Association Between Neural Network And System Dynamics To Predict Dialysis Dose During Hemodialysis

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Abstract- The total dialysis dose, expressed as Kt/V, has been widely recognized to be a major determinant of morbidity and mortality in hemodialyzed patients. Many different factors influence the correct determination of Kt/V, such as urea sequestration in different body compartments, access and cardiopulmonary recirculation. These factors are responsible for urea rebound after the end of the hemodialysis session, causing poor Kt/ V estimation. In this work, system dynamics model was combined with a neural network (NN) method for early prediction of the Kt/V dose. Two different portions of the urea concentration-time profile provided by the system dynamics (on-line urea monitor) were analyzed: the entire curve A and the first half B, using an NN to predict the Kt/V and compare this with that provided by the system dynamics model. The NN was able to predict Kt/V is the middle of the 4h session (B data) without a significant increase in the percentage error (B data: 6.65%±2.51%; A data: 5.62%±8.65%) compared with the system dynamics Kt/ V.

Key words: System dynamics, Artificial intelligence, Neural networks, Urea kinetic modelling, Hemodialysis, Dialysis adequacy.

I. INTRODUCTION

Since the re-analysis of the National Cooperative Dialysis Study by Gotch and Sargent, total dialysis dose, expressed as Kt/V (where K is the clearance of the dialyzer plus residual renal clearance, t is the treatment time, and V is the total body water volume), is considered to be a major determinant of morbidity and mortality in hemodialyzed patients and has become a widely used index for the expression of treatment adequacy [1-8]. Numerous methods are available to quantify the hemodialysis dose, most based on the theory that uremic mortality and morbidity are related to low molecular-weight nitrogenous solutes, and that urea is a satisfactory indicator of these compounds. Despite the existence of formal mathematical variable-volume single and double pool models for the calculation of Kt/V [9], these have been largely replaced by 'clinician-friendly' kinetic methods [10-12]. Most of these techniques require the extraction of blood samples at different stages of the dialysis session.

All of these approaches have been used to predict the equilibrated $_{eq}$Kt/V, without waiting for 30-90 min post-dialysis to take a true equilibrated urea sample. The true equilibrated Kt/V requires waiting for this period following the session, because the blood urea concentration rises to a new equilibrium over this period, this phenomenon being known as 'urea rebound'. These estimation approaches do, however, require waiting until the end of the hemodialysis session.

Another alternative for computing the total dialysis dose is the measurement of the urea removed by using the system dynamics model (Hemodiadynamics) [13,14]. This can be accomplished using a dialysis simulator based on system dynamics approach that was built for analyzing the dynamic implications of implementing adequate hemodialysis dose. This dialysis simulator evaluates the effect of dialysis policies on session performance, quantifying, optimizing dialysis efficiency and monitoring dialysis performance online. The model was validated for clinical use to help staff achieve the desired dialysis performance and make the correct responses to poor processes of care that impede adequate dialysis. In many fields of clinical medicine, artificial neural networks (ANN) have been used successfully to solve complex and chaotic problems without the need of mathematical models and a precise understanding of the mechanisms involved [15–17]. Pharmacodynamic analysis [18–20] (cyclosporin dosage adjustment [21], heparin pharmacokinetics during hemodialysis [22]), time-course and diagnosis of chronic nephropathies (IgA nephropathy [23], glomerular vs tubular renal disease [24]), allograft tolerance and function (chronic and acute allograft rejection [25–28]), diagnosis of renal transplant rejection [29], prediction of cytomegalovirus disease after renal transplantation [30], stratification of cardiac risk in renal transplantation [31] and hemodialysis efficiency evaluation (urea kinetic modelling [32,33]) are only a few examples of the artificial intelligence opportunities. However, because of several existing methods for calculating delivered dialysis dose, Kt/V values can, in fact, be different for the same set of pre-/post dialysis blood urea concentrations. These methods require waiting until the end of the session to know or estimate the true Kt/V dose. This means that the adequacy of the hemodialysis can be gauged only after the session is over. It would therefore be very advantageous to have a method for within-dialysis prediction of the true Kt/V dose, because it would provide the possibility of making an on-line correction of the treatment to achieve the prescribed dose. In this work, we present a neural network (NN) approach for the analysis of the urea kinetic time profile given by the system dynamics dialysis simulator. In this application, we analyze the information carried at different time intervals with the aim of early estimation of Kt/V.

II. SUBJECTS AND METHODS

A. Patients

The study was done on 50 patients clinically stable that gave their informed consent to participate. They are 23 male and 27 female patients, with ages ranging 28-73 years (48±13, mean and SD), and dialysis therapy duration ranging 6-96 months (32±28). The etiology of renal failure was chronic glomerulonephritis (11 patients), vascular nephropathy (9 patients), diabetic nephropathy (11 patients), hypertension (7 patients), interstitial chronic nephropathy (5 patients), unknown cause (4 patients), and other etiologies (3 patients). The vascular access was through a native arteriovenous fistula (45 patients), and a permanent jugular catheter (5 patients).

B. Hemodialysis Procedure

Patients had dialysis three times a week, in 3-4 hour sessions, with a pump arterial blood flow of 300-350 mL/min, and flow of the dialysis bath of 500 mL/min. The dialysate consisted of the following constituents: sodium 141 mmol/l, potassium 2.0 mmol/l, calcium 1.3 mmol/l, magnesium 0.2 mmol/l, chloride 108.0 mmol/l, acetate 3.0 mmol/l and bicarbonate 35.0 mmol/l. hollow-fibre polysulphone and cellulose diacetate dialyzers were used. The dialysis technique was conventional hemodialysis, no patient being treated with hemodiafiltration. The hemodialysis session conditions were kept stable throughout the study. A Fresenius model 4008B dialysis machine equipped with a volumetric ultrafiltration control system was used in each dialysis. Fluid removal was calculated as the difference between the patients' weight before dialysis and their target dry weight.

C. System Dynamics Urea Simulator [13,14]

The model discussed in [13] was developed using Vensim DSS v 4.0a simulation software for formulating, analyzing and comparing various policies to determine optimum level of dialysis parameters for improved session performance. The simulation results with base case values and with different test scenarios are presented in [13]. The base case values were selected based on the experts experience in the field of nephrology and the insights from the research literature. The following variables were extracted from the dialysis records and patient charts: sex, age, height, pre-dialysis weight, blood flow rate, dialysate flow rate, dialyzer surface area, dialyzer ultrafiltration coefficient K_{uf}, pre-HD blood urea concentration (BUN), desired ultrafiltration volume, dialysate temperature, type of dialysate, systolic blood pressure and actual equipment effectiveness. The system dynamics dialysis simulator then calculates the dialysis output variables such as Kt/V, post-dialysis blood urea concentration, post-dialysis urea distribution volume, actual ultrafiltration volume, probability of complications, normalized protein catabolic rate (nPCR), session degradation and session performance. The whole structure of the model was presented in [13]. The Modeled Dialysis Adequacy ($_{Sp}$Kt/V) and Modeled Post BUN structure will be described here from the overall stock & flow diagram to show how the model can be used for the estimation of the amount of urea removed during a single dialysis and the dialysis adequacy Kt/V.

- **Definition of Subsystems parameters and Variables**

    - **Calculated Dialysis Adequacy (Kt/V)** – This is the amount of dialysis dose received per dialysis. It is a dimensionless variable measured using a relative scale (varying from 0 to 2).

    - **Pre BUN** is the concentration of blood urea nitrogen before dialysis treatment session.

    - **Residual Renal function** is an indication of remaining GFR, it also reflects remaining endocrine functions and degree of renal dysfunction.

    - **Urea Reduction** – This is the ratio of the post blood urea nitrogen to the pre blood urea nitrogen that indicates the removal rate of urea. It is a dimensionless variable measured as a decimal value between 0 and 1.

- **Dialysis Session Schedule** – Dialysis treatment is carried out at specific time interval. This variable determines when to initiate dialysis treatment cycle. This is assumed as an exogenous variable and hence is not changed for the simulation time period

- **Urea Generation Rate** – It is defined as the generation rate of urea nitrogen that can be estimated from the urea nitrogen removal rate. The generation rate of urea is linked to the protein nitrogen appearance rate because most protein nitrogen is excreted as urea. A low pre-dialysis or time-averaged plasma urea level may be found in patients in whom urea removal is inadequate but in whom the urea generation rate is also low (e.g., due to poor protein intake). It is measured in milligrams per minute (mg/min)

- **Initial Urea distribution volume ($V_{initial}$)** – This is the anthropometric volume of distribution of urea that may be calculated by Watson formulae derived from stature, age, and gender [35]. It is defined as the volume of water a patient's body contains. The body is about 60 percent water by weight. If a patient weighs 70 kilograms, V will be 42 liters. It is measured in deciliters (dL)

- **Urea Distribution Volume (V_t)** – This is the modeled volume of distribution of urea It is also a tool that is used to assess dialysis adequacy and it must be monitored over time during dialysis. It is measured in deciliters (dL)

- **Modeled Dialyzer Clearance (In Vivo)** – This is the measured dialyzer clearance during session. The clearance of a dialyzer is defined as its volumetric rate of removal of a particular blood solute, i.e. the amount of solute removed from the blood per unit time, divided by the incoming blood concentration. Therefore, inlet and outlet blood urea concentrations (C_{in} and C_{out}) can be used to directly measure the in vivo dialyzer performance if simultaneous blood flow measurements (Q_b) are available. It is defined as the product of the urea extraction ratio [ER = (Cin -Cout)/ Cin] and blood flow rate (Q_b). It is measured in deciliters per minute (dL/min).

- **Access Recirculation Fraction (AR)** – During hemodialysis, some of the blood entering the dialyzer inlet has flowed from the dialyzer outlet without passing through the peripheral capillaries. This flow of dialyzed blood from dialyzer outlet to inlet is termed recirculation and is quantified as the flow rate of recirculated blood entering the dialyzer, expressed as a fraction of the extracorporeal blood flow rate. This fraction is calculated in the model on the basis of the discrepancy between the expected clearance (K_{de}) and modeled clearance (K_{dm}). Recirculation significantly impairs the efficiency of the hemodialysis treatment and it can also be a sign of a pending access problem. It is a dimensionless variable measured using a relative scale (varying from 0 to 1).

- **Ultrafiltration Volume** – This is the amount of actual ultrafiltration volume during session. It is defined as the difference between the pre-dialysis and post-dialysis weights. It is measured in deciliters.

- **Session Performance** – This is a measure of how dialysis session being developed is, i.e., how likely it is to be successful for the patient. It is defined as the overall dialysis session efficiency as a function of dialysis adequacy and dialysis complications. It is a dimensionless variable measured using a relative scale (varying from 0 to 1; 0 corresponds to total failure and 1 corresponds to total success).

- **The Modeled Dialysis Adequacy (Kt/V) Subsystem**

  The Modeled Dialysis Adequacy (Kt/V) Subsystem is shown in figure 1. The calculated dialysis adequacy is based on the second-generation Daugirdas formula in [34], but it was modified to be used from the systems perspective. The Calculated Dialysis Adequacy stock (Dimensionless) is fed into by adequacy increasing rate (Dimensionless/Minute) and is depleted by adequacy decreasing rate (Dimensionless/Minute). The Calculated Dialysis Adequacy stock is an integral of the adequacy increasing rate less the adequacy decreasing rate.

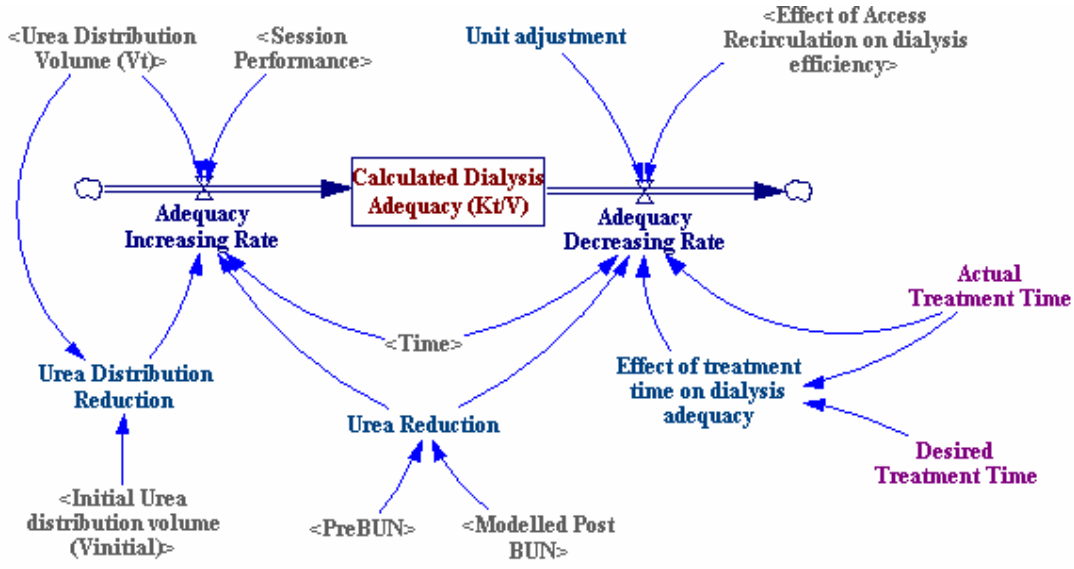

Fig. 1 The Dialysis Adequacy Subsystem

Calculated Dialysis Adequacy (t) = Calculated dialysis adequacy (0) + ∫ [adequacy increasing rate- adequacy decreasing rate] dt (1)

Calculated Dialysis Adequacy (0) = 0 (2)

The rate of increasing adequacy increases with increase in urea reduction and ultrafiltration rate. An increase in the ultrafiltration rate leads to a decrease in the urea distribution volume and this drives up the dialysis adequacy. Equation (3) represents the adequacy increasing rate:

Adequacy increasing rate = IF THEN ELSE (Session Performance = 1, 0, ZIDZ ((4-3.5 * Urea Reduction) * 0.55 * (Urea Distribution Reduction/"Urea Distribution Volume (Vt)"), Time) (3)

If the session performance is 100 %, this means that the dialysis adequacy reached the desired value. Hence, there is no increase in the adequacy after reaching the value desired. Otherwise, the adequacy increasing rate is driven by the amount of urea removed during session and the reduction in urea distribution volume. The urea reduction is a ratio of the modeled post-BUN to the pre-BUN. The ZIDZ function is used to returns 0 when dividing by 0 to start simulation at initial time.

The rate of decreasing adequacy is determined by the amount of urea removed and the small amount of urea generated during dialysis. The recirculation and the adherence to treatment duration also cause a decrease in the dialysis adequacy. Equation (4) represents the adequacy decreasing rate:

Adequacy decreasing rate = (ZIDZ (Ln (Urea Reduction – Unit adjustment * (Actual Treatment Time/60)), Time)) * Effect of Access Recirculation on dialysis efficiency * Effect of treatment time on dialysis adequacy (4)

The product of unit adjustment and prescribed treatment time term adjusts the post-/pre-BUN ratio, R, for urea generation and is a function of session length. For a session length of 3–4 hours, the generation term is about 0.024–0.032. The ratio of the actual treatment time to the desired treatment time determines the effect of the treatment time on dialysis adequacy. The ratio of the reduction of dialyzer clearance by access recirculation (AR) to expected dialyzer clearance determines the effect of the access recirculation on dialysis adequacy.

- **The Modeled post BUN Subsystem**

  The Modeled post BUN Subsystem is shown in figure 2. The Modeled post-BUN stock (mg/dL) is fed into by BUN increasing rate (mg/dL/Minute) and is depleted by BUN decreasing rate (mg/dL/Minute). The Modeled post-BUN stock is an integral of the BUN increasing rate less the BUN decreasing rate. If the urea removal is inadequate, then dialysis is inadequate. It is measured in milligrams / deciliter (mg/dL).

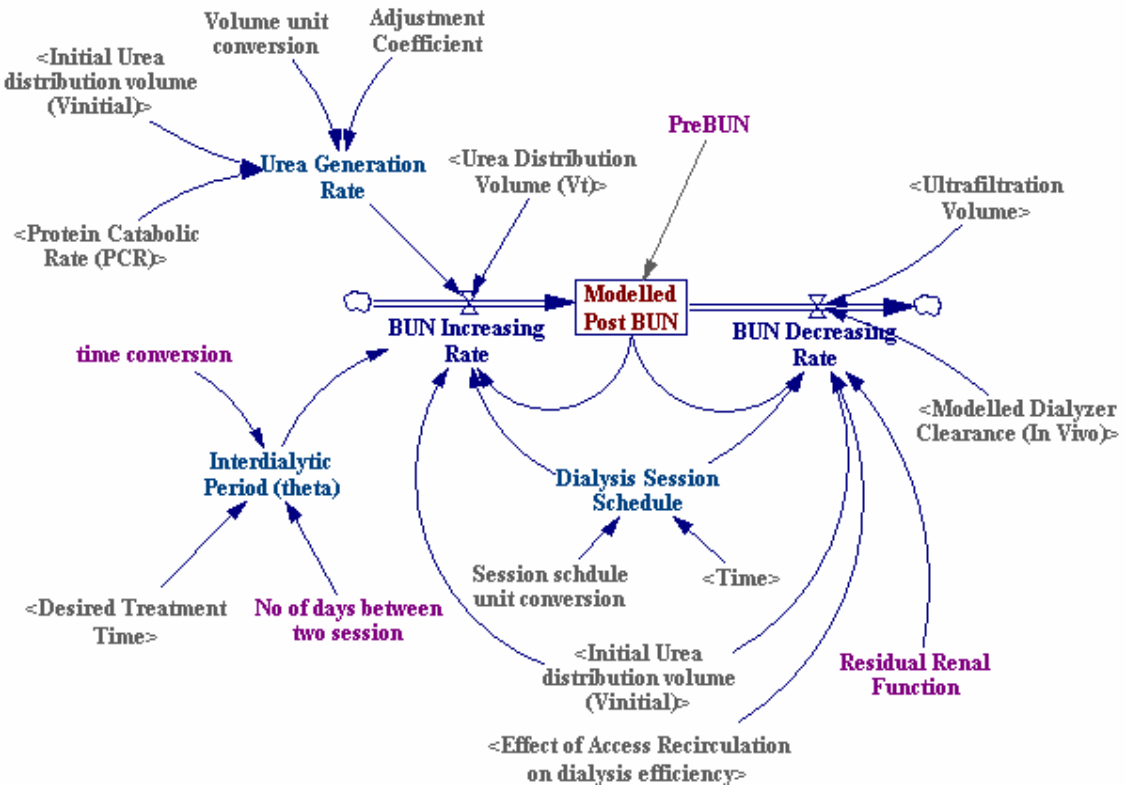

Figure 2 The Modeled Post-BUN Subsystem

Modeled Post-BUN (t) = Modeled Post-BUN (0) + ∫ [BUN increasing rate – BUN decreasing rate] dt (5)

Modeled Post-BUN (0) = pre-BUN (mg/dl) (6)

Dialysis session schedule is a binary variable. It takes the value of 1 during the dialysis treatment session and 0 during the interdialytic period. Dialysis session schedule is determined by the Interdialytic period and the duration of dialysis treatment. It is also noted that dialysis treatment is completed periodically at equal intervals. Thus the duration of session determines the dialysis interval and the interdialytic period (theta) determines the number of days the dialysis would be carried out and can be calculated as follows:

Interdialytic Period (theta) = (No of days between two session × 24 × 60) – Desired Treatment Time (7)

Dialysis Session Schedule = PULSE TRAIN (INITIAL TIME, duration of session, "Interdialytic period (theta)", FINAL TIME) (8)

The amount of urea generated after dialysis depends on the nutritional status or the dietary protein intake of the patient and urea distribution volume. It increases with the increase in the interdialytic period. The generation rate of urea nitrogen can also be estimated from the urea nitrogen removal rate and the intensity or the rate of dialysis that was given. The urea generation rate is calculated according to the Borah method [36].

The increasing rate of urea or the pre-BUN can be estimated by the model based on the following equation [37]:

BUN Increasing rate = IF THEN ELSE (Dialysis Session Schedule = 0, (((Urea Generation Rate * "Interdialytic Period (theta)") + (Modeled Post BUN * "Urea Distribution Volume (Vt)")) / "Initial Urea distribution volume ($V_{initial}$)") / "Interdialytic Period (theta)", 0) (9)

The model generates a series of sawtooth BUN patterns based on the measured $_{sp}$Kt/V and various hypothetical values of g. As the values for g are increased, the height of the sawteeth will rise.

For each value of g, the model assumes that every dialysis has the same $_{sp}$Kt/V (except for ultrafiltration) and runs the simulation until the pre-dialysis BUN (computed for either Monday, Wednesday, or Friday) stabilizes. The model then compares the stabilized pre-dialysis BUN with the actual measured value. If the value is too high, the model inputs a lower value of g and redoes the computation. The model keeps adjusting the value for g until the predicted pre-dialysis BUN value matches the actual value.

BUN decreasing rate = IF THEN ELSE (Dialysis Session Schedule = 1, (((Modeled Dialyzer Clearance (In Vivo) + Residual Renal Function)*Modeled Post BUN)/("Initial Urea distribution volume ($V_{initial}$)"-Ultrafiltration Volume)*Effect of Access Recirculation on dialysis efficiency), 0) (10)

The rate of decreasing BUN during session increases as the dialyzer clearance rate and ultrafiltration rate increases. The residual renal function has an effect on the urea removal during dialysis because a minority of patients with significant residual kidney function (K_r), when unaccounted for, may result in an underestimation in the actual total delivered dose of hemodialysis. Because of the short duration of impact, urea clearance provided by residual kidney function (K_r) contributes little to the intradialytic drop in BUN concentration. However, the long interdialytic interval more fully reveals the impact of K_r, which is manifest in the pre-dialysis BUN concentration and the normalized protein catabolic rate (nPCR).

The pre-dialysis BUN concentration is lowered, and the nPCR is reduced. When K_r is zero, the interdialytic rise in the BUN concentration is linear; if Kr > 0, the rise in BUN will be more shallow and curvilinear resulting from continuous kidney urea excretion. The access recirculation also affects the BUN reduction because it lowering of the urea concentration of the blood flowing into the dialyzer by 5%-40%. The amount of urea removed in the dialyzer is equal to the volume of blood cleared multiplied by dialyzer inflow urea concentration. Although dialyzer clearance remains unchanged, the amount of urea removed is reduced because of the reduced urea concentration at the dialyzer inlet throughout dialysis. It was shown from simulation results that the urea follows a double exponential removal profile in the body as shown in figure 3.

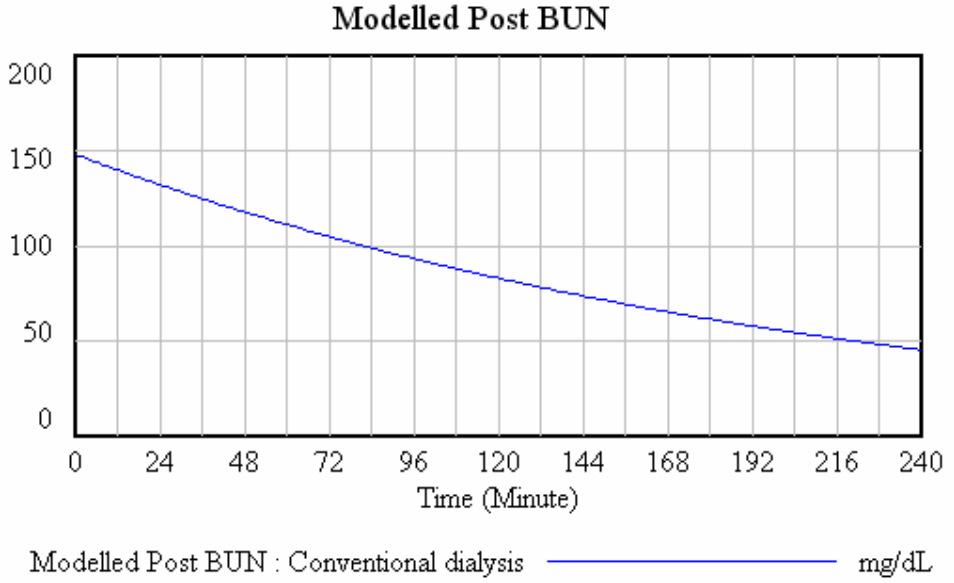

Fig. 3 Modeled Post BUN

D. Study Design

We curve-fitted the modeled post-BUN time profile of using a mono-exponential regression equation:

$$U(t) = U_{\infty} + U_C \cdot e^{-(t-t_0)/\tau} \qquad (11)$$

Where U is the predicted urea concentration at $t = \infty$; U_C is the extrapolated urea concentration at the beginning of curve analysis minus the urea concentration at infinity U_∞ (excess of urea at t_o over urea at infinity U_∞); t_o is the time at which curve analysis was begun; and τ is the time decay constant. The model parameters $\{U_\infty, U_C, \tau\}$ were recorded. The parameter t_o was fixed at time zero and so was not used as an input parameter.

Two models were built corresponding to the complete urea time profile, model A, and to the first half, model B. Although the bi-exponential behaviour of urea kinetics is well-established, we modeled the system dynamics urea time profile with a mono-exponential model, because this model requires fewer parameters than the bi-exponential model for analysis by NN, thus improving the NN estimate by reducing the input dimension-complexity of the NN. In all cases, we found a high regression coefficient between the fitted curve and the observed values for the mono-exponential ($R > 0.97$). The parameters estimated from models A and B were used to feed a neural network to predict their corresponding Kt/V values (Kt/V_{NNA} and Kt/V_{NNB}, respectively). The results were compared between each model and the system dynamics dialysis simulator value.

E. Neural Network.

NNs are mathematical models that grew out of early attempts to model the behaviour of the human central nervous system. They usually consist of a set of simple processing units ('neurones') that are highly interconnected through coefficients called weights ('synapses'). The NNs resemble the brain in two main aspects

(a) Knowledge is acquired by the network from its environment through a learning process
(b) Inter-neuron connection strengths, known as synaptic weights, are modified during the learning process and used to store the acquired knowledge [38].

In this work, an NN called a multi-layer perceptron was used, which is a well known neural network model widely used in biomedical applications; it was trained by a supervised learning algorithm, which means that, during the learning process, input data are presented to the NN, and an error correction strategy is used to update the synaptic connections to minimize the error (or cost function) between the NN output and the true value (desired output). Multi-layer perceptrons (MPs) have been successfully applied to the estimation of equilibrated urea (and also to equilibrated Kt/V) from blood-side measurements [39]. The MP is a feed-forward NN with one input layer (equal in size to the number of input variables used in the analysis), hidden layers (none, one or several) and an output layer. Each layer is connected to the next by numerical coefficients called 'weights'. The NN is trained in an iterative process, with input/output pairs keeping this 'learned' knowledge for future recall. After that, the NN can be used with new inputs not seen during the training phase. The NN was trained with a modified back-propagation algorithm, which is a supervised learning strategy consisting in the modification of the weight values to minimize an error function when an input/output pair is presented to the network. The algorithm used to train the NN was the Levenberg-Marquardt (LM) training algorithm [40], which is a non-linear least squares algorithm applied to batch training of multi-layer perceptrons (all the inputs are presented to the NN before the weights are updated). The transfer function of the hidden nodes was the logistic-sigmoid function, and a linear function was used for the output node.

F. Study analysis

1. **Neural network architecture (size) selection**: To achieve the best NN architecture for this problem, different network sizes (in this case, different numbers of nodes in the hidden layer) were tried. For each of the urea models A and B, we proceeded as follows: the patient records consisting of U_∞, U_C, τ were randomized in their order of presentation and then separated into two sets (training and test sets), as follows:

- Pair set 1: training set first 70% of the samples; test set remaining 30%
- Pair set 2: training set last 70% of the samples; test set first 30%

For each pair set, three NNs of the same size, but differing in initialization weights, were trained to study the stability and robustness of the NN. We used a range of two to seven hidden nodes. The following parameters were analyzed: the average, the standard deviation and the maximum-minimum values over all training tests of

(i) The mean-squared error between the NN output and the system dynamics Kt/V
The mean and standard deviation of the difference between the estimated and the system dynamics Kt/V

(ii) The mean and standard deviation of the error between the estimated and the system dynamics Kt/V, when the estimate was expressed as a percentage of the system dynamics model value. The final architectures were chosen for models A and B on the basis of minimum mean-squared error accompanied by minimum values for (ii) and (iii) in the above list. The result of this process is shown in Table 1.

Table 1 NN estimation performances

M	HN	Error		%Error		MSE
		mean	Standard deviation	mean	Standard deviation	
A	4	–0.049 ± 0.059	0.331 ± 0.023	–0.450 ± 0.034	20.768 ± 0.324	0.065 ± 0.022
B	4	0.031 ± 0.048	0.213 ± 0.011	–0.301 ± 3.648	15.453 ± 0.521	0.034 ± 0.006
M: model; HN: hidden nodes						

2. Final model validation, generation of results:

NNs were chosen, three pair sets were made with different combinations of 80% and 20% of the samples. This increment in the percentages, compared with the training set used to decide the NN size, was made to improve the generalization properties of the NN. The samples employed the jack-knife validation method:

- Pair set 1: training set first 80%; test set last 20%
- Pair set 2: training set last 80%; test set first 20%
- Pair set 3: training set from 10% to 90%; test set first 10% and last 10%.

This implies that the NN models were tested over 27 patients ($46 \times 0.2 \times 3 = 27$), which is more than 50% of the patients. The best weights (giving minimum mean-squared error) of three different training sessions over each input/output training set were chosen as the final NN models.

III. RESULTS AND ANALYSIS

The complete processing flowchart is shown in Fig. 4. The urea values from the system dynamics model are subject to curve-fitting. This yields the three input parameters for the NN, which then predicts the Kt/V.

The Kt/V estimations made by the NN models were analyzed as follows:

(a) Regression of model A against the system dynamics model as the independent variable

(b) Regression of model B result against the system dynamics, expressed as % error of model B against the system dynamics as the independent variable.

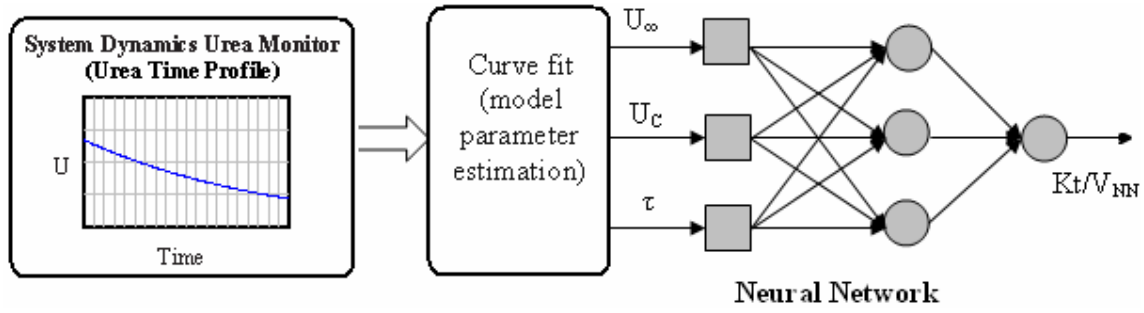

Fig. 4 Flowchart for neural network. Urea concentration-time profile curve fitting process yields" three parameters" {U_∞, U_C, τ } that are input parameters for network consisting of input, hidden and output nodes'. Network-calculated Kt/V is" compared with true value for each case, and synaptic weights" between neurons are adjusted to minimize error of estimate

1. Kt/V Estimation

Table 2 and Fig. 5 show the results of the regression analysis of model A against the system dynamics model for urea estimation. The regression is highly significant, r-squared approaching 74%. The 95% prediction limits of the estimate, at a low Kt/V of 1.0, are evenly distributed around the reference value, giving estimates between 1.2 and 0.8. The regression line consistently underestimates higher values of Kt/V. For example, at a Kt/V of 1.8, the 95% prediction limits range from 1.8 to approximately 1.2. The mean percentage error of model A against the system dynamics was 5.62%±8.65.

Table 2 Regression of Kt/V estimates from model A against system dynamics

	Linear regression (Y=a + bX)			
model	**a**	**b**	**R**	**RMSE**
Kt/V_{NN} against Kt/V_{SD}	0.310	0.701	0.861	0.095

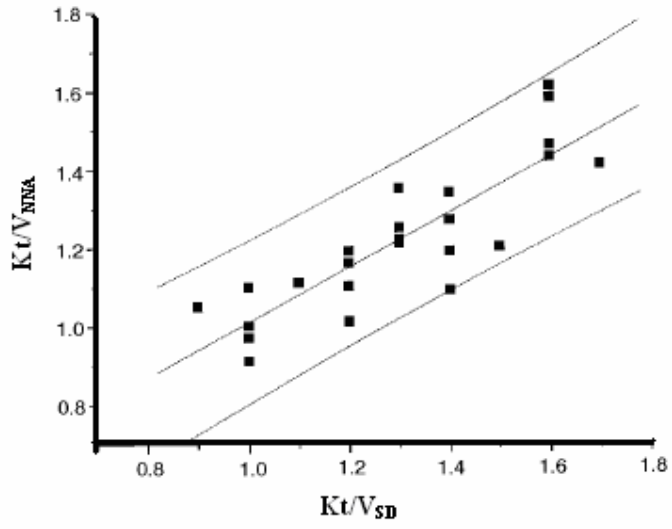

Fig. 5 Regression result for Kt/V from model A against system dynamics value plotted in absolute values" of Kt/V. Regression line and 95% prediction limits" are shown

Fig. 6 shows the results for model B. We calculated the error in model B estimates (Kt/V_{NNB}) compared with the value of the system dynamics Kt/V as:

$$\text{Error} = 100 \cdot \frac{Kt/V_{NNB} - Kt/V_{SD}}{Kt/V_{SD}} \qquad (12)$$

I.e. percent error, and plotted this against Kt/V_{NNB}. Points lying above the zero error line indicate over-estimation by model B. The significance of the vertical line will be explained in discussion section. The mean error of model B against the system dynamics was 6.65%±2.51.

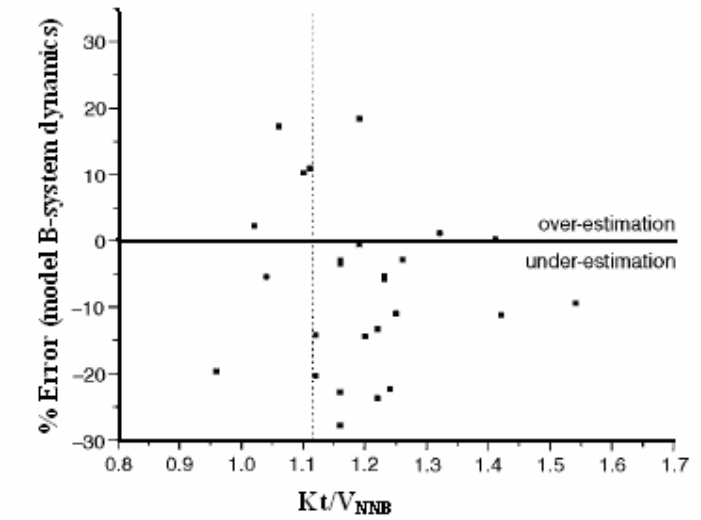

Fig. 6 Estimation error of model B compared with system dynamics value plotted against model B estimate of Kt/V. Points" above horizontal line are over-estimates; points" below are underestimates. Vertical line is" proposed decision threshold. Patients" lying to left of this" line are considered to have significant chance of low, final Kt/V

DISCUSSION

The objective of this study was to find out if a neural network was capable of predicting the value of Kt/V given by the system dynamics simulation model, and, more specifically, if the neural network was capable of predicting Kt/V during the hemodialysis session, so that remedial measures could be undertaken if the predicted Kt/V were too low. Neural networks of the type used here are best kept simple to improve the chance of the algorithm finding a general, rather than local, minimum error. This motivated us to use a single exponent representation of the urea time profile, supported by high values for R^2 in each fired case. Our first finding was that the regression of model A against the system dynamics was satisfactory, yielding a value of 0.86 for the regression coefficient, it should be remembered that these are clinical data, for which this magnitude of R is considered to be good. The fired line correctly estimated low values of Kt/V and progressively under-estimated increasing values of Kt/V. The width of the 95% prediction band was approximately ±0.2 units of Kt/V. Once we had decided that the neural network was capable of estimating the system dynamics Kt/V over the full period of dialysis, we then tested its predictive ability using only the first half of the dialysis period. Obviously, if we have a system dynamics available, we are not at all interested in the result of model A in practical terms, because the system dynamics has by then given us the result.

We are, however, very interested in model B, because it may predict the result at the halfway point of dialysis, allowing us to take corrective action if the predicted value is too low. Our finding is that model B could be useful in this context. As the only data available during dialysis is the prediction from model B, we must select a critical value for the predicted Kt/V from model B, which is used as a decision level for the implementation of corrective measures in the rest of the session. The value we chose was a predicted Kt/V close to 1.1, shown as a vertical line in Fig. 6. The basis for this choice is as follows: the lower-right quadrant of Fig. 6 shows those patients who were under-estimated by model B. All of these patients will achieve a satisfactory Kt/V close to, or exceeding, the generally accepted target value of 1.2. Of the three patients lying in the upper-right quadrant, two were close to zero error and above 1.2, whereas the remaining patient was overestimated by around 18%, would not be treated and would represent a 'false negative'. The upper-left quadrant represents the most serious cases, over-estimated by 10% or more and destined to achieve a Kt/V of about 1. These patients should be treated to improve their final dose. They represent 'true positives' in the present context. The lower-left quadrant contains patients under-estimated by model B, who would be treated to improve their final Kt/V if the model B 1.1 decision threshold were accepted. These patients might have achieved a final Kt/V close to 1.2 on their own and could be considered as 'false positives'.

The important conclusion to be drawn from this analysis is that model B shows a promising performance in the setting of a decision threshold for corrective intra-dialysis measures. A lack of sufficient patients with low final values of Kt/V prevents us from a more rigorous analysis, but we feel that these results should be of interest to those working in the field. We used only three parameters as inputs to the neural network, all related to the urea concentration-time curve, it would be interesting, in the future, to develop neural networks ranging from patient-specific networks, built up over many dialysis sessions, to networks concerning specific characteristics, for example gender-based networks and dialyzer-specific network to optimize for factors affecting the time-constant of the urea curve.

CONCLUSIONS

This work suggests that much information about final Kt/V is carried in the first stage of hemodialysis treatment. It would be useful to adopt an integrated methodology, i.e., a combination of both neural network and system dynamics methodology, for various applications because this would give us an opportunity to combine the advantages of both techniques. Both approaches should be considered as complimentary approaches and can be used effectively for various applications. The neural network approach could be further developed to make on-line treatment modifications to achieve a prescribed dose, thus improving treatment quality.

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