Hoe de efficiëntie van hemodialyse meten?

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Een van de nefrologen van het
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Hasselt

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Hemodialyse-efficientie
intro 1

- Gezonde nieren:
  - functioneren 10.080 min/week
  - met regulatie van filtratie, reabsorptieve en endocriene functies
  - Filtratie capaciteit voor kleine moleculen: circa 1200 l/Week

  (Hoe meten we de nierfunctie?: creatinineklaring: 100 ml/min)

- Dialyse
  - 720 tot 1.440 min/week (3 maal 4 tot 8 uur per week)
  - enkel filtratie (door diffusie, convectie, ultrafiltratie)
  - filtratiecapaciteit voor kleine moleculen 150 tot 200 l/week

  En toch is tot decades overleving met dialyse mogelijk.

Hemodialyse-efficiëntie
intro 2

Hoeveel dialyse is genoeg?

Zo veel mogelijk, als 2 gezonde nieren ⟷ **Niet meer dan nodig**

Hemodialyse-efficiëntie
intro 3

Hemodialyse-efficiëntie
intro 4

Continue kwaliteitsverbetering (Accreditering)

Hemodialyse-efficiëntie

0. Introductie

1.Wat? en voor wie?

2.Welke parameters?

Kt/V en zijn geschiedenis

3.Hoe?

4. Besluit

Hemodialyse-efficiëntie
Wat?

1. Wat

‘**Dialysis-adequacy’: adequaatheid**

Patiënt georiënteerd

- ↓ Mortaliteit
- ↓ (minimaliseert) morbiditeit
  van dialyse en chronische nierinsufficiëntie
- ↑ (behoud van) Kwaliteit van leven:
  maximaliseert welzijn
  en behoud sociale onafhankelijkheid.

Hemodialyse-efficiëntie voor wie?

1’. En voor wie?

- Bedrijf/Ziekenhuis: winst?
- Werk-organisatie van artsen en verpleging?
- Patiënt?
- Overheid?

2012 QIP (Quality Incentive Program) USA
Pay for performance (- 2 % financiering zo niet gehaald) ipv fee for service:
3 clinical measures
- anemia management,
- **hemodialysis adequacy**
- vascular acces type

3 reporting measures:
- dialysis savety events
- attestation of administering a patient satisfaction survey
- attestation of patient mineral metabolism monitoring

Am J Kidney Dis. 2012 Nov;60(5 Suppl 1):S5-13; quiz S14-7. doi: 10.1053/j.ajkd.2012.07.002

Hemodialyse-efficientie, geschiedenis 1

- 1965
  - HD: 3 maal per week,
  - >20 uur per week,
  - Mortaliteit aan dialyse < 10 % jaar (USA)

- 1981: **NCDS: National Cooperative Dialysis Study**

  RCT: hoog vs laag ureum voor dialyse, midweek, TAC

  korte (194-199 min) vs lange (269-271 min) dialyse (p: 0.056)

  → ureum klaring en nPCR is belangrijk, maar niet dialysetijd

  te kleine patiëntenaantallen?, exclusie van diabetespatiënten, cellulose kunstnieren

- 1985: Gotch: mechanistische analyse NCDS: **Kt/Vureum**

  Kt/V 0.95 à 1 is voldoende voor adequate dialyse,

  kortere tijd kan gecompenseerd worden door hogere klaring van ureum → kortere dialyse, 3 tot 2 uur per sessie → mortaliteit ↑24.5%/jaar

Hemodialyse-efficiëntie, geschiedenis 2

- 1985-1990

  Japanse en Europese **observationele** studies: betere overleving dan in USA door langere dialyse?

- 1990

  Kt/V 1.2 -1.3 als standaard

- 1991 Bernard Chara, Tassin: 3 x 8 uur per week, low flux

  'We suggest that patient **survival** should be considered as the best overall index of adequacy of dialysis'

- 1992 Belding H Scribner

  'Adequate control of **blood pressure** now must become a **part of the definition of adequacy of dialysis** along with an adequate dose of dialysis and adequate intake of protein'.

Hemodialyse-efficiëntie geschiedenis 3

- 1995

  NKF-KOQI: sp Kt/V ureum: (1.2 -) 1.3

  zo 3 maal hemodialyse per week

- 1997

  Japanse dialyse registratie:

  dialysetijd korter dan 5 uur: predictor voor dood

- 2000

  NKF-DOQI update: spKt/V ureum 1.3 (single pool)

  eKt/V 1.05 (double pool, equilibrated)

Hemodialyse-efficiëntie geschiedenis 4

- 2002

  Hemodialysis (**HEMO)** Study Group, NIH sponsored (NEJM 2002; 247:2010-2019)
  - Van 03.1995 tot 10.2000
  - 190 min vs 219 min (+ 15%)
  - Qb: 311 vs 375 ml/min (+ 20%)
  - spKt/V en eKt/V: 1.32 en 1.16 vs 1.71 en 1.53

  → 'patients undergoing hemodialysis thrice weekly appear to have no major benefit from a higher dialysis dose higher than the recomended by current US guidelines'

  Twardowski 2013: 'if the higher dosis is achieved mainly by indreased dialyser blood flow' (NDT 2013: 28:826-232)

Hemodialyse-efficiëntie geschiedenis 5

- 2006

  DOPPS observational study

  1. duur van dialysesessie ~ lagere mortaliteit (ook nog na rekening te houden met case mix, Kt/V, gewicht, non-adherence: tot 4.5 uur)
  2. hoge Kt/V is beter indien met langere dialyseduur
  3. UFrate > 10 ml/kg/uur is geassocieerd aan hoger risico op mortaliteit en intradialytische hypotensie (bevestigd in re-analyse HEMO)

- 2010

  Frequent Hemodialysis Network Trial Group: n=245, RCT, NIH fundend:

  in-center, 12 maanden, circa 52 jaar oud, 10.4 vs 12.7 uur per week, Qb 402 vs 396 ml/min, Qd 710 vs 747 ml/min

  geen overlevingsverschil tussen 5-7 maal per week en 3 maal per week

  (control group: 8.7% mortaliteit, wel betere bloeddrukbeheersing, lage fosfor, lagere LVmass, welbevinden beter, N ENGL J MED 2010; 363:2287-2300

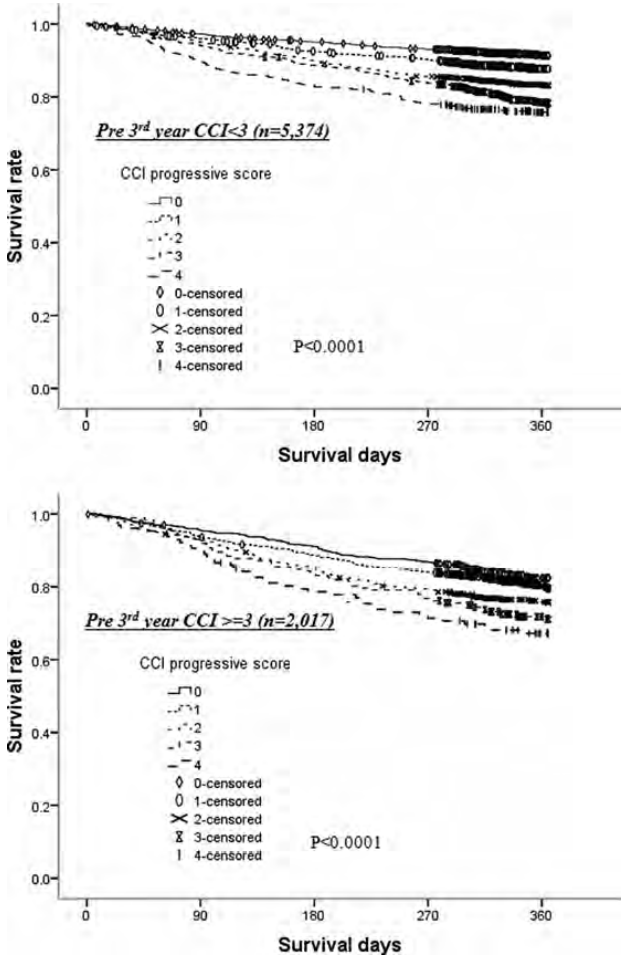
- 2011

  Frequent Hemodialysis Network Nocturnal Trial: onvoldoende recrutering,

  3 x 4 uur vs 6 x nachtelijke dialyse; n= 87: type II statische fout

- Geen effect (*Kidney International* (2011) **80,** 1080–1091)

Hemodialyse efficiëntie: te laat?



Nephrol Dial Transplant (2013) 28: 1005–1012

Hemodialyse efficientie: complex!

Table 2. HRs and 95% CIs for mortality from all causes and cardiovascular disease by marital status in haemodialysis patients[a]

	Marital status		
	Married	Single	Divorced/widowed
Number of patients	795	146	123
Person-years	3198	602	461
All causes			
Number of cases	286	41	58
Mortality rate	89.4	68.1	125.9
Multivariate-adjusted HR (95% CI)	1 (reference)	1.51 (1.06–2.16)	1.28 (0.95–1.73)
Cardiovascular disease			
Number of cases	131	22	32
Mortality rate	41.0	36.5	69.5
Multivariate-adjusted HR (95% CI)	1 (reference)	1.68 (1.03–2.76)	1.73 (1.15–2.60)

HR, hazard ratio; CI, confidence interval.
[a]Morality rate was defined as number of deaths per 1000 person-years. Multivariate-adjusted HRs were estimated by adjusting for age, sex, duration of haemodialysis, cause of renal failure, body mass index, systolic blood pressure, total cholesterol, HDL cholesterol, hsCRP, albumin, co-morbid conditions (stroke, myocardial infarction and cancer), current smoking, regular alcohol consumption, education level and job status.

Nephrol Dial Transplant (2013) 28: 1013–1020

Adequate hemodialyse parameters 1

- Welbevinden van de patiënt (fysisch, mentaal, sociaal)
- Voedingstoestand: malnutritie is erger dan obesitas; PCR (protein catabolic rate), serumalbumine, SGA
- Bloedvolume per dialyse (ruwe parameter: minstens zoveel liter als iemand weegt)
- Kt/V ureum
- Klaring van middle en grote moleculen: beta2-microglobuline
- Euvolemie: Ultrafiltratie (<8 ml/kg/uur; ‘slow ultrafiltration’), vullingstoestand (klinisch, BCM, echocardiografie,echo sushepatische vaten, echo longen)
- Adequate bloeddrukcontrole (Mr Clyde Shields and dr. Scribner 1960, Dr. Charra in Tassin, 1983): door volumecontrole en zoutbeperking (voeding en dialysaat)
- Lage frequentie van intradialytische hypotensie

Adequate hemodialyse: parameters 2, niet exhaustief

- Controle van anemie, kalium, metabole acidose, fosfor, metabolic bone disease
- Vaatacces: % av-fistel, katheter gerelateerde complicaties (bacteriemie)
- Hospitalisatie-frequentie, re-hospitalisatie binnen 30 dagen
- Dialysewaterkwaliteit
- Kunstnier, voorbereiding kunstnier
- Anticoagulatie
- Sterilisatiemethodiek
- Educatie van patiënt en familie
- Voorbereiding naar transplantatie
- Mobiliteit
- Transport van en naar de dialyse-afdeling
- Ondersteuning door diëtiste en sociale dienst
- Hemodialyse produkt: HDP

Adequate hemodialyse: parameters 3: een buitenbeentje

Table I. Various values of the Hemodialysis Product (HDP), as well as the corresponding expected clinical findings.

Hours per Dialysis Session	Dialysis Sessions per Week	HDP*	Clinical Results
3	3	27	Totally inadequate. Severe malnutrition.
4	3	36	Inadequate. A high percent of the U.S. dialysis population is malnourished.
5	3	45	Borderline. Some malnutrition, BP control difficult.[8-12]
8	3	72	Only 3 days/wk schedule has proven to be adequate.[8-12]
5	4	80	No data yet available.
3	5	75	No data available. BP control should be easy.
2–3	6	72–108	Preliminary data: Good well-being. BP control possible if sodium intake is limited.
8	6	288	Best so far because PO_4 normalized. BP control very easy.[16,17]

**Hemodialysis Product = (hours/dialysis session) x (dialysis sessions/week)^2*

Hemodialyse efficiëntie: ureum

- Ureum
  - Relatief non-toxisch
  - Kleine molecule, 60D
  - Ongeladen
  - Getransporteerd tussen vochtcompartimenten via aquaporines: gemakkelijk
  - NCDS: keuze voor ureum omdat het een maat is voor voedselinname en dialyseklaring

- Niet representatief voor klaring van proteïne gebonden uremische toxines, middle molecules, andere kleine en water-oplosbare uremische toxines:
  bvb Natrium en Fosfor: negatief geladen: trager transport.

- Andere biomarker?: Erythrocyte glutathione transferase (eGST): marker van lange termijn epuratieve efficientie van dialysebehandelingen?

KT/V ureum: bepaling van geleverde dialysedosis?

- URR : ureum reductie ratio
- Kt/Vureum (genormeerde ureum klaring)
  → UKM: Urea Kinetic Modeling:
  - individualisatie dialyse?
  - evaluatie of geleverde dialysedosis overeenkomt met voorgeschreven dosis
  - meting ureumproduktie tussen dialyses in: nPCR
- Maar:

Restdiurese

Ultrafiltratie: verlaagd V: verhoogd postdialyse ureum (spKt/V)

Ureumproduktie tijdens dialyse (spKt/V)

Recirculatie:

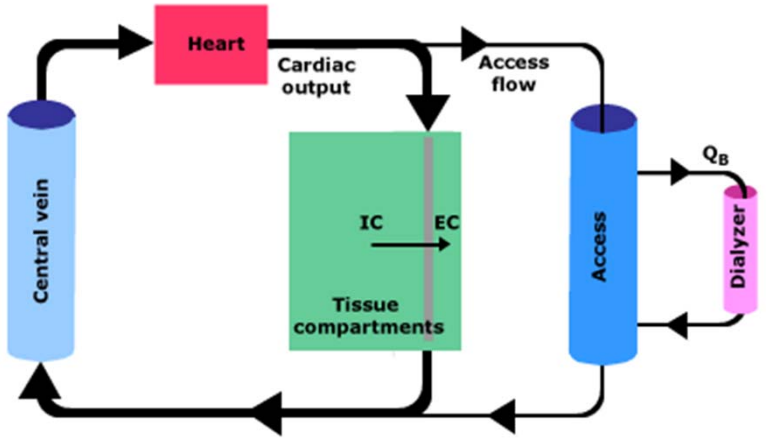
in de av-fistel

bij av-fistel ook cardio-pulmonair: 3 tot 7 % (hoger bij laag hartdebiet en hoge fistelbloedflow)

Rebound: eKT/V (equilibrated Kt/V: ureum postdialyse is hoger: eKt/V < spKt/V)

Hemodialyse efficiëntie

Schematic figure demonstrating the relationship between urea clearance and equilibration when the access is parallel to the circulation in hemodialysis

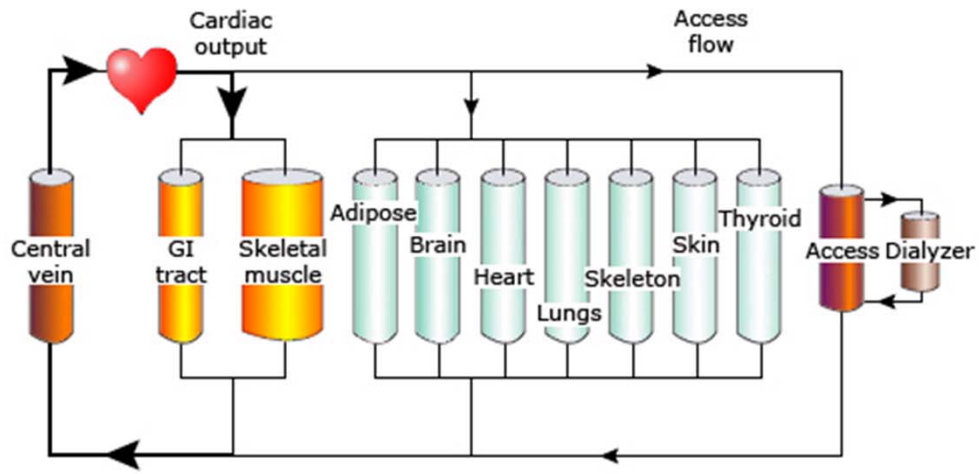


Schematic representation of standard hemodialysis in which flow through the access is in parallel with the systemic circulation. The degree to which urea is removed is dependent upon the rate of urea equilibration between intracellular stores (IC) and the extracellular fluid (EC). Slow equilibrators will have a lower BUN during dialysis but a slower rate of total urea removal.

UpToDate®

Hemodialyse efficiëntie:

Schematic figure showing urea stores versus perfusion in different organs during hemodialysis



The different tissue compartments represent areas of the body with variable degrees of perfusion from the heart and urea sequestration. Within the gastrointestinal tract and skeletal muscle, the ratio of blood flow to urea content is low. These organs therefore sequester up to 80 percent of the total body urea, leading to urea rebound and reduced dialysis efficiency.

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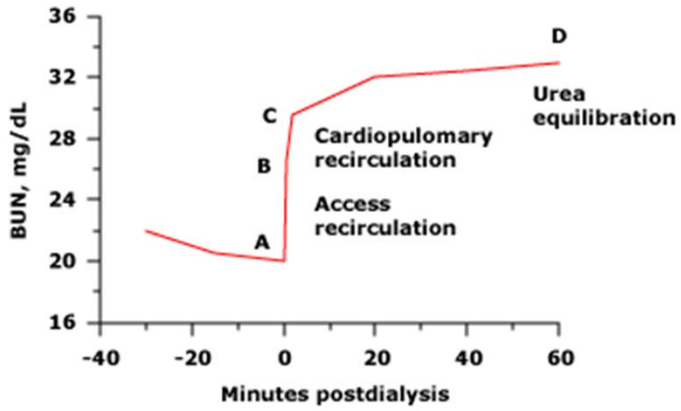
Hemodialyse efficiëntie:

Changes in blood urea nitrogen measured at different times after dialysis



Sequential changes in BUN measured at the end of and after hemodialysis. A is the immediate postdialysis sample; B is an immediate postdialysis sample taken from the limb opposite the vascular access to eliminate access recirculation; C is delayed for two minutes to eliminate the effect of cardiopulmonary recirculation; and D is delayed for one hour when urea equilibration should be complete.

Data from Depner, TA, Kidney Int 1994; 45:1522.

UpToDate®

Hemodialyse-efficientie: KT/V ureum

- Kt/V via bloednames: gouden standaard

  moeilijk

  Bloedname voor en na dialyse: juiste techniek, altijd dezelfde techniek, Dougirdas.

- Kt normeren voor V: formule van Watson:

  V (L, male) = 2.447 + (0.3362 x wt [kg]) + (0.1074 x Ht [cm]) - (0.09516 x age [years])
  V (L, female) = -2.097 + (0.2466 x wt [kg]) + (0.1069 x Ht [cm])

  met huidig lichaamsgewicht of ideaal lichaamsgewicht

  of 0.67 x lichaamsgewicht

  of lichaamsoppervlakte

  of levermassa

  of ‘resting energy expenditure’ REE

  of ‘bioelectrical resistance’

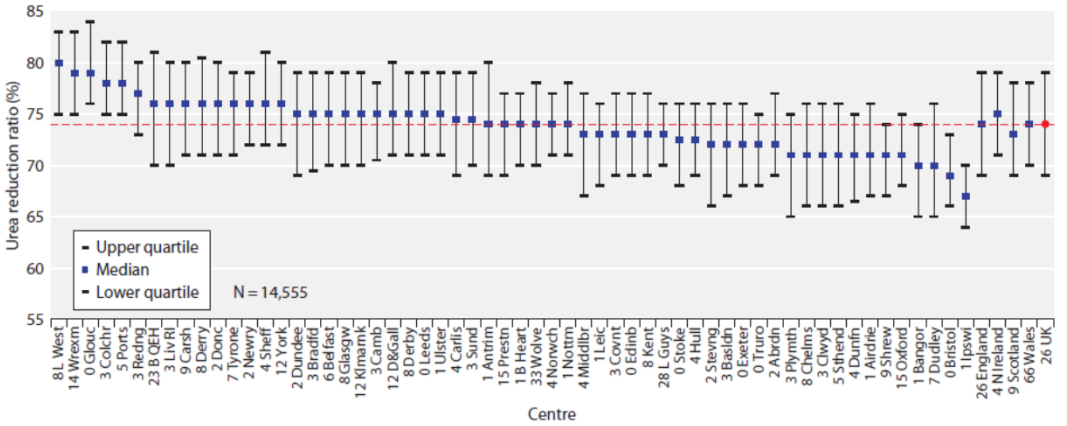


Fig. 7.1. Median URR achieved in prevalent patients in each centre, 2010

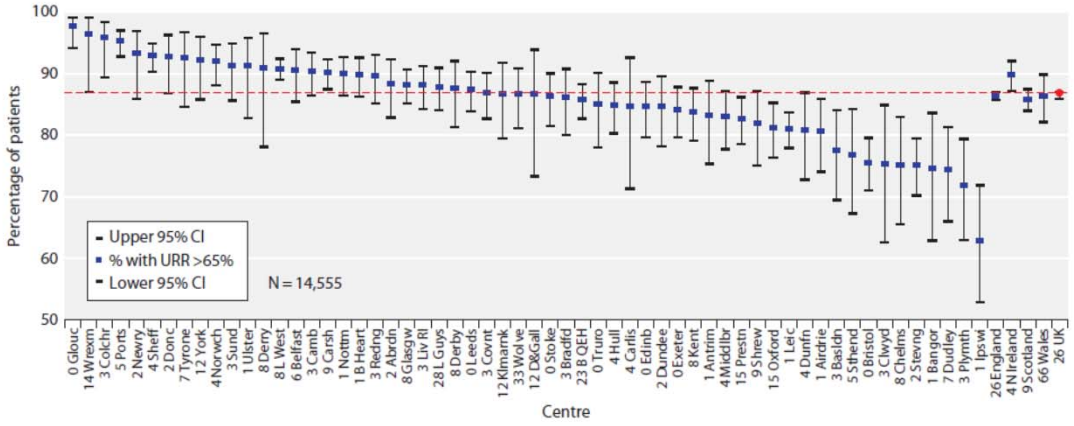


Fig. 7.2. Percentage of prevalent patients with URR >65% in each centre, 2010

The Kt/V - Worldwide Measure for Dialysis Dose

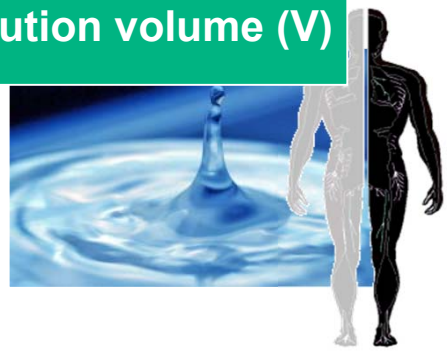
What is Kt/V?

Treatment time (t)

Urea Clearance (K)

Kt/V

Urea distribution volume (V)

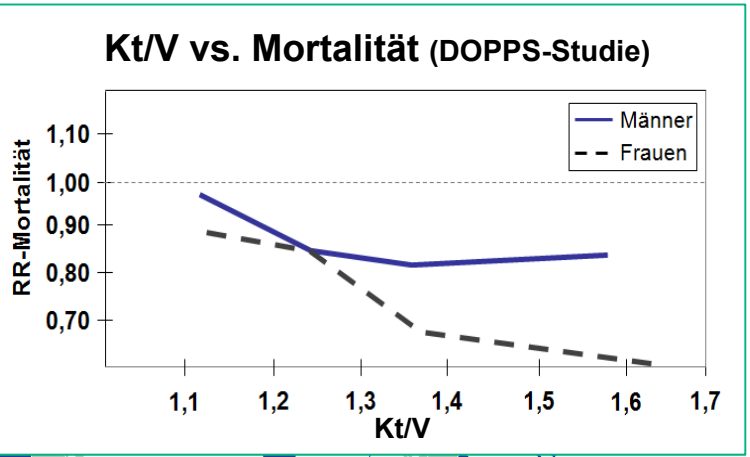


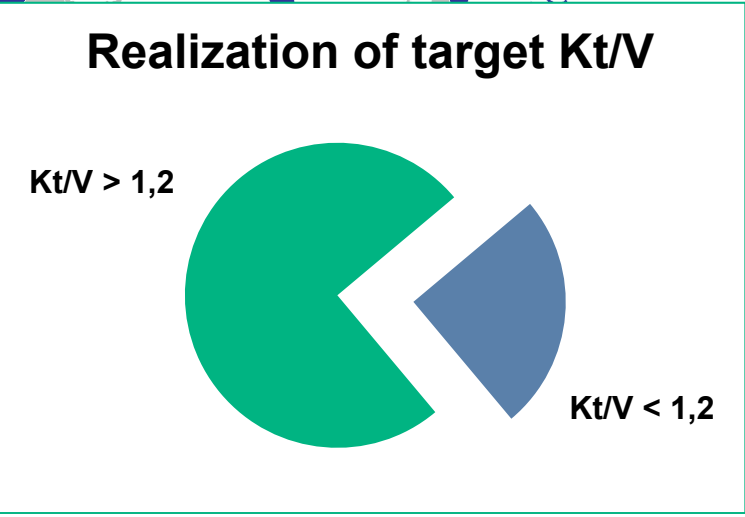
Example:

$$Kt/V = \frac{245\ ml/min * 300\ min}{54.000\ ml} = 1,36$$

Why Kt/V?

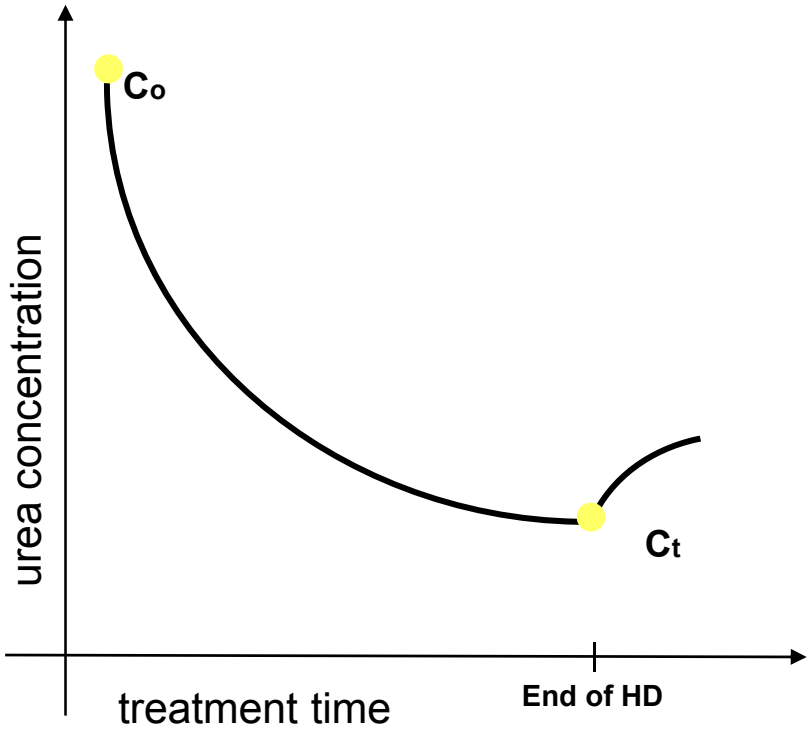
- Coherence between mortality and Kt/V is prooven
- Minimum dose in every treatment should be Kt/V ≥ 1,2
- The Kt/V is often checked only once a quarter
- Up to 25% of dialysis patients does not realize their minimum dose





Quantification of extracorporeal blood treatments

- **Quantification of dosage is calculated by elimination of urinary excreted substances according to the native kidney function**



- **Urea is used as surrogate parameter for low-molecular uremic toxins**
- **Urea elimination gives information about the dialysis dose**
- **Urea can be almost completely eliminated during dialysis due to its molecular size**

Quantification of extracorporeal blood treatments

Urea reduction rate [URR] $= \left(1 - \frac{C_t}{C_0}\right) \cdot 100\ (\%)$

- Most simple formula for calculating the dialysis dose

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Kt/V $C_t = C_0 * e^{-\frac{K*t}{V}} = \frac{K \cdot t}{V} = -\ln\left(\frac{C_t}{C_0}\right)$

- Is used in the daily routine on the basis of the urea concentration pre and post HD

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The problem with both methods:

Ultrafiltration / urea generation during dialysis and the urea rebound are not considered

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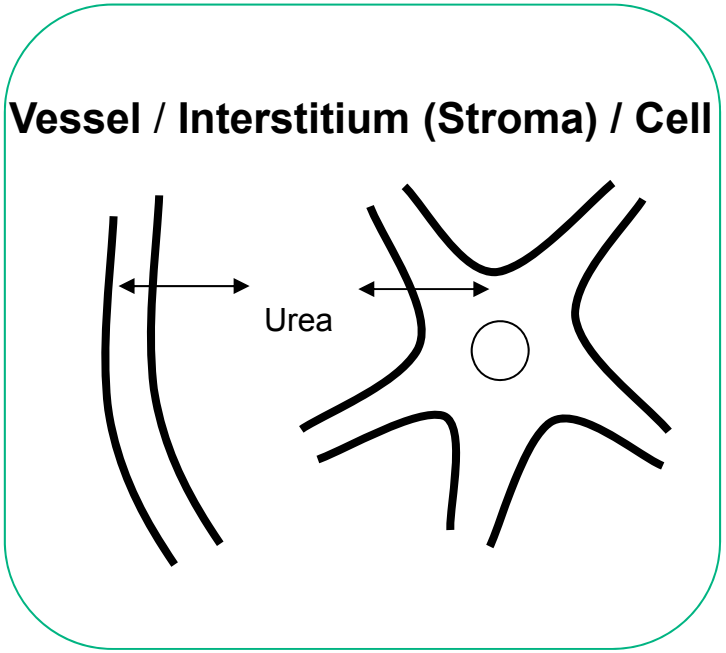
single-pool-Kt/V [spKt/V] $= -\ln(R - 0{,}008 \cdot T) + (4 - 3{,}5 \cdot R) \cdot \frac{UF}{W}$

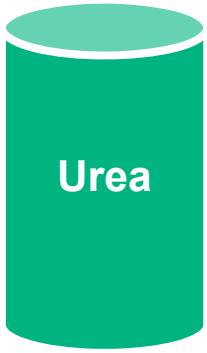
- Ultrafiltration and urea generation during dialysis are considered

Quantification of extracorporeal blood treatments



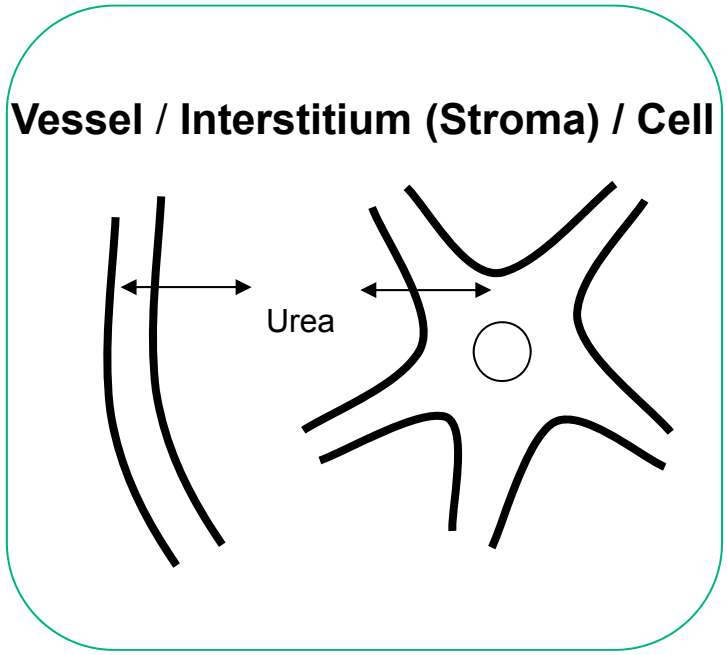
Single-pool model:

Ultrafiltration and urea generation are considered.



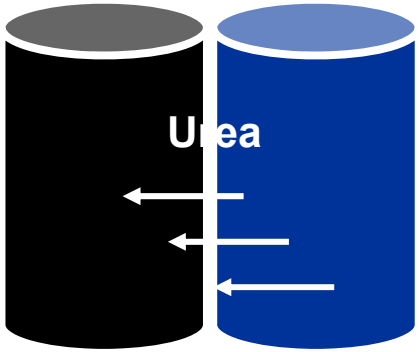
- Assumption that the body is 1 compartment

Quantification of extracorporeal blood treatments



Double-pool model:

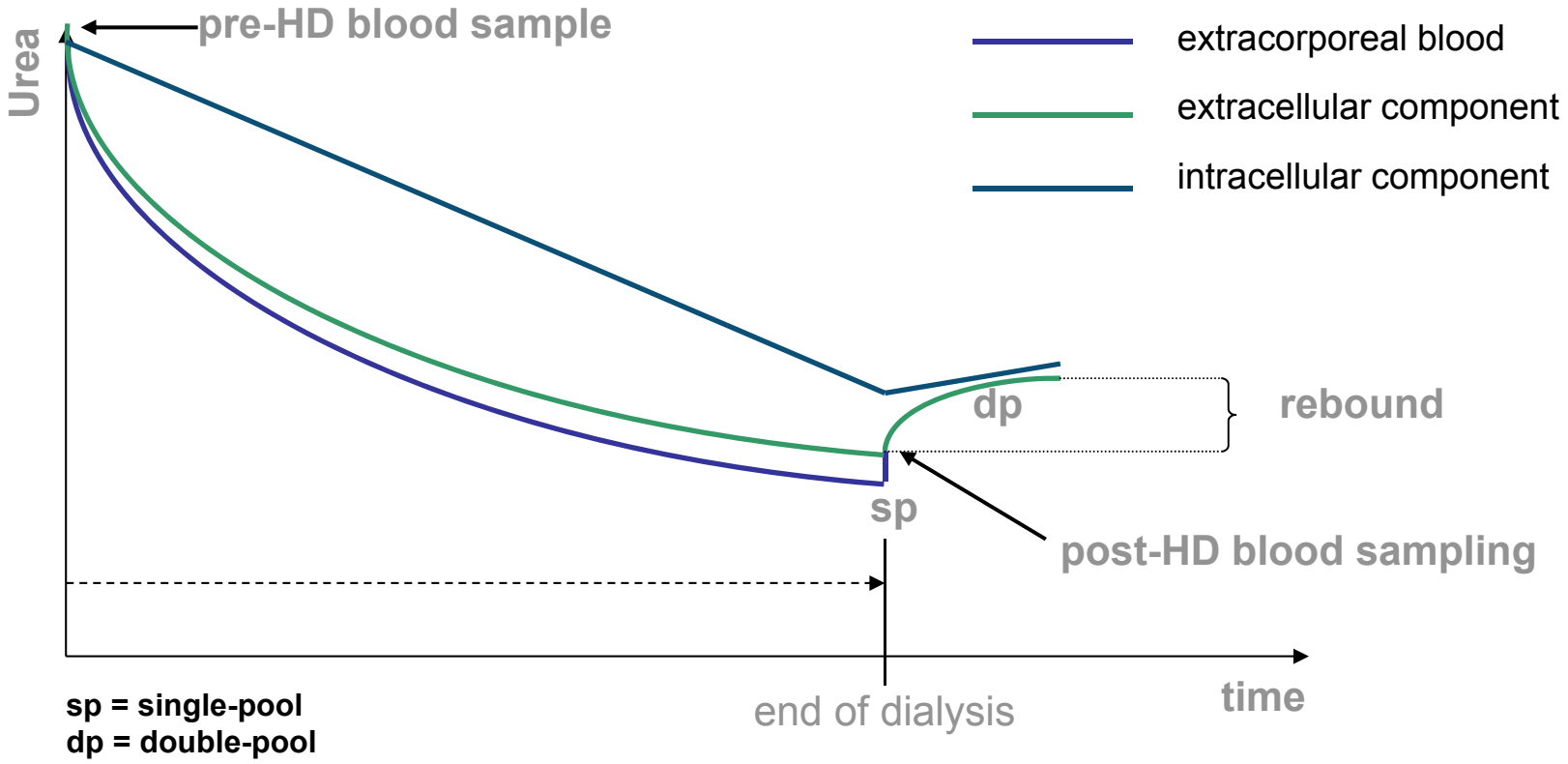
Assumption that there are 2 compartments



- Rebound is taken into consideration
- (eKt/V is lower than spKt/V)

Quantification of extracorporeal blood treatments

Kt/V-calculation [clinical routine]



Quantification of extracorporeal blood treatments

Urea reduction rate [URR] $= \left(1 - \frac{C_t}{C_0}\right) \cdot 100\ (\%)$

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Kt/V $C_t = C_0 * e^{-\frac{K*t}{V}} = \frac{K \cdot t}{V} = -\ln\left(\frac{C_t}{C_0}\right)$

- Is used in the daily routine on the basis of the urea concentration pre and post HD

single-pool-Kt/V [spKt/V] $= -\ln(R - 0{,}008 \cdot T) + (4 - 3{,}5 \cdot R) \cdot \frac{UF}{W}$

- Ultrafiltration and urea generation during dialysis are considered

equibrilated-Kt/V [eKt/V] $= spKt/V - \frac{0{,}6}{T} \cdot spKt/V + 0{,}03$

- Urea rebound after dialysis is taken into account

Determination process [clinical routine] of Daugirdas Kt/V [spKt/V / e Kt/V]

- The Kt/V result depends to a great degree on the correct determination of pre- and post-dialysis urea concentrations in the serum.

The following procedure is recommended*:

- **Take a pre-dialysis blood sample from the dialysis needle immediately prior to dialysis start, before the dialysis hose system is connected or sodium chloride has been injected into the venous or arterial needle.**
- **Once the dialysis period is complete, stop the dialysate and UF flow and reduce blood flow to 100ml/h in order to prevent recirculation.**
- **After 15 seconds take a blood sample as close as possible to the arterial dialysis needle**

(*European Best Practice Guidelines for Hemodialysis Part 1, Section II, Hemodialysis adequacy)

Variables in Kt/V determination [Daugirdas]

Observations in the daily routine and studies have shown:

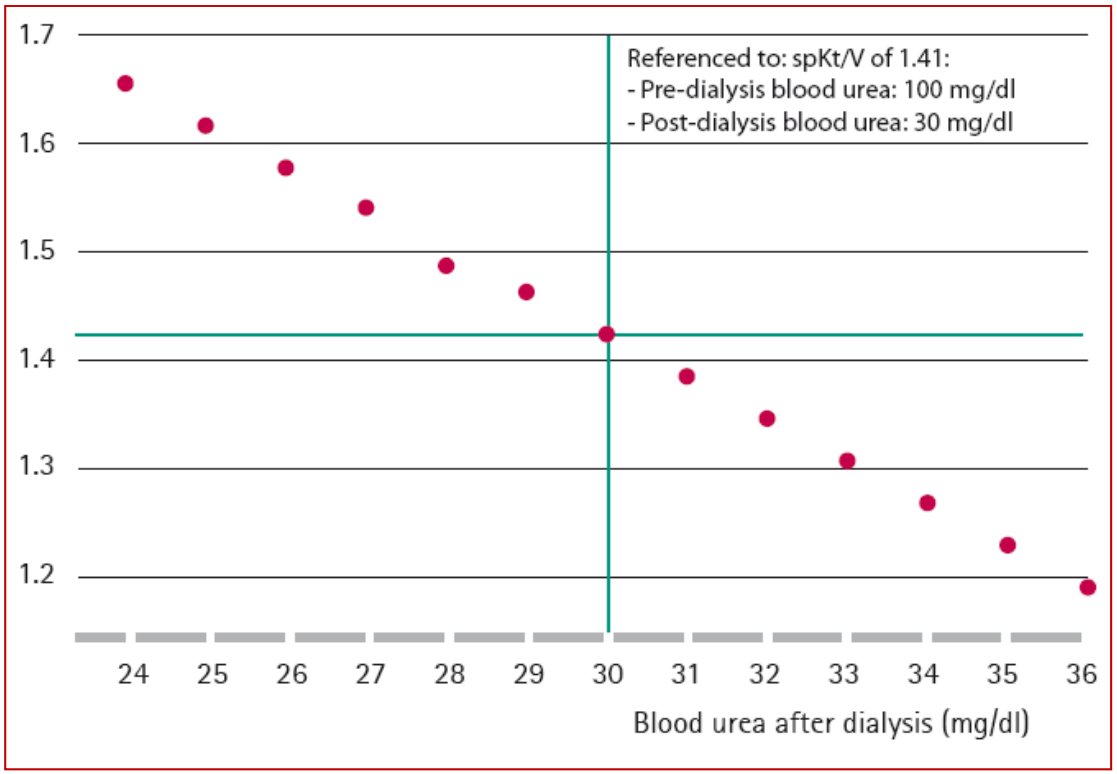
Recommendations are not followed due to various reasons.

Timing and method of blood sampling have a significant influence on the result!

Variation in blood sample collection for determination of haemodialysis adequacy. Council on Renal Nutrition National Research Question Collaborative Study Group. JA Beto, VK Bansal, TS Ing, JT Daugirdas.1998.

Variables in Kt/V determination [Daugirdas]

Influence of the post-dialysis blood (urea) sample on the spKt/V value



- Indeed, little variations in the urea concentrations have a significant impact on the Kt/V!

Kt/V Determination [Daugirdas]

- **Reference Method**

- Widely used all over the world
- Results are available after dialysis
- Extensive & expensive
- Accuracy (≤ ± 30%) strongly depends on timing of post-dialytic blood sample

- **Information about dialysis dose in only 1 of 36 dialysis sessions**

Additional sources of errors

- decline of dialyzer-clearance during HD
- shunt- and cardio-pulmonary recirculation
- slower urea-mobilisation in the peripheral vessels due to a low blood pressure
- error in consequence of estimation of „V“

→ Kt/V measurement: Avoids bad dialysis, but does not guarantee good dialysis.

Monitoring of dialysis dose in every treatment?

YES!

- For various reasons administered dialysis dose is not realized in every treatment
- The Kt/V determination by using blood samples is usually done in long time intervals.
- To ensure a high treatment quality at all - an adequate dialysis dose should be administered in every single treatment.

Monitoring Dialysis Dose
Methods

- **Methods for Online- / Real-time monitoring of dialysis dose**

I. **Electrolyte Clearance of dialyzer**

II. **Sampling of spent dialysate**

III. **Urea determination by Urease**

IV. **UV-Absorbance in spent dialysate**

Monitoring Dialysis Dose
Methods

Companies and Products

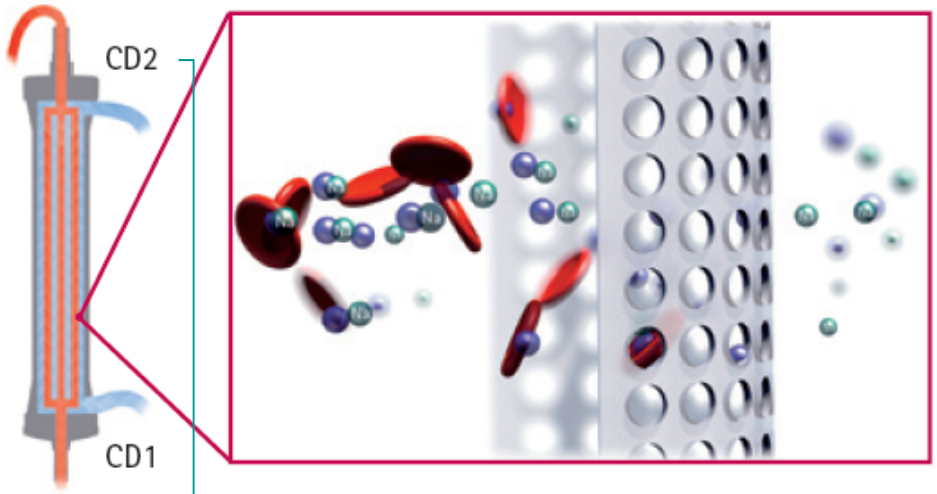
Manufacturer	Product	Measuring principle
Fresenius Medical Care	OCM Kt/V	Determination of filter clearance "K" using sodium dialysance
GAMBRO	Diascan®	
NIKKISO	-	Calculation only

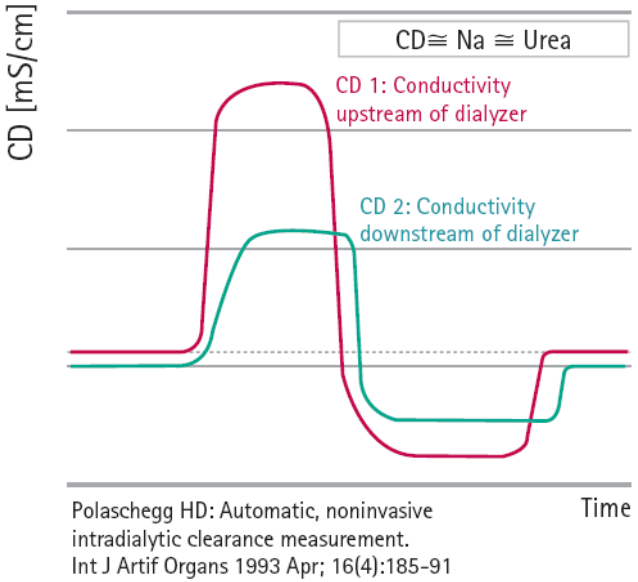
Monitoring Dialysis Dose

Methods

I. Electrolyte Clearance of dialyzer

- Determination of filter clearance "K" using sodium dialysance
- The measured sodium dialysance is used as surrogate parameter for urea clearance





Polaschegg HD: Automatic, noninvasive intradialytic clearance measurement. Int J Artif Organs 1993 Apr; 16(4):185-91

- Change of conductivity is measured downstream the dialyzer (2nd probe)

Monitoring Dialysis Dose

Methods

Measuring Accuracy Electrolyte Clearance

Parameter	Accuracy		Accuracy Kt/V
K	5%	OCM Kt/V Diascan®	?
t			
V			

EDTA Poster Presentation: Kt/V- A Measure of Dialysis Dose: How Precise is it? Abbas S., W.H. Xie, S. Stiller, H. Mann. Aachen, Germany 2009.

Monitoring Dialysis Dose
Methods

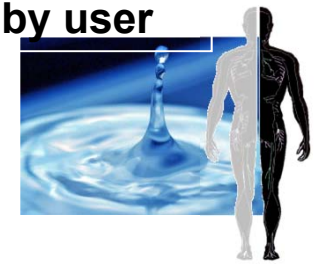
Calculation of the Kt/V

Measured Dialyzer Clearance (K)

Documented Treatment Time (t)

Kt/V

Urea distribution volume (V) – manually set by user



Monitoring Dialysis Dose

Methods

Measuring Accuracy Electrolyte Clearance

Parameter		Accuracy
K	→	5%
t	→	0%
V		

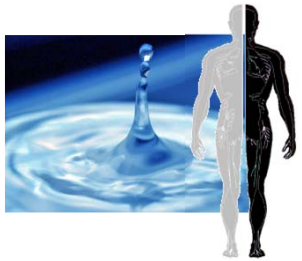
→ **Accuracy Kt/V** ?

EDTA Poster Presentation: Kt/V- A Measure of Dialysis Dose: How Precise is it? Abbas S., W.H. Xie, S. Stiller, H. Mann. Aachen, Germany 2009.

Monitoring Dialysis Dose

Methods

Determination of the Urea Distribution Volume V



V

A: Watson Formula

B: Bioimpedance Spectroscopy

Monitoring Dialysis Dose
Methods

A: Determination of V with Watson formula

- Differentiation between male / female

Formula for male patients:
V (litre)= 2,447 – 0,09516 x age (years) + 0,1074 x height (cm) + 0,3362 x dry weight (kg)

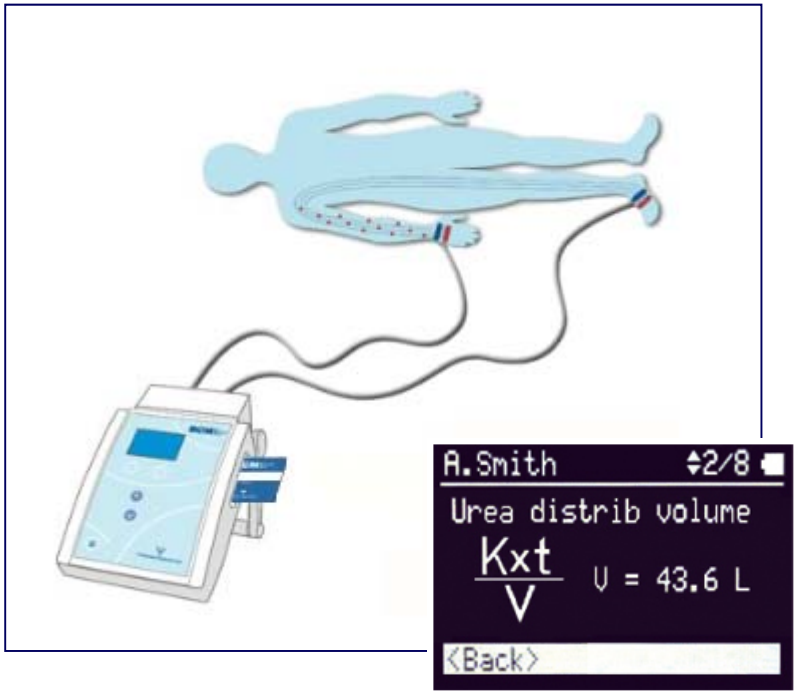
Formula for female patients:
V (litre) = -2,097 + 0,1069 x height (cm) + 0,2466 x dry weight (kg)

- Developed for 700 healthy Americans
- Imprecise results for huge group of dialysis patients (old / malnourished)

Monitoring Dialysis Dose
Methods

B: Measuring V with Bioimpedance Spectroscopy

For example **BCM** (Body Composition Monitor):



- Measurement of electric resistence in the human body (intra and extra-cellular water behaves like electric resistivs (ICW + ECW) / cell membrans behave like capacitors.

  Total body water: TBW = ECW/ICW

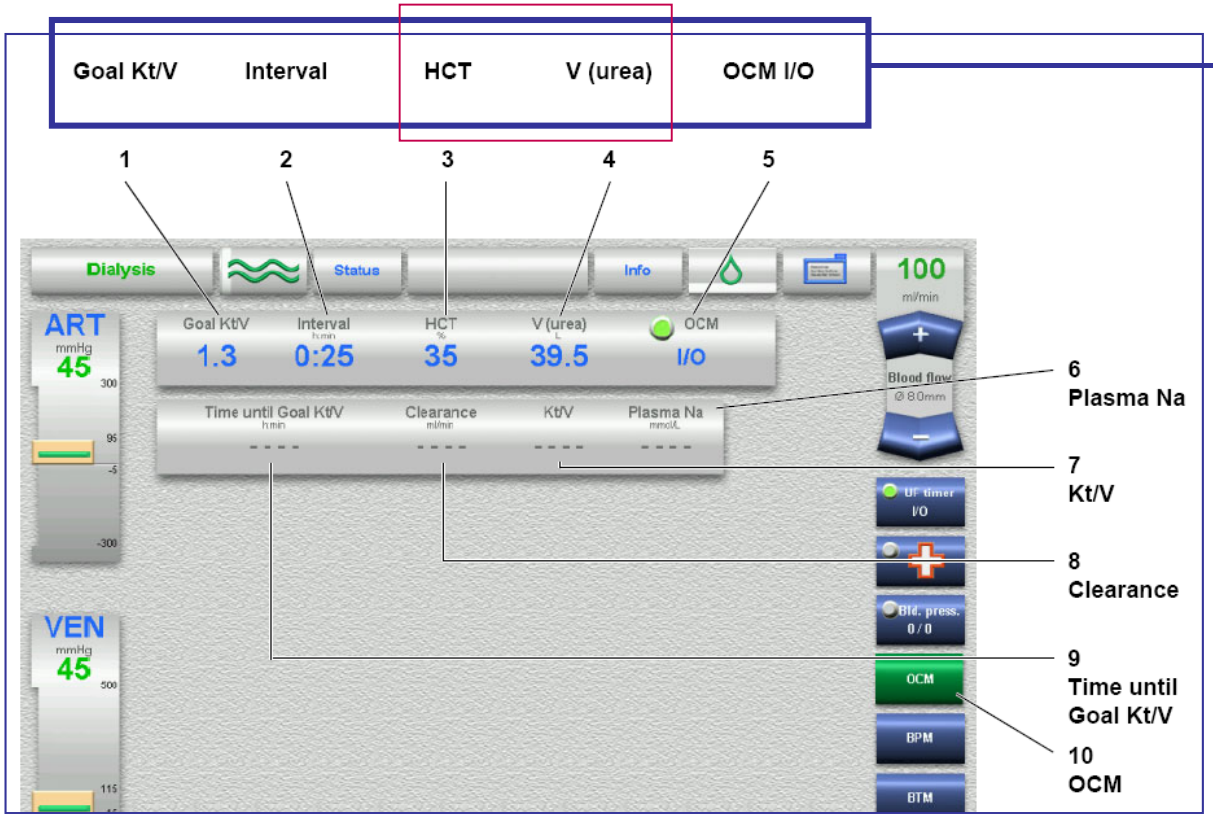
- Possibly false results for important dialysis patient groups:
  - Malnourished patients
  - Amputated patients
  - Diabetic patients

- Extra disposables required
- Expensive extra device

Monitoring Dialysis Dose

Methods

Required Parameters



Setting Parameters

- **Haematocrit [%]**
- **Urea distribution volume (V) If calculated by Watson formula are additionaly needed:**
  - **sex**
  - **age**
  - **height**
  - **weight**

Monitoring Dialysis Dose

Methods

Measuring Accuracy Electrolyte Clearance

Parameter	Accuracy		Accuracy Kt/V
K	5%		
t	0%		
V_{BS}	8%		9,3%
V_{Watson}	15%		15,9%

EDTA Poster Presentation: Kt/V- A Measure of Dialysis Dose: How Precise is it? Abbas S., W.H. Xie, S. Stiller, H. Mann. Aachen, Germany 2009.

Monitoring Dialysis Dose
Methods

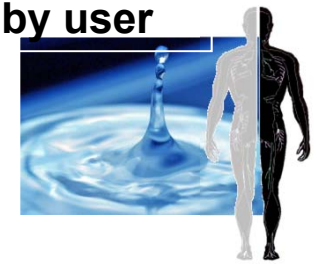
Calculation of the Kt/V

Measured Dialyzer Clearance (K)

Documented Treatment Time (t)

Kt/V

Urea distribution volume (V) – manually set by user



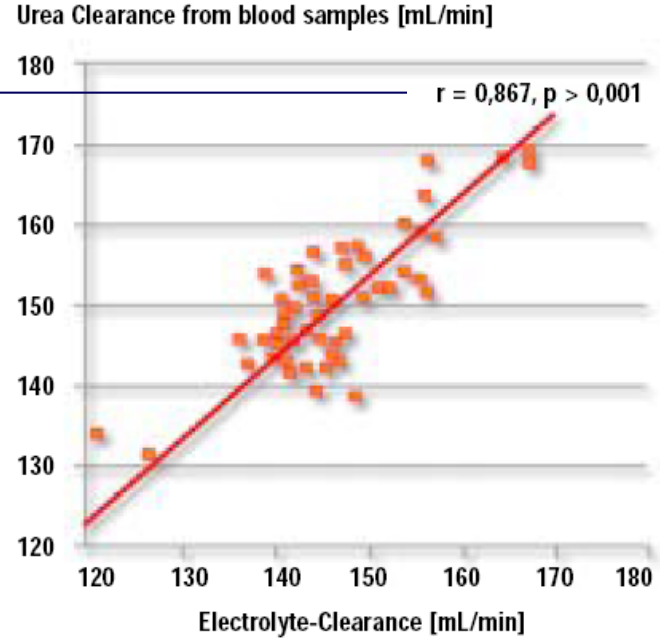
Decisive Parameter for Kt/V accuracy

Monitoring Dialysis Dose
Methods

Measuring Accuracy Electrolyte Clearance

Customer Brochure OCM:

Correlation between Urea Clearance and Electrolyte-Clearance r = 0,867



Kuhlmann U, Goldau R, Samadi N, Graf T, Gross M, Orlandini G, Lange H. Accuracy and safety of online clearance monitoring based on conductivity variation. Nephrol Dial Transplant 2001; 16: 1053-1058

- **This is also no information about correlation between blood-Kt/V and OCM-Kt/V.**

Art. Nr. 7324831/4 GB (2g/h/b 05.03)

Monitoring Dialysis Dose
Methods

GAMBRO

Diascan

ARTIS Operator's Manual

11.2 Procedures

It is possible to use the Diascan function only with the following treatment modes:

- Hemodialysis (DN)
- Isolated UF

- **No Single-Needle Treatment**

- **No Hemodiafiltration**

Monitoring Dialysis Dose
Methods

Fresenius Medical Care

oCm Kt/V

The measurement will not be started if the following treatment procedures have been selected:
- ONLINE*plus*™ HF treatment
- Single-Needle

- **No Single-Needle Treatment**

- **No Hemofiltration**

Monitoring Dialysis Dose
Methods

Restrictions Competitors Electrolyte Clearance

- **Adjustment of sodium conductivity is always linked to a risk of sodium overload for patients.**
- **To avoid this measurements can not be generated permanently throughout the entire treatment time.**
- **Phases of high sodium concentrations have to be equated with phases of low concentrations.**
- **Measurements are merely information at particular points of time during dialysis sessions.**

(Gambro: Measurements can be repeated every 15, 30 or 60 minutes. / FMC every 25 min at minimum)

Monitoring Dialysis Dose
Methods

Restrictions Competitors Electrolyte Clearance

- **Furthermore it is not possible to change treatment parameters during measuring phases (Gambro: 1 Phase = 6 min.)**

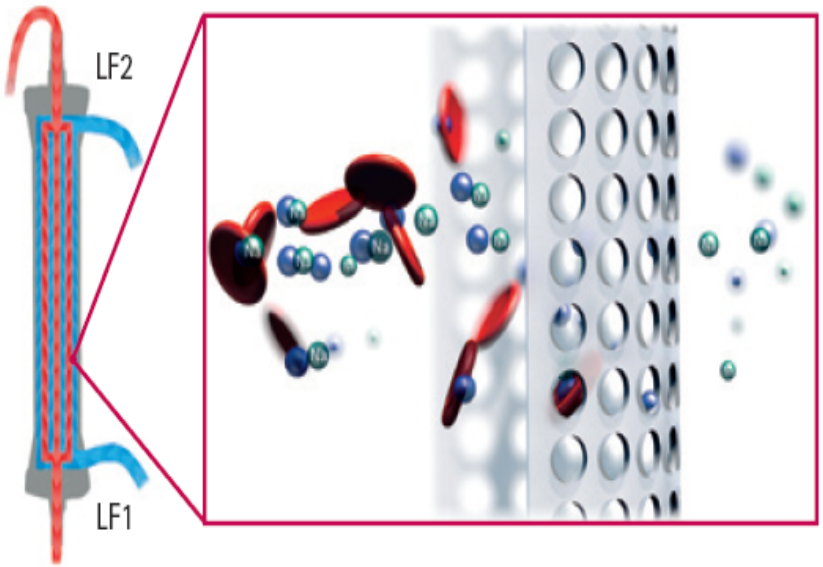
  Parameters that are not allowed to change are:
  - Blood- / dialysateflow
  - Ultrafiltration rate / ultrafiltration volume
  - Conductivity
  - Temperature

- **Measurements get aborted when parameters are changed.**

Monitoring Dialysis Dose
Methods

Summary Electrolyte Clearance

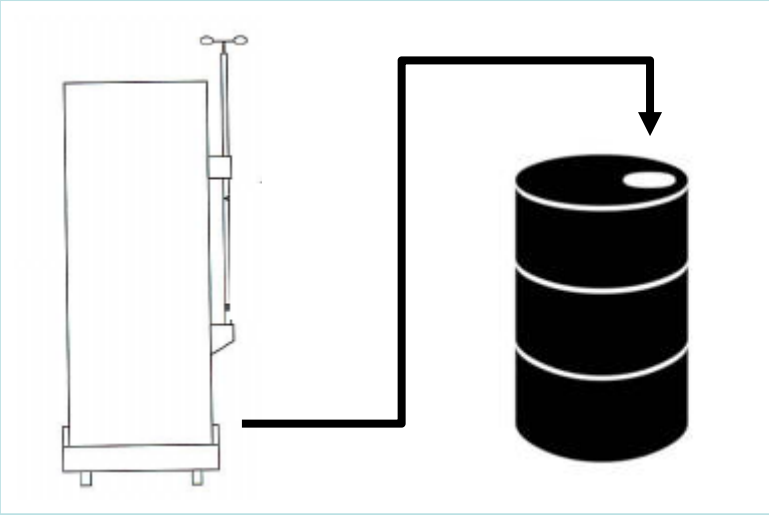
- Sodium Clearance (OCM / Diascan) merely measures the dialyzer
- Only Periodic Measurements
- Requires determination of urea distribution volume (V)
- Not for all treatment modes and hence not for all patient groups
- Restricted Market Acceptance



Monitoring Dialysis Dose
Methods

II: Sampling of spent dialysate: Solute Removal Index

- **Whole amount of spent dialysate from one dialysis session is collected**
- **Urea concentration is determined**



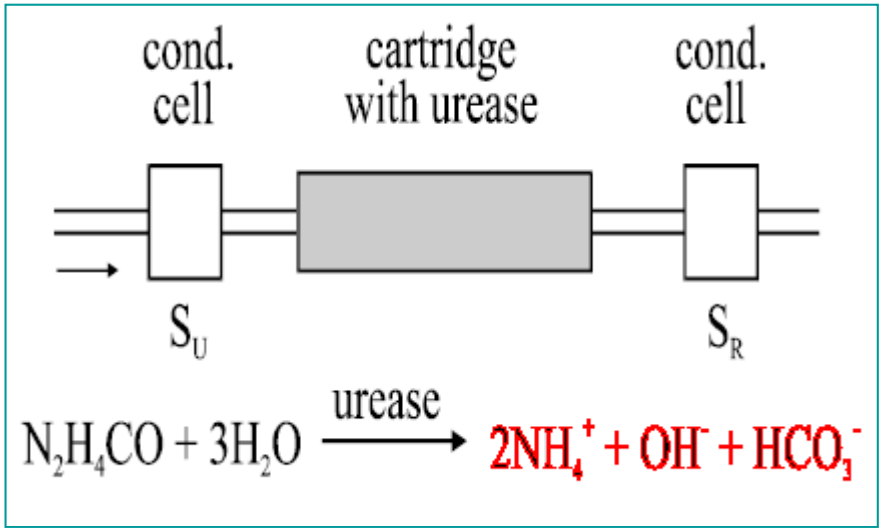
- **≥ 120 liters spent dialysate**
  (DFflow 500ml/min | 240 min session time)
- **Non-applicable for daily use!!!**

Monitoring Dialysis Dose
Methods

III. Urea determination by Urease

Urease: Enzyme that catalyzes the hydrolysis of urea into carbon dioxide and ammonia.

Stand alone device



- Ultrafiltrate or Dialysate passing at a small flow rate a conductivity cell (S_U)
- A cartridge containing urease and a second conductivity cell (S_R) are in series.
- Urea is broken down by Urease
- This results in a change in electric conductivity which is calibrated for the urea concentration

cf: Stiller S., Al-Bashier A., Mann H.: On-line Urea Monitoring during hemodialysis: A Review. Saudi J Kidney Dis Transplant 2001; 12(3): 364-374

Monitoring Dialysis Dose
Methods

Summary Urea determination by Urease

- **Measuring urea concentration in spent dialysate**
- **Online urea concentration monitoring**
- **Calibration might pose an obstacle for a regular application[1]**
- **Unit is an expensive separate device**
- **Due to high costs for single use urease cartridges are those systems restricted to research purposes (Lindsay and Sternby 2001)**

cf: Stiller S., Al-Bashier A., Mann H.: On-line Urea Monitoring during hemodialysis: A Review. Saudi J Kidney Dis Transplant 2001; 12(3): 364-374

Monitoring Dialysis Dose

Methods

Methods I. – III.

Electrolyte Clearance

Strength

- Applicabe for daily use

Weakness

- Measuring only sodium clearance
- V must be determined
- No spKt/V / eKt/V / URR

Sampling of spent dialysate

Strength

- Measurement in spent dialysate
- Measuring Urea
- Precise

Weakness

- Non-applicabe for daily use
- Expensive apparatus

Urea determination by Urease

Strength

- Measurement in spent dialysate
- Measuring Urea
- Precise

Weakness

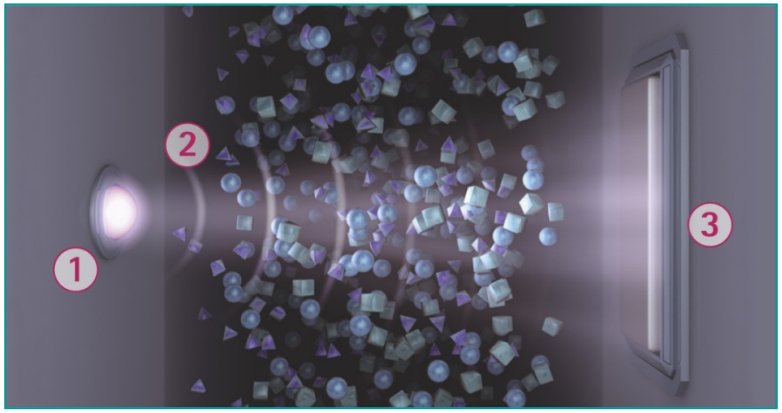
- Non-applicabe for daily use
- Calibration required
- Expensive follow-up costs

Monitoring Dialysis Dose

Adimea

- **The Adimea measurement principle**

Utilisation of the principles of spectroscopy for determining the reduction of urinary excreted substances in the dialysate drain



- **A light source ① transmits ultraviolet light through the dialysate flowing to the drain.**
- **The particles contained in the dialysate absorb the light depending on the concentration ②.**
- **This absorption is detected by a sensor ③.**

➲ **This provides the system with information about the curve of molar reduction in the urea.**

Monitoring Dialysis Dose

Adimea

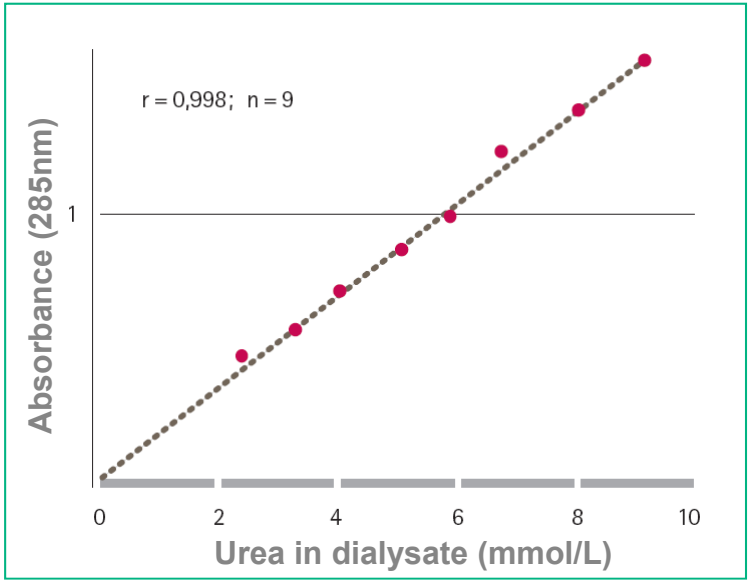
Approved by several Publications:

- **Fridolin et al: On-line monitoring of solutes in dialysate using absorption of ultraviolet radiation: Technique description.**

  The international Journal of Artificial Organs / Vol. 25 / no. 8, 2002 / pp. 748-761. Nephrol Dial Transplant (2003) 21: 2225-2231

- **Uhlin et al: Estimation of Delivered Dialysis Dose by On-Line Monitoring of the Ultraviolet Absorbance in the spent Dialysate.**

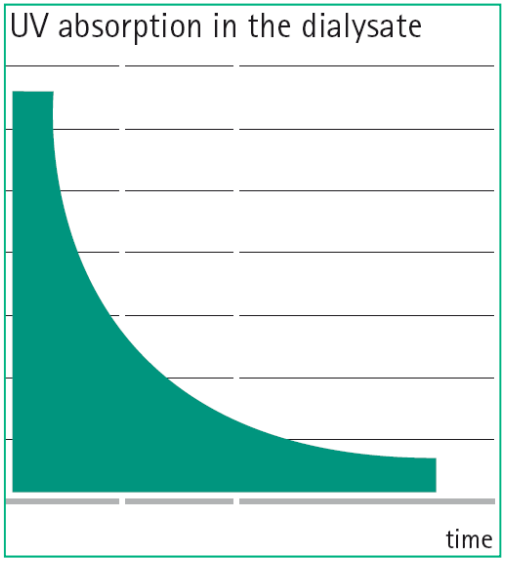
  American Journal of Kidney Diseases, Vol 41, No 5 (May), 2003: pp 1026-1036



Monitoring Dialysis Dose

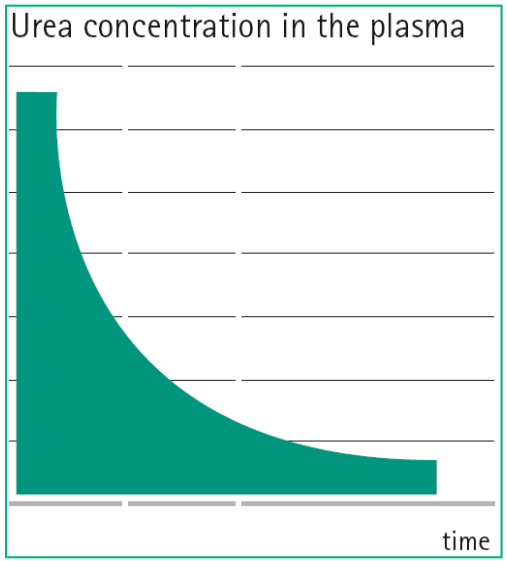
Adimea

The measured curve for light absorption is almost identical to the curve for urea concentration:



correlates

± 2%



Kt/V can be determined directly on the basis of the curve.

$$A_t = A_0 \cdot e^{-\left(\frac{K}{V}\right) \cdot t}$$

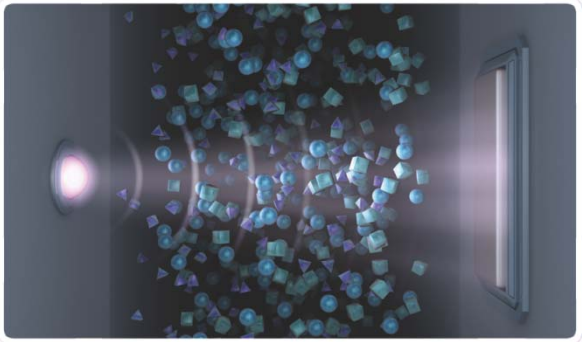
$$C_{Bt} = C_{B0} \cdot e^{-\left(\frac{K}{V}\right) \cdot t}$$

Monitoring Dialysis Dose

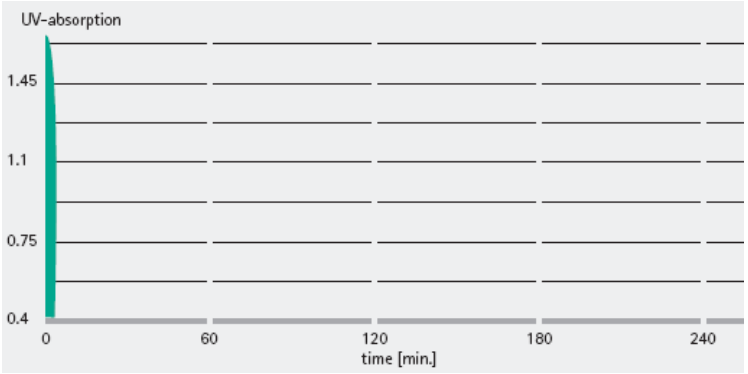
Adimea

Treatment start*

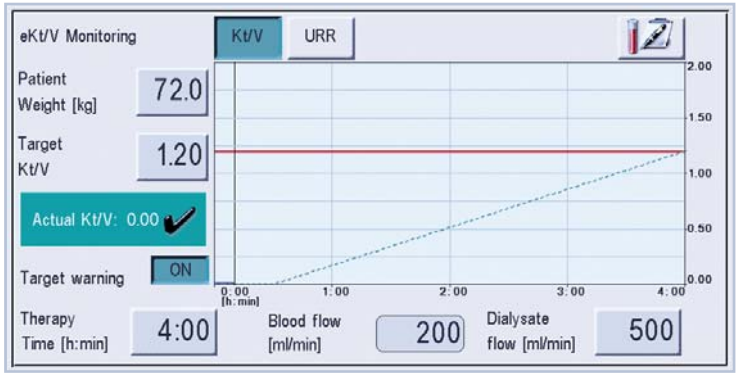
High molar concentration in the dialysate ...



... entails high UV absorption



Absorbed UV waves provide information about the quality of the dialysis



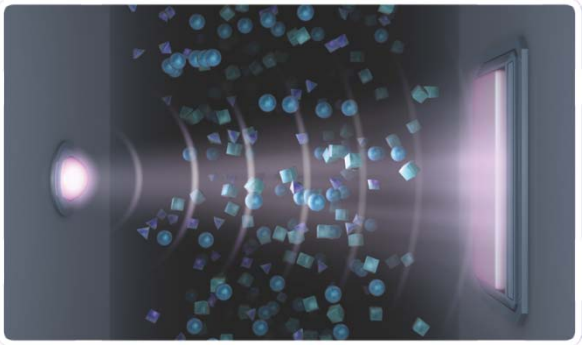
* (sample treatment curve)

Monitoring Dialysis Dose

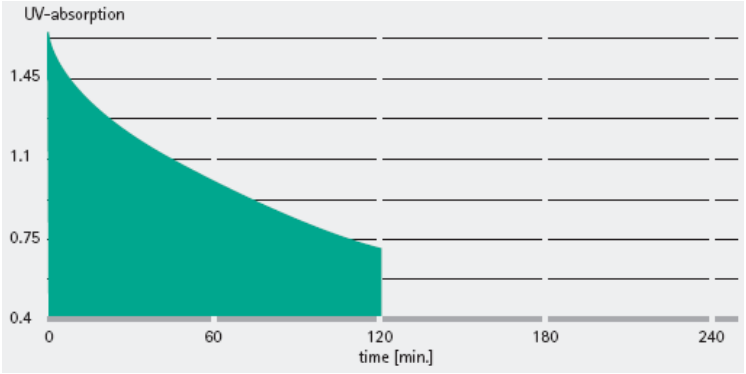
Adimea

In the middle of the treatment*

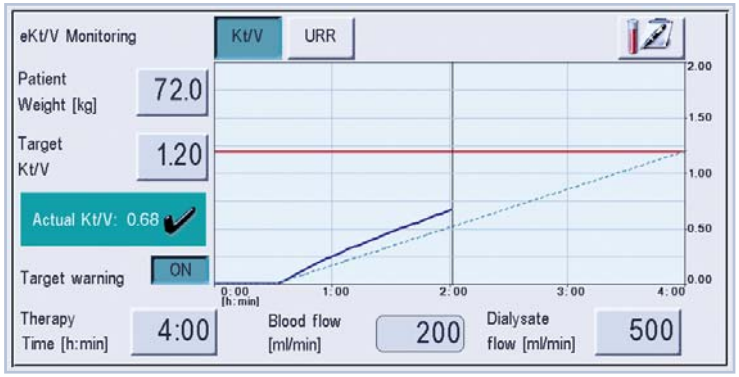
As molar concentration decreases ...



... the absorption of UV waves is also reduced



The progress of the dialysis progress can be seen quickly and easily



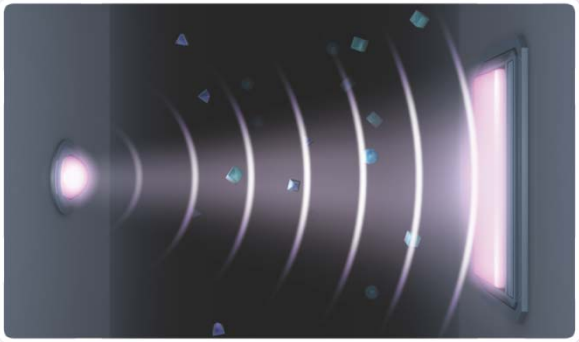
* (sample treatment curve)

Monitoring Dialysis Dose

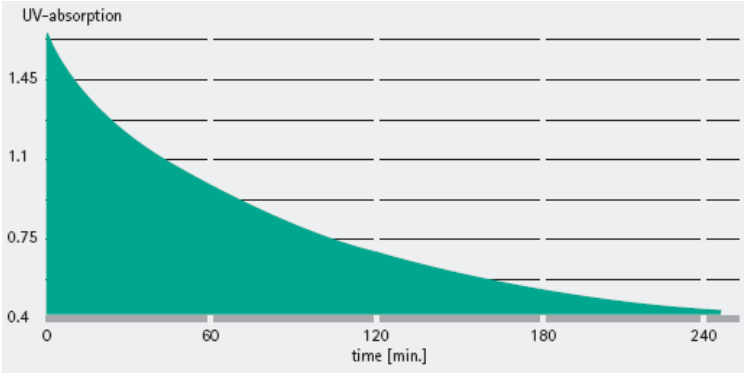
Adimea

Treatment end*

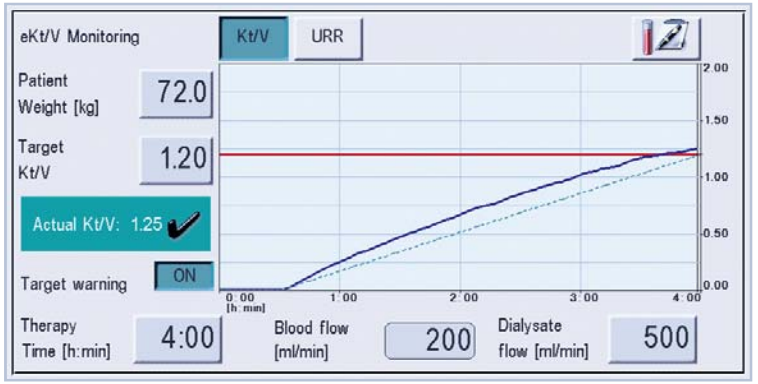
The few remaining molecules ...



... hardly absorb any UV light



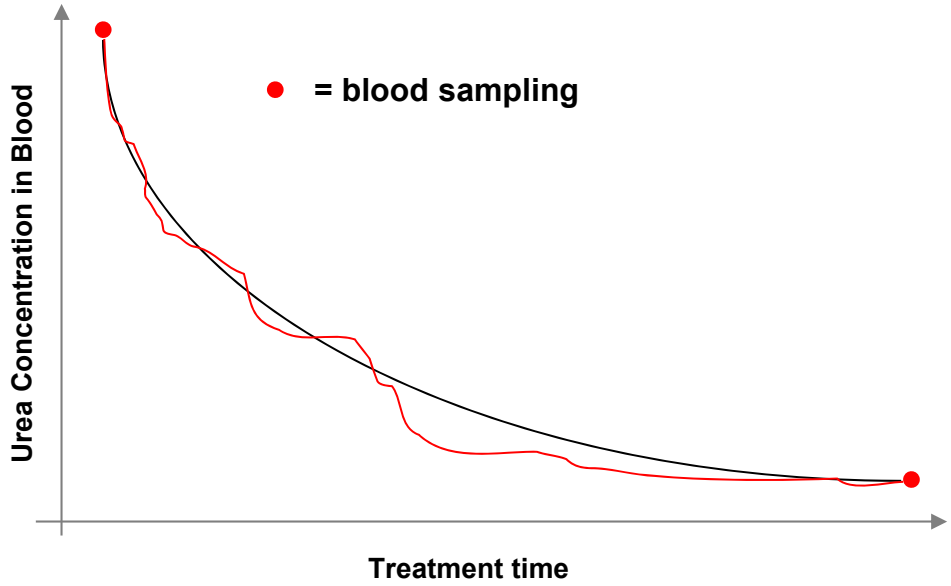
Easy to understand display of actual dialysis efficiency



* (sample treatment curve)

Adimea
Clinical Data

- **Kt/V-Determination using Daugirdas-Formulas**



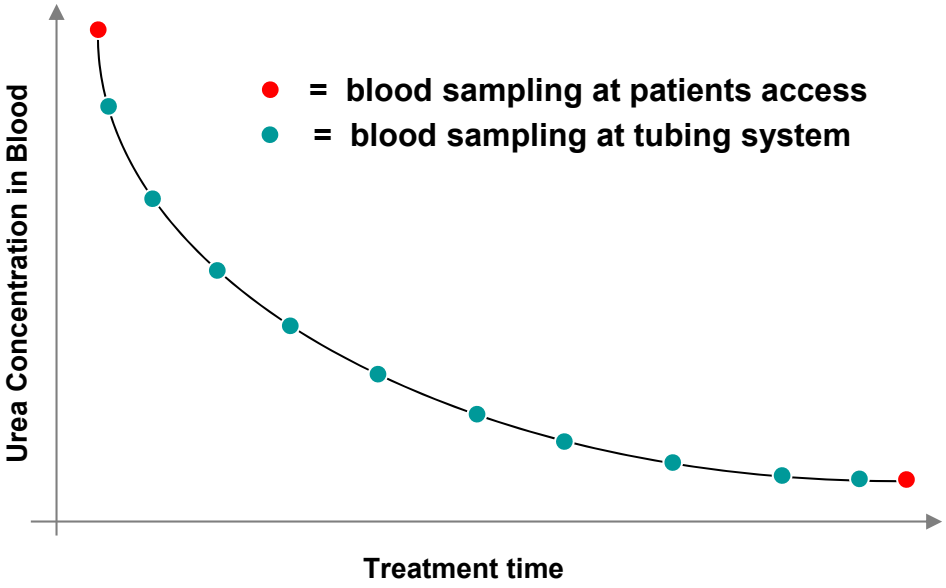
single-pool-Kt/V [spKt/V]

$$=-\ln(R - 0{,}008 \cdot T) + (4 - 3{,}5 \cdot R) \cdot \frac{UF}{W}$$

Does this procedure make sense?

Adimea
Clinical Data

- **Precise Blood Kt/V determination using…**



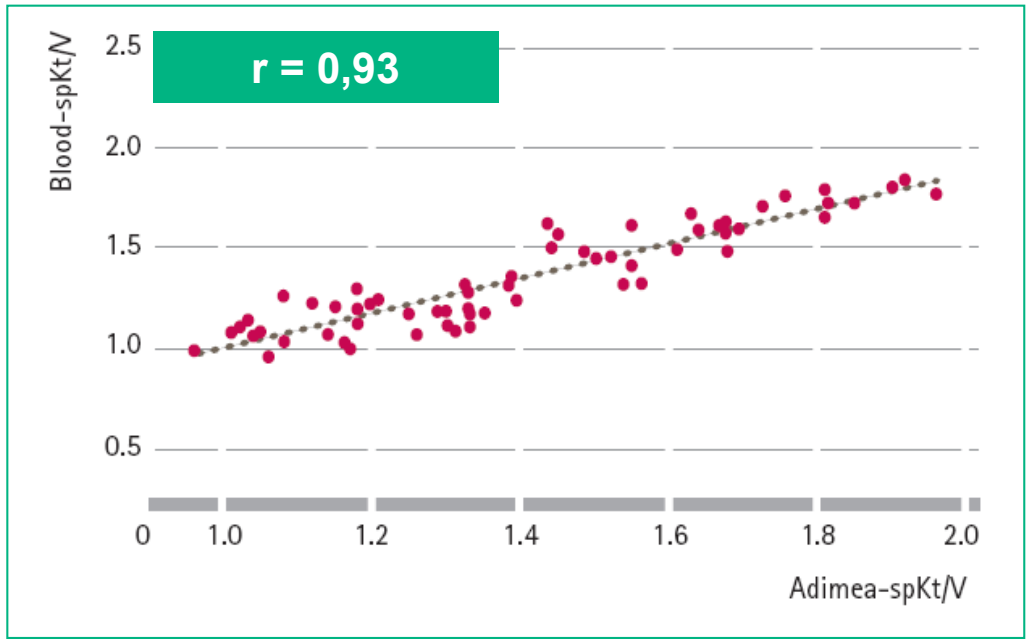
gold standard

- Intention:
  Precise determination of blood-Kt/V under routine conditions
- Method:
  Controlled blood sampling (study conditions / every 20-minutes)

Assure correct Kt/V values based on blood samples!

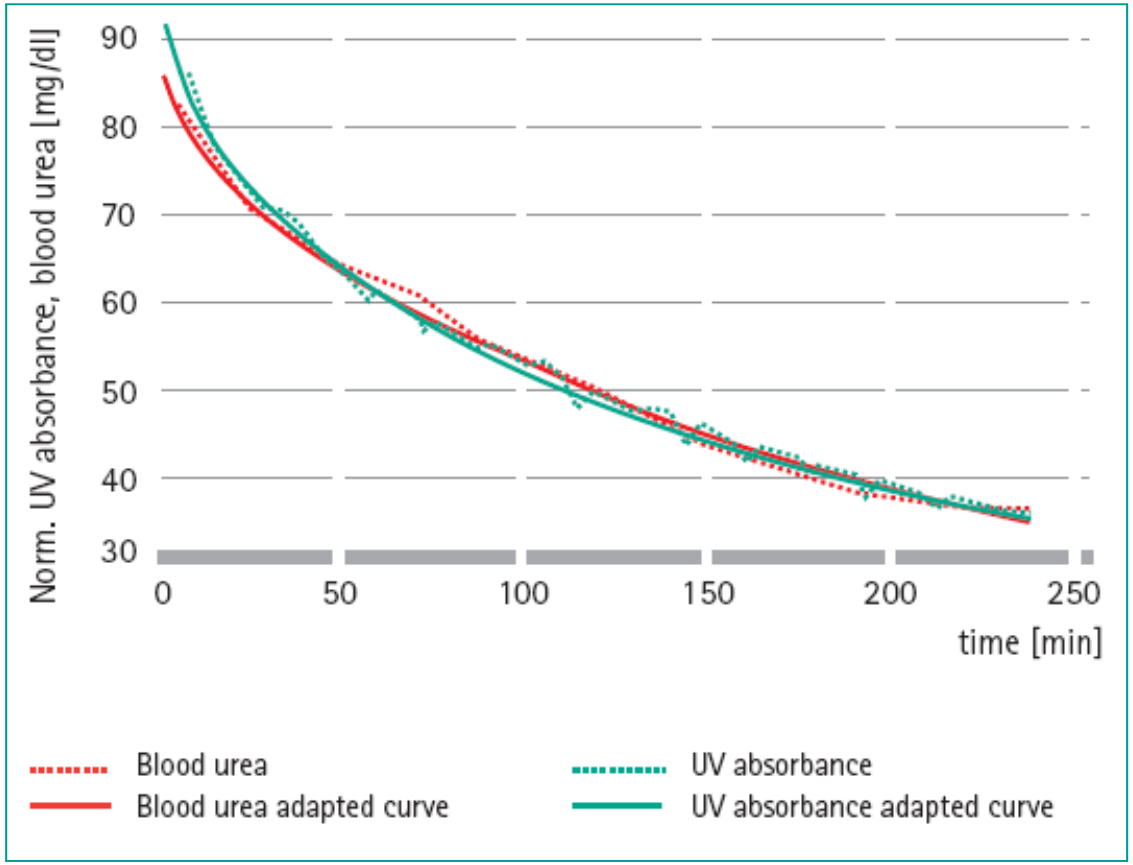
Adimea
Clinical Data

Blood-Kt/V (gold standard) vs. **Adimea-Kt/V**



Non-systematic error: only 7 %

Adimea
Clinical Data



[2] Werner, Günthner et al., [B. Braun Avitum AG, Melsungen], 2009.

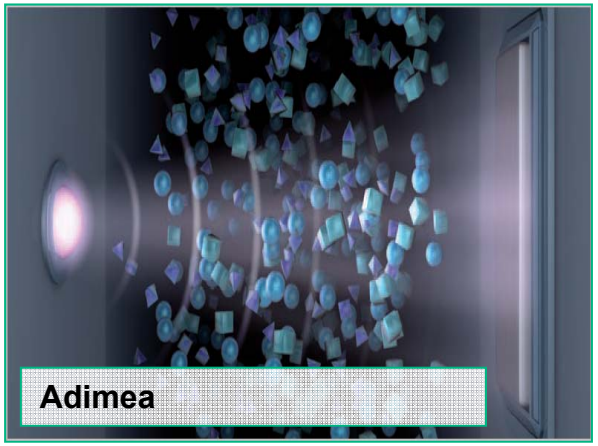
Sample treatment

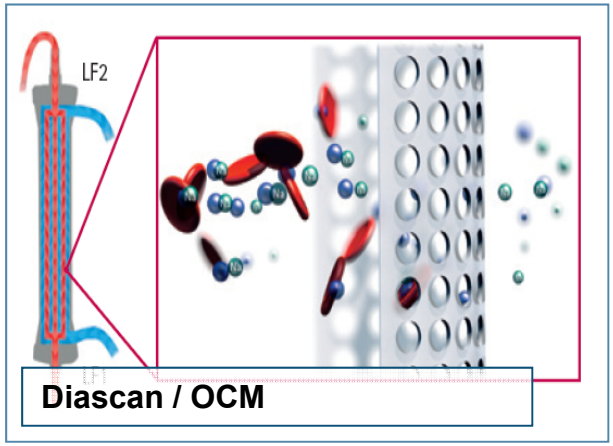
UV absorption signals vs. serum urea values (at 20-minute measurements).

Reveals the excellent correlation:

Deviation for this treatment only 5 %

Adimea | Decisive Key Arguments





Characteristics

- Continuous Measurements in spent dialysate
- Goal-oriented paramater adaption in every treatment type
- Result can be seen directly
- No „V“ determination required
- No follow up costs for service or extra disposables

- No real-time monitoring
- Usually done only once a month or once a quarter
- Adaptiopns on parameters not until before next dialysis session
- Accuracy pending on timing of blood samplings
- manpower requirements

- Unapplicable in SN therapies
- Restrictions in HF / HDF modes
- Only periodic measurements
- Manual determination of Urea distribution volume „V“ required
- No URR / spKt/V / eKt/V
- Frequent calibration (OCM)

Hemodialyse-efficientie besluit 1

- Mortaliteit is verbeterd aan dialyse en wordt nu vooral bepaald door co-morbiditeit, meer nog dan door leeftijd.
- ‘De patiënt sterft aan dialyse, niet door dialyse’.
- Voornaamste doodsoorzaak van dialysepatienten blijft cardiovasculair, waarvan de oorzaken ook al van voor de dialysestart terug te vinden zijn.
- Klaring van kleine moleculen door dialyse als parameter van dialyse adequaatheid is dan ook erg beperkt, alhoewel een waardevolle parameter van de afgeleverde dialysedosis.
- Kt/V
  - voorheen als maximum toe te dienen zorg geinterpreteerd
  - nu als minimum en belangrijk maar niet enige onderdeel van de gehele zorgpakket.

Hemodialyse-efficientie besluit 2.

- Van efficiënte
  over adequate
  naar optimale hemodialyse!

- Met medewerking van de patiënt en het hele nefro-logische team!

Referenties

- http://www.cari.org.au/dialysis_adequacy_published.php
- KDIGO
- EBPG for hemodialysis, 2007
- UpToDate
- Braun