WHAT IS

ON-LINE CLEARANCE

MONITORING ?

PRINCIPLE OF THE OCM

OCM is an;

ELECTROLYTE BASED
[namely Sodium (Na +)]

UREA CLEARANCE MEASUREMENT

without the need for any additional blood sampling !

PRINCIPLE OF THE OCM

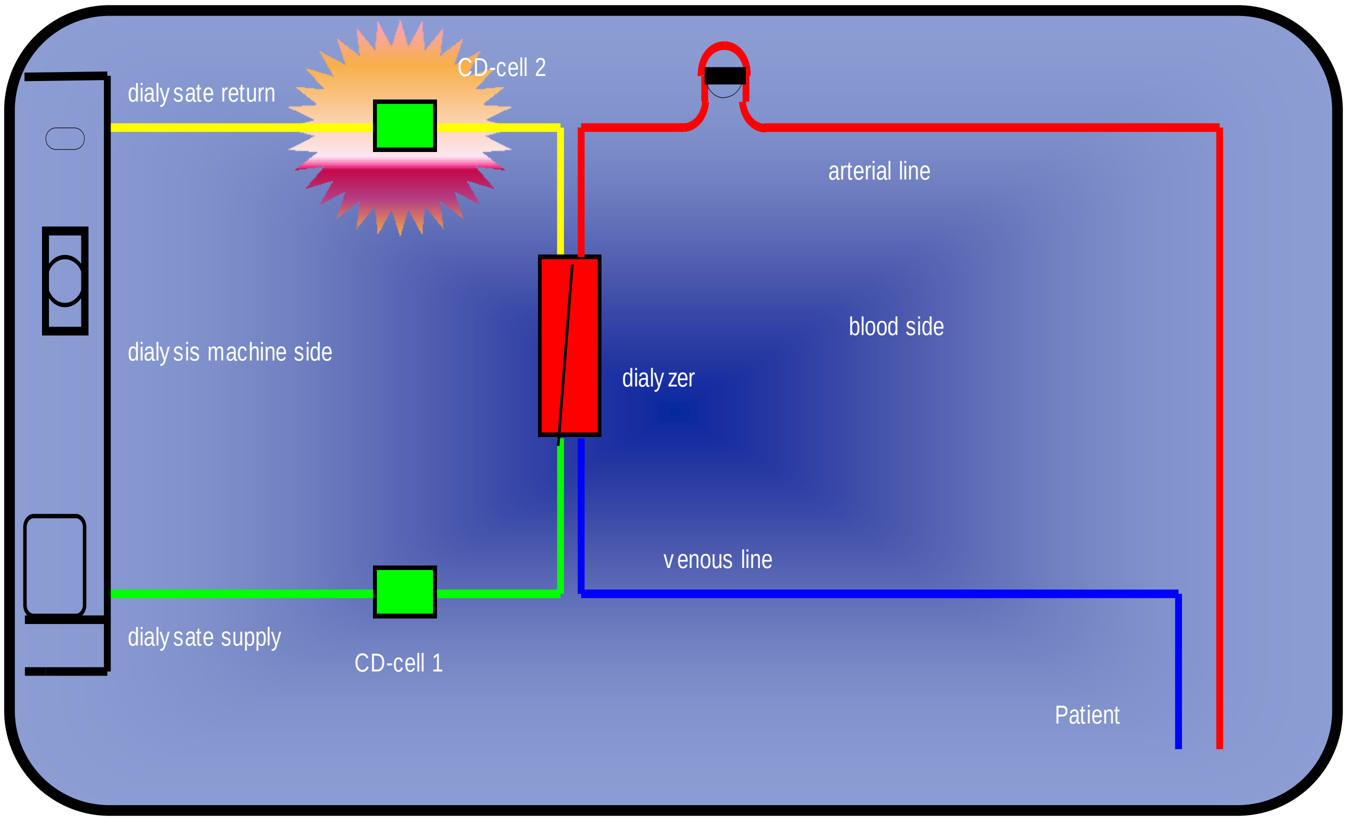
Achieved by;

- additional fitting of a second **CONDUCTIVITY** cell in the return dialysate line
- no other hardware modification has to be made

WHY ????

On-Line Measurement

PRINCIPLE OF THE OCM



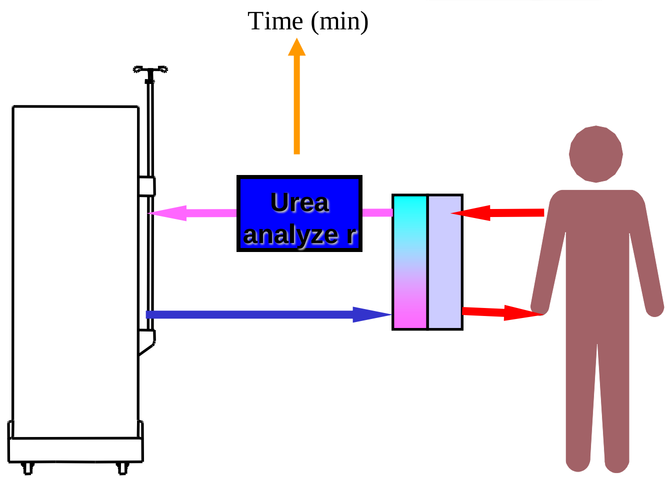
PRINCIPLE OF THE OCM

Non-invasive approach

- Sodium chloride (NaCl) and Urea diffusion coefficients are almost equal
- therefore NaCl dialysance is comparable to urea clearance
- intradialytic adjustments of therapy
- multiple immediate and precise clearance information every session
- less expensive in materials, no additional operating costs e.g. laboratory

ON-LINE CLEARANCE MONITOR

PRINCIPLE OF THE OCM



Principle: continuous measurement of urea concentration in the effluent dialysate by means of:

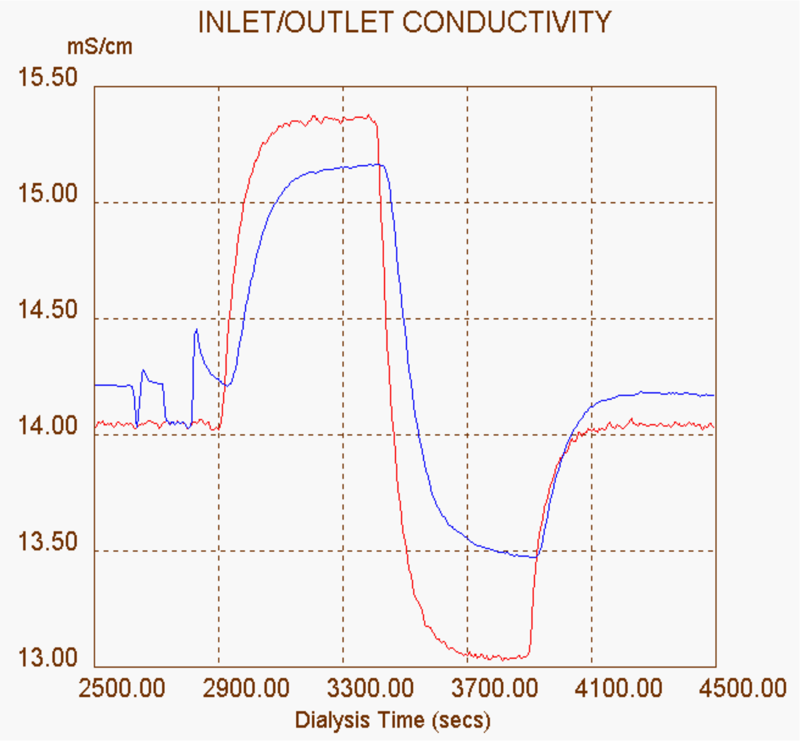
- **enzymatic** urea breakdown combined with ion sensitive electrodes or measurement of electrical conductivity
  misc.. references

- **optical** methods (e.g. UV 254 nm)
  Gal G, Grof J: Continuous UV photometric monitoring of the efficiency of hemodialysis. Int J Artif Organs 1980 Nov;3(6):338-41

Advantage: provides **complete** set of UKM data

Problem : prohibitive **operating costs**

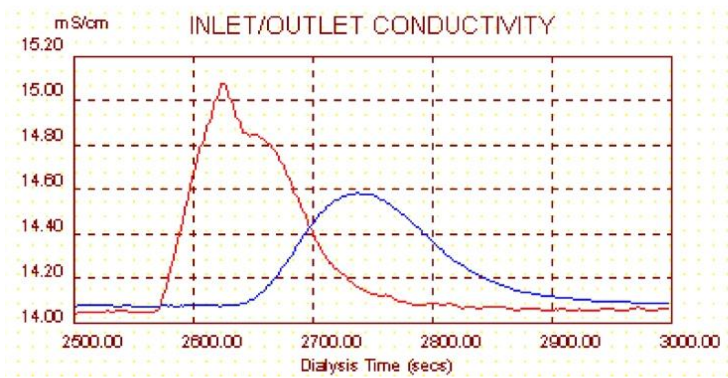
PRINCIPLE OF THE OCM

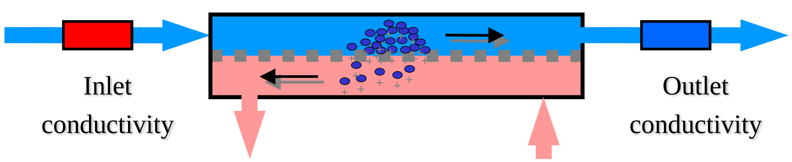


Step-profile

- increase of dialysate inlet conductivity of 10% above base level for approx.. 5min.
- Followed by the same decrease to base level,
- with recordings of conductivity from the inlet and outlet dialysate lines,
- together with dialysate flow an UF rate
- known process since 1983 but never clinically tested

PRINCIPLE OF THE OCM





Principle:

- Modification of a dialysate conductivity pulse during dialyser passage

Influencing factor(s):

- membrane transport properties at given flows for the solute used in the pulse (Na^+ as surrogate for urea)
- ...

Result:

- sodium dialysance, finally converted to effective in vivo dialyser urea clearance

OCM RESULTS

Study design:

- 20 patients, 52 ±17 years
- ten treatments monitored by OCM per patient (4008H with OCM option)
- 3 OCM tests per treatment

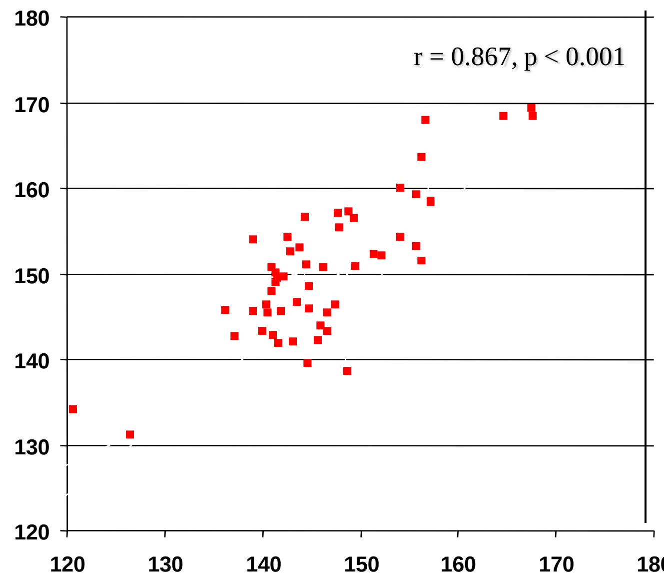
Treatment parameters:

- treatment time 3-5 h
- blood flow range 200 - 250 ml/min
- dialysate flow 500 ml/min
- dialyser: PSu 1.8m²
- mean UF volume 1.8 ± 0.4 l/HD

Parameters measured:

- conductivity pre/post dialyser
- blood urea, arterial / venous
- dialysate urea (2% sampling)
- total recirculation

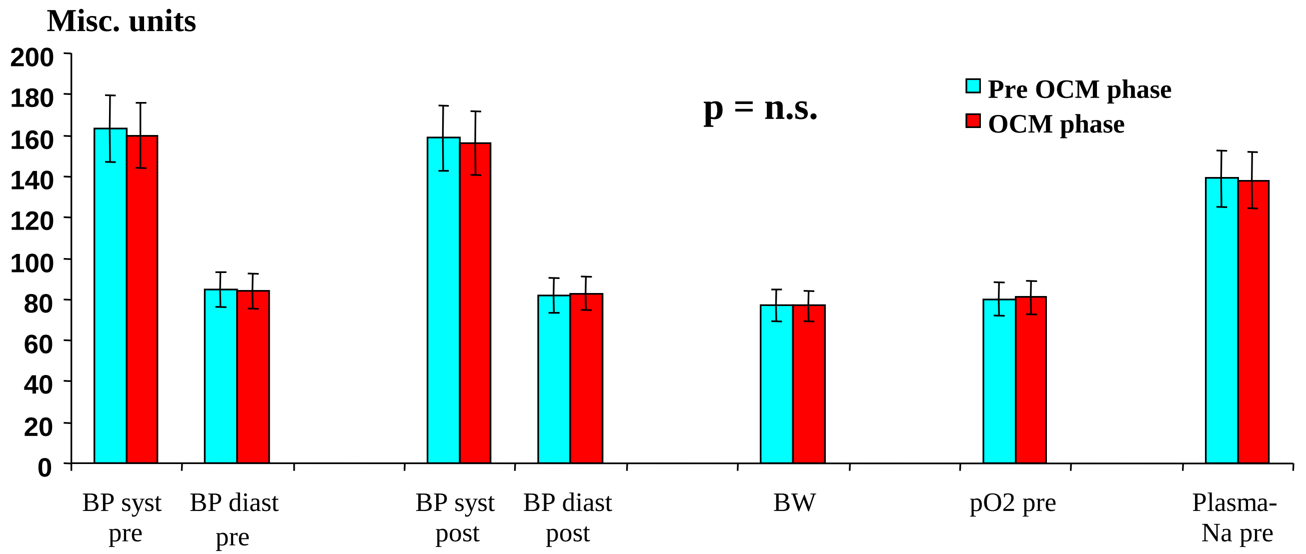
Blood side urea clearance [ml/min]



Electrolyte clearance [ml/min]

Kuhlmann U, Goldau R, Samadi N, Graf T, Orlandini G, Lange H: Accuracy and safety of online clearance monitoring based on conductivity variation. Abstr. EDTA 1999, 249

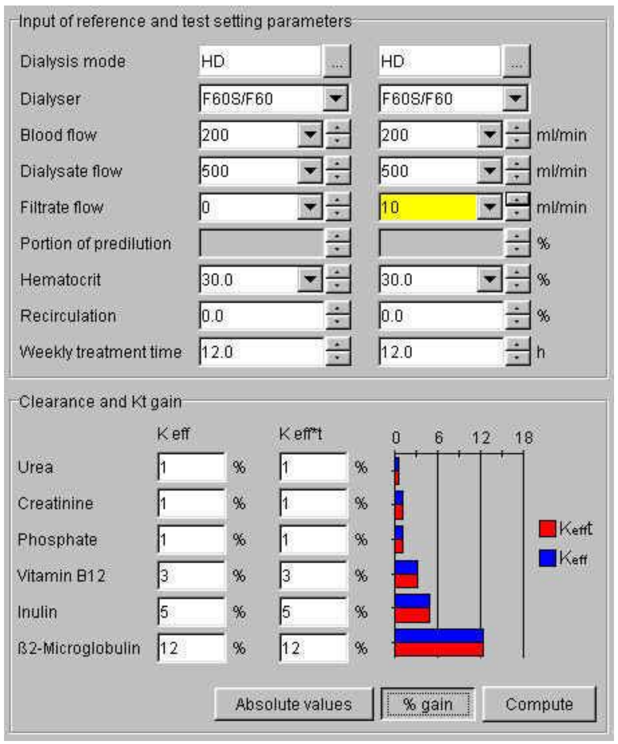
OCM RESULTS

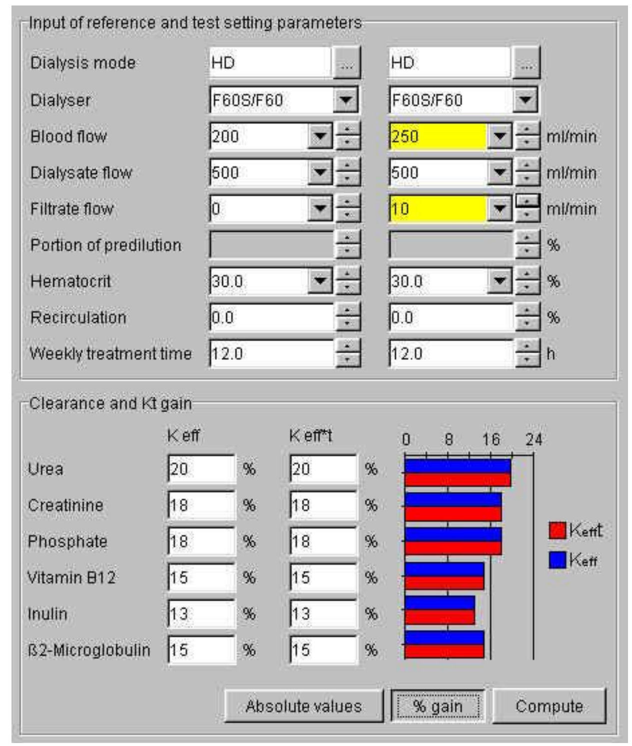


	Plasma Na before OCM pulse [mmol/l]	Plasma Na after OCM pulse [mmol/l]	Sodium balance per pulse [mmol]
N	211	211	329
Mean	**138.4**	**138.6**	**4.02**
± SD	1.4	1.4	18.8

Kuhlmann U, Goldau R, Samadi N, Graf T, Orlandini G, Lange H: Accuracy and safety of online clearance monitoring based on conductivity variation. Abstr. EDTA 1999, 249

CLEARANCES AT DIFFERENT BFR/UFR





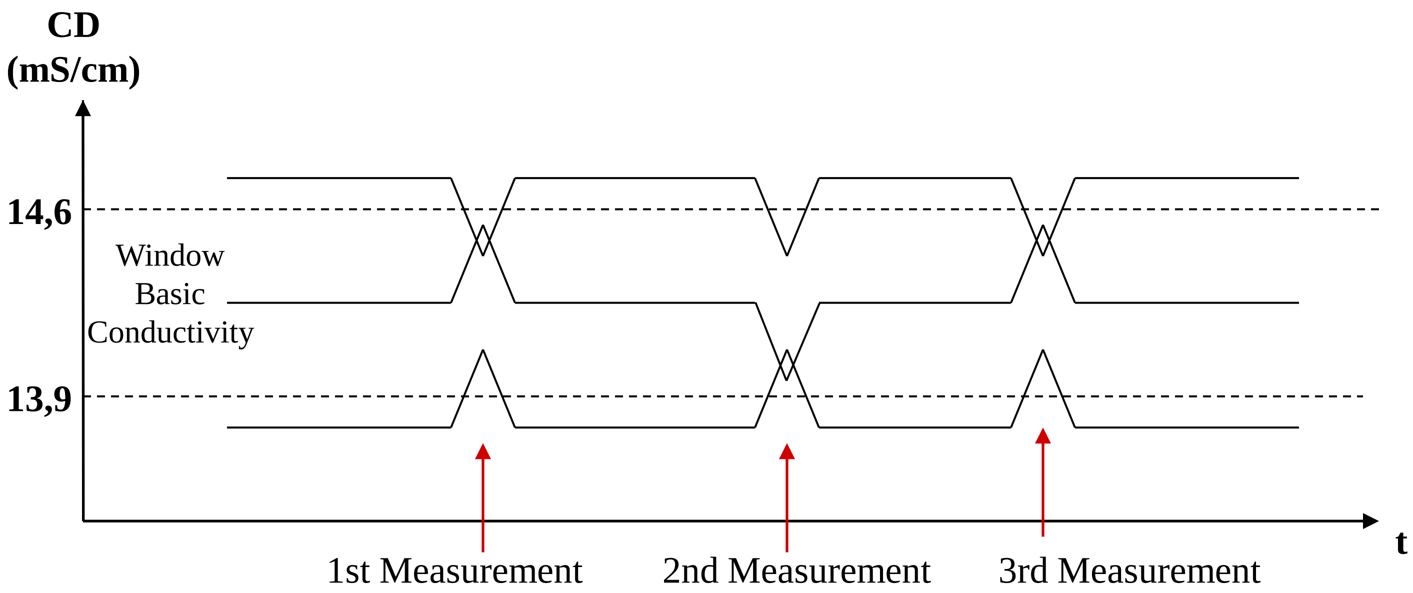
Data from: FMC Clearance Calculation Tool

PRINCIPLE OF THE OCM

A measurement

- max. conductivity 15.7 mS/cm
- min. conductivity 12.8 mS/cm
- depending on the base conductivity the measurement direction will alternate
- if the conductivity is below 13.9 mS/cm the conductivity will be raised
- if the conductivity is above 14.6 mS/cm the conductivity will be lowered
- if the conductivity is within these ranges then the direction of the pulse will alternate

PRINCIPLE OF THE OCM



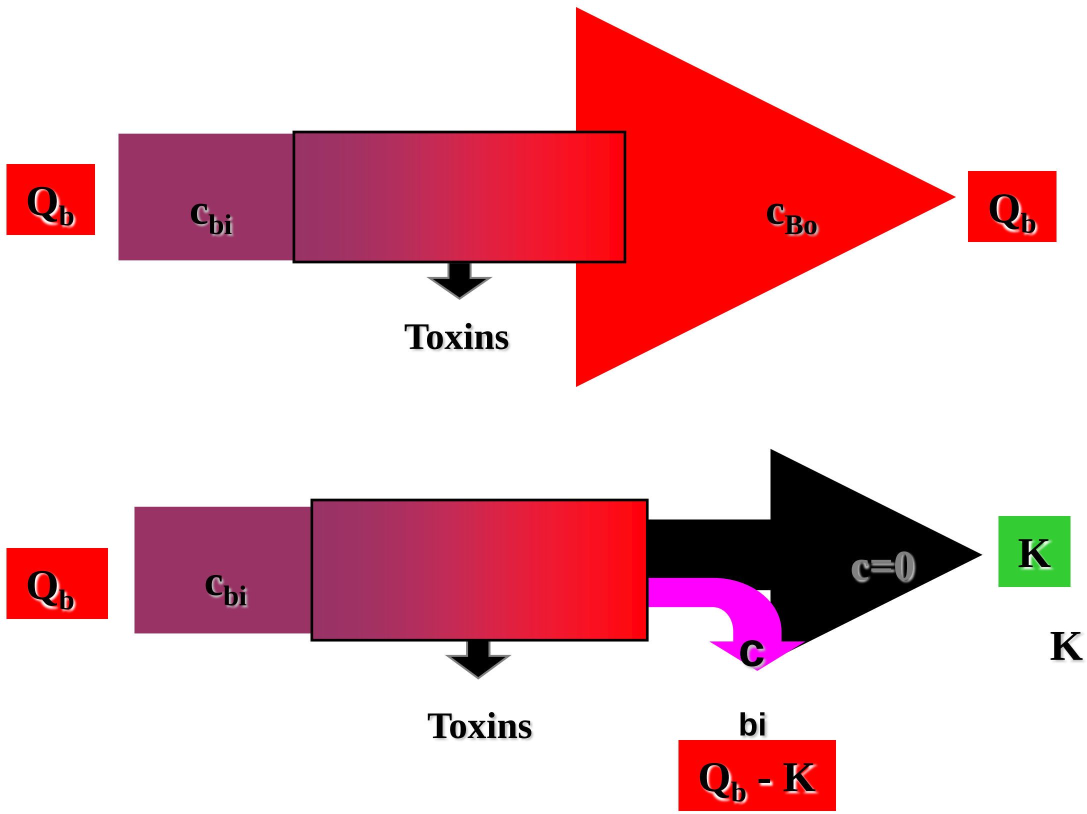
ON-LINE CLEARANCE MONITOR

Fresenius Medical Care

DEFINITION

- CLEARANCE
- DIALYSANCE,
- Kt/V

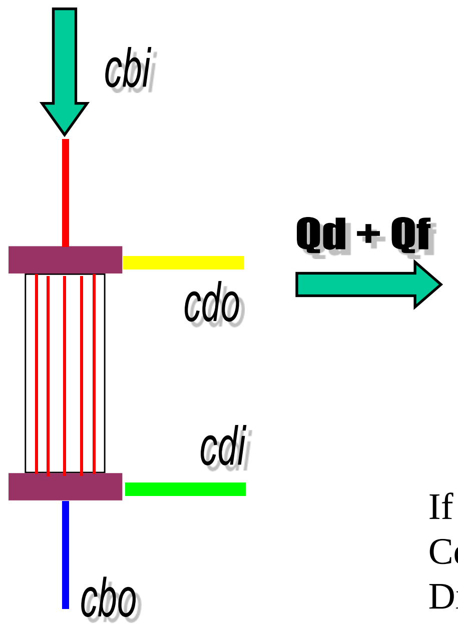
CLEARANCE



The clearance for a certain solute is the (theoretical) flow K cleared completely from this solute:

$$K = Q_b \bullet \frac{c_{bi} - c_{bo}}{c_{bi}}$$

CLEARANCE, DIALYSANCE



$$Dialysance_{eff} = K = \frac{Extracted\ Mass\ Flow}{Concentration\ Gradient}$$

$$K = (Qd + Qf) * \frac{cdo - cdi}{cbi - cdi}$$

Clearance = Dialysance (cdi = 0)

If a substance to be dialysed is not contained within the dialysate this Cdi = 0 the dialysance is then called clearance.
Dialysance can be expressed when it contains only Cbi and not Cbo

b = blood
c = concentration
d = dialysate
i = inlet
o = outlet

Kt/V

$$\frac{Kt}{V} = \frac{effective \quad Dialysance \quad * \; t_{Treatment}}{Patients \quad Distribution \; Volume} \left[\frac{ml}{l}\right]$$

Unit of a drug dose

V (Urea) normally determined by clinical measurement.

- **Watson Formula**

  males $V = 2.447 - 0.095 \cdot a + 0.107 \cdot h + 0.336 \cdot w$

  females $V = -2.097 + 0.107 \cdot h + 0.247 \cdot w$

- **Hume-Weyers Formula**

  males $V = -14.013 + 0.195 \cdot h + 0.297 \cdot w$

- **Empirical Formula**

  V = sex, weight/kg, height/cm and age

- **Daugiradas**

- **Mellit-Cheek - Paediatrics**

Kt/V

Kt/V urea

is the recommended minimum dialysis dose expressed as a value according to the DOQI guidelines and the NCDS as;

- **1.2**

single pool prescribed value should be;

- **>1.3**

assessment of the Kt/V is normally performed by costly and time consuming blood urea concentration analysis

Kt/V

Urea based KT/V per session has risen last decade and is highly correlated to URR.

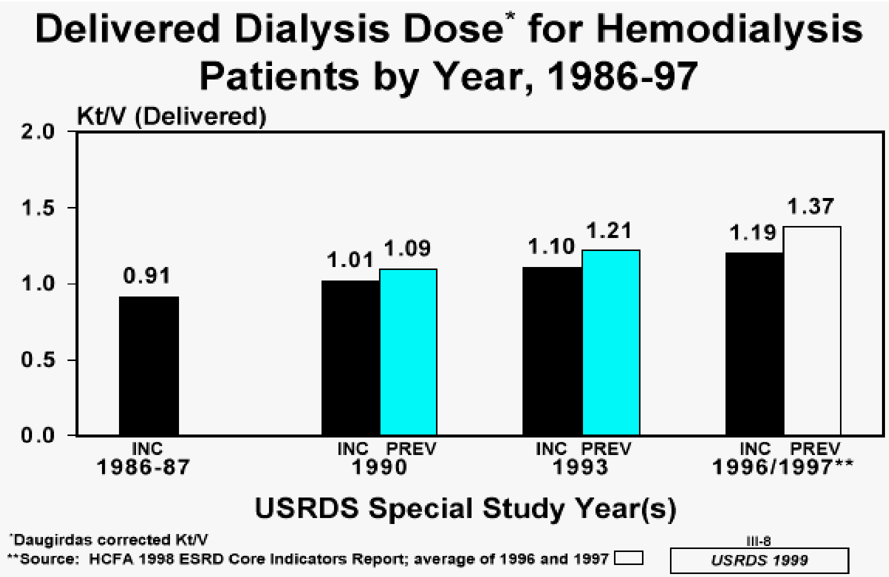


Figure III-8

Delivered dose of dialysis for hemodialysis patients, by year, 1986-1997. Source: Special Analysis; HCFA 1998 ESRD Core Indicators Report.

Kt/V

$$URR = \frac{\text{Pre - Post Dialysis Blood Urea Nitrogen (BUN)}}{\text{Pre Dialysis BUN}} [\%]$$

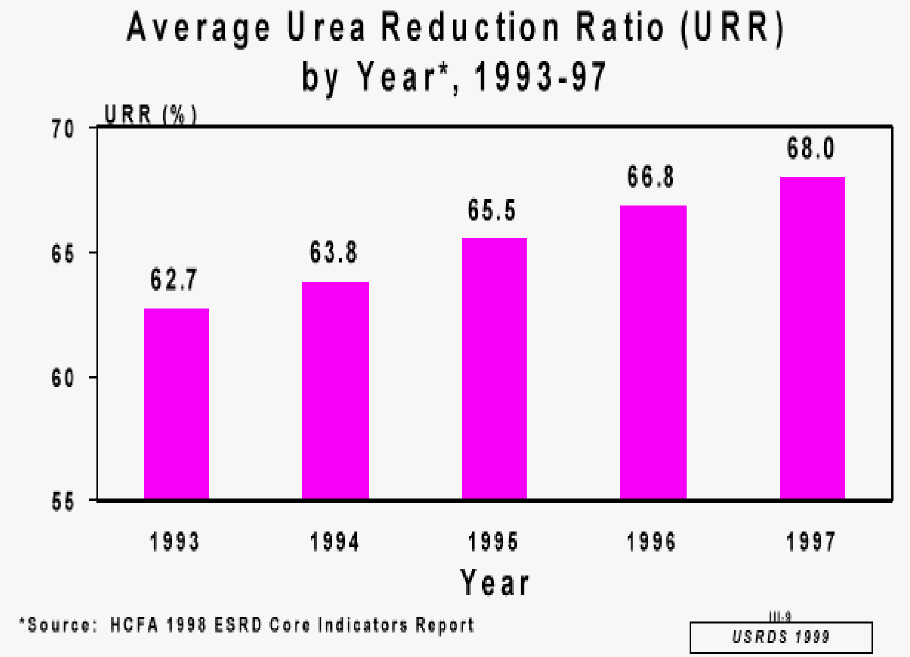
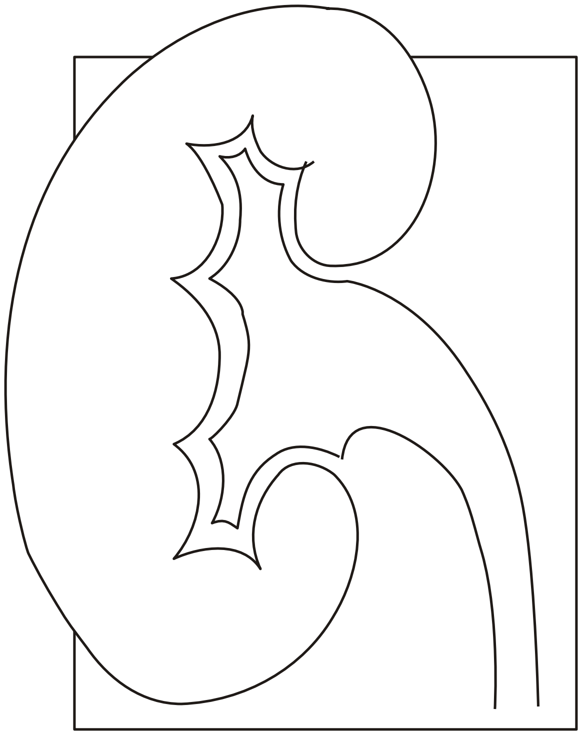


Figure III-9

Average urea reduction ratio by year, 1993-1997. Source: HCFA 1998 ESRD Core Indicators Report.

Kt/V



- Inadequate dialysis increases the morbidity and mortality rates
- The national Co-operative Dialysis Study (NCDS) demonstrated that the normalised treatment dose Kt/V, is correlated with Protein Catabolic Rate PCR, and morbidity /mortality
- Changes in Kt/V are followed by changes in PCR

ON-LINE CLEARANCE MONITOR

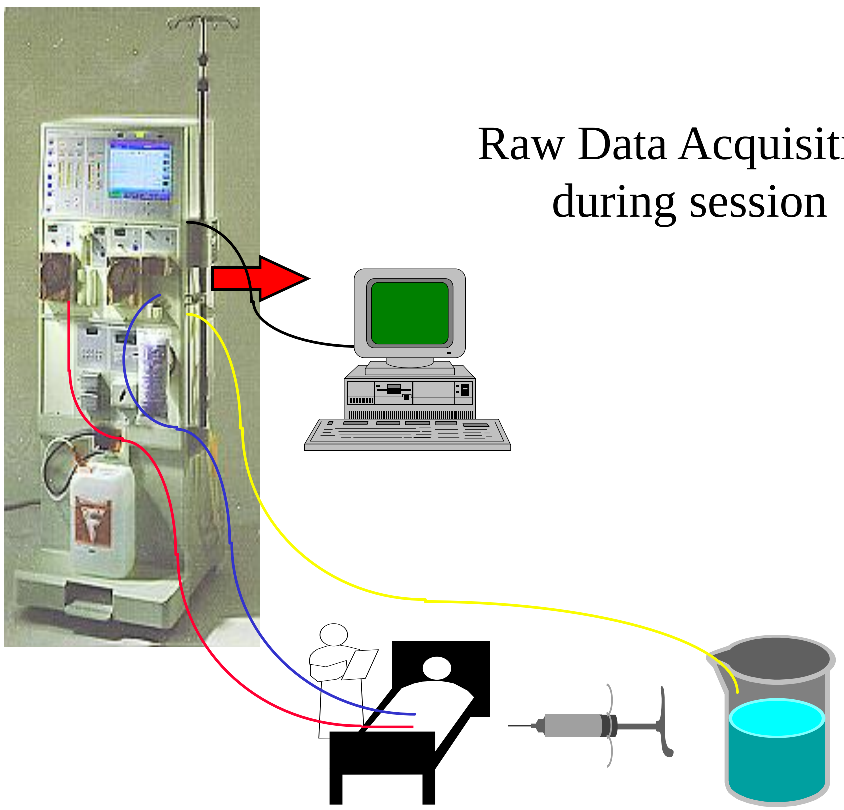
Kt/V

Today		OCM
Blood Samples expensive, not practical	Dose Assessment $\frac{Kt}{V} > 1.2$?	Dialysate side: K, t low costs : 1 CD cell
Once a week or less	**Frequency**	4-6 times per session
Retrospective	**Detection of Irregularities**	Continuous, “ON LINE”
Patients Blood, Staff, Syringes, Lab costs	**Current efforts**	1 Calibration / Year
6-8% (SD)	**Accuracy of K**	5% (SD)
uncomfortable	**Handling**	Button push
Impractical, uncommon	**Session Quality Assurance**	Standard

ON-LINE CLEARANCE MONITOR

Fresenius Medical Care

Kt/V CURRENT PROCEDURE



Raw Data Acquisition
during session

- **Time consuming**
- **Expensive**
- **Labour Intensive**

What factors can affect the outcome of the Prescribed Kt/V

UNDERDOSAGE OF DIALYSIS

Results in:

- increased long term mortality rates
- ureamic related symptoms e.g. oedema
vascular instability
nausea / vomiting
- disturbed electrolyte metabolism
- bad nutritional status
- increased comorbidity factors
- significant decrease in the Quality Life
- increase in treatment costs due to poor health

Expected Remaining Lifetimes for U.S. Population (1995), All ESRD Patients[1] (1997) and Dialysis Patients (1997) by Age, Race and Sex

	U.S. Population, 1995[2]				ESRD population, 1997[4]				Dialysis population[3,4], 1997			
	Black		White		Black		White		Black		White	
Age	M	F	M	F	M	F	M	F	M	F	M	F
0-14	61.1	69.7	68.7	74.8	26.7	24.3	32.6	30.0	18.0	16.2	16.9	15.4
15-19	51.7	60.2	59.2	65.2	22.2	19.6	24.6	23.3	18.6	16.6	16.2	15.2
20-24	47.2	55.4	54.5	60.4	19.3	17.0	21.3	20.0	16.4	14.4	14.0	12.9
25-29	42.9	50.6	49.9	55.5	16.5	15.3	17.9	16.8	14.1	13.0	11.4	10.4
30-34	38.6	46.0	45.2	50.6	14.2	13.5	15.1	14.3	12.2	11.6	9.4	8.7
35-39	34.5	41.4	40.7	45.8	12.4	11.8	12.7	12.3	10.8	10.5	8.0	7.5
40-44	30.5	36.9	36.1	41.0	10.7	10.1	10.6	10.3	9.5	9.0	6.9	6.8
45-49	26.7	32.6	31.7	36.3	9.0	8.6	8.8	8.4	8.1	7.8	6.1	5.9
50-54	23.0	28.4	27.3	31.7	7.7	7.2	7.1	6.7	7.0	6.7	5.2	5.0
55-59	19.6	24.4	23.2	27.3	6.6	6.0	5.7	5.4	6.1	5.7	4.4	4.3
60-64	16.4	20.6	19.3	23.0	5.4	5.3	4.5	4.4	5.1	5.0	3.7	3.8
65-69	13.6	17.1	15.7	19.1	4.3	4.5	3.6	3.5	4.1	4.4	3.2	3.2
70-74	11.0	13.9	12.5	15.4	3.6	3.6	2.9	2.9	3.5	3.6	2.8	2.8
75-79	8.8	11.1	9.7	12.0	2.9	3.0	2.5	2.5	2.9	3.0	2.4	2.4
80-84	6.8	8.4	7.2	8.9	2.5	2.5	2.0	2.1	2.5	2.5	2.0	2.1
85+	5.1	6.2	5.2	6.3	1.9	2.1	1.7	1.7	1.9	2.1	1.6	1.7

[1] Includes patients treated with either dialysis or transplantation.

[2] Ventura SJ, Peters KD, Martin JA, Maurer JD. Births and Deaths: United States 1996. Monthly vital statistics report, Vol 46 No. 1, supp 2. Hyattsville, MD; National Center for Health Statistics, 1997: Table 16

[3] Mortality followup is censored at transplant.

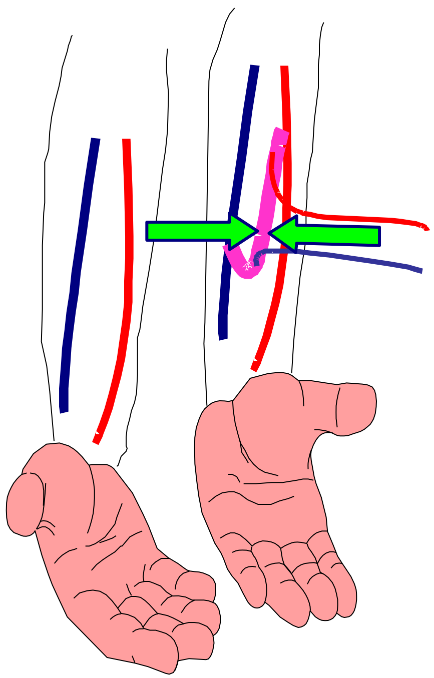
[4] Death rates used for these calculations exclude dialysis unrelated deaths.

Source: Reference Table D.2 and Special Analysis

USRDS 1999

ON-LINE CLEARANCE MONITOR

FACTORS AFFECTING OUTCOME



- Fistula flow
- Stenosis or Occlusion can occur due to increasing age resulting in decreased access blood flow
- Fistula recirculation
- High pre-pump arterial pressures

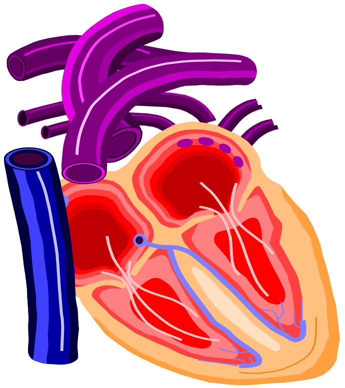
Typical Blood Flow : 0.8 - 1 l /min

ON-LINE CLEARANCE MONITOR

Fresenius Medical Care

FACTORS AFFECTING OUTCOME

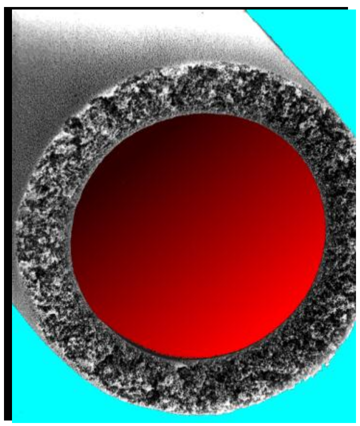
- Heart insufficiency
- Generalized electrolyte or fluid disequilibrium
- Arterial blood pressure problems
- Cardiopulmonary recirculation



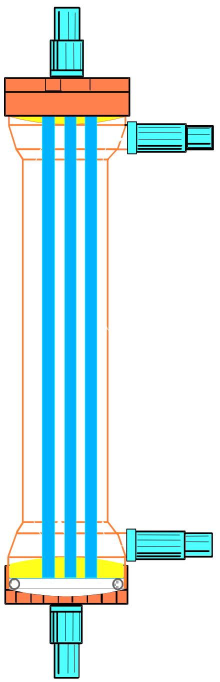
may result in reduced cardiac output and insufficient vascular transport properties from diuretic toxins together with a

- Reduction of treatment time
- Reduction in blood flow

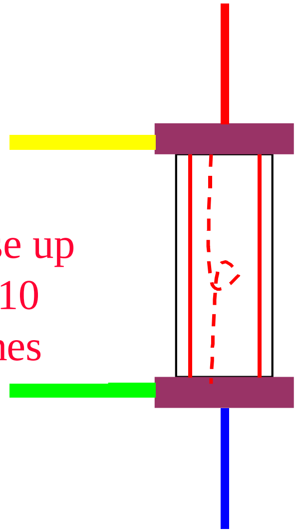
FACTORS AFFECTING OUTCOME



- surface of the filter
- type of membrane
- anticoagulation
  (consequent clotting)
- dialysate flow
- overestimation of the dose of dialysis
  due to post dialysis rebound
- air bubbles



FACTORS AFFECTING OUTCOME



Reuse up to 10 times

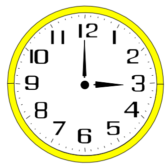
REUSE

- Reduces affectivity due to
  1. fibers clotting,
  2. protein occlusion of the micropores
- in countries where reimbursement is low
- loss of active surface area

KT/V_{urea}: Various Sources for Technical Errors

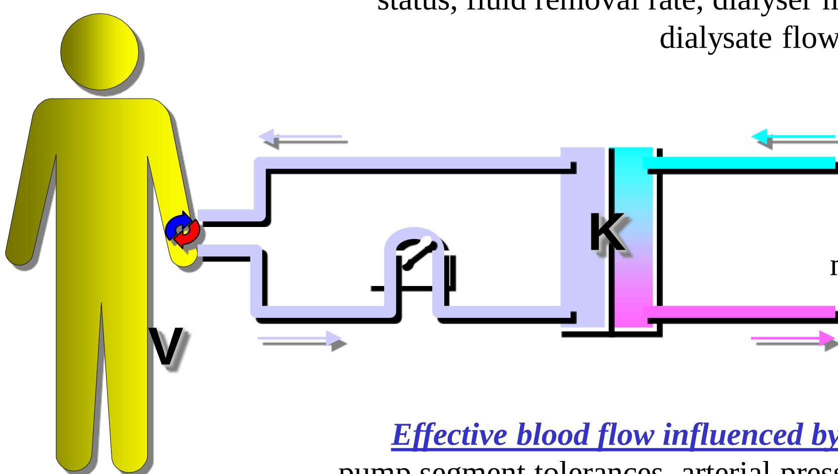
$$\frac{K \times t}{V}$$

t



Effective treatment time may be not correct

In vivo clearance influenced by
effective blood flow, blood composition, anticoagulation status, fluid removal rate, dialyser manufacturing tolerances, dialysate flow ...



Dialysate flow influenced by
machine settings, flow fluctuations ...

Effective blood flow influenced by
pump segment tolerances, arterial pressure, access recirculation ...

OPERATION OF THE

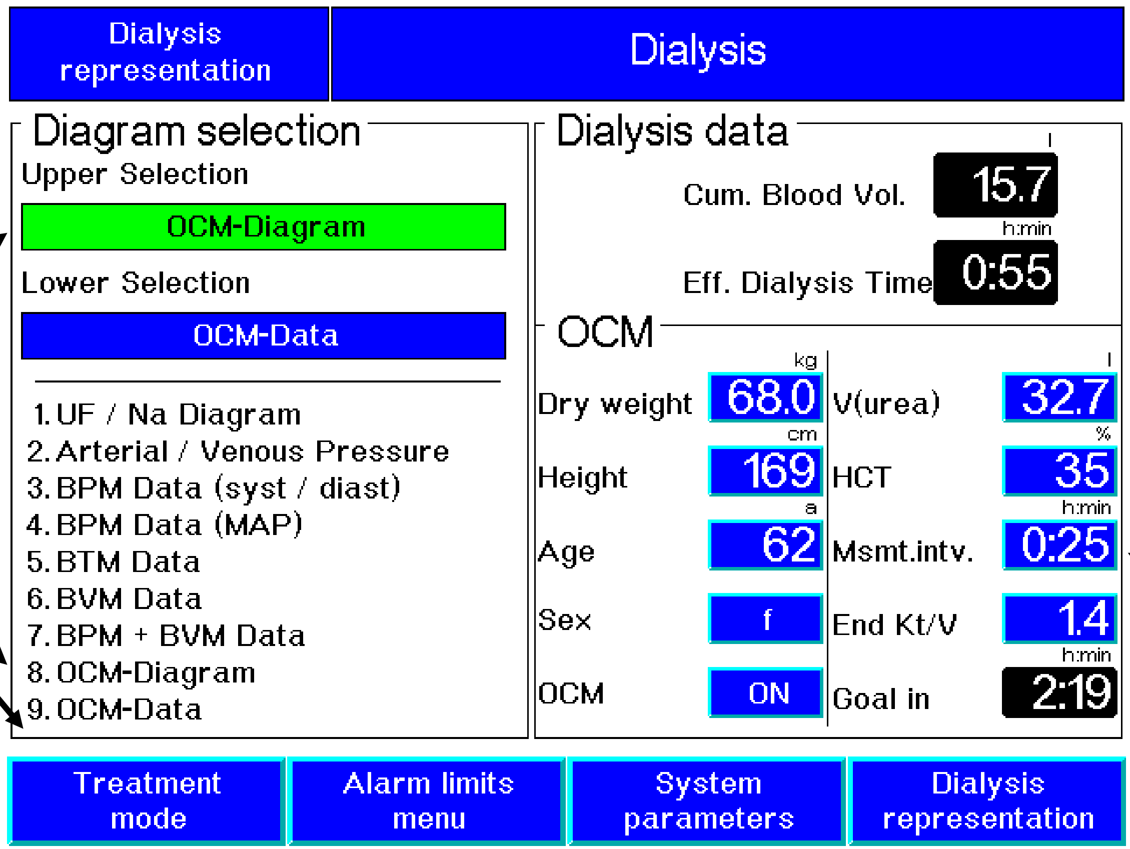
OCM

ON-LINE CLEARANCE MONITOR

Fresenius Medical Care

OCM SCREEN

Select the graphs you wish to be displayed
either No. 8, or No. 9 in the dialysis representations screen



If V urea is unknown at the start after entering Wt,kg, S and age and pressing Confirm it will automatically be calculated

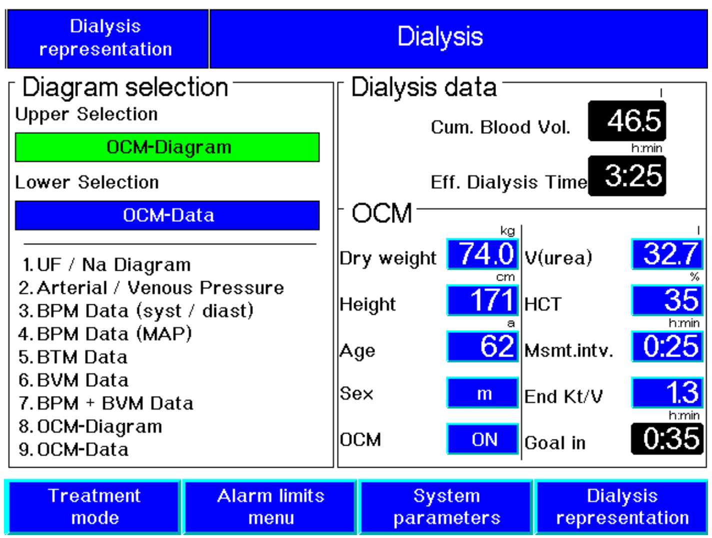
Msmt.intv. = the time interval between each measurement

ON-LINE CLEARANCE MONITOR

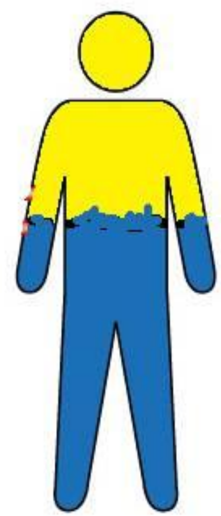
Fresenius Medical Care

OCM SCREEN

Example 2



Distribution Volume of Urea Vurea



Body mass 30-35%

Water 60-65%
V=liters

ENTERING THE DATA

- **Dry Weight** **= g**
- **Height** **= cms**
- **Age** **= yr.**
- **Gender** **= M/F**

All are necessary for the calculation of Volume of Urea V (Urea)

HCT
required for the calculation of

- K (clearance)
- Plasma Na +

Once the **CONFIRM** key is pressed

Volume of **Urea** is automatically calculated / litres

It is advised to enter the **Vurea** if it is known

ENTERING THE DATA

Enter UF and Dialysate Data as normal

- connect patient
- switch On UF
- if required select the OCM Data and Diagram in the Dialysis Representations Screen to be displayed on the main screen

CLEARANCE CALCULATION

- updated every minute
- during CPHT/Diasafe rinsing no dialysate flow therefore the clearance = 0
- following a CPHT the clearance drops approx. ⅔ rd of the mean value

MEASUREMENT TIME INTERVAL

• minimum interval	=	25 min.
•(maximum interval	=	9h 47 min)
• Total measurement time	**=**	**11 min**

- if there is less than 12 min. of UF time remaining the measurement will not be performed
- 1 min for stable CD - 10 min measurement
- commences as soon as the optical detector sees blood
- in intervals of 12.5 min due to the PHT
- stable conductivity must be achieved and remain stable for 60 sec, otherwise the measurement will be aborted.

MEASUREMENT TIME INTERVAL

Cyclic Pressure Holding Test

• bypass mode for approx. 20 sec
• dialysate flow is stopped
• flow is included in the clearance calculation

Diasafe Rinsing

• is delayed during a measurement until it is completed

Conductivity Changes

• if any changes are made during the measurement, it will be aborted
• during a measurement the conductivity limits are opened for approx.. 3.5 min. and if these are changed at this time the measurement will be aborted

ON-LINE CLEARANCE MONITOR

Fresenius Medical Care

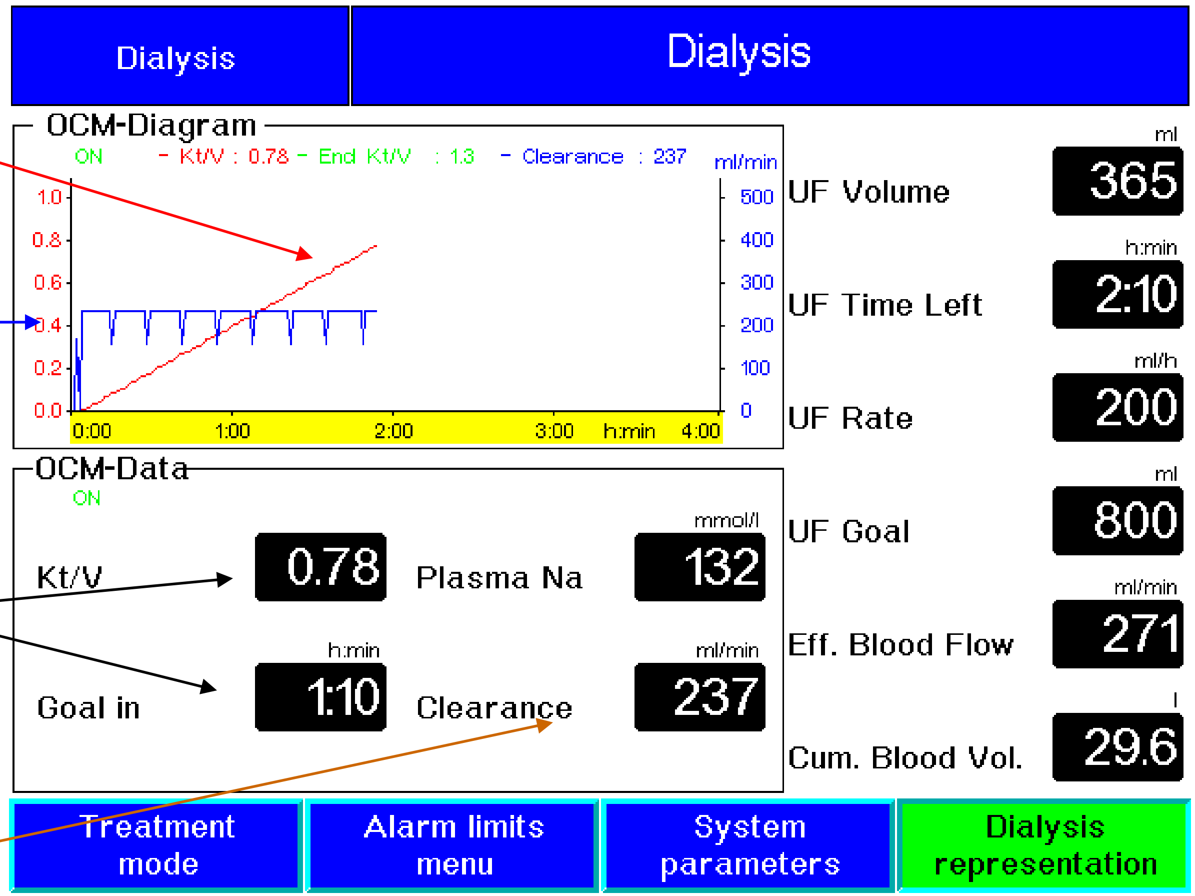
OCM DATA SCREEN

KT/V linear increase during the treatment

Dialyser Clearance value
(also showing the troughs for the cyclic pressure holding test)

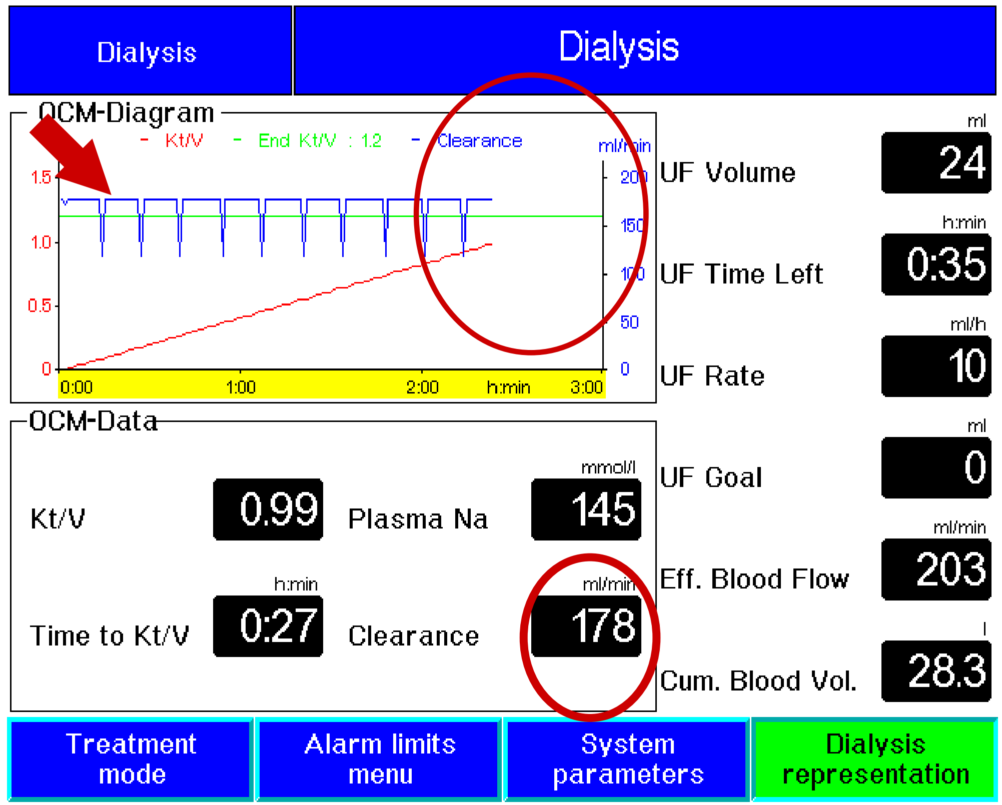
Kt/V result appears following the first measurement

Clearance value is shown once the value is > 70 ml/min



OCM DATA SCREEN

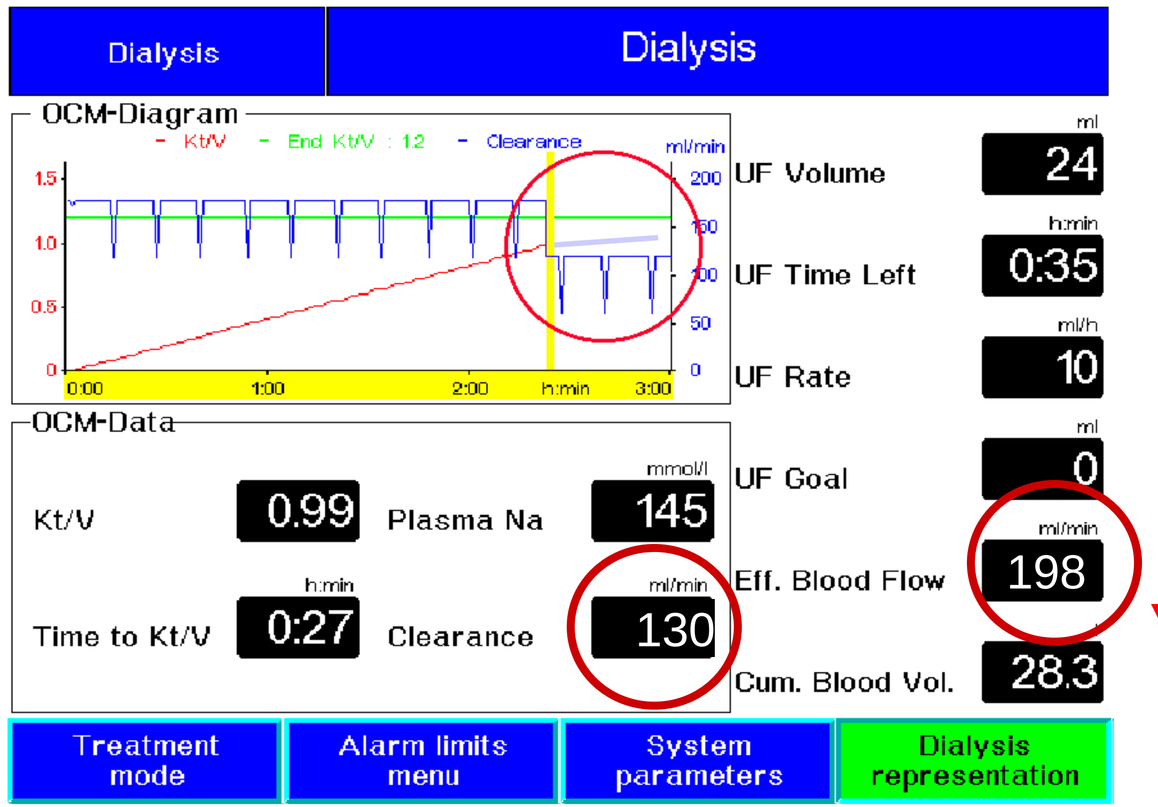
Here we can see the calculated clearance and a steady rise in the Kt/V as expected.



OCM DATA SCREEN

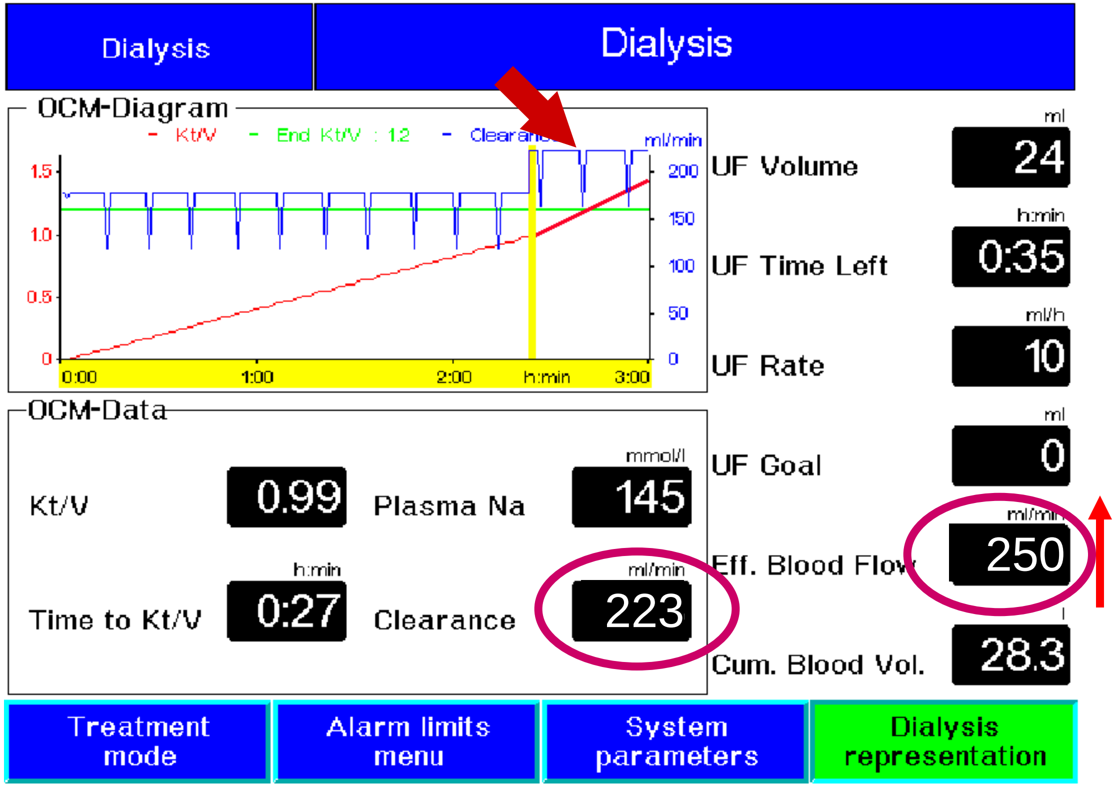
Here the clearance has changed and therefore the graphics also change to depict the new calculated clearance

- Blood flow reduced?
- Fibres clotting?



OCM DATA SCREEN

Here we can see the result on both clearance and Kt/V after increasing the Blood Flow rate



OCM DATA SCREEN

Kt/V

- minimum Kt/V should be **1.2**

- each time a measurement is performed this value will increase towards the selected Kt/V

- the time required to achieve this value will be shown on the screen this may exceed the dialysis time, but is the necessary time required depending on dialyser, bloodflow etc.

OCM DATA SCREEN

Plasma Na+

- corresponds to the sodium concentration in the patients plasma
- calculated once the clearance is **> 70 ml/min**
- allows for the adaptation of the sodium concentration in the dialysate to physiological value of the patient
- shows the trend of the serum sodium during the dialysis

OCM ADJUSTMENT

Requirements;

- performed every 100 treatments
- once UF Goal has been achieved
- optical detector must not see blood
- dialysate lines in the shunt interlock
- stable conductivity
- adjustment time approx. 7.5 min.
- Cleaning key is disabled
- audible alarm generated

Failure of the Adjustment

- dialysate alarm
- water alarm
- dialysate the flow is switched off
- conductivity is changed
- power failure
- emptying/disconnecting the biBag
- bicarbonate probe is placed into the rinse port
- fill programme
- optical detector sees blood or becomes opaque
- dialysate flow falls below 250 ml/min
- cleaning programme is activated
- shunt cover is opened

OCM ADJUSTMENT

ATTENTION !!

- 20 opportunities for the adjustment (120 treatments)
- otherwise OCM is deactivated
- engineer must then recalibrate the machine
- message displayed after UF Goal reached / optical detector has sensed opaque fluid

OCM CONDITIONS

OCM measurements will commence providing the following are **not** being used;

- UF/Na+ profiles number 1,5,or 6, UF time > 180 min.
- Single - Needle Click-Clack
- Battery power

The **OPTICAL DETECTOR MUST SEE BLOOD** for the OCM Measurement to commence

OCM CONDITIONS

Failure of the calculated data

- ultrafltraton rate > 90% of the effective blood flow rate
- effective blood flow < 0 ml/min
- excessive arterial blood flow fluctuations

ISO UF

- providing a calculation was successfully performed prior to starting the ISO

BVM Closed Loop

- BVM may impair the calculation therefore a measurement will be performed at the next available possibility

SUMMARY

1. There is an established correlation between the dose of dialysis terms of Kt/V_{urea} and the relative risk of death in HD patients.
2. Comparisons between prescribed and delivered doses of dialysis show that there is a significant portion of "no delivery" in routine haemodialysis.
3. Procedures to monitor the delivered dose of dialysis on a routine basis are most desirable.
4. Online urea monitoring is perfect (because it delivers all data required for a full scale UKM procedure) but it is associated with prohibitive costs.
5. Alternatively, effective in vivo dialyser urea clearance can be measured by means of pre / post dialyser conductivity at nearly zero costs.
6. Such an automated procedure currently is the best tool for dose assessment in routine HD.