



Getting better, every day

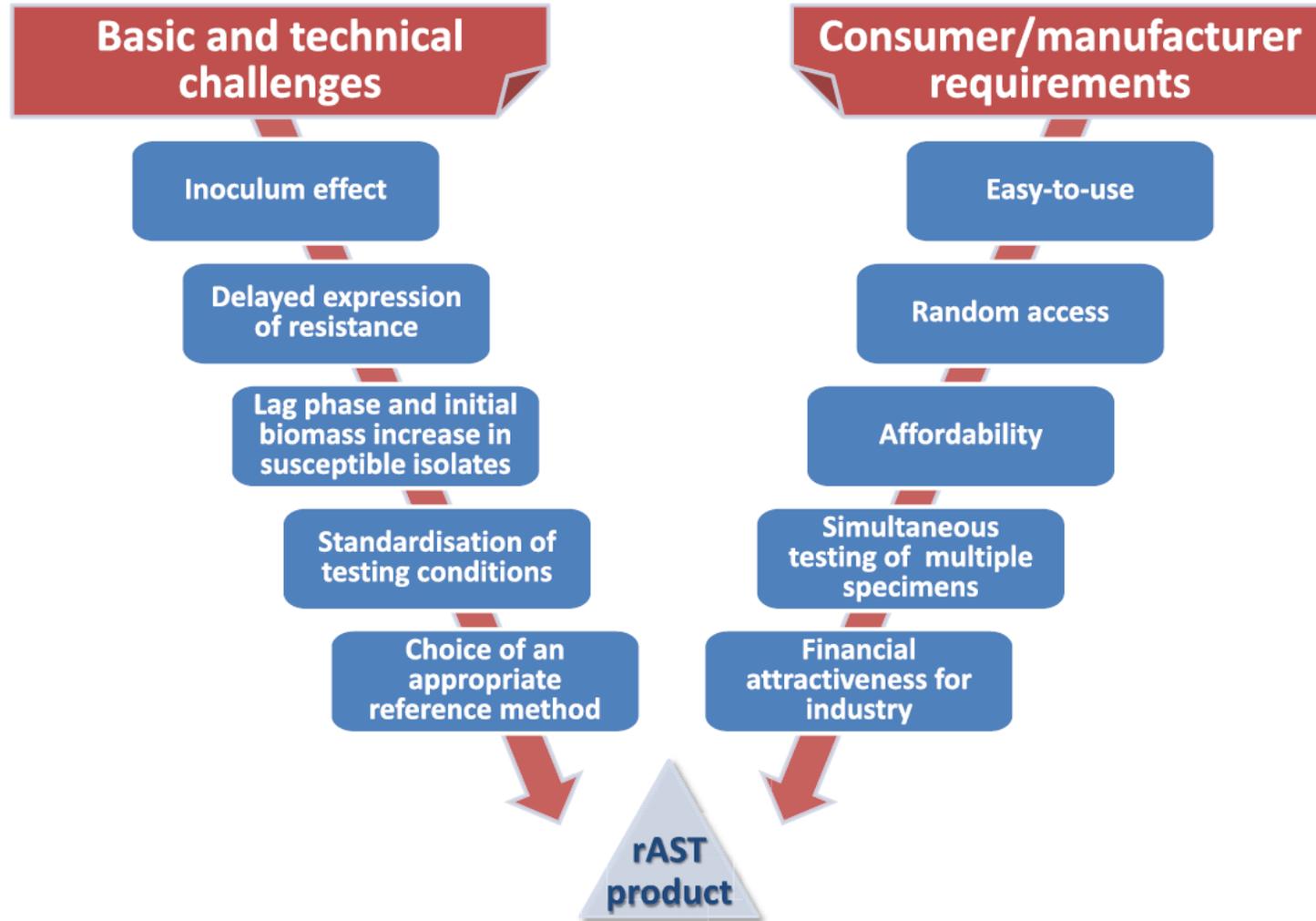


dRAST trial in Turku University Hospital, Turku, Finland

NordicAST WS, Malmö, 29.5.2024

Kaisu Rantakokko-Jalava

Getting better, every day



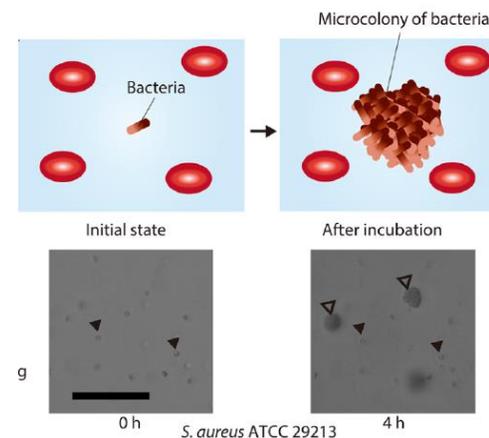
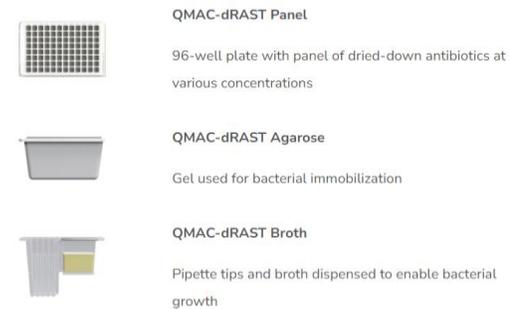
Clinical microbiologist's requirements

- Should cover species and antibiotics/resistance mechanisms relevant with regard to empiric treatment
- Should reduce time to result significantly (without 24/7 processing)
- Should replace routine testing in applicable species
- Should be operable also by non-bacteriology technicians

Fig. 3. Challenges and requirements of rapid antimicrobial susceptibility testing (rAST).

dRAST (Quantamatrix, South Korea)

- MIC-method; automated microscopy analyzes bacterial growth in agar in the presence of antimicrobials (range 3-7 MIC dilutions); results in 6 hours
- Species: a wide range of gram-negatives, gram-positives only staphylo- and enterococci, no fastidious species
- Antimicrobials: 18 in gram-neg and 17 in gram-pos EUCAST panel, plus ESBL and MRSA screens, expert system for interpretations
- random access, 12 samples simultaneously, simple sample preparation, no daily maintenance, easy QC
- Several publications compare dRAST to various reference methods with gram-positive and/or gram-negative bacteria, categorical agreement >90%
Choi J 2017, Huh HJ 2018, Grohs P 2020, Wong 2022



Aims and methods

- Trial period 3.7.2023 – 19.1.2024
- Aiming to get knowledge about
 - Performance of dRAST in comparison to routine method
 - Direct disc diffusion with overnight incubation (dilution w. gram-negative, staph)
 - Standard disc diffusion
 - Discrepancies resolved by broth microdilution (Sensititre)
 - Critical resistance with regard to empiric treatment
 - Results of antimicrobials recommended for definitive therapy according to local guidelines
 - Turnaround time (feasibility with regard to opening hours)
 - Possible clinical impact

Strains

- Positive blood culture flasks with rapid ID (Maldi-TOF MS) indicating a species suitable for dRAST (n=153)
- Strains from collection, including strains obtained from the NordicAST CPE study, spiked in BC (n=35)

	n	prospective samples	strain collection
Enterobacterales			
Escherichia coli	40	32	8
Klebsiella pneumoniae complex	23	10	13
Citrobacter spp.	4	3	1
Enterobacter cloacae complex	7	3	4
Klebsiella aerogenes	4	3	1
Klebsiella oxytoca	4	4	0
Morganella morganii	2	2	0
Proteus mirabilis	3	1	2
Providencia rettgeri	1	0	1
Serratia spp.	1	1	0
	89	59	30
Other gram-negatives			
P. aeruginosa	13	12	1
Acinetobacter spp.	3	3	0
S. maltophilia	1	1	0
	17	16	1
Gram-positives			
S. aureus	40	40	0
E. faecalis	14	12	2
E. faecium	12	10	2
S. epidermidis	10	10	0
CNS, non-epidermidis	6	6	0
	82	78	4
Total	188	153	35

Time to result

	Time to result dRAST (h:min)			
	n	median	min	max
Enterobacterales	95	6:45	4:36	7:48
Other gram-negatives	16	6:45	6:36	7:12
Staphylococci	54	6:42	6:36	7:48
Enterococci	30	7:12	6:36	7:48

Same day clinical impact most likely for results ready by 15:00. However, ID on call until 22:00.

Detection of critical resistance

E. coli and *K. pneumoniae*

Species	n	ESBL*	CPE*	Comment on performance of dRAST
<i>E. coli</i>	40	2+1 3*CTX-M	0+5 1*VIM 1*IMP 1*NDM 2*OXA-48 group	3/3 ESBLs detected (+ one false positive by Expert system) CPEs: except for one strain with OXA-48, meropenem-MIC was >0.125 mg/L (EUCAST cutoff). Strain with NDM: mero interpretation false S (MIC 2) (ref R >32) One strain with CMY, mero interpretation S (ref I)
<i>K. pneumoniae</i> cplx	23	0+2	0+11 2 VIM 6 OXA-48 -group, 1 KPC 1 NDM 1 NDM+OX A-48	2/2 ESBLs detected. Both had elevated meropenem-MIC, dRAST detected one but missed the other All CPE strains had meropenem-MIC >0.125 (!) One strain with VIM: meropenem interpretation S (MIC 0.5), reference I (MIC 4)

Other gram-negatives

- Enterobacter cloacae complex, 3 CPE strains
2/3 dRAST meropenem MIC >0.125 mg/L (S), ref I
1/3 dRAST meropenem MIC >16 mg/L (R), ref R
- Proteus mirabilis, 1 CPE (NDM)
dRAST meropenem MIC 16 (R), ref 22 mm/MIC ?
- Citrobacter freundii, 1 CPE (NDM)
dRAST meropenem MIC 0.5 mg/L (S), ref 17 mm/MIC?
- Acinetobacter baumannii: dRAST correctly identified meropenem resistance in two A. baumannii strains

S. aureus

- Among 40 tested strains, 9 (8+1) were MRSA
- FOX screen in dRAST correctly identified 8, expert system one
- In addition, one false positive MRSA screen
- Inducible clindamycin resistance missed in 3/3 strains
- Erythromycin, gentamycin: consistent results
- Levofloxacin: 2 (5%) major errors (false R)

Enterococci

- *E. faecalis*, 4/14 strains were VRE (1 *vanA*, 3 *vanB*)
 - all detected by dRAST
 - No very major errors
 - Major errors: gentamycin high (1), linezolid and teicoplanin (2)
- *E. faecium* 2/12 strains were VRE (1 *vanA*, 1 *vanB*)
 - both detected by dRAST
 - Very major error with ampicillin (2 strains)

Preliminary conclusions

- dRAST detected ESBLs, CPE, MRSA and VRE relatively well
 - in 27/29 CPE, mero MIC > EUCAST cutoff (0.125 mg/L)
 - However, the expert system currently cannot utilize the MIC-value, only S/I/R
- Otherwise dRAST tended to underestimate ertapenem and meropenem MICs and overall resistance for piperacillin-tazobactam in gram-negatives

Clinical microbiologist's requirements

Partly
(except for
cefuroxime, and
pneumococcus/penicillin)

Should cover species and antibiotics/resistance mechanisms relevant with regard to empiric treatment

Yes

Should reduce time to result significantly (without 24/7 processing)

No

Should replace routine testing in applicable species

Yes, except for releasing the results

Should be operable also by non-bacteriology technicians

Clinical analysis ongoing

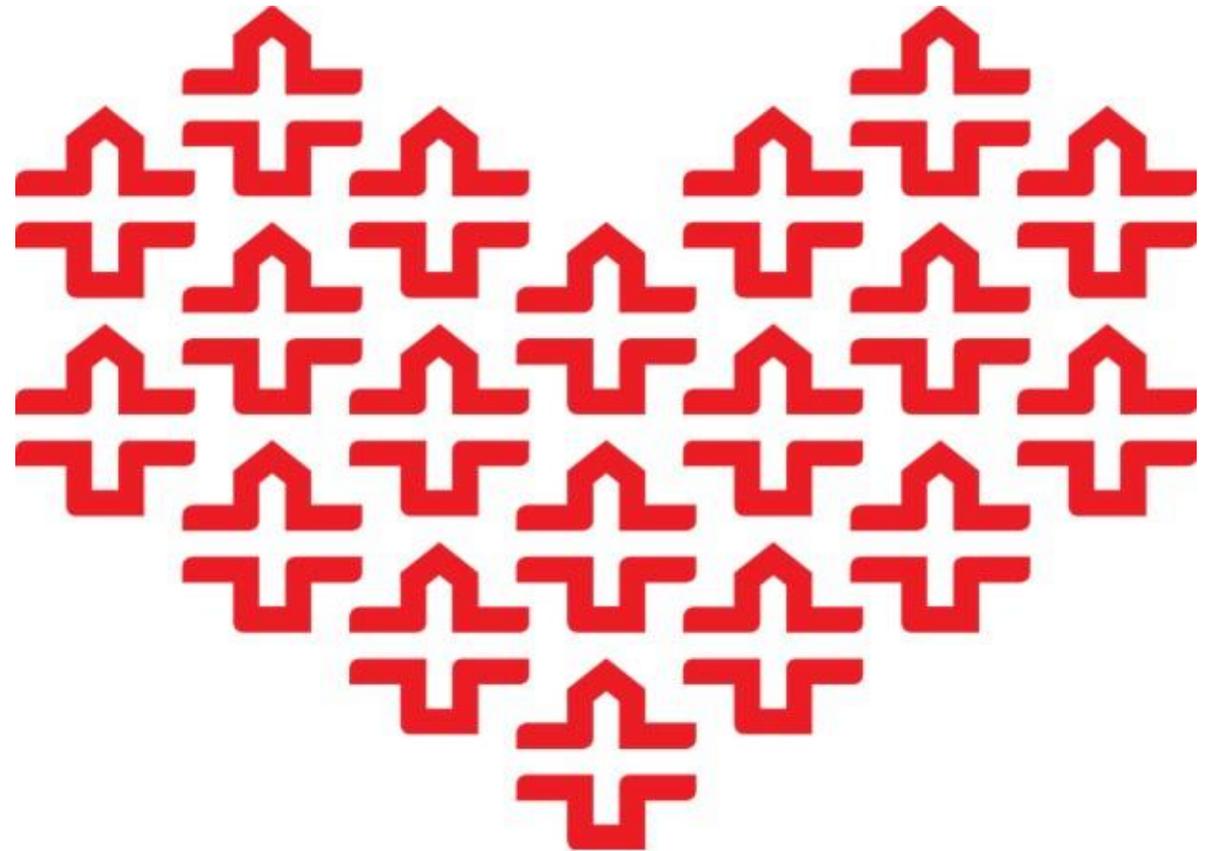
- Possible clinical impact

Empiric treatment vs results in 153 prospective clinical samples
Benefit of rapid AST vs rapid ID

- In the Finnish setting, rapid ID (+rapid detection of major resistance mechanisms) would most probably be a more cost-effective approach

Thanks to

**Dina Riihiaho
Annukka Pietikäinen
Eveliina Lassila
Katariina Haimakka
Tiina Partanen
Jacqueline Sirvidas
Ville Pirhonen**



Getting better, every day