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Evaluation of the Hitachi 911 for Routine Urine Analysis and for Measurement of Various Special Serum Analytes

By *Jan P. van Straalen, Anja Leyte, Joop A. Weber, Jozef P. M. C. Gorgels* and *Gerard T. B. Sanders*

Laboratorium voor Algemene Klinische Chemie, Academisch Ziekenhuis bij de Universiteit van Amsterdam, Amsterdam, The Netherlands

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Summary: The Boehringer Mannheim Hitachi 911 is a selective analyzer for 35 different methods including 3 ion-selective electrode (ISE) methods. We have evaluated this analyzer primarily to obtain objective information on its applicability for routine urine analyses in our laboratory. We also implemented appropriate assays for various special serum- and whole blood-tests, some for the first time on the Hitachi 911 and some with modified settings. Analytical evaluation involved NCCLS EP5-T2 (imprecision), NCCLS EP6-P (linearity), *Krouwer* 27 (multifactor) and *Passing & Bablok* (method comparison) evaluation protocols. With the exception of evidence of systematic erroneous sample predilution, overall results were favourable. Practicability of the Hitachi 911 was judged by simulating daily routine. During a period of two weeks, daily urine samples were rerun on the Hitachi 911, leading to a gain of about 50% in total processing time. It was concluded that the Hitachi 911 meets the requirements in terms of analytical performance, reliability, versatility and speed for an analyzer to be used in a routine (urine) setting, while having a distinct role in special (serum/whole blood) measurements.

Introduction

In our 1000 bed academic hospital a relatively large number of urine analyses are performed daily. In looking for a replacement for our dedicated analyzer for urinalysis, we realized that not many data specifically concerning urine are available as a basis for selection. The choice of a new clinical chemistry analyzer requires the objective assessment of its analytical and practical performance. The former aspect is nowadays evaluated routinely with the use of one or more defined protocols and algorithms. Based on previous experience (1) we have decided to use evaluation protocols developed by the American National Committee for Clinical Laboratory Standards (NCCLS) for this study. Thus, NCCLS EP5-T2 (EP5) and EP6-P (EP6) (2, 3) are one-at-a-time protocols used for testing imprecision and linearity, respectively. The EP5 protocol provides data on within-run, run-to-run, day-to-day and total imprecision. Linearity according to the EP6 protocol is either present or absent; in the latter case, and for very precise assays (1), quantification of the deviation from linearity is possible with the use of the data generated in the *Kroll & Emancipator* algorithm (4, 5). The multifactor *Krouwer* 27 protocol (6, 7) provides a simultaneous estimation of various variables, including drift and carry-over. In addition, methods can be compared according to *Passing & Bablok* (8), relating the measurement of analytes by new tests and/or analyzers to reference- or standard methods. In the present study, we have used the above protocols and algorithms to evaluate the performance of the Hitachi 911 for assays measuring the following analytes: sodium, potassium, calcium, phosphate, urea, creatinine, glucose and total protein in urine. We also tested determinations of lactate, iron, ferritin, haptoglobin, transferrin, digoxin, vitamin B_{12} and folate in serum, and cyclosporin in whole blood.

Next to the analytical quality, the practicability performance of an analyzer plays an important role in the medical laboratory. This was evaluated as follows: following the manufacturers' instructions with respect to calibration and control frequency, we gained information on various aspects of daily use of the Hitachi 911 in routine

practice. For a period of 15 days and extrapolated to one year, all routine urine samples were analyzed both using the present methods and on the Hitachi 911, and turnaround times were compared.

Materials and Methods

Analyzer

The Hitachi 911 is a selective access analyzer with a capacity of 35 different tests including 3 ISE methods. Its output rate is 360 tests per hour without ISE and 720 tests per hour with ISE. The ISE unit (indirect method) consists of three flow through electrodes measuring sodium, potassium and chloride. By means of two reagent-arms, one to four reagents can be added to a sample. The optical system contains a halogen lamp, a wavelength grating device and twelve wavelength dependent diodes. The instrument has flexible measuring windows allowing measurements from 3 to 16.5 minutes. The measurement cycle is 20 seconds. All assays are performed at 37 °C. The reagents are kept refrigerated at 10 °C.

Assays

The Hitachi 911 has so called defined channels for fixed applications (i. e. reagents provided by Boehringer Mannheim (BM)), and open channels which give the user the opportunity to program analytical parameter settings freely. In total, 22 tests were installed during the evaluation period (not all are discussed here) (tab. 1). Urine assays were performed as described by the manufacturers (tab. 1), except for the following cases which involved modifications in the settings defined by BM: calcium, glucose and total protein. For calcium and glucose, this related to the calibration methods used and was intended to improve the linearity and the

Tab. 1 Overview of assays investigated on the Hitachi 911. Suppliers: BM: Boehringer Mannheim; SYVA: Syva diagnostics. Type of analysis: 2: 2 point end; 3: 2 point rate; 4: multipoint rate. Sample volume (1*): 11 times prediluted sample; Sample volume (2*): 26 times prediluted sample.

Analyte	Method (supplier)	Type of analysis	Calibration type	Wavelength (nm) (prim./-sec.)	Sample volume (µl)	Reagent 1 (µl)	Reagent 2 (µl)	Reagent 3 (µl)	Reagent 4 (µl)
Sodium, Potassium	ISE		linear		20	1220	600	–	–
Calcium	Cresolphthalein (BM)	2	linear	340/700	10	250	100	–	
Phosphate	Molybdate (BM)	2	linear	340/700	5 (1*)	250	–	110	–
Urea	Urease (BM)	3	linear	340/415	4 (1*)	320	80	–	–
Creatinine	Jaffe (BM)	3	linear	505/570	2	250	–	50	–
Glucose	Hexokinase (BM)	2	spline	340/415	3	250	50	–	–
Protein	Benzothonium-Cl (BM)	2	spline	505/700	15	250	–	100	135
Iron	Ferrozine (BM)	2	linear	570/700	20	250	–	50	–
Transferrin	Tina-quant (BM)	2	logit-log	600/700	3	330	–	70	–
Ferritin	Tina-quant (BM)	2	logit-log	800	10	190	–	50	–
Cyclosporin	EMIT (SYVA)	2	logit-log	340/700	30	150	70	–	–
Digoxin	Cedia (BM)	4	linear	570/660	18	100	–	140	90
Lactate	Enzymatic (BM)	2	linear	340/376	4	200	50	50	–
Haptoglobin	Immunoturbidimetric	2	logit-log	340/700	4 (2*)	200	–	43	–

linear range. In the original BM calcium determination, a 2 point calibration was employed (0 and 2.5 mmol/l), whereas our application involved a 5 point calibration (0, 1.25, 2.50, 3.75, and 5 mmol/l) calculated with linear regression. The BM glucose determination, also with a two point calibration (0 and 20 mmol/l), was modified to involve a 5 point calibration (0, 5, 10, 25 and 50 mmol/l) calculated with cubic spline curve fitting. It is important to note that as with patient samples, the calibration samples with a glucose concentration of 25 mmol/l or higher are automatically prediluted (eight times, 30 µl + 210 µl) by the analyzer. The total protein assay was modified with a third reagent (surfactant or Brij 35, 100 g/l final), to be added just before the cuvette washing step. This reagent prevents contamination of the cuvettes with denaturated proteins. Furthermore, one analyte was measured with dual settings: ferritin, using two different calibration characteristics namely

(a): „lower extended range"-measuring range 0–400 µg/l and 15 µl sample volume (Ferritin 1);

(b): „normal range"-measuring range 0–800 µg/l and 5 µl sample volume (Ferritin 2).

Calibration

An aqueous solution with the following composition was used for the calibration of all urine analytes except sodium, potassium and total protein: calcium 2.5 mmol/l, phosphate 25 mmol/l, urea 250 mmol/l, creatinine 8.75 mmol/l, glucose 5 and 200 mmol/l.

Sodium and potassium were calibrated with the BM Na^+, K^+, Cl^- standards.

Total protein was calibrated with Preciset U/CSF Protein (BM).

The following calibration materials were used for the serum tests:

CFAS protein (BM) for transferrin;

Preciset Ferritin (BM) for ferritin;

Orion calibration set (Orion Diagnostica, Espoo, Finland) for haptoglobin.

Digoxin and cyclosporin were calibrated with standards provided by BM (CEDIA digoxin calibrators) and Syva Diagnostica (Syva Diagnostica, San Jose, CA, USA), respectively.

Calibrators included in the CEDIA vitamin B_{12} and folate test kit (Microgenics Corporation, Concord, USA) were used for these analytes.

Diluted lactic acid calibrator (BM) was used for the calibration of lactate.

A Fe^{2+} solution from Baker chemicals (J. T. Baker Inc, USA) was used as a calibrator for the determination of iron.

Imprecision protocol

Imprecision was tested according to the NCCLS EP5 protocol (2). This protocol involves the measurement of analyte concentrations at two levels, twice per day in duplicate for twenty days, followed by calculation of within-run, between-run, run-tu-run and total imprecision. As sample material various commercial control preparations were used:

Urinorm (Instruchemie, Hilversum, the Netherlands) for the urine analytes;

Bio-Rad (Anaheim, CA, USA) Lyphocheck immunoassay control levels 1, 2 and 3 for digoxin, ferritin and B_{12}/folate;

Bio-Rad Liquicheck immunology control (human) levels 1 and 2 for haptoglobin and transferrin;

Bio-Rad Lyphocheck whole blood control (human) levels 1, 2 and 3 for cyclosporin;

Precinorm U and Precipath U (BM) for iron;

Precinorm S and Precipath S (BM) for iron and lactate;

Precinorm TDM levels 1, 2 and 3 (BM) for digoxin, and

Precinorm P and Precipath P (BM) for haptoglobin, transferrin, and ferritin.

Data were checked on outliers. When an outlier exceeded 5.5 times the standard deviation of the test it was removed from the data set (2).

Linearity

Linearity was tested according the NCCLS EP6 protocol (3). As starting material for the urine analytes we used distilled water ("low") and an aqueous solution with appropriate concentrations of the various analytes ("high"). Two human serum pools were used ("low" and "high"). In some cases (ferritin and digoxin) we had to spike the pooled serum with a stock solution. The spiking method complied with the recommendations of the NCCLS (3). Following the EP6 protocol, mixtures of the low and high pool were made according to the following scheme: low, 3 low + 1 high, 2 low + 2 high, 1 low + 3 high, high. The 5 level mixtures were then tested in two separate runs in quadruplicate. Data were plotted on an x,y linear-linear graph plot and examined visually. In addition, the lack of fit (LOF) of the linear model was determined mathematically with the following algorithms:

$$\begin{aligned}
LOF &= RSS - T_E \\
RSS &= \text{Residual sum of squares} \\
RSS &= [20 \cdot \Sigma(\Sigma y^2) - (\Sigma y)^2] / 20 - [20 \cdot (\Sigma(x \cdot \Sigma y)) \\
&\quad - (4 \cdot \Sigma x) \cdot (\Sigma y)]^2 / 20 \cdot [80 \cdot \Sigma x^2 - (4 \cdot \Sigma x)^2] \\
T_E &= \text{Remainder sum of squares} \\
T_E &= \Sigma[\Sigma y^2 - (\Sigma y)^2]
\end{aligned}$$

Then,

$$G = 5(LOF)/T_E.$$

G was compared with the appropriate critical value of the F distribution. If G was smaller than this critical value, the hypothesis of a linear fit was not rejected. For very precise assays, data with clinically acceptable linearity may be statistically declared non-linear (1). For this reason data from the EP6 observations were also evaluated with the BMD-P5R polynominal regression calculation program (BMDP Statistical Software Inc, USA) in order to obtain 1st, 2nd and 3rd order polynomes. The 3rd order polynomes were imported in the *Kroll & Emancipator* algorithm (4, 5) to obtain quantitative measures of relative non-linearity. (Results < 2.5%, from this algorithm, indicate a good linear fit).

Drift and carry-over

Drift and carry-over were evaluated according to the *Krouwer* 27 protocol (6, 7) with which one can discriminate between linear drift, quadratic drift and concentration dependent drift. In addition, this protocol quantitates the sample related carry-over independently. A further result of the *Krouwer* 27 protocol provides an estimation of the (non)-linearity and within-run imprecision. In single runs three concentration levels of human serum [low (± 0), medium (mixture of low and high) and high (maximum detectable value)] were analyzed nine times in a sequence as prescribed. During the evaluation period the protocol was run in duplicate and the results were interpreted separately.

Method comparison

The methods investigated on the Hitachi 911 (tab. 1) were compared with those currently in use in our hospital. With the

exception of sodium and potassium, urine assays were compared with measurements using a continuous flow system (SMA II) from Technicon (Technicon Inc, Tarrytown, New York, USA). The following analytes were measured spectrophotometrically: calcium (cresolphthalein complexing method), phosphate (molybdate UV method), urea (diacetylmonoxime method), creatinine (alkaline pricrate method), and glucose (glucose oxidase-peroxidase method), for more detailed descriptions see l. c. (9). Sodium and potassium measured on the Hitachi 911 by indirect ISE were compared with flame emission spectrometry (SMA II). Cyclosporin, digoxin and ferritin were compared with the radioimmunoassay methods used in our hospital: cyclosporin was determined with CYCLO-Trac® reagent provided by Incstar (Incstar, Minnesota, USA); reagents for the determination of digoxin and ferritin were obtained from Diagnostic Products Corporation (Diagnostic Products Corporation, Los Angeles, USA). Transferrin and haptoglobin were compared with a nephelometric- and turbidimetric method, respectively. For transferrin we used reagents from Behringwerke (Behringwerke AG, Marburg, Germany) adapted on a Behring nephelometer type 200. The turbidimetric determination of haptoglobin was performed using reagent from Atlantic antibodies (Incstar, Minnesota, USA) adapted on a COBAS BIO analyzer (Hoffmann La Roche, Switzerland). Iron was measured using the same assay on both the Hitachi 911 and the Hitachi 747.

Statistics

For calculation of imprecision, linearity and *Krouwer* 27 parameters, we used EVAL-KIT software (CKCHL, Tilburg, the Netherlands). *Passing & Bablok* mathematics (8) were used for the calculation of the method comparison parameters.

Practicability performance

Practicability assessment was performed in the following manner: during a period of 15 working days we reanalysed our daily urine routine samples on the Hitachi 911. All actions were administrated such as number of (re)-calibrations because of reagent change and sample reruns, and in addition turnaround time was assessed.

Results and Discussion

General

Results for vitamin B_{12} and folate tests are not included in this paper. Although no proper methodology was available, we nevertheless attempted to implement these assays on the Hitachi 911. However, we did not succeed: within-run coefficients of variation (CVs) were routinely over 15%. This may relate to the fact that the Hitachi 911 does not allow the incubation times of over 15 min that are recommended by the assay manufacturer. We did not pursue this any further.

Imprecision

Data for the within-run, run-to-run, day-to-day and the total imprecision for the urine analytes are summarized in table 2. Imprecision data for the serum- and whole blood tests are given in table 3. It should be noted that the way imprecisions are calculated in this protocol (2) may lead to within-run CVs being larger than day-to-day CVs (e. g. calcium, 2.76 mmol/l). For all urine analytes, acceptable CVs were found: total CVs were less than 3.0%, except for total protein (3.5% at the low control level). With regard to creatinine, sodium and potassium, these results are in agreement with those found in a recently published multicentre Hitachi 911 evaluation predominantly focussed on serum and plasma analytes (10). Some of the control materials appeared not to be suitable for this kind of imprecision evaluation: for iron in Precinorm S and Precipath S inexplicable shifts in measured levels were noticed, whereas the use of Precinorm U and Precipath U resulted in CVs ranging from 1.1 to 3.2%,

Tab. 2 Imprecision of urine assays performed on the Hitachi 911. Imprecision was quantitated using the NCCLS EP5-T2 protocol (2) as described in Materials and Methods.

RD: creatinine, reduced volume; DL: creatinine, sample predilution.
CV: coefficient of variation (for calculations, see figure 1).

Analyte	Mean concentration	Within-run CV (%)	Run-to-run CV (%)	Day-to-day CV (%)	Total CV (%)
Sodium	68.47 mmol/l	0.64	0.85	1.11	1.34
Sodium	134.13 mmol/l	0.46	0.86	0.69	0.98
Potassium	49.95 mmol/l	0.56	0.80	2.00	2.12
Potassium	96.92 mmol/l	0.66	1.12	2.80	2.94
Calcium	1.42 mmol/l	1.41	1.41	1.41	1.41
Calcium	2.76 mmol/l	2.54	2.17	1.44	2.90
Phosphorus	19.68 mmol/l	1.78	1.37	1.37	2.13
Phosphorus	38.81 mmol/l	1.42	1.21	0.98	1.65
Urea	206.17 mmol/l	0.90	1.32	1.17	1.63
Urea	405.44 mmol/l	1.24	1.06	0.85	1.43
Creatinine RD	7.96 mmol/l	1.26	1.76	1.63	2.14
Creatinine DL	15.33 mmol/l	1.44	1.96	1.89	2.54
Glucose	6.89 mmol/l	1.31	1.45	1.02	1.74
Glucose	65.21 mmol/l	1.49	2.61	2.02	2.93
Total protein	0.57 g/l	1.75	1.75	1.75	3.50
Total protein	2.09 g/l	0.96	1.44	2.39	2.87

Tab. 3 Imprecision of serum and whole blood assays performed on the Hitachi 911.
Imprecision was quantitated using the NCCLS EP5-T2 protocol (2) as described in Materials and Methods.
Ferritin 1: new set points; Ferritin 2: extended measuring range. CV: coefficient of variation (for calculations, see figure 1). Information on the controls is provided in Materials and Methods.

Analyte	Mean concentration	Within-run CV (%)	Run-to-run CV (%)	Day-to-day CV (%)	Total CV (%)
Iron Precinorm S	10.04 µmol/l	2.79	2.69	15.04	15.34
Iron Precinorm U	15.31 µmol/l	2.09	2.35	2.29	3.20
Iron Precipath S	39.16 µmol/l	1.20	3.32	25.92	26.02
Iron Precipath U	22.93 µmol/l	1.31	2.44	2.53	3.18
Lactate Precinorm S	2.71 mmol/l	1.11	1.48	1.85	2.21
Lactate Precipath S	1.99 mmol/l	1.51	2.02	1.51	2.52
Digoxin 370-1	0.39 µg/l	15.38	10.26	23.08	25.64
Digoxin 370-2	1.69 µg/l	2.96	4.14	6.51	7.69
Digoxin 370-3	3.04 µg/l	1.97	3.29	4.28	5.26
Digoxin TDM-1	0.87 µg/l	9.22	6.92	8.07	11.53
Digoxin DTM-2	1.83 µg/l	2.74	2.19	6.02	6.57
Digoxin TDM-3	3.21 µg/l	2.18	2.18	5.30	5.61
Ferritin 1 Precinorm P	76.28 µg/l	2.61	5.55	5.20	6.78
Ferritin 1 Precipath P	327.37 µg/l	3.81	5.98	6.54	8.24
Ferritin 2 Precinorm P	78.52 µg/l	1.94	4.72	4.56	5.82
Ferritin 2 Precipath P	325.31 µg/l	1.63	2.92	5.49	5.98
Haptoglobin Precinorm P	1.27 g/l	3.16	3.16	3.16	4.73
Haptoglobin Precipath P	2.22 g/l	1.81	4.06	4.51	5.42
Transferrin Precinorm P	3.44 µg/l	1.75	2.33	2.04	2.91
Transferrin Precipath P	4.37 µg/l	2.06	2.29	1.60	2.52
Cyclosporin 561	97.57 µg/l	6.48	6.66	4.63	8.04
Cyclosporin 562	261.98 µg/l	4.44	3.27	6.42	7.51

comparable to previously published findings (10). Furthermore, controls provided by Bio-Rad showed extremely high CVs for ferritin, haptoglobin and transferrin, ranging from 9 to 16%. This is possibly caused by instability of these materials. As an alternative, we measured these analytes in Precinorm P and Precipath P for the EP5 protocol; this reduced the variation to 2.5 to 5.5%. For cyclosporin only one set of controls is available: Bio-Rad Lyphochek whole blood control. The rather high CVs for cyclosporin appear to be inherent to this material, since calibrators and patient material performed notably better. However, the EP5 procedure was not repeated with human material.

Linearity

Table 4 shows the results of the linearity evaluation for those analytes tested. In the specified ranges, all tests except the one for calcium were accepted as linear. For urinary calcium, if measured according to the serum specifications, linearity is lost above 5 mmol/l (calcium BM). Adaptation of the calcium calibration settings (see Introduction) to a 5 point instead of a two point procedure improved linearity (by visual inspection) up to approximately 9 mmol/l (calcium AMC) (fig. 1). It should be noted that although the glucose determination was linear up to a theoretical concentration of 200 mmol/l, the measured values were incorrect (glucose BM). Figure 2 illustrates that for all samples that were prediluted (i. e. with first measurement values higher than 20 mmol/l), final values of glucose concentration were about 20% lower than expected. Apparently, sample predilution by the Hitachi 911 is characterized by a systematic error. As a pragmatic solution, we have adapted the calibration procedure to include standards with values above 20 mmol/l, therefore requiring predilution, resulting in a correct response in the higher concentration range (glucose AMC) (fig. 2). The success of this problem solving procedure moreover indicates that the dilution error relates to the sample and/or diluent handling by the Hitachi 911. The error is therefore predicted to cause problems in any assay using sample predilution without calibration predilution.

Drift and carry-over

Drift and carry-over were tested for the same analytes as in the linearity evaluation (tab. 4), according to the *Krouwer* 27 protocol (6, 7). No significant drift or sample carry-over could be demonstrated with this sensitive protocol (data not shown).

In addition, total protein determination was tested for carry-over between serum and urine samples by using a sample tray intermittently filled with human serum and urine. Even in these extreme circumstances (total protein concentrations varying between 0 and 2.5 g/l), no carry-over was established.

Tab. 4 Linearity.
K & E: *Kroll & Emancipator* relative non-linearity (4, 5);
BM: original settings according to Boehringer Mannheim;
AMC: changed settings as described in Materials and Methods.

Analyte	x upper limits	x lower limits	y upper limits	y lower limits	*K & E* (%)
Sodium	200.00 mmol/l	0.00 mmol/l	203.00 mmol/l	1.60 mmol/l	0.227
Potassium	200.00 mmol/l	0.00 mmol/l	200.00 mmol/l	0.18 mmol/l	0.590
Calcium (BM)	10.00 mmol/l	0.00 mmol/l	7.73 mmol/l	0.00 mmol/l	2.814
Calcium (AMC)	10.00 mmol/l	0.00 mmol/l	9.43 mmol/l	0.00 mmol/l	0.484
Phosphate	50.00 mmol/l	0.00 mmol/l	49.60 mmol/l	0.00 mmol/l	0.052
Urea	500.00 mmol/l	0.00 mmol/l	516.00 mmol/l	0.00 mmol/l	0.066
Creatinine	25.00 mmol/l	0.00 mmol/l	24.18 mmol/l	0.00 mmol/l	0.396
Protein	3.00 g/l	0.00 g/l	2.99 g/l	0.00 g/l	0.492
Glucose (BM)	200.00 mmol/l	0.00 mmol/l	178.00 mmol/l	0.00 g/l	0.131
Glucose (AMC)	200.00 mmol/l	0.00 mmol/l	200.00 mmol/l	0.00 mmol/l	1.152
Iron	216.50 µmol/l	3.83 µmol/l	208.70 µmol/l	2.84 µmol/l	0.383
Ferritin (1)	319.00 µg/l	12.30 µg/l	406.63 µg/l	12.27 µg/l	1.052
Ferritin (2)	611.00 µg/l	12.30 µg/l	933.40 µg/l	12.66 µg/l	0.743
Digoxin	4.07 µg/l	0.14 µg/l	4.09 µg/l	0.19 µg/l	1.287

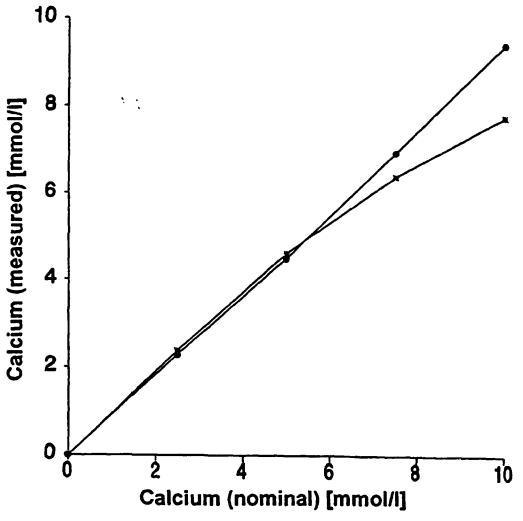

Fig. 1 Improved linearity of modified calcium assay.
Five calcium level mixtures were prepared as prescribed for linearity evaluation according to the NCCLS EP6 protocol (3), and calcium was measured using either the original BM settings (*; two point calibration) or the modified settings (●; five point calibration) as described in Materials and Methods.

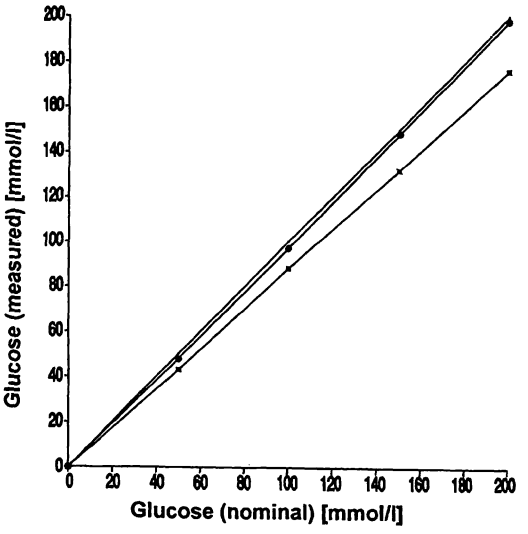

Fig. 2 Sample predilution error.
Five glucose level mixtures were prepared as prescribed for linearity evaluation according to the NCCLS EP6 protocol (3). Glucose was measured (involving sample predilution if [glucose] higher than 20 mmol/l) using a two point calibration without calibrator glucose concentrations above 20 mmol/l and therefore without calibrator predilution (*), and using a five point calibration with calibrator glucose concentrations above 20 mmol/l (●). (·): nominal [glucose] = measured [glucose].

Method comparison

The results of the method comparisons according to *Passing & Bablok* (8) are combined in table 5 including the measured ranges. For each method, samples were equally divided over the measuring range. In general, correlations between measurements on the Hitachi 911 and measurements with the currently used methods were acceptable. An optimal correlation was found for sodium and potassium measured with the Hitachi 911 ISE in comparison with a flame emission spectrometer. The glucose determinations correlated poorly in the lower section of the measuring range caused by the incapability of the SMA II to discriminate glucose values between 0–5 mmol/l. Data in this concentration range were not included in the statistical evaluation.

Assessment of practibility

Practicability evaluation related to the performance of the analyzer in daily routine use. This was investigated as follows: complying with the recommendations of the

Tab. 5 Method comparison for analytes measured on the Hitachi 911 and with reference or standard methods.
Method comparison was performed according to *Passing & Bablok* (8) as described in Materials and Methods. n: number of samples; Syx: standard error of estimated y; r: coefficient of correlation; (U): urine; Ferritin (1): new set points; Ferritin (2): extended measuring range.

Analyte	Compared with	n	Range	Linear regression	S_{yx}	r
Sodium (U)	SMA	119	1 – 240 mmol/l	y = 0.997 x + 1.001	2.90	0.999
Potassium (U)	SMA	119	1 – 130 mmol/	y = 1.032 x + 0.803	1.16	0.999
Calcium (U)	SMA	55	1 – 9 mmol/l	y = 0.953 x – 0.043	0.11	0.998
Phosphate (U)	SMA	119	1 – 50 mmol/l	y = 1.028 x – 0.803	1.41	0.993
Urea (U)	SMA	119	50 – 500 mmol/l	y = 1.058 x + 0.460	11.88	0.996
Creatinine (U)	SMA	118	0.7 – 22 mmol/l	y = 0.989 x – 0.079	0.41	0.996
Protein (U)	Protein Analyzer	108	0.1 – 7.5 g/l	y = 0.945 x – 0.053	0.17	0.992
Glucose (U)	SMA	43	5.0 – 219 mmol/l	y = 0.966 x – 0.771	2.10	0.998
Ferritin (1)	RIA	98	4 –4500 µg/l	y = 0.939 x – 4.636	101.69	0.989
Ferritin (1)	RIA	79	4 – 450 µg/l	y = 0.915 x – 4.028	47.51	0.867
Ferritin (2)	RIA	98	4 –4500 µg/l	y = 1.046 x – 4.785	95.56	0.992
Ferritin (2)	RIA	79	4 – 450 µg/l	y = 1.039 x – 4.879	65.24	0.827
Ferritin (1)	Ferritin (2)	99	4 –4500 µg/l	y = 1.128 x + 1.280	50.86	0.998
Ferritin (1)	Ferritin (2)	78	4 – 450 µg/l	y = 1.154 x + 0.298	10.80	0.993
Transferrin	Nephelometry	99	0.7 – 5.0 g/l	y = 0.867 x + 0.047	0.18	0.970
Iron	Hitachi 747	100	1 – 70 µmol/l	y = 0.987 x – 0.312	1.20	0.990
Cyclosporin	RIA	59	55 – 300 µg/l	y = 0.886 x + 5.867	14.94	0.964
Digoxin	RIA	75	0.5 – 3 µg/l	y = 1.063 x – 0.098	0.23	0.953
Haptoglobin	Cobas Bio	89	0.03– 5 g/l	y = 1.130 x – 0.240	0.18	0.843

test- and analyzer manufacturer with respect to calibration frequencies and reagent stability (calibration was every 24 hours and upon reagent renewal; controls were included in every run with an interval of 30 samples), all clinical requests for routine urine analyses were reanalyzed on the Hitachi 911 for a period of 15 working days. A daily average of 23 (SD = 13) patient urine samples with 3 (SD = 3) test requests each were processed. Data obtained on the reagents, calibrators and controls used were extrapolated to a one-year period using the total amount of test requests from 1993 (see Materials and Methods). It was noted that for some tests (e. g. total protein) the daily requests are less than the samples necessary for calibration and control. As a result, the costs of these tests are strongly influenced by the relatively numerous calibrations. The turnaround time for the daily routine load of urine samples was two hours, meaning a considerable shorter analyzer occupancy than in our present laboratory setting with the SMA II requiring four hours. Clearly, this leaves enough room for the use of the Hitachi 911 in measurements of various special serum and whole blood analytes, as intended.

Overall conclusion

From the results presented it can be deduced that notwithstanding its problems with sample predilution, the Hitachi 911 is a good alternative to the SMA II for routine urine chemistry. With appropriate precision, all measurements including total protein can be made from a single tube. The analyzer has enough speed and versatility to combine its use in urinalysis with the acceptable performance of several homogeneous immunoassays and other measurements of special serum or whole blood analytes.

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J. P. van Straalen
Department of Clinical Chemistry
Academic Medical Centre
F1-217.1, Meibergdreef 9
NL-1105 AZ Amsterdam
The Netherlands