

Quick Reference

Nx STAGE

Achieving more intensive
critical care therapy
for your patients.

SMART • SIMPLE • SECOND NATURE

Frequency

- Daily ICU therapy (vs. every other day) reduces mortality by 41%
Schiffel et al, N Engl J Med 2002.

Delivery

- CRRT improves hemodynamic stability and volume control versus conventional therapies
- Extended daily therapies (8–12 hrs) may offer comparable stability with simplified staffing, anticoagulation, and patient logistics
Kumar, et al, Am J Kidney Dis 2000.

Dose

- High dose CVVH (35 ml/kg/hr or above, or ~60 liters daily for an average patient) reduces mortality by 28% vs. standard dose CVVH
Ronco, et al, Lancet 2000.
- Even higher doses of convective therapy (45 ml/kg/hr or above) may benefit certain patient subgroups, particularly patients with sepsis
Ronco, et al, Lancet 2000; Honore, et al, Crit Care Med 2000.

Timing

- Earlier therapy initiation may improve survival
Gettings, et al, Intensive Care Med 1999; Ronco, et al, Lancet 2000.

Actual vs. intended delivery:

- Actual therapy time and dose can fall short of that prescribed by over 33%.

Venkataraman, et al, J Crit Care 2002.

Nursing shortage:

- Lower staffing ratios increase patient mortality, and increasing workload of existing nurses compounds the situation (increasing turnover, burnout, etc.)

Needleman, et al, N Engl J Med 2002; Aiken, et al, JAMA 2002.

Equipment:

- Limitations in flow rates with some current equipment may preclude delivery of the intensive therapies described in clinical literature

Product literature review.

Fluid volumes:

- Higher requirements increase handling time and complexity

Limitations of traditional scale-based systems.

Filter Function

- Higher blood flows may lead to improved filter function and fewer treatment interruptions due to clotting
Holt, et al, Anaesth Intensive Care 1996.

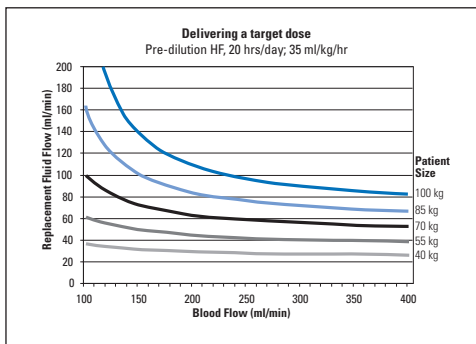
Therapy Delivery

- Higher blood flows can lead to higher effluent saturation:*

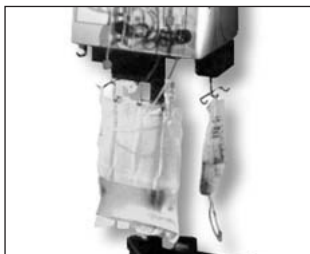
 - Higher clearance per liter of fluid (more dose), or
 - Same dose with less fluid (less \$\$), or
 - Same clearance in less time (schedule flexibility)

The NxStage Cartridge and Cycler are uniquely designed to deliver a full range of flows to address your ICU patient needs.

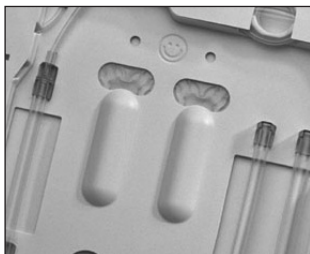
*See questions 7 and 8 for additional detail.



Source: Clark, et al, Artificial Organs, 2003 (in press).

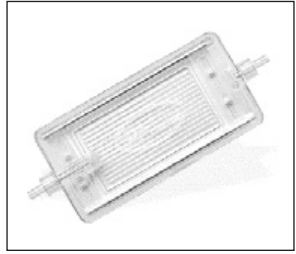


vs.



Fluid handling tasks are daunting in high intensity therapies with scale-based systems. NxStage System One makes this practical with the only volumetric balancing system in its class.

- Volumetric balancing eliminates scales, and thus
 - No waste bags and waste bag changes
 - No splash and injury risk from waste bag changes
 - No limit on the number of clean bags to be hung
 - No scale nuisance alarms
 - No scale calibration or waste bag nuisance alarms
- By simplifying fluid management, allows nurse more time to spend with patient



- **Protection from inadvertent exposure to fluid contamination, particularly given high fluid volumes**
The NxStage System One is compatible with optional IV filters, to reduce exposure risk to inadvertent air, particulate, bacteria, and endotoxin contamination in replacement fluid
- **“Foolproof” engagement of safety systems**
All NxStage System One safety systems are automatically engaged with “drop-in” cartridge loading
- **Reliable volume control**
Regular fluid balancing self-checks throughout NxStage treatment ensure accuracy without need for manual calibration



Cyclor

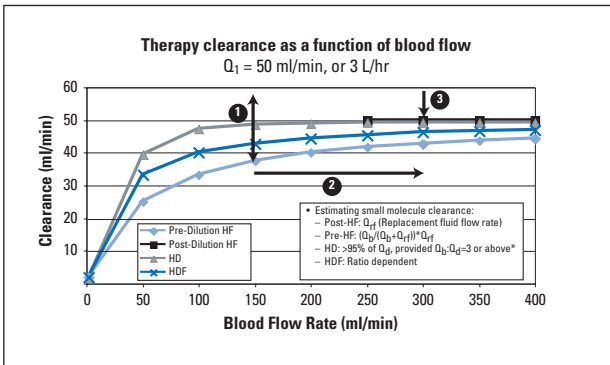
- Drop-in loading and automated prime
- Touch screen interface (OneView) to simplify training, troubleshooting, and charting
- Wide operating ranges to maximize flexibility
- Freedom from water processing and compact design for crowded ICU environment

Cartridge

- “No intervention” prime with NxStage Cartridge Express
- No drip chambers or blood air/interface to address circuit clotting risk
- Low resistance tubing set and high performance blood pump header to optimize blood flow out of a given blood access
- Balancing system integrated into cartridge to eliminate calibration and maintenance needs



- Small molecule clearance can be improved by increasing blood flow (Q_b) and/or fluid flow (dialysate – Q_d ; replacement fluid – Q_{rf}) rates
- Blood flow implications on therapy efficiency are generally less obvious than those of RF or dialysate flows



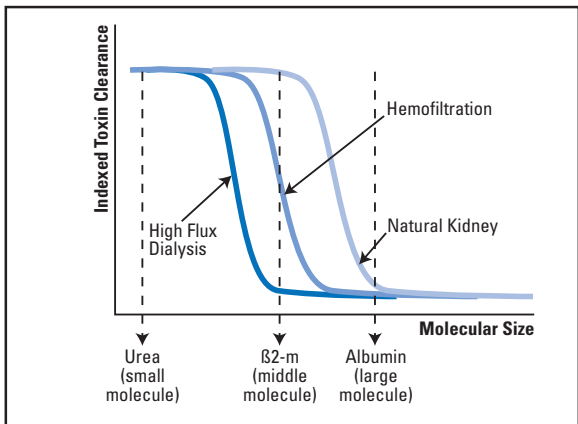
Note: Standard kinetic modeling. Assumes HDF uses pre-dilution mode and mix is 50% HD/50% HF.

*Simplification with $K_0A = 440 \text{ ml/min}$. Diffusive clearance is driven by a complex relationship between BFR, dialysate flow, and dialyzer properties.

1. Therapy efficiencies differ with post-HF > HD > HDF > pre-HF.
2. Efficiency grows and differences between therapies decrease as blood flow increases
3. Clearance levels of post-dilution HF are not achievable until a certain blood flow is reached due to hemoconcentration considerations

IMPLICATION: Opportunities to most efficiently deliver a choice of therapies increase when higher patient blood flows are achieved: higher clearance per liter of fluid or same clearance with less fluid or same clearance in less time.

- Convection more efficiently removes a broader range of solutes than diffusion, particularly in the middle molecular range



McCarthy, et al, Seminars in Dialysis 2003.

- HF > HDF > HD
Burnet, et al, JASN 2001.
- Despite lower small molecule (urea) clearance efficiency, pre-dilution HF can have higher large molecule removal than post-dilution (due to reduced hemoconcentration and polarization effects)
Li, et al, JASN 2001.
- Many suspected ARF toxins lie in the middle molecular range, e.g., pro-inflammatory mediators, β 2-microglobulin, and myoglobin
Trojanov, et al, Nephrol Dial Transplant 2003; Winchester, et al, Blood Purif 2003.
- Ronco and Honore studies were conducted in convective mode (post-dilution hemofiltration)
- The naturally functioning kidney is based on convection

Dosing guidelines:

- No definitive dosing guidelines for Acute Renal Failure exist
“For stable patients with ESRD, a dose response relationship has been shown for delivering clearance versus outcome. Recent evidence supports a similar relationship for patients with ARF. However, a dose range has not been established.”

“No recommendations can be made for specific dialysis dosing for patients with specific diseases at this time.”

ADQI Summary Statements.

Illustrative benchmarks (expressed as daily clearance volume for an average patient)

- Ronco (CRRT)
 - High dose (35 ml/kg/hr) 55–60 L/day
 - Higher dose (45 ml/kg/hr) 75–80 L/day
 - Venkataraman (conventional CRRT) 25–30 L/day
 - Marshall (SLEDD/extended daily) 40–50 L/day
 - Schiff (Daily Intermittent) 30–35 L/day
 - Conventional intermittent therapy 30–35 L every other day
- All normalized using EKR from original publications and Liao, et al (In Press); Artificial Organs.

To increase solute (e.g., BUN) reduction

- Primary approach: Increase replacement fluid or dialysate flow rates, as appropriate
- Secondary approach: Increase blood flow to enable higher clearances, increase therapy efficiency

Practicality of higher blood flows

- Previous ICU studies of intermittent dialysis showed average blood flows of 200–290 ml/min (average of approximately 250 ml/min)
Teehan, et al, J Intensive Care Med 2003.
- Extracorporeal volume is independent of blood flow

Therapy Options

Isolated Ultrafiltration (without fluid)

Hemofiltration (with IV fluid) – post-dilution or pre-dilution

Hemodialysis (with dialysate)

Weight and Dimensions

H x W x D (cm) 39 x 37 x 46

Weight ~ 30 kg (35 kg with warmer)

Flow Rates

Blood 50–600 ml/min

Prescription fluid Up to 12 l/hr

Fluid removal Up to 2.4 l/hr

Processors

Dual system for safety and control.

Power Requirements (Cycler)

Voltage 100–240 VAC

Power 200 W

Frequency 50/60 Hz

Warmer Capability

At 200 ml/min fluid flow, warms 22°C (room temperature) fluid to 37°C and removes air.

Safety and Control Systems

Arterial Pressure Fixed: -50 to -500 mmHg; user programmable

Venous pressure Fixed: 20, 400 mmHg; locking low-adjustable limit

Effluent pressure Fixed: 20, 1500 mmHg; locking low-adjustable limit

Air Detection Ultrasonic – venous (with redundancy), arterial, and prescription fluid

Temperature Thermistor alarms at 39°C

Blood Leak Optical sensor

TMP Maximum 500 mmHg

Other

Safety Standards IEC 60601-1; EN 60601-1; UL-2601-1; CSA 601.1-M90

EMC Standards IEC 60601-1-2:2001

Drip Proof IPX1

Cartridge and Filter (with optional NxStage Cartridge Express)

High flux polyethersulfone filter; Gamma sterilized

Blood Volume

Tubing Set ~100 ml

Total 205–225 ml with preattached hemofilter

Membrane Area 1.5 m²

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Who can tell me more?

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