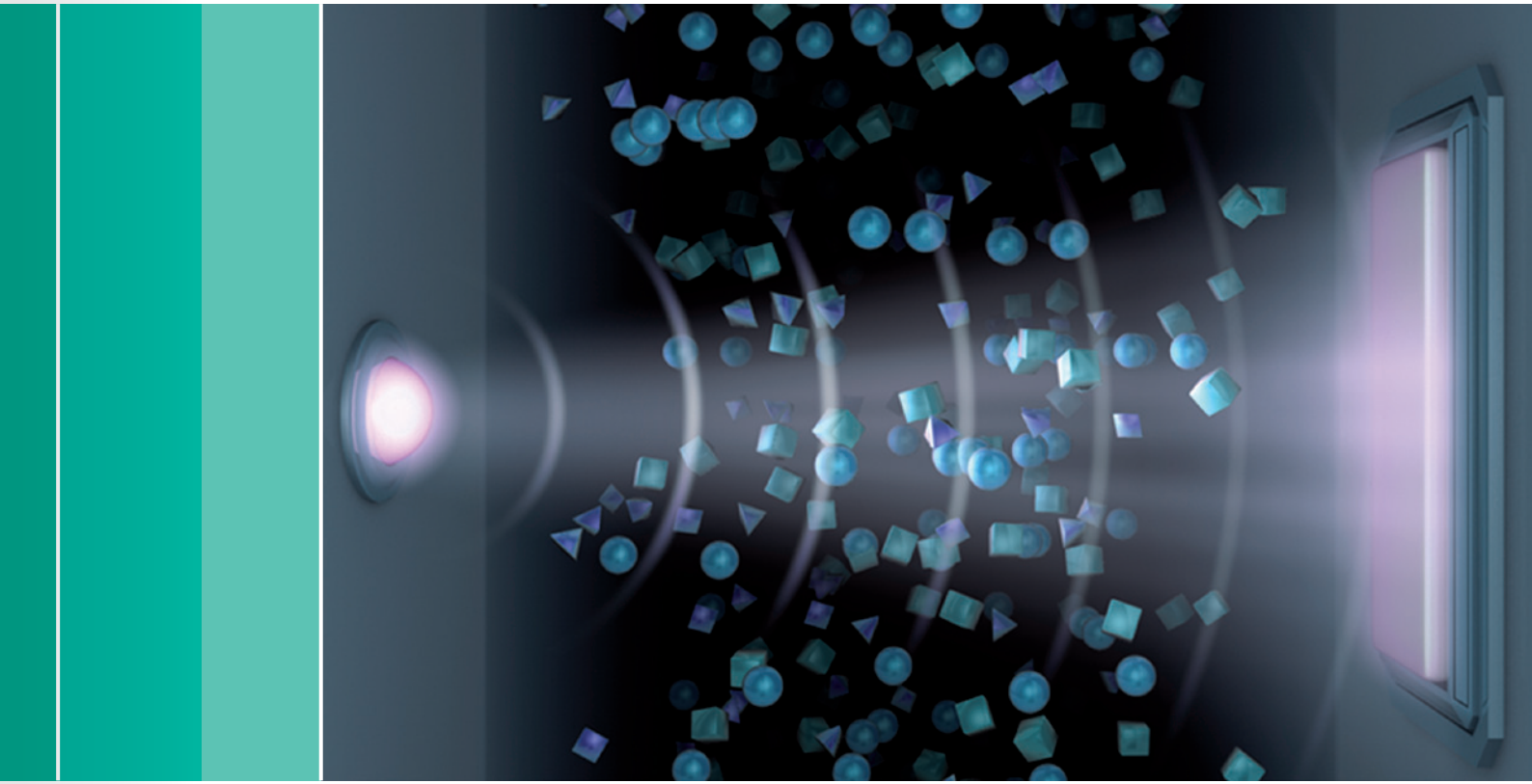
Adimea

User Guide – Case studies from clinical practise



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SHARING EXPERTISE

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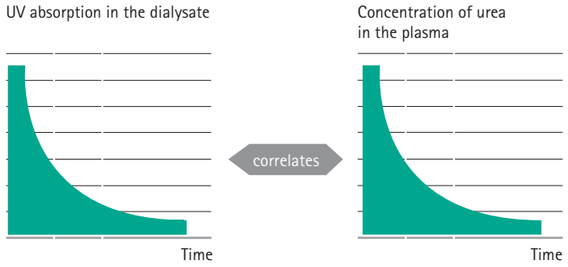
1. Introduction

Adimea product intent and operating principle

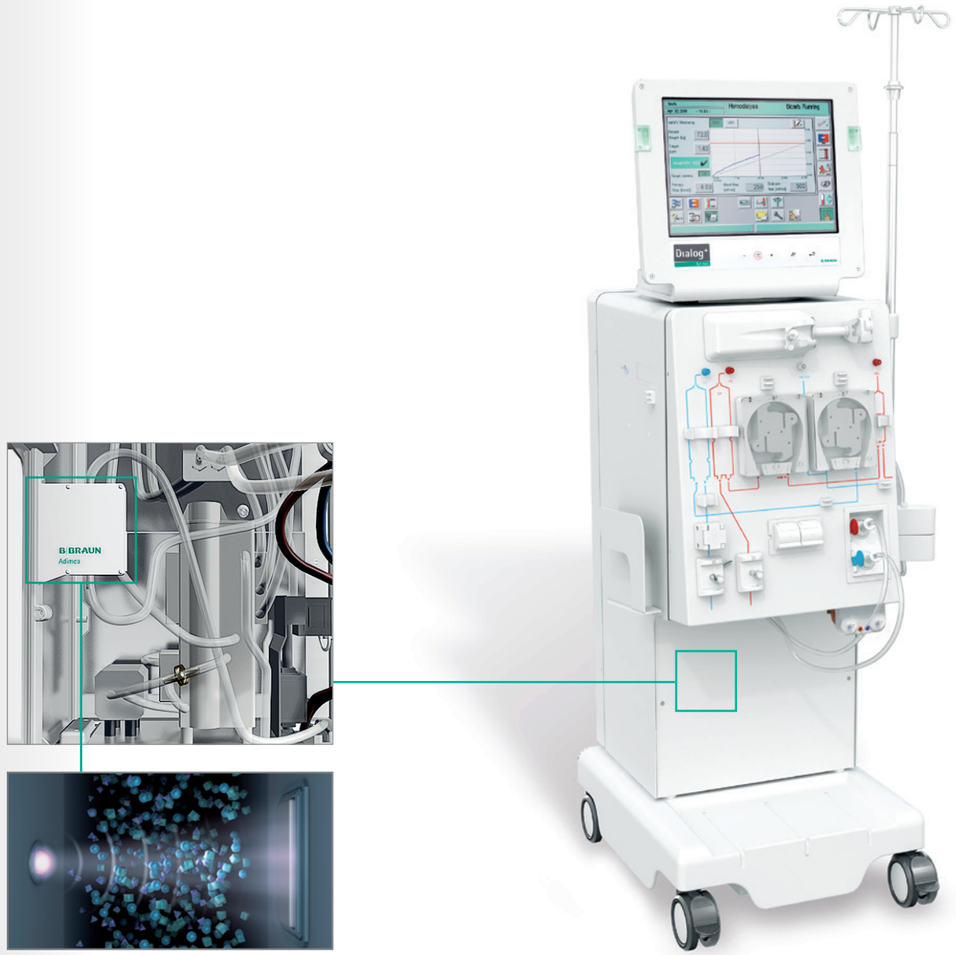
The product name Adimea stands for Accurate Dialysis Measurement.
The real-time measurement system can determine the Kt/V accurately during each dialysis session.

The benefits of daily measurement are obvious:
the user is able to adjust parameters during treatment (blood flow, dialysate flow rate, dialysis duration are especially relevant parameters) to model the Kt/V. A minimum spKt/V of 1.2 is associated with a reduced mortality risk for the patient.[1, 2, 3] Therefore Kt/V is one of the most relevant quality parameters in almost all health systems throughout the world (e.g. KDOQI and EBPG). Experience in the field using Adimea has shown that Kt/V frequently fluctuates from one treatment to the next. If Kt/V is only checked monthly or quarterly, it may be months before sub-optimal dosing is discovered. By measuring online during every therapy, the innovative Adimea system is able to identify sub-optimal dosing immediately, support timely adjustments in treatment parameters and also eliminate common process-related factors influencing the previous reference method (taking of blood samples).[4]

The measurement principle of Adimea is simple: a UV light sensor which is built into the dialysate drain of the Dialog+, measures light absorption and hence the change in concentration of urinary excreted substances as they flow out. The more particles are removed, the more UV lightwaves are absorbed by these particles in the spent dialysate. Over the course of treatment the concentration decreases, resulting in a reduction in light absorption. (See example on pages 6 and 7)



The light absorption course which is accurately recorded by the Adimea measurements corresponds almost exactly to the course of the concentration of urea in the blood. This is the critical measurement for determining Kt/V, which is presented in real-time on the Dialog+. Studies have validated the accuracy of the system.[5]



References:
[1] Held PJ, Port FK, Wolfe RA, et al: The dose of hemodialysis and patient mortality. Kidney Int 50:550-556, 1996, [2] Owen W, Lew N, Liu Y, Lowrie E, Lazarus M: The urea reduction ratio and serum albumin concentration as predictors of mortality in patients undergoing hemodialysis. N Engl J Med 329:1001-1006, 1993, [3] Port FK, Ashby VB, Dhingra RK, Roys E, Wolfe RA: Dialysis dose and body mass index are strongly associated with survival in hemodialysis patients. J Am Soc Nephrol 13:1061-1066, 2002
[4] Daugirdas JT, Tattersall JE. Automated monitoring of hemodialysis adequacy by dialysis machines: potential benefits to patients and cost savings. Kidney Int. 2010 Nov; 78(9):833-5., [5] Castellarnau A, Werner M, Günthner R, Jakob M. Real-time Kt/V determination by ultraviolet absorbance in spent dialysate: technique validation. Kidney Int. 2010 Nov; 78(9):920-5.

1. Introduction

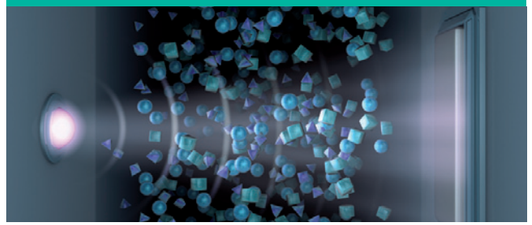
Adimea operating principle – treatment example

Measurement in dialysate

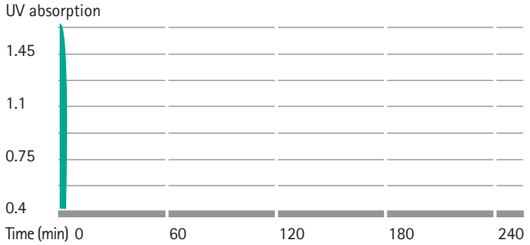
UV light absorption

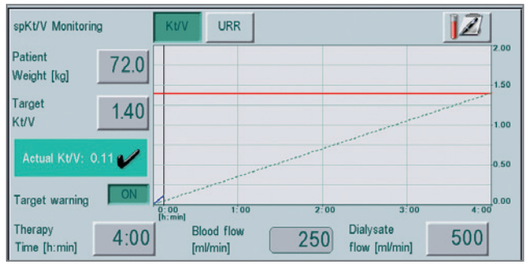
Real-time Kt/V

Start of dialysis

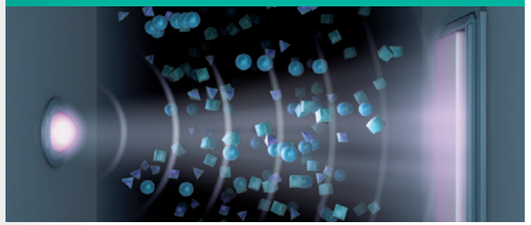


High concentration of substances – high light absorption

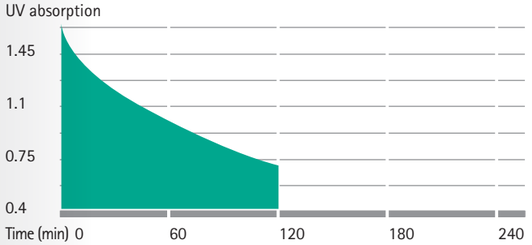


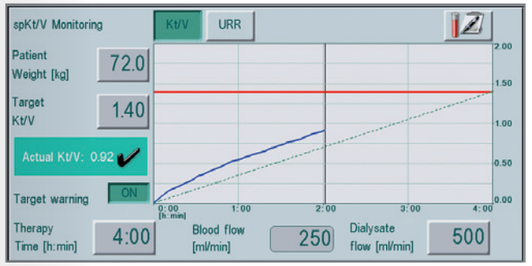


Half-way through treatment

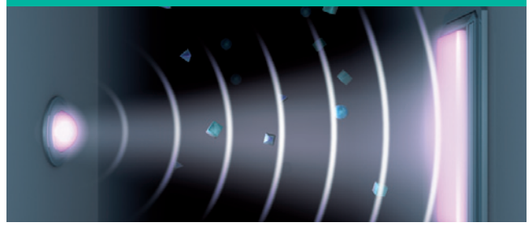


Exponential reduction over time

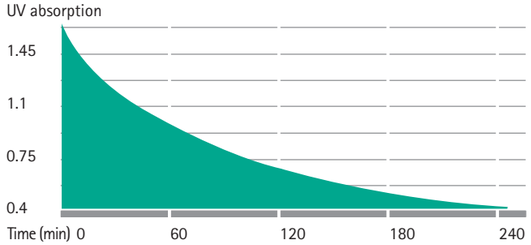


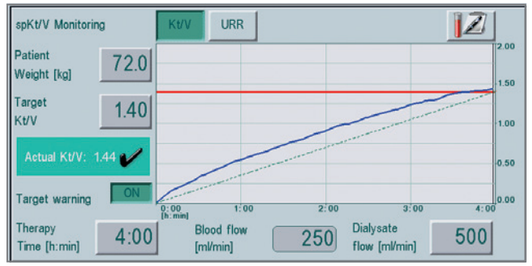


End of dialysis



Low concentration of substances – low light absorption





2. The Kt/V Navigation System

Support when administering high-quality treatments

To reach the planned objective as directly as possible at the same time as optimising resources, is a requirement of modern navigation systems. Adimea fulfils this requirement:

1. Individual patient objectives are set at the start of dialysis.
2. Over the course of the treatment the user can quickly and clearly see whether the treatment complies with the planned "route" and whether the objective that has been set can be achieved (eg Kt/V > 1.2).
3. If problems develop, the system offers the user the ability to alter the parameters while treatment is still ongoing and to adapt treatment to the current circumstances to achieve the objectives.
4. Any adjustments made are incorporated in real-time and represented in the measurements.

A standard feature of the Dialog+ is a simple and clear user menues.

**The user is constantly aware of the objective:
Achieving adequate dialysis dose every treatment.**

Only one setting to start the system!

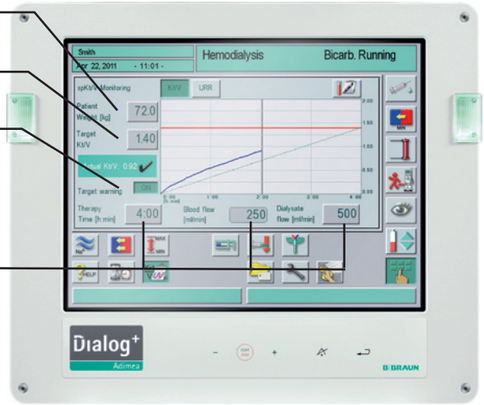
1

Enter weight (current wet weight before dialysis)

Check or set Kt/V target value

Is target (value) warning active?
Only then will the system notify the user in the event of impending suboptimal dose (yellow signal lamps)

Simple and rapid access
Overview of relevant treatment parameters



Simple overview of ongoing treatment

Switch between Kt/V and urea reduction ratio (URR)

Kt/V data storage
(only in conjunction with Patient Therapy Card or Nexadia)

Real-time overview of Kt/V
(graphical and numerical)

3. Application during treatment

Continuous information about the administered dialysis dose

Dialog⁺ informs the user quickly and clearly via the signal lamps about the current treatment situation.

Green indicates: everything is ok.

If the Adimea target (value) warning is activated, a predicted suboptimal dosing may be the reason for a change to the yellow warning status.

If this happens, the user can immediately assess the treatment status by looking at the dialysis machine.

If the Kt/V is too low, treatment parameters can be simply and rapidly adjusted to model the Kt/V. (The next section describes in detail which parameters can be changed and how this is done). After a short wait (usually 3 to 7 minutes) the effect of the change can be viewed on the screen.

If the clearance performance improves, the device immediately switches back to the green status. If the changes are not successful, further adjustments can be made.

4. Adjusting treatment parameters

Adimea offers direct control of 3 important influencing factors

One crucial benefit of real-time measurement is the ability to model dialysis conditions while dialysis is still on-going. This makes targeted oriented treatment possible. Kt/V is thus directly dependent on effective dialysis time, blood flow rate and dialysate flow rate.

Blood flow rate | **Dialysate flow rate** | **Effective dialysis time**

Changes in blood flow and or dialysate flow influence clearance. A longer dialysis time means more time to remove urinary excreted substances. The case studies on the following pages demonstrate what effects changes in the parameters have on the treatment status.

Adjustments to treatment parameters during dialysis sessions must be agreed with the physician.

Case study I

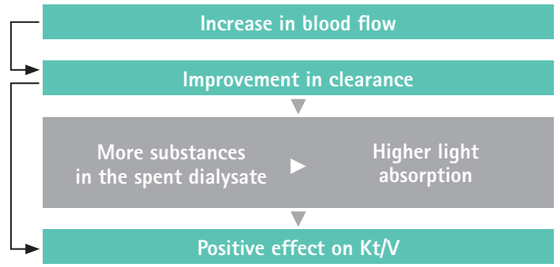
Increasing blood flow ➲ increases Kt/V

Blood flow rate is very important regarding small molecule clearance. A higher flow-rate means a larger volume of blood is treated. More urinary excreted substances can pass through the dialyser and be removed per minute and hence also over the duration of treatment. This improves clearance. Naturally, one requirement is that the dialyser can also transport the larger quantity of substances. The use of large membrane surfaces is generally beneficial. A blood flow rate increase of between 200 to 350ml/min has pratically a linear effect on the Kt/V administered[6]. Adjusting blood flow – if the general status and in particular the vascular access of the patient allow – should be the first choise to optimize Kt/V. ⚠

Effect of the change on the course of treatment:

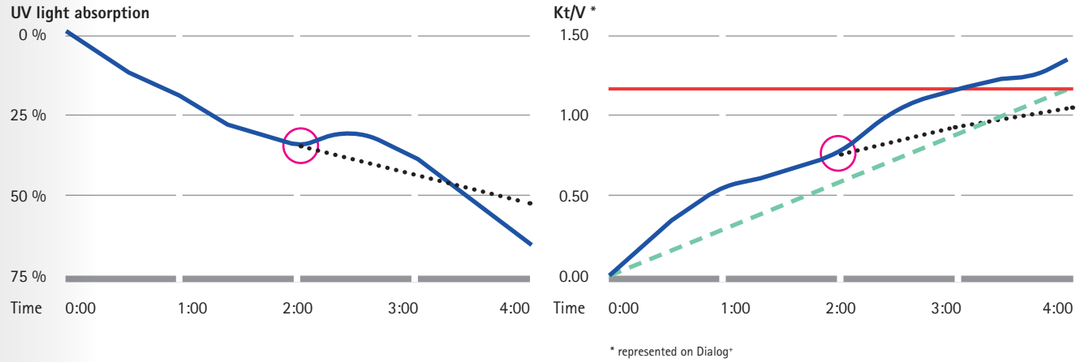
- Adimea target value warning after 2 hours and 5 minutes treatment time
- User intervention: increase in blood flow rate (+50 ml/min)

The higher blood flow improves clearance and hence the efficacy of dialysis.



⚠ Adjustments to treatment parameters during dialysis sessions must be agreed with the physician.

References: [6]) Hörl, W.; Wanner C.: Dialyseverfahren in Klinik und Praxis (Dialysis procedures in the clinic and surgery). Technik und Klinik. 2004. Georg Thieme Verlag (Stuttgart)



Result

After the blood flow rate was adjusted, the patient achieved his target Kt/V during this treatment.

Actual treatment curve (including change in treatment parameters)
Predicted treatment curve without adjustment in treatment parameters
Kt/V orientation line (Dialog+ screen)
Target Kt/V
User intervention time point

Case study II

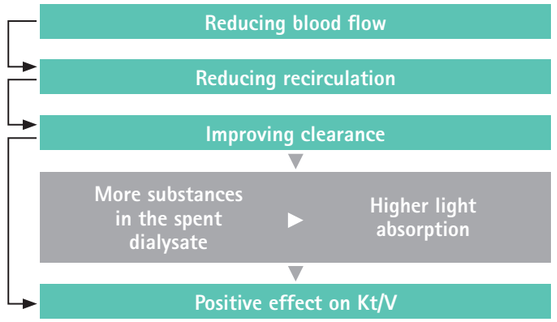
Reducing blood flow ➲ increases Kt/V

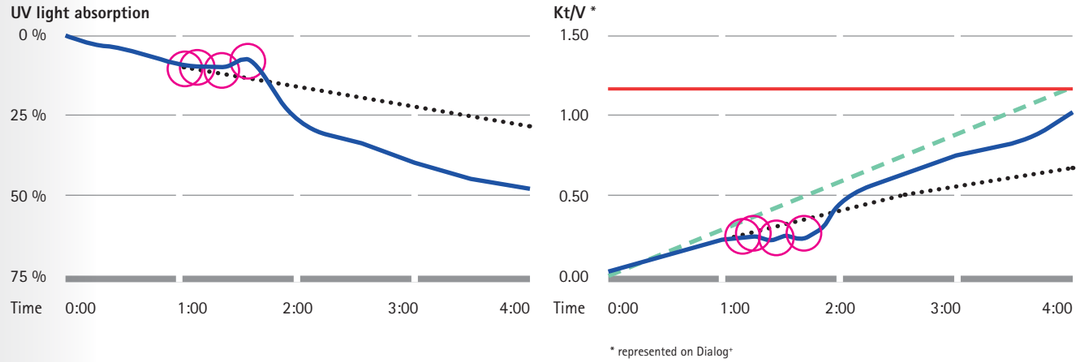
Increasing blood flow as described in the first case study may not achieve the desired effect in some patients: the higher the blood flow rate, the higher the probability of recirculation in the shunt. Recirculation means that cleaned blood flows through the dialyser without previously having been enriched with urinary excreted substances in the body of the patient. So an increase in flow may cause clearance performance to decline in this circumstance. Therefore in specific circumstances it may make sense to reduce the patient's blood flow to increase the Kt/V. ⚠

⚠ Adjustments to treatment parameters during dialysis sessions must be agreed with the physician.

Effect of the change on the course of treatment:

- Adimea target value warning after 1 hour and 3 minutes' treatment time
- User intervention: in the case presented, the blood flow rate was initially increased in several stages (at 5 to 7 minute intervals by a total of +80 ml/min) to increase clearance and hence the efficacy of dialysis. However, this did not result in a positive effect on the Kt/V.
- After assessing treatment and patient status (close position of needles / poor access ▸ recirculation?) it was decided to reduce blood flow (-60ml/min compared with the baseline value) to minimise a possible shunt recirculation
- After a few minutes an increase in Kt/V was recorded. This suggests that there was significant recirculation in the shunt which was able to be reduced by decreasing blood flow.





Result

The target Kt/V could not be achieved by the end of dialysis because of the decline in efficacy in the first 90 minutes of treatment. However a significantly better Kt/V than the predicted value could be achieved. (1.01 vs 0.72)

Case study III

Increasing dialysate flow ➲ increases Kt/V

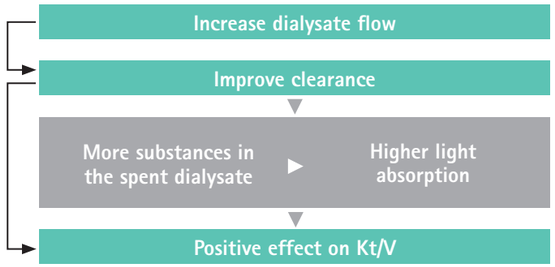
Increasing the flow of dialysate has less of an effect on clearance than blood flow. Despite this, the effect should not be underestimated. The higher flow of dialysate increases the concentration gradient in the dialyser – and clearance is increased due to better diffusion. ⚠

It makes sense to adjust this parameter, especially when the blood flow is already very high and more urea is offered to the dialyser via the blood flow than can be removed.

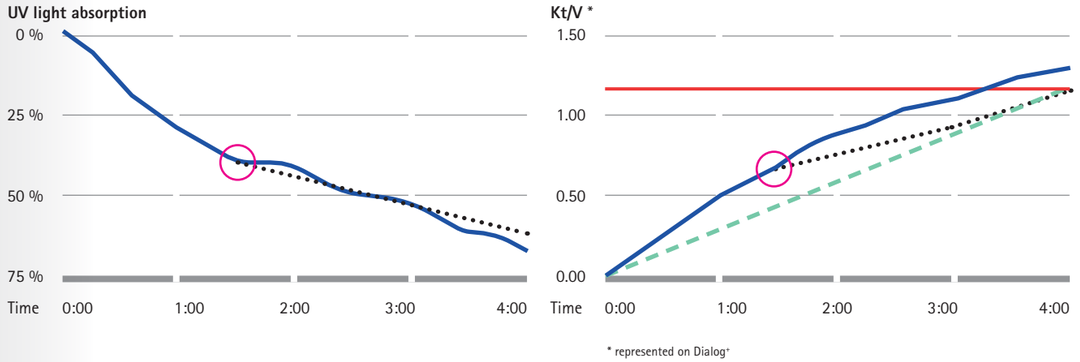
Effect of the change on the course of treatment:

- Adimea target value warning after 1 hour and 31 minutes' treatment time
- User intervention: increase in dialysate flow rate (+50 ml/min)

The higher dialysate flow changes the concentration gradient – clearance and hence efficacy of dialysis can therefore be improved. The change gave the patient a higher Kt/V at the end of treatment than if there had been no intervention. Increasing the flow of the dialysate has less of an effect on clearance than altering blood flow. Accordingly, this is reflected in smaller changes in the course of the Kt/V. An increase in the dialysate flow from 500ml/min to 800 ml/min while maintaining blood flow the same at 300 ml/min increases Kt/V by aprroximately 10 %. In the example shown, this translates as follows: the increase in dialysate flow improved clearance ▸ the concentration of substance in the spent dialysate was thereby increased ▸ more light was absorbed ▸ the UV light absorption curve flattens outfor a short time. In contrast, the Kt/V increases as more particles of substance are removed.



⚠ Adjustments to treatment parameters during dialysis sessions must be agreed with the physician.



Result

The target KtV was achieved by adjusting dialysate flow.

Actual treatment curve (including change in treatment parameters)
Predicted treatment curve without adjustment in treatment parameters
Kt/V orientation line (Dialog+ screen)
Target Kt/V
User intervention time point

Case study IV

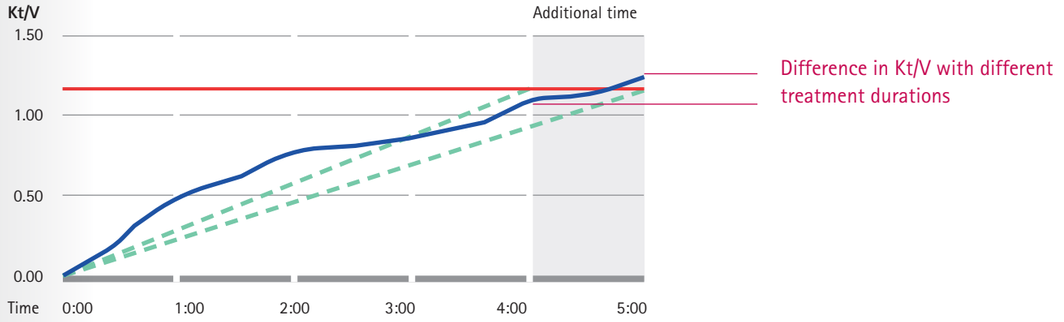
Extending dialysis time ➲ increases Kt/V

Extending dialysis time - if practical - is the most effective way to influence dialysis dose. Longer effective dialysis time means longer time to remove urinary excreted substances. Extending this parameter is also medically the most sensible measure, since not only does this influence the clearance of urea, but it also has a positive effect on fluid balance and middle molecule elimination.

Effect of the change on the course of treatment:
The treatment course presented shows that with longer treatment running times there is correspondingly more time available to achieve the target Kt/V. In other words: more time available to remove urinary excreted substances.

In the treatment example presented, the Kt/V was achieved with a set dialysis time of 5 hours and no warning messages were generated. In contrast, with the 4-hour treatment after approx. 2 hours and 10 min'. of treatment the system would have generated a Kt/V target value warning. Without adjustment, the Kt/V target value cannot be achieved.

Longer dialysis time
→ **More time to remove urinary excreted substances**
→ **Higher Kt/V at the end of dialysis**



* represented on Dialog+

Result

By extending dialysis time the Kt/V can normally be achieved without any change in flow parameters. This highlights the significance of longer dialysis times.

Actual treatment curve (including change in treatment parameters)
Predicted treatment curve without adjustment in treatment parameters
Kt/V orientation line (Dialog+ screen)
Target Kt/V
User intervention time point

5. Recording and interpreting the daily measurements

The daily measurements with Adimea enable the dialysis dose to be monitored while each treatment is ongoing. Storing the relevant Kt/V data on Patient Therapy Card or in the Nexadia data management system additionally enables a comprehensive retrospective evaluation of the treatment status.

For example, trends in the course of the Kt/V can be observed and assessed. Cases from clinical practice show that steadily falling Kt/V values could indicate a developing shunt stenosis (see example). Therefore, because of the data storage, Adimea offers additional support, including in the interpretation of shunt conditions.

Recommendation based on the conditions in the example below: Check shunt conditions.

Smith

Apr 22, 2011 - 13 00 -

Preparation Acknowledge data!

Therapy date and time [dd.mm.yyyy h:min]	Target Kt/V [-]	Patient weight [kg]	Actual therapy time [h:min]	Average blood flow [ml/min]	Average dialysate flow [ml/min]	Act.URR [%]	Act.Kt/V [-]	spKt/V
14.03.2011 08:05	1.40	65.8	04:05	245	500	75	1,43	
16.03.2011 08:08	1.40	65.5	04:03	250	500	75	1,43	
18.03.2011 08:10	1.40	65.3	04:00	255	500	76	1,45	
21.03.2011 08:01	1.40	65.8	04:05	250	500	74	1,41	
23.03.2011 07:58	1.40	65.5	03:58	245	500	66	1,25	
25.03.2011 08:05	1.40	65.1	04:05	230	500	57	1,08	
28.03.2011 08:03	1.40	65.6	04:10	235	500	61	1,14	
30.03.2011 08:11	1.40	65.5	04:00	240	500	53	1,01	
01.04.2011 08:06	1.40	65.7	04:05	240	500	51	0,98	

Almost consistent treatment parameters Decreasing Kt/V trend

In association with the evaluation of the Kt/V reference value from the blood sampling, data storage of the daily Kt/V values with Adimea offers a crucial benefit: If the blood Kt/V differs significantly from the stored Adimea measurements, improper handling during blood sampling could be the reason for an incorrect blood Kt/V value. One possible consequence is misinterpretation of the treatment status. If the prescription is adjusted immediately – based on only a single Kt/V value – long-term suboptimal dosing may be the result. It is also conceivable that during a treatment e.g. due to frequent interruptions in treatment, only a low Kt/V was achieved. The user should consider whether treatment parameters should be adjusted to prevent suboptimal dosing during dialysis based on a single measurement.. Evaluation of the long-term Kt/V values would show that the patient is normally achieving his target Kt/V and no adjustment in parameters needs to be carried out.

For comparison: blood Kt/V 1.16 (determined from pre and post-dialysis blood sample)

Recommendation: no adjustment in treatment parameters.

Smith

Apr 22, 2011 - 13 00 -

Preparation Acknowledge data!

Therapy date and time [dd.mm.yyyy h:min]	Target Kt/V [-]	Patient weight [kg]	Actual therapy time [h:min]	Average blood flow [ml/min]	Average dialysate flow [ml/min]	Act.URR [%]	Act.Kt/V [-]	spKt/V
14.03.2011 08:05	1.40	65.8	04:05	245	500	75	1.43	
16.03.2011 08:08	1.40	65.5	04:03	250	500	75	1.43	
18.03.2011 08:10	1.40	65.3	04:00	255	500	76	1.45	
21.03.2011 08:01	1.40	65.8	04:05	250	500	72	1.41	
23.03.2011 07:58	1.40	65.5	03:58	245	500	76	1.45	
25.03.2011 08:05	1.40	65.1	04:05	250	500	74	1.42	
28.03.2011 08:03	1.40	65.6	04:10	245	500	75	1.43	
30.03.2011 08:11	1.40	65.5	03:30	230	500	61	1.15	
01.04.2011 08:06	1.40	65.7	04:05	250	500	76	1.45	

Almost consistent Kt/V values Lower blood flow / shorter treatment time than usual

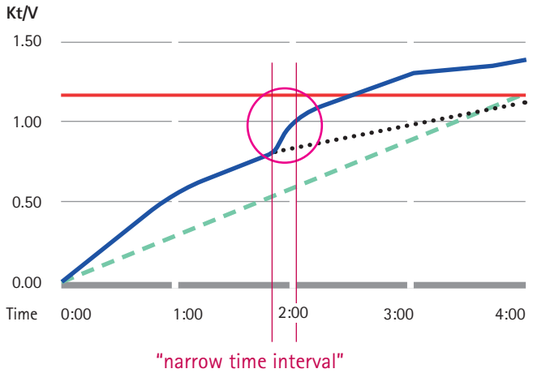
6. Typical curves and their significance

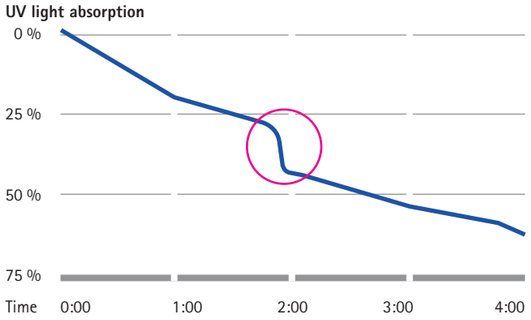
Sharp rise in Kt/V curve

Due to a variety of physiological conditions, every dialysis patient will have an individual Kt/V or URR curve shape. This is attributed to the reaction of the patient to the processes of dialysis which triggers a different and individual mobilisation of small molecule substances in each patient. However there are Kt/V curves that can arise under specific circumstances in all patients and allow conclusions to be drawn about certain events during dialysis. One example of this is a significantly rising Kt/V over a relatively short period of dialysis (10 – 15 minutes).

This may be due to two influencing parameters which have an identical effect in principle:

1. **Sudden and severe filter clotting**
2. **Sudden and severe recirculation**



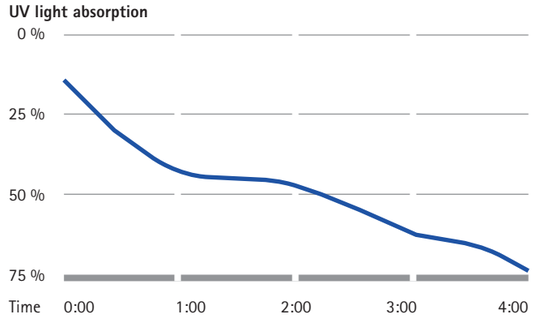


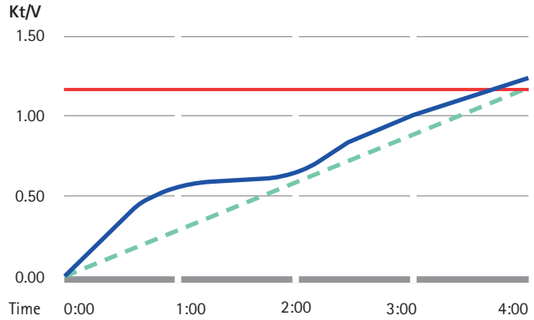
Both events lead to a drastic reduction in the spent dialysate of urinary excreted substances. Clotting blocks the membrane, recirculation prevents the blood being enriched by urinary excreted substances in the body of the patient. If this happens, the UV sensor suddenly measures fewer substances in the discharge from the dialysis equipment without receiving the information that the initial parameters have changed. This leads to a slight overestimation of the Kt/V at the end of this single treatment. The intelligent software of the system highlights the influence to a narrow time interval. Despite the slightly fluctuating Kt/V value, this situation is of decisive benefit to the user as evaluation of the treatment curve on the graph makes the influencing factors obvious: the filter can if necessary be checked for clotting or the poor needle positioning corrected.

Flattening of the Kt/V curve

A phenomenon that is frequently observed in clinical practice is the flattening of the Kt/V curve over a limited time period during the course of treatment. This flattening can often be observed in individual patients at the same time point each treatment.

The reason for this is that mobilisation of small molecule substances from the second and third compartments takes place to a different speed for each patient. A large quantity of substances flows rapidly out of the spaces in the cells and between the cells into the cleaned blood. The concentration of substance in the dialysate discharge remains temporarily constant – which means that the Kt/V does not increase. After some time the processes slow down causing the concentration of substance in the dialysate discharge from the machine to fall again steadily. Why individual patients show this very rapid mobilisation for a short time has not yet been established. The redistribution of fluids between the compartments could provide one possible explanation. A flattening of the curve can often be observed when blood pressure falls.





Actual treatment curve (including change in treatment parameters)
Predicted treatment curve without adjustment in treatment parameters
Kt/V orientation line (Dialog⁺ screen)
Target Kt/V
User intervention time point

7. Glossary

Name	Explanation
Clearance	Generally clearance describes the removal of a certain substance from a system in the body. In the particular case of dialysis this is normally considered to be the elimination of urea from the body of the patient.
KDOQI	Guidelines on the treatment of patients with chronic kidney disease: Kidney Disease Outcome Quality Initiative (KDOQI). Published by the USA organisation „National Kidney Foundation“ (NKF).
EBPG	Guidelines on the treatment of patients with chronic kidney disease: European Best Practise Guidelines (EBPG). Published by the European organisation „European Renal Association“ (ERA).
First compartment	Intravascular space (Fluid space within the blood vessels)
Second compartment	Interstitium (Spaces between the cells)
Third compartment	Intracellular space (Fluid space in the cells)
Kt/V	Quality parameter for assessing the effectiveness of dialysis. (K=urea clearance / t=dialysate time / V=urea distribution volume of patient)
spKt/V	single-pool Kt/V. Calculation model of Kt/V according to Daugirdas. Urea generation during dialysis as well as effects of ultrafiltration are included in the determination of Kt/V by this model

Important information

The case studies presented show example curves of individual treatment situations. In routine clinical practice, adjustments of blood flow, dialysate flow and dialysis time may provide differing results. Altering parameters during ongoing treatment must be tailored to the situation of the individual patient. Changes in parameters must therefore always be agreed with the treating physician.

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