Test Performance of the FilmArray Gastrointestinal Panel (BioFire) From a Clinical Trial Study in Hawaii

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Abstract

Background

A wide variety of microorganisms can contribute to infectious gastroenteritis. These pathogens often exhibit similar clinical presentations, thereby necessitating specific diagnostic testing. These infectious agents contribute to significant morbidity and sometimes exhibit serious sequelae (e.g. HUS). Current laboratory methods for detecting stool pathogens are often labor-intensive, lengthy in turn-around-time and may lack sensitivity. This study reports on the clinical test performance of a multiplexed nested RT-PCR platform, the FilmArray Gastrointestinal (GI) Panel [FA-GI] (BioFire Diagnostics, Inc.) as a clinical trial site.

Materials and Methods

In this clinical study, the FA-GI (detects 23 stool pathogens, FDA-cleared on 5/5/2014*) was used to test 144 residual, delinked stool specimens collected in Cary-Blair media from patients with suspected gastrointestinal disease. Comparator testing consisted of bacterial stool culture, including both routine and selective culture. Discordant results were confirmed using PCR testing and bi-directional sequencing.

Results

Bacterial stool pathogens were detected in only 9.7% (14/144) of the specimens using traditional culture methods compared to an overall pathogen detection rate of 42.4% (61/144) using the FilmArray GI Panel. Negative results were observed in 57.6% (83/144). The clinical sensitivity for most pathogens was 100% (i.e. EPEC at 95.2%). The specificity ranged from 96.7 to 100%. Single infectious agents were detected in 73.8% (45/61). Co-infections were observed [2 at 19.7% (12/61), 3 at 6.6% (4/61)]. EPEC was the most frequently detected bacterial pathogen at 39.3% (24/61) and *Campylobacter* was next at 16.3% (10/61). Traditional detection methods missed 40% (4/10) of the *Campylobacter,* 17% (1/6) of the *Salmonella* and did not detect the *Vibrio cholerae* and *Vibrio parahaemolyticus.* Finally, the cost of traditional methods ($89 to $390) would most likely compare favorably with the FilmArray GII Panel.

Conclusions

The FilmArray GI panel revealed increased test performance (4.4-fold increase), decreased turn-around-time and possible cost savings. Use of this rapid panel would allow for a more optimal choice of appropriate therapy, improved infection control and may even lessen the possibility of complications often seen with some GI pathogens.

*Abstract modified on 5/5/2014. The BioFire Gastrointestinal FilmArray Panel was FDA-cleared for 22 pathogens, excluding *Aeromonas spp.*

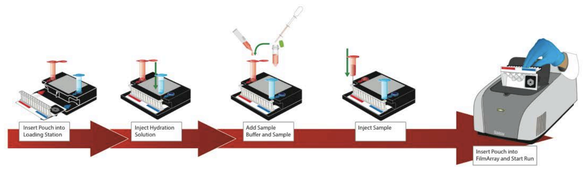
Materials and Methods

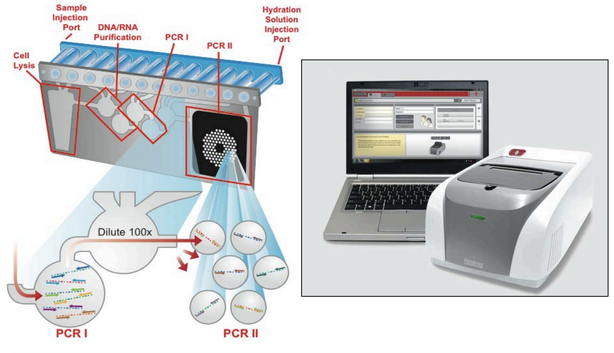
Specimen Collection, Culture, PCR and Antigen Testing

Specimens (n=144) were collected and transported in Cairy-Blair. Traditional culture methods were employed for detecting GI pathogens using routine and selective media. This included the following: SBAP+/- Amp, MAC, MAC Sorb, HE, SS, Campy-SBAP, CIN, GN broth and TCBS. Comparator methods included stool culture (DLS) and PCR with bi-directional sequencing (BFDx Lab).

FilmArray Gastrointestinal (GI) Panel (BioFire)

The FA-GI employs a reagent freeze-dried pouch that stores all of the necessary reagents for sample preparation, reverse transcription, PCR and detection. Separate nucleic acid extraction is not required and hands-on-time is about 5 min for a total amplification and detection time of about 60 minutes. The FA-GI employs a highly sensitive, nested multiplex PCR in an enclosed pouch to avoid any amplicon contamination. Finally, using endpoint melting curve analysis, the FA-GI software automatically generates a result for each target in an individualized patient report. Bi-directional sequencing was considered the gold standard.





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We wish to thank the clinical and molecular staff of the Microbiology Department at Diagnostic Laboratory Services, Inc. (The Queen's Medical Center) for their superior technical support.

Results

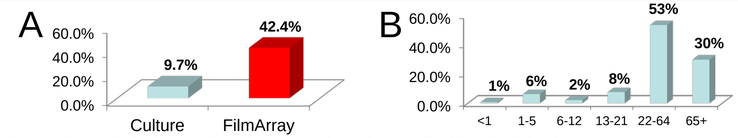

Figure 1 **A**. Detection of GI pathogens with culture vs FA-GI. **B**. Patient age demographics

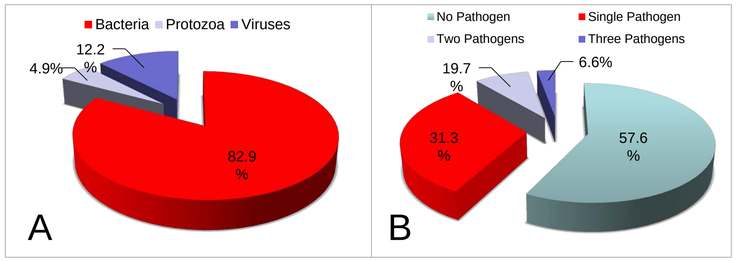

Figure 2 **A**. Categories of GI pathogens detected. **B**. GI pathogens detected as co-infections.

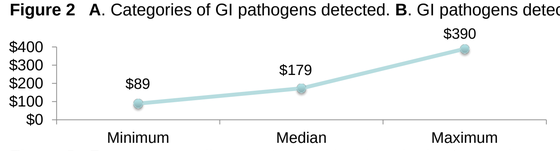

Figure 3. Range and median cost for traditional methods of detection

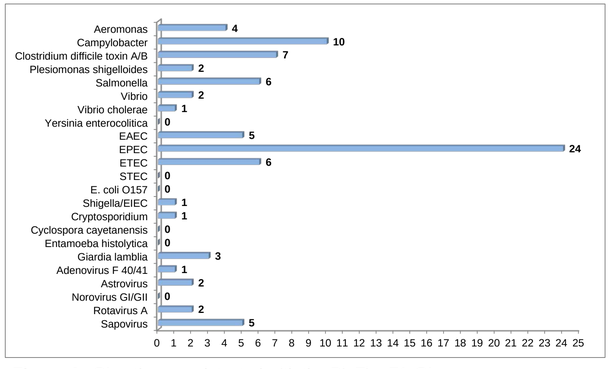

Figure 4. GI pathogens detected with the BioFire FA-GI

Table 1. Detection rate of pathogens by FilmArray vs traditional methods

Pathogen	FilmArray	Culture/EIA	Traditional Method Detection Rate
Campylobacter	10	6	60%
Salmonella	6	5	83%
Giardia lamblia	3	2	66%

Table 2. FA-GI panel results prior to discrepant analysis.

Bacteria	Sensitivity/PPA			Specificity/NPA		
	TP/TP + FN	%	95% CI	TN/TN + FP	%	95% CI
Aeromonas	4/4	100	39.8-100	140/140	100	97.4-100
Campylobacter	6/6	100	54.1-100	134/138	97.1	92.7-99.2
Clostridium difficile	6/6	100	54.1-100	137/138	99.3	96-100
Plesiomonas shigelloides	0/0	-	-	142/144	98.6	95.1-99.8
Salmonella	5/5	100	47.8-100	138/139	99.3	96.1-100
Vibrio	0/0	-	-	142/144	98.6	95.1-99.8
Vibrio cholerae	0/0	-	-	143/144	99.3	96.2-100
Yersinia enterocolitica	0/0	-	-	144/144	100	97.5-100

Diarrheagenic *E. coli/Shigella*	Sensitivity/PPA			Specificity/NPA		
	TP/TP + FN	%	95% CI	TN/TN + FP	%	95% CI
EAEC	5/5	100	47.8-100	139/139	100	97.4-100
EPEC - Algorithm	20/21	95.2	76.2-99.9	119/123	96.7	91.9-99.1
ETEC	4/4	100	39.8-100	138/140	98.6	94.9-99.8
STEC	0/0	-	-	144/144	100	97.5-100
E. coli O157	0/0	-	-	144/144	100	97.5-100
Shigella /EIEC - culture	0/0	-	-	143/144	99.3	96.2-100
Shigella /EIEC - PCR	0/0	-	-	143/144	99.3	96.2-100

Parasites	Sensitivity/PPA			Specificity/NPA		
	TP/TP + FN	%	95% CI	TN/TN + FP	%	95% CI
Cryptosporidium	1/1	100	2.5-100	143/143	100	97.5-100
Cyclospora cayetanensis	0/0	-	-	144/144	100	97.5-100
Entamoeba histolytica	0/0	-	-	144/144	100	97.5-100
Giardia lamblia	3/3	100	29.2-100	141/141	100	97.4-100

Viruses	Sensitivity/PPA			Specificity/NPA		
	TP/TP + FN	%	95% CI	TN/TN + FP	%	95% CI
Adenovirus	1/1	100	2.5-100	143/143	100	97.5-100
Astrovirus	2/2	100	15.8-100	142/142	100	97.4-100
Norovirus	0/0	-	-	144/144	100	97.5-100
Rotavirus	2/2	100	15.8-100	142/142	100	97.4-100
Sapovirus	4/4	100	39.8-100	139/140	99.3	96.1-100

Conclusions

1. The FA-GI (BioFire) has an improved detection rate (4.4 fold) for a variety GI pathogens as compared with conventional methodologies (Figure 1A).
2. The FA-GI (BioFire) can detect multiple pathogens simultaneously with high sensitivity and specificity (Figure 2B, Table 2).
3. The cost of traditional methods, as ordered by the physician, ranges from $89 (stool culture only, including shiga toxin) to $390 (stool culture plus *Vibrio*, *Yersinia*, O&P exam, and *Crypto/Giardia* EIA). These prices do not include the additional cost of detection for GI viruses (approximately $400), which is included in the FA-GI.
4. The detection rate of FA-GI is superior to traditional method (Table 1) with very high sensitivity and specificity (Table 2).
5. The turn-around-time of FA-GI is less than traditional methods (62 minutes for FA-GI versus several days for traditional methods).
6. A drawback of FA-GI is that only one sample can be run per hour, and multiple machines and sequential runs may be needed for high volume laboratories.

Selected References

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