A Flow Measurement Guide
for Industry Bioengineers

DIALYSIS / RENAL REPLACEMENT

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Transonic Applications

Transonic began partnering with outside companies shortly after its inception in 1983 to develop innovative devices. Soon, a robust Transonic/Customer synergy developed between Transonic and device manufacturers and this vital Customer/Manufacturer relationship has become part of Transonic's DNA. It lies at the heart of the development of all Transonic products.

Our applications range from utilizing standard products straight off the shelf to creating such novel designs that they would not be recognized as a Transonic product. Together with our collaborators, Transonic has striven to push the limit on flow measurements including ultra-low flow applications in novel measurement mediums. Transonic customized Flowsensors and Flowboards are being used in a wide range of products and applications including:

Mechanical Circulatory Support Devices including:

1. Heart Lung Machines
2. Extracorporeal Membrane Oxygenation (ECMO) circuits
3. Artificial Hearts (AH)
4. Ventricular Assist Devices (VADs)

Renal Replacement Devices: Hemodialysis Machines

Organ Preservation Devices

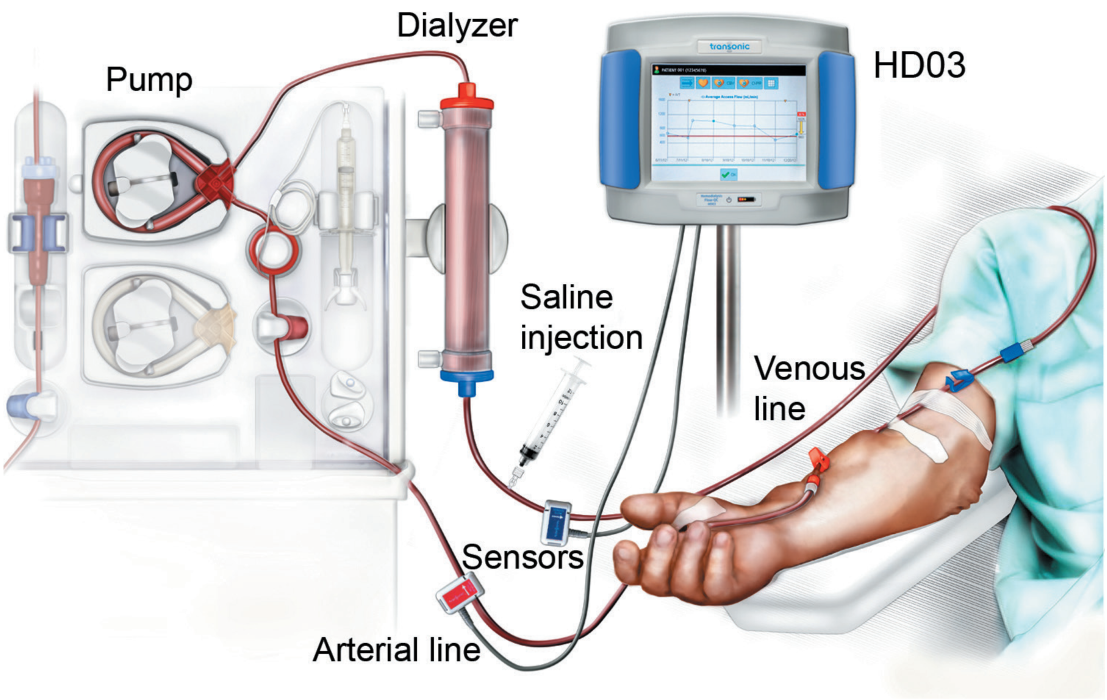
Treatment Delivery /Therapy Devices

1. Anesthesia Delivery / Pain Management Systems including:
2. Organ Infusion Pumps
3. Urodynamic System / Urometer
4. Pediatric Hydrocephalus
5. Endometrial Ablation
6. Ocular Surgery

Many More Possibilities

A sampling of the broad spectrum of Transonic application will be presented along with the solutions that Transonic offers for each application.

Renal Replacement



Schematic of Transonic HD03 Hemodialysis System with its touch screen computer/monitor and Flow/dilution Flowsensors clipped onto the arterial and venous tubing lines.

Delivered Blood Flow (DBF)

Renown nephrologist Dr. Thomas Depner studied the wear and cavitation of tubing at different pressure pump settings and recognized that actual pump flow can differ from a pump's setting during hemodialysis. He identified the need for a way to independently measure delivered blood flow to verify the flow set by the pump during prolonged blood pump procedures such as dialysis and ECMO. Not only did his observation spur development of the Transonic Hemodialysis Monitor that measures delivered pump flow directly with transit-time ultrasound Flowsensors applied to the outside of dialysis lines, but also to the incorporation of Transonic Flowboards and Flowsensors into dialysis machines.

DBF Confirms Dose Delivery

Sufficient flow needs to be delivered to the hemodialysis patient for dialysis to occur and for the patency of the vascular access to be maintained. However, actual delivered blood flow (the blood flow in the dialysis lines) to the hemodialysis patient can differ from the flow that the hemodialysis machine (pump) is set at for a variety of reasons.

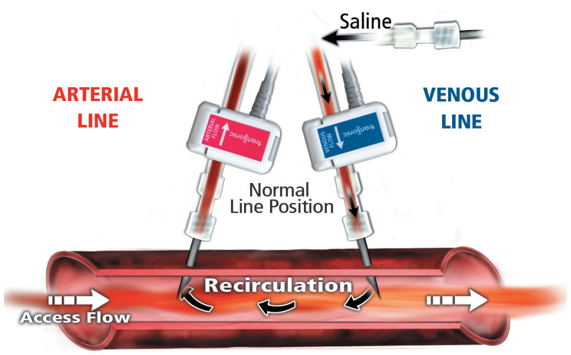
Delivered blood flow also can be measured in catheter patients.

Renal Replacement cont.

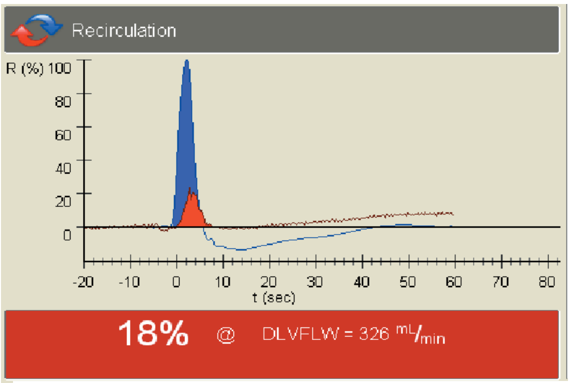
Access Recirculation

Transonic can also measure access recirculation in fistulas, grafts and catheters. To measure vascular access recirculation, Flow/dilution Sensors monitor the blood's ultrasound velocity (1560 - 1590 m/sec). The greater the protein concentration in the blood, the faster ultrasound will travel. When a bolus of isotonic saline (velocity in blood is 1533 m/sec) is injected into the blood, the blood protein concentration is diluted. Flow/dilution Sensors detect the reduced ultrasound velocity.[10]

When recirculation occurs, the saline indicator returns immediately to the arterial line (Fig. 3.3) where the diluted blood is detected by the arterial sensor. The Monitor's software converts the data into conventional dilution curves (Fig. 3.4). The first blue curve indicates the saline dilution as blood flows through the venous sensor. The second red curve represents saline dilution as flow passes through the arterial sensor. Recirculation is calculated as a ratio of the area under the arterial curve to the area under the venous curve.



Recirculation Measurement. Saline is introduced into the venous sensor with the dialysis lines in normal position. Access recirculation (back flow) through the vascular access into the arterial needle is measured.



A blue venous (upper) dilution curve followed by a red (lower)arterial curve. The ratio of the areas under the curves indicates 18% recirculation.

Access Recirculation (R%)

Recirculation (Fig 2) is assessed by injecting 10 ml of 0.9% NaCl solution (V_V) into the venous port that generates the area (S_{ven}) in the venous sensor (Fig 3):

$$V_v = S_{ven} \times Q_b \quad (1)$$

The immediate appearance of a dilution curve (Fig 3) with area (S_r) identifies recirculation. The amount of recirculated indicator (V_r) is proportional to the area under the concentration curves (S_r) from the arterial dilution sensor times dialyzer flow:

$$V_r = S_r \times Q^*_b \quad (2)$$

Recirculation is the ratio of the volume of recirculated indicator to the volume of injected indicator:

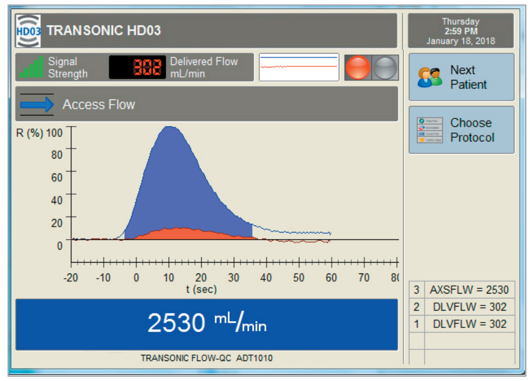
$$R\% = \frac{V_r}{V_v} \times 100\% = \frac{S_r}{S_{ven}} \times 100\% \quad (3)$$

Renal Replacement cont.

Vascular Access Flow

Vascular Access flow measurements are performed in arteriovenous grafts and fistulas created by reversing the hemodialysis blood lines at their needle connections. The dialyzer removes blood from the venous side of the access and returns the blood to the arterial side to create the mixing conditions needed for an indicator dilution measurement of access flow. When saline is introduced into the venous line, it dilutes the blood's protein concentration and reduces ultrasound velocity. This blood protein concentration change is detected first by the sensor clipped onto the venous blood line. The Monitor's software generates a venous dilution curve. The diluted blood from the venous line then enters the access and mixes with the incoming access flow. Upon reaching the arterial needle, a portion of mixed blood is removed from the access by the dialyzer. This diluted blood is then detected by the arterial sensor and the Monitor's software generates an arterial dilution curve. Access flow is calculated from the ratio of the area under the venous curve to the area under the arterial curve.

Hemodynamics of access flow measurement with lines reversed by Krivitski Method. Line reversal creates an artificial recirculation loop with a mixing site at the arterial side of the access.



Result showing flow/dilution curves and AF measurement of 680 ml/min flow.

Access Flow (Q_a)

With the Krivitski Method™, access flow is measured by reversing the dialyzer lines (Fig 5): the arterial inlet removing the blood is now downstream from the venous outlet, the outlet needle faces the access stream for complete mixing. In this case, the flow between the needles (Q_{mix}) is the sum of access flow (Q_a) and dialyzer blood flow (Q_b) .

$$Q_{mix} = Q_a + Q_b \qquad (4)$$

Ten milliliters (10 ml) of isotonic saline (V_v) is injected into the venous line. The area under the dilution curve (S_{art}) recorded by the arterial sensor (Fig 4) is determined by the flow at the site of mixing.

$$Q_{mix} = \frac{V_v}{S_{art}} \qquad (5)$$

Access flow follows from Eq. 4 and Eq. 5:

$$Q_a = Q_{mix} - Q_b = \frac{V_v}{S_{art}} - Q_b \qquad (6)$$

Finally, using Eq. 1 and Eq. 6:

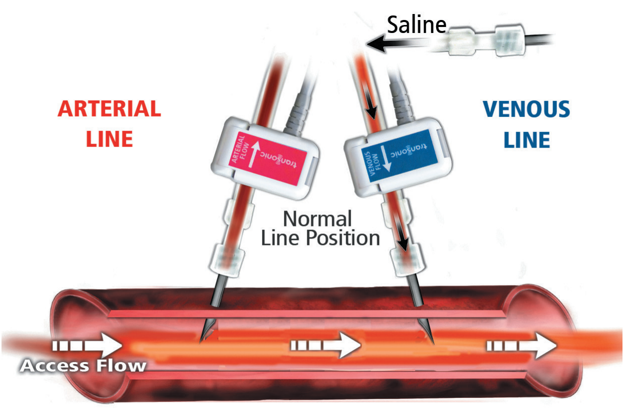
$$Q_a = Q_b \times \left(\frac{S_{ven}}{S_{art}} - 1\right) \qquad (7)$$

Renal Replacement cont.

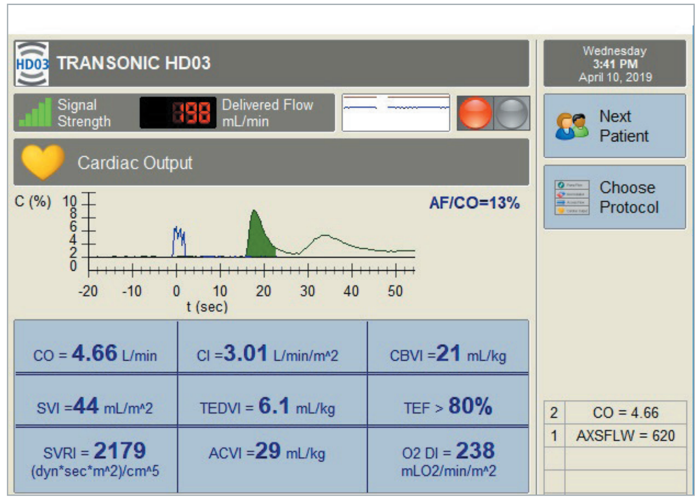
Cardiac Output (CO)

With the lines connected normally, 30 ml of 0.9% NaCl (V_V) is injected into the venous line. After the indicator traverses the heart and lung, the dilution curve is recorded in the arterial line. Cardiac output is calculated from the area (S_{CO}) of the dilution curve by the classic equation:

$$CO = V_v / S_{co}$$



Cardiac Output Measurement. Saline is introduced into the venous line with dialysis lines in normal position. The arterial sensor measures the saline concentration of blood from which Cardiac Output is calculated.



Flow-QC screen reports Cardiac Output, (CO); Cardiac Index (CI); Central Blood Volume Index (CBVI); Stroke Volume Index (SVI); Total End Diastolic Volume Index (TEDVI); Total Ejection Fraction (TEF); Systemic Vascular Resistance Index (SVRI); Active Circulation Volume Index (ACVI); Oxygen Delivery Index (O_2DI). Software also displays Height, Weight, Heart Rate, Blood Pressure, Peripheral Resistance, Central Blood Volume Index, Systemic Cardiac Index and Stroke Volume.

Renal Replacement References

Theory & Validations

Krivitski NM, "Theory and Validation of Access Flow Measurement by Dilution Technique during Hemodialysis," Kid Int'l, 1995; 48(1): 244-250. (Transonic Reference # HD1T)

Depner TA, Krivitski NM, MacGibbon D, "Hemodialysis Access Recirculation (Rc) Measured by Ultrasound Dilution," ASAIO J 1995; 41(3): M749-M753. (Transonic Reference # HD6V)

Krivitski NM, Depner, TA, "Cardiac Output and Central Blood Volume during, Hemodialysis: Methodology," Adv Ren Replace Ther 1999; 6(3): 225-232. (Transonic Reference # HD8T)

Gold Standard

Garland JS *et al,* "Are Hemodialysis Access Flow Measurements by Ultrasound Dilution the Standard of Care for Access Surveillance?" Advances in Renal Replacement Therapy 2002; 9(2): 91-98. (Transonic Reference # HD263A) *Ultrasound indicator dilution is the current Gold Standard for measurement of vascular access recirculation and access flow. Ultrasound indicator dilution is the method of choice for monthly surveillance of vascular access grafts in adherence to NKF-K/DOQI guidelines*

McCarley PB *et al,* "Vascular Access Blood Flow Monitoring Reduces Access Morbidity and Costs," Kidney Int 2001; 60: 1164-7. (Transonic Reference # HD11190) *"Vascular access blood flow monitoring along with preventative interventions should be the standard of care in chronic hemodialysis patients."*

Vascular Access Flow

Aragoncillo I *et al,* "Adding access blood flow surveillance reduces thrombosis and improves arteriovenous fistula patency: a randomized controlled trial," J Vasc Access. 2017 Apr 20:0. (Transonic Reference # HD11190) *"QA-based surveillance combining Doppler ultrasound and ultrasound dilution reduces the frequency of thrombosis, is cost effective, and improves thrombosis free and secondary patency in autologous AV."*

Dialysis Adequacy

Delivered Blood Flow

MKimata N *et al,* "Study of discrepancies between recorded and actual blood flow in hemodialysis patients," ASAIO J. 2013 ;59(6): 617-21(Transonic Reference # HD9860A) *"HD efficiency must be carefully monitored, especially in patients with high blood flow."*

Recirculation

MacDonald JT *et al,* "Identifying a New Reality: Zero Vascular Access Recirculation Using Ultrasound Dilution," ANNA J 1996; 23(6): 603-8. (Transonic Reference # HD4T) *Zero recirculation is a reality, thanks to ultrasound dilution's ability to separate CPR from access recirculation.*

Cardiac Output

Haag S, Artunc F *et al,* "Systemic haemodynamics in haemodialysis: intradialytic changes and prognostic significance," Nephrol Dial Transplant. 2018 Mar 26. (Transonic Reference # HD112305A) *Hemodynamic monitoring identifies a significant number of HD patients with cardiac impairment who are at risk for increased mortality*

MacRae JM *et al*, "The Cardiovascular Effects of Arteriovenous Fistulas in Chronic Kidney Disease: A Cause for Concern?" Seminar in Dialysis 2006; 19: 349-352. (Transonic Reference # HD7337A) *A thorough cardiac assessment should be performed in patients with CAD prior to placing an AVF. Regular careful evaluations are necessary in patients with cardiac disease and AVFs. Patients with high flow fistulas (flow greater than 2L/min) and increasing LVEDV are recommended to have a flow reduction procedure on their AVF.*

Pediatric

Ashoor IF *et al,* "Arteriovenous Access Monitoring with Ultrasound Dilution in a Pediatric Hemodialysis Unit," Blood Purif 2015; 39(1-3): 93-8. (Transonic Reference # HD10296) *"UD screening is very sensitive in detecting hemodynamically significant stenosis and can decrease AV access thrombosis rates."*

Goldstein SL, Allsteadt A, "Ultrasound Dilution Evaluation of Pediatric Hemodialysis Vascular Access," Kidney Int 2001; 59: 2357-2360. (Transonic Reference # HD11190) *Ultrasound indicator dilution (UD) is a valid indicator of access flow in children. "When the uncorrected flow value reported by UD is corrected for patient body surface area, UD is predictive for the presence or absence of severe AV graft stenosis, regardless of patient size."*

Comparison of Methodologies

Lopot F *et al,* "Comparison of Different Techniques of Hemodialysis Vascular Access Flow Evaluation," Int J Artif Org 2003; 12:1055-1063. *"Ultrasound dilution (Krivitski Method): Very high reproducibility and the negligible impact of changes in blood flow on the accuracy of vascular access flow measurement justifies its current status as the reference method for vascular access flow evaluation. "*