Evaluation of Pima CD4 Point-of-Care Device in Western Kenya for Potential use in Field Settings

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Abstract (updated)

BACKGROUND: Pre-treatment loss to follow-up has been cited as a barrier to effective antiretroviral treatment programs. The use of CD4 point-of-care (POC) testing has shown promise in some studies in improving linkage to care and treatment. One major challenge for POC devices rollout is the feasibility for use in field settings by lay health workers. We validated the PIMA CD4 POC against conventional platform on both capillary and venous blood with lay health workers and lab technicians in western Kenya under field conditions.

METHODS: In Phase I, performance of the PIMA device was evaluated against the FACSCalibur on 280 venous blood samples. In Phase II, paired capillary and venous blood samples collected from 147 patients, were tested by both the lab technician and lay counselor using PIMA POC and assessed against the conventional laboratory based FACS Calibur platform. Statistical analyses included agreement (Bland-Altman tests), correlation and accuracy determination (sensitivity and specificity) at clinical relevant cut-off (≤350 cells/mm^3 for ART initiation eligibility).

RESULTS: PIMA CD4 compared favorably with the conventional FACSCalibur on venous blood (Table 1). In addition good correlation and low biases were observed with the PIMA CD4 results from lay counsellor and lab technician on both venous and capillary blood (Tables 2-3). The sensitivity and specificity at treatment eligibility cut-off in Phase I comparison with venous blood was 93% and 90% respectively. In Phase 2 sensitivity and specificity on venous blood was 100% and 98% respectively for the laboratory technician and 94% and 95% respectively for the lay counsellor. Using capillary blood the sensitivity and specificity was 79% and 98% respectively for the lab technician and 86% and 99% for the lay counsellors (Table 3).

CONCLUSIONS: PIMA results compared favorably with the conventional FACSCalibur on both venous and capillary blood regardless of the cadre of staff thus showing the potential utility of this device in primary health care and field settings without impacting more burden on the limited laboratory health care personnel in resource limited settings.

Background

- Scaling up of antiretroviral therapy (ART) programs has increased demand for CD4 T cell count tests
- CD4 T cell counts are used in HIV-positive patients;
  - For initiation of ART,
  - To direct empiric treatments of suspected opportunistic infection
  - To identify patients failing therapy in resource-poor settings.
- However, access to CD4 testing is hampered by lack of laboratory infrastructure: often patients travel long distances or samples transported to where such facilities are available under cold chain conditions.
- Pre-treatment loss to follow-up can be a barrier to effective ART programs
- CD4 POC testing may reduce this by improving linkage to care and ART initiation
  - Demonstrated ability of POC CD4 to reduce loss to follow up by 50% (Jani et al, 2011)
- Key implementation challenge is accuracy of POC CD4 when operated by lay health workers in field settings, compared to laboratory based methods

Objectives

In-laboratory validation of POC CD4 device performance and accuracy: we assessed the new PIMA POC CD4 system (including the reagents and software) versus the predicate system (IVD Tritest™ CD3/CD4/CD45 reagent with Trucount™ tubes and Multiset software on the FACSCalibur™ flow cytometer) in the determination of absolute CD4 and/or %CD4 to assess performance characteristics

- Of PIMA CD4 versus FACSCalibur performed by laboratory technologist using capillary and venous blood specimens
- Of laboratory and lay health workers in the use of POC CD4 for CD4 enumeration under laboratory and field conditions, respectively

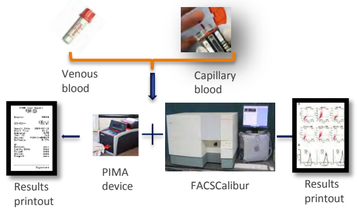
Ethical Approval

By the KEMRI Ethical Review Committee and CDC Institutional Review Board

Study Design

- Cross-sectional study of adults PIMA and FACSCalibur CD4 testing between Feb to Apr 2013 in the ISO15189 accredited KEMRI/CDC HIVR laboratory
- Inclusion Criteria
  - HIV infected adults already enrolled in an existing HIV care and treatment programme
  - Willing to provide written informed consent to draw venous and capillary blood

Laboratory Procedures



Statistical analysis

- Concordance correlation and linear regression were used to assess overall performance of PIMA
- Duplicate Coefficient of Variation and Bland Altman analyses were used to assess agreement of the PIMA and FACSCalibur
- Specificity and Sensitivity were used for misclassification analysis

Results

Table 1: Correlation and Misclassification Analysis of PIMA on Venous Blood by CD4 category (n=427)

	Cells/µL		*Pima Lab tech (Venous)
FACSCalibur (Venous)		CCC (%)	96 (91,94)
	<350	Absolute Mean bias	46 (26, 52)
		Sensitivity (%)	93 (85, 97)
		Specificity (%)	90 (87,93)
	<500	Sensitivity (%)	94 (90,97)
		Specificity (%)	84 (79,89)

N.B. CCC = Concordance Correlation Coefficient; Pima bias is towards lower CD4 count by 46 cells/µL

Table 2: Correlation and Misclassification Analysis of PIMA by staff cadre on Venous Blood (n=147)

	Cells/µL		Pima Lab tech (Venous)	Pima Lay HW (Venous)
FACSCalibur (Venous)		CCC (%)	91 (89,94)	87 (84,91)
	<350	Absolute Mean bias	66 (53, 78)	86 (72, 100)
		Sensitivity (%)	100 (86,100)	94 (77, 99)
		Specificity (%)	98 (93, 100)	95 (89, 98)
	<500	Sensitivity (%)	97 (88,100)	100 (93,100)
		Specificity (%)	84 (74,91)	76 (65,84)

N.B. Both Venous specimens drawn by lay health workers

Table 3: Correlation and Misclassification Analysis of PIMA by staff cadre on Capillary Blood (147)

	Cells/µL		Pima Lab tech (Capillary)	Pima Lay HW (Capillary)
FACSCalibur (Capillary)		CCC (%)	94 (93,96)	93 (91,95)
	<350	Absolute Mean Bias	36 (25,48)	44 (32, 57)
		Sensitivity (%)	79 (62, 90)	86 (67, 93)
		Specificity (%)	98 (93,100)	99 (94, 100)
	<500	Sensitivity (%)	96 (87, 99)	82 (72, 90)
		Specificity (%)	96 (87, 99)	82 (72, 90)

Figure 1:Linear Regression Analysis of FACSCalibur vs PIMA with Venous Sample

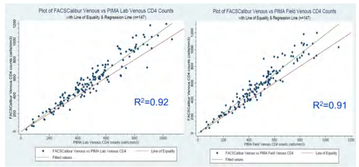


Figure 2: Bland-Altman plot of FACSCalibur vs PIMA

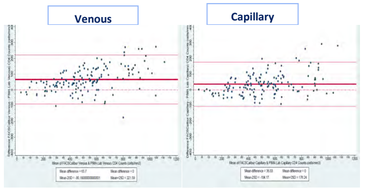
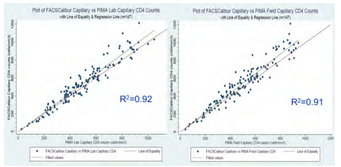


Figure 3: Linear Regression Analysis of FACSCalibur vs PIMA with Capillary Sample



Summary and Conclusion

- PIMA results compared favorably with conventional FACSCalibur on both venous and capillary specimens, regardless of the cadre of staff, in this laboratory validation
- PIMA CD4 POC correctly identifies majority of patients requiring ART, with a mean bias favoring earlier treatment initiation (46 cells/ml)
- POC CD4 testing has potential to enhance HIV care and treatment programs without burdening laboratory technicians in resource limited settings
- Randomized clinical trial on the impact of PIMA CD4 on linkage to HIV care is warranted (and ongoing at our site).
- ART program impacts of the bias of PIMA should be explored using a cost effectiveness approach (also planned).

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