Human vs Machine: A Systematic Review of Automated Bead-Based Multiplex Immunoassay Performance

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Introduction

- Autoimmune diseases are important contributors to morbidity and mortality in the United States. Researchers have identified more than 20 subtypes of antinuclear antibodies (ANAs), which are the hallmark of autoimmune diseases (1).
- Reliable, rapid ANA tests with acceptable sensitivity and specificity are in high demand for the timely diagnosis and treatment of autoimmune diseases (2,3).
- The gold standard for ANA detection is manual indirect immunofluorescence (IIF) with Hep-2 cells. This method is highly sensitive but has several flaws. It relies heavily on highly skilled morphologists which may lead to reader bias, and increased inter-laboratory variation (2,4).
- This study is a systematic review of the currently available multiplexed systems (i.e., Bioplex 2200, AtheNA Multi-Lyte ANA and FIDIS Connective 10) that might serve as alternative methods for detection of ANAs in the diagnosis of autoimmune diseases (5).

Methods

1. In the present study, we employed the Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols (PRISMA-P) to review research articles on the use of multiplexed systems in the diagnosis of systemic lupus erythematous (SLE), and analyze the participants, interventions, comparators and the outcomes (PICO).
2. PubMed with MeSH terms, CINAHL and Web of Science were searched to identify relevant studies.
3. Study selection and appraisal were conducted independently by three reviewers and analysis was performed to synthesize the data.

Results

- The literature search identified 193 potentially relevant articles. Further examination of the titles and abstracts resulted in 24 articles for which the full text was assessed in detail.
- Sixteen of the full-text articles met the specified criteria to be included in the review. After further consideration only 13 articles were included in the present review.
- RNP, SS-A, SS-B, Sm, Scl-70, Jo-1, centromere B, chromatin, ds-DNA and histone were the major antinuclear antibodies (ANA) tested, but not every study included all of them.
- The AtheNaA Multi-Lyte ANA and ANCA Test system, AtheNA MultiLyte ANA II Test system, the Bioplex 2200 or the FDIS were the multiplex systems used in the articles.
- Five of the 13 included studies reported positive predictive and negative predictive values for either the antibodies that correlated with SLE or specific antibodies.

Sensitivity (%)

	Author (reference number)							
	Avanis, et al. (10)	Biagini, et al. (6)	Copple et al.(7)	Copple et al.(7)	Copple et al. (7)	Bardin et al. (8)	Bruner et al.(9)	Infantino, et al. (11)
Multiplex system	AtheNA Multi-Lyte Systems	AtheNA Multi-Lyte Systems	AtheNA Multi-Lyte System	FIDIS connectiv e 10	QUANTA Plex™ ENA 8	Bioplex 2000	Bioplex 2000	Bioplex 2000
SS-A	27.6	68	15-20	20-25	20-25			
SS-B	5.4	27	11-15	5	0-5			45.5
Sm	5	73	20-25	10	10-15		83	
RNP	8.1	82	35	30	20-25		92	
Scl-70	2	9	5-10					
dsDNA	9.7	59				70	71	
Jo-1							80	
Ro60								68.2
Ro52								45.5
La							92	
Ribo-P							92	

Specificity (%)

	Article reference number							
	6	7 (A)	7 (B)	7 (C)	8	9	10	11
SS-A	100	100		98				
SS-B	17			99				94.7
Sm	81							
RNP	83			97			92.5	
Scl-70			99	99				
dsDNA	76.9		93		96	80		
Jo-1			99			99		
CpB								
La								
Ribo-P								
Ro60								93.2
Ro52								95.5

Results (continued)

- Seven studies reported the sensitivity and specifity for the following antibodies; SS-A, SS-B, Sm, RNP, Scl-70, dsDNA, Jo-1, centromere protein B (CpB), La, ribosomal P (Ribo-P), Ro60, and Ro52. Copple et al. (ref. 7) tested three systems: A-BMD, B-INOVA, C-Athena
- In general, all three multiplex systems (AtheNA Multi-Lyte ANA-II test system, FIDIS connective 10, Bioplex 2200) demonstrated higher specificities (>80%), but lower sensitivities (<80%) in the detection of ANA for SLE diagnosis.
- The ability to distinguish between types of SLE was reported in one article by Op De Beeck et al.
- No study reported the cost efficiency, turnaround time, improvement of healthcare or the ability to distinguish between SLE.

Discussion

- This systematic review provided preliminary evidence that the commercially available bead-based multiplex systems provide variable sensitivities and specificities in the diagnosis of SLE.
- Default cut-off values for each machine play an important role in the diagnosis, so it is suggested that the cut off values of each system should be established before it is used in the clinical laboratory.
- There is no significant difference in the diagnostic efficiency between different brand names.
- This review is limited by a small sample pool of articles that were mostly industry-funded.

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