Image interpretation of urine cultures using the APAS® Independence – artificial intelligence in the routine clinical laboratory.

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Despite significant developments in automation, microbiology remains a highly manual and labour-intensive discipline. Additionally, as pathology test numbers continue to grow, the acquisition and allocation of appropriate staff resources and knowledge has become increasingly challenging.

The APAS® Independence is an in-vitro diagnostic instrument using artificial intelligence and machine learning technology to automate culture plate imaging, analysis and interpretation. APAS Independence appears to offer microbiology laboratories the ability to augment the skills of scientific staff, reduce workload and increase efficiencies.

An *in situ* evaluation of the APAS Independence was carried out in the microbiology laboratory, St Vincent's Pathology, Melbourne. The results of 3665 urine cultures analysed using APAS Independence were compared to those of microbiologists performing traditional culture reading techniques.

We investigated potential gains in laboratory efficiency and collected feedback from scientific and technical staff regarding the instrument's usability.

CLEVER CULTURE SYSTEMS

APAS INDEPENDENCE

APAS Independence operation parameters

The APAS Independence was run in accordance with manufacturer's instructions, using Analysis Module version AM_007-1.0.0.

Methods

Standard urine processing methodology at St Vincent's Pathology Melbourne

All urine samples received in microbiology have automated chemistry and microscopy performed using Aution Hybrid AU-4050 System (ARKRAY Inc, Japan). In addition, urines are cultured, using a 1ul calibrated loop, onto a Horse Blood Agar/Brilliance UTI chromogenic agar (Thermo Fisher Scientific Australia, product PP2249) bi-plate and incubated aerobically at 35°C for 18 hrs. Generally, interpretation of culture plates occurred at three levels.

St Vincent's classification	Definition	APAS classification
No growth	No colony-forming units (CFU) detected	No growth
No significant growth (NSG)	An estimated < 10^7 CFU/L detected	Doubtful
Significant growth (SIG)	An estimated ≥ 10^7 CFU/L detected	Probable or Review

No growth was included in the NSG group for analyses.

APAS Independence reporting compared to standard laboratory workflow

A total of 881 agar plates were first analysed by APAS Independence and then assessed and reported by the laboratory independently. Results reported by St Vincent's Pathology were extracted from the laboratory information system. The primary analysis variable was bacterial growth enumeration of the bi-plate, classified as 0, 10^6, 10^7 and 10^8+ CFU/L. Similarly, APAS Independence calculated the enumeration for each agar of the bi-plate using the largest enumeration of the two agars. This allowed for direct comparison with enumerated results generated by St Vincent's Pathology standard workflow (SVP). A subset of samples were evaluated using a multiclass composite reference standard method, allowing discrepant results to be resolved in an unbiased manner via simulation. An additional 2119 samples were processed and used for investigation of microbiologist variability, which is not presented here.

Incorporation of APAS Independence into routine workflow

A total of 665 samples received in the laboratory were routinely processed by APAS Independence. In order to do this, routine workflow was investigated and subsequently improved to facilitate processing afforded by the instrument. During this time laboratory efficiencies and staff utilization were measured, and feedback from staff involved in the both the process of specimen preparation and agar reading was sought.

Results - APAS Independence vs St Vincent's Pathology standard workflow

Table 1: Confusion matrix outlining average sample classifications by SVP and APAS Independence after the unbiased discrepant resolution method.

		APAS Independence	
		NSG	SIG
SVP	NSG	333	37
	SIG	35	476

These data demonstrated a high level of agreement (91.8%, Table 1). Where there was SVP SIG and APAS NSG disagreement (n=35), a large percentage were urogenital and skin contaminants at low levels above the 10^7 threshold, and 2 were slow growing alpha-haemolytic streptococci presenting as a hazy growth after 18 hours. Of these two, one sample would have flagged for Review under normal SVP workflow by virtue of a raised white blood cell count, and APAS Independence would re-route the plate away from an NSG plate classification, to an SIG plate classification.

Sensitivity and specificity were estimated and 95% confidence limits presented using the Wilson score method [1] within the unbiased discrepant resolution method [2]. Sensitivity is defined as the probability of APAS Independence detecting significant growth where SVP has determined significant growth, and specificity as the probability of APAS Independence reporting non-significant growth where SVP has determined non-significant growth. All analysis was performed in R 3.4.3 [3] and the results can be seen in Table 2.

Table 2: Significant growth sensitivity of APAS

Parameter	Estimate	Lower	Upper
Significant growth sensitivity	0.932	0.894	0.958
Significant growth specificity	0.901	0.851	0.939

Potential gains in laboratory efficiency

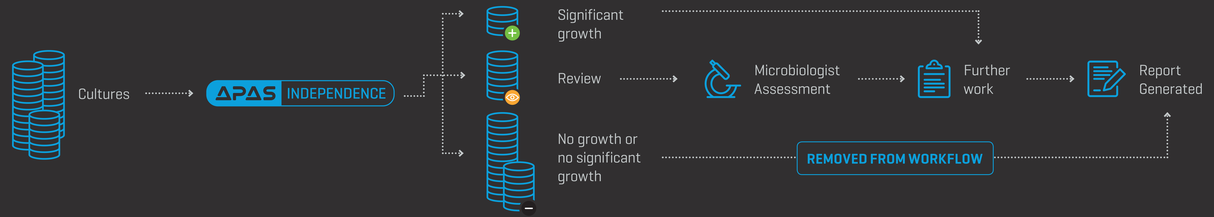
The changes that APAS Independence enabled in specimen processing workflow allowed for simplification of tasks and considerable time savings. Workflow analysis determined that 40% of laboratory assistant time could be saved while processing specimens.

During the evaluation, APAS Independence was not interfaced to the laboratory's information system. Considering that approximately 70-80% of urine cultures return results of no growth or no significant growth, there exists a potential for significant reduction (up to an estimated 50%) in microbiologist time for reporting.

Operator feedback

Microbiologists rated the instrument's usability on a scale from 1 to 5, with 1 being "very complex to use" and 5 being "very easy to use". Three of the four microbiologists rated APAS Independence usability as 5, whilst the other rated it as 4. They considered the availability of imaged cultures to be a key feature, along with the speed of APAS Independence in both sorting and reading agar plates. Both the microbiologist and laboratory assistant groups cited the benefits of a simplified workflow, particularly in specimen set-up, as a major advantage of the instrument.

[1] Newcombe RG. Two-sided confidence intervals for the single proportion: Comparison of seven methods. Statistics in Medicine 1998;17:857–72.
[2] Brenton L, Jardine D, Waters MJ, Stanford T, Giglio S. Clinical evaluation of APAS® Independence: automated imaging and interpretation of urine cultures using artificial intelligence, integrating a novel method for unbiased discrepant resolution. Manuscript submitted for publication.
[3] R Core Team. R: A language and environment for statistical computing. Vienna, Austria: R Foundation for Statistical Computing; 2017.



Conclusions

APAS Independence performed with a high level of sensitivity and specificity and facilitated operational efficiencies in both specimen processing and culture reading.

By removing the negative and non-significant urine cultures from the hands of microbiologists, APAS Independence allows for the redirection of microbiologist time to more complex tasks. Users reported a high level of engagement with the technology, most frequently citing the instrument's ease of use, high-quality image resolution and accuracy as the primary benefits.