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# Minimally Invasive Sutureless Anastomosis of an AV Hemodialysis Graft

An overview of the InterGraft™ Vascular Anastomotic Connector System and a case report from the first-in-human study.

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End-stage renal disease (ESRD) is a worldwide public health problem. There are more than one million ESRD sufferers worldwide. In the United States alone, 571,000 ESRD patients underwent treatment in 2009; since 2000, a 12% increase in the incidence rate of ESRD has been observed in patients who are ≥ 75 years of age. Conventional three-times-weekly hemodialysis is the most common treatment, accounting for approximately 91% of all treatments.[1] To perform hemodialysis, an arteriovenous (AV) vascular access is needed to remove blood for dialysis filtration and return the blood to the body. Due to the need for surgical healing and development, the access is ideally prepared several weeks or months in advance of anticipated need. A significant challenge in managing patients with ESRD is providing immediate access when needed, along with consistent and sustained access. Despite the magnitude of the resources committed to the treatment of ESRD and the substantial improvements in the quality of dialysis therapy, these patients continue to experience significant morbidity and mortality and a reduced quality of life.

Vascular access has frequently been referred to as the Achilles' heel of dialysis because of the high morbidity and mortality rates due to infection, thrombosis, and ultimate access failure. Of the three types of AV vascular access—fistulas (AVFs), grafts (AVGs), and central venous catheters (CVCs)—the type used is influenced by factors such as the expected time course of renal failure and the condition of the patient's vasculature. While AVFs are considered the gold standard, synthetic grafts are also widely used because venous pathology at the time of access creation limits AVF. Furthermore, the failure rate of AVFs to mature and become suitable for dialysis may be as high as 60%; therefore, many ESRD patients will require an AVG access at some point during the disease course.[2,3] Establishment of long-term dialysis access remains a significant challenge, especially in patients with multiple previous failed access sites and in the elderly.[4-6] With continued treatment needed in an increasingly older ESRD population, the increased use of AVGs may also be needed.[7,8]

**Figure 1. The InterGraft™ Vascular Anastomotic Connector System includes a Venous InterGraft™ Connector (top) and an Arterial InterGraft™ Connector (bottom). The InterGraft™ Connectors are vascular prostheses and are designed with a nitinol framework that is encapsulated in ePTFE.**

Grafts are relatively easy to place using standard tunneling techniques. Expanded polytetrafluoroethylene (ePTFE) is the most common graft material.[3] Newer self-sealing multilayered PTFE configurations and other graft materials have recently been introduced, offering the potential for earlier access.[9,10] Compared with AVFs, grafts have a greater incidence of recurrent stenosis, especially at the venous anastomosis, and require more salvage interventions to maintain patency for dialysis.[3] The pathogenesis of venous stenosis is composed of a cascade of events resulting in endothelial and smooth muscle injury that results in neointimal hyperplasia and, ultimately, flow-limiting stenosis.[11] With the conven-

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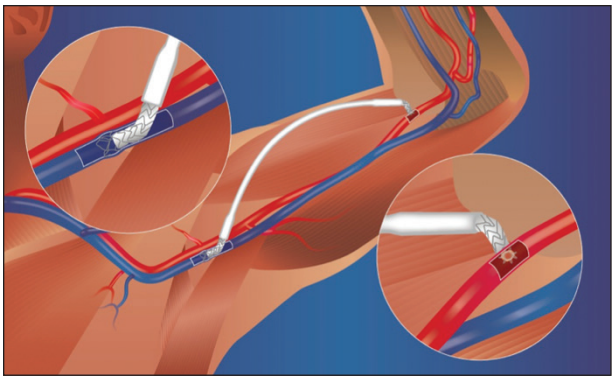

**Figure 2. Upper arm AVG with anastomoses using the Venous and Arterial InterGraft™ Connectors.**

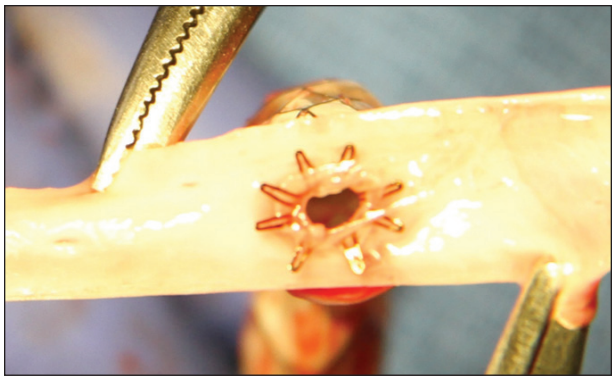

**Figure 3. Longitudinal incision of canine femoral artery in which Arterial InterGraft™ Connector flange has been deployed. Flange tines and central 4-mm-diameter inflow orifice are shown.**

tional end-to-side venous anastomosis, the vessel wall is subjected to turbulent, nonlaminar flow and low shear stress at the toe and heel of the anastomosis, sites that correspond to the development of intimal hyperplasia. As neointimal hyperplasia progresses, there is a decrease in the blood flow, leading to stenosis and thrombosis. In addition to these hemodynamic factors, the trauma of surgical graft implantation due to relatively large incision sites and sutured anastomoses contributes to increased healing time and possible complications. These observations point to the need for new devices and techniques to optimize AVG flow dynamics and healing, resulting in the reduction of stenosis and other complications.

The InterGraft™ Vascular Anastomotic Connector System (InterGraft™ System, Phraxis™, Inc.) was developed for minimally invasive AV anastomosis of a standard, 6-mm-diameter hemodialysis graft. The InterGraft™ System includes a Venous InterGraft™ Connector and an Arterial InterGraft™ Connector that are each designed for transcatheter delivery and deployment using customized delivery systems. The Connectors have a self-expanding nitinol framework that is encapsulated with expanded ePTFE (Figure 1). The inner ePTFE lumen (blood contact surface) is carbon impregnated.

The Venous Connector is a flexible, flared, self-expanding endoprosthesis designed for coaxial placement in veins approximately 4 to 7 mm in diameter at the target venotomy site (Figure 2). The flared end allows for vessel expansion of up to 10 mm and includes anchoring barbs that extend into the vein wall. The Venous Connector is delivered via an 11-F sheath and over a guidewire that is up to 0.018 inches in diameter.

The Arterial Connector is designed for end-to-side anastomosis to the target artery, using a low-profile flange for attachment to the artery wall while also allowing for distal blood flow (Figure 2). The Arterial Connector has a flexible midsection that allows for up to a 90° angle of introduction and is designed for use in arteries approximately 3.5 to 6 mm in luminal diameter. The flange end is configured with eight evenly spaced tines around a 4-mm-diameter inflow orifice (Figure 3). The Arterial Connector is delivered via a 7-F sheath and over an 0.014-inch guidewire.

The graft ends of the InterGraft™ Connectors exit from the vessels and are manually fitted within a conventional vascular access graft that has been tunneled under the skin. The graft tunneling and connections are made through small skin incisions, thereby reducing surgical trauma and facilitating the overall healing time as compared with standard sutured anastomoses. Anastomoses with the InterGraft™ System may improve the local vessel wall shear stresses and promote laminar flow, thereby improving patency. Computational fluid dynamics modeling demonstrated a graft flow rate of approximately 1 L/min when the AV pressure difference was approximately 100 mm Hg. The maximum wall shear ranged from 265 to 180 Pa, and thus below the threshold to cause mechanical hemolysis (800 Pa) and below the level thought to stimulate hyperplasia.[12]

A first-in-human clinical study of the InterGraft™ System is currently underway at the Sanitario Italiano in Asuncion, Paraguay. The study is a prospective, single-center, nonrandomized, one-arm design. Graft anastomosis and overall implant procedural outcomes, patency throughout a 6-month follow-up period, and adverse events will be evaluated. A case report from the study, with outcomes through 30 days, is presented.

## CASE REPORT

The patient is a 64-year-old man with a history of hypertension, diabetes mellitus, and ESRD. He underwent hemodialysis treatment for the previous 3 weeks via a CVC. Baseline angiographic evaluation showed that the vascular anatomy in the left upper arm was suitable for placement

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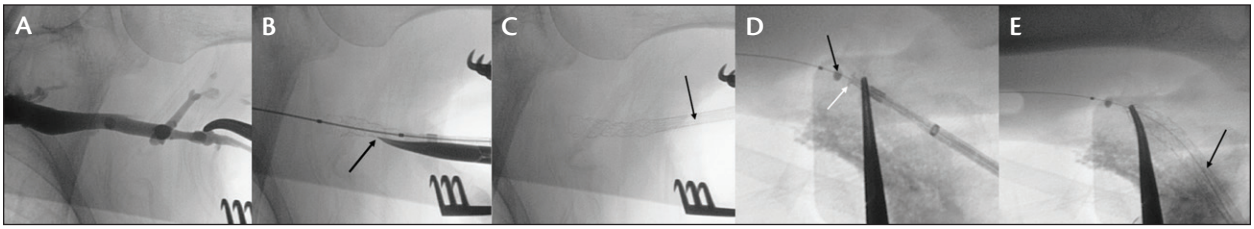


**Figure 4. Deployment of the InterGraft™ Connectors. Imaging of axillary vein to determine target venotomy site for introduction of the Venous InterGraft™ Connector (A). Deployment of Venous InterGraft™ Connector (B); clamp tip (arrow) marks the site at which Connector exits from the vein. Fully deployed venous InterGraft™ Connector (C); note the straight pattern of the nitinol framework (arrow) that is fitted within the graft. The Arterial InterGraft™ Connector flange has been deployed (white arrow) and the positioning balloon (black arrow) has been inflated (D); clamp tip marks the exit site from the artery wall. The extravascular segment of the Arterial InterGraft™ Connector (arrow) has been deployed (E).**

of an AVG with anastomoses using the InterGraft™ System. Written informed consent was obtained, and the patient was entered into the study. The target outflow axillary vein was located deep within the axilla and would have been a challenging location for conventional suturing of the outflow anastomosis (Figure 4A).

After local anesthesia, the patient's upper arm was prepared and draped in the usual fashion. Small skin incisions were made at the target venotomy and arteriotomy sites, and a 6-mm-diameter PTFE graft (Atrium Flixene vascular graft, Maquet Vascular Systems) was tunneled into position via the incision sites. The target venotomy site in the axillary vein was exposed, and the vein was accessed using a micropuncture needle. An 11-F introducer sheath was placed, and the guidewire was inserted. The Venous InterGraft™ delivery system, containing the preloaded Connector, was prepped, then introduced over the guidewire. Under fluoroscopic guidance, the Venous Connector was positioned using the radiopaque marker bands on the delivery system and while observing the location of a clamp tip that was placed at the planned venotomy site (Figure 4B). The Connector was deployed using a pin-and-pull technique. The delivery system was removed, and the protruding end of the Connector was gently grasped with fingers to control bleeding and fitted within the venous end of the tunneled graft (Figure 4C). The graft was flushed with heparinized saline solution and clamped. A single stay suture was placed to secure the Connector to the graft (Figure 5A).

Next, the target brachial artery was exposed and accessed using a micropuncture needle. A 7-F introducer sheath was placed, and the guidewire was inserted. The Arterial InterGraft™ delivery system with preloaded Connector was prepped, then introduced over the guidewire. Under fluoroscopic guidance, the Connector was positioned using radiopaque marker bands located on the delivery system sheath and on a positioning balloon. The flange end of the Connector was deployed first. The positioning balloon was then inflated and

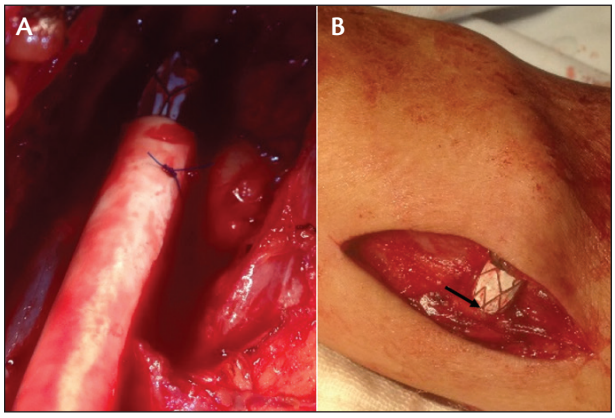


**Figure 5. Graft connected to axillary vein using the Venous InterGraft™ Connector. A single stay suture has been placed as a failsafe measure to secure the graft to the Venous Connector (A). The Arterial InterGraft™ Connector flange (arrow) is deployed within the wall of the brachial artery, creating an end-to-side anastomosis (B). The Connector exits perpendicular to the artery, then the flexible segment of the Connector bends approximately 45° as it is inserted into the graft and positioned around the margin of the biceps.**

gently retracted to secure the flange to the artery wall (Figure 4D). The remainder of the Connector was then deployed using a pin-and-pull technique (Figure 4E). The balloon was deflated, and the delivery system was removed from the body. The protruding end of the Connector was gently grasped with fingers to control bleeding and was fitted within the arterial end of the tunneled graft. The graft was unclamped, allowing blood flow through the AV circuit. Observation of the arteriotomy site showed that the Arterial Connector was properly secured to the artery wall and there was no leaking (Figure 5B). The incision sites were closed. The graft was evaluated by ultrasound the next morning, and flow was observed. The graft had an audible bruit and palpable thrill. Following the evaluation, the patient was discharged according to local standard procedure.

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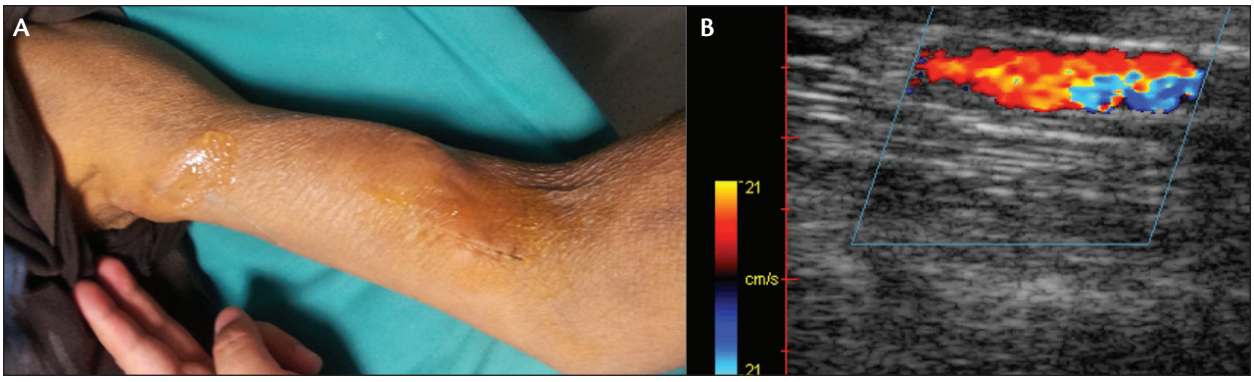


**Figure 6. At 2 weeks after the procedure, the incisions were healed, and there was minimal swelling in the arm (A). Ultrasound evaluation of the InterGraft™ Connectors and graft at 30 days showed that the Connectors and graft were widely patent (B).**

A follow-up evaluation was performed 2 weeks after the procedure. The incisions were observed to be nicely healed, with minimal swelling in the upper extremity (Figure 6A). Ultrasound evaluation at 30 days showed that the InterGraft Connectors and graft were widely patent (Figure 6B). There were no adverse events reported since discharge, and the graft is being used successfully for hemodialysis access.

## RESULTS AND CONCLUSION

The over-the-wire graft anastomosis procedure with the InterGraft™ System described in this case allowed for minimally invasive creation of the venous and arterial anastomoses. The novel InterGraft™ System shows promise as a valuable interventional tool and may be particularly useful for anastomosis of a hemodialysis access in patients with centrally located target outflow veins that cannot be readily accessed using standard surgical methods.

By providing a minimally invasive method for creating an AVG access, the InterGraft™ System allows the procedure to be performed by a variety of physicians skilled in graft tunneling methods and interventional techniques, such as interventional radiologists and nephrologists, in addition to vascular surgeons. A large percentage of ESRD patients present with an urgent need for hemodialysis, and use of temporary venous catheter access is the only option currently available. Unfortunately, catheter use even for short periods can result in higher rates of infection, thrombosis, morbidity, and mortality. Graft anastomosis using the InterGraft™ System offers the possibility of a faster postoperative recovery. Use of the InterGraft™ System with newer self-sealing grafts may also allow for earlier graft cannulation, thereby reducing the need for temporary catheter access.

The InterGraft™ System is not currently marketed. Phraxis™ anticipates that a clinical study of the InterGraft™ System will be performed in the United States under an investigational device exemption beginning in early 2015. ■

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