# Relationship Between Effective Ionic Dialysance and In Vivo Urea Clearance During Hemodialysis

Robert M. Lindsay, MD, Bernard Bene, MD, Nicolas Goux, MSc, A. Paul Heidenheim, MSoc, Christina Landgren, PhD, and Jan Sternby, PhD

• **Effective ionic dialysance (EID) can be measured from dialyzer inlet and outlet conductivity changes following two steps of dialysate conductivity. Relationships between EID and in vivo urea clearances were studied four times per hemodialysis treatment in eight patients, each undergoing six hemodialysis treatments (192 data sets). Dialyzer blood flow was varied from 190 to 500 mL/min. Dialysate flow was constant (751 to 771 mL/min), and a standard dialyzer (700 HG; Cobe, Lakewood, CO) was used. Double samples were drawn for arterial, venous, and dialysate urea measurements. Two laboratory values were missing. Twelve unreliable laboratory values indicated by divergent results were excluded. Urea clearances were calculated by formulae converting whole-blood to blood-water urea clearances. EID was measured using Diascan (Gambro-Dasco, Medolla, Italy). Mass balance was checked by comparison of dialysate and blood-water urea clearances. Divergent results between dialysate and blood-water urea clearance values led to the exclusion of an additional three laboratory values. A small error (4.2%) in urea mass balance was found (dialysate greater than blood-water urea clearances). A total of 175 data sets were compared. EID showed excellent correlation with blood-water urea clearances ($r = 0.92$) over the line of identity, with a mean difference of –3.5 mL/min (–1%), and similarly with dialysate urea clearances ($r = 0.92$; mean difference, –13.4 mL/min; –5%). For both blood- and dialysate-side comparisons, differences increased with greater clearances. Because EID is an effective clearance and urea clearance is a measure of dialyzer clearance, the curves were corrected for cardiopulmonary recirculation; access recirculation was zero (Transonic monitor; Transonic Systems Inc, Ithaca, NY). For cardiopulmonary recirculation correction, cardiac output and access flows were assumed to be 6.4 L and 1.46 L/min. Corrected data show EID correlates with blood-side urea clearance ($r = 0.92$), with a mean difference of +7.3 mL/min (3.3%), and is constant over the range of clearances. EID correlated with dialysate urea clearance ($r = 0.92$) with virtually no difference. The difference on the blood side is consistent with the urea mass balance error found. These data indicate that EID using Diascan can provide an accurate indication of effective urea clearances obtained during hemodialysis and is of value in monitoring dialysis adequacy.**


**INDEX WORDS: Ionic dialysance; urea clearance; hemodialysis (HD) adequacy.**

DELIVERING AN adequate dose of dialysis is a major issue in the treatment of patients on maintenance hemodialysis therapy. In recent years, there has been increased awareness of delivered dose of dialysis as an important predictor of patient outcome. Because of this, both the United States and Canada have set guidelines for the delivered dose of dialysis, using urea as a surrogate molecule (Dialysis Outcomes Quality Initiative and Canadian Practice Guidelines).[1,2] A multitude of factors may influence the delivery of the prescribed dialysis dose, eg, effective time on dialysis is less than prescribed, inaccurate blood pump calibration, access and cardiopulmonary recirculation, inadequate dialyzer clearance caused by reuse or clotting, and other factors. Urea kinetic monitoring is often performed at monthly intervals, but this may not accurately mirror all treatments.[3] Urea clearance is traditionally used as a measure of dialyzer efficiency and is usually calculated from blood-side clearance measurements. However, blood-side measurements do not take recirculation and inaccurate blood flows into consideration and require blood sampling. It has been suggested that an on-line noninvasive method to measure effective ionic dialysance (EID) can be used to monitor dialyzer efficiency during treatment. The Diascan, which is incorporated into the Integra dialysis machine (Gambro-Dasco, Medolla, Italy), uses a dialysate-based conductivity measurement in which outlet conductivity is measured at two steps of known dialysate conductivity at the dialysate inlet.

Measurements and calculations are automatically performed at regular intervals during the

*From the Optimal Dialysis Research Unit, London Health Sciences Centre–Victoria Campus, The University of Western Ontario, London, Ontario, Canada; and Gambro AB Therapy Systems Research, Lyon, France, and Lund, Sweden.*

*Received December 28, 2000; accepted in revised form May 4, 2001.*

*Address reprint requests to Robert M. Lindsay, MD, London Health Sciences Centre, 800 Commissioners Rd E, London, Ontario, Canada N6A 4G5. E-mail: robert.lindsay@lhsc.on.ca*



*0272-6386/01/3803-0016$35.00/0*
*doi:10.1053/ajkd.2001.26874*

treatment. Mathematical models are used to calculate the EID of the dialyzer. Several workers[4-7] have shown a relationship between EID and urea clearance and that it is possible to use ionic dialysance as an indicator of treatment efficiency. Monitoring EID thus is made easy at every dialysis treatment without the need for additional equipment or disposables. Published studies to date[6,7] have elucidated the relationship between ionic dialysance and urea clearance, focusing on the EID range of 150 to 225 mL/min. In North America, larger dialyzers and greater blood flows are used to achieve greater clearances. This study was designed to explore the relationship between EID and urea clearance during treatment with high blood flow rates (Qbs) and large surface area high-efficiency dialyzers.

The primary aim of the study is to compare the EID, measured by the Diascan, with blood- and dialysate-based urea clearance measurements.

## METHODS

### *Study Design*

This study is a single-center open-label study design evaluating the Diascan during 48 dialysis treatments. Eight patients were included and evaluated during six hemodialysis treatments; four data sets per treatment were obtained, giving a total of 192 data points. The study period used a 1-week familiarization phase (prephase) and a 1-month study phase. Staff was trained on equipment and study procedures during the prephase. The study was approved by the Ethics Review Board of The University of Western Ontario (London, Ontario, Canada), and written informed consent was obtained from all participating patients.

### *Patients and Dialysis Treatments*

The eight patients (five men, three women) had end-stage renal failure and routinely were undergoing dialysis in the Adam Linton Dialysis Unit of London Health Sciences Centre (Ontario, Canada). These patients all had arteriovenous accesses (five arteriovenous fistulae, three synthetic grafts) that were known to be functioning well, had been shown previously to have blood access flow rates in excess of 1,000 mL/min, and therefore had zero access recirculation under normal hemodialysis conditions. Access flow and access recirculation measurements were performed using the Transonic HD01 monitor (Transonic Systems Inc, Ithaca, NY). Dialysis treatment time varied according to the patient's individual prescription, but all were in excess of 4 hours. All dialysis started and ended in the usually prescribed manner; however, dialyzer Qbs were varied at intervals from the prescribed rate of 450 mL/min to allow measurements to take place (discussed later). Dialyses were performed using the high-performance Cobe 700 HG dialyzer (Cobe, Lakewood, CO) using the Integra (Gambro-Dasco) dialysis machine fitted with the Diascan (Gambro-Dasco) device. Dialysate flow rates (Qds) were held constant during each treatment and were in the range of 750 to 775 mL/min. Ultrafiltration rates depended on each patient's requirements per dialysis and did not exceed 1 L/h. Changes in ultrafiltration rate were made when clinically indicated, but were kept constant during sampling periods (discussed later). Dialysate sodium composition was prescribed at 140 mmol/L.

### *Diascan Measurement Principle*

The EID measured by the Diascan can be defined as the dialysance of mobile electrolytes through the dialysis membrane corrected for recirculation and ultrafiltration. EID is derived from measurements of dialysate conductivity ($Cd_{out}$) at outlet ($Y_1$ and $Y_2$) corresponding to two different set points of dialysate conductivity at inlet ($X_1$ and $X_2$).

$$EID = [Qd + Qf]*[1 - (Y_1 - Y_2)/(X_1 - X_2)]$$

where Qf is ultrafiltration flow rate. This principle has been described extensively by Petitclerc et al.[4] The Diascan is programmed to measure EID every 30 minutes during the dialysis procedure. After the measurement of $CD_{out}$ ($Y_1$) at the prescribed value of dialysate conductivity ($X_1$), the set value of dialysate conductivity is changed by 1 ms/cm for 2 minutes ($X_2$). The value of $CD_{out}$ is then measured at the end of this phase ($Y_2$).

The set value of dialysate conductivity is then moved back to the prescription value, and the EID is computed. To ensure an accurate reading, the Diascan requires a stable period of 6 minutes on both blood and dialysate sides. During this period, there should be no injections into the blood circuit or changes made in Qb or ultrafiltration rates. The 6-minute period starts before the measurement of $Y_1$ and ends after the measurement of $Y_2$.

### *Sampling Method*

Diascan measurements were automatically made at 30-minute intervals during the dialysis treatment. Sampling of study parameters was performed according to a predetermined schedule of four Diascan measurements per treatment. Two minutes before the Diascan measurement, a Qb between 190 and 500 mL/min was assigned in random order. Qb was set according to the reading from a Transonic HD017 monitor (Transonic Systems Inc, Ithaca, NY), and not the Integra machine blood pump setting. Other treatment parameters were kept stable during the Diascan measurement period. Immediately after completion of the Diascan measurements, samples were drawn in duplicate from the arterial and venous blood catheters and effluent dialysate catheter. All treatment parameters, such as Qb (both machine and Transonic), Qd, ultrafiltration rate, ionic dialysance, and time were recorded. Immediately after drawing the samples, an access recirculation measurement was made using the Transonic monitor. Qb was then returned to the prescribed value, and the procedure was repeated with the next Diascan measurement. The reason that Qbs from both the Integra machine and Transonic HD01 monitor were obtained is the concern that the Qb shown by the dialysis machine may overestimate the real Qb through the dialyzer because of the

**Table 1. Difference Between Paired Laboratory Measurements**

| Variable | No. | Range* | Mean | SE | Median | IQR† | Extreme‡ |
|---|---|---|---|---|---|---|---|
| Arterial urea (mmol/L) | 192 | −1.4 to +1.5 | 0.035 | 0.027 | 0 | 0.4 | ±1.2 |
| Venous urea (mmol/L) | 191 | −0.5 to +1.3 | −0.006 | 0.015 | 0 | 0.2 | ±0.6 |
| Dialysate urea (mmol/L) | 191 | −1.1 to +0.9 | −0.012 | 0.017 | 0 | 0.2 | ±0.6 |

*Samples for urea were taken in duplicate and labeled A and B. The difference of B in relationship to A for each pair was recorded, with sign (±) taken into account. The range in difference values is given.

†IQR is the distance between the 25th and 75th percentile for the range of the differences of the paired urea values.

‡The extreme limits for differences in paired urea values was taken as $3 \times IQR^2$. Differences in paired results (A versus B) that were beyond this extreme range led to the exclusion of the mean (of A and B) urea value from data analysis.

effect of prepump arterial pressure, inaccuracies in pump calibration, or changes to the pump segment of the blood tubing set during dialysis. When calculating conventional urea clearances, the Qb given by the dialysis machine is commonly used, with the potential for significant errors, especially at high flows. To eliminate as much as possible the effect of inaccurate Qbs, the Transonic HD01 monitor Qb was used as the gold standard for calculations.

### *Blood and Dialysate Samples*

Blood and dialysate samples were analyzed using the Paramax urea nitrogen reagent (Dade Diagnostics of PR Inc, Aguada, PR). Total-protein levels in blood samples were analyzed using the Paramax total-protein reagent (Baxter Diagnostics Inc, Deerfield, IL). Hematocrit on blood samples was determined by microcentrifugation.

### *Accuracy of Laboratory Values*

Two samples were drawn from the arterial blood catheter, venous blood catheter, and effluent dialysate line at each measurement time to permit cross-checking of laboratory values for arterial, venous, and dialysate urea. The objective was to identify laboratory values likely to be unreliable and exclude these data points from further analysis. Unreliable laboratory values are indicated by widely divergent results between the paired samples.

The frequency distribution of the difference between pairs of laboratory values was examined for each of the three variables. Properties of these distributions are listed in Table 1. All distributions were significantly skewed and thus analyzed using the nonparametric procedure of creating box and whisker plots. In this procedure, the distribution of cases about the median is examined to identify outliers and extreme cases, which lie 1.5 to 3 box lengths and more than 3 box lengths from the median, respectively. A box length corresponds to the interquartile range (IQR), the distance between the 25th and 75th percentiles. Extreme cases, which showed very large differences between paired laboratory values relative to the rest of the assays, were excluded from further analysis. Outliers were examined for key-punch and transcription errors. Laboratory values not received back from the laboratory were handled as missing data.

Cases also were screened using the precision specifications given in the literature in the testing kits. Means and coefficients of variation (SD divided by the mean, expressed as a percentage) were reported for multiple measurements of a standard sample of a fixed composition. The SD for test measurements was 0.8 mmol/L for serum urea. Because the number of measurements behind these specifications was not reported in this literature, it was not possible to determine SEM and confidence intervals. As an alternative, a maximum difference between paired laboratory values equal to 2 SDs was chosen for screening purposes.

As an additional check, the mass balance error between blood-water and dialysate-side clearances was evaluated.

The mean urea value for all remaining pairs of urea values was taken and used in clearance calculations.

### *Diascan Measurement Data*

All data points obtained for the Diascan measurements were used in the final evaluation.

### *Data Analysis*

Urea clearances, calculated from standard equations using both blood-water concentrations and blood-water flow rates, are detailed in the Appendix. These urea clearances were then compared with their corresponding EID values by linear regression and Bland-Altman analyses.

## RESULTS

### *Integra Machine Versus Transonic Monitor Qbs*

Qbs set by the Integra machine were varied from 190 to 500 mL/min. A comparative analysis of Qb by the Integra machine versus the Transonic Monitor was performed using regression analysis. The scatter plot and regression line are shown in Fig 1. There was a very strong and highly significant linear relationship between the two alternative measures ($r = 0.981$; $P < 0.00001$). The residuals were normally distributed, but there was increased variability along the range of values. The plot of the difference between the two methods by the mean of both measurements (Bland-Altman analysis) shows increased variance and a greater magnitude of difference along the range of values, with the

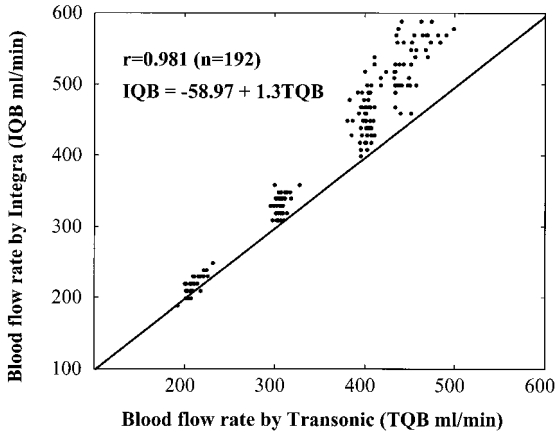


**Fig 1. Comparison of Qbs indicated by the Integra machine (IQB) versus measured by the Transonic monitor (TQB). A strong linear relationship is seen between these alternative measures ($r$ = 0.981; $P$ < 0.0001; IQB = 1.3; TQB = –59). Residuals were normally distributed, but there was increasing variability along increasing range of values. The line is the line of identity.**

Integra measurements becoming greater than Transonic measurements at greater Qbs (Fig 2; $r$ = 0.831; $P < 0.00001$). For this reason, the Transonic Qb is used for all further analyses of data in this study.

*Accuracy of Laboratory Values*

Two laboratory urea values in total were missing, one in blood and one in dialysate.

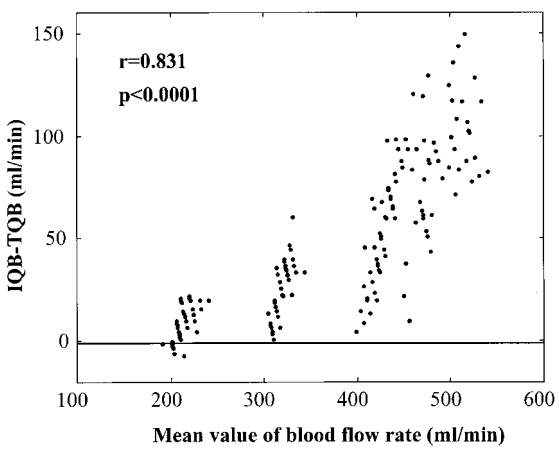


**Fig 2. Bland-Altman analysis of Integra machine (IQB) versus Transonic monitor (TQB) Qbs shows increased variance and greater magnitude of the difference between IQB and TQB along the range of values, with IQB becoming greater than TQB at greater Qbs. This pattern is highly significant ($r$ = 0.831; $P$ < 0.0001).**

Twelve pairs of urea measurements (four arterial, one venous, and seven dialysate) had differences that lay beyond the limits for extreme values (ie, > 3 IQRs from the median; Table 1) and were eliminated from further analysis. No paired urea values were found to have a difference that exceeded twice the SD for test measurements reported by the test kit manufacturer. An additional three urea values were excluded from analysis after examination of the mass balance error, in which the difference between the blood- and dialysate-side urea clearances was outside 3 IQRs (±60 mL/min) of the frequency distribution of those parameters. This left 175 data sets for urea clearances.

*EID Versus Urea Clearances*

The relationship between EID and blood-water urea clearance (kub, equation 1; Appendix) is shown over the line of identity in Fig 3. The relationship is strong and highly statistically significant ($r$ = 0.92; $P < 0.0001$). Values of Qd used to calculate urea dialysate-side clearances (kud, equation 2; Appendix) ranged from 751 to 771 mL/min. The corresponding relationship between EID and dialysate urea

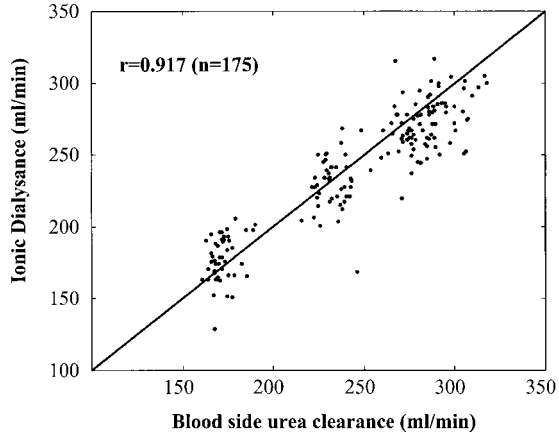


**Fig 3. Relationship between EID and blood-water urea clearances (kub, equation 1; Appendix). A strong and statistically significant ($r$ = 0.92; $P$ < 0.00001) linear relationship (EID = 0.83 kub + 38) is shown. Data are plotted over the line of identity. It appears from the scatter plots that variances between ionic dialysance and blood-side urea clearances are increasing at greater clearance values, with EID values becoming lower than blood-side urea clearances.**

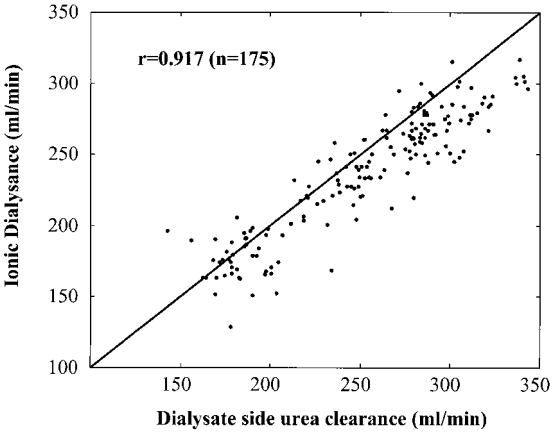


**Fig 4. Relationship between EID and dialysate-side urea clearance (kud, equation 2; Appendix). This figure shows a strong and significant ($r = 0.92$; $P < 0.00001$) linear relationship (EID = 0.81 kud + 34) between the two sets of data plotted over the line of identity. As shown in Fig 3, scatter plots suggest increasing variance between the sets of results at greater clearance values, with EID clearances less than dialysate-side urea clearances at greater values of clearance.**

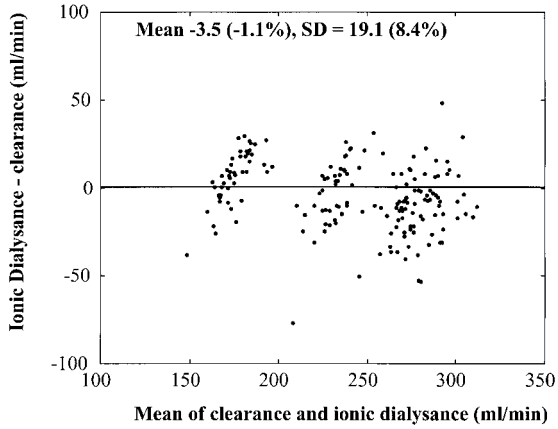


**Fig 5. Bland-Altman analysis of data in Fig 3 indicates an overall mean difference between EID and blood-side urea clearance of –3.5 ml/min, approximately –1%. However, the difference between EID and blood-side urea clearance increases significantly ($P < 0.01$) over the range of values.**

clearance (Fig 4) shows the same strong correlation and is also highly significant ($r = 0.92$; $P < 0.00001$). As seen in these scatter plots, these relationships appear to be linear. In accordance with the assumptions of regression analysis, residuals were normally distributed. However, the assumption of constant variance of y for all levels of x appears to be violated in both sets of clearance data, with variances increased at greater clearance levels. Bland-Altman analyses of data plots (Figs 5 and 6) show statistically significant trends ($P < 0.01$) over the range of values. EID clearances are less than the blood- or dialysate-side urea clearances at greater ranges of clearance.

Blood-side urea clearances using Qbs indicated by the Integra machine were also calculated (kub, equation 1; Appendix). They also showed by regression analysis a strong and significant linear relationship with corresponding EID clearances ($r = 0.87$; $P < 0.001$). As expected, knowing the inherent error in Integra Qb, the relationships diverged between measures, especially toward the greater end of clearance values. Because of the error, no further data comparisons using blood-side urea clearance with Integra Qb values were made.

### *EID Versus Urea Clearances Corrected for Cardiopulmonary Recirculation*

Because the Diascan provides an effective clearance with access and cardiopulmonary recirculation and potential inaccuracies in Qd determination accounted for, blood and dialysate urea clearance values were corrected for cardiopulmonary recirculation. There was no case of access recirculation and, as previously indicated, only clearances calculated using the Transonic Moni-

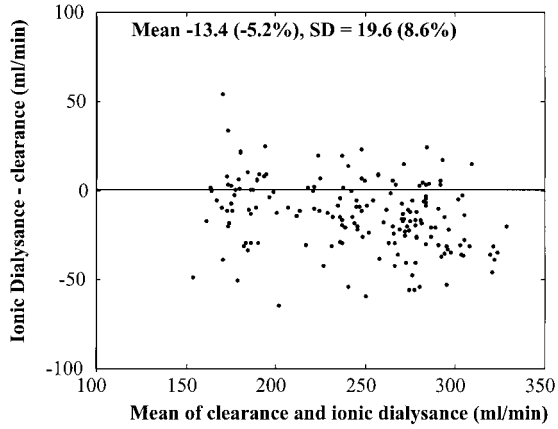


**Fig 6. Bland-Altman analysis of data in Fig 4 shows an overall difference between ionic dialysance and dialysate-side urea clearances of a mean –13.4 mL/min; approximately –5%. However, this difference increases significantly ($P < 0.01$) over the range of clearance values.**

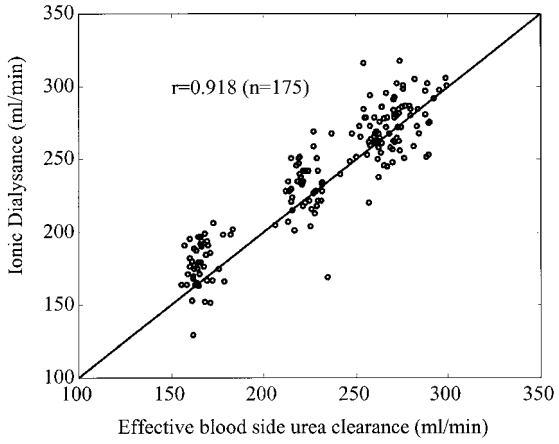


**Fig 7. The plot of EID against the effective blood-side urea clearance (shown in Fig 3) corrected for cardiopulmonary recirculation ($k_{corr}$, equation 7; Appendix). Data are plotted over the line of identity and show a highly significant correlation ($r = 0.92$; $P < 0.0001$) that appears to be constant over the range of values. (Regression equation: EID = 0.9 $k_{corr}$ + 30.)**

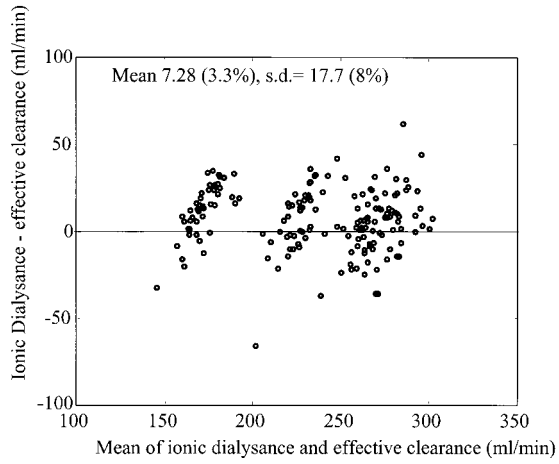


**Fig 8. Bland-Altman analysis of data in Fig 7 shows that overall ionic dialysance tends to be greater than the effective (corrected for cardiopulmonary recirculation) blood urea clearance by approximately 7 mL/min, a difference of 3.3%. However, this difference is shown to be constant over the range of clearance values.**

tor Qb were used. To do this, we applied the correction to the data according to equation 7 (Appendix), in which we assumed a cardiac output of 6.8 L/min and an access flow of 1.46 L/min. This assumption was based on results of a separate study performed to examine the relationship between access flow and cardiac output in Adam Linton Dialysis Unit (London Health Sciences Centre) patients with arteriovenous fistulae and grafts.[8]

Corrected data in Fig 7 showed EID correlated highly with blood-water urea clearance ($r = 0.92$; $P < 0001$), and this correlation holds over the range of clearance values (Fig 8). However, Fig 8 indicates that these corrected data show a 3.3% difference in favor of EID over the blood-side urea clearance. Correcting the dialysate-side urea clearance gave a correlation of $r = 0.92$ ($P < 0.0001$; Fig 9), with a mean difference of only –1.7 mL/min (–0.63%) and also constant over the range of values (Fig 10).

### *Dialysate-Side Versus Blood-Side Urea Clearances*

Figure 11 shows plots of dialysate-side versus blood-side urea clearance over the line of identity. Although data correlate ($r = 0.94$), it can be seen that the plots are not equally distributed over the identity line. Dialysate-side clearances appear to be greater than blood-side clearances. A Bland-Altman–like analysis was performed expressing the difference between the dialysate- and blood-side clearances as a percentage of their mean and plotting this against the mean of dialysate and blood-water urea clearances. These data are shown in Fig 12 and indicate a urea mass balance error of 4.1% that is constant over the range of clearances.

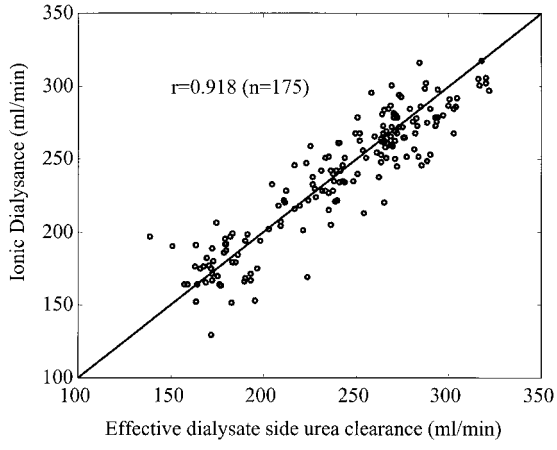


**Fig 9. The plot of EID versus effective dialysate urea clearance in which effective clearance is clearance data shown in Fig 4 corrected for cardiopulmonary recirculation ($k_{corr}$, equation 7; Appendix). Data plots are over the line of identity and show a significant correlation ($r = 0.92$; $P < 0.0001$) that appears to be constant over the range of values. (Regression equation: EID = 0.89 $k_{corr}$ + 26.)**

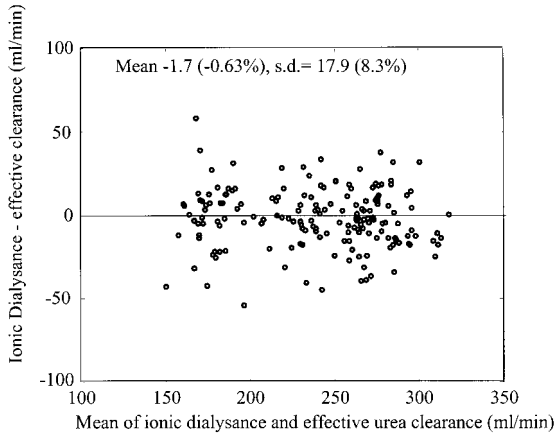


**Fig 10. Bland-Altman analysis of data in Fig 9 that confirms that any variability between ionic dialysance and effective dialysate urea clearance is constant over the range of values, with a mean difference of only –1.7 mL/min, or – 0.63%.**

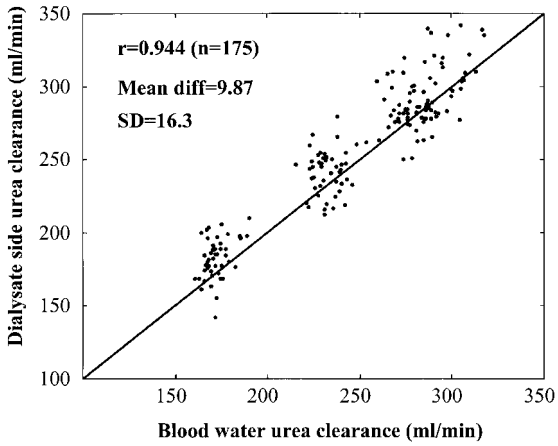


**Fig 11. The plot of dialysate-side urea clearance (kud) versus blood-side urea clearance (kub) is shown over the line of identity. Data show a significant linear correlation ($r$ = 0.94; $P$ < 0.0001). It can be seen that the plots are not equally distributed over the identity line. Dialysate-side clearances appear to be greater than blood-side clearances. This mass balance error is approximately 10 mL/min overall. (Regression equation: kud = 0.96 kub +18.)**

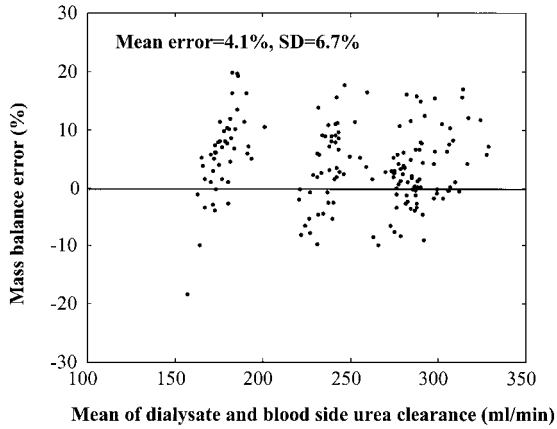


**Fig 12. Data from Fig 11 are used to express the mass balance error (difference between dialysate- and blood-side urea clearances expressed as a percentage of the mean clearance value) plotted against the mean of dialysate- and blood-side urea clearances. This shows an overall mean mass balance error of 4.1% that is constant over the range of clearances.**

## DISCUSSION

This study shows that EID by Diascan gives a result that correlates very closely with dialysate-side urea clearances corrected for cardiopulmonary recirculation (Fig 9). Bland-Altman analysis shows this correlation to hold over clearance values ranging from 150 to nearly 300 mL/min and that there is virtually no difference between the two sets of data. This close correlation is especially encouraging considering that the same correction factors were applied to all eight patients, ie, an access flow rate of 1.46 L/min and a cardiac output of 6.8 L/min plus equation 7 (Appendix). In retrospect, access flow rates and cardiac outputs should have been measured on each individual patient during each experimental dialysis session to allow each urea clearance value to be individually corrected. This was not done. When data analysis was performed, the separation between EID and urea clearances only at greater clearance values was noted. Because EID values were less than urea clearances at this point and EID is an effective clearance, the possibility that cardiopulmonary recirculation caused this separation was then entertained.

A separate study of the same dialysis population from which these eight patients were selected provided data that the mean cardiac output for our population was 6.8 ± 1.8 (SD) L/min, with a mean access flow rate of 1.46 ± 0.6 L/min and a ratio of access flow to cardiac output of 0.21 ± 0.06.[8] This study also suggested that this ratio remains fairly constant in the absence of access dysfunction.[8] The eight patients on this current study were selected on the basis of having well-functioning accesses with flow rates known to be in excess of 1 L/min. Their cardiac outputs can be assumed to be in proportion;

therefore, whatever the actual values for cardiac outputs and access flows were, the mean values used in the clearance correction would seem reasonable. A similar close correlation is held between EID and blood-side water urea clearances that are also corrected for cardiopulmonary recirculation (Fig 7). However, in this case, Bland-Altman analysis shows that although the correlation holds true over the range of clearances, there is a slight difference of approximately 3%, with the EID tending to just overestimate blood-side water urea clearances (Fig 8). This 3% difference would seem to be accounted for by the urea mass balance error of just more than 4% found when dialysate clearances were compared with blood-water urea clearances (Figs 11 and 12).

Why this urea mass balance error exists is not certain. There could be many explanations. One possible reason is that calibration of the Transonic device was performed with dialysis fluid at room temperature, whereas both hematocrit and temperature are known to affect the measurement. Although Qb measurements used in the comparisons were performed using a calibrated Transonic device (the Integra Qb measurement regarded as erroneous, Fig 1), 4.1% is not a large error. There could also be some error in the calculation of blood-water flow, eg, the constant 0.72 for water fraction in red blood cells might be different depending on patients' total-body water content (equations 5 and 6; Appendix). It would be unlikely that this relates to accuracy of laboratory values because unreliable laboratory values, indicated by widely divergent results between twin samples, were discarded (a total of 12 pairs of measurements; 5 blood and 7 dialysate). The rest of the double samples showed very good precision. Regardless of the explanation, the error with the blood-side clearance measurement is very small. Intuitively, the dialysate-side measurements should be more reliable because they do not require corrections for blood-side water urea contents, and Qd and ultrafiltration rate are generally accurately recorded by most dialysis machines. This therefore suggests that the use of EID by Diascan may be a very useful clinical tool, especially because it is a true effective clearance incorporating not only the actual capabilities of the dialyzers and dialysis machine (eg, blood pump), but also the effect of all forms of recirculation. The only effect not included is urea distribution into different parts of the body (multiple body pools of urea), which causes the whole-body clearance to be approximately 10% to 15% less.[6] The EID value given by the Diascan may be more accurate than even the corrected clearance values obtained from dialysate-side measurement. It must be remembered that in these experiments, unreliable laboratory values were discarded, whereas all Diascan measurements were taken. There is no published information to date on the reproducibility of EID measurements by Diascan. However, separate in vitro studies performed in our laboratory indicated that these measurements are reliable and reproducible, with a variability on test/retest of approximately 3% (unpublished data).

The Diascan device makes repeated measurements during each dialysis treatment. It therefore is an ideal device to use for the continuous supervision of treatment efficiency. It can be used to detect changes during an individual treatment and bad conditions during a particular treatment in comparison with the normal situation. Changes during the treatment could, eg, be induced by clotting or decreased blood flows caused by needle problems. Reversed needles and blood flow settings left unintentionally low are examples of situations that will cause the clearance during the entire treatment to be lower than normal.

An average effective urea clearance (K) can be given for each dialysis treatment; time is easily and accurately measured, and therefore the effective $K \times t$ can be given for every treatment. Extrapolating to a delivered Kt/V presents some difficulties because an independent measure of V would be required. Petitclerc et al[7] showed a good correlation between delivered Kt/V measured by direct dialysis quantification and by the conductivity measurement. Conversely, Manzoni et al[9] found on eight patients that the Kt/V value determined by EID plus an assumption that the urea distribution volume corresponded to 55% of body weight was underestimated by 22% compared with direct dialysis quantification studies. They believed the difference was caused by both an overestimate of urea distribution volume (+17%) and an underestimate of the effective

urea clearance (–11%). The reason for this difference between the findings of Petitclerc et al[7] and Manzoni et al[9] is not certain. In the report by Manzoni et al,[9] there is no indication of the stability of dialysate- or blood-side urea measurements. Also, the mean effective urea clearance used by Manzoni et al[9] to calculate Kt/V was based on a single-pool assumption for the evolution of the urea concentration, whereas volume (V) was determined by direct quantification. This means that the dose (Kt/V) calculated from urea concentrations will be overestimated because of both recirculation and two-pool effects. Nevertheless, their data showed that EID and urea clearance proved to be closely related; thus, the effective urea clearance could be derived according to a regression equation. Gotch et al,[10] using a similar technology (Fresenius Medical Care, Lexington, MA), also reported that EID closely predicts effective urea clearance with a coefficient of variation of only 6.7% and thus can provide inexpensive automatic measurements of delivered Kt/V every dialysis session. These studies, supplemented by the current data, support the concept that this technology may be of considerable clinical benefit to dialysis patients, even when undergoing high-efficiency dialysis treatments, common in North America.

## APPENDIX

*Equations*

Clearance calculations are made according to:

1. Urea blood side:

$$kub = [uaw * qbar - uvw * qbvr]/uaw$$

where kub is blood-side urea clearance in milliliters per minute, uaw is arterial urea blood-water concentration in millimolar, qbar is arterial blood-water flow rate in milliliters per minute, uvw is venous urea blood-water concentration in millimolar, and qbvr is venous blood-water flow rate in milliliters per minute.

2. Urea dialysate side: $kud = ud * qdqf/uaw$

where kud is dialysate-side urea clearance in milliliters per minute, ud is dialysate urea concentration in millimolar, and qdqf is dialysate flow plus ultrafiltration rate in milliliters per minute.

Blood-water concentrations in these equations are calculated according to:

3. Arterial urea:

$$uaw = ua/[1 - 0.00107 * pta]$$

where ua is arterial urea concentration in millimolar and pta is arterial total-protein concentration in grams per liter.

4. Venous urea:

$$uvw = uv/[1 - 0.00107 * ptv]$$

where ptv is venous total-protein concentration in grams per liter.

Blood-water flows are calculated according to the following:

5. Arterial:

$$qbar = [0.72 * hta + (1 - hta) * (1 - 0.00107 * pta)] * qb$$

where hta is arterial hematocrit in percent.

6. Venous:

$$qbvr = [0.72 * htv + (1 - htv) * (1 - 0.00107 * ptv)] * [qb - ufr * 1000/60]$$

where htv is venous hematocrit in percent, qb is blood flow rate in milliliters per minute, and ufr is ultrafiltration rate in liters per hour.

7. Correction for cardiopulmonary recirculation is calculated according to:

$$k_{corr} = \frac{k}{1 + k/[CO - Qa]}$$

where k is clearance in milliliters per minute, CO is cardiac output in milliliters per minute, and Qa is access flow in milliliters per minute.

## REFERENCES

1. National Kidney Foundation: DOQI Clinical Practice Guidelines for Hemodialysis Adequacy. Am J Kidney Dis 30:S15-S66, 1997 (suppl 3)

2. Goldstein MB, Deziel C, Hirsch DJ, Hoult P, Levin A, Sohi P, Taub KJ, Watson D: Clinical practice guidelines for the delivery of hemodialysis. J Am Soc Nephrol 10:S306-SS310, 1999 (suppl 13)

3. LeFebvre JMJ, Spanner E, Heidenheim AP, Lindsay RM: Kt/V (urea): Patients do not get what the physician prescribes! ASAIO Trans 37:M132-M133, 1991

4. Petitclerc T, Goux N, Reynier AL, Bene B: A model for non-invasive estimation of in-vivo dialyser performances and patient's conductivity during hemodialysis. Int J Artif Organs 16:585-591, 1993

5. Polaschegg HD: Automatic non-invasive intradialytic measurements. Int J Artif Organs 16:185-191, 1993

6. Daugirdas JT, Schneditz D: Postdialysis urea rebound: Measurement, prediction and effects of regional blood flow. Nephrol Dial Transplant 23:166-173, 1994

7. Petitclerc T, Bene B, Jacobs C, Jaudon MC, Goux N: Non-invasive monitoring of effective dialysis dose delivered

to the hemodialysis patient. Nephrol Dial Transplant 10:212-216, 1995

8. Pandeya S, Lindsay RM: The relationship between cardiac output and access flow during hemodialysis. ASAIO J 45:135-138, 1999

9. Manzoni C, Di Filipo S, Corti M, Locatelli F: Ionic dialysance as a method for on-line monitoring of delivered dialysis without blood sampling. Nephrol Dial Transplant 11:2023-2030, 1996

10. Gotch F, Peter H, Panlilio F, Folden T, Keen M: On-line measurement of delivered Kt/V during dialysis. J Am Soc Nephrol 6:600A, 1995 (abstr)