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The evaluation of the performance of the MBT STAR-BL Test for the rapid detection of carbapenemase activity in *Enterobacteriaceae*

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Objectives

MALDI-TOF MS technology enabled the rapid identification of bacteria, however the culture-based antimicrobial susceptibility methods require overnight incubation and thus, hamper the time advantage obtained by this new technology. A novel method, the MBT STAR-BL test, based on the investigation of the breakdown of beta-lactam agents due to enzymatic activity of beta-lactamases on the MALDI-TOF MS platform, holds the potential to rapidly detect important resistance mechanisms. In this study we aimed to assess the performance of MBT STAR-BL test for the rapid detection of carbapenemase production in *Enterobacteriacae*.

Methods

MBT STAR-BL test (Bruker Daltonics, Germany) was used for the investigation of carbapenemase activity in a collection of 56 clinical isolates harboring carbapenemase genes (*Klebsiella pneumoniae;* n = 53, *Escherichia coli;* n = 3). The isolates were incubated in ertapenem and meropenem containing incubation solutions for 3 hours and then centrifuged. Supernatant (1 µl) was transferred onto the MALDI target plate and matrix solution was added. The analysis was performed on a MALDI-TOF MS instrument (microflex LT, Bruker Daltonics, Germany). Positive control strains containing carbapenemase genes (KPC, IMP, VIM, OXA-48 and NDM-1) and negative control strains lacking any carbapenemase gene but containing genes for extended-spectrum beta-lactamase (TEM, SHV and CTX-M) and AmpC beta-lactamase production were also included.

Results

All control strains exhibited the expected results (Figure 1). The results obtained for the clinical isolates are outlined in Table 1. Negative results for ertapenem hydrolysis were observed in three OXA-48 positive *K. pneumoniae* isolates. And negative results for meropenem hydrolysis were obtained for two OXA-48 positive *K. pneumoniae* isolates, and two NDM-1 + OXA-48 positive *K. pneumoniae* isolates. However, when ertapenem and meropenem results were evaluated together, all isolates exhibited positive results for carbapenem hydrolysis with at least one of the antimicrobial agents tested.

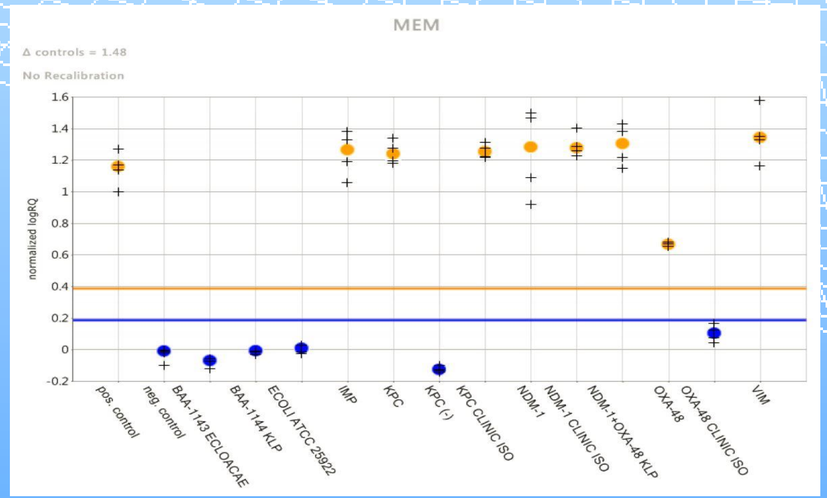

Figure 1. Exemplary study result obtained by STAR-BL test for both clinical and reference isolates with meropenem. **Note:** Isolates below the blue bar are negative for meropenem hydrolysis, isolates above the orange bar are positive for meropenem hydrolysis according to the interpretation of MBT STAR-BL software.

Table 1. The performance of MBT STAR-BL test for the detection of carbapenemase activity in carbapenemase gene positive clinical *Enterobacteriaceae* isolates (n = 56)

Carbapenemase gene	n	Carbapenem Hydrolysis		STAR-BL Result		
		ETP	MEM	POS	IND	NEG
KPC	2	2/2	2/2	2/2	-	-
OXA-48	16	13/16	14/16	16/16	-	-
NDM-1	8	8/8	8/8	8/8	-	-
NDM-1 + OXA-48	28	28/28	26/28	28/28	-	-
IMP + OXA-48	1	1/1	1/1	1/1	-	-
VIM + OXA-48	1	1/1	1/1	1/1	-	-
Total	56	53/56	52/56	56/56	-	-

ETP: ertapenem, **MEM:** meropenem, **POS:** positive, **IND:** indeterminate, **NEG:** negative

Conclusion

- The STAR-BL (selective testing of antibiotic resistance–beta-lactamase) module integrated into the MALDI-TOF MS system produced highly accurate results for the isolates tested.
- The analysis of carbapenemase activity for both ertapenem and meropenem was found to increase the sensitivity of the method.
- The MBT STAR-BL test is able to detect the carbapenemase activity within hours and thus, offers an option to laboratories that already possess a MALDI-TOF MS instrument to rapidly detect this highly important resistance mechanism.