

qualitatively detect IgG antibodies against SARS-CoV-2 antigens. The Abbott assay detects IgG against the viral nucleocapsid (N) protein, while the DiaSorin assay uses antigen derived from the viral spike (S) protein. Here we evaluate the performance of these two assays at our institution.

**Methods:** 45 patient samples (serum or plasma) were tested for anti-SARS-CoV-2 IgG by both the Abbott and DiaSorin assays. The samples were previously characterized at a national reference laboratory using the Abbott assay or by an in-house PCR-based test for SARS-CoV-2 RNA. Samples yielding discordant results across platforms were further tested using the EUROIMMUN Anti-SARS-CoV-2 ELISA (IgG) assay at the reference laboratory.

**Results:** 22 samples tested negative for SARS-CoV-2 by the reference lab Abbott assay, and 23 tested positive by the same reference lab test (n = 13) or by an in-house PCR-based test (n = 10). The 22 samples characterized as negative again tested negative by both the Abbott (in-house) and DiaSorin assays (100% NPA). Among the 23 samples characterized as positive, all 23 tested positive by the Abbott assay (100% PPA), while only 15 tested positive by the DiaSorin assay (65% PPA). For each of the 8 discordant cases, samples were further tested by EUROIMMUN assay, which targets the S protein; 7 of the 8 samples tested negative by this assay, in agreement with the DiaSorin test results. Thus, for the discordant cases, testing for IgG against N (in-house and reference lab Abbott assays) gave positive results, while testing for IgG against S (DiaSorin and EUROIMMUN assays) mostly gave negative results.

**Conclusion:** These findings highlight the importance of the differences between various SARS-CoV-2 antibody tests, and providers should be aware of the specific antigenic target(s) in each test. Selection of a specific assay may depend on the need to assess past exposure to SARS-CoV-2 (for which a nucleocapsid target may be more sensitive) or to detect neutralizing antibodies (for which a spike target may be more relevant). This also has implications for disease surveillance as reliance on anti-spike antibodies alone may underestimate infection prevalence.

**Disclosures:** All Authors: No reported disclosures

#### 419. Diagnostic Utility of a Ferritin to Procalcitonin Ratio to Differentiate Patients with COVID-19 from Those with Bacterial Pneumonia

Katherine C. Jankowsky, MD<sup>1</sup>; Peter Hyson, MD<sup>1</sup>; Jin Huang, BS<sup>1</sup>; Daniel B. Chastain, PharmD<sup>2</sup>; Carlos Franco-Paredes, MD, MPH<sup>1</sup>; Kristine M. Erlanson, MD MS<sup>1</sup>; Andres Henao-Martinez, MD<sup>1</sup>; Leland Shapiro, MD<sup>1</sup>; <sup>1</sup>University of Colorado Denver, School of Medicine, Aurora, Colorado; <sup>2</sup>UGA, Albany, Georgia

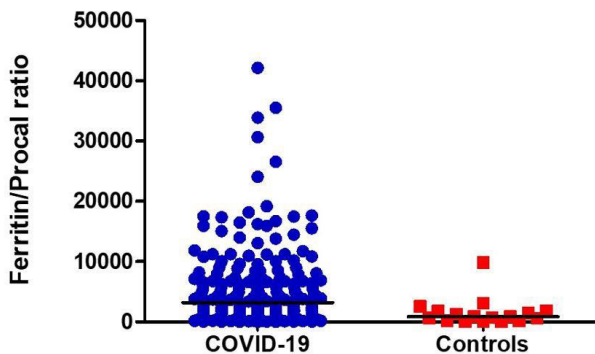
**Session:** P-13. COVID-19 Diagnostics

**Background:** Accurate, rapid, inexpensive biomarkers are needed to differentiate COVID-19 from bacterial pneumonia, allowing effective treatment and antibiotic stewardship. We hypothesized that the ratio of ferritin to procalcitonin (F/P) reflects greater viral activity and host response with COVID-19 pneumonia, while bacterial pneumonia would be associated with less cytotoxicity (lower ferritin) and more inflammation (higher procalcitonin), thus a lower F/P ratio.

**Methods:** We conducted a retrospective study of adult patients admitted to a single University hospital in the US through May 2020, during the COVID-19 pandemic. We compared F/P ratio of patients diagnosed with COVID-19 or bacterial pneumonia, excluding patients with COVID-19 and bacterial co-infections. In a logistic regression, we controlled for age, sex, body mass index (BMI), diabetes (DM), and hypertension (HTN). We used a receiver operating characteristic analysis to calculate the sensitivity and specificity of F/P values for the diagnosis of COVID-19 versus bacterial pneumonia.

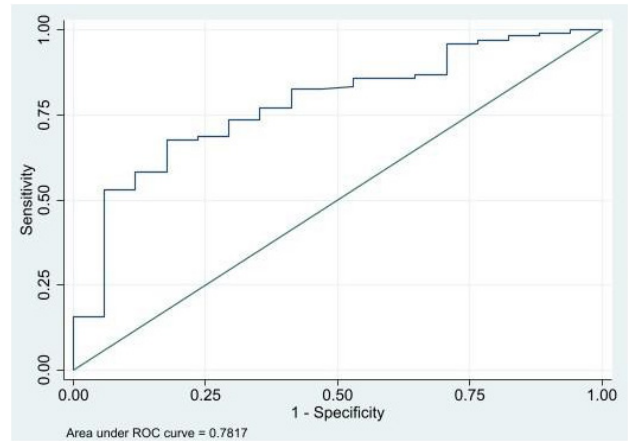
**Results:** Of 218 patients with COVID-19 and 17 with bacterial pneumonia, COVID-19 patients were younger (56 vs 66 years, p=0.04), male (66% vs 24%, p=0.009), had higher BMI (31 vs 27 kg/m<sup>2</sup>, p=0.03), and similar rates of HTN (59% vs 45%, p=0.3) and DM (32% vs 18%, p=0.2). The median F/P ratio was significantly higher in patients with COVID-19 (3195 vs 860, p=0.0003, Figure 1). An F/P ratio cut-off of  $\geq 1250$  generated a sensitivity of 78% and a specificity of 59% to correctly classify a COVID-19 case (Figure 2). When adjusted for age, gender, BMI, DM, and HTN, a ratio  $\geq 1250$  was associated with significantly greater odds of COVID-19 versus bacterial pneumonia (OR: 4.9, CI: 1.5, 16.1, p=0.009).

Figure 1. Ferritin to Procalcitonin Ratios of patients with COVID-19 and patients with Bacterial Pneumonia (controls).



Black line represents medians. P=0.0003

Figure 2. Receiver Operating Characteristic Analysis of Ferritin to Procalcitonin Ratio Cut-off Values Predicting COVID-19 Diagnosis.



**Conclusion:** We observed an elevated F/P ratio in patients with COVID-19 compared to those with bacterial pneumonia. A F/P ratio  $\geq 1250$  provides a clinically relevant increase in pre-test probability of COVID-19. Prospective studies evaluating the discriminatory characteristics of F/P ratio in larger cohorts is warranted.

**Disclosures:** All Authors: No reported disclosures

#### 420. Diagnostic Utility of Chest CT scan for COVID-19, in the Early Stage of the Pandemic in Brooklyn, New York

Rachel Gibbs, MD Candidate<sup>1</sup>; Lung H. Fu, n/a<sup>2</sup>; Michael Silver, MS<sup>2</sup>; Zachary S. Lockerman, MD MBA<sup>2</sup>; Monica Ghitan, MD<sup>2</sup>; Edward Chapnick, MD<sup>2</sup>; Yu Shia Lin, MD<sup>2</sup>; <sup>1</sup>Ben Gurion University of the Negev, Wellesley, Massachusetts; <sup>2</sup>Maimonides Medical Center, Brooklyn, New York

**Session:** P-13. COVID-19 Diagnostics

**Background:** Diagnosis of coronavirus disease 2019 (COVID-19) in the early weeks of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pandemic in New York City posed unique challenges. Due to inadequate testing availability and long turnaround times, decisions on which patients to isolate were problematic. With sensitivity comparable to reverse transcription polymerase chain reaction (RT-PCR), the absence of ground glass opacities (GGOs) on chest CT scan was useful to rule out COVID-19. We evaluated the specificity of chest CT scan findings for COVID-19 along with other clinical and laboratory findings.

**Methods:** A retrospective chart review was done of 182 adult patients who were tested for SARS-CoV-2 by RT-PCR and underwent a chest CT scan while admitted to Maimonides Medical Center between March 1 to 23, 2020. Cases were defined as those with a positive RT-PCR result or who were treated for COVID-19. Negative cases were defined as those with negative RT-PCR and an alternative diagnosis confirmed by an ID physician. Beyond March 23, almost all newly admitted patients were isolated.

**Results:** There were 111 COVID-19 positive and 71 COVID-19 negative patients. Of the COVID-19 patients, 61% were male and 39% female, 56% white, 20% Hispanic, 14% black, 9% Asian, 36% Jewish, 35% had diabetes mellitus (DM), 50% had hypertension and 42% had cardiovascular disease. Clinical symptoms, signs, and laboratory values for COVID-19 positive and negative groups were not significantly different. COVID-19 patients had significantly higher BMI (p = 0.001). On chest CT scan, bilateral or unilateral, peripheral distribution and lower lobar GGOs were over 80% specific for COVID-19. The frequency of GGOs was significantly higher when chest CT scans were done during the second week of illness compared to the first week (p = 0.0195). Jewish patients were associated with higher rates of death (p = 0.0475) and underlying DM was associated with higher rates of ARDS, AKI, intubation, ICU admission and death (p < 0.05) compared to other demographic and comorbid groups.

**Conclusion:** Chest CT scan is an important component in the diagnostic process for patients with suspected COVID-19 infection, especially during the second week of symptoms. The findings may aid clinical decisions in the setting of a second surge of SARS-CoV-2.

**Disclosures:** All Authors: No reported disclosures

#### 421. If at first you do not succeed.... Repeat SARS-COV2 PCR testing

Stephanie M. Shea, MD<sup>1</sup>; Gopi Patel, MD<sup>1</sup>; Sarah Schaefer, MD<sup>2</sup>; Michael D. Nowak, MD<sup>3</sup>; Emilia Mia. Sordillo, MD, PhD<sup>1</sup>; Alberto Paniz-Mondolfi, MD, PhD<sup>1</sup>; Melissa R. Gitman, MD<sup>1</sup>; <sup>1</sup>Icahn School of Medicine at Mount Sinai, New York, New York; <sup>2</sup>Icahn School of Medicine at Mount Sinai Hospital, New York, New York; <sup>3</sup>The Mount Sinai Hospital, New York, NY

**Session:** P-13. COVID-19 Diagnostics

**Background:** Nucleic Acid Amplification Tests (NAATs) of nasopharyngeal specimens (NPS) have become standard for diagnosis of SARS-COV2. IDSA guidelines suggest repeat testing after 24-48 h when initially negative and clinical suspicion persists. We characterized patients from whom initial NPS were NAAT-negative, but

repeats were NAAT-positive, in order to identify which patients might benefit from repeat NAAT for SARS-CoV-2, and the appropriate interval.

**Methods:** We conducted an IRB-approved retrospective review of laboratory and electronic medical record data for all patients evaluated for SARS-CoV-2 infection at the Mount Sinai Health System, whose initial NAATs were done between March 16 – March 30, 2020, and who were retested within one month. NAATs were performed on NPS in viral transport medium using the Roche Diagnostics cobas® 6800 SARS-CoV-2 Test. Baseline patient characteristics, clinical and radiographic findings were identified.

**Results:** Of 235 patients eligible for inclusion, 172 (70.5%) were initially NAAT-negative, and 118 (68.6%) remained NAAT-negative over 1 month follow up. 54 (31.4%) converted to NAAT-positive over the next 1-month. Of patients who became NAAT-positive, 31 (57.4%) were inpatients who converted results within a single admission; the average interval was 6d 7h between the NAAT-negative and NAAT-positive results, and the minimum interval was 10.5 h. Symptoms examined for correlation for conversion to NAAT-positive were: fever, cough, shortness of breath, and combined nausea/vomiting/diarrhea. Duration of symptoms reported at triage did not appear to affect time to conversion to NAAT-positive. No individual symptom was more likely to be associated with conversion to NAAT-positive. However, time to conversion to NAAT-positive was shorter for patients with multiple symptoms. In general, chest radiography (CXR) findings correlated with NAAT results; interval to NAAT-positive was shorter for patients with worsening CXR findings.

**Conclusion:** Our data supports repeat testing in patients with multiple clinical symptoms suggestive of SARS CoV-2 infection and negative initial NP test results. Further studies are needed to determine the true clinical sensitivity and specificity of SARS-CoV-2 NAAT assays.

**Disclosures:** All Authors: No reported disclosures

#### 422. Performance Evaluation of a Rapid and Easy-to-Use COVID-19 Test

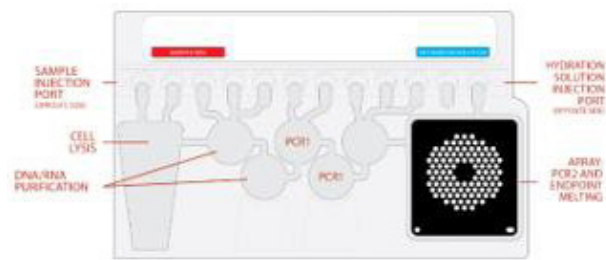
Corike Toxopeus, PhD<sup>1</sup>; Brian Jones, PhD<sup>1</sup>; Jessica Brown, BS<sup>2</sup>; Mark Gurling, PhD<sup>1</sup>; Cynthia Andjelic, PhD<sup>1</sup>; Cynthia L. Phillips, PhD<sup>3</sup>; <sup>1</sup>BioFire Defense, LLC, Salt Lake City UT USA, Utah; <sup>2</sup>Biofire Defense, Salt Lake City, Utah; <sup>3</sup>BioFire Defense, Salt Lake City, Utah

**Session:** P-13. COVID-19 Diagnostics

**Background:** The BioFire® COVID-19 Test is a qualitative test for use on the FilmArray® 2.0 and Torch systems for the detection of SARS-CoV-2 RNA in nasopharyngeal swabs (NPS) in transport media. This test received Emergency Use Authorization from the FDA.

A closed, disposable pouch contains all the necessary reagents for sample preparation, nucleic acid extraction, reverse transcription, polymerase chain reaction (PCR), and amplified nucleic acid detection to identify RNA from SARS-CoV-2 virus in an NPS specimen. Internal controls monitor all stages of the test process. Once an NPS sample (0.3 mL) is loaded into the system disposable pouch (Figure 1), the fully automated test returns results within an hour. As an additional resource, the BioFire COVID-19 Test External Control Kit (+) includes positive external control material that may be used for quality control and laboratory verification.

Figure 1. BioFire COVID-19 Test Disposable Pouch



**Methods:** The following were evaluated:

- Limit of Detection (LoD)
- Positive and Negative Percent Agreement (PPA and NPA, respectively) for clinical contrived samples and a limited number of clinical specimens
- Exclusivity

**Results:** • LoD

The LoD was evaluated using live SARS-CoV-2 virus (cultured from the USA\_WA1/2020 strain obtained from World Reference Center for Emerging Viruses and Arboviruses (WRCEVA)). The LoD was determined to be 3.3E+02 GC/mL (2.2E-02 TCID<sub>50</sub>/mL).

- Clinical Contrived

Accurate detection of virus in clinical matrix was demonstrated at various LoD levels using thirty contrived individual unique clinical samples (PPA), and 66 individual unique negative clinical specimens (NPA).

- Clinical Samples

Positive samples were collected from patients presenting with signs or symptoms of COVID-19, and who were previously identified as positive for SARS-CoV-2 by another EUA test. Negative samples were collected in 2018, and therefore presumed negative for SARS-CoV-2.

- Exclusivity

The potential for cross-reactivity was evaluated for six viruses from the same genetic family as SARS-CoV-2, and for an additional 30 high priority organisms/viruses. No cross-reactivity was observed.

Table 1. SARS-CoV-2 Virus Test Results at 1x and 0.1x LoD for the BioFire COVID-19 Test

xLoD	Concentration Tested		Test Result (% Detection)		
	GC/mL	TCID <sub>50</sub> /mL	Detected	Equivocal	Not Detected
1x	3.3E+02	2.2E-02	20/20 (100%)	0/20 (0%)	0/20 (0%)
0.1x	3.3E+01	2.2E-03	14/20 (70%)	5/20 (25%)	1/20 (5%)

Table 2. Clinical Contrived and Negative Testing with the BioFire COVID-19 Test

	Agreement with Known Analyte Composition			
	PPA	%	NPA	%
<b>Overall Agreement</b>	30/30	100%	66/66	100%
<b>95% CI</b>	[88.6 – 100]		[94.5-100]	

Table 3. BioFire COVID-19 Test Performance Summary

Virus	PPA			NPA		
	TP/(TP + FN)	%	95% CI	TN/(TN + FP)	%	95% CI
SARS-CoV-2	9/10*	90%	59.6-98.2%	5/5	100%	56.6-100.0%

\*One sample had a late Ct value when originally evaluated on the NECOV19 test. When the sample was retested on the NECOV19 test, the result was negative. These results indicate a near-LoD level of SARS-CoV-2 virus and/or sample degradation.

**Conclusion:** The BioFire COVID-19 Test reliably detects SARS-CoV-2 virus RNA in clinically relevant samples.

**Disclosures:** Corike Toxopeus, PhD, BioFire Defense, LLC. (Employee, stock owner) Brian Jones, PhD, BioFire Defense, LLC (Employee, own stock) Jessica Brown, BS, BioFire Defense (Employee, Stock owner) Mark Gurling, PhD, BioFire Defense, LLC (Employee) Cynthia Andjelic, PhD, BioFire Defense (Employee, Other Financial or Material Support, Own stocks) Cynthia L. Phillips, PhD, BioFire Defense (Employee, Scientific Research Study Investigator, Shareholder) BioFire Defense (Employee, Scientific Research Study Investigator, Shareholder)

#### 423. SARS-CoV-2 NGS Assay Powered by Biotia COVID-DX Software

Dorothy Nagy-Szakal, MD PhD<sup>1</sup>; Mara Couto-Rodriguez, MS<sup>1</sup>; Joseph Barrows, MS<sup>2</sup>; Heather L. Wells, MPH<sup>3</sup>; Marilynne Debieu, PhD<sup>1</sup>; Courtney Hager, BS<sup>1</sup>; Kristin Butcher, MS<sup>2</sup>; Siyuan Chen, PhD<sup>2</sup>; Robert Boorstein, MD PhD<sup>3</sup>; Christopher Mason, PhD<sup>1</sup>; Niamh B. O'Hara, PhD<sup>1</sup>; <sup>1</sup>Biotia, Brooklyn, New York; <sup>2</sup>Twist Bioscience, South San Francisco, California; <sup>3</sup>Lenco Diagnostic Laboratories, Brooklyn, New York

**Session:** P-13. COVID-19 Diagnostics

**Background:** COVID-19 had spread quickly, causing an international public health emergency with an alarming global shortage of COVID-19 diagnostic tests. We developed and clinically validated a next-generation sequencing (NGS)-based target enrichment assay with the COVID-DX Software tailored for the detection, characterization, and surveillance of the SARS-CoV-2 viral genome.

**Methods:** The SARS-CoV-2 NGS assay consists of components including library preparation, target enrichment, sequencing, and a COVID-DX Software analysis tool. The NGS library preparation starts with extracted RNA from nasopharyngeal (NP) swabs followed by cDNA synthesis and conversion to Illumina TruSeq-compatible libraries using the Twist Library Preparation Kit via Enzymatic Fragmentation and Unique Dual Indices (UDI). The library is then enriched for SARS-CoV-2 sequences using a panel of dsDNA biotin-labeled probes, specifically designed to target the SARS-CoV-2 genome, then sequenced on an Illumina NextSeq 550 platform. The COVID-DX Software analyzes sequence results and provides a clinically oriented report, including the presence/absence of SARS-CoV-2 for diagnostic use. An additional research use only report describes the assay performance, estimated viral titer, coverage across the viral genome, genetic variants, and phylogenetic analysis.

**Results:** The SARS-CoV-2 NGS Assay was validated on 30 positive and 30 negative clinical samples. To measure the sensitivity and specificity of the assay, the positive and negative percent agreement (PPA, NPA) was defined in comparison to an orthogonal EUA RT-PCR assay [PPA [95% CI]: 96.77% [90.56%-100%] and NPA [95% CI]: 100% [100%-100%]]. Data reported using our assay defined the limit of detection to be 40 copies/ml using heat-inactivated SARS-CoV-2 viral genome in clinical matrices. In-silico analysis provided >99.9% coverage across the SARS-CoV-2 viral genome and no cross-reactivity with evolutionarily similar respiratory pathogens.

**Conclusion:** The SARS-CoV-2 NGS Assay powered by the COVID-DX Software can be used to detect the SARS-CoV-2 virus and provide additional insight into viral titer and genetic variants to track transmission, stratify risk, predict outcome and therapeutic response, and control the spread of infectious disease.

**Disclosures:** Dorothy Nagy-Szakal, MD PhD, Biotia (Employee) Mara Couto-Rodriguez, MS, Biotia (Employee) Joseph Barrows, MS, Biotia, Inc. (Employee, Shareholder) Heather L. Wells, MPH, Biotia (Consultant) Marilynne Debieu, PhD, Biotia (Employee) Courtney Hager, BS, Biotia (Employee) Kristin Butcher, MS, Twist Bioscience (Employee) Siyuan Chen, PhD, Twist Bioscience (Employee) Christopher Mason, PhD, Biotia (Board Member, Employee, Shareholder) Niamh B. O'Hara, PhD, Biotia (Board Member, Employee, Shareholder) Twist (Other Financial or Material Support, I am CEO of Biotia and Biotia has business partnership with Twist)