



Perfusion Assessment with the SPY System after Arterial Venous Reversal for Upper Extremity Ischemia

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Background: The timing and pattern of reperfusion following arterial-venous reversal (AVR) in patients with terminal ischemia of an upper extremity is not well understood.

Methods: The current case series describes the timing and pattern of reperfusion observed in patients with terminal upper extremity ischemia who underwent AVR and repeated postoperative indocyanine green (ICG) angiography between 2004 and 2009. For all included patients, the SPY Near-Infrared Perfusion Assessment System permitted visualization of ICG-labeled blood flow for 60-second sampling periods at scheduled postoperative time points; outflow and rate and amplitude of inflow were objectively quantified with SPY-Q Analysis Toolkit image analysis software.

Results: The series comprised 6 male patients (mean age, 46 years) who presented with upper extremity ischemia related to hypothenar hammer syndrome ($n = 2$), embolism with patent foramen ovale ($n = 2$), atherosclerosis ($n = 1$), and avulsion amputation of the thumb ($n = 1$); the patient with the avulsion amputation was diagnosed with thromboangiitis obliterans at the time of replantation. AVR was successful in all 6 patients. In 5 of 6 patients, ICG angiography and SPY-based visualization/quantification showed that venous outflow and arterial inflow gradually normalized (versus unaffected digits) between postoperative days (PODs) 0 and 3 and was maintained at long-term follow-up (≥ 3 months); for the patient who underwent thumb replantation, perfusion normalized between POD 3 and month 5 follow-up.

Conclusions: AVR effectively reestablished blood flow in patients with terminal upper extremity ischemia. ICG angiography with SPY technology revealed that, in most cases, kinetic curves, timing, and patterns of perfusion gradually normalized over several PODs. (*Plast Reconstr Surg Glob Open* 2014;2:e185; doi: 10.1097/GOX.000000000000138; Published online 22 July 2014.)

Terminal ischemia of the upper extremity is challenging for the reconstructive surgeon and, if untreated, results in ulcer formation and eventual amputation. The diffuse nature of this disease often precludes focal endovascular interventions such as angioplasty, stenting, or thrombectomy and extravascular interventions such as resection

and reconstruction. Lack of a distal arterial target precludes effective bypass grafting. In this situation, a salvage procedure, venous arterialization or arterial-venous reversal (AVR), has been used.¹ With AVR, the healthy venous system is used to convey oxygenated blood past the diseased arterial system and retrograde into the poorly perfused capillary bed.

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Once in the arterial system, flow can then move antegrade back into the venous system. Although the efficacy of AVR has been described,²⁻⁵ the anecdotal nature of such reports, the small number of patients involved, and poor understanding of the physiology of this unconventional approach have limited its widespread adoption.

Insuring adequate reperfusion of the affected region is a matter of primary importance when managing patients with terminal ischemia and a potentially unsalvageable limb. With AVR for such cases, the timing and pattern of reperfusion is not well understood. The SPY Near-Infrared Perfusion Assessment System (distributed by LifeCell Corp., Branchburg, N.J.; manufactured by Novadaq Technologies Inc., Richmond, BC, Canada), which utilizes indocyanine green (ICG), is an imaging technology that allows real-time visual assessment of superficial blood flow. The ICG fluorescent molecule binds tightly to serum lipoproteins in the intravascular space, making its fluorescence an excellent marker for blood flow. Additional SPY software (SPY-Q Analysis Toolkit, distributed by LifeCell Corp.; manufactured by Novadaq Technologies Inc.) allows for quantitative analysis of blood flow based on ICG fluorescence intensity. Surveillance of tissue perfusion using ICG fluorescence has been validated over a number of years in numerous clinical situations, including breast reconstruction, abdominal wall reconstruction, head and neck reconstruction, and gastrointestinal procedures.^{6,7} The current report describes a series of 6 patients with terminal ischemia of an upper extremity for which ICG surface angiography was used to define the timing, pattern, and completeness of reperfusion after AVR was performed.

METHODS

This was a retrospective review of patients with upper extremity terminal ischemia for which AVR was performed between 2004 and 2009. All procedures were performed by the same surgeon at a

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single center. Patient charts were reviewed to define patient demographics, cause of ischemia or initiating disease, and timing, pattern, and completeness of revascularization after AVR.

AVR was performed as previously described by Pederson.⁸ In general, once the region of ischemia was defined, a LeMaitre valvulotome (LeMaitre Vascular, Burlington, Mass.) was used to destroy valves to the bases of the fingers in the affected area. Non-contributory vein branches were ligated to avoid venous hypertension in the nonischemic, normally perfused portion of the hand. AVR was performed by transposing and repairing a dorsal vein end-to-side or end-to-end to a flowing artery proximal to the level of occlusion (Fig. 1). Although end-to-end repair is technically easier, these involved vessels are typically large enough so that similar patency rates can be achieved with end-to-end and end-to-side repairs. An end-to-side repair is more likely to maintain patency of small arterial branches in the vicinity of the anastomosis and can be converted to an end-to-end repair if there is a problem.

ICG angiography utilizing the SPY system was used to measure surface perfusion in the target area of the affected extremity after AVR and in an unaffected control digit. It allowed a real-time, uninterrupted, 60-second “digital video snapshot” of the progression of surface perfusion. ICG angiography digital images were captured for the target and control regions intraoperatively before AVR (baseline), intraoperatively immediately after AVR postoperative day 0 (POD 0), and on POD 1 and POD 3 at the bedside. At long-term follow-up (≥ 3 months), ICG angiography was performed to determine the continued efficacy of revascularization. Clinical monitoring of perfusion also included assessment of color, turgor, warmth, and capillary refill every 2 hours in the transitional care intensive care unit during the first 24 hours postoperatively and then every 4 hours until discharge. External pen Doppler examination was also performed at these intervals and at the long-term follow-up visit to assess ongoing patency of flow reversal in the bypass vein.

All patients received a 5-day course of intravenous dextran-40 at 25 mL/h starting at the time of AVR completion. The first patient in the series received an additional 5-day course of therapeutic intravenous heparin and therapeutic oral warfarin for 2 weeks after discharge. The heparin and warfarin components of the regimen were eliminated for subsequent patients.

SPY Near-infrared Perfusion Assessment

At each scheduled assessment time point, ICG (2.5 mg/mL) was administered via an intravenous bolus through a peripheral line followed by a 10 mL

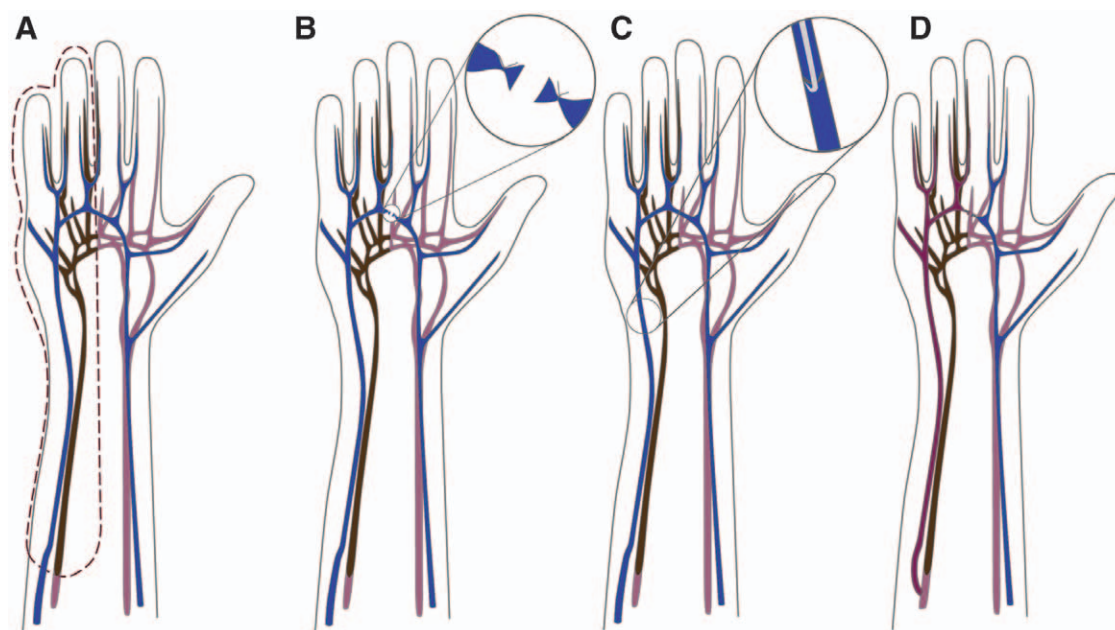


Fig. 1. Diagrammatic representation of an AVR. Note that the ulnar artery is occluded from the forearm to the distribution of the digital arteries at the fourth and fifth digits. The dotted line illustrates the region of poor arterial flow (A). Noncontributory veins or those whose flow are outside of the region requiring arterialization are ligated (B). A valvulotome is used to disrupt valves and allow retrograde flow (C). The dorsal vein is then transposed and repaired to a healthy artery proximal to the occlusion arterializing the venous system and providing flow to the ischemic capillary beds (D).

flush of normal saline. The SPY near-infrared laser diode array was used to excite the ICG molecules. The coupled high-definition camera was used to monitor and record the real-time video of fluorescence on the skin surface. The $18.5 \times 13.5 \text{ cm}^2$ study area allowed simultaneous visualization and comparison of the treatment and control regions. Additionally, static digital images of the fluorescence pattern were captured every 4 seconds over a total sampling period of 60 seconds. Utilizing the SPY software (SPY-Q Analysis Toolkit), kinetic curves illustrating the rate of inflow, outflow, and peak amplitude of the fluorescence at the fingertips were created. Data from all 6 patients were used to calculate average kinetic curves, timing, and patterns of perfusion; these parameters were compared between the treated target area and the unaffected control area.

RESULTS

Between 2004 and 2009, a total of 6 patients underwent an upper extremity AVR and were included in the current case review. Demographic and clinical characteristics are summarized in Table 1. All patients were male. Five patients complained of worsening cold intolerance, rest pain, and color changes in their digits at the time of presentation. Preoperative angiography helped confirm the absence of distal arterial targets for conventional bypass surgery in these patients and was the basis for their referral for microsurgical evalu-

ation. The sixth patient presented with acute crush avulsion amputation of his left thumb at the proximal phalangeal level. AVR was required for this patient due to Buerger's disease (thromboangiitis obliterans) identified at the time of thumb replantation.

All AVR procedures were successful. Five patients had resolution of cold intolerance and rest pain at POD 1. The patient with thumb replantation had no sensation at POD 1 and could not be similarly evaluated. Postoperative swelling occurred in all patients and resolved completely by 2 weeks. There were no

Table 1. Demographic and Clinical Characteristics of AVR Patients

Characteristic	Patients (N = 6)
Age, mean (range), y	45 (38–56)
Male, n (%)	6 (100)
Race, n	
White	5
Polynesian	1
Ischemia etiology, n	
Hypothenar hammer syndrome	2
Embolicism with patent foramen ovale	2
Atherosclerosis	1
Avulsion amputation of thumb with underlying thromboangiitis obliterans	1
History/comorbid factors	
Deep venous thrombosis (prior)	1
Hypertension	1
Insulin-dependent diabetes mellitus	1
Tobacco smoker	1

complications associated with utilizing the ulnar or radial artery. At POD 3, the emergence of venous egress or outflow was noted in all patients except the patient with thumb replantation. At the long-term follow-up visit (≥ 3 months), all 6 patients had reperfusion and patency of their bypass veins determined by ICG angiography and Doppler, respectively. The pattern of reperfusion was similar in all patients. The averaged kinetic curves of treated digits and control digits are illustrated in Figure 2.

Case Examples

Case 1 involved a 45-year-old motorcycle mechanic diagnosed with ulnar hypothenar hammer syndrome who was referred by a vascular surgeon with worsening rest pain, cold intolerance, and intermittent white or blue discoloration (Fig. 3). Arteriogram revealed significant ulnar artery thrombosis. There was no evidence of a hamate or other wrist bone fracture. Laboratory findings included normal complete blood counts and coagulopathy workup. Surgical exploration confirmed a lack of distal arterial targets for bypass graft. AVR was performed utilizing the basilic vein transposed to the ulnar artery proximal to the occlusion. Immediate (POD 0) ICG angiography revealed improvement from baseline in the level of perfusion, but incomplete perfusion or arterial insufficiency at the fingertip at 60 seconds

(Fig. 4). At POD 1, arterial insufficiency was resolved; flow reached the fingertip within the 60-second assessment period; however, the rate and amplitude of inflow was reduced relative to the control area evaluated (See video, Supplemental Digital Content 1, which displays arterial insufficiency resolved at POD 1. ICG fluorescence now reaches the fifth fingertip at approximately 15 seconds and peaks at 45 seconds. This video is available in the “Related Videos” section of the Full-Text article on PRSGo.com or available at <http://links.lww.com/PRSGO/A42>). There was no egress or venous outflow in the 60-second period. POD 3 was characterized by continued increase in the rate and amplitude of inflow, peak amplitude similar to that observed in the unaffected control area, and, for the first time, the beginnings of venous outflow (See video, Supplemental Digital Content 2, which shows continued increase in the rate and amplitude of inflow and peak amplitude similar to the unaffected control area. These trends persisted at long-term follow-up, with normalization of rate of inflow and rate and amplitude of outflow, with amplitude approximating control digit values. This video is available in the “Related Videos” section of the Full-Text article on PRSGo.com or available at <http://links.lww.com/PRSGO/A43>). Long-term evaluation showed persistence of these trends with normalization of rates of inflow and outflow, with peak amplitude approximat-

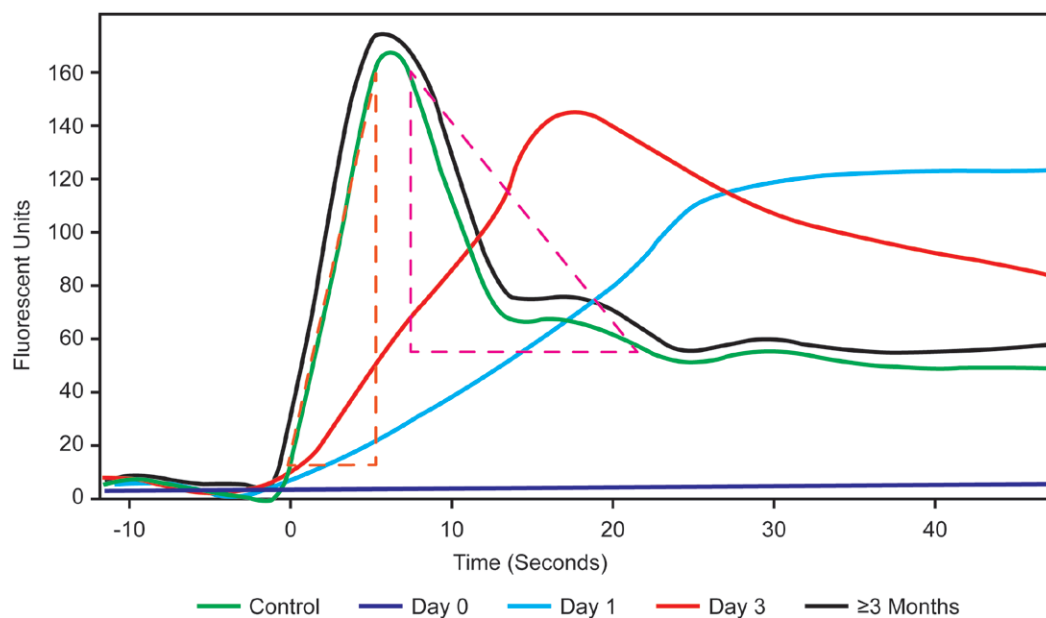


Fig. 2. Average kinetic curves for ICG detected at the control and treatment fingertips at POD 0, POD 1, POD 3, and long-term follow-up. Broken line triangles represent the slope or rate of inflow (orange) and outflow (pink) for the control kinetic curve. The average kinetic curves of the treatment fingertips illustrate arterial insufficiency or lack of inflow at POD 0. This is followed by progressive improvement in the rate of arterial inflow at POD 1 and 3 with normalization approximating the control on long-term follow-up. Venous insufficiency or lack of outflow marks POD 1 but begins to resolve in 5 of 6 patients by POD 3. The increased rate of outflow noted at POD 3 is associated with the trend toward improved inflow rate and amplitude. Rate of inflow, outflow, and amplitude normalize by 3 months.

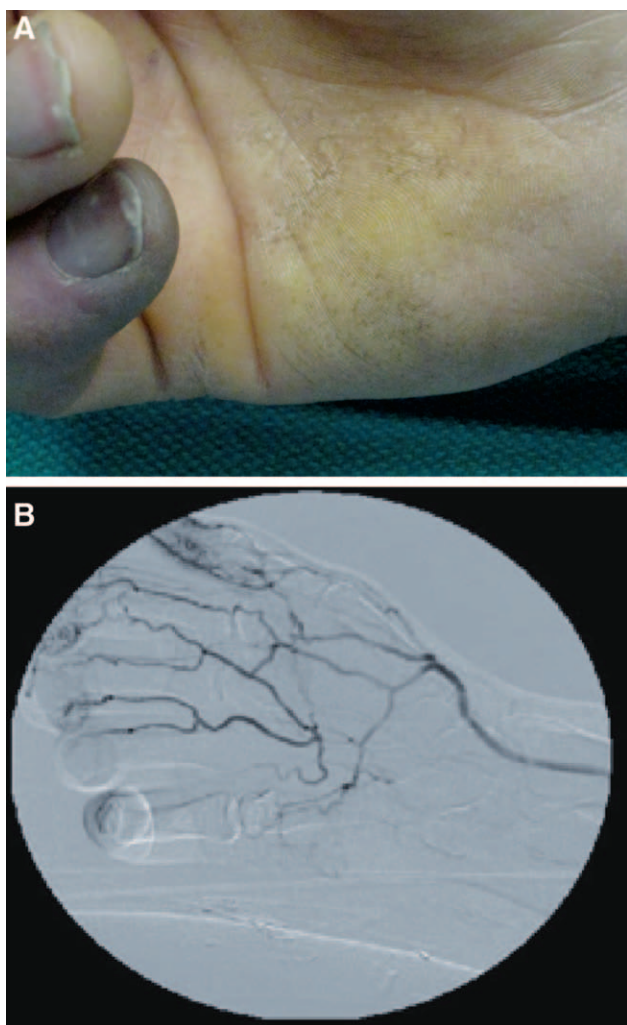


Fig. 3. Case 1. Left fifth cyanotic finger (A) and angiogram revealing significant ulnar artery and deep and superficial arch occlusion without sufficient compensation from the superficial arch from the radial artery to support the fifth digit (B). The fourth digit is perfused by flow from the radial artery to the residual superficial arch. There is no target for potential bypass grafting.

ing values seen in control digits. Color and capillary refill could not be distinguished clinically between treated and control digits (Fig. 5). The timing and pattern of AVR-induced reperfusion observed for the other nonreplant patients in this series were consistent with those seen in case 1.

Case 2 involved a 53-year-old big-rig tire installer with a 20 pack-year smoking history who was referred for replantation of his left thumb following its acute crush avulsion amputation at the proximal phalangeal level caused by a metal wheel part while at work. He was taken to the operating room for the purpose of replantation of the amputated thumb. Exploration revealed luminal occlusion of both digital arteries throughout their course. Subsequent histology

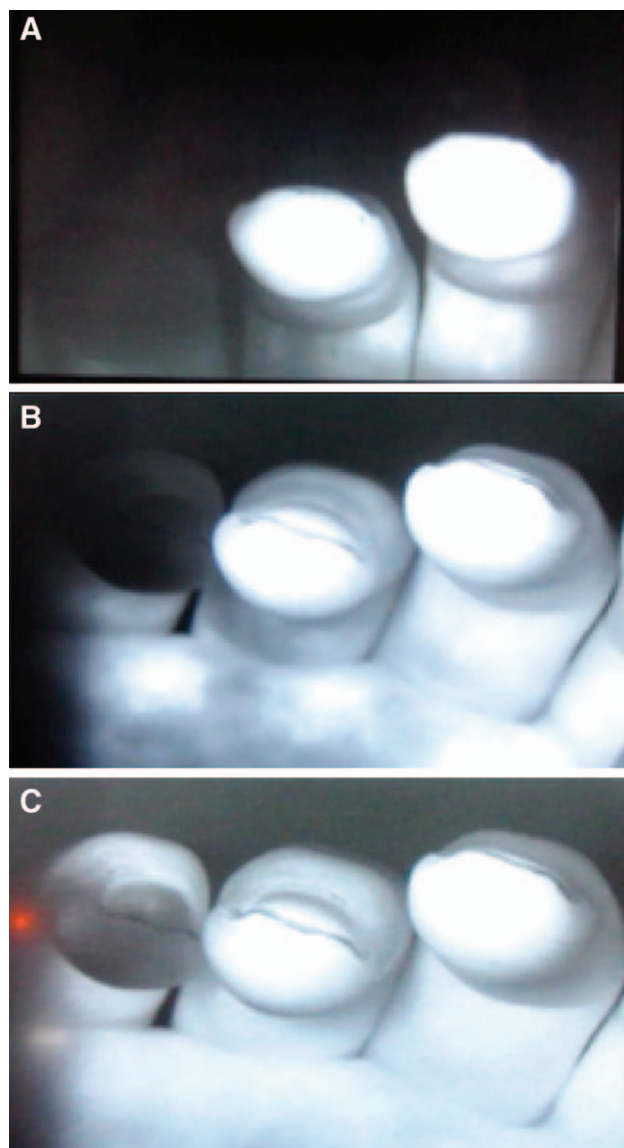
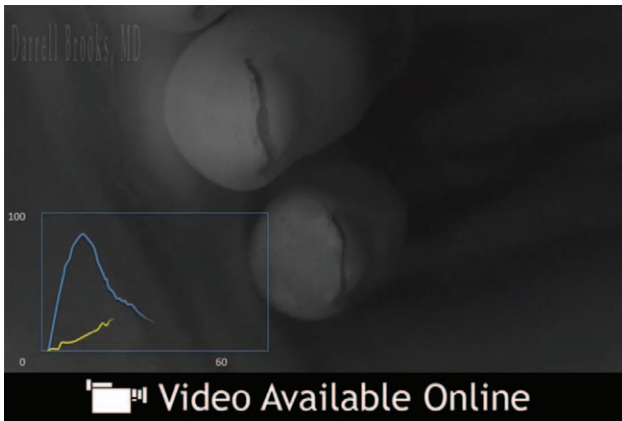


Fig. 4. Case 1. ICG fluorescent angiograms illustrating the 60-second perfusion of the hand prearterialization (A), 30 seconds postarterialization (showing improvement in the level of inflow; B), and 60 seconds postarterialization (showing continued improvement but persistent arterial insufficiency at the fingertip at POD 0; C). Note the persistent fifth finger arterial insufficiency at 60 seconds.

revealed fibroluminal stenosis with central vascular recanalization consistent with late thromboangiitis obliterans (Fig. 6). In this patient, AVR provided blood flow through the dorsal venous system (Fig. 7) achieved via bypass graft from the dorsal radial artery to a dorsal vein located at the proximal radial aspect of the replanted portion of the thumb. Venous outflow was restored by repair of a dorsal vein at the ulnar midaxillary line of the thumb. The crossing branches between these vessels were clipped to decrease blood flow rerouting away from the distal thumb capillary



Video Graphic 1. See video, Supplemental Digital Content 1. Case 1: Video shows arterial insufficiency resolved at POD 1. ICG fluorescence now reaches the fifth fingertip at approximately 15 seconds and peaks at 45 seconds. This video is available in the “Related Videos” section of the Full-Text article on PRSGo.com or available at <http://links.lww.com/PRSGO/A42>.

beds. The timing and pattern of reperfusion was similar to the other patients presented in this series except that there was no evidence of venous outflow or venous sufficiency by POD 3 based on ICG angiography. The patient did not return for long-term follow-up with SPY angiography until month 5. At that time, not only did Doppler evaluation reveal continued patency of the arterialized dorsal vein, but repeat ICG angiography revealed maturation of arterial and venous flow dynamics [completion of a leftward shift of the thumb’s kinetic curve mirroring that of its control (Fig. 8) and real-time visual fluorescent patterns and



Video Graphic 2. See video, Supplemental Digital Content 2. Case 1: Video shows continued increase in the rate and amplitude of inflow and peak amplitude similar to the unaffected control area. These trends persisted at long-term follow-up, with normalization of rate of inflow and rate and amplitude of outflow, with amplitude approximating control digit values. This video is available in the “Related Videos” section of the Full-Text article on PRSGo.com or available at <http://links.lww.com/PRSGO/A43>.

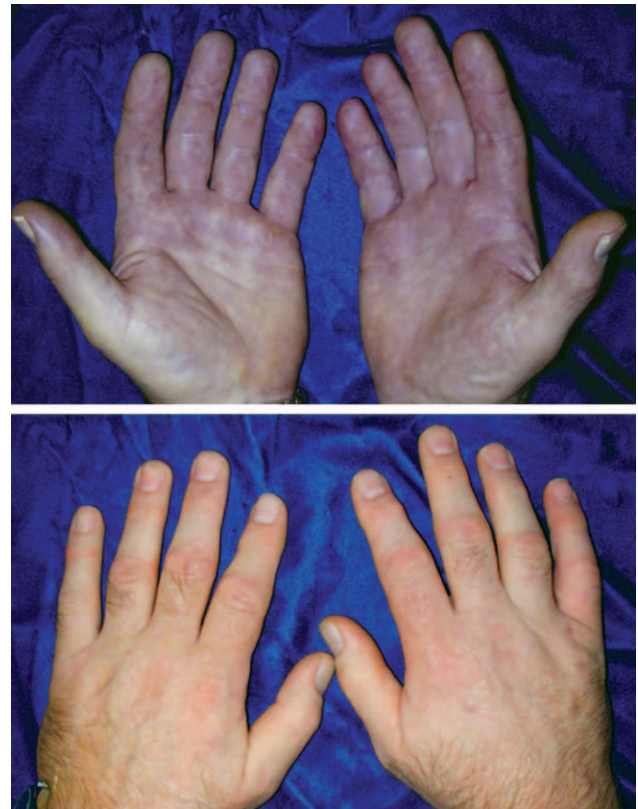


Fig. 5. Case 1. Three months after AVR, no signs or symptoms of arterial or venous insufficiency have returned.

timing making the arterialized digit indistinguishable from the control digit (See video, Supplemental Digital Content 3, which shows that Doppler evaluation of the arterialized dorsal vein revealed patency. This video is available in the “Related Videos” section of the Full-Text article on PRSGo.com or available at <http://links.lww.com/PRSGO/A44>; See video, Supple-

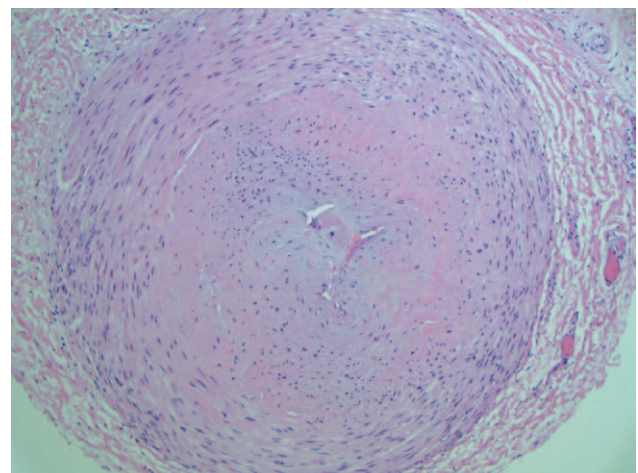


Fig. 6. Case 2. Hematoxylin and eosin stain of a representative histological section of the digital arteries revealing fibro-luminal stenosis with central vascular recanalization consistent with late thromboangiitis obliterans.



Fig. 7. Case 2. Two weeks after replantation by AVR, the thumb has complete soft-tissue survival, good color, and resolution of swelling.

mental Digital Content 4, which shows similar peak amplitudes and simultaneous rates of arterial inflow and venous outflow consistent with normalization of the kinetic curves and maturation of the vascular circuits. This video is available in the “Related Videos” section of the Full-Text article on PRSGo.com or available at <http://links.lww.com/PRSGO/A45>].

DISCUSSION

Although AVR has been shown to be an effective approach to terminal ischemia of the upper extremity,²⁻⁵ no study has given insight into the timing and pattern of reperfusion after AVR. In the current series of patients, assessment after AVR with ICG angiography visualized using the SPY system along with the SPY-Q software not only allowed real-time visualization of the reperfusion pattern but also quantified reperfusion in terms of rates of inflow, outflow, and peak amplitude.

As has been established in a wide variety of intraoperative settings,^{6,7} postoperative ICG angiography using the SPY system proved a reliable means of precisely visualizing blood flow and quantifying inflow and outflow rate and amplitude in the current series of patients. Prior reports (and the current series) have also documented the validity of using perfusion kinetics derived from SPY-Q software, in which perfusion within the target area is compared with that within an unaffected nearby control area of tissue, yielding accurate evaluations of vascular patency and perfusion sufficiency.⁹ A major benefit of this system compared with other monitoring techniques is the

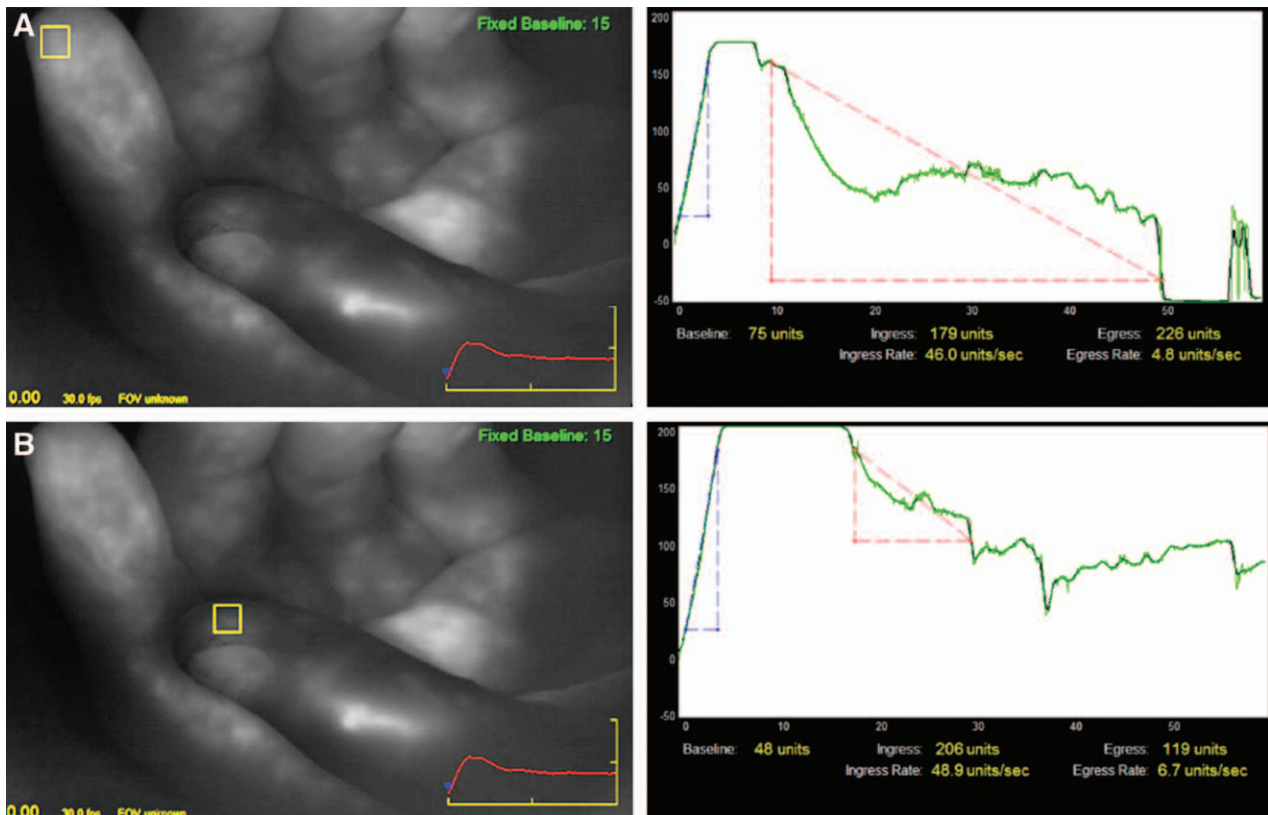


Fig. 8. Case 2. Kinetic curves obtained 5 months after AVR for the control index finger (A) and the thumb (B) replanted by AVR. Yellow boxes define the study area for each digit. Note the comparable inflow and outflow rates. Real-time visual appreciation of the pattern and timing of the inflow and outflow circuits not only illustrates the normalization of flow kinetics in the arterialized thumb but also demonstrates the utility of the SPY technology.



Video Graphic 3. See video, Supplemental Digital Content 3. Case 2: Video shows that Doppler evaluation of the arterialized dorsal vein revealed patency. This video is available in the “Related Videos” section of the Full-Text article on PRSGo.com or available at <http://links.lww.com/PRSGO/A44>.

real-time visualization that it allows. In addition, the SPY system allows a global ability to monitor an entire area rather than a limited spot.

The present findings indicate that AVR does not result in immediate restoration of flow into the capillary bed, but instead gradual development of arterial sufficiency, followed by venous sufficiency, and finally a normal perfusion pattern. The gradual changes documented by the blood flow kinetic curves obtained in this series of patients may represent the maturation of flow from the bypass vein into the arterial system and then back into the venous system. Such angiography on POD 0 revealed a pattern of improved creeping flow in the skin without a direct entry into the arterial system, at least not to the extent that would allow flow to the fingertip in a 60-second period. By POD 1, arterial insufficiency was resolving, with increased inflow kinetics and amplitude. This may mark the maturation of pathways from the vein to the capillary beds. Clinically, this was accompanied by resolution of rest pain on POD 1. Between POD 1 and POD 3, there was an emergence of venous outflow, possibly marking maturation of flow from the arterial to venous systems. From previous work involving perfusion patterns after replantation,¹⁰ we know that venous outflow has a direct impact on the rate and amplitude of arterial inflow; low or insufficient venous outflow decreases arterial inflow rate and amplitude. In line with this, we observed that as venous insufficiency resolved on POD 3, arterial inflow and amplitude also similarly improved. Between POD 3 and long-term follow-up (≥ 3 months), there was normalization of the venous and arterial kinetics relative to perfusion kinetic curves observed for an unaffected control area in the same patient. At some point in this recovery period, flow into the arterial and out of the venous channels matured and became comparable with that seen in unaffected digits.



Video Graphic 4. See video, Supplemental Digital Content 4. Case 2: Video shows similar peak amplitudes and simultaneous rates of arterial inflow and venous outflow consistent with normalization of the kinetic curves and maturation of the vascular circuits. This video is available in the “Related Videos” section of the Full-Text article on PRSGo.com or available at <http://links.lww.com/PRSGO/A45>.

The phenomenon of maturation of flow from the arterial to venous systems we observed is not unprecedented. Arterialized venous flaps are another example of tissue perfused by an unconventional vascular circuit.¹¹ Similar to AVR, the arterialized venous flap uses arterial flow into the venous system, which in turn serves as an eventual conduit into the capillary system. Theories regarding how this unconventional vascular pathway works include the concept of “reverse flow,”¹² in which it is proposed that flow progresses from vein to the venules and then continues retrograde into the capillary beds. Such systems may also achieve perfusion via “arterial-venous shunting,”¹³ where flow travels retrograde through incompetent arterial-venous shunts from the veins to the arterioles and then antegrade into the capillary beds.

That venous insufficiency began to resolve in all patients except the patient with the replanted thumb by POD 3 could be explained by the fact that only 1 outflow vein was repaired in the replanted thumb. Theoretically, maturation of flow into 1 outflow vein might be more difficult in this situation and take longer to mature. This is in contrast to the other patients in whom multiple normal outflow veins still existed. Venous insufficiency resolved in the replanted thumb with maturation of flow through the repaired vein or with the healing of veins in the periphery sometime between POD 3 and ≥ 3 months.

Swelling, which lasts approximately 2 weeks, marks the postoperative course of arterialized venous flaps. This is similar to observations in our study and those reported in the literature.⁸ This could represent tissue reaction during the vascular channel maturation period.

Use of the SPY system altered the author's appreciation of what was occurring postoperatively regarding flow. Seeing the initial perfusion and then reaching the expected milestones of perfusion allowed decision making with confidence. The ability to confirm existence and improvement of flow allowed subsequent adjustment in the conservative anticoagulation regimen used with the initial case. Experience with the SPY system can allow the surgeon to develop flow dynamic expectations. We may potentially decrease our protocol interventions and get the patient home earlier in cases where such expectations are met. If such expectations are not met in a case, however, the surgeon may decide to increase anticoagulation or prolong hospitalization. The use of the SPY system has been beneficial in cases such as AVR, as reported here, and should be evaluated regarding additional possible applications in assessing reperfusion on a microsurgical ward.

There are myriad causes of ischemia of the upper extremity, as detailed by Pederson and Neumeister.¹⁴ This study dealt with only 3 of these: embolic (4 patients), atherosclerotic (1 patient), and thromboangiitis obliterans (1 patient). Although AVR has been shown to be effective in other chronic causes of upper extremity ischemia such as peripheral arterial disease, vasculitis, insulin-dependent diabetes mellitus, and lupus erythematosus, the timing and perfusion characteristics in this study may not be representative of those disease processes. The relatively healthy venous and capillary systems in our patients contributed to the efficacy and consistency of AVR in this series. Although AVR may be less effective in other situations in which the venous or capillary systems are more involved in the disease process, this salvage technique may still represent the patient's only alternative to amputation. Patient expectations need to be managed accordingly in such cases. SPY angiography may play an even greater role in these populations, possibly directing anticoagulation and duration of hospitalization. Additional study of the timing and perfusion patterns in these patients is required.

CONCLUSIONS

AVR was a valuable and effective technique for the current series of 6 patients with terminal ischemia and an otherwise unsalvageable portion of the upper extremity. Repeated ICG angiography using the SPY system over the postoperative recovery period permitted description of the timing and pattern of perfusion after AVR. This information is key for establishing our expectations for postoperative recovery in patients who undergo this procedure. This unique window into the progression of flow into the capillary bed and out of the venous system increases our understanding of AVR physiology and may hopefully encourage surgeons to use this technique not

only as salvage when no other approach is possible, but also in cases where AVR might be technically less demanding and more reliable than traditional bypass procedures to small distal arterial targets in the hand.

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