38.5h ± 32.8h
- Mean time to BC speciation: 71.7h ± 39.3h
- Mean time to T2B result: 3.6h ± 0.2h – 7.70hr ± 1.38h
- T2Bacteria demonstrated 90% per patient sensitivity and specificity, negative predictive value of 99.7%, and a per-assay specificity of 98% depending on the number of samples tested
- Potential advantages of T2B over BC:
  - Detect bacteremia several days before BC (3-5 hours versus 2-3 days)
  - If probable and possible BSIs were assumed to be true positives missed by blood culture, per-patient specificity of T2Bacteria was 96%
  - Diagnose infections missed by BC
  - Detect patients with antecedent antibiotics
  - Detect patients with extra-blood site infections

ECCMID, April 2019

The T2Bacteria assay is a sensitive and rapid detector of bacteremia that can be initiated in the emergency department and has potential to favorably influence subsequent therapy

Voigt, C, Silbert, S, Widen, R, et al.

- Evaluated n=137 patients admitted through the emergency department (ED) with blood samples run on T2Bacteria and blood culture
- Relative to blood culture, T2Bacteria showed 100% PPA and 98.4% NPA
- Conclusion: “In this ED population, the T2Bacteria assay was a rapid and sensitive detector of bacteremia from common ESKAPE pathogens and showed the theoretical potential to influence subsequent patient therapy, ranging from antibiotic de-escalation to faster time to effective therapy.”
- T2Bacteria covered 70% of all species detected by blood culture
- Evaluation of potential impact on therapy showed the majority of patients would have benefited from the T2Bacteria result

Journal of Antimicrobial Chemotherapy, April 2018

T2Bacteria magnetic resonance assay for the rapid detection of ESKAPEc pathogens directly in whole blood

DeAngelis, G., Posteraro, B., DeCarolis, E., et al.

This prospective study was conducted at Gemelli Hospital, Rome, IT with 129 adult patients in the ICU and ED:

- T2Bacteria Panel achieved faster time to species ID than BC: 5.5h ±1.4h vs. BC 25.2h ± 15.2h (P<0.001) and faster time to negative results 6.1h ± 1.5h vs. BC 120.0h ± 0.0h (p<0.001)
- T2Bacteria performed with a sensitivity and specificity of 90% and 98% respectively according to true-infection criteria

MAD-ID, May 2018 *Manuscript in process*

Early experience with the T2Bacteria Research Use Only (RUO) Panel at a community hospital

Weisz, E., Newton, E.C., Estrada, S., and Saunders, M.

This prospective study was conducted at Lee Health, Fort Myers, FL in 28 adult patients presenting to the ED:

- The T2Bacteria RUO Panel allowed testing from whole blood samples and provided final results within 4 hours
- T2Bacteria RUO Panel provided positive and negative results approximately 20 hours and 122 hours sooner than BCs, respectively (p<0.001)
- T2Bacteria RUO Panel detected 5 organisms not identified by BC
- Study identified >30 opportunities for de-escalation of coverage based on negative results for *S. aureus* or *P. aeruginosa*

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T2 Biosystems®

T2Bacteria® Panel

ASM Microbe, June 2018 *Manuscript in process*

Evaluation of the T2Bacteria Panel compared to standard blood culture at Ochsner Medical Center

Ogawa, M., Wargo, C., Marty-Vigo H., et al.

This blinded, prospective study was conducted at Ochsner Medical Center, New Orleans, LA in 137 adult subjects presenting to the ED:

- T2Bacteria demonstrated an overall average of 100% sensitivity and 98% specificity
- T2Bacteria did not miss any growth from BC of a bacteria species on panel and detected true positives
- The study suggests that T2Bacteria can provide highly sensitive and specific results in hours vs. days for a standard BC

ASM Microbe, June 2018

Validation of a rapid diagnostic test on whole blood for early identification of pathogens in patients in the intensive care unit

Pickens, C., Qi, C., Malcynzski, M., et al.

This a combined prospective and retrospective study conducted by Northwestern University with 91 retrospective samples and 58 prospective samples from patients admitted to the ICU:

- The T2Bacteria RUO Panel was 87% sensitive and 95% specific for the detection of six different organisms compared to BC; The calculated specificity is limited by comparison to BC because many studies demonstrate that BC itself is poorly sensitive
- As further support, the T2Bacteria RUO Panel detected organisms in the blood when BC was negative but evidence of infection in the urine or lung was available; A positive T2Bacteria Panel RUO result in this setting may indicate poor source control, inappropriate antibiotics or poor host defenses

IDWeek, October 2018 *Manuscript in process*

Implementation of the T2 Biosystems T2Bacteria Panel in a level-one trauma center, safety net hospital

Robinson, C., Jackson, R., Sauaia, A., and Cohen, M.

This prospective study was conducted at Denver Health, Denver CO with I74 adult patients presenting to the ED and from the Surgical ICU:

- The T2Bacteria Panel correctly identified 91% infections defined by the study's clinical definition of bacteremia
- BC identified 29 patient infections, 10 of which were potentially false positive
- Investigators concluded that T2Bacteria's much faster results than BC and high specificity make it a tool that can be used in the emergency department and surgical ICU settings

T2MR® Technology

Science Translational Medicine, 2013

T2 Magnetic Resonance enables nanoparticle-mediated rapid detection of candidemia in whole blood

Neely, L.A., Audeh, M, Phung, N.A., et al.

T2 magnetic resonance (T2MR) diagnostic platform approach:

- Blood-compatible polymerase chain reaction is followed by hybridization of the amplified pathogen DNA to capture probe–decorated nanoparticles.
- Hybridization yields nanoparticle microclusters that cause large changes in the sample's T2MR signal
- With this T2MR-based method, pathogens can be detected directly in whole blood, thus eliminating the need for analyte purification.

T2Candida® Panel

Diagnostic Microbiology and Infectious Disease, April 2018

Diagnosing candidemia with the T2Candida Panel: An instructive case of septic shock in which blood cultures were negative

Clancy, C.J. and Nguyen, M.H.

This case study by UPMC investigators highlights how T2Candida can identify proven candidemia patient cases that are missed by concurrent BCs, and guide early treatment. In addition:

- Due to high PPV, patient populations in which T2Candida should have the greatest clinical utility include patients: admitted to the ICU, with febrile neutropenia, with septic shock, with LVAD + evidence of active infection, and admitted to ICU + at high risk for candidemia based on clinical prediction models
- T2Candida may be particularly useful in targeting antifungal treatment to patients with septic shock who also have other risk factors for candidemia
- Anticipated NPVs remain exceptional (≥99%) in most settings in which the test will be employed

Journal of Antimicrobial Chemotherapy, March 2018

Impact of rapid, culture-independent diagnosis of candidaemia and invasive candidiasis in a community health system

Patch, M.E., Weisz, E., Cubillos, A., et al.

This retrospective two-phase study was conducted at Lee Health, Fort Myers, FL with 100 adult patients with suspected candidemia:

- The mean time to appropriate therapy from the first positive BC was 34h (range 1-92h; 53%>24h; In contrast, the time to initiation of appropriate antifungal therapy was only 6 h (range 1–13 h) from the time of blood draw in the T2Candida-positive patients in Phase 2 (P=0.00147)
- There were no statistically significant differences in length of hospital or ICU stay, in all-cause 30 day readmissions or in mortality; However, an 8 day reduction in length of stay was noted in Phase 2 (Table 1)
- The major findings in this study are the decreased time to initiation of targeted antifungal therapy when a T2Candida-directed treatment strategy was employed versus that of a BC-directed therapy approach and the avoidance of empirical therapy in 58.4% (101/173) of T2Candida-negative patients
- The decreased utilization of empirical micafungin therapy observed in Phase 2 would result in a total savings of US$48,400 (or $280 per tested patient) in antifungal costs alone when compared with historical control data from Phase 1

IDWeek, October 2018

Incorporating T2Candida testing into rational antifungal management

Shields, R.K., Clancy, C.J., Marini, R.V., et al.

In this single center prospective trial, 114 adult patients residing in the ICU, University of Pittsburgh Medical Center, Pittsburgh, Pennsylvania, were evaluated with T2Candida. Results demonstrated:

- Targeted antifungal management approaches resulted in decreased antifungal usage and shorter times to start of antifungal therapy among patients with invasive candidiasis
- Median antifungal days of therapy per patient were reduced by 11 days (p=0.0005) and shorter times to start antifungal therapy among patients with invasive candidiasis
- Combining proven, probable, and possible cases, 12% (15/125) of patients were diagnosed with invasive candidiasis using T2 or BC results, compared to only 6% (7/125) of patients if BC results were used alone

Journal of Clinical Microbiology, April 2018

The efficacy of T2 Magnetic Resonance assay in monitoring candidemia after the initiation of antifungal therapy: The Serial Therapeutic and Antifungal Monitoring Protocol (STAMP) trial

Mylonakis, E., Zacharioudakis, L.M., Clancy, C.J., et al.

This multi-center prospective trial was conducted with 188 adult patients with a BC positive for yeast. Designated as the STAMP trial, the study was designed to investigate the performance of T2MR assay as a monitoring tool for post-therapy clearance of candidemia compared to BCs:

- This study provides evidence that T2MR might outperform BCs in monitoring the clearance of *Candida* spp. in candidemic patients who are on antifungal treatment
- Based on the log rank test, there was a statistically significant improvement in post-treatment surveillance using the T2MR assay compared to BC (P = 0.004)

Clinical Infectious Diseases, May 2018

Detecting infections rapidly and easily for candidemia trial, Part 2 (DIRECT2): A prospective, multi-center study of the T2Candida Panel

Clancy, C.J.,Pappas, P.G., Vazquez, J., et al.

This multi-center prospective trial, known as DIRECT2 was conducted among 14 U.S. centers with 152 adult hospitalized patients. The DIRECT2 study finds strong, reliable performance of the T2Candida Panel on real patient samples:

- The median time to detection of *Candida* by diagnostic BCs and subsequent species identification was 3.4 days; In comparison, the T2Candida Panel provides diagnostic results in an average time of 4.4 hours
- T2Candida detected almost twice as many confirmed infections as BC in patients receiving antifungal therapy
- This indicates T2Candida is a more effective diagnostic tool for patients treated with pre-emptive or empiric antifungal therapy
- T2Candida was 89% sensitive in patients with positive BCs, a result that was remarkably similar to the analytic sensitivity of 91.1% for contrived blood samples in the DIRECT trial