

# Urine Based Rapid Molecular Diagnostic Test Evaluation for Pulmonary Tuberculosis with Potential for Point of Care: Cape Town Cohort

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## Background

- Current sputum-based diagnostic tests for tuberculosis (TB) do not serve all target populations making optimal diagnosis difficult.
- TB diagnosis among sputum scarce patients is challenging for timely diagnosis and treatment initiation.
- *Mycobacterium tuberculosis* (*M. tb*)- specific transrenal (Tr) DNA from urine is a potential target for a molecular test to fill the gap in TB diagnosis.

## Material/Methods

- Spot urine, blood and sputum samples from 428 adults with suspected pulmonary TB (164 HIV positive, 263 HIV negative) were collected at three clinical sites in Cape Town, South Africa.
- Tr-DNA was isolated from 4 ml of EDTA urine using an in-house method optimized for DNA fragments  $\geq 38$  bp.
- A rapid double stranded primer-based PCR method targeting the *M. tb*- specific Direct Repeat region was applied for Tr-DNA detection. The isolated DNA was tested in triplicate using the automated molecular analyser Alere™ q – (figure-1) with a single use cartridge containing internal controls (positive and negative).
- The Tr-DNA test has a short time to result of 45 minutes.



Figure 1 – Alere q analyser & cartridge

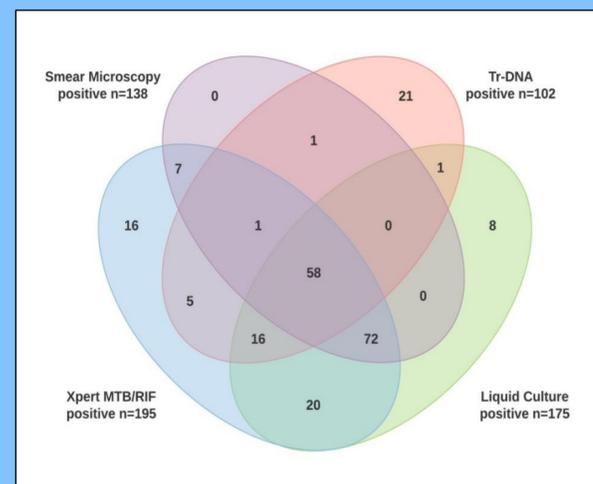


Figure 2 – Venn diagram comparing four TB diagnostic tests

## Results

- An overall sensitivity of 42.86% and specificity of 88.61% was achieved in comparison to the liquid MGIT culture (Table-1). Among HIV-infected TB patients the sensitivity and specificity were 45.24% and 89.04%, respectively.
- Combination of smear microscopy and Tr-DNA increased the sensitivity to 83.82% (smear microscopy alone 75.14%) with 96.61% specificity.
- Venn diagram (figure-2) for all four TB diagnostic tests is shown.

Table 1 – Tr-DNA Assay sensitivity and specificity

Tr-DNA Test	Reference Test (liquid MGIT culture)		
	Positive	Negative	Sum
<b>Positive</b>	75	27	102
<b>Negative</b>	100	210	310
<b>Sum</b>	175	237	412
Sensitivity (95%CI)	Specificity (95%CI)	Positive predictive value	Negative predictive value
<b>42.86%</b> (35.42 – 50.54%)	<b>88.61%</b> (83.86 – 92.36%)	<b>73.53%</b>	<b>67.74%</b>

## Conclusion

- This multi-center concept study indicates that Tr-DNA has a high specificity and modest sensitivity. Although unsuitable as a stand-alone test, in combination with smear microscopy, it may have the potential to aid TB diagnosis in HIV endemic regions where sputum scarce and extra-pulmonary TB is not uncommon.