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# Comparison of Cepheid Xpert Flu/RSV XC and BioFire FilmArray for Detection of Influenza A, Influenza B, and Respiratory Syncytial Virus

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**The Xpert Flu/RSV XC was compared to the FilmArray respiratory panel for detection of influenza (Flu) A, Flu B, and respiratory syncytial virus (RSV), using 128 nasopharyngeal swabs. Positive agreements were 100% for Flu A and RSV and 92.3% for Flu B. The Xpert may be useful in clinical situations when extensive testing is not required and may serve an important role in laboratories already performing broader respiratory panel testing.**

Respiratory viral infections are among the most common acute infections in patients presenting to the emergency department (1). Optimization of care for such patients involves accurate and rapid diagnostics (2). Rapid detection can optimize management by limiting administration of unnecessary antimicrobials and ancillary diagnostic tests (3, 4), while enhancing decision making on infection control practices and the allocation of health care services (5). For example, the average duration of empirical oseltamivir was reduced by 50% when using rapid influenza testing, compared to our previous method that had a longer turnaround time for results (6). Moreover, prompt initiation of antiviral therapy may shorten the duration and severity of illness, contributing to decreased transmission of disease, fewer missed work and school days, and fewer bacterial coinfections (3, 7).

Although they provide results rapidly, antigen assays can exhibit low sensitivity (8, 9). Rapid molecular assays have thus become the mainstay of testing for respiratory viruses in many clinical laboratories. Many provide results within 1 to 2 h. One such assay is the BioFire FilmArray respiratory panel (FilmArray) (BioFire Diagnostics, Salt Lake City, UT), a multiplex nucleic acid amplification test for the qualitative detection and differentiation of 20 respiratory pathogens from nasopharyngeal (NP) swabs within ~1 h. Assay targets include influenza A (including subtypes H1, H3, and H1-2009), influenza B, and respiratory syncytial virus (RSV), among other viruses and bacteria (10).

In late 2014, Cepheid received clearance from the Food and Drug Administration for the Xpert Flu/RSV XC (Xpert) (Cepheid, Sunnyvale, CA), a molecular test for the detection and differentiation of influenza A, influenza B, and RSV. Unlike the FilmArray, the Xpert cannot discriminate among influenza A strains. The assay is performed on Cepheid's GeneXpert system, an automated platform that performs extraction, amplification, and detection within 63 min using a single disposable cartridge. Acceptable specimens include NP swabs and nasal aspirates/washes.

We sought to compare the performance of the Cepheid Xpert Flu/RSV XC with the BioFire FilmArray respiratory panel and to determine its potential utility in our laboratory, where we were routinely using the FilmArray for influenza and RSV testing. We performed a verification study using a convenience sample of 128 archived NP swab specimens in viral transport medium collected from patients at The University of Chicago Medicine and previously tested for clinical purposes using the FilmArray. Patient ages ranged from 17 months to 93 years, with a median age of 35 years; 29.7% of tested specimens were from children. Eighty-four of these specimens were stored at −80°C, and the remaining 44 specimens were stored at 4°C for a maximum of 3 days before being tested on the Xpert. Specimens were brought to room temperature, vortexed, and tested. Testing and interpretation of results were done according to the assays' package inserts. The specimens initially tested as follows: 37 positive for influenza A (including 12 samples of subtype H1 2009 and 25 samples of subtype H3), 36 positive for influenza B, 37 positive for RSV, and 20 negative for influenza A, influenza B, and RSV (8 of these were positive for other targets on the FilmArray). One specimen was positive for influenza A and RSV, and another was positive for influenza B and RSV.

Results were reported as detected or not detected. Each of the 128 specimens provided 3 results (influenza A, influenza B, and RSV), for a total of 384 test results. Of these, 381 (99.2%) were in initial agreement, with a Cohen's kappa coefficient ($\kappa$) of 0.98. All 3 initially discordant results involved the influenza B target (Table 1). There was therefore a 100% positive agreement for influenza A and RSV ($\kappa = 1$) and 92.3% for influenza B ($\kappa = 0.94$; 95% confidence interval, 0.88 to 1.01). The presence of other viruses did not interfere with the assay.

To our knowledge, this is the only study comparing the Xpert Flu/RSV XC with the BioFire FilmArray respiratory panel. In one recent study (11), the Xpert Flu/RSV XC assay was compared to laboratory-developed tests and the older Xpert Flu assay, and the researchers reported that the sensitivity of influenza detection was improved compared to that with the Xpert Flu assay. Another study compared the Xpert Flu/RSV XC assay with singleplex PCR tests routinely used in their laboratory and reported sensitivities/specificities of 97.8%/100% and 97.9%/100% for influenza and RSV, respectively (12).

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**TABLE 1** Concordance of the Xpert Flu A/Flu B/RSV with the BioFire FilmArray

| Result with Cepheid Xpert Flu/RSV XC | Result with BioFire FilmArray | | | | | |
|---|---|---|---|---|---|---|
| | Flu A | | Flu B | | RSV | |
| | Positive | Negative | Positive | Negative | Positive | Negative |
| Positive | 37 | 0 | 36 | 0 | 37 | 0 |
| Negative | 0 | 91 | 3 | 92 | 0 | 91 |

In this study, the Xpert Flu/RSV XC showed nearly perfect agreement (99.2%) with the BioFire FilmArray respiratory panel. We consider this assay acceptable for patient testing. However, how would this assay be of use in clinical laboratories already performing the FilmArray or another multiplex PCR for respiratory viruses?

In our hospital, the Xpert would have been a welcome addition during the last influenza season (2014-2015), when the prevalence of the primary circulating influenza strain was known and a high volume of testing had to be performed, taxing our use of the FilmArray. Specifically, we would have used the Xpert in two situations: first, for the immunocompetent outpatients with a suspected viral respiratory illness during the peak of the season, including those who required prompt management in the emergency department; and second, for the employees with mild respiratory symptoms who had to be sent home if positive for influenza.

A possible limitation of this study is the use of archived specimens that were previously tested fresh using the FilmArray platform. Moreover, the comparison of platforms was not performed in parallel. Although it is possible that these issues affected assay performance, this did not appear to significantly affect the results, as the assays showed near-perfect correlation.

In summary, the multiplexing of molecular assays has generated many options for respiratory virus testing. The laboratory can determine how to allocate and balance the use of these assays to optimize patient care and overall processes within the hospital and laboratory. Targeted testing for influenza and RSV might be most appropriate in certain clinical situations and during the peak of the influenza season, whereas more extensive panel testing might be better suited for sicker patients and/or during a time of decreased influenza prevalence.

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