New Technology: First Look

The Role of Cryopreserved Femoral Vein Graft in Hemodialysis Access Surgery

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ABSTRACT **Cryopreserved allografts have demonstrated resistance to infection similar to that of autogenous tissue when used for the treatment of prosthetic arterial bypass graft infections. As the number of hemodialysis access procedures increases, prosthetic hemodialysis graft infection has become a significant problem. We have used the cryopreserved femoral vein as an alternative conduit in the treatment of prosthetic arteriovenous (AV) hemodialysis graft infections. Forty-eight cryopreserved femoral vein AV graft procedures were performed. The 1-year primary graft patency rate was 49%, while the secondary graft patency rate was 75%. No subsequent cryopreserved allograft infections occurred. The cryopreserved femoral vein graft is a safe, durable, and infection resistant conduit for the treatment of prosthetic AV hemodialysis graft infections.**

Keywords **Cryopreserved femoral vein, infected prosthetic bypass graft**

The use of allografts is not a new concept. The first allograft implant was performed by Alexis Carrel in 1912, when he interposed the jugular vein of a dog into the thoracic aorta of another dog.[1] The jugular vein allograft was patent on necropsy examination 2 years later, but almost half a century passed before D. Emerick Szilagyi et al. in 1957 reported the use of arterial allografts in the human abdominal aorta.[2] Unfortunately, in follow-up extending to 15 years the arterial allografts had become aneurymal,[3] and this curbed the

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enthusiasm for allografts as arterial conduits. Nevertheless, interest continued in the role of allografts for the treatment of infected prosthetic arterial grafts.

In 1975, Wesley Moore and colleagues[4] demonstrated the resistance of allografts to infection in the dog model. In Moore's study, the femoral artery was inoculated with *Staphylococcus aureus* and 3 days later an arterial bypass was performed through this field. One group of dogs had the contralateral femoral artery used as a bypass conduit (autogenous graft), the second group underwent bypass using femoral artery from other dogs (allograft), while the third group had dacron grafts placed. The autogenous and allograft bypass graft groups performed equally well with very few late infections (8% autogenous and 17% femoral artery allografts) versus an 88% infection rate in the dacron graft group. Recent animal experiments have confirmed Moore's initial observations that arterial allografts have a lower potential for infection than prosthetic grafts when placed in an infected field.[5,6]

Clinical experience with human allografts continues to grow. Vogt and colleagues from Zurich, Switzerland reported a series of 34 human allografts used in the treatment of prosthetic vascular graft infections. At follow-up extending to 3 years, he reported a 91% freedom from reinfection rate[7] and subsequent reports have supported Vogt's findings.[8–13]

The use of allografts for hemodialysis access has been limited, but Baraldi et al. reported on 59 patients who underwent fresh and cryopreserved saphenous vein allograft replacement for recurrent prosthetic arteriovenous (AV) graft failures.[14] Baraldi et al. reported a 1-year primary patency rate of 72%, however, there was no improved graft patency over polytetrafluoroethylene (PTFE) to justify the additional expense of using cryopreserved allografts.

INDICATIONS FOR THE USE OF CRYOPRESERVED FEMORAL VEIN IN HEMODIALYSIS ACCESS

In 1973, only 11,000 patients in the United States received hemodialysis.[15] Today, however, more than 210,000 are on chronic hemodialysis, and dialysis access procedures are the most commonly performed vascular operation. Thirty percent of hospital admissions for renal failure patients result from complications of AV access.[15] The National Kidney Foundation has published guidelines and recommendations on the care of hemodialysis patients entitled the Dialysis Outcome Quality Initiative (DOQI).[16] One of the many findings identified by the DOQI guidelines was an increased number of hemodialysis AV graft operations compared with primary AV fistulas. This trend likely does not reflect a change in the surgeon's approach to angioaccess, but rather a change in patient demographics which limits the surgeon's ability to create a primary AV fistula. For example, in the United States today, approximately 45% of renal failure patients are older than 64 years of age[16] and lack the superficial venous anatomy necessary to create primary AV fistulas. As a result, surgeons are forced to perform prosthetic AV grafts which unfortu-

nately increase the potential number of graft complications such as multiple failures and infection (Fig. 1).

Over the past 3 years, the hemodialysis graft infection rate at our institution has been 12%, which is comparable with other reported graft infection rates.[17] Although limited "puncture site" infections may be treated by local resection and reconstruction "around" an infected field, most prosthetic graft infections require excision, which often leads to a delay for a subsequent angioaccess procedure and prolonged wound care. The significant morbidity associated with infected AV grafts led us to investigate the use of cryopreserved femoral vein allografts as an alternative conduit for hemodialysis access.

SURGICAL TECHNIQUE

The superficial femoral vein allograft is harvested by standard procurement teams within a 24-hour window from the time of death. The vein is placed into a cryoprotective medium and undergoes a slow freeze process down to a liquid nitrogen temperature of −168°C. The tissue is quarantined until serology markers for common viral diseases (i.e., hepatitis A, B, C, HIV type

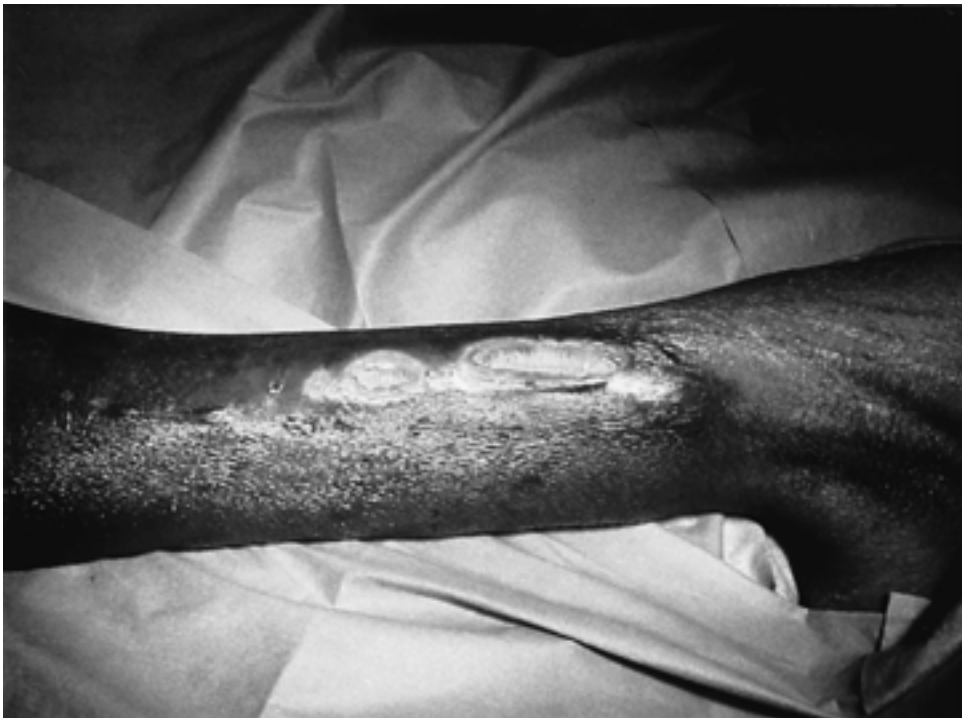

Fig. 1 Infected hemodialysis graft eroding through the skin.

1 and 2) and bacterial cultures are negative; the tissue is then released for clinical use. There is a small theoretical risk of viral disease transmission with the use of any human tissue or organ, but there have been *no* reported cases of viral or bacterial disease transmission from more than 39,500 vascular allograft implants. The effect of cryopreservation on viral inactivation, however, remains unknown.

ABO blood-type compatibility is recommended between donor and allograft recipient.[18] A cryopreserved femoral vein graft may be shipped overnight to any center in the United States and the dry-ice packing maintains graft viability for 72 hours. An alternative to ordering and shipping allografts at the time of operation is to store the grafts in a liquid nitrogen freezer unit at individual centers, thus making the grafts available for urgent cases. To prepare the allograft, it is placed in a warm water bath (37–42°C) for a "rapid thaw" which gives the best cellular viability. Using a series of solutions provided by the manufacturer (CryoLife, Inc., Kennesaw, GA), the graft is prepared for implantation (Fig. 2).

A cryopreserved femoral vein graft is usually less than 24 cm in length, which is shorter than the standard PTFE graft (45 cm). Because of this

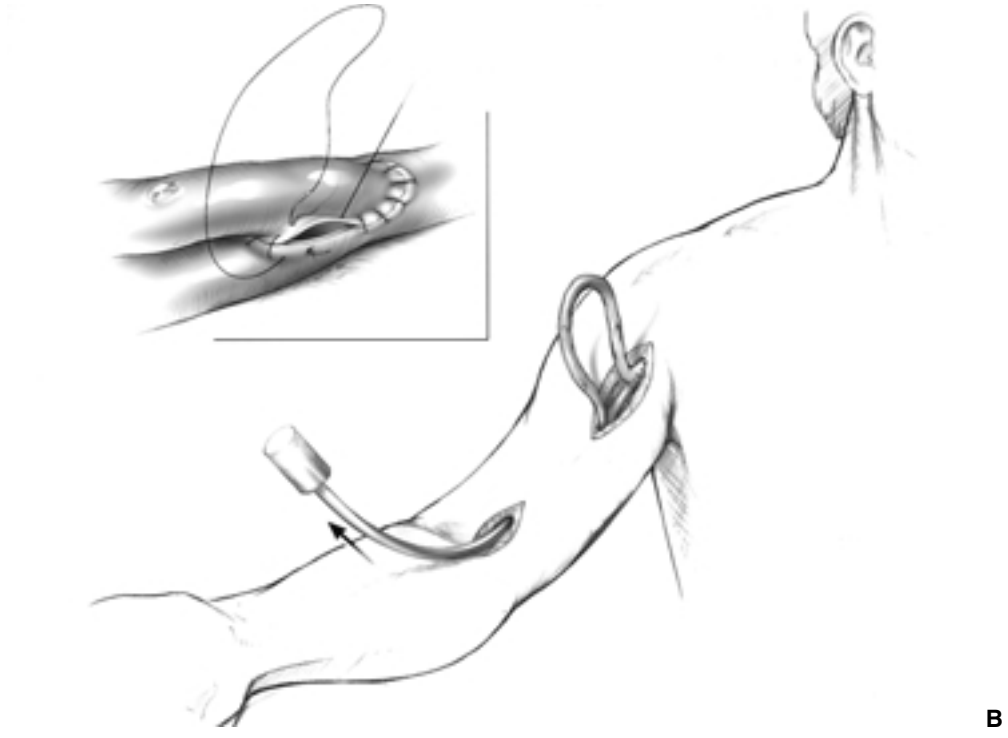

Fig. 2 **(A)** The venous anastomosis. **(B)** *Careful* tunneling of the cryopreserved femoral vein to prevent injury.

length limitation, it is mandatory to measure the distance between the arterial and venous anastomotic sites prior to opening the cryopreserved femoral vein. For example, when operating for AV graft infection in the upper arm, it is wisest to expose the brachial artery and vein at a more proximal location. The cryopreserved femoral vein may then be tunneled away from the infected graft and the anastomoses completed and the incisions closed prior to excision of the infected graft. The venous anastomosis is constructed first (Fig. 3) and the graft is irrigated with 2000 units of heparin in a 10 mL lactated ringers solution. The valves in the cryopreserved femoral vein prevent backbleeding (Fig. 4), therefore, a clamp is not necessary to control backbleeding of the cryopreserved femoral vein graft while the arterial anastomosis is constructed. Because of the large diameter of the cryopreserved femoral vein, the graft is "tapered" at the arterial end with a double row of 6–0 polypropylene suture until a 6 mm oriface remains (See Figure 4). The arterial anastomosis is then constructed in a standard end to side fashion. The cryopreserved

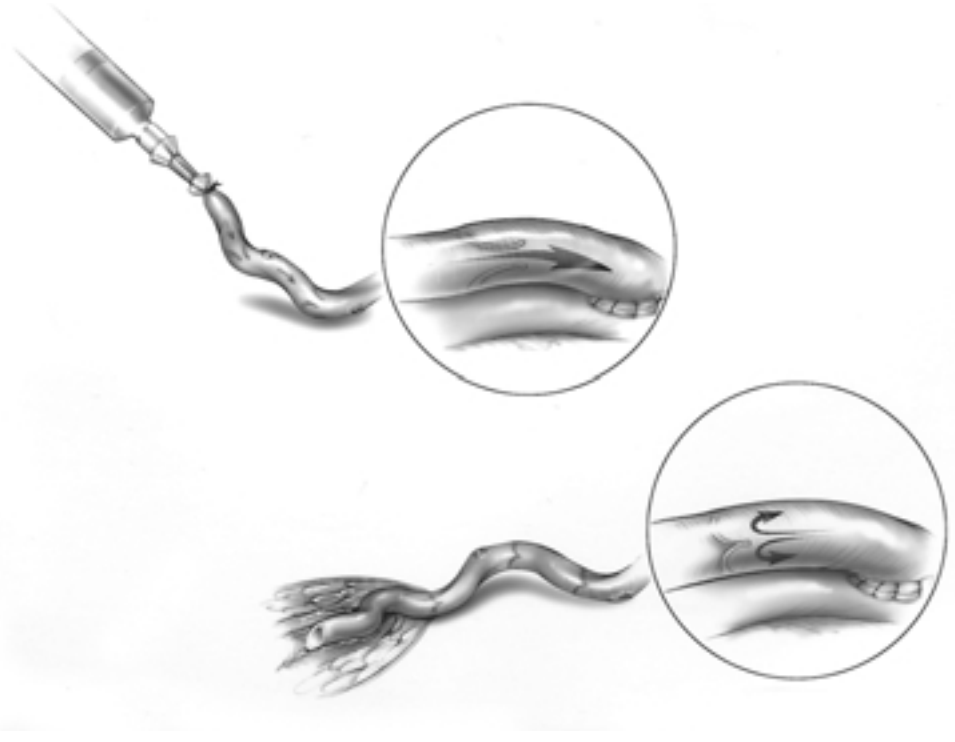

Fig. 3 The graft is flushed with 2000 units of heparin mixed in lactated ringer's solution. The valves within the cryopreserved femoral vein graft prevent backbleeding, therefore, the arterial anastomosis can be performed without the use of a clamp on the graft.

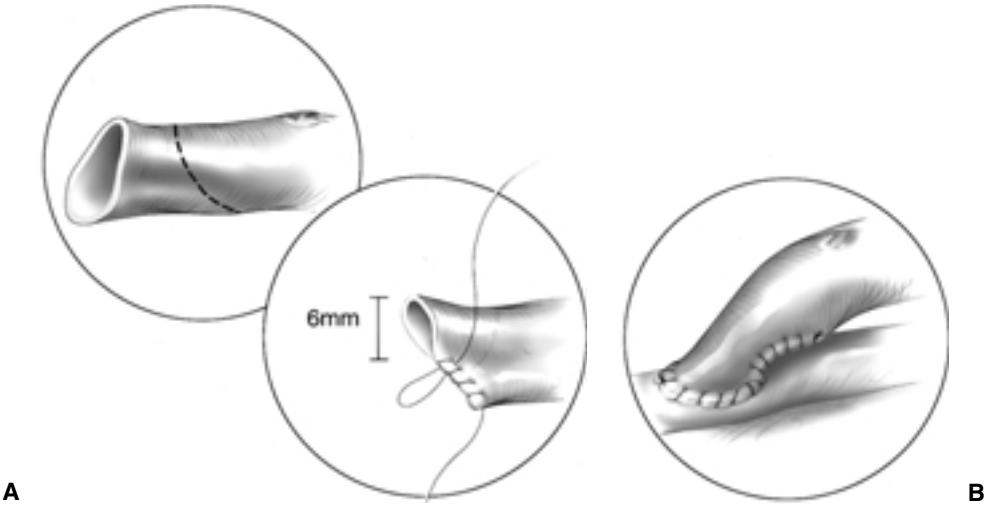

Fig. 4 The arterial end of the cryopreserved femoral vein graft is "tapered" **(A)** by cutting the graft at an angle and **(B)** the sewing a double row of 6-0 polypropylene suture.

femoral vein AV graft is allowed to mature for 10 to14 days before it is accessed.

CLINICAL EXPERIENCE

The results of a prospective study that consisted of 44 patients who underwent 48 cryopreserved femoral vein AV grafts has been reported.[17] Twenty patients had prosthetic AV graft infections with no available access in the contralateral arm because of multiple previous failed AV grafts or central venous occlusion. The other 14 patients had ongoing bacteremia and sepsis from nonsurgical causes and placement of a new prosthetic AV graft was contraindicated. Ten other patients had multiple failed AV grafts, and a "last ditch" placement with a cryopreserved femoral vein, into a compromised venous outflow tract, was attempted.

The 12-month primary patency rate was 49% with a 75% secondary patency rate (Figs. 5 and 6),[17] which is similar to other reported primary and secondary patency rates for prosthetic AV grafts.[19–21] These initial results demonstrate that cryopreserved femoral vein AV grafts are reasonably durable and can be successfully salvaged using standard thrombectomy and graft revision techniques. It is of interest to note that when a stenosis developed at the distal end of the cryopreserved femoral vein graft, it spared the native axillary vein which usually remained patent. This is quite a different pattern than the often-reported venous stenosis that occurs with prosthetic AV graft failures. In our experience, if the cryopreserved femoral vein graft ultimately failed, another prosthetic AV graft may be placed with a low risk of infection.[17]

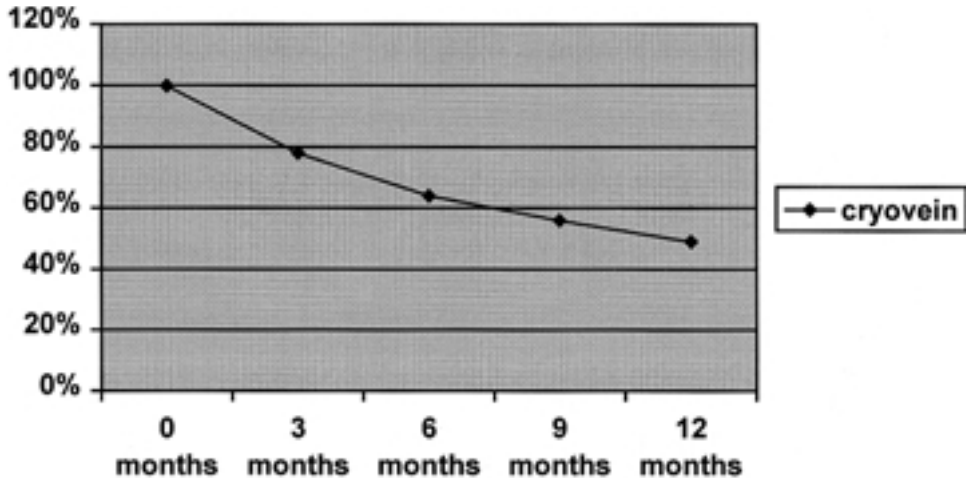

Fig. 5 Primary patency of the cryopreserved femoral vein AV graft.

The most significant finding from this study was the absence of subsequent infection in follow-up extending to 3 years in the cryopreserved femoral vein group.[17] Despite 82% of our patients presenting either with an infected AV graft, bacteremia, or sepsis, *none* of the cryovein implants became infected. Seventy seven percent of the infected prosthetic AV grafts in this study cultured gram positive organisms: 50% *Staphylococcus aureus* and 27% *Staphylococcus epidermidis.* Experience, therefore, is limited with the use of

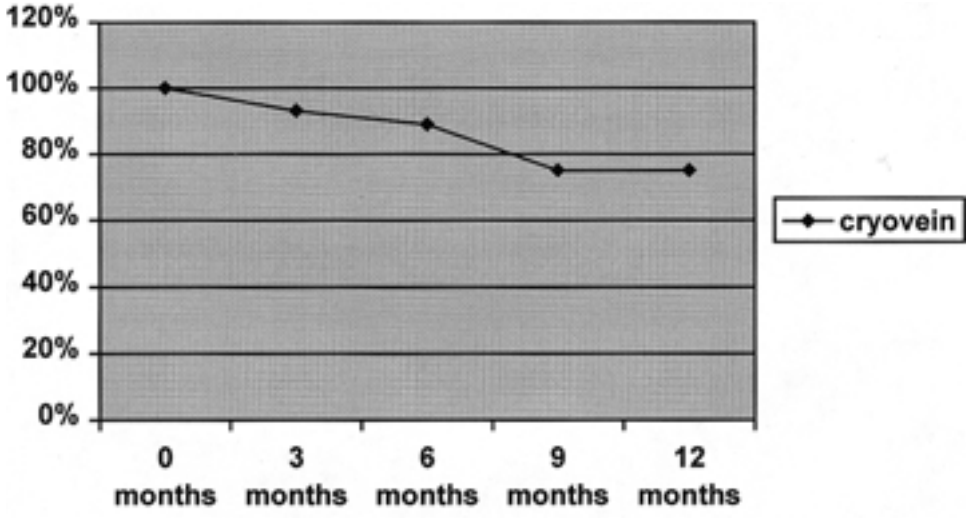

Fig. 6 Secondary patency of the cryopreserved femoral vein AV graft.

cryopreserved femoral vein grafts in the presence of more virulent gram negative infections. Nevertheless, based on these results, we believe that a cryopreserved femoral vein may be safely implanted in the presence of infections with a low risk of recurrent infection. Ongoing studies on the ability of cryopreserved femoral vein to withstand more virulent bacterial pathogens will hopefully demonstrate the ultimate role of these grafts.

COST ISSUES ON THE USE OF CRYOPRESERVED ALLOGRAFTS

In this era of healthcare finance constraints, an issue that must be addressed is the cost of the cryopreserved femoral vein which is $2500. To offset this cost, one must analyze the course of treatment for a patient with an infected AV graft. At operation, the infected prosthetic AV graft must be excised and due to the high risk of reinfection if a new PTFE graft was placed, even in a remote location, a long-term dialysis catheter is often necessary. Subsequent outpatient procedures, therefore, are required with this conventional graft excision therapy adding additional costs for the patient and the hospital. With the cryopreserved femoral vein graft, however, it may be placed at the time of the infected AV graft excision and accessed 10 days later, thus saving the patient another operation and hospitalization.

To evaluate this concept, a study of 33 patients was performed: 20 patients underwent cryopreserved femoral vein implantations for prosthetic AV graft infection compared with 13 patients who had infected prosthetic AV grafts excised with placement of long term hemodialysis catheters.[22] The hospital length of stay for the cryopreserved femoral vein treated patients averaged 2.4 days (range 1 to 11 days) compared with 8.1 days (range 1 to 22 days) for the graft excision and dialysis catheter group.[22] Wound care and sepsis delayed hospital discharge in both groups, however, the increased hospital length of stay in the graft excision group was because of the need for daily systemic antibiotics to "sterilize" the bloodstream prior to placement of a long-term hemodialysis catheter and subsequent prosthetic AV graft. In our institution, the cost of a surgical floor bed is $310 per day, a dialysis catheter placement in the radiology suite is $610, an outpatient AV graft procedure hospital cost is $2100 and a PTFE graft costs $395. This $3415 hospital cost is readily offset by an avoidance of a subsequent PTFE graft placement after resolution of infection and bacteremia. A cryopreserved femoral vein AV graft, however, offers the advantage of a shortened hospital length of stay by avoiding continuous intravenous antibiotics to "sterilize" the bloodstream prior to placement of a dialysis catheter and/or AV graft, the benefit of a durable graft that will avoid a recurrent graft infection, and the probability that the cryopreserved femoral vein will become the most appropriate and cost-effective treatment for AV graft infections.

CONCLUSION

Cryopreserved femoral vein is an appropriate alternative conduit in the treatment of infected hemodialysis grafts. The 12-month primary patency rate of 49% and secondary patency rate of 75% for the cryopreserved femoral vein demonstrates similar durability to PTFE AV grafts. No cryopreserved femoral vein grafts developed subsequent graft infections. After excision of an infected AV graft, it is often necessary to "sterilize" the bloodstream, prior to placement of an indwelling dialysis catheter and other prosthetic graft. Placement of a cryopreserved femoral vein allows access of the graft within 10 days and avoids the necessity for prolonged intravenous antibiotic treatment, shortening the hospital length of stay. The cryopreserved femoral vein offers the advantages of an infection resistant, durable conduit that may become the most efficacious and cost-effective treatment for AV graft infection.

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Expert Commentary

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The use of allograft vascular conduits has fascinated surgeons for almost a century. They offer the potential benefits of living tissue compared with their prosthetic counterparts. Despite this acute interest, however, allografts have yet to find a routine place in the daily practice of vascular surgery. As noted by the authors, the early experience with allografts showed them to be prone to later degeneration into aneurysms. Use of allografts as bypass conduits has been disappointing, with the grafts proving to be prone to frequent early failure.[1–3] The causes of graft failure are no doubt multifactorial, but rejection has been identified as a major contributor. Both humoral and cell-mediated responses have been identified.[4] For infrainguinal grafts at least, low dose immunosuppression is not adequate to forestall this response and prevent graft occlusion,[5] and few are willing to accept the risk of high dose immunosuppression to achieve graft patency.

That the grafts themselves are in fact living tissue even after cryopreservation, has been well documented.[6–9] The grafts remain alive with the passage of time if they remain patent. It would appear that the allograft tissue itself becomes replaced by recipient cells with the passage of time. Explanted allograft bypass grafts demonstrate either complete replacement by host cells or a mosaic of donor and recipient cells.[10] The graft is not a passive collagen tube but a living dynamic structure that continues to express procoagulant and anticoagulant factors and demonstrate an endothelial lining.

Their living tissue quality presumably accounts for their resistance to infection when compared with prosthetic grafts. It would appear from the work by Matsuura et al.[11] that this well documented attribute of allograft vein conduits applies to hemodialysis applications as well. Some have even used allograft artery or vein for in situ replacement of infected prosthetic grafts rather than the "extra-anatomic" routing advocated by the authors. The grafts demonstrate comparable patency with that of their prosthetic counterparts, even without the use of anticoagulation or immunosuppression. The approach would appear to be cost-effective despite the high cost of the graft itself as the overall length of stay for these patients is reduced. This may ultimately prove to be the single most prevalent niche indication for use of allograft bypass grafts.

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The Last Word

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We want to thank Dr. Carpenter for his comments. The viability of the cells within the cryopreserved allografts must play an important role in the resistance of these vascular conduits to infection. Like any tissue or organ transplant, these allografts are prone to an immune response. We have not seen any complications related to acute rejection, and the patency rates are similar to PTFE. We feel the larger diameter and the high flow/low resistance characteristics of this hemodialysis conduit are important factors in our improved patency rates.