

## Advances in Tunneled Central Venous Catheters for Dialysis: Design and Performance

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### ABSTRACT

Over 70% of patients initiating chronic hemodialysis in the United States have a tunneled central venous catheter (CVC) for dialysis as their first blood access device. Tunneled CVC have requirements that are unparalleled by other access devices: high blood flow rates at moderate pressure drops without obstruction, minimal trauma to the vein, resistance to occlusion by fibrous sheathing, prevention of infection, avoidance of clotting, biocompatibility, avoidance of lumen collapse and kinking and breaks, resistance to antiseptic agents, place-

ment with minimal trauma, and radiopaque appearance on X-ray. This publication reviews the numerous designs for tunneled CVC and evaluates the advantages and disadvantages of each design. A catheter that self-centers in the superior vena cava (Centros™) is described, along with early clinical results. Current challenges and future directions for tunneled CVC for dialysis are discussed, included means to diminish catheter-related infections, catheter tip clotting, fibrous sheathing, central venous stenosis, and external component bulk.

### Prevalence and Problems of Central Venous Catheters for Hemodialysis

Over 70% of patients initiating chronic hemodialysis in the United States have a tunneled central venous catheter (CVC) as their first blood access device (1). As shown by Centers for Medicare Services (CMS) and in Fig. 1, at 90 days of dialysis the catheter is still the access of choice, used in patients in whom the fistula or graft has not matured, was not workable, or was not indicated (2). Over the period from 2002 to 2005 the number of grafts being used at 90 days decreased and the number of fistulas increased, but the percentage of catheters being used remained about the same.

Many patients would be better served if an arteriovenous (AV) fistula had been placed some months earlier, and if it were fully developed and functional when dialysis was implemented. However much this is the desired course, it is not often the actual course. In all of the single-minded enthusiasm of the Fistula First program, we sometimes forget that tunneled CVC are used in patients starting dialysis because they offer advantages. As summarized by Beathard (3,4) tunneled CVC for

dialysis have advantages (noted in Table 1) as well as some significant disadvantages:

The requirements for a tunneled CVC for dialysis are actually multiple and stringent, unlike requirements for any other access device (5):

- High blood flow rates at moderate pressure drops, with few instances of outflow failure and pressure alarms regardless of patient fluid status and catheter position relative to the vein wall.
- Minimal trauma to the vein intima to avoid thrombosis and venous stenosis.
- Resistance to occlusion by fibrous sheathing.
- Prevention of bacterial migration around the catheter after placement.
- Avoidance of contamination of the catheter lumen.

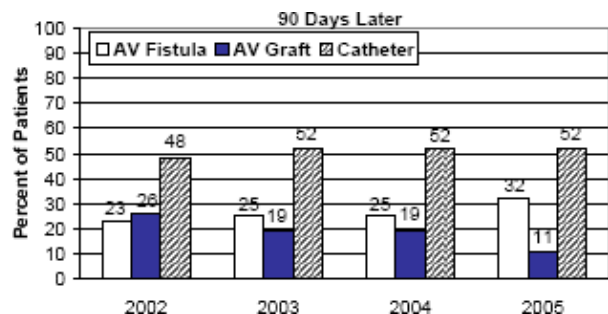


Fig. 1. Distribution of access types 90 days after initiation of chronic outpatient dialysis (CMS 2006 report [2]).

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**TABLE 1. Advantages and disadvantages of tunneled central venous catheters for dialysis**

| Advantages   | Disadvantages  |
|--|--|
| Universally applicable (functional in nearly 100% of patients) | High morbidity caused by thrombosis and infection          |
| Ability to insert into multiple sites                          | Risks of permanent central venous stenosis or occlusion    |
| Maturation time not required                                   | Discomfort and cosmetic disadvantage of external appliance |
| Venipuncture not required                                      | Lower blood flow rates, requiring longer dialysis times    |
| No hemodynamic consequences (no CP recirculation)              |  |
| Ease and low cost of placement and replacement                 |  |
| Ability to provide access over a period of months              |  |
| Ease of correcting thrombotic complications                    |  |

- Avoidance of seeding of the outside of the catheter during bacteremia.
- Avoidance of clotting at the tip or within the catheter.
- Biocompatibility of the catheter surfaces, avoiding removal of white cells or platelets.
- Avoidance of lumen collapse under negative pressure.
- Avoidance of kinking of catheter segments at points of bending.
- Physical strength and integrity to avoid breaks or disconnections of any component (ability to replace broken connectors is desirable).
- Resistance to antiseptic agents that might be applied at the skin exit site.
- Placement procedures with minimal trauma, difficulty and risk.
- Radiopaque appearance on X-ray, for evaluation of location during placement and after use.

Each tunneled CVC has a risk of failing one or more of these requirements, and each failure results in significant medical problems.

The use of dual lumen CVC for removing and returning blood during dialysis is commonplace now but in the late 1970s this concept revolutionized dialysis (6). Before the development of CVC for dialysis, dialysis was possible only with an arterial access, through an internal/external AV silicone shunt or through separate catheters placed into an artery and a vein and removed after each treatment.

The development of CVC for dialysis was not simple, especially for single-body catheters. Drawing blood from a central vein at 200–400 ml/min is a delicate and somewhat unpredictable process. The pressure in central veins is much lower than in arteries and vein walls are thinner and more distensible, even though the flow of blood through central veins is the same as through central arteries. Removal of blood through the ports of a CVC in a vein creates a negative pressure around these ports because of direct suction and because of the Ber-

noulli effect. This negative pressure can cause the vein wall to collapse around the ports and obstruct flow into the ports, even if the flow through the vein is much higher than the flow of blood through the catheter. If a fibrous tissue sheath forms around the catheter and reaches the tip or if clots form around the tip, the entry port to the catheter becomes smaller and the velocity of blood flow is increased. The increased blood velocity creates a greater negative pressure around the ports, and increases the tendency to pull the vein wall over the tip.

There are four classic approaches to the problem of providing sufficient blood outflow through dual-lumen CVC for dialysis:

- Place the removal and return lumens within the right atrium, where the tips cannot rest against a venous wall and only one lumen usually rests against the atrial wall.
- Position the catheter with the removal lumen on the inside of the catheter curve, directing this lumen away from the vein wall and toward the bloodstream.
- Use a large catheter so that the removal lumen cannot be blocked by a small clot or a small amount of fibrous tissue.
- Provide multiple blood entry ports in all directions around the circumference of each catheter tip so that some of the ports are always facing away from the vein wall.

There are problems of and limitations on each of these approaches. Positioning the tips of the removal and return lumens at the middle of the atrium is somewhat difficult, especially as the relative positions of the catheter and the heart change when the patient stands up after lying on the procedure table, and as the removal lumen is shorter than the return lumen. Positioning the catheter so that the removal lumen is on the inside of the catheter curve is not always easy as the catheter course through the subcutaneous tissue and central veins is rather complex and tortuous. Placing a larger catheter is always more difficult and somewhat more traumatic than placing a smaller catheter, especially if the larger catheter is not round in shape. Providing multiple side holes in all directions around the catheter tips requires that two catheters be placed, or that one catheter must separate into two separate tips. Side holes in a catheter also have disadvantages. If they are too large or too many, blood will quickly flow through the tip of the catheter after placement and between uses, removing catheter lock solutions and promoting clotting at the tip. If the side holes are too small or too few then blood will flow in and out only through the tip of the catheter, thus diminishing any advantage of the side holes. Further, any single-body catheter that becomes covered by a sheath will lose function, whether there are side holes or not. Sheathing of catheters occurs only where the catheter contacts a vein or atrial wall (7). When sheathing develops it is difficult to correct by tissue plasminogen activator infusion, stripping or catheter replacement (8).

A newer solution to the problem of obtaining unrestricted blood removal through the catheter is to design the distal part of the catheter so that it rests against the wall of the superior vena cava (SVC) and supports the

removal lumen in the center of the vena cava. This approach, used in the Centros™ catheter (Angio-dynamics, Inc., Queensbury, NY), is described below.

### Types of CVC for Dialysis and a Short History

Central venous catheter for dialysis are classified into either “acute” or “chronic” catheters, depending on whether the catheters are expected to be used for only several days or months to years. Acute CVC are designed to be placed with a minimum amount of effort. Historically, acute catheters for dialysis were relatively rigid, pointed catheters with a conically shaped tip that could be advanced into the vein directly over a guidewire. The catheter body dilates the entry site as it is advanced into the vein. Acute CVC for dialysis have no subcutaneous cuff or locking device and a short linear tunnel. More recently some acute catheters have become available with soft tips similar to that of chronic tunneled catheters. The tract around the guidewire is dilated and the catheter is stiffened using a stylet, then advanced over a guidewire in a manner similar to over-the-wire placement of a tunneled catheter (described below).

Tunneled CVC for dialysis are soft, blunt-tipped catheters with a subcutaneous Dacron® “cuff” (INVISTA S.à r.l., Wichita, Kansas) for tissue in-growth or a plastic “grommet” to immobilize the catheters below the skin surface. Tunneled CVC are generally

placed through internal jugular veins into the SVC with the goal of placing the tips of the catheter at the junction of the SVC and the right atrium. Alternative venous access points are external jugular veins, subclavian veins, and femoral veins. Due to their blunt shape tunneled CVC have traditionally been placed through a “split sheath,” which is a cylindrical thin-walled plastic device advanced into the vein over a dilator. The dilator has a central lumen that follows the guidewire. The guidewire and dilator are then removed and the split sheath opening is closed with a finger or valve to prevent excessive bleeding. The catheter is then inserted through the split sheath into the central vein. The split sheath is split along two preformed grooves, and the halves are retracted around the catheter, leaving the catheter in position within the central vein. More recently, techniques have been developed to allow placement of tunneled CVC to be performed over a guidewire placed through a previously dilated tract, in a manner similar to acute CVC for dialysis. A plastic catheter or stylet within the catheter stiffens the catheter to allow it to follow the guidewire more easily.

Tunneled CVC for dialysis have a curved subcutaneous tunnel leading from the vein insertion site to a distant exit site. The cuff or plastic grommet fixes the catheter in position and prevents bacteria at the exit site from migrating around the catheter. The cuff also serves as the outer limit for a fibrous tunnel that leads to the entrance point of the central vein. This tunnel is similar

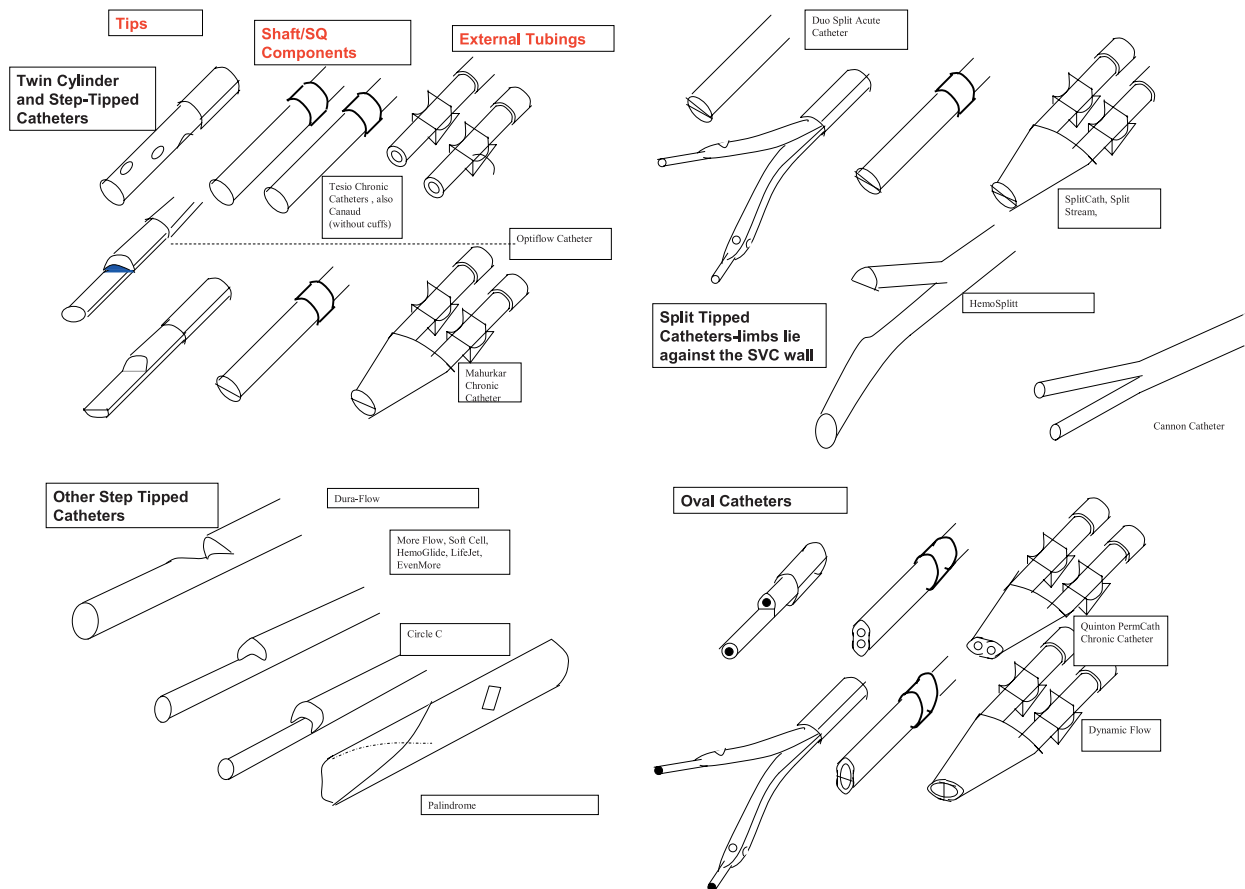


FIG. 2. Various designs of tunneled central venous catheters for dialysis.

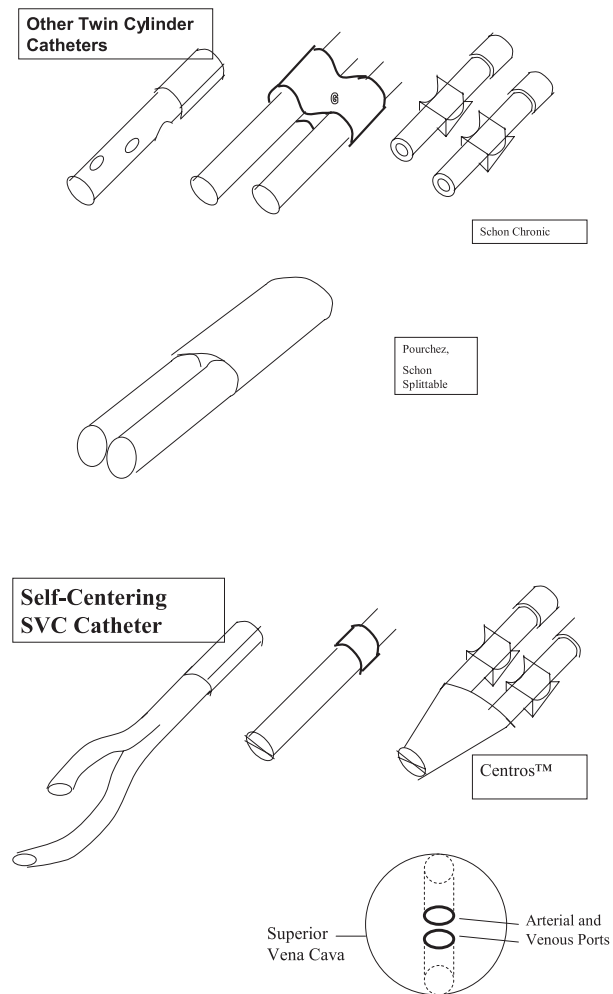


FIG. 2. (Continued)

to a vein wall and is contiguous with the internal jugular vein (or other vein of insertion), creating a passageway for blood or air when the catheter is removed. The tunnel stops at the Dacron cuff where it melds into the fibrous tissue surrounding the cuff. Without the cuff, as in acute catheters, this tunnel continues all of the way to the skin exit site over time, creating potential for back-and-forth movement of the catheter and potential pericatheter bacterial migration around the catheter.

A pictorial history of tunneled dialysis catheters is included in Fig. 2, and this history is discussed more fully in a recent review (5). Canaud et al. devised a catheter system composed of two 10 French catheters, each placed into the vena cava and with tips leading to the right atrium. Flow rate was excellent over many months of use (9,10). Tesio added subcutaneous cuffs and the catheter became more popular. More recent versions of the Canaud catheters have included a subcutaneous plastic grommet to fix the catheter limbs in place; the Schon catheter has a similar device. Quinton designed the PermCath dual lumen chronic catheter, an oval-shaped chronic catheter of about 20 French circumference and including two cylindrical 8 French lumens (11,12). Mahurkar designed a chronic CVC of soft materials and blunt tips and double-d blood flow lumens (13). The Ash Split Cath chronic catheter has a double-d

configuration in the mid-body, but separates into two separate distal tips, each with side holes in all directions. The Palindrome catheter is a double-d catheter with both lumens having the same length, but with oppositely angled and symmetrical side ports (14). The Centros™ catheter has outward bends of the tips that contact the inferior vena cava in two places and inward bends to place the arterial and venous ports in the middle of the vena cava. No side holes are needed as the ports do not rest on the venous wall (15).

### Advantages and Disadvantages of Various Tunneled CVC Designs

#### Hydraulic Performance of Tunneled CVC Versus Grafts and Fistulas with Needles

In spite of the wide variety of designs of tunneled CVC for dialysis there are few comparative studies to define advantages of one design over another. The best way to characterize the effectiveness of flow in a dialysis access is to determine the “conductance” of the access, which is the flow rate divided by the pressure drop on the arterial (blood removal) limb (4,5). Merely describing the achieved blood flow rate was during an entire dialysis is not very descriptive, as the blood flow rate depends upon many factors such as number of pressure alarms, volume status of the patient, physician’s prescription, pressure gradients, etc. There have been few comparative studies showing how the hydraulic conductance of catheters compares to needles, though one by Twardowski in 1999 was helpful. In this publication he showed that although there is considerable scatter, the hydraulic conductance of most catheters is similar to a 16 gauge needle in a graft or fistula during dialysis.

#### Split-Tip Catheters Versus Single-Body Step-Tips

The basic concept of the Split Cath is to provide side holes around each limb of the catheter, similar to a Canaud or Tesio catheter. This assures that even if each limb lies against the surface of the vena cava or atrium that some side holes will be facing the lumen, and away from the wall. In vitro studies demonstrate the hydraulic advantage of this design, using models as shown in Fig. 3. Mareels et al. performed studies using computational flow dynamics and particle imaging and demonstrated that the Split Cath design had a considerably lower shear rate than any other catheter design, with only 32% of the tip portion having a shear stress over 10 Pa as shown in Fig. 4. However, the downside of the Split Cath design was that it also creates areas of stagnation in the tip, with blood residence time at this location over 0.03 seconds (16).

Clinically which is better, catheters with a split tip or a single body? Several studies have shown a slight advantage of the Split Cath over step-tip catheters. Trerotola et al. performed a randomized study of 12 end-stage renal disease (ESRD) patients receiving 14 F Split Cath catheters placed versus 12 patients receiving 13.5 F Hickman catheters (17). Weekly for 6 weeks the blood

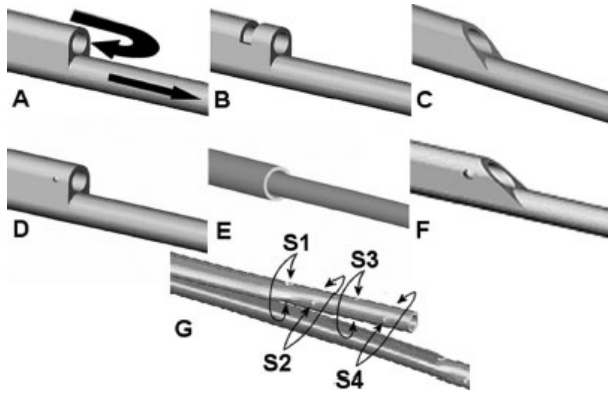


FIG. 3. Types of catheters evaluated in CFD and PIV studies (16). (A) Cut straight; (B) cut straight with slot; (C) cut angle; (D) cut straight with hole; (E) concentric; (F) cut angle with hole; (G) Ash split.

flow rate was measured using Transonic flow monitors, while the blood pump was set at speeds of 200, 300, 350, 400 ml/minute and as high as possible with sustained flow. The measured blood flow rate at the highest pump setting was  $422 \pm 12$  ml/minute for the Split Cath and  $359 \pm 13$  for the Hickman ( $p < 0.005$ ) as shown in Fig. 5. Recirculation was significantly less at all pump settings for the Split Cath patients ( $p = 0.01-0.06$ ), though for both catheters it remained below 6% as shown in Fig. 6.

Long-term functional survival of CVC is probably the most significant measure of the success of their use. One problem with such studies is a lack of firm definitions for patency failure or catheter-related bloodstream infection (CRBSI), to serve as endpoints. Many catheters are

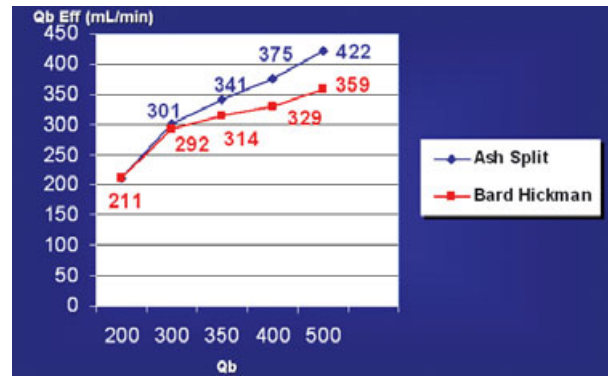


FIG. 5. Relationship between roller pump setting of dialysis machine and actual flow rate by Transonic™ device, for Split Catheter and Bard Hickman (17).

removed in these studies for presumed failure to flow or sepsis. In the Trerotola study above, the Split Cath had slightly better 6 week survival than the Hickman catheter. Richard et al. performed a randomized study comparing the Split Cath, Opti-Flow, and Tesio catheters in 113 placements in ESRD patients (18). Maximum (effective) blood flow rates were compared between the catheters immediately after placement, and 30 and 90 days after placement. Blood flow rate tended to be higher with the Split Cath but results were not significantly different. Failure-free survival of the catheters was analyzed with an average follow-up of 120 days. Though statistically not significant, predicted lifespan appeared higher for the Split Cath and Tesio catheters than the Opti-Flow. Placement complications occurred only with Tesio and Opti-Flow catheters. These results are shown in Fig. 7.

Table 2. Parameters Calculated in the Tip Zone of the Arterial Lumen of Each Catheter

|                            | Cut Straight (Reference) | Cut Angle | Cut Straight Hole | Cut Angle Hole | Cut Straight Sleeve | Concentric | Ash Split-Based                       |
|----------------------------|--------------------------|-----------|-------------------|----------------|---------------------|------------|---------------------------------------|
| Flow division              |                          |           |                   |                |                     |            |                                       |
| End-opening                | 100%                     | 100%      | 48.8%             | 46.6%          | 18.0%               | 100%       | 6.6%                                  |
| Side entrance              | N/A                      | N/A       | 51.2%             | 53.4%          | 82.0%               | N/A        | S4: 4.2% S3: 8.6% S2: 15.6% S1: 65.0% |
| Avg. SS                    | 12.6 Pa                  | 16.3 Pa   | 14.2 Pa           | 14.6 Pa        | 12.8 Pa             | 44.8 Pa    | 11.6 Pa                               |
|                            |                          | +29%      | +13%              | +17%           | +2%                 | +255%      | -8%                                   |
| % Vol. SS > 10 Pa          | 41.8%                    | 54.7%     | 45.8%             | 47.9%          | 41.0%               | 87.9%      | 32.2%                                 |
|                            |                          | +31%      | +10%              | +15%           | -2%                 | +110%      | -23%                                  |
| % Vol. RT > 0.015 s        | 16.8%                    | 13.9%     | 9.8%              | 10.2%          | 19.7%               | 18.9%      | 60.8%                                 |
|                            |                          | -17%      | -42%              | -39%           | +17%                | +13%       | +262%                                 |
| % Vol. RT > 0.030 s        | 0.1%                     | 2.6%      | 0.1%              | 0.1%           | 2.7%                | 8.3%       | 31.2%                                 |
|                            |                          | x26       | x1                | x1             | x27                 | x83        | x314                                  |
| Avg. SS where RT ≤ 0.015 s | 10.7 Pa                  | 15.3 Pa   | 13.4 Pa           | 13.7 Pa        | 10.6 Pa             | 37.1 Pa    | 11.0 Pa                               |
|                            |                          | +43%      | +25%              | +28%           | -1%                 | +247%      | +3%                                   |
| Avg. SS where RT > 0.015 s | 21.3 Pa                  | 22.7 Pa   | 21.3 Pa           | 22.6 Pa        | 22.0 Pa             | 77.6 Pa    | 12.0 Pa                               |
|                            |                          | +6%       | 0%                | +6%            | +3%                 | +264%      | -44%                                  |
| Platelet Lysis Index       | 0.0071                   | 0.0448    | 0.0154            | 0.0249         | 0.0497              | 0.1260     | 0.0357                                |
|                            |                          | x6.3      | x2.2              | x3.5           | x7.0                | x17.7      | x5.0                                  |

SS, Shear stress; RT, blood residence time.

The following parameters were calculated in the tip zone of the arterial lumen of each catheter: (1) tip volume average SS, (2) percentage of tip volume with SS > 10 Pa, (3) percentage of tip volume with RT > 0.015 second, (4) percentage of tip volume with RT > 0.030 second, (5) average SS in zones with RT ≤ 0.015 second, (6) average SS in zones with RT > 0.015 second, and (7) Platelet Lysis Index. Percentages show relative difference compared with reference case.

FIG. 4. Measured shear rate and residence time for various parts of various catheter designs (16).

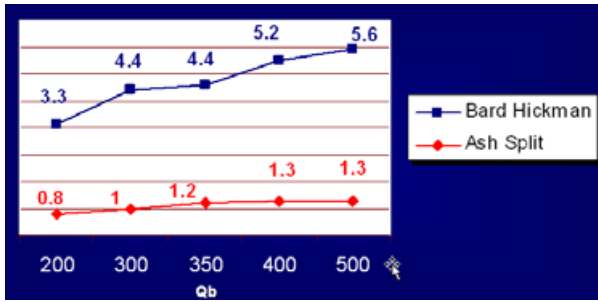


FIG. 6. Recirculation in forward flow measured by Transonic, for recently placed Split Caths versus Bard Hickman (17).

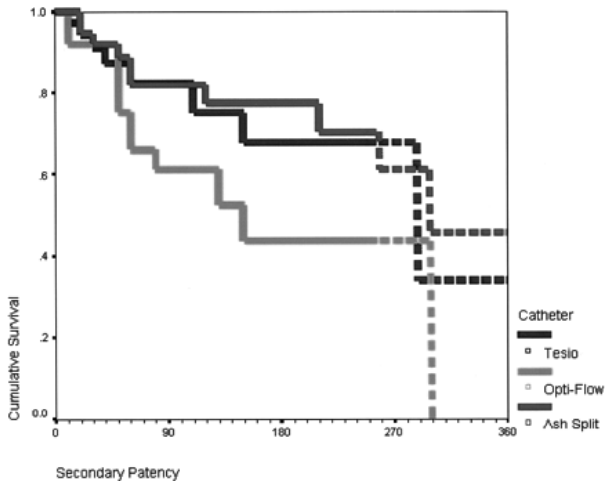


FIG. 7. Survival of catheters to primary failure, for Split Cath, Optiflow, and Tesio catheters (19).

Trerotola et al. also performed a randomized study comparing the Split Cath and Opti-Flow catheters in 132 placements in ESRD patients (19). Complications during placement were no different for the two catheters and ranged 15–17% (mostly, kinking). Opti-Flow delivered significantly higher flow rates when tested at 1 month, but there was no significant difference in flow at 6 months. Recirculation was always lower with the Split Cath catheter but not always significantly different. The Split Cath had significantly longer half-life, partly due to lower infection rate but also due to some mechanical failures of the Opti-Flow. Postulating on reasons that the Split Cath might have lower infection rates, the authors suggested that the “self-cleaning” function of the Split Cath, with high velocity flow through the side holes created by the “step down” tip, may diminish fibrin sheath and therefore decrease the opportunity for bacterial colonization. The results of seven non-randomized studies of the Split Cath confirming catheter survival rates of about 9 months on average are summarized in our review in *Seminars in Dialysis* (5). However, the overall longevity of Split Caths is not any better than that of Tesio catheters, which have been shown to have up to 2 years of assisted function (20).

## Side Holes Versus No Side Holes in Tunneled CVC

As discussed above regarding the Split Cath design, catheter side holes have advantages and disadvantages. They can decrease the overall resistance and provide lower shear rate and better flow in the short run, especially on the arterial side. However, they also can create relative dead space at the end of the tip promoting clotting. They allow flow of blood through the tip to wash out locking solution almost as soon as the catheter is filled with it (5,21,22). Side holes also allow clots to adhere to the catheter tip, a process facilitated by lumens with rough edges. Tesio/Canaud catheters have six side holes in a spiral shape. It is not uncommon for these catheters to clot completely within several hours after placement. Removing the clot with forceful irrigation, using the catheter for dialysis and then re-locking the catheter with heparin usually results in a catheter that functions for a long time. Presumably this is because the catheter becomes “biolized” or protein-coated and is therefore more resistant to clotting.

Side holes can also increase overall catheter resistance. To understand this, it is important to understand more about how blood flows within a catheter. A curious phenomenon is that the relationship between flow and pressure is not the same on both lumens of the catheter. As shown in Fig. 8, the higher the blood flow rate, the higher the hydraulic resistance on the arterial side. The relationship between flow and pressure is not a straight line as it is on the venous lumen (23). The best explanation for this phenomenon is given by Fricker et al., who demonstrated that at the arterial inlet port, blood enters the catheter as a “developing” flow pattern, not a parabolic or developed flow pattern, as shown in Fig. 9. This “plug” flow results in higher shear at the catheter inner surface. The higher the flow rate, the greater the distance it takes the blood to develop parabolic flow within the catheter lumen, and the greater the hydraulic resistance of the catheter (24). Also, the more complicated the tip shape, the greater the distortion of flow and the greater the distance of developing flow, as shown in Fig. 10. If the tip is blocked and all of the flow is through the side holes, then hydraulic resistance can increase markedly

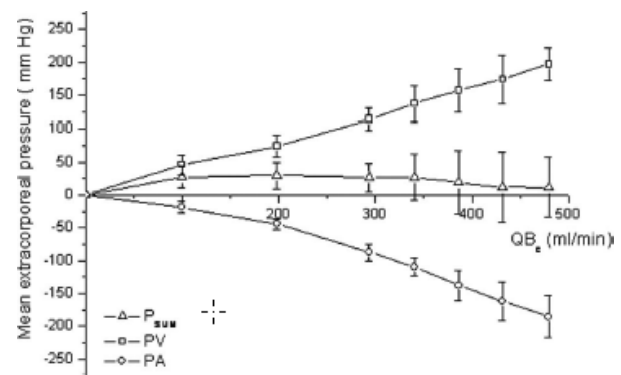


FIG. 8. Relationship between flow and pressure during in vitro experiments with DD catheters. The hydraulic resistance of the venous lumen is fairly constant, but that of the arterial lumen increases with increasing flow (23).

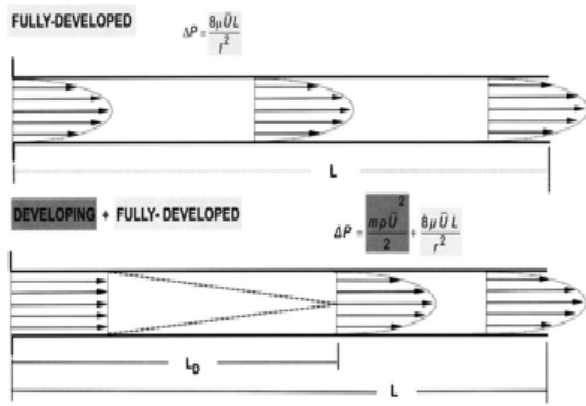


FIG. 9. Depiction of the difference between fully developed and developing flow within dialysis catheters. At the arterial inlet port, blood enters as developing flow rather than parabolic flow, and this flow has high resistance. The higher the flow rate, the greater the proportion of developing flow in the catheter lumen (24).

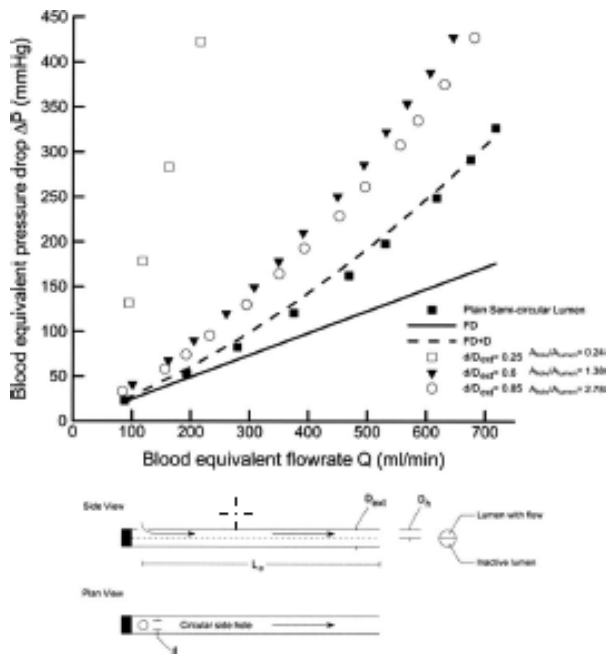


FIG. 10. Effect of side-hole tip geometry on the relationship between flow and pressure. The more complicated the tip design, the less developed is the flow pattern and the greater the catheter resistance (24).

with blood flow rate, regardless of the size of the side holes (24).

Do side holes provide any advantage clinically? Tal et al. performed a prospective study of Mahurkar-type single-body tunneled catheters, comparing catheters with side holes to catheters without side holes (25). On removal, many of the catheters with side holes had adherent clots, while those without side holes had fewer adherent clots, as shown in Fig. 11. In a follow-up of over 12 weeks there was a slightly higher flow rate for catheters with side holes, though without a significant difference. Surprisingly there was a significantly higher rate inci-

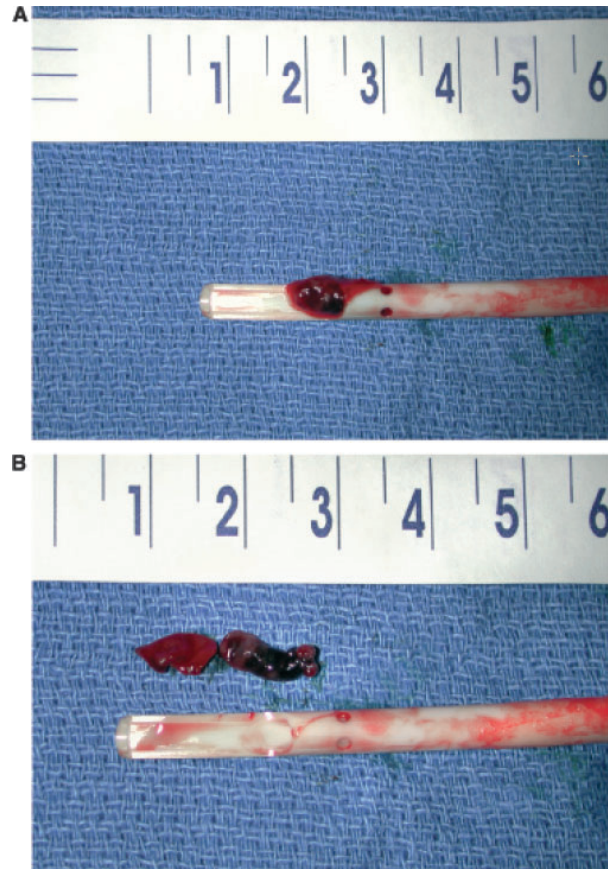


FIG. 11. Clots adherent to the side holes of Mahurkar-type step catheters, in the study by Tal et al. (25).

dence of CRBSI in the catheters with side holes versus those without (2.54/1000 catheter days versus 0.254/1000 catheter days). The authors surmised that clots adherent to the catheter tip served as a nidus for infection, after seeding from systemic bacteremia or lumen contamination.

Thus, side holes have advantages and disadvantages. If a catheter limb rests against a vein or atrial wall and the tip is blocked by sheath or thrombus, side holes allow continued flow though at a higher hydraulic resistance. However if a catheter tip can be positioned away from a wall, as in the atrium or within the SVC blood stream, then side holes would not be necessary and in fact disadvantageous.

### Symmetric Tipped Tunneled CVC, the Palindrome™

In 2005 Tal reported on a new catheter design with symmetric tips and biased ports, as shown in Fig. 12 (14). In an animal study the percentage recirculation was compared to that of step-tip and split-tip catheters, immediately after placement. All of the catheters were run in reverse flow and tips placed in the SVC or the right atrium. As shown in Fig. 13, the Palindrome had less recirculation than any of the other catheters. Surprisingly, all catheters had slightly more recirculation when placed in the atrium than in the SVC. The step-tip

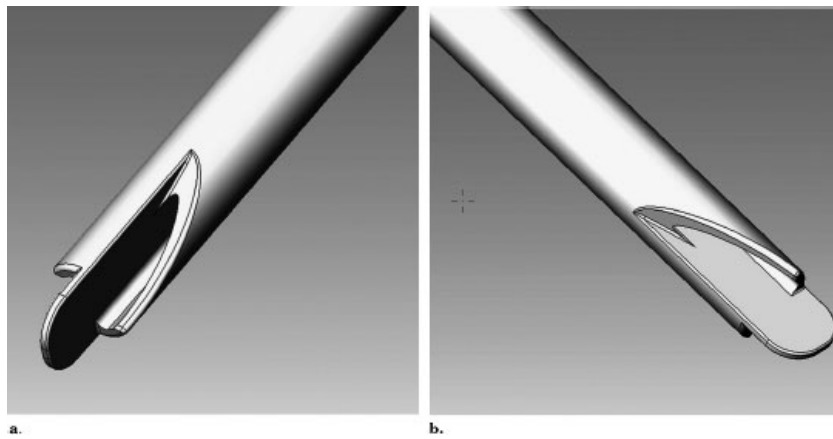


FIG. 12. The symmetrical Palindrome catheter of Dr. Tal, with bias-cut ports. Kinetic energy carries returning blood downstream, and pressure gradient brings blood through the closest part of the removal blood lumen (14).

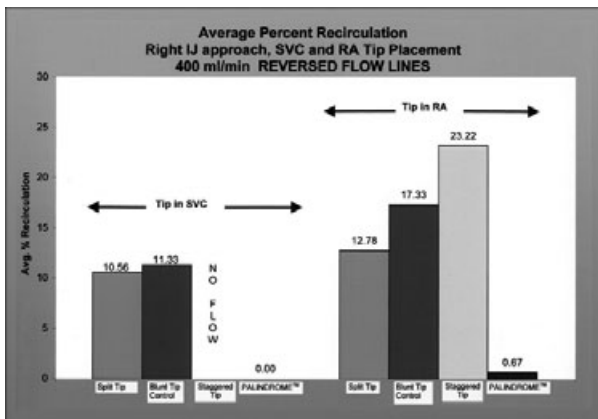


FIG. 13. Recirculation rates with reversed flow for step tip, split tip and Palindrome catheters, in an animal model (14).

catheters had no flow when placed in the SVC of the pig though the split tip and Palindrome allowed flow.

In the patient and over time, any catheter lying on the vein or atrial wall will be affected by sheaths, clots, and the relation of the catheter tip to the vascular surfaces, and these factors affect recirculation. In a recent survey of recirculation in a dialysis unit, Moossavi et al. measured recirculation in patients with step-tip, split tip and symmetrical (Palindrome) catheters, while the catheters were run in the usual flow direction. All tunneled catheters delivered the same recirculation, between 6% and 8%. Acute dialysis catheters however delivered blood flow with 23% recirculation. Though the Palindrome catheter appears successful, there are no clinical data yet showing that it diminishes recirculation or has higher flow rates over time than other catheters (26).

### Self-Centering SVC Catheter, the Centros™

The idea of the Centros™ catheter is fairly simple. The best way to avoid complete sheathing of the catheter is to hold a portion of the catheter in the middle of the vena cava. As shown in Fig. 2, the Centros™ catheter has a distal end that is planar with two outward bends of

the distal tips that create two points of contact with the SVC. The ports bend inward from the contact points. The contact points center the catheter in the vena cava and place the ports in a position away from the wall of the vein wall. Side holes are not necessary as the ports should not be in contact with the vena cava wall and therefore should not become occluded. If fibrous sheathing near the ports is avoided the blood flow rate of the Centros™ should be maintained over many months of use, and recirculation should be minimal (in vitro tests demonstrate zero recirculation). The catheter is designed to be placed in the lower third of the SVC rather than within the atrium, so placement is made easier. In some versions a gently preformed curve of the apex of the catheter matches the usual arc of the subcutaneous tract.

There is some prior evidence that a catheter supported within the SVC will remain free of sheathing and thrombosis. In 1998 Kohler and Kirkman reported an animal trial in which single lumen 3.2 mm diameter catheters were placed in the SVC of pigs, and left for 1–8 weeks (27). No anticoagulant was administered and the catheters were not used for infusion or blood removal. Some of the catheters had a 2 cm diameter loop attached to them, to center the tip in the distal SVC. During placement of the catheters without a loop, fluoroscopy demonstrated a continued relative motion of the catheter and vena cava wall with each heartbeat; however, catheters with the loop remained stationary at the point of contact with the vena cava wall. As shown in Fig. 14 when the loop catheters were examined at the end of the 8 week period, the SVC and catheter were completely free of fibrous sheathing and thrombosis. In pigs with nonlooped catheters the catheter was completely covered by sheath and thrombus, the SVC was nearly occluded, and there was a much greater number and size of intimal lesions. From this study it is apparent that a catheter which is supported in the vena cava by two points of contact should have considerably less sheathing and fibrosis, and therefore more constant flow over time, versus straight, single-body or split-tip catheters.

In June 2007 the FDA approved the Centros™ catheter for use in dialysis access. A small number of these

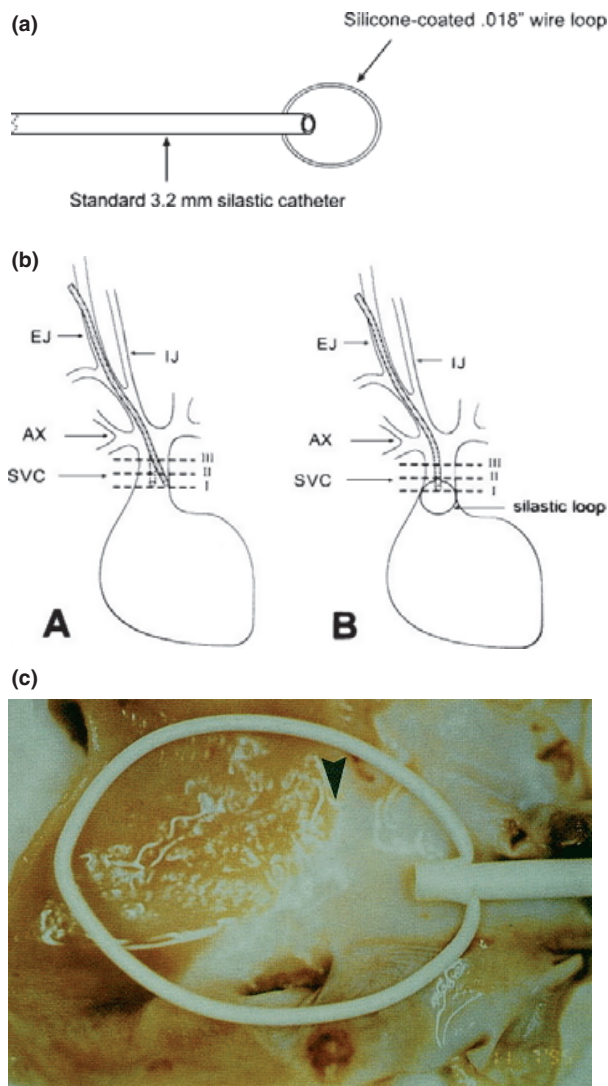


FIG. 14. (a) Catheter design of Dr. Kohler with loop to support the distal tip in the middle of the vena cava. (b) Position of loop in SVC. (c) Appearance of SVC near tip of catheter, 8 weeks after placement (27).

catheters was created of 28 and 24 cm length (hub to tip) and a gentle bend at the expected apex (as in Fig. 2). All catheters had a self-sealing opening on the venous limb to allow threading over a single guidewire, though this feature is not needed for placement through a split sheath. After IRB approval we initiated a clinical trial at four independent centers (Ash SR, Clarian Arnett Health, Lafayette, IN; Asif A, University of Miami, Miami, FL; Yevzlin AS, University of Wisconsin, Madison, WI; Samaha AL, Kidney and Hypertension Center, Cincinnati, OH) to determine the hydraulic properties of the catheter and permanence of flow. Inclusion criteria were quite broad:

- Adult patients initiating or continuing in-center HD who were scheduled to receive a tunneled dialysis catheter in the right IJ vein;
- Patients who may have had a prior tunneled catheter for dialysis in the right IJ site were eligible for inclusion in the study; and

- Patients were expected to require use of the catheter for more than 45 days.
- Exclusion criteria were few:
- Patients with a prior history of right IJ vein thrombosis, or
  - With documented stenosis of the right IJ, innominate, or SVC;
  - Patients in whom the catheter would be placed into the same site as an existing catheter; and
  - Patients who were unable to sign a consent form.

Nine catheters were placed into patients, in all cases through the right IJ, under local anesthesia using fluoroscopy, ultrasound, and a 16 French split sheath. Tips of the catheters were placed in the lower third of the SVC rather than in the atrium. An example of a post-placement X-ray is in Fig. 15. The catheters were used three times per week for outpatient hemodialysis treatments. Once per week at the start of dialysis, the blood pump was set to deliver a negative arterial pressure of  $-200$  mmHg on the arterial line. The blood flow rate associated with this modestly negative pressure was recorded ( $Q_{b-200}$ ). The same measurement was also performed on 120 prevalent DD tunneled CVC for dialysis in 20 dialysis centers, as part of a study of catheter locks. In the current study, reasons for catheter removal were recorded as were any significant problems with the catheters.

Figure 16 demonstrates the average  $Q_{b-200}$  flow rate for all nine catheters, over the 7-week study. The mean  $Q_{b-200}$  was 390 ml/minute ( $SD \pm 49$ ) at catheter insertion and was 401 ml/minute ( $SD \pm 80$ ) at 7 weeks of use (NS). By comparison, 120 standard tunneled dialysis IJ catheters being used in several dialysis units had a lower  $Q_{b-200}$ , 348 ml/minute ( $SD \pm 64$ ,  $p < 0.05$ ). During 7 weeks of follow-up, one of the nine self-centering catheters was removed due to presumed exit

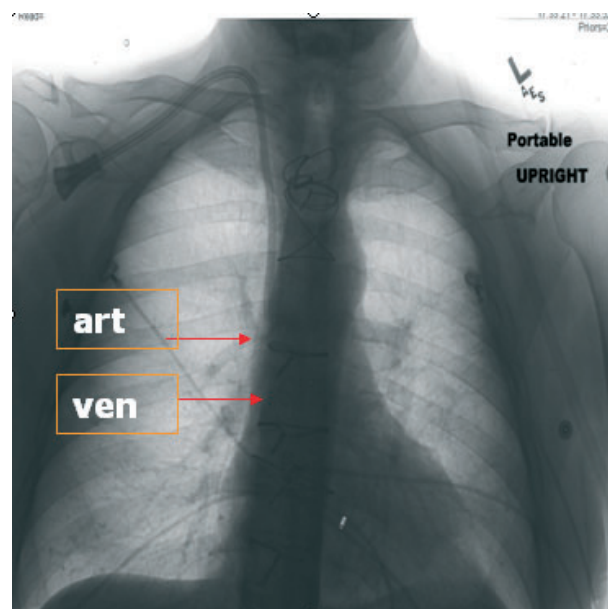


FIG. 15. X-ray of chest showing placement of the Centros tips in the lower third of the SVC.

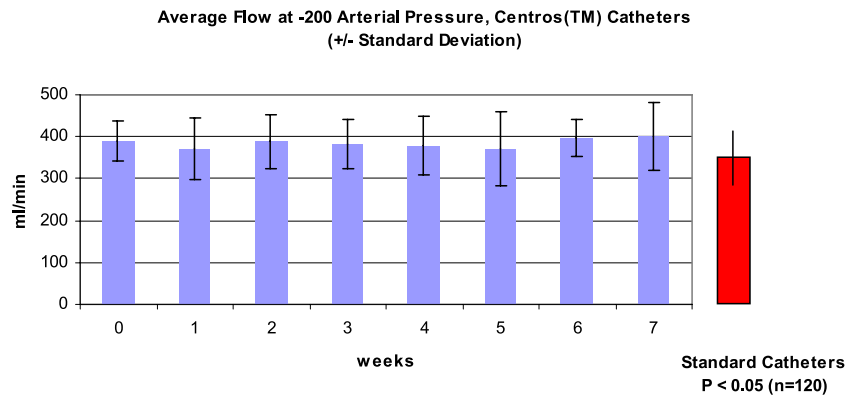


FIG. 16. Flow rate of the Centros catheters at modestly negative arterial side pressure (QB<sub>-200</sub>), over 7 weeks of dialysis use. For comparison, same measurement carried out on 120 prevalent DD tunneled dialysis catheters.

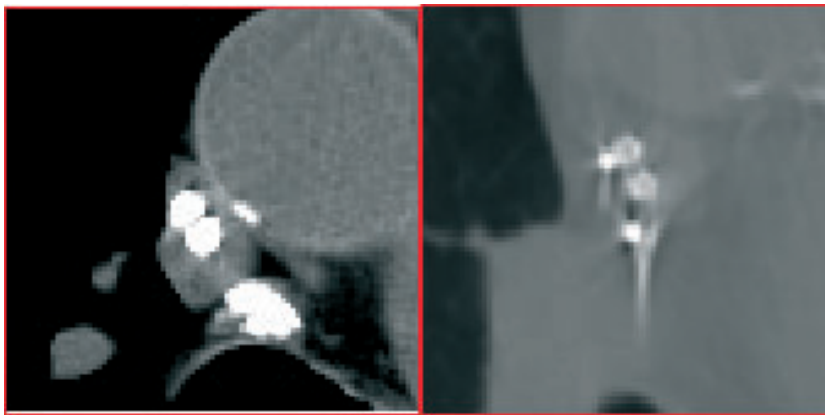


FIG. 17. CT scans of the chest taken 4 months after Centros placement in two patients, demonstrating that the catheter limbs form a plane within the vena cava and at least one port is separated from the vena cava wall. The SVC on the right includes two pacemaker wires.

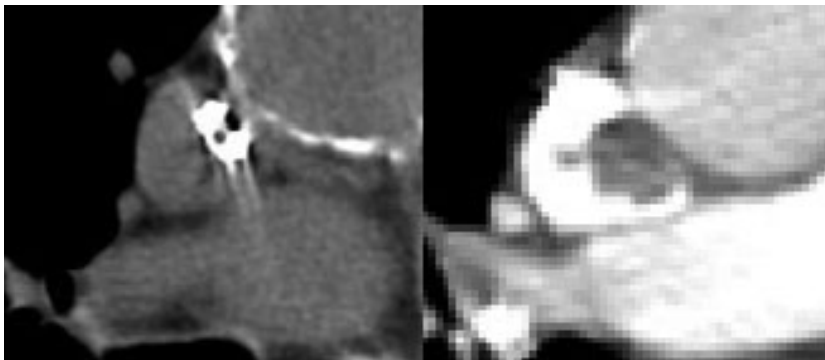


FIG. 18. CT scans of two patients with Split Cath catheters in place for several months. Note that both limbs of the catheter lie against the vena cava wall. Clot surrounds the catheter in the CT angiogram on the right.

infection, and one was removed when no longer needed. No catheter failed to provide adequate flow for dialysis during the study.

At the end of the study catheters continued to be used for dialysis, in some patients for up to 6 months. Two patients volunteered for a computed tomography (CT) scan of the chest after 4 months of catheter use. Figure 17 demonstrates that the catheters were in the expected position, limbs in a plane across the vena cava with at least one distal limb separated from the

wall of the vena cava. No sheath was seen but of course a standard CT could not detect sheaths of less than 1 mm thickness. For comparison, Fig. 18 includes two CT scans performed on patients with Split Cath catheters, demonstrating that both limbs of these catheters are adjacent to the vena cava wall, as is always the case. One of these Split Cath catheters has a clot or sheath covering the catheter. At removal, none of the Centros™ catheters exhibited any resistance to retraction, and none came out with remnants

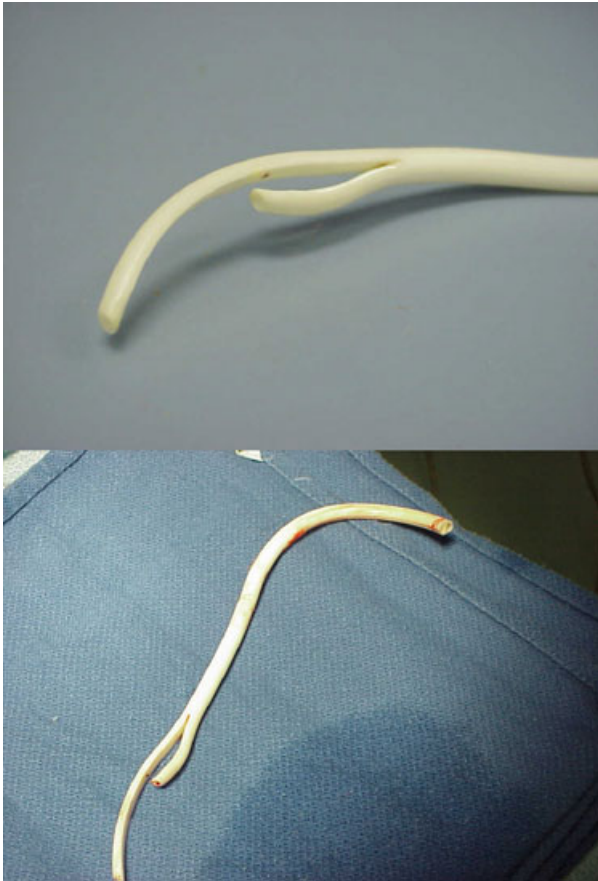


FIG. 19. Appearance of Centros™ catheters after removal and gently rinsing with sterile saline. The only signs of any thin sheath was in a few catheters, near the jugular vein entrance sheath.

of any thickened sheath. In fact most catheters were remarkably free of any clots or evidence of sheath as shown in Fig. 19.

This preliminary study indicates that the self-centering Centros™ catheter provides highly acceptable flow rate at modest negative pressure, without deterioration in flow rate over 7 weeks of use. This high flow rate occurred despite positioning of the tips of the catheter in the SVC (rather than within the atrium). The Centros™ catheter is now being marketed widely. The study showed no evidence of any significant sheathing of the catheters. Two large multi-center studies are planned for the catheter, one observational and one randomized versus a standard split-tip catheter.

### Current Challenges and Future Directions for Tunneled CVC for Dialysis

The advent of successful tunneled CVC for dialysis has been a great advance for patients with ESRD, both for beginning hemodialysis and for continuing dialysis. Tunneled CVC now allow dialytic support of patients for many months if needed, allowing patients to be supported long enough for fistulas and

grafts to be created, corrected, and become the best long-term access choices.

In spite of advances, tunneled CVC still have significant problems and limitations. For each of these problems, there will someday exist a solution which will advance the technology and benefits of tunneled CVC for dialysis:

- *Catheter-related infections:* Catheter materials, chemical impregnation methods, or catheter locks are now being investigated to kill bacteria in the biofilm layers both on the outside and inside of tunneled CVC, in order to decrease this most common complication of the catheters. Two recent reviews have confirmed that every antibacterial catheter lock that has been studied in randomized, prospectively controlled trials has demonstrated a 50–80% decrease in the incidence of CRBSI (28,29). The antibacterial effect of impregnated chemicals and new catheter materials in a tunneled CVC must remain for many months rather than a week or so (as with acute catheters), and this implies the need for some method of regeneration of the active component over time, or use of covalently bound enzymatic or catalytic materials.
- *Catheter tip clotting:* As mentioned above, catheters without side holes have some advantage in avoiding clotting. Catheters which open and close at the tip would allow the catheter to retain anticoagulant and completely avoid blood clotting within the ports.
- *Catheter fibrous sheathing:* As described above, one solution for catheter sheathing may be a catheter which centers itself in the vena cava (the Centros™). Other approaches include chemical impregnation of the catheter to prevent the growth of macrophages and fibroblasts around the catheter bodies, though this is likely to be difficult as the irritation of the vein wall by the catheter is such a strong stimulus for sheath formation.
- *Central venous stenosis:* Methods to distribute or diminish “wear” on the vena cava must be evolved to avoid this serious and still frequent complication. Avoiding use of acute dialysis catheters diminishes the frequency of central venous stenosis. Catheters that are supported at only two points in the SVC diminish the contact area of the catheter to the vein but might increase wear at two points. Whether these catheters diminish the risk of SVC stenosis in the long run is unclear.
- *External component bulk:* Patients bandage and keep dry the hubs, extension tubings, clamps, and connectors, but many also complain about the general bulk of the catheter components on their bodies. Also, the preclusion of showering is a real bother to many patients. Subcutaneous ports were proposed as one solution (LifeSite, BioLink) but clearly are not the answer for most long-term patients. Eventually more radical skin-level “connectology” will be necessary.

- *External component breakage*: More durable yet still light-weight components are possible. Simplifying the entire catheter design to limit the size and number of glued connections is a partial solution.

With a few more improvements, tunneled CVC for dialysis could become a painless, effective and safe long-term access for the majority of dialysis patients and perfectly acceptable as an alternative to AV grafts. For those patients in whom they are possible, the fistula will likely remain the optimal access for some years.

### Conflict of Interest

Dr. Ash is Chairman and Director of Research for Ash Access Technology, Inc., the originator of the Split Cath™ and Centros™ catheter designs.

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