Abbott

POINT OF CARE

WHITE PAPER: VERIFICATION OF THE i-STAT® SYSTEM WITHIN AUGSBURG HOSPITAL

THE RESULTS SHOWN HERE ARE SPECIFIC TO ONE HEALTH CARE FACILITY AND MAY DIFFER FROM THOSE ACHIEVED BY OTHER INSTITUTIONS

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INTRODUCTION

Fast and precise determinations of activated clotting time (ACT) are essential during cardiopulmonary bypass (CBP) surgery to monitor the degree of heparin-induced anti-coagulation. An inaccurate ACT puts patients at risk for thrombosis and haemorrhage and risks damage to the extracorporeal circuit.[1] However, there are a number of challenges that hinder the evaluation of ACT and subsequent patient care:

- ACT tests with some traditional analysers can lead to highly variable results, raising doubts about the accuracy of critical ACT results and requiring re-testing[1,2]
- Traditional analysers require periodic quality control (QC) checks that interrupt patient testing[3]
- Inadequate centralised QC of Point of Care (POC) methods and equipment often prevents the testing and maintenance of equipment[1]

This white paper describes the rationale behind the implementation of the *i-STAT System* at Augsburg Hospital where mechanical ACT testing had been used for many years. Data, collected on site, are described which compare the precision of the *i-STAT System* to its traditional, mechanically-based ACT testing device.

OVERVIEW OF AUGSBURG HOSPITAL

Located in Augsburg, Germany, the Augsburg Hospital is a teaching hospital for the Ludwig-Maximilians-University in Munich.[4,5]

- Consists of 25 clinics and institutes, including the Clinic for Heart and Thoracic Surgery
- Houses more than 5400 employees, including specialists and supportive personnel
- In 2012, more than 1000 CPB operations were performed on site

RATIONALE FOR i-STAT SYSTEM IMPLEMENTATION

Traditional, mechanical methods of testing ACT were previously used at Augsburg Hospital for several years within its cardiovascular operating room (CVOR). The switch to the *i-STAT System*, an IT-integrated POC device, was driven by five main objectives:

- Integration with the hospital's established Conworx system[6]
- Improved efficiency
- Reduced workload for QC (e.g. one liquid solution for all instruments and electronic documentation of QC)
- Consolidation of POC testing technology across different clinics and tests
- Elimination of paper documentation and verification

METHODOLOGY

The *i-STAT System*, which uses biochemical methods to measure activated clotting time-kaolin (ACT-K), was compared to the system that was previously in use (Hemochron Signature+).

Method comparison

1. Both the *i-STAT* analyser and comparative analyser were configured for Pre-Warm settings.
2. Method comparison testing:
   Duplicate testing was performed on the *i-STAT System* and a comparative system for most method comparison samples. The Syy and Sxx determined from pooled averages of the duplicate results were used for the imprecision element of the Deming regression calculations. Only the first of the duplicates was used to calculate slope, intercept and the r value (correlation coefficient).

i-STAT CONTROL LOT NUMBERS	
i-STAT Control Level 1 Lot Number(s)	261053, 271049
i-STAT Control Level 2 Lot Number(s)	271053

RESULTS

Electronic QC for the i-STAT System is efficient and in accordance with guidelines

- Measurements take slightly longer on the *i-STAT System* than the comparator device
- The *i-STAT System* QC is easily customisable to be in accordance with the Guidelines of the German Federal Medical Council (RiliBÄK*)
- Testing did not need to be stopped for electronic QC, unlike the comparator device
- Required single liquid solution
- QC results were sent to Conworx POCcelerator™ and did not need to be re-documented on paper and sent to the lab for verification

The i-STAT System results strongly correlate with those from the previously used comparator product within the therapeutic range

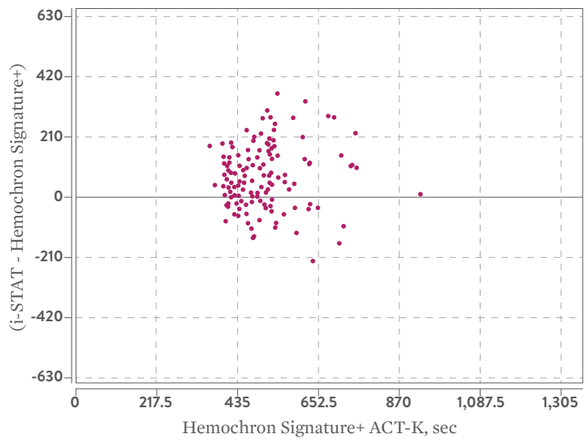
The *i-STAT System* uses a unique biochemical method to perform ACT testing, which measures the conversion of a thrombin substrate other than fibrinogen, which forms a measurable electroactive compound. This method is different from mechanical ACT testing, which detects the formation of blood clots.[7] Differences between the testing methods could potentially lead to differences in ACT measurements. Therefore, *i-STAT* ACT-K sample measures were compared to those of the previously-used comparator product using both a difference analysis and a regression analysis.

Difference analysis:

A difference analysis showed that the time measures between the two devices differed substantially within the therapeutic range.

ACT-K DIFFERENCE PLOT

i-STAT (WB) – Hemochron Signature+ (WB)



TEST	RANGE	EXCLUDE OUTLIERS	N	AVERAGE DIFFERENCE	S_D†
ACT-K	350.01 – 400.00		6	107.33	67.27
	400.01 – 450.00		45	34.00	71.65
	>450.00		90	69.83	125.60

* Guideline of the German Medical Association for Quality Assurance of Laboratory Medical Examinations
† S_D is the standard deviation of the differences

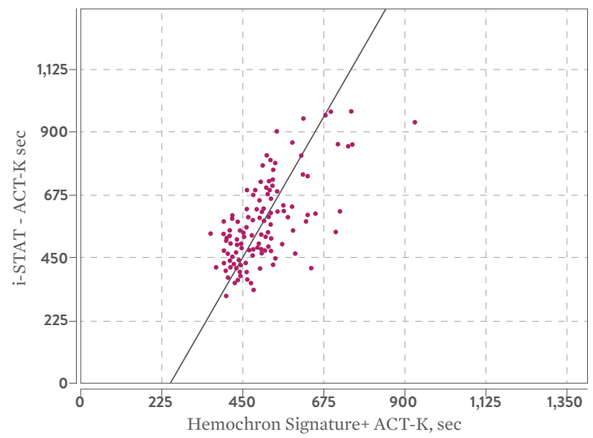
Regression analysis:

To determine the strength of correlation between the i-STAT System and the comparator product, a Deming regression analysis was performed. The calculated r value, or correlation coefficient, from the regression analysis, is a measure of how closely data points fall near the regression line. It is dependent on the data range used in its calculation, as well as the amount of random error present in the methods, and is not necessarily a good measure of how well the methods compare.

The strength of the correlation in this test (r=0.67) was significant (N=141; P=0.001; according to Pearson's two-tailed correlation coefficient table).[8] This indicates that the therapeutic range used with the comparator product can be applied to the *i-STAT System*.

ACT-K REGRESSION PLOT

i-STAT (WB) vs. Hemochron Signature+ (WB)



TEST	N	EXCLUDE OUTLIERS	Sxx	Syy	SLOPE	Y-INTERCEPT	Sy.x	r
ACT-K	141		42.70	27.67	2.2	-562.7	110.37	0.67

Sxx is the mean difference between duplicates on the comparative (X) method in the method comparison study.
Sy.x is the standard error of the estimate. The average dispersion of the data around the regression line.
Syy is the mean of the differences between duplicates on the Y method of the method comparison study.

RESULTS CONTINUED

Duplicate differences were greater for the comparator product than for the i-STAT System

In order to determine the CV of the devices, samples were tested on both systems (*i-STAT*: N=142 and comparator product: N=136). The comparator product had more divergent duplicates than the *i-STAT system* **(see figures opposite)**.

- Of the samples tested in duplicate and within the therapeutic range (<450s), only a single sample had a duplicate difference larger than 50s (55s; 3% of samples) on the *i-STAT System* while the comparator device had eight samples with differences larger than 50s (15% of samples)
- In 7% of the duplicate measurements on the comparator device, one of the duplicate measurements fell out of range (>1000s) while the other one was in range (<900s). These discrepancies did not occur on the *i-STAT system*
- 148 samples were tested in this method comparison study. Of these, there were 134 duplicate results available for the *i-STAT* and 121 for the comparator product. The average difference between the *i-STAT* duplicates was 26.3 seconds, 30% better than the average difference of 37.4 seconds for the comparator product

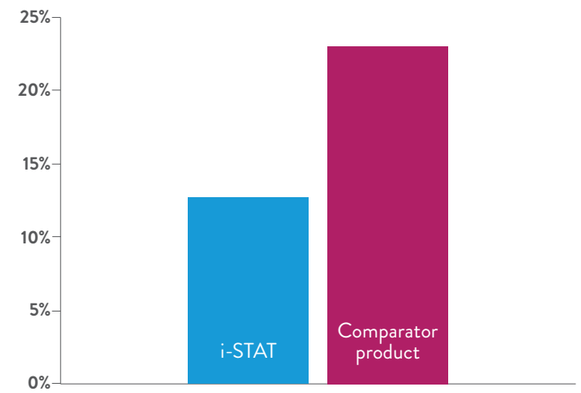
THE i-STAT SYSTEM DEMONSTRATED PRECISION WITH A COEFFICIENT OF VARIATION (CV) ≤5%

The *i-STAT* precision was further tested using two different control samples: level 1 (<450s) and level 2 (>450s). The calculated CVs were as follows:

- Level 1: 4.68% (N=25)
- Level 2: 5.08% (N=18)

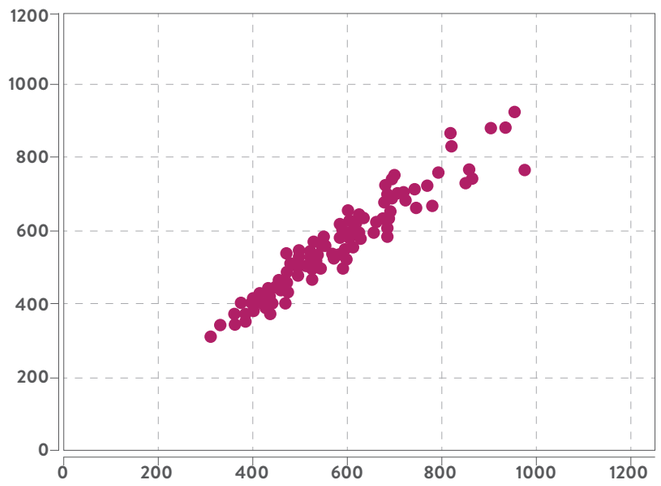
The comparator product, while not tested during this study, is described as having a CV of <10%.[3]

REPRODUCIBILITY i-STAT VS. COMPARATOR PRODUCT

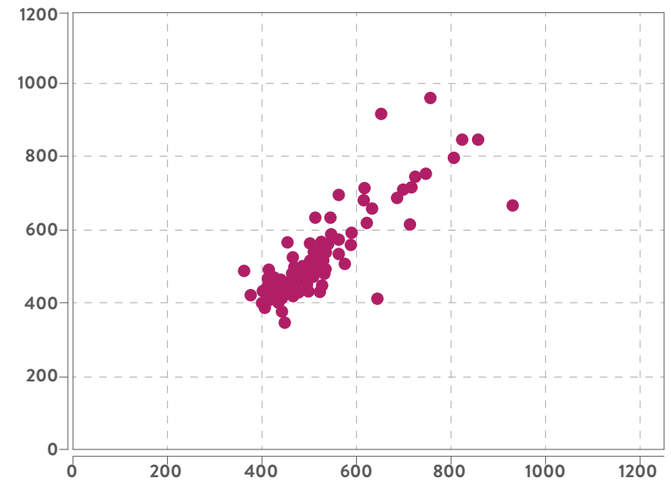


Differences between duplicate results >50 seconds

i-STAT SYSTEM SAMPLE DUPLICATES



COMPARATOR DEVICE SAMPLE DUPLICATES



DISCUSSION

This white paper describes both the implementation and ease of use of the *i-STAT System* within Augsburg Hospital along with data comparing the precision of the *i-STAT System* with the Hemochron Signature+ in a clinical setting.

The Guidelines of the German Federal Medical Council (RiliBÄK) include detailed documentation instructions concerning lab procedures and corresponding results, and the creation of standard operating procedures (SOPs) and a quality management handbook. According to its guidelines, in the case of out of range results of control samples, immediate corrective actions must be implemented including the lockout of further use. The entire process, including corrective actions taken, the outcome, and root cause, needs to be documented and verified.[9] The previous ACT testing device used by Augsburg Hospital in the CVOR led to difficulties in adhering to the RiliBÄK recommendations as it resulted in time-consuming documentation.

The *i-STAT System*, with built in QC and customisation features, allows local, state, or national accreditation requirements to be easily followed. The analyser features:[10]

- Internal electronic checks and calibration during each test cycle
- Customisable QC checks and lockout for both Electronic Simulator and liquid QC controls
- Digital documentation of QC data via the Conworx POCcelerator
- Simple integration with many, third party, laboratory and hospital information systems

One benefit noted was that the periodic internal Electronic Simulator testing by the *i-STAT* was unobtrusive compared to the testing system of the comparator product. The internal Electronic Simulator testing occurred for the *i-STAT System* as a 20 second step before commencing patient measurements.[10] The comparator product's electronic QC is required after every eight hours of use, uses dedicated cartridges[3] and, in the environment of Augsburg hospital, took up to 300–500 seconds (depending on device settings) to perform. From the user's perspective, the QC tests were requested without warning and at irregular intervals. Although the QC tests could be discontinued to allow patient testing, it was felt that the *i-STAT System* potentially provided more safety due to its regular, internal QC testing that did not interrupt patient testing.

The *i-STAT System* simplified the documentation procedure required by RiliBÄK. The device stores QC results as distinct records and transmits them to the Conworx POCcelerator via the downloader for easy viewing. Furthermore, The Data Manager is designed to easily connect to typical laboratory or hospital information systems.[10] In the case of Augsburg Hospital, the *i-STAT System* was easily integrated with the third-party, Conworx system.[6] This paperless process simplified documentation and verification, improving the workflow and maintenance of the analysers.[10]

The measurement time for the *i-STAT System* was slightly longer than the comparator device. However, this was not considered to be an obstacle to implementing the *i-STAT System* within the hospital environment. Furthermore, out-of-range blood samples measured with the comparator device took more than 1005 seconds (approximately 17 minutes) to analyse. Moreover, the troubleshooting guidelines for the comparator device require repeat test taking when samples are out-of-range.[3] This often led to additional blood sampling and additional testing time, again, up to 17 minutes.

In transitioning from the previously-used comparator device, it was necessary to determine if the *i-STAT System* could be used within the same therapeutic range. The i-STAT Kaolin ACT test is calibrated to match the Hemochron Celite FTCA510 using prewarmed reagent.[7] As the hospital previously used the Hemochron Signature+ model, additional comparison testing was warranted.

Although the sample results of the *i-STAT System* differed from those acquired by the comparator device within the therapeutic range, the correlation between the two was found to be significant, ensuring the easy incorporation of the *i-STAT System* into CVOR protocols. Furthermore, the precision displayed by *i-STAT System* was ≤5% while the comparator device has a published precision of <10% when measuring patient samples in a clinical setting.

The implementation experience was also a factor in the decision to use the *i-STAT System* since April 2015:

- The *i-STAT* was successfully integrated in the Augsburg Hospital CVOR and Conworx system within one week
  - Approximately 150 staff members were trained and are now confident using *i-STAT*, including anaesthetic staff, nurses, and doctors
  - Abbott Point of Care personally trained staff and left a positive impression

OVERALL, THE i-STAT SYSTEM WAS JUDGED TO BE A PRECISE AND AN EFFICIENT MEANS OF POC ACT TESTING FOR THE FOLLOWING REASONS:

- Testing did not have to be stopped for electronic QC
- Validation with paper documentation at the central laboratory was not needed
- The tested precision was adequate for the *i-STAT System* (CV of ≤5%)
- The precision gave clinicians relief from the doubt of variable results, which were often found with the previously-used mechanical system, and reduced the need to delay care during re-testing of samples
- The system was easy to integrate into Augsburg Hospital's existing IT system

CONCLUSIONS

- *i-STAT* gives clinicians a reliable ACT result, freeing them of doubt in their decision-making and enhancing patient care
- Through precise, biochemical ACT testing, *i-STAT* optimises patient safety in the CVOR potentially by eliminating interruptions in patient testing
- *i-STAT* enables seamless integration of results with hospital IT systems, streamlining workflow and maximising efficiency
- *i-STAT* is simple to integrate and implement in CVOR departments

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Intended Use Information
The i-STAT Kaolin Activated Clotting Time (KaolinACT) test is an in vitro diagnostic test that uses fresh, whole blood, and is used to monitor high-dose heparin anticoagulation frequently associated with cardiovascular surgery.

For In Vitro Diagnostic use only

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