

# Evaluation of the Analytical Performance of the Nova StatSensor Creatinine Meter for Blood Testing

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**Background and Objective:** For reliability of laboratory results, all methods, instruments, and reagents should be evaluated. The Nova StatSensor creatinine meter is a hand-held device for determination of creatinine concentration in the whole blood. Therefore, the device has to be validated or verified before performing.

**Material and Method:** Observational analysis method with cross sectional design was used in this evaluation. The commercial reagents and coded samples were prepared for linearity, precision, accuracy, and interference studies.

**Results:** The linear measurement range of 1.3 to 9.5 mg/dL was verified with the recovery results between 91.6 to 105.0%. Total imprecision demonstrated by coefficient of variation (CV) was 6.4 to 8.9 CV%. Linear regression was  $y = 0.946x + 0.103$ ,  $r = 0.992$ ,  $r^2 = 0.984$ . The bias was calculated from our data using regression equation. Our results demonstrated the accuracy was acceptable. Glucose level of 200 mg/dL and 400 mg/dL created the high difference between baseline creatinine (1.2 mg/dL and 2.8 mg/dL) and creatinine measured in the presence of interference was 25.0%, 16.7%, 14.3%, and 19.7% respectively.

**Conclusion:** Our results demonstrated that the device provides reliable creatinine measurement and could be used in point-of-care testing. Use of this device in diabetic patients with high glucose level of  $\geq 200$  mg/dL is not recommended.

**Keywords:** Analytical performance, Creatinine meter, POCT

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A currently dramatic increase in using contrast media in image analysis induce kidney risks such as contrast-induced nephropathy (CIN) and nephrogenic systemic fibrosis in patients with impaired renal function<sup>(1,2)</sup>. To avoid kidney problems induced by radio-contrast media using in computed tomography (CT) or magnetic resonance imaging (MRI) procedures, the need to assess patients' kidney function before they undergo radiologic procedures with contrast agents is concerned<sup>(3)</sup>. Therefore, it is important to measure serum creatinine and calculate for estimating the glomerular filtration rate (eGFR). However, many patients arrive for CT or MRI without having recent creatinine results or eGFR available in their medical records. Consequently, several hospitals have prompted to implement point-of-care testing (POCT) for rapid creatinine assessment of patients' kidney function. The Nova StatSensor creatinine is a hand-held point-of-care (POC) device designed to perform laboratory testing

at or near the site where clinical care is delivered<sup>(4)</sup>. Although the device has been recently approved in North America, an evaluation of POC instruments before implementation is required due to limitation of reliability of its performance when compare with central laboratory equipment.

The objectives of the present study were to evaluate the reliability of creatinine result performed by the Nova StatSensor, therefore the assessment of linearity, precision, accuracy, and interference was designed. The central laboratory results, using Jaffe rate method, was assigned as a comparative method used for comparative study. In addition, due to concept of validation/verification has just been recently purposed, then only a few studies and data are available especially in developing countries. Therefore, the authors also aimed to demonstrate the evaluation process and data as to be a basic data for other laboratories in the same region.

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## Material and Method

### Setting

The present study included the assessment of linearity, precision, accuracy, and interference were

followed Clinical and Laboratory Standards Institute (CLSI) guidelines. It was submitted to the Institutional Review Board (IRB) of the hospital for approval (project registration number 155-18-11), and was waived due to no data linked to patients. Patient specimens were assigned a number code to remove any identification. Laboratory staff that operated the meters was trained to be familiar with the device before the present study. Routine daily QC was performed as manufacturer's recommendation<sup>(5)</sup>. The present study was conducted at the Laboratory Department, Bumrungrad Hospital, Bangkok, Thailand.

### **Blood samples and materials**

Five linearity solutions from Nova StatSensor creatinine linearity kit (Cat No.44037, Lot numbers 5509170241, 5509182242, 5509173243, 5509170244, and 5509180245) were used for linearity experiment. Three levels of Nova StatSensor quality control (QC) materials (Level 1, Cat No.43921, Lot numbers 5010350241; Level 2, Cat No.43922, Lot numbers 5010350242; and Level 3, Cat No.43923, Lot numbers 5010350243) were used in precision study. Forty heparinized specimens with hematocrit between 30 to 60% were randomly selected from daily tested specimens at central laboratory. One milliliter (1 mL) each was taken from eight specimens daily for five days. All samples were coded to remove any identification, and were used for comparative study. Then more two heparinized samples collected in the same way as done for comparative study were used for interference study. D(+)-Glucose (Merck), molecular weight 180.16 g/mol, Cat No.1.08337.100, Lot number K38076537833) was used for preparation of 20% spiked glucose solution for interference study.

### **Method evaluation**

#### **Linearity**

Nova StatSensor commercial creatinine linearity kit (range of 1.3-9.5 mg/dL, levels of 1.3, 2.2, 4.0, 6.4, and 9.5 mg/dL) was used to evaluate the linearity or analytical measurement range (AMR) of the device. Each level was performed in duplicate and the recovery between 90 to 110% of each concentration from the assigned values was expected for linearity<sup>(6,7)</sup>.

#### **Precision**

Within-run and between-day (20 office days) were assigned by repeating analysis (n = 20) of three levels of QC materials (level 1 = 0.5-1.4 mg/dL, level 2 = 1.5-2.8 mg/dL, level 3 = 4.5-7.5 mg/dL).

The precision was expressed by coefficient of variation (CV). The CV of  $\leq 10\%$  of each level was accepted<sup>(3,4,8,9)</sup>.

#### **Accuracy**

Forty heparinized samples were used for comparative study between Nova StatSensor (test method) and Jaffe rate method (Beckman Coulter DxC 800, Synchron<sup>®</sup> System) of the central laboratory (comparative method). The kinetic alkaline picrate is used in Jaffe rate method to determine the concentration of creatinine in samples such as serum, plasma, or urine. Creatinine from the sample combined with the reagent, produces a red color complex, which the absorbance is read at 520 nm. The concentration of the creatinine in the sample is directly measured from the observed rate measurement<sup>(10,11)</sup>. Deming linear regression and Pearson's correlation coefficient (r) and coefficient of determination ( $r^2$ ) were used for evaluation the results. The accuracy was accepted if they were within 0.2 mg/dL limit when creatinine level < 1.0 mg/dL and 20% if creatinine level of > 1.0 mg/dL<sup>(12-14)</sup>.

#### **Interference**

Interference study was performed by spiking two heparinized samples with high concentration glucose. Creatinine in each sample was determined as baseline before samples were spiked. Two heparinized samples were prepared to have glucose level of 200 mg/dL and 400 mg/dL. Each sample was measured for creatinine by Nova StatSensor in duplicate. A  $\geq 15\%$  difference between baseline creatinine and creatinine measured in the presence of interference (glucose 200mg/dL and 400 mg/dL) was considered significant<sup>(4,15)</sup>.

### **Results**

Evaluation of the analytical performance of the Nova StatSensor creatinine meter for blood testing was done for validation/verification of linearity, precision, accuracy, and interference. The results of the study were described and demonstrated by tables and figures as followings.

Linearity study results using Nova StatSensor commercial creatinine linearity kit (range of 1.3-9.5 mg/dL) was verified with the recovery results between 91.6 and 105.0% are demonstrated in Table 1 and Fig. 1.

Precision of Nova StatSensor was determined from within-run and between-day imprecision studies.

**Table 1.** Linearity study was performed by using Nova StatSensor commercial creatinine linearity kit (range of 1.3-9.5 mg/dL). The recovery results between 91.6-105.0% were demonstrated. The linearity between 1.3-9.5 mg/dL was verified

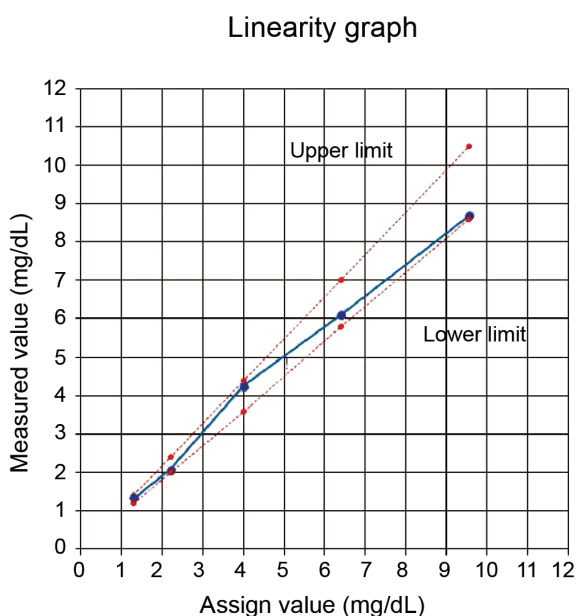
Linearity kit	Assigned value (mg/dL)	Nova StatSensor		Mean (mg/dL)	Recovery (%)
		1 <sup>st</sup> test (mg/dL)	2 <sup>nd</sup> test (mg/dL)		
Level 1	1.3	1.36	1.31	1.3	100.0
Level 2	2.2	2.09	2.06	2.1	95.5
Level 3	4.0	4.10	4.39	4.2	105.0
Level 4	6.4	6.22	5.99	6.1	95.3
Level 5	9.5	8.58	8.77	8.7	91.6

Total imprecision was calculated as well. All precision results are shown in Table 2. The % CV of within-run, between-day, and total imprecision of level 1, 2, and 3 were 5.5%, 4.7%, 4.1%, 4.5%, 7.6%, 4.9%, 7.1%, 8.9, and 6.4% respectively. All CV results were  $\leq 10\%$ . The results demonstrated the precision of the device was acceptable.

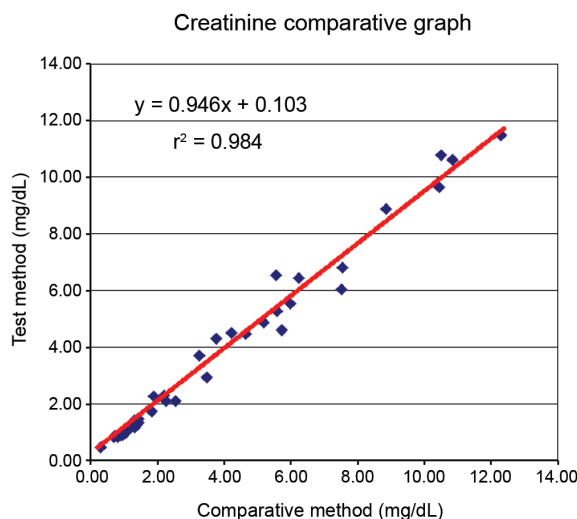
Forty heparinized specimens with hematocrit between 30 and 47%, and creatinine between 0.3 and 12.3 mg/dL were used for comparative study between Nova StatSensor (test method) and Jaffe rate method (Beckman Coulter DxC 800, Synchron<sup>®</sup> System) of

the central laboratory (comparative method). The comparative graph is demonstrated by Fig. 2. The regression equation and correlation (r) were calculated. The authors regression equation was  $y = 0.946x + 0.103$ ,  $r = 0.992$ ,  $r^2 = 0.984$ . The  $r^2$  value demonstrated high correlation. Then, the bias was calculated from our data using our regression equation. Our bias of creatinine  $< 0.1$  mg/dL was very from 0.0 and 0.2 mg/dL, and bias of creatinine  $> 1.0$  mg/dL was varied from 0.3 and 19.7%. Our comparative study demonstrated that the device had acceptable accuracy.

Two heparinized samples were spiked with high concentration glucose were used for interference study. The difference between baseline creatinine and



**Fig. 1** The linearity results are presented by linearity graph. All levels from 1.3-9.5 mg/dL are verified and represented by solid line, and located within acceptable area (recovery  $\pm 10\%$ , upper limit and lower limit, dash lines)



**Fig. 2** The comparative results of 40 samples, creatinine range between between 0.3-12.3 mg/dL, are demonstrated by comparative graph, with regression equation was  $y = 0.946x + 0.103$ , and  $r^2 = 0.984$ . Our  $r^2$  value demonstrated high correlation

**Table 2.** Within-run and between-day imprecision were determined for evaluation of precision of Nova StatSensor. Total imprecision was calculated as well. The results shown all %CV were  $\leq 10\%$ . The results demonstrated the precision of the device were acceptable

	Level 1	Level 2	Level 3
Within-run imprecision			
Mean creatinine (mg/dL)	1.05	2.27	6.11
Standard deviation (mg/dL)	0.06	0.11	0.25
Within-run imprecision (%CV)	5.50	4.70	4.10
Between-day imprecision			
Mean creatinine (mg/dL)	1.01	2.14	6.21
Standard deviation (mg/dL)	0.05	0.16	0.30
Between-day imprecision (%CV)	4.50	7.60	4.90
Total imprecision (%CV)	7.10	8.90	6.40

**Table 3.** Two samples with baseline creatinine of 1.2 mg/dL and 2.8 mg/dL. Interference determination was studied by adding high glucose concentration to till glucose level of 200 mg/dL and 400 mg/dL was achieved. The difference between baseline creatinine and creatinine measured in the presence of interference was 25.0%, 16.7%, 14.3% and 19.7% respectively

	Baseline Cr (mg/dL)	1 <sup>st</sup> test (mg/dL)	2 <sup>nd</sup> test (mg/dL)	Average (mg/dL)	Difference* (%)
Sample No. 1					
Glucose 200 mg/dL	1.2	1.4	1.6	1.50	25.0
Glucose 400 mg/dL	1.2	1.4	1.4	1.40	16.7
Sample No. 2					
Glucose 200 mg/dL	2.8	3.3	3.1	3.20	14.3
Glucose 400 mg/dL	2.8	3.3	3.4	3.35	19.7

\* A difference between baseline creatinine and creatinine measured in the presence of interference (glucose 200 mg/dL and 400 mg/dL)

creatinine measured in the presence of interference was calculated. The results of the present study are shown in Table 3. The present results demonstrated that at high glucose level of 200 mg/dL and 400 mg/dL, creatinine results performed by the device should be concerned.

### Discussion

The Nova StatSensor creatinine meter was evaluated for linearity, precision, accuracy, and interference using commercial reagents and coded removed identification samples and compared against central laboratory values.

Although measurement range claimed by manufacturer is 0.3 to 12.0 mg/dL, the available of Nova StatSensor commercial creatinine linearity kit are 1.3, 2.2, 4.0, 6.4, and 9.5 mg/dL. Linearity study results using Nova StatSensor commercial creatinine linearity kit at levels of 1.3, 2.2, 4.0, 6.4, and 9.5 mg/dL

were assessed and the recovery results were 100.0%, 95.5%, 105.0%, 95.3%, and 91.6%, respectively (Table 1). Therefore, measurement range verified by the present study was 1.3 to 9.5 mg/dL. These results were consistent with some previous studies<sup>(4,16)</sup>. Yet the lowest and highest level of 1.3 to 9.5 mg/dL are narrower than the manufacturer's claimed, the highest of 9.5 mg/dL is high enough for clinical decision to evaluate the renal function of patients before radio-contrast study. The lowest of 1.3 mg/dL seemed to be not low enough for kidney function judgment; anyhow, it was limitation of reagents provided. The authors' laboratory approved a measurement range of Nova StatSensor from 1.3 to 9.5 mg/dL. Any creatinine level of lower than 1.3 mg/dL is concerned, however, the total precision of lower results at mean levels of 1.01, and 1.05 mg/dL was 7.1 CV% (Table 1) and the accuracy study of results from 0.3 to 1.0 mg/dL were acceptable (Fig. 1). All the present information was

prepared and informed clinicians for their decision. More detail will be further discussed below. In general, POC instruments do not perform as well as those in the central laboratory therefore any doubt of results getting from POCT should be confirmed by more reliable methods performed in the central laboratory. Actually linearity is not the performance characteristic that needs to be validated. Never the less it is important to determine the measurement range of a method to set the lowest and highest results that are reliable and can be reported<sup>(7)</sup>. Although the measurement range has already been claimed by the manufacturers, check those claims by laboratory before services are required<sup>(6)</sup>.

Two important performance characteristics that need to be validated are precision and accuracy. A replication experiment is typically performed by obtaining test results on at least 20 samples of the same material and then calculating the mean, standard deviation, coefficient of variation. The replication experiment estimates the random error caused by factors vary in the operation of method. Ideally, the test variation should be small. The present study (Table 2) demonstrated that Nova StatSensor had acceptable precision with total imprecision of 6.4 to 8.9 CV%. The present results were not different from instruction information when compared with the manufacturer's imprecision of 8, 6, and 4 CV% at creatinine levels of 1, 5, and 10 mg/dL, respectively<sup>(5)</sup>. Regarding accuracy, a comparative experiment is planned and performed to estimate inaccuracy or systematic error. Forty different patient specimens with creatinine levels cover the entire measurement range claimed by manufacturer were tested by comparative method (Beckman Coulter DxC 800, Synchron<sup>®</sup> System used by central laboratory method) and test method (Nova StatSensor, Nova Biomedical). Linear regression equation from the present results was  $y = 0.946x + 0.103$ ,  $r^2 = 0.981$  (Fig. 1). The authors' correlation was very good; in another words 98.1% of our data were linear with low intercept (0.103 mg/dL) and almost perfect slope (0.946). The bias was calculated from our data using our regression equation. The authors found that the presented bias of creatinine  $< 0.1$  mg/dL varied from 0.0 to 0.2 mg/dL, and bias of creatinine  $> 1.0$  mg/dL varied from 0.3 to 19.7%. Regarding to manufacturer's criteria our results demonstrated that the device had acceptable accuracy. Results of the precision and accuracy were similar to studies of other authors as well<sup>(4,17)</sup>.

Interference study is performed to estimate the systematic error caused by materials that may be

present in the specimen being analyzed. Glucose is one of the common and potential interferences, so the authors designed a study performed by spiking two heparinized samples with high concentration glucose. Two heparinized samples were spiked to have a glucose level of 200 mg/dL and 400 mg/dL (Table 3). The presented difference between baseline creatinine and creatinine measured in the presence of interference (glucose 200 mg/dL and 400 mg/dL) were 25.0%, and 16.7% for baseline creatinine of 1.2 mg/dL, and 14.3%, and 19.7% for baseline creatinine of 2.8 mg/dL. Almost all these differences were  $\geq 15\%$ , and considered significant. The authors also noticed that glucose interference caused false positive or higher creatinine results. Although up to 500 mg/dL of glucose is informed to exhibit no interference by the manufacturer's instruction<sup>(5)</sup>, the present results demonstrated that the level of glucose  $> 200$  mg/dL should be concerned. The authors recommend to avoid the performing of creatinine by the device in those patients who have glucose  $> 200$  mg/dL. Further study for interference by glucose should be encouraged.

This is the first report of an analytical evaluation of the Nova StatSensor creatinine meter for whole blood in Thailand. The authors found that the precision in terms of total imprecision is in acceptable criteria with broad measurement range that can cover the clinical requirement for patients who arrive for CT or MRI without having recent creatinine results or eGFR available in their medical records. The results of creatinine performed by the device correlated very well with central laboratory measurements. In conclusion, the presented results demonstrated the device provides reliable creatinine measurement and could be used in point-of-care testing. However, the authors recommended that using in diabetic patients with high glucose level should be avoided.

#### Acknowledgements

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#### Potential conflicts of interest

Meditop Co., Ltd. was support reagents and consumables for this study.

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## การประเมินความสามารถในการตรวจวิเคราะห์ครีเอทีนินในเลือดของเครื่อง Nova StatSensor

ชญาณิชฐ์ ศรีหงส์, กวินัญญาณี แพ่งสภา, กัณญอร เชื้อบุญมี, ยงยุทธ โฉมพันธ์ุ, นวพรรณ จารุรักษ์

**ภูมิหลังและวัตถุประสงค์:** เพื่อผลการตรวจวิเคราะห์ทางห้องปฏิบัติการที่น่าเชื่อถือ วิธีการ เครื่องมือ และน้ำยา จะต้องได้รับการประเมินก่อนการนำมาใช้ เครื่อง Nova StatSensor creatinine meter เป็นเครื่องขนาดมือถือที่ใช้สำหรับตรวจวิเคราะห์ระดับ creatinine ในเลือดครบส่วน ดังนั้นจึงต้องได้รับการประเมินโดยการทำ method validation หรือ verification ก่อนการใช้งาน

**วัสดุและวิธีการ:** รูปแบบการวิจัยสำหรับการศึกษานี้ใช้ observational analytical method แบบตัดขวาง น้ำยาเชิงพาณิชย์ และตัวอย่างเลือดผู้ป่วยที่เลือกใช้ซึ่งได้รับการลบข้อมูลสืบค้นถึงผู้ป่วยได้รับการจัดเตรียม เพื่อใช้ในการศึกษาพิสัยการตรวจวิเคราะห์ ความแม่นยำ ความถูกต้อง และสารรบกวน

**ผลการศึกษา:** ผลการประเมินพิสัยการตรวจวิเคราะห์มีค่าระหว่าง 1.3 ถึง 9.5 มก./มล. และมีค่า recovery อยู่ระหว่างร้อยละ 91.6 ถึง 105.0 ส่วนค่าความแม่นยำรวมแสดงด้วยค่าสัมประสิทธิ์ของความแปรปรวนมีค่าร้อยละ 6.4 ถึง 8.9 สมการถดถอยเชิงเส้นมีค่า  $y = 0.946x + 0.103$ ,  $r = 0.992$ ,  $r^2 = 0.984$  ซึ่งผ่านเกณฑ์การยอมรับ การศึกษาสารรบกวนพบว่ากลูโคสที่ระดับ 200 มก./มล. และ 400 มก./มล. รบกวนการตรวจวิเคราะห์ creatinine ที่ระดับ 1.2 มก./มล. และ 2.8 มก./มล. ถึงร้อยละ 20.5, 16.7, 14.3 และ 19.7 ตามลำดับ

**สรุป:** ผลการศึกษานี้แสดงว่าเครื่องตรวจวิเคราะห์นี้ที่เป็นเครื่องสำหรับใช้ ณ จุดที่ดูแลรักษาผู้ป่วยมีความน่าเชื่อถือ ส่วนการใช้ในผู้ป่วยเบาหวานที่มีระดับน้ำตาล  $\geq 200$  มก./มล. นั้นไม่แนะนำ

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