The T2Candida Panel Identifies 3.55 Times More On-Panel *Candida* Species Compared to Conventional Blood Culture

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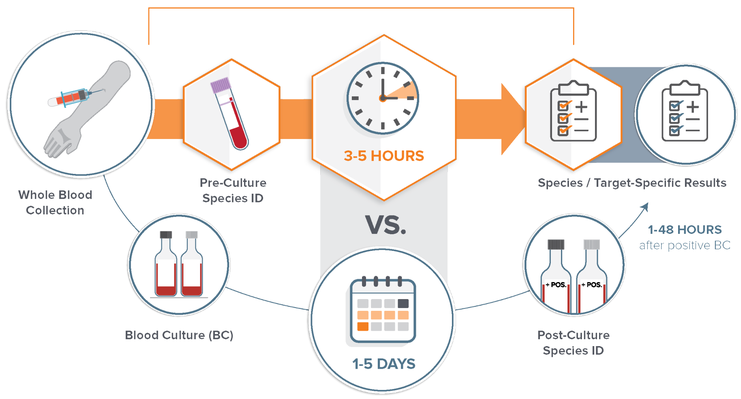
Background

- The T2Candida® Panel is an FDA-cleared and CE-marked culture-independent *in vitro* diagnostic test that identifies common species that cause fungal sepsis utilizing T2 Magnetic Resonance Technology (T2MR).
- This FDA-cleared panel detects *Candida albicans, Candida tropicalis, Candida parapsilosis, Candida krusei,* and *Candida glabrata* directly from whole blood within 3-5 hours.
- The T2Candida Panel has been demonstrated to be highly sensitive with a sensitivity of 91.1% and a limit of detection (LoD) of 1-3 CFU/mL.[1]
- The T2Dx Instrument detects intact pathogen cells[2] → both active and non-proliferating/stationary cells
- The purpose of this study is to quantify the rate at which T2Candida detects on-panel species compared to blood culture in studies evaluating T2Candida.

Rapid Culture-Independent Species ID with T2 Biosystems



Methods

INCLUSION:

Publications, presentations, and abstracts evaluating the T2Candida Panel were systematically screened and included if the study reported organism level detection data for both the T2Candida panel and conventional blood cultures.

EXCLUSION:

Studies were excluded if organism level data were not available for both on and off-panel organisms. Data relating to bacterial species and the T2Bacteria Panel were excluded from analyses.

OUTCOMES:

The primary outcome is the ratio of on-panel organisms identified overall by the T2Candida Panel compared to conventional blood cultures.

Results

Table 1: Included Studies

Author	Year	Location	T2C Tested	Patient Population
Mylonakis, E[1]	2015	USA	1501	Blood Culture Ordered
Cendejas-Bueno, E[3]	2021	Spain	97	Medical-surgical PICU
Cruz, H[4]	2023	Portugal	34	ICU
Lucignano, B[5]	2022	Italy	106	Pediatric Sepsis
Seitz, T[6]	2022	Austria	85	ICU
Birk, N[7]	2023	USA	870	ICU
Zacharioudakis, IM[8]	2023	USA	216	ICU
Krifors, A[9]	2022	Sweden	101	Surgical ICU
O'Donnell, M[10]	2023	USA	155	Medical ICU

Table 2: Time to Pathogen Detection and Ratio of T2Candida Panel vs Blood Culture Pathogen Detection

Author	T2C Positive	Time to Species ID T2C (h)	BC Positive	Time to Species ID BC (h)	Δ (h)	T2C+/ BC+ Ratio
Mylonakis, E[1*]	36	4.2	7	> 120	115.8	5.1
Cendejas-Bueno, E[3]	7	NA	2	NA	NA	3.5
Cruz, H[4]	5	5.7	2	70.3	64.6	2.5
Lucignano, B[5]	10	3.7	4	125.5	121.8	2.5
Seitz, T[6]	9	5	1	85.6	80.6	9
Birk, N[7]	79	NA	22	NA	NA	3.6
Zacharioudakis, IM[8]	5	NA	3	NA	NA	1.7
Krifors, A[9]	9	NA	2	NA	NA	4.5
O'Donnell, M[10]	14	5.6	7	60	54.4	2
Total	**174**		**50**		**3.5**	
Time (mean)	**4.8 h**		**92.3**		**87.5**	

* Prospectively collected samples ONLY

Results

Figure 1: Additional BSI Causing Pathogen Detection with the T2Candida Panel (1,3-6,10)

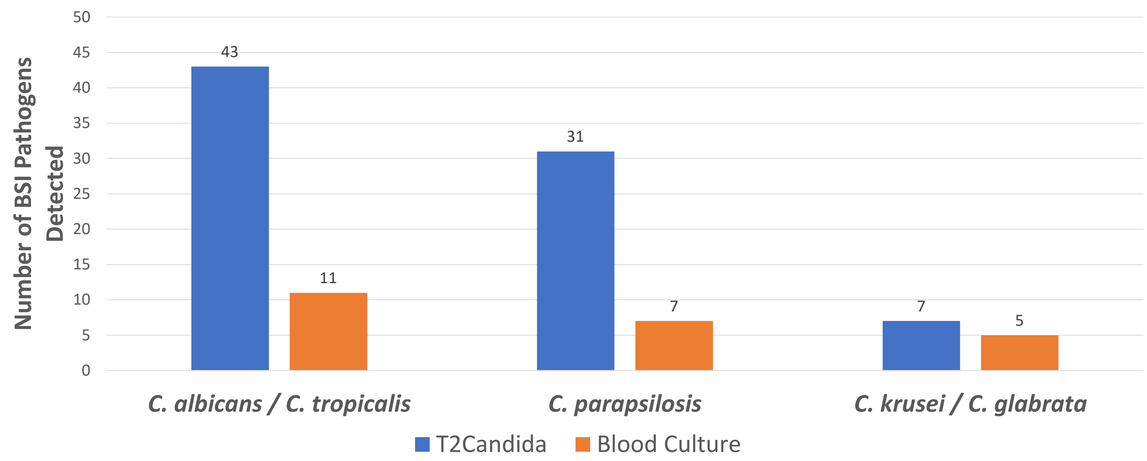


Table 3: Ratio of Additional Pathogens Detection with the T2Candida Panel Compared to Conventional Blood Culture (1,3-6,10)

Species	No. BSIs Pathogens Identified	T2C+/ BC+ Ratio
C. albicans / C. tropicalis	43	3.9
C. parapsilosis	31	4.4
C. krusei / C. glabrata	7	1.4
Total	**81**	**3.5**

Table 4: Clinical Adjudication of T2Candida Positive – Blood Culture Negative Cases(3,5,6,10)

Author	No. of T2C+/ BC- cases	Adjudication*
Cendejas-Bueno, E[3]	5	5/5 = Pathogen identified in other cultures
Lucignano, B[5]	6	6/6 = Probable or Possible IC
Seitz, T[6]	8	8/8 = True infections
O'Donnell, M[10]	7	2/7 = Probable or Possible IC±

* Adjudication process and definitions varied by study, ±Eighty percent of false-positive cases were attributed to C. parapsilosis, a skin commensal

- Across 9 studies, a total of n=3,165 T2Candida Panels were prospectively collected and tested.
- A total of n=1,656 were tested in the USA and n=1,509 were tested outside of the US.
- The T2Candida Panel identified 3.5 times more on-panel organisms than conventional blood cultures.
- For prospective interventional clinical studies (n=4) describing complete or partial clinical adjudication of T2C+/BC- cases, 21/26 (81%) were deemed true, probable or possible infections.(3,5,6,10)

Conclusion

- The highly sensitive T2Candida Panel identified 3.5 more on-panel organisms, directly from whole blood within 4.8 hours, compared to conventional blood cultures at 92.3 h across 9 clinical studies.
- T2Candida Panel has the potential to improve care by allowing clinicians to optimize antifungal therapy through added identification of BSI-causing pathogens that otherwise were missed by conventional blood culture.
- Future studies are needed to evaluate the impact of these added detections compared to conventional blood cultures.

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10. O'Donnell M, Shields RK, Marini RV, et al. Stewardship-Guided T2Candida Testing Shortens Time to Antifungal Treatment and Reduces Antifungal Usage Among Medical Intensive Care Unit Patients With Septic Shock. *Open Forum Infect Dis* 2023;10(11):ofad538.

T2Direct Diagnostics™ Critical Workflow Steps

T2Biosystems®

GLOVE CHANGING

Put on fresh gloves prior to:

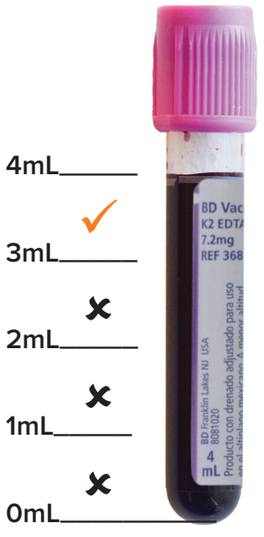
- Work area preparation
- Obtaining samples and opening outer packaging for all Panel components
- Removing Panel components from packaging and assembling Panel for loading
- Unloading completed Panel
- Work area preparation after unload

SAMPLE COLLECTION

Tube Type: 4 mL K_2EDTA or K_3EDTA, purple top Vacutainer® tubes (BD #367861, 367862 or equivalent)

Volume: At least 3 mL are required

Sample Preparation: Ensure that the sample is at room temperature and inverted 8-10 times prior to use

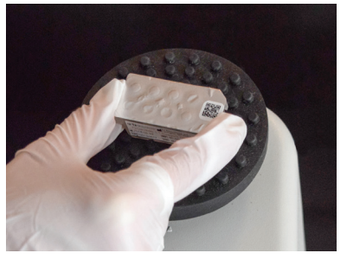


REAGENT TRAY MIXING

Shake: Mix the reagents in the Reagent Tray by shaking in a horizontal motion until contents are homogeneous

or

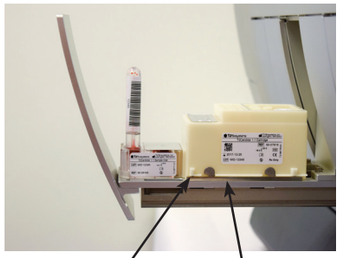
Vortex: Securely hold the Reagent Tray upright and push down onto the center of the vortex head cover for 5 seconds until contents are homogeneous



Tap: Displace trapped air in the Reagent Tray by firmly tapping it on the work prep area. Visually confirm there are no bubbles.

PANEL SEATING

When loading the fully assembled Panel onto the T2Dx, ensure that it is level and in full contact with the metal rails and seated on the location pins. Location pins are not visible when the Panel is securely seated in the drawer.



PANEL LABEL AND REAGENT TRAY COVER REMOVAL

Follow the T2Dx touchscreen prompts for loading the fully assembled Panel.

Remove the Cartridge Label

Remove the Reagent Tray Cover (T2Bacteria Only)

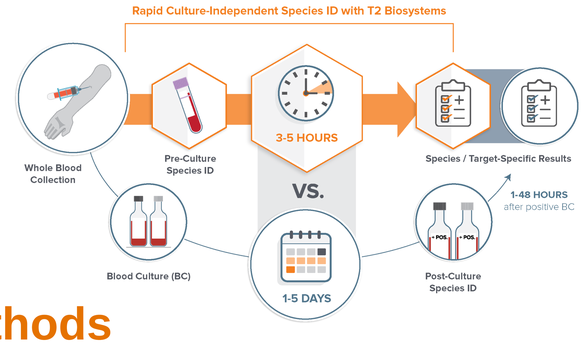
The T2Bacteria Panel Identifies 3 Times More On-Panel Bacterial Pathogens Compared to Conventional Blood Culture

Oscar E. Guzman, PharmD, BCPS, BCCCP, FCCM[1] ; Brian C. Bohn, PharmD, BCIDP[1]

[1]T2 Biosystems, Lexington, MA, USA

Background

- The T2Bacteria® Panel is an FDA cleared and CE marked culture independent *in vitro* diagnostic test that identifies common species that cause bacterial sepsis utilizing T2 magnetic resonance technology.
- This FDA cleared panel detects *Enterococcus faecium*, *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, and *Escherichia coli* directly from whole blood within 3-5 hours.
- The CE-marked panel also has *Acinetobacter baumannii* as a sixth target.
- The T2Bacteria Panel has been demonstrated to be highly sensitive with a sensitivity of 90% and a limit of detection (LoD) of 2-11 CFU/mL. [13]
- The purpose of this study is to quantify the rate at which the T2Bacteria Panel detects on-panel species compared to blood culture in studies evaluating the T2Bacteria Panel.



Methods

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Publications, presentations, and abstracts evaluating the T2Bacteria Panel were systematically screened and included if the study reported organism level detection data for both the T2Bacteria panel and conventional blood cultures.

EXCLUSION:
Studies were excluded if organism level data were not available for both on and off-panel organisms. Data relating to *Candida* species and the T2Candida Panel were excluded from analyses.

OUTCOMES:
The primary outcome is the ratio of on-panel organisms identified overall by the T2Bacteria Panel compared to conventional blood cultures.

Results

Table 1: Included Studies

Author	BC Method	Year	Location	Population
Bonura C[1]	Bactec FX	2023	Italy	ICU
Cruz H[2]	Bactec FX	2023	Portugal	ICU
Parajo Pazos N[3]	Bactec FX	2023	Spain	ICU
Giacobbe DR[4]	Bactec FX	2022	Italy	ICU
Lucignano B[5]	Bactec 9240, Bactec 70FX	2022	Italy	Pediatrics Sepsis
Seitz T[6]	BacT/ALERT FN Plus	2022	Austria	ICU
Krifors A[7]	BacT/ALERT VIRTUO	2022	Sweden	SICU
Quirino A[8]	BacT/ALERT VIRTUO	2022	Italy	Suspected BSI
Paggi R[9]	Bactec FX	2021	Italy	ICU
Drevinek P[10]	Bactec FX	2021	Czech	ICU
Douka E[11]	Bactec 9240	2020	Greece	ICU
Walsh TJ[12]	Bactec FX	2019	USA	HemOnc
Nguyen MH[13]	BacT/ALERT, Bactec FX, VersaTREK	2019	USA	Suspected BSI
DeAngelis G[14]	BacT/ALERT VIRTUO	2018	Italy	ED

Results

Table 2: Time to Pathogen Detection and Ratio of T2Bacteria Panel vs Blood Culture Pathogen Detection

Author	T2B Positive	Time to Species ID T2B (h)	Blood Culture Positive	Time to Species ID Blood Culture (h)	Δ (h)	T2B+/ BC+ Ratio
Bonura C[1]	48	4.91	21	93.64	88.73	2.29
Cruz H[2]	51	6.1	29	42.6	36.5	1.76
Parajo Pazos N[3]	20	NR	6	NR	36.9	3.33
Giacobbe DR[4]	11	NR	3	NR	NR	3.67
Lucignano B[5]	131	4.4	39	65.7	61.3	3.36
Seitz T[6]	9	4.3	3	41.5	37.2	3.00
Krifors A[7]	28	NR	8	NR	NR	3.50
Quirino A[8]	18	4.5	8	NR	NR	2.25
Paggi R[9]	28	3.7	11	37.6	33.9	2.55
Drevinek P[10]	16	6.1	9	62	55.9	1.78
Douka E[11]	13	3.5	4	84	80.5	3.25
Walsh TJ[12]	11	3.7	4	12.5	8.8	2.75
Nguyen MH[13]	190	3.61	41	71.7	68.1	4.63
DeAngelis G[14]	30	5.5	12	25.2	25.2	2.50
Total	**n = 604**		**n = 198**			**3.05**
Time (mean)	4.6 h		53.6 h		**48.5 h**	

NR = not reported

Figure 1: Additional BSI Causing Pathogen Detection with the T2Bacteria Panel

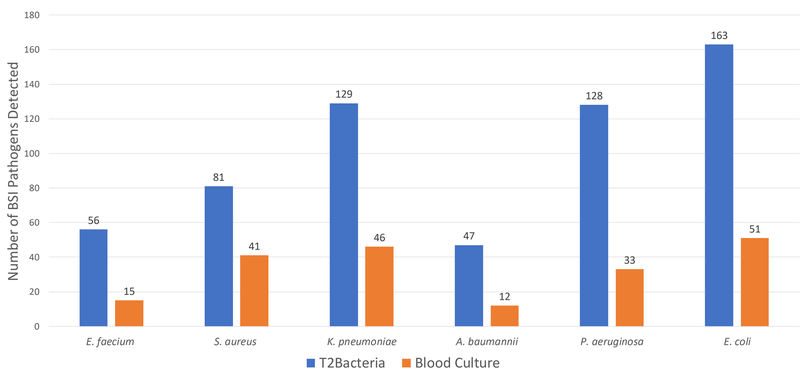

Table 3: T2Bacteria Panel Analytic Performance

Specific Bacteria Detected	Compared to Gold Standard (Blood Cultures)	
	Sensitivity (95%CI)	Specificity (95%CI)
E. faecium (n=56)	80% (51.91% to 95.67%)	98.47% (97.95% to 98.89%)
S. aureus (n=81)	87.8% (73.80% to 95.92%)	98.45% (97.93% to 98.87%)
K. pneumoniae (n=129)	93.48% (82.10% to 98.63%)	97.01% (96.32% to 97.60%)
A. baumannii (n=47)	83.33% (51.59% to 97.91%)	97.49% (96.56% to 98.23%)
P. aeruginosa (n=128)	100% (89.42% to 100%)	96.74% (96.03% to 97.35%)
E. coli (n=163)	86.27% (73.74% to 94.30%)	95.96% (95.19% to 96.65%)
T2Bacteria Panel	**89.9% (84.83% to 93.72%)**	**97.34% (97.08% to 97.59%)**

Results

- Across 14 studies, a total of 2998 T2Bacteria Panels were tested.
- A total of n=1511 were tested in the USA and n=1487 were tested outside of the US.
- The primary blood culture test methods included the Bactec (FX, 70FX or 9240) system (n=1227), and BacT/ALERT (FN Plus or VIRTUO) system (n=344), Bactec or Bact/ALERT or VersaTEK (n= 1427).
- The T2Bacteria Panel identified 604 on-panel organisms compared to 198 identifications from conventional blood cultures.
- The T2Bacteria Panel identified 3.05 times more on-panel organisms (n=406) than conventional blood cultures.
- The T2Bacteria Panel identified the following additional pathogens compared to conventional blood culture
  - ***E. faecium*** **(n=41), T2B+/BC+ Ratio = 3.73**
  - ***S. aureus*** **(n=40), T2B+/BC+ Ratio = 1.97**
  - ***K. pneumonia*** **(n=83), T2B+/BC+ Ratio = 2.8**
  - ***A. baumannii*** **(n=35), T2B+/BC+ Ratio = 3.91**
  - ***P. aeruginosa*** **(n=95), T2B+/BC+ Ratio = 3.87**
  - ***E. coli*** **(n=112), T2B+/BC+ Ratio = 3.19**
- For studies (n=8) describing complete or partial clinical adjudication of T2B+/BC- cases, 430/503(85.5%) were deemed true infections.
- The sensitivity and specificity of the T2Bacteria Panel among these 14 studies was 89.9% and 97.34%.

Conclusion

- The highly sensitive T2Bacteria Panel identified 3.05 more on-panel organisms, directly from whole blood within 4.6 hours compared to conventional blood cultures at 48.h across 14 clinical studies.
- T2Bacteria Panel has the potential to improve care by allowing clinicians to optimize antibiotic therapy through added identification of BSI causing pathogens that otherwise were missed by conventional blood culture.
- Future studies are needed to evaluate the impact of these added detections compared to conventional blood cultures.

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