



Nucleic Acid Detection in Patients Whose HIV RNA Levels are Near the Lower Limit of Detection: Implications for Endpoint Determination in HIV Vaccine Trials

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Background

- HIV vaccines elicit humoral immune responses that confound serological diagnosis of HIV infection.
- The most promising vaccines also induce cellular immune responses that are hoped will prevent infection and/or lower viral set point.
- Some proportion of both HIV infected and uninfected vaccine recipients will have positive serology results and undetectable viral RNA.

Objectives

- This study compares several nucleic acid detection strategies in HIV-vaccine naïve individuals who are either HIV seropositive with suppressed viral load or seronegative but at risk for infection.

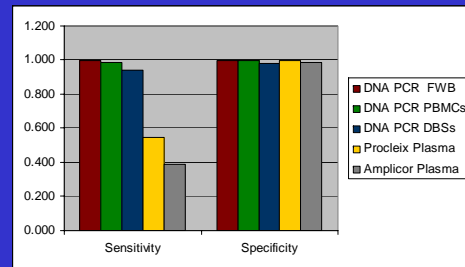
Methods

- Study participants (n=338) were enrolled at Brown University/Miriam Hospital (Providence, Rhode Island) into one of two groups: HIV seropositives having reported undetectable viral RNA (prior 3 months, n=155) and at-risk individuals without history of HIV infection (n=183). Ninety-four percent of the HIV infected participants were on anti-retroviral medications.
- EIA and Western Blot (WB) were performed on serum to confirm HIV sero-status.
- HIV-1 Viral RNA load was determined by the Roche Amplicor HIV-1 Monitor Test V1.5, ultrasensitive method.
- The Procleix HIV-1 Discriminatory assay was used to detect HIV viral RNA in plasma.
- HIV DNA was detected using the Roche Amplicor HIV-1 DNA assay V1.5. ROC analysis of all data points provided an Optical Density value of > than 0.74 for positive/negative discrimination. An absorbance value of > or = 0.8 was selected as the cutoff value for a positive test determination in this study.

- Frozen whole blood, PBMCs and dried blood spots (DBS) on 903 cards were tested in the Roche Amplicor HIV-1 DNA assay V1.5.
- Sensitivity and Specificity calculations were made using EIA/WB as the Gold Standard.

Results

	DNA PCR FWB	DNA PCR PBMCs	DNA PCR DBSs	Procleix Plasma	Amplicor Plasma
Sensitivity	1.00 (.9765-1.00)	0.987 (.954-.998)	0.942 (.893-.973)	0.548 (.447-.648)	0.387 (.288-.484)
Specificity	1.00 (.980-1.00)	1.00 (.980-1.00)	.978 (.945-.994)	1.00 (.951-1.00)	0.984 (.953-.997)



Conclusions

- DNA PCR using any studied specimen types, is significantly more sensitive for qualitative HIV diagnosis than either of the studied RNA detection methods in HIV infected subjects having well-controlled disease.
- DNA detection assays merit strong consideration for infection status determination in HIV vaccine recipients.