The newly developed Cepheid Xpert® HIV-1 VL compared to the established Abbott RealTi*me* HIV-1 viral load measurement

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Background:
The GeneXpert® platform is well established for performing different molecular diagnostics assays. The ease of usage, the random access capability and the rapid turn-around time make the platform very interesting for a broad spectrum of applications. We compared the newly developed Xpert® HIV-1 VL assay to the broadly used Abbott m2000 RealTi*me* HIV-1 viral load assay. Special focus was put on reproducibility of results in the low viral load range and linearity in HIV-1 subtype B and non-subtype B viruses..

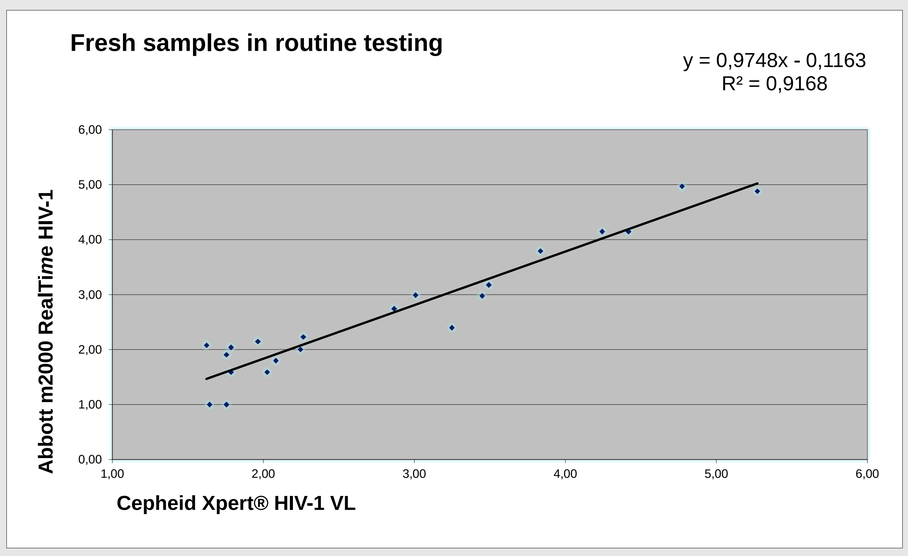

Figure 1: 100 fresh clinical samples in daily routine comparrison
Diagrammed are all 21 samples that resulted with the Xpert-assay above the detection limit of 40 copies/mL (log 1.6)

Results:

79 of the 100 fresh samples were below the detection limit of 40 cop./mL in the Xpert® HIV-1 VL and 82 of the samples were below the detection limit of 40 cop./mL in the Abbott m2000 RealTi*me* HIV-1. While only 11 of those samples showed a detection signal with RealTi*me* HIV-1, 22 did with the Xpert® HIV-1 VL leading to an overall concordance of 77% (see Tab. 1 and Fig. 1).
Intra- and inter-assay variations were low and comparable up to superior to RealTi*me* with intra-assay %CV ranging from 2.5% for samples with a viral load of 2.4 log cps/mL to 7.8% with 1.8 log cps./mL (s. Tab. 2).
Linearity on the diluted samples was shown for all three subtypes tested, **B, CRF01_AG** and **CRF02_AE** by using a simple linear regression model with slopes of 0.99; 0.99 and 0.97, intercepts of 0.07; 0.01 and 0.13 and coefficients of determination (R^2) of 0.99; 0.98 and 0.99, respectively (s. Fig. 2).

Methods:
Fresh (n=100) and diluted (n=225) patient samples spread over the clinical relevant range of viral load with a focus on low viremia were tested. The Xpert® HIV-1 VL uses the same cartridge format as the other assays on the GeneXpert® platform.
Fresh samples from daily clinical routine were tested in direct comparison to the Abbott m2000 RealTime HIV-1 viral load assay. Three high viral load samples from different HIV-1 subtypes (B, CRF01_AE, CRF02_AG) were diluted to following target concentrations: 100000 cop./mL, 10000 cop./mL, 1000 cop./mL, 500 cop./mL, 250 cop./mL, 125 cop./mL, 63 cop./mL, 31 cop./mL and 15 cop./mL (log 5; 4; 3; 2.7; 2.4; 2.1; 1.8; 1.49 and 1.18 cop./mL respectively). Each dilution step was tested in 5 replicates. To better assess reproducibility in the low ranges, dilutions of subtype B with 250 cop./mL, 125 cop./mL, 63 cop./mL were tested in 10 replicates with the Xpert® HIV-1 VL and the Abbott m2000 RealTi*me* HIV-1.

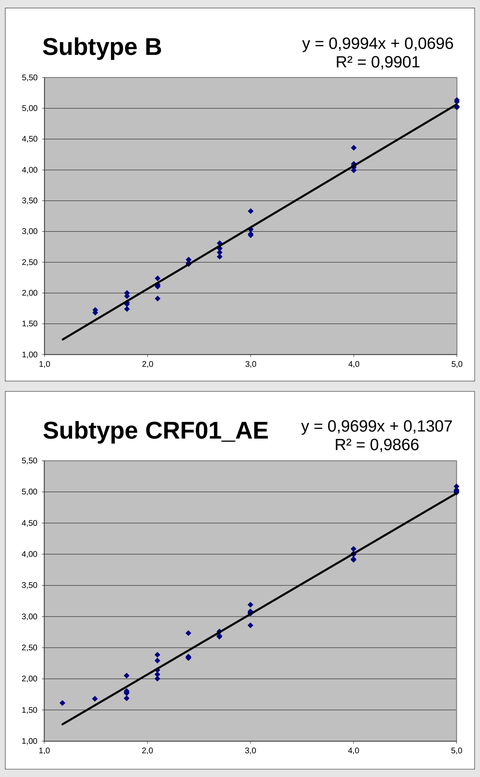

Figure 2:
Linearity in log copies/mL in eight dilution steps
beginning with log 5 down to log 1,18
HIV-1 in subtypes
B, CRF01_AE and CRF02_AG

Conclusions:

A high correlation between the Abbott m2000 RealTi*me* HIV-1 and the Xpert® HIV-1 VL could be shown. The higher detection rate below detection limit might hint to a slightly higher sensitivity of the Xpert® HIV-1 VL. The assay showed excellent linearity and robust reproducibility.
The random access capability, the easy usage and the rapid time to result of only 90 minutes make the GeneXpert® platform and the Xpert® HIV-1 VL a valuable tool in clinical routine, especially for urgent samples.

Table 1: 100 fresh clinical samples in daily routine comparison
nd = not detected; quant.= quantificated

100 fresh samples		Abbott m2000 RealTi*me* HIV-1			
		nd	<40	quant.	sum
Cepheid Xpert® HIV-1 VL	nd	54	3	0	57
	<40	15	6	1	22
	quant.	2	2	17	21
	sum	71	11	18	100

Table 2: Reproducebility in the low end
10 subtype B replicates per dilution step
intra-assay variance calculated

Dilution Log c/mL / test	mean	standard deviation	variance
2.4 expert	2,52	0,064	2,5324
2.4 m2000	2,43	0,115	4,7499
2.1 expert	2,12	0,100	4,7463
2.1 m2000	2,15	0,177	8,2085
1.8 expert	1,88	0,146	7,7765
1.8 m2000	1,87	0,147	7,8671