Evaluation of the QuickMIC rapid AST assay for blood cultures in a clinical setting

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1 AMR is a challenge for empirical therapy

The changing landscape of antimicrobial resistance poses a challenge for empirical therapy, increasing the need for antimicrobial susceptibility testing (AST) to guide treatment. However, traditional methods such as broth microdilution (BMD) are comparatively slow and with high variability, typically allowing +-1 log2 dilution steps of variation. New rapid AST methods usually show low precision or narrow range, sometimes only measuring one single concentration point. We have developed a lab-on-a-chip gradient method (Figure 1) for rapid AST directly from positive blood cultures with high precision and resolution.

Here we evaluate the speed, precision and accuracy in comparison to current methods.

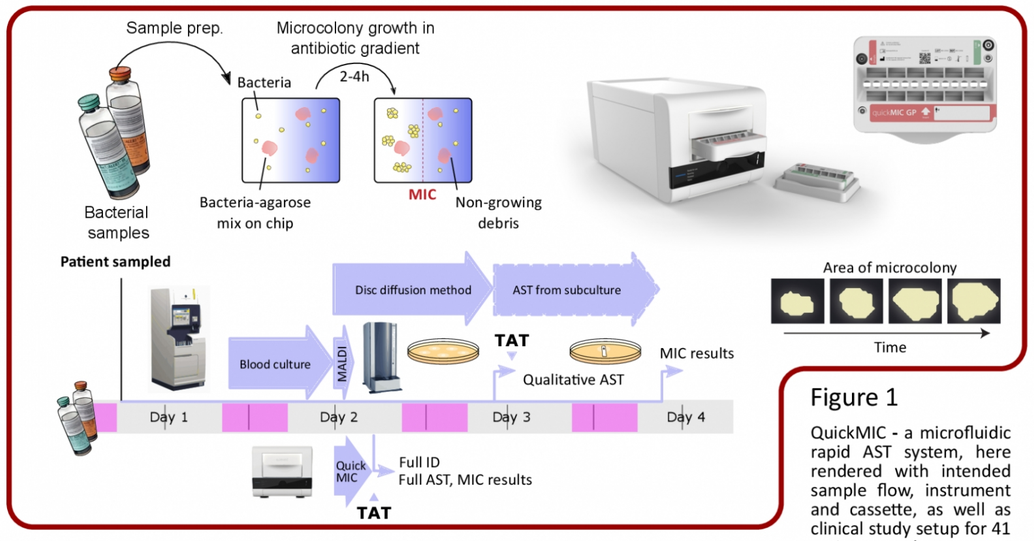


Figure 1

QuickMIC - a microfluidic rapid AST system, here rendered with intended sample flow, instrument and cassette, as well as clinical study setup for 41 patient samples.

2 QuickMIC provides precise MIC results in 2-4 h

Essential agreement with BMD for the spiked strains was overall 89.2% (n = 893), and the repeatability of QM was overall 44% from target MIC (SD normalized to range). Times to result for QM were on average 180 min (SD: 24 min). Regression analysis indicated that the QuickMIC method is robust with regards to initial inoculate and time after blood culture positivity, but significant variations exist with regards to SIR category, species and antibiotic ($p<0.05$). Total turn-around-time (TAT) when compared to disc diffusion for clinical samples were 33.0h for QM (SD: 7.2h) and 52.9h (SD: 9.3h) respectively (Fig. 2a, n=41), and the overall categorical agreement was 96.4%. 50% of sample TAT was in the Transport time and Blood culture incubation categories (Fig. 2b).

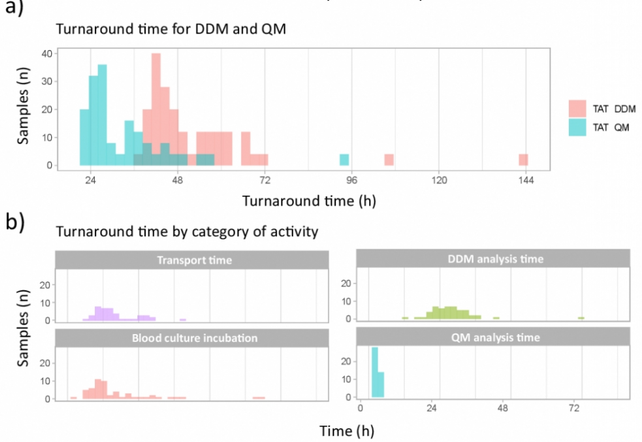
Essential agreement with BMD (89 strains)

AMI	CEP	CIP	COL	CTA	CTV	CTZ	GEN	MER	PIT	TIG	TOB	Total
75.5	87.5	93.3	77.6	90.7	95.9	92.2	95.1	83.1	92.0	93.9	85.7	**89.2%**

Categorical agreement with disc diffusion (41 samples)

AMI	CIP	CTA	CTZ	GEN	MER	PIT	TOB	Total
88.2	100.0	94.9	97.4	93.9	97.4	94.9	94.9	**96.4%**

Figure 2 Overview and detailed breakdown of the sample to result turnaround times for the 41 patient samples.



3 Methods used

QuickMIC was compared to BMD with respect to accuracy and repeatability by running 89 spiked clinical strains using the QM GN panel. Regression analysis was used to identify important factors affeting likelihood of achieving EA. QuickMIC was also compared with rapid disc diffusion for 41 clinical patient samples, with regard to turnaround time and categorical agreement, for 8 antibiotics.

4 We conclude:

- **QuickMIC can provide rapid and precise antibiotic susceptibility data directly from positive blood cultures.**
- **Times-to-result and interexperiment variability is low compared to traditional methods.**
- **The rapid AST system enables 40% reduction in AST turnaround time, which could have a positive impact on quality of care and antibiotic stewardship.**

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