Clinical Evaluation of a Semi-Quantitative Multiplex Molecular Assay for the Identification of Bacteria, Viruses, and Fungi in Lower Respiratory Specimens*

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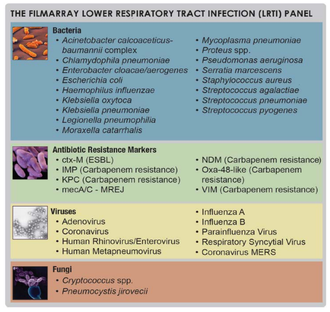
Introduction

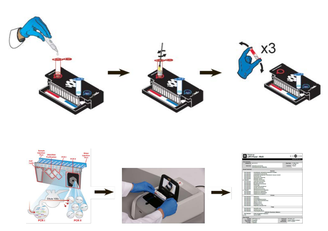
Lower respiratory infections can be caused by an array of bacterial, viral, or fungal organisms. These infections can carry high morbidity and mortality in hospitalized patients with co-morbidities. Rapid and accurate identification of these organisms is central to selection of the appropriate antimicrobial regimen; however, culture methods are slow and insensitive, and molecular tests are not available or are not routinely ordered on these specimens. We evaluated the research use only FilmArray® Lower Respiratory Tract Infection Panel (LRTI, BioFire Diagnostics, Salt Lake City, UT) for detection of respiratory pathogens in sputum and bronchioloalveolar lavage (BAL) specimens.

Methods and Instrumentation

A total of 57 BAL and 48 sputum were collected from inpatients aged 18 years and older with symptoms of respiratory tract infection at 8 hospitals in the US. All specimens were tested using the LRTI assay, which identifies 17 bacterial agents (14 reported semi-quantitatively when the target genomic is present at or above 10^4 copies/mL) in addition to 2 fungal and 9 viral agents (reported qualitatively). Select resistance mechanisms including mecA/C, ctx-M, KPC, VIM, IMP, NDM, and OXA-48 are also detected. In this study, identification results for LRTI were compared to standard of care (SOC) methods including culture and PCR based on clinician order. Chart review was conducted to determine type and duration of antibiotic (abx) therapy for each subject. No fungal targets were detected in this evaluation.



Workflow



Conclusions

- FilmArray® LRTI demonstrated a positive percent agreement (PPA) of 94.7% (18/19) and 95.8% (23/24) for bacterial ID targets in BAL and sputum specimens, respectively.
- Use of a molecular comprehensive etiology panel aids in the identification of potential pathogens in complex specimens or after the initiation of antibiotic therapy.
- Results from the FilmArray® LRTI may aid in earlier identification of respiratory pathogens and optimization of antibiotic therapy.

*The assays described in this poster have not been evaluated for IVD use by regulatory agencies

Table 1. Comparison of FilmArray® LRTI and culture in BAL (n=57)

Organism	SOC+/FA+	SOC+/FA-	SOC-/FA+	SOC-/FA-	Total	PPA	NPA
A. baumannii	0	0	0	57	57	ND	100%
Enterobacter	4	0	0	53	57	100%	100%
E. coli	1	0	0	56	57	100%	100%
H. influenzae	2	0	3	52	57	100%	94.6%
K. oxytoca	0	0	1	56	57	ND	98.3%
K. pneumoniae	2	0	1	54	57	100%	98.2%
M. catarrhalis	1	0	1	55	57	100%	98.2%
Proteus	0	0	0	57	57	ND	100%
P. aeruginosa	3	1	1	52	57	75.0%	98.1%
S. marcescens	2	0	0	55	57	100%	100%
S. agalactiae	0	0	0	57	57	ND	100%
S. pneumoniae	0	0	0	57	57	ND	100%
S. pyogenes	0	0	0	57	57	ND	100%
S. aureus	3	0	4	50	57	100%	92.6%
Total	**18**	**1**	**11**	**768**	**798**	**94.7%**	**98.6%**

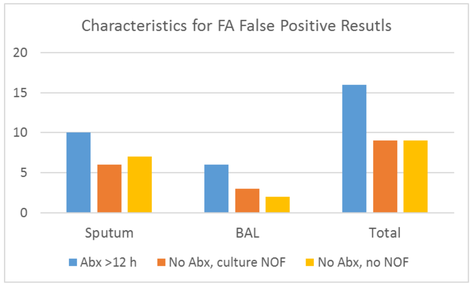
FA: FilmArray® LRTI; SOC: Standard of care; ND: Not determined

Table 2. Comparison of FilmArray® LRTI and culture in Sputum (n=48)

Organism	SOC+/FA+	SOC+/FA-	SOC-/FA+	SOC-/FA-	Total	PPA	NPA
A. baumannii	2	0	1	45	48	100%	97.8%
Enterobacter	0	0	1	47	48	ND	97.9%
E. coli	1	0	2	45	48	100%	95.7%
H. influenzae	0	0	4	44	48	ND	91.7%
K. oxytoca	0	0	1	47	48	ND	97.9%
K. pneumoniae	2	0	2	44	48	100%	95.7%
M. catarrhalis	0	0	0	48	48	ND	100%
Proteus	1	0	1	46	48	100%	97.9%
P. aeruginosa	6	0	2	40	48	100%	95.2%
S. marcescens	2	0	0	46	48	100%	100%
S. agalactiae	1	0	2	45	48	100%	95.7%
S. pneumoniae	0	0	3	45	48	ND	93.8%
S. pyogenes	0	0	0	48	48	ND	100%
S. aureus	8	1	4	35	48	88.9%	89.7%
Total	**23**	**1**	**23**	**625**	**672**	**95.8%**	**96.5%**

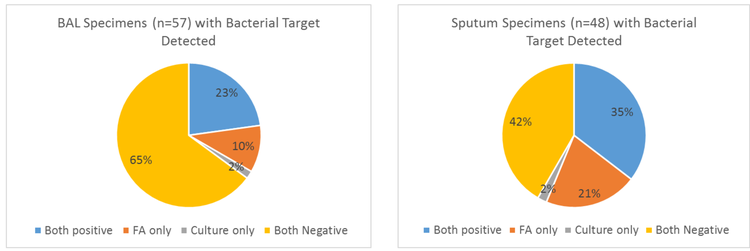
FA: FilmArray® LRTI; SOC: Standard of care; ND: Not determined

Figure 1. Classification of false positive results

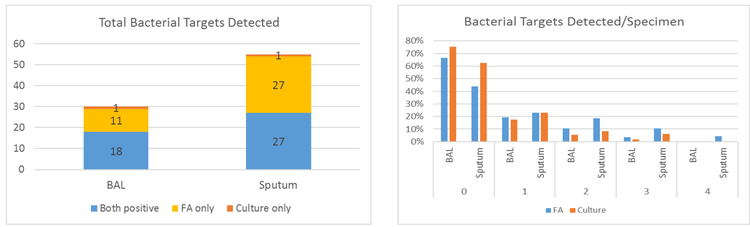


FilmArray® (FA) had a larger number of false positive (i.e. culture negative) results sputum vs. BAL specimens. The majority of false positive results (18/34, 52.9%) were observed in patients who received antibiotic therapy for >12h prior to specimen collection, which may have impacted recovery of these organisms in culture. Another 9/34 (26.5%) of cultures were reported to contain normal oral flora (NOF) which may have obscured the penitential pathogen

Figure 2. Qualitative comparison of FilmArray® LRTI and culture (n=105)



FilmArray® (FA) detected a potential pathogen in 43% more BAL specimens and 60% more Sputum specimens.



FilmArray ® (FA) identified 67% more total bacterial targets in BAL and 100% more targets in Sputum compared to culture. Additionally, FA identified multiple potential pathogens (up to 4) in 14% of BAL and 34% sputum specimens compared with 7% and 16% of routine cultures, respectively.

Table 3. Detection of viral targets by FilmArray® LRTI

	FA Viral Target	SOC order	FA Bacterial Target	Bacterial Culture	Abx[a]
BAL	Adenovirus	None	None	NOF	Van, Azm
BAL	RSV	None	None	Negative	Van, Cfz
BAL	Coronavirus	None	None	Negative	Van, Tzp
BAL	Coronavirus	None	None	NOF	Van,Tzp
BAL	hRV/EV	None	None	Negative	Azm, Tob Mtz
BAL	hRV/EV	CMV, EBV	*M. catarrhalis* (10^4)	NOF	None
BAL	hRV/EV	None	*S. aureus* (10^5)	NOF	Azm, Mem, Van
BAL	hRV/EV	None	*E. coli* (10^4)	NOF	Etp, Van
SPU	hRV/EV	None	*S. agalactiae* (10^5)	NOF	Ctx, Lvx
BAL	hRV/EV	HSV, EBV	*P. aerugonosa* (10^5) *K. oxytoca* (10^4)	*P. aeruginosa* (10^4)	Amx, Tzm, Dap
			A. baumannii (10^4) *P. aeruginosa* (10^5)	*A. baumannii* *P. aeruginosa*	Cfz
SPU	hRV/EV	None	*S. aureus* (10^7)	*S. aureus*	
BAL	hRV/EV	None	*M. catarrhalis* (>10^7)	*M. catarrhalis* (>10^5)	Ctx Van
BAL	hRV/EV	None	None	*P. aeruginosa*	Van

NOF: Normal oral flora; SOC; Standard of care
[a]Patient received antibiotic(s) within 24 h of specimens collection

FilmArray® (FA) detected a viral pathogen in 12.4% (13/105) of specimens. Of these, 69% (9/13) were positive for rhinovirus/enterovirus; eight of which were also positive for a bacterial target. Of the remaining 5 specimens positive for a viral target ,2 were positive for coronavirus, and one each was positive for rhinovirus/enterovirus, adenovirus and RSV. None of these 5 specimens were positive for bacterial pathogens; however, all five patients were receiving multiple antibiotics. Only 2/13 specimens with a virus detected by LRTI had a viral SOC test ordered.