

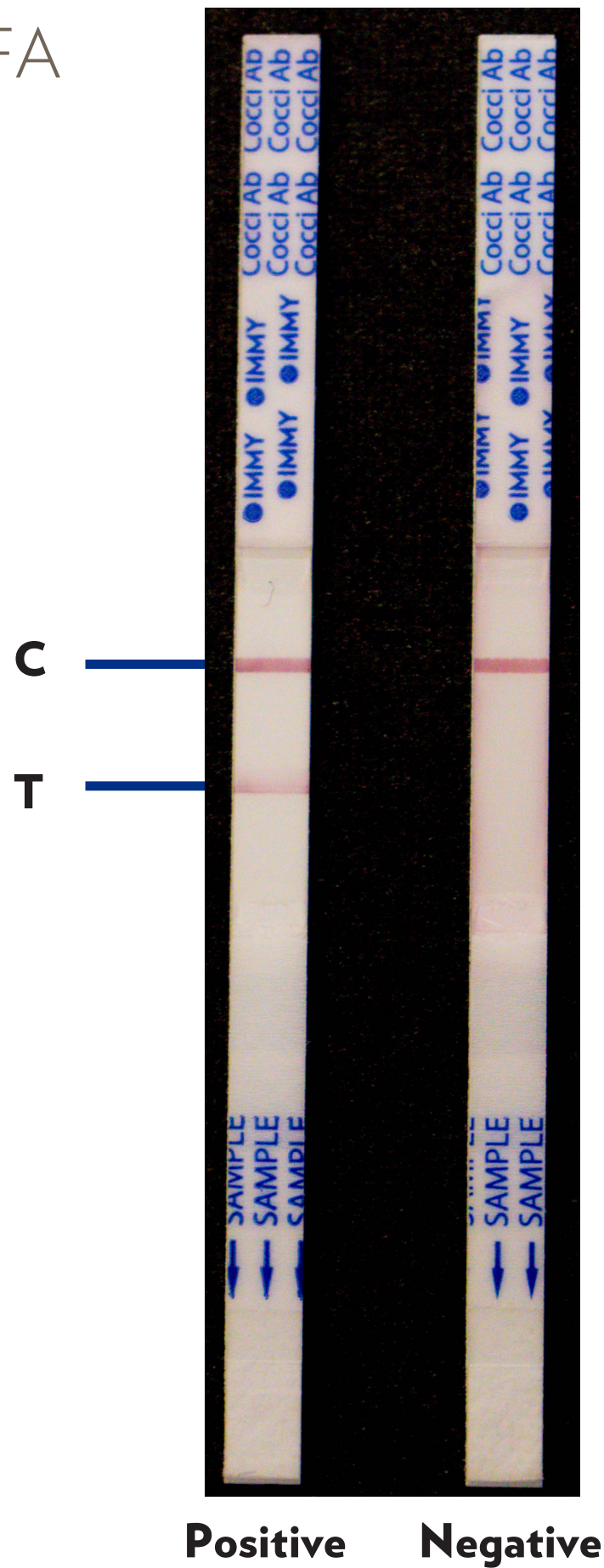
RAPID DETECTION OF ANTI-COCCIDIOIDES ANTIBODIES USING THE sōna™ COCCIDIOIDES Ab LATERAL FLOW ASSAY

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ABSTRACT

Coccidioides, the causative agent of San Joaquin Valley Fever, is a fungal agent endemic to the arid regions of the Americas. Due to the difficulties associated with fungal culture, the dominant method of diagnosis is serology. Typical serological diagnosis methods require from 48 to 72 hours using technologies like immunodiffusion or complement fixation. IMMY has developed a new 20 minute lateral flow assay for the detection of antibodies against *Coccidioides* sp. and it was compared to these typical serological methods. Specimens were considered reactive for antibodies against *Coccidioides* if positive in two out of three different traditional assays: immunodiffusion, complement fixation and ELISA. A two by two diagnostic table and an ROC curve was developed comparing the assays. The area under the ROC curve was 0.885 (95% confidence interval (CI) = 0.801, 0.942, standard error 0.0377, p<0.001) for the sōna™ *Coccidioides* Ab assay. The assay had 100% sensitivity (95% CI: 91.1 - 100) and 76.92% specificity (95% CI: 63.2 - 87.5) when compared to the reference method. In this study, the positive predictive value was 76.92% and the negative predictive value was 100%.

Figure 1: The CTA2003 LFA strips for the detection of antibodies against *Coccidioides* species.



INTRODUCTION

Coccidioides, the causative agent of San Joaquin Valley Fever, is a fungal agent endemic to the arid regions of the Americas. Due to the difficulties associated with fungal culture, the dominant method of diagnosis is serology. Coccidioidomycosis serology can be a laborious, time consuming and expensive process. It is for this reason that many hospitals rely on send out diagnostic testing from reference laboratories. IMMY has developed a lateral flow assay designed to quickly rule out negative cases, near the point of care. Reduced turnaround time, cost-savings and enhanced anti-microbial stewardship are benefits of the assay, in addition to those provided by more rapid patient management. The IMMY sōna™ *Coccidioides* Ab lateral flow could be an effective tool for ruling out potential *Coccidioides* infections.

METHODS

Ninety-two human serum samples (52 positive, 42 negative) were characterized by the University of California, Davis Coccidioidomycosis Serology Laboratory and IMMY. Specimens were considered positive if reactive in two of any of the regularly performed assays: complement fixation, immunodiffusion or quantitative immunodiffusion (performed at UC-Davis) and Premier® *Coccidioides* EIA manufactured by Meridian Bioscience (performed at IMMY). These specimens were kindly provided to IMMY for the evaluation of sōna™ *Coccidioides* Ab lateral flow assay (CTA2003). Briefly, specimens were diluted to 1:441 in specimen diluent and tested on the sōna™ *Coccidioides* Ab. After 20 minutes, results were interpreted by two operators. A ROC analysis was performed to determine assay sensitivity and specificity.

PROCEDURE

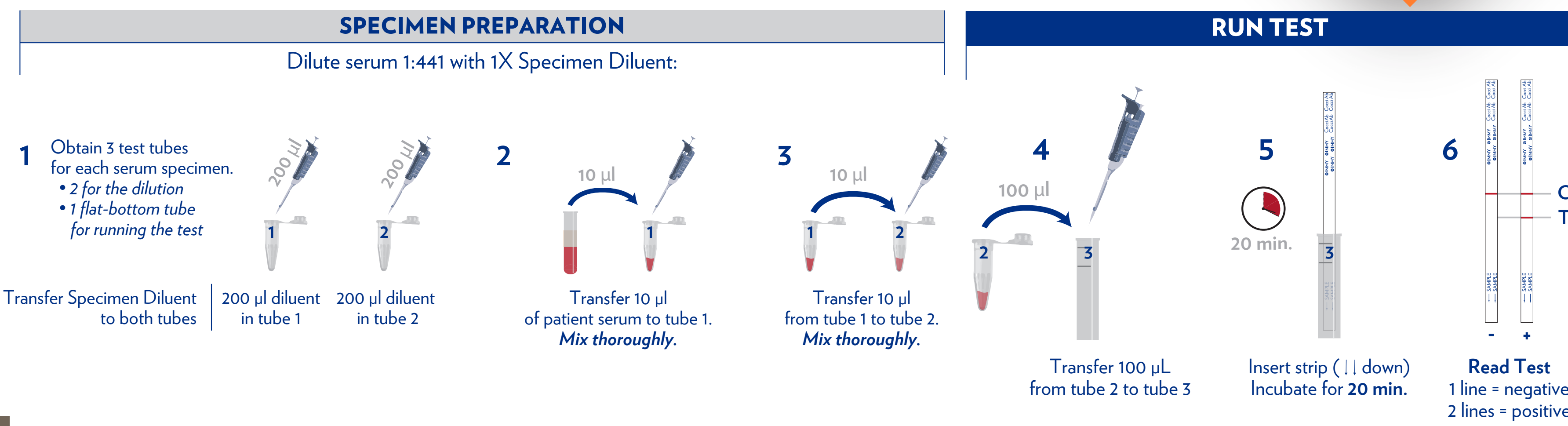


Figure 2: The CTA2003 LFA Procedure

RESULTS

The area under the ROC curve was 0.885 (95% confidence interval (CI) = 0.801,0.942, standard error 0.0377, p<0.001) for the sōna™ *Coccidioides* Ab assay. The assay had 100% sensitivity (95% CI: 91.1 - 100) and 76.92% specificity (95% CI: 63.2 - 87.5) when compared to the EORTC criteria. The positive predictive value was 76.9% and the negative predictive value was 100% (Figure 3).

	IgM+	IgG+	Total+
ID	20	26	40
EIA	23	37	40
CF*	-	-	19/40

* CF does not distinguish IgG/IgM

Table 1: Specimen Characterization Table

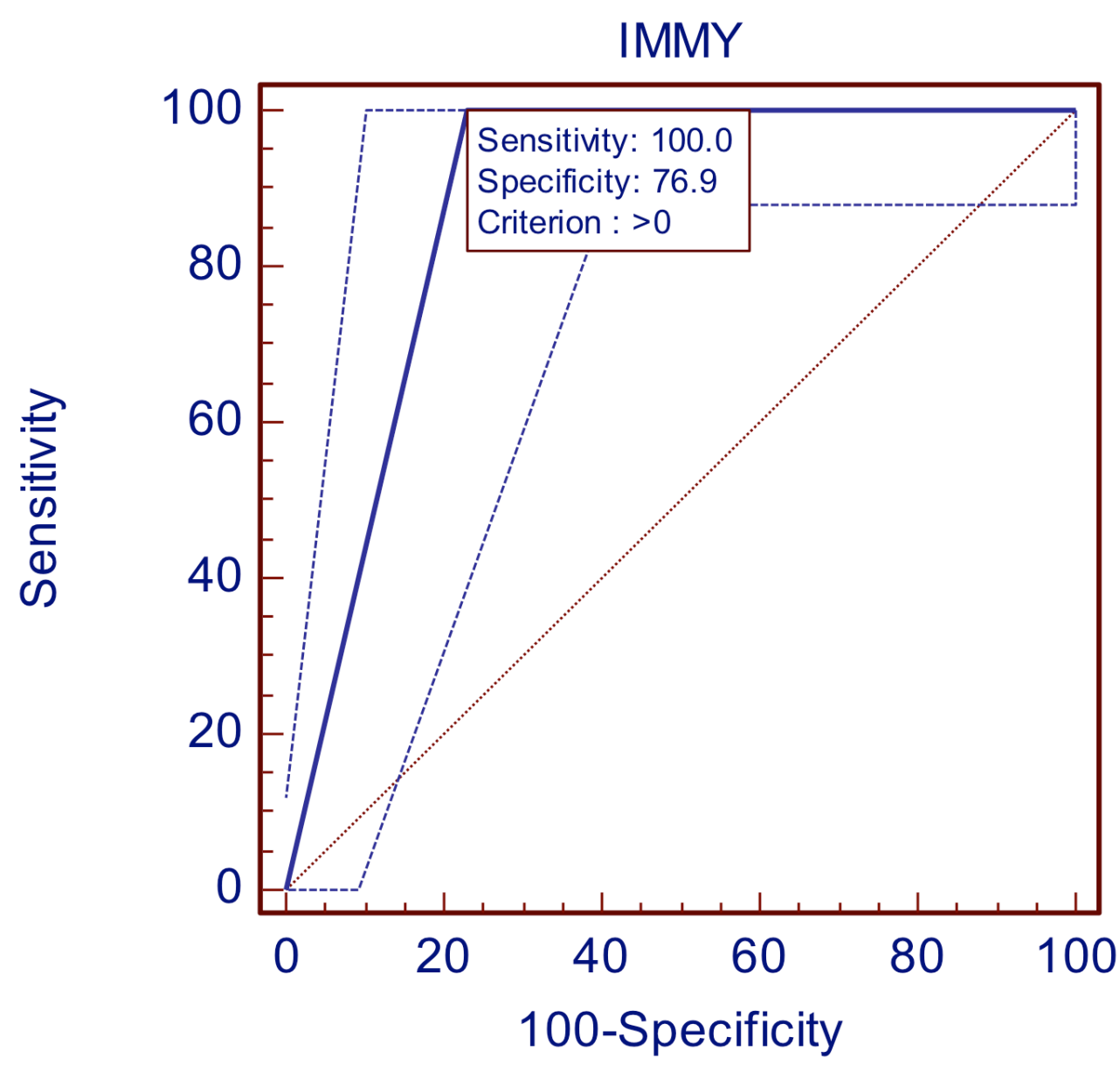


Figure 3: ROC analysis of the CTA2003 kit vs characterized specimens

EORTC

	Probable	Negative	Totals
IMMY Positive:	40	12	52
IMMY Negative:	0	40	40
Totals	40	52	

		95% CI
Sensitivity	100.00%	91.11 % to 100.00%
Specificity	76.92%	63.16% to 87.46%
Positive Likelihood Ratio	4.33	2.64 to 7.12
Negative Likelihood Ratio	0.00	
Disease Prevalence	43.48%	33.17% to 54.22%
Positive Predictive Value	76.92%	63.16% to 87.46%
Negative Predictive Value	100%	91.11 % to 100.00%
ROC Area Under Curve	0.885	0.801 to 0.942
Standard Error (p<0.001)	0.0377	

Table 2: 2x2 Contingency Table and Statistical Analysis

CONCLUSIONS

The sōna™ *Coccidioides* Ab test is a rapid immunoassay that detects anti-*Coccidioides* antibodies. The high negative predictive value of the assay allows for a 20 minute screen to rule out patients suspected of having Valley Fever. Management of this population of patients can be significantly improved by ruling out Valley Fever, allowing physicians to better direct treatment. Patients positive on the sōna™ *Coccidioides* Ab test can then be referred to more traditional serology techniques to confirm the presence of antibodies to *Coccidioides*.

REFERENCES

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