Techniques in Vascular and Interventional Radiology

Sclerotherapy with Adjunctive Stasis of Efflux (STASE) in Venous Malformations: Techniques and Strategies

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Venous malformations are very commonly encountered in interventional radiologic practice. Indications for therapy are clearly defined based on the lesion's impact on patient's quality of life. Screening laboratory coagulation studies in patients with historical or lesion morphologic risk factors often reveal abnormal coagulation parameters consistent with localized intravascular coagulation or more severe coagulopathic states. These may require chronic or periprocedural medical management to avoid potentially life-threatening disseminated intravascular coagulation or other thromboembolic phenomena. Once a multidisciplinary decision to treat a venous malformation is made, one must decide between percutaneous and/or surgical techniques. Sclerotherapy with adjunctive stasis of efflux (STASE) techniques have become the mainstay of therapy for most venous malformations as they are well-tolerated and effective. STASE techniques work primarily by (i) the administration of sclerosant(s) exerting an inhibitory and/or endotheliocidal effect on venous malformation endothelium leading to thrombosis, involution, and fibrosis, and secondarily via adjunctive outflow occlusion using any combination of local compression, balloons, gelatin, coils, laser, radiofrequency, or adhesives to improve sclerosant penetration and dwell-time in the lesion. Adhesives alone can fill the lesion to facilitate surgical resection in some cases. Common sclerosants in modern practice include sodium tetradecyl sulfate, bleomycin, polidocanol, ethanol, and hypertonic saline. Most agents can be given directly in unmodified or "neat" form or can be mixed with a gas to form a sclerofoam or embolic such as gelatin to form a sclerogel. Choice and method of sclerosant delivery in each patient is based on the intraluminal lesion volume, architecture, vital structure proximity, agent toxicity, viscosity, and level of experience of the interventional radiologist with that particular agent. Multi-session STASE therapy usually reduces symptoms of chronic pain or mass with low risk of known complications of skin or nerve impairment, compartment syndrome, hemoglobinuria, deep venous thrombosis, or pulmonary phenomena.

KEYWORDS Venous malformation, Low-flow malformation, Vascular anomalies, Sclerotherapy, Embolization, STASE

The following discussion is primarily intended to acquaint the interventional radiologist with the rationale and physical concepts supporting the full spectrum of sclerotherapy with adjunctive stasis of efflux (STASE) techniques and strategies in the treatment of venous malformations. Diagrammatic illustrations accompany or represent case images wherever possible as angiographic snap-shots alone are often unable to completely demonstrate the multiple underlying steps of a dynamic process. This will be preceded by a brief overview of preprocedure medical management issues relevant to the interventionalist. Hopefully, the broader exposure and incorporation of these techniques and practices will provide the

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interventional radiologist greater facility and flexibility in making the appropriate intraprocedural decisions best suited to the individual venous malformation and the patient.

Clinical Presentation and Evaluation of the Patient

Venous malformations are the most common of all vascular anomalies seen in referral.[1] With a prevalence of over 1%, it is inevitable that a referral for a vascular anomaly will come to *every* interventional radiologist.[2,3] Depending one's local practice milieu, referral for a venous malformation will usually come from a medical specialty such as vascular, plastic or orthopedic surgery, dermatology, or hematology.[4] As one becomes established, an increasing number of referrals will come from primary care practitioners. It is essential in any patterns of referral that patient evaluation must be made to incorporate a multidisciplinary group of physicians in that institution or group of institutions that are well-versed in the current classification, diagnosis, and multidisciplinary management of all vascular anomalies.[4,5] This cannot be stressed enough.[6]

The typical venous malformation patient will present with a multiyear or near life-long history of a deep or superficial mass or purplish discoloration on the skin that may or may not be gradually increasing. The patient will often complain of dull (but sometimes focally sharp) pain or swelling in the region associated with any one or more of the following: Activity, direct contact/trauma, dependent positioning, during sleep or other sedentary periods or related to certain times of the menstrual cycle. Symptoms are often not related to lesion size. On inspection, the lesion can be solitary or multifocal and distributed within a region, can be ecchymotic, and can be associated with varices. On palpation, the lesion is usually soft, compressible, and nonpulsatile. Beside Doppler examination will reveal little or no venous waveforms and definitely no arterial waveforms.[7]

A detailed review of the imaging workup of a venous malformation in the context of a fulsome differential diagnosis of other vascular anomalies or neoplastic or inflammatory conditions that may mimic a venous malformation in clinical presentation are beyond the scope of this technical discussion. However, one point merits emphasis; if a given lesion by reliable history has relatively recent onset, that is, less than 2 years (particularly in an adult population), is rapidly increasing in size or degree of pain, or has any diagnostic imaging features considered atypical for a vascular malformation, an image-guided biopsy is most likely indicated.[7,8] Once again, this kind of decision should be entered into in concert with a multidisciplinary team.

Indications/Contraindications for Intervention

Assuming appropriate clinical and imaging workup and correct diagnosis of a venous malformation, the interventional radiologist with the multidisciplinary team must first ascertain if the lesion *should* be treated and only then decide *if* the lesion can be treated by percutaneous or other means. A significant minority, if not majority of patients seeking medical attention do not need any intervention at all other than reassurance that the lesion is not neoplastic and may only need conservative measures. These include compression garments, avoidance of certain activities, and aspirin or oral nonsteroidal anti-inflammatory agents in the appropriate setting.[9]

When and when not to intervene in a venous malformation is best described by Lee et al in situations where the patient has *one absolute* indication or 2 *relative* indications while also considering potential contraindications best described by Burrows (Table 1).[10,11]

Patient Preparation for Intervention

Consent

As with any other elective procedure, it is best to meet with the patient in a clinic setting separate in time and place from the angiography suite to fully describe the (i) etiology and natural history of the disease process, (ii) STASE technique, (iii) lesion and sclerosant-specific risks of the procedure including skin blistering, ulceration/necrosis, hyperpigmentation, nerve impairment, contracture formation, compartment syndrome, deep venous thrombosis and pulmonary embolism, and other pulmonary sequelae, (iv) likely need for serial procedures each carrying with them the possibility of pain, swelling, and immobility.[4] Depending on the patient, lesion location, and agent chosen, one can make preparation for anesthesiology attendance versus conscious sedation if necessary.

Addressing Critical Preprocedure Hematologic Concerns

All 3 factors of Virchow's triad; altered blood flow, endothelial injury, and hypercoagulability are present in a venous malformation. Slow stagnant blood flow within a and structurally and functionally abnormal endothelialized vasculature without valves constantly stimulates the coagulation cascade, with repeated injury from clotting and hemorrhage further adding to a feedback loop. Not unsurprisingly, a significant number of venous malformations present with a distinct coagulopathy known as localized intravascular coagulation (LIC).[12-14] This entity is characterized by an elevation in d-dimers (>0.5 μg/mL or 500 μg/L), fibrin degradation products (>10 μg/mL or 10 mg/mL), and in some cases, decreased fibrinogen levels (<150 mg/dL or 1.5 g/L). Depending on the series, 33%-88% of patients have some degree of d-dimer elevation and approximately 5% with decreased fibrinogen levels.[14-17]

The detection of LIC and coagulopathy is important for 3 reasons. First, painful flareups may be associated with aggravation of those hematologic parameters associated with LIC and therefore conservative (eg, compression garments) or medical treatment directed to this portion of the

Table 1 Indications and Contraindications for Sclerotherapy Specific to Venous Malformations (Adapted/modified from Lee[10] and Burrows[11])

Indications (Require One Absolute or Two Relative Indications)		Contraindications
Absolute	**Relative**	
Hemorrhage (especially if recurrent)	Disabling pain and/or discomfort of a progressive nature	Proximity of the vascular lesion to major nerve trunks, especially in the presence of pre-existing neuropathy
Secondary complications of chronic venous hypertension	Functional disability or impairment affecting daily activity and the quality of life	Lesions involving or near the airway or orbit
Lesions located at a life and/or limb threatening region (eg, proximity to the airway)	Cosmetically severe deformity accompanying physical and/or psychological disability and severe negative impact on the quality of life	VM with extensive cutaneous involvement
Lesions threatening vital functions (eg, seeing, hearing, eating or breathing)	Vascular-bone syndrome with rapid progress of long bone growth discrepancy accompanied by significant pelvic tilt and/or compensatory scoliosis	VM involving the deep veins of the lower extremities
	Lesions located at a region with a high risk of complication (eg hemarthrosis; deep vein thrombosis)	Presence of severe consumption coagulopathy
	Lesions with recurrent infection and sepsis	Patent foramen ovale with history of right to left shunt
		Chronic pulmonary embolic disease with decreased reserve

coagulation cascade, that is, low molecular-weight heparin (LMWH) or direct anti-Xa agents may control and improve patient symptoms.[12,14,18-21] Second, patients with coagulopathy are more likely to develop painful phleboliths, thrombophlebitis, deep venous thrombosis, and pulmonary embolism and therefore must be identified to allow appropriate thromboprophylaxis.[15,17] Third, and most importantly to the interventional radiologist, minor sclerotherapy among other factors can cause LIC to rapidly progress onto disseminated intravascular coagulation (DIC) either intra- or postprocedurally with life-threatening consequences.[13]

The interventional radiologist must ensure patients are screened for risk of LIC and sent for appropriate lab studies, and where appropriate, be treated medically both periprocedurally and/or chronically. In assessing risk, large lesion volume greater than 250-500 mL, multifocality, truncal location, spongiform appearance, venous ectasia, malformations associated with overgrowth syndromes, and combined lesions such as Klippel-Trenaunay, (KTS) blue rubber bleb nevus syndrome or Congenital Lipomatous Overgrowth, Vascular malformations, Epidermal nevi, and Spinal/Skeletal anomalies (CLOVES), have found to be associated with a greater risk of LIC/coagulopathy and should prompt evaluation with platelet count, PT, aPTT, d-dimer and fibrinogen levels.[22] If STASE therapy is considered and the patient has one or more of a history of thrombosis, a family history of thrombosis, venous ectasia, low platelet count, a d-dimer level 5 times control, or a low fibrinogen level, the patient may be started on LMWH 0.5 mg/kg sc bid for 14 days pre- and postprocedure after initial consultation with a hematologist.[13,23,24] Similar risk factors in the setting of an elevated d-dimer and either decreased fibrinogen or chronic pain may be an indication for chronic LMWH or direct oral anticoagulants (DOACs) such as dabigatran or rivaroxaban, however, should always be managed in consultation with a hematologist.[17,20,21] In cases of intervention in KTS or CLOVES, one may consider temporary IVC filter placement (Table 2).[25]

Once the patient workup is thought to be complete prior to an intervention, one may consider reviewing a checklist to ensure all matters have been addressed (Table 3).

In the Case Room Before Administration of Therapy

Room Set-up

After time-out procedure and administration of conscious sedation, or anesthesiologist administered locoregional or general anesthesia, the patient is sterilely draped and prepped with all possible access points to the lesion visible though a fenestrated drape. Colorless skin prep is preferred as it best allows one to detect subtle skin changes during intervention that may portend complication. Relevant cross-sectional imaging should be made readily accessible and visible to the operator for immediate reference. High-quality ultrasound at musculoskeletal/small parts settings with a sterilely-prepped transducer is secured into the field. The image intensifier position and fluoroscopic imaging should be tested over the expected site of the lesion to avoid delays that could lead to loss of access after the lesion is first entered. The lesion can also be compressed to lower the volume of the lesion to

Table 2 Hematologic Considerations for Intervention in Venous Malformations

Characteristics	Assessment	Action	
Large lesion size Multifocality Venous ectasia Overgrowth syndrome Combined lesions such as Klippel Trenaunay syndrome, blue rubber bleb nevus syndrome, CLOVES	Increased risk of LIC or other coagulopathy	Warrants complete blood count (platelets), PT/INR, aPTT, d-dimer, fibrinogen level	
Patient history of previous thrombosis Family history of thrombosis Venous ectasia Low platelet count d-dimer 5× normal Low fibrinogen level	Increased risk of developing procedure-induced DIC	Preprocedure Hematologist may recommend: 14 days preprocedure: 0.5 mg/kg LMWH sc bid × 7 days 7 days preprocedure: Recheck labs if normal: Continue current dose if persistently abnormal: increase to 1.0 mg/kg LMWH sc bid × 7 days	Postprocedure Hematologist may recommend: Same as maximum preprocedure dose × 14 days OR until ambulating (whichever is LONGER)

Table 3 Pre-STASE 12-Point Checklist

1. Multidisciplinary team referral/involvement
2. Clinical history and imaging findings consistent with diagnosis of venous malformation confirmed
3. Biopsy (if necessary)
4. Patient seen in office prior to intervention
5. Baseline medical photography obtained
6. Laboratory – hematologic evaluation performed (if coagulopathy risk factors present)
7. Firm indication(s) for therapy established
8. Informed patient consent obtained in advance of procedure including description of nature of disease process, STASE technique, expected postprocedure course, lesion-specific risk of complications, and likely need for multisession therapy)
9. Anesthesiology and/or hematology consultation arranged (if necessary)
10. Preprocedure/postprocedure thromboprophylaxis regimen established, and prescription given to patient (if necessary)
11. Physiotherapy consultation/regimen post-therapy coordinated (if necessary)
12. One to 3 sessions of scleroembolotherapy separated by 3 weeks to 3 months scheduled/slated based on individual lesion

increase the effectiveness of sclerotherapy.[11] All anticipated access supplies should be ready and assembled on the table, with sclerosant and embolic agents immediately available.

Access and the Phlebographic Phase

Simply put, access is everything in vascular anomaly percutaneous intervention. Malpositioned, unstable, or ill-conceived access can prematurely end a procedure or lead to catastrophic complications. There are many variations in technical apparatus for access and with experience, one should settle on a system that works best for them. We present a baseline modifiable system that provides minimal dead space, maximum flexibility, and durable security when transitioning between the diagnostic phlebographic and the scleroembolic phases of the procedure at any given access point.

When a chosen access needle is advanced to the desired depth of the lesion, it should have as little of its remaining length outside the body. Too much free needle is inherently unstable, requires undue supervision, and predisposes to loss of access. This can not only lead to contrast extravasation, obscuring the lesion, and prematurely ending a procedure, but can also lead to extravasation of sclerosant with potential grave consequences. As such, we use 21, 23, or 25-gauge butterfly needles for more superficial lesions and nontrocar 21 gauge 4 or 7 cm or longer needles if necessary or deeper lesions. Low-profile two-in-one needle-fine cannula combinations can also provide improved security provided the lesion's target lumen can accommodate the slightly increased size and the operator can manage the additional technical demands without traumatizing the access site.[11] The needle or cannula should be attached to connecting tubing that is as short or low volume as possible with just enough length to allow operator comfort and not risk loss of access from inadvertent traction. Low-catheter volumes are important, particularly in low capacity lesions. During a media transitions, one does not have the luxury to permit overly large volumes of saline or contrast to clear though lines into the lesion before a chosen scleroembolic agent arrives as the former may fill the lesion and not allow administration of the latter, or worse still, could lead to rupture of the lesion and extravasation of sclerosant (Fig. 1).

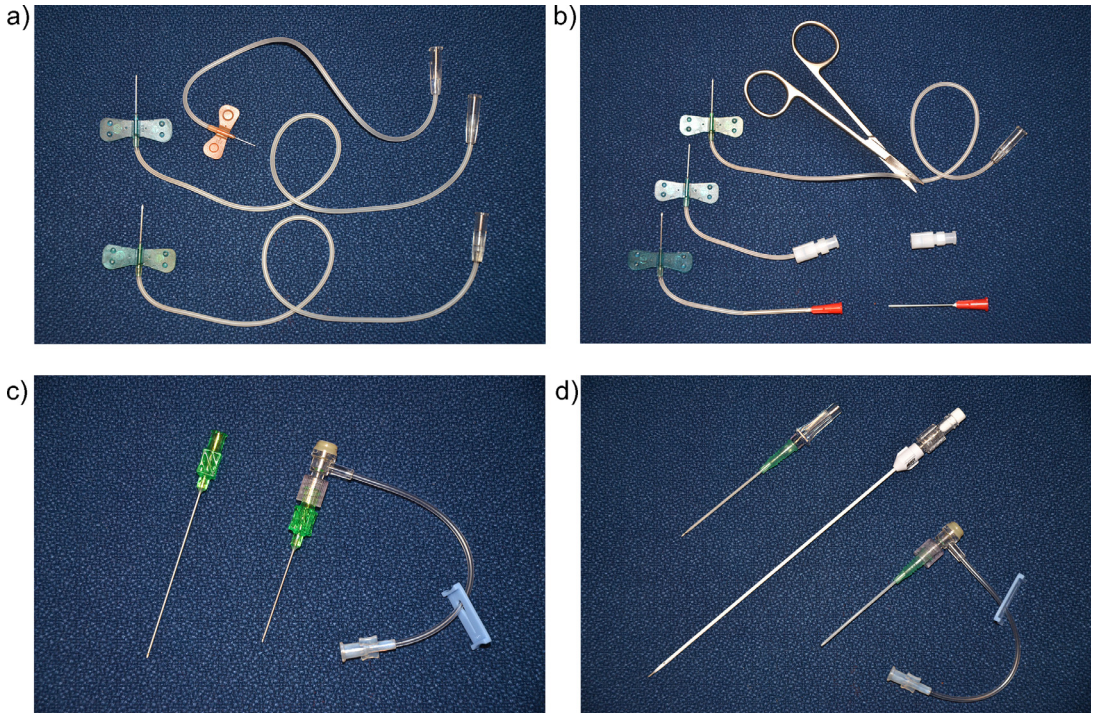

Figure 1 Needles and connection tubing used for initial percutaneous access of venous malformations. (a) Unmodified 21, 23, and 25-gauge butterfly needles most appropriate for use in more superficial venous malformations. (b) To reduce volume during media transitions, the butterfly needle tubing can be shortened by cutting the tubing and attaching a bare-end catheter to Luer adapter. If not available, one can gently hold the bare cut end with a clamp and very carefully insert a blunt needle with a second clamp. (c) Typical 7 and 4 cm 21-gauge needles used in combination with low volume T-connector extension tubing, (d) Variety of needle-short catheter combinations that may be appropriate for more durable access in lesion access sites that may have a slightly larger lumen.

For phlebography, we usually connect the tubing to a three-way stopcock attached to an "in-line" 10 cc syringe containing saline and an "orthogonal" 10 cc syringe containing contrast. It is critically important to use color-coded or color-labeled all syringes during a STASE procedure as confusion can lead to inadvertent sclerosant administration. By convention at our institution, saline is labeled green (safe), contrast is labeled blue, sodium tetradecyl sulfate is labeled yellow or orange (caution), ethanol is labeled red (greatest danger), and ethiodized oil white (lipid). When dealing with finer or lower capacity lesions structures, or head and neck lesions, 5, 3, or even 1 cc syringes can be used for their finer control and sensory feedback. Some advocate using silicone-free syringes that may keep sclerofoams stable for longer periods of time. Whichever access needle/device is chosen, a maximally oblique course under real-time ultrasound guidance will provide the most secure and safe access. It is also critical within any given lesion to access the deeper/dependent portions of the venous malformation, particularly if a sclerofoam administration is being considered. Sclerofoams are obviously less dense than blood and will rise within the lesion. Overly superficial access will not allow treatment of deeper component of the lesion. The needle of the flushed apparatus and then advanced obliquely into the malformation under real time ultrasound guidance, preferably with one operator advancing the needle slowly and a second operator *gently* aspirating on the "in-line" saline syringe looking for the subtlest of "flashes" of blood in the needle hub prompting an immediate stop. It is very important to engage the malformation antegradely versus upon withdrawal as the latter will have higher propensity to extravasate. The stopcock is switched to contrast, and the least volume needed to confirm intraluminal positioning is injected (Fig. 2).

The lower viscosity and density of diluted contrast will more fully and evenly penetrate the lesion unlike full-strength contrast which can sequester in more dependent portions of the lesion shielding the endothelium from the effects of incoming sclerosant. Full-strength contrast may permit lower administered volume in smaller lesions. Contrast is further injected to define volume of distribution and whether the lesion is cavitary, spongy, or dysmorphic.[7] Venous drainage may appear diminutive or nearly absent (Type I), normal appearing (Type II), enlarged and rapidly filling (Type III), or the lesion may consist entirely of dysmorphic hypertrophied venous channels (type IV).[26,27] Establishing the pattern of venous drainage from a venous malformation is by far the most important goal of the initial phlebogram as it determines the ease with which a sclerosant or embolic material is likely to remain unassisted within the lesion and therefore dictates choice and preparation of sclerosant, site of delivery, and the need for adjunctive control of efflux from the malformation (Fig. 3).

During the initial phlebographic phase and throughout the later intervention one must always confirm that the access site

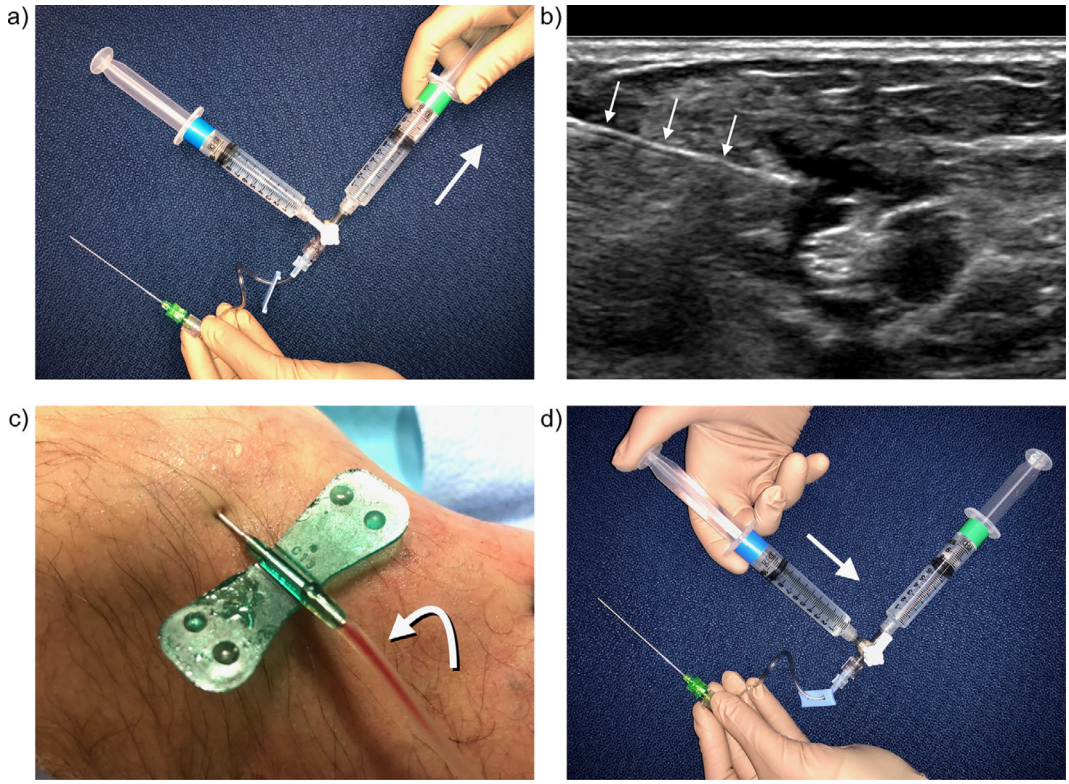

Figure 2 Technique and device setup for initial percutaneous access of the venous malformations. (a) The access needle is connected via short tubing and a three-way stopcock to an "in-line" syringe containing saline (green) and an "orthogonal" syringe containing contrast (blue). The needle is advanced while gently aspirating on the saline syringe. (b) Access needle (small white arrows) entering a heterogeneous venous malformation obliquely at a low angle under ultrasound guidance. (c) Flash of blood (curved white arrow) signaling intra vascular access and halting further needle advancement, (d) Stopcock is opened to contrast which is then gently injected to first confirm intraluminal positioning and then perform phlebography.

remains intraluminal and that there are no (a) straight lines or broad arcs of contrast outside the malformation suggesting extralesional extravasation or (b) regions of serpentine irregular filling defect or short arcs of contrast in or near the lesion suggesting intra or perilesional extravasation (Fig. 4).

Choice and Preparation of Therapeutic Agents

A complete review of the pharmacology, characteristics, and complication profile of the many scleroembolic agents available for STASE are beyond the scope this discussion, however, a brief overview is presented below.

Sodium tetradecyl sulfate (STS) has become one of the most commonly used sclerosing agents in venous malformations. It is an anionic surfactant, and causes thrombosis, intimal necrosis, and fibrosis. It can be administered in pure or "neat" in 1 or 3% form and with the addition of intravenous contrast, sclerosant progression through the lesion can be monitored under "positive roadmap" techniques. The conversion of sclerosant into foam is advocated because of its increased viscosity leads to greater "dwell-time," endothelial contact, and greater effectiveness per unit dose.[28] STS agent can be easily transformed into a higher viscosity sclerofoam using Tessari technique by mixing 3 mL 3% sodium tetradecyl sulfate with 0.5 mL ethiodized oil and 6.5 mL air to total 10 mL volume.[29] This preparation is best for a "negative roadmap" techniques as the foam is less radiodense than contrast, however, many combinations abound. This agent can also be foamed with a higher concentration of ethiodized oil and less air rendering it more radiodense allowing the foam to be traced on "positive roadmap." The 3% dose range is from 6-20 mL per session or 0.5 mL/kg.[11,30]

Polidocanol is another surfactant with anesthetic properties that behaves and acts on endothelium in similar ways to STS and is available in various liquid or foam preparations from 0.25%-4.0% (Fig. 5).

Ethanol is (100% v/v dehydrated ethanol) is historically a very well-known sclerosant and is still widely used. Ethanol rapidly denaturing blood proteins, lyses and denudes endothelium, denuding and fractures intima to the internal elastic lamina ensuring permanent closure.[31] The agent often used neat, however, can also be diluted up to 50% or mixed with various contrast water or lipid-soluble agents to increase viscosity. It can also be administered in a gel form from either the manufacturer or prepared by the operator.[32-34] Irrespective of method, ethanol must be used very cautiously to avoid phenomena of non-target embolization and must be NOT be administered to a patient at a rate greater than 0.1 mL per kg per 10 minute interval and NOT greater than a

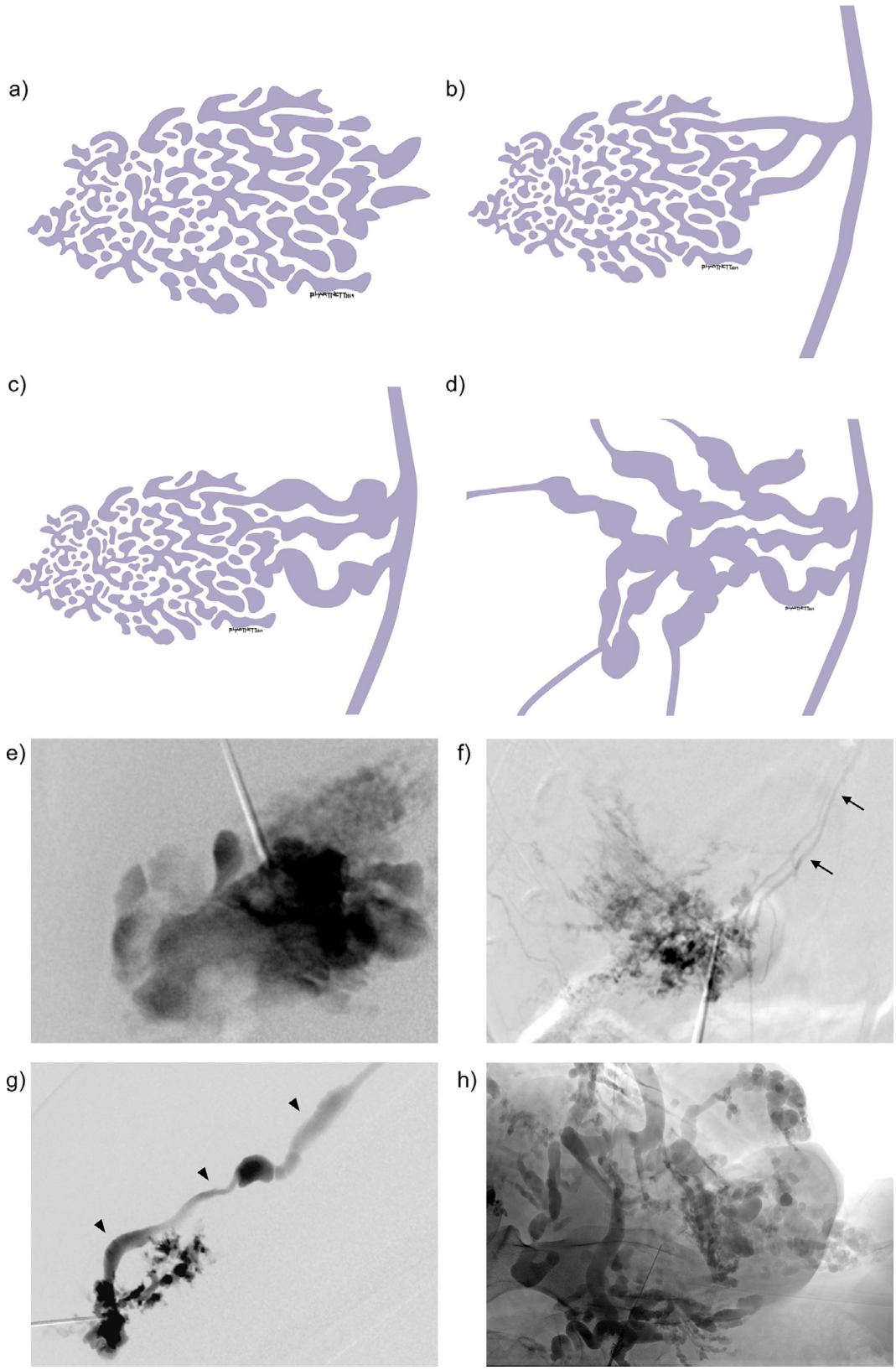

Figure 3 Puig[26,27] classification of venous malformations based on pattern of venous drainage or efflux on phlebography. (a) Type I venous malformation demonstrating negligible venous drainage, (b) Type II lesion with normal small draining veins before entering normal deep veins, (c) Type III anatomy revealing abnormal enlarged or tortuous draining veins, (d) Type IV lesion consisting predominantly of enlarged dysmorphic venous structures, (e) Type I phlebogram of a venous malformation with no detectable venous drainage, (f) Type II anatomy on phlebography with normal small draining veins (small black arrows), (g) Type III findings demonstrating underfilling of a venous malformation due to rapid efflux through an abnormal enlarged draining vein (black arrowheads), Type IV venous malformation phlebogram consisting of multiple dysmorphic enlarged venous structures.

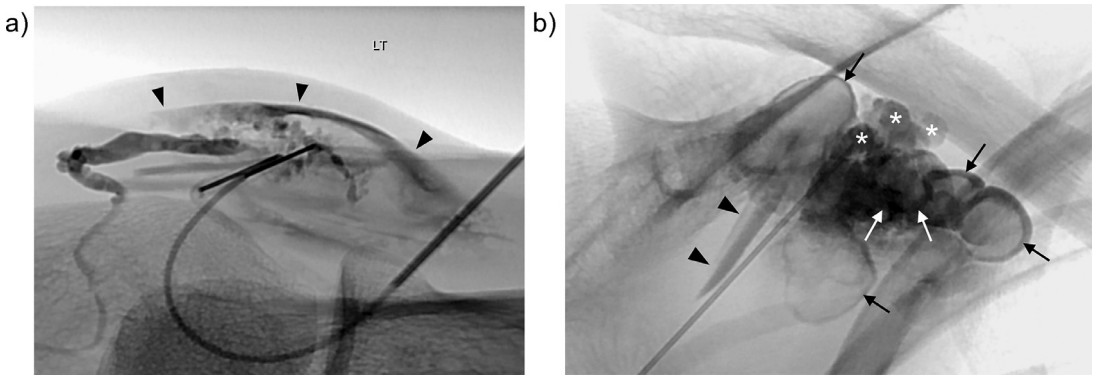

Figure 4 Patterns of extravasation during percutaneous access in venous malformations. (a) Although intravascular access was achieved in this elbow venous malformation, continued contrast injection into a relatively low volume lesion has produced a wide arc of contrast away from the lesion consistent with extralesional extravasation (black arrowheads). (b) Supraclavicular venous malformation with contrast in the true lumen of the malformation (white asterisks), however, there is also intralesional extravasation (white arrows) leading to perilesional extravasation (black arrows) and extralesional extravasation (black arrowheads).

total dose of 50 mL or 0.5-1.0 mL per kg per case as this may increases the risk of cardiovascular collapse.[31,11]

Bleomycin is historically a proven effective treatment of lymphatic malformations but has been found to be a potent therapeutic option in venous malformations and may be more effective than other agents in certain scenarios.[35-37] Bleomycin is particularly well-suited in mucosal lesions or regions susceptible to swelling.

Bleomycin probably works by inducing endothelial mesenchymal transition through the mTOR pathway which may underlie its serotherapeutic effect.[38] As such, the agent is much gentler with a much lower complication profile, however, there are risks of skin hyperpigmentation and ulceration especially if injected too superficially.[36] Hyperpigmentation can occur diffusely or at focal areas of pressure or vascular microtrauma as occurs with adhesive sites form tape or EKG

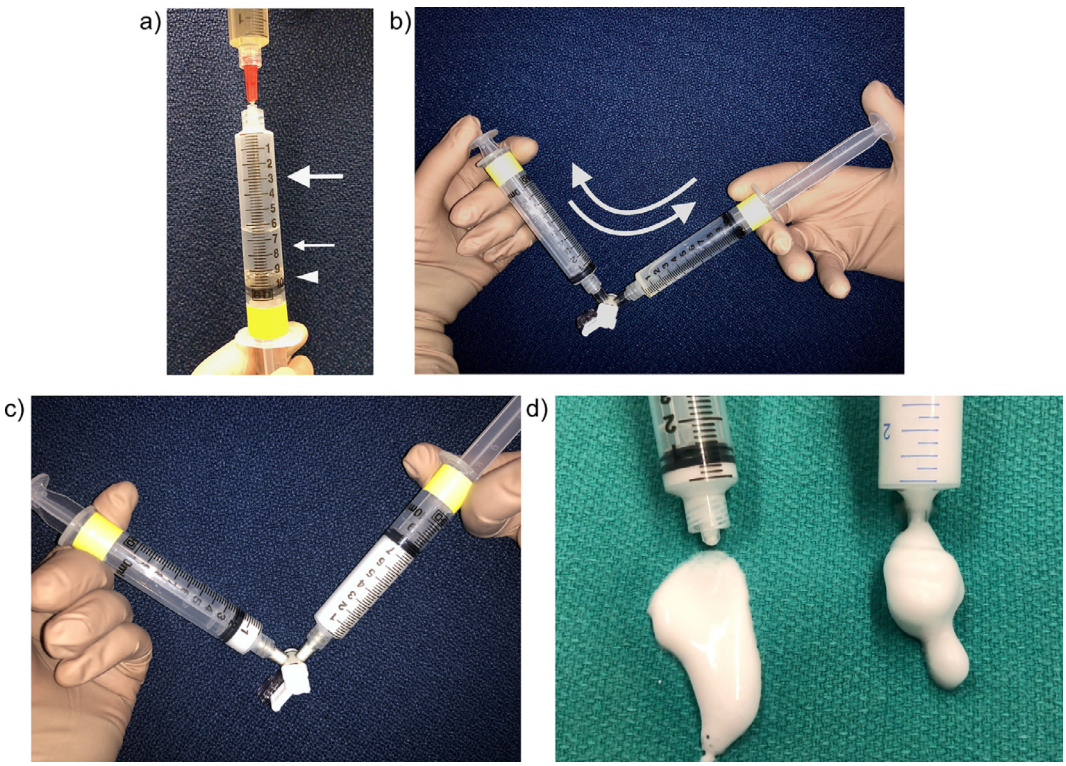

Figure 5 Creation of sclerofoam. (a) Typical ingredients using 3 mL 3% sodium tetradecyl sulfate (small arrow) and 0.5 mL ethiodized oil (arrowhead) diluted with 6.5 mL room air (large arrow) to total volume of 10 mL, (b) Syringe in Fig 5a) oscillated with another 10 mL syringe via three-way stopcock using Tessari technique, (c) Resultant white sclerofoam created between syringes, (d) Appearance and consistency of sodium tetradecyl sulfate sclerofoam (left side, from black-labeled syringe) and polidocanol foam (right side, from blue labeled syringe).

electrodes.[39] One must be wary of rarely reported but devasting complications of flagellate erythema, acute lung toxicity or pulmonary fibrosis.[40-43] There is a report of one infant with acute pulmonary toxicity after one session of 1.2 mg/kg bleomycin and a case of pulmonary hypersensitivity reaction occurring in one patient after a second session of only 0.28 mg/kg or 0.4U/kg.[41,42] As such, there is ongoing academic debate as to safe per session and cumulative lifetime doses. Common recommendations include a maximum dose of 10-15 U per session and 90-100 U maximum cumulative life-time dose in adults and 0.5-1.0 mg/kg per session and cumulative maximum of 1.0 mg/kg in children.[35,44,45,43,46,47] One should endeavor to keep oxygenation under anesthesia to the lowest acceptable limits as hyperoxia may predispose to pulmonary toxicity.[44] Irrespective, baseline plain film chest and pulmonary function tests with follow-up are recommended for any patient receiving bleomycin for scleroembolic therapy.

Bleomycin can be prepared in a number of ways. The most common is 1.0 U per mL of 1:1 normal saline and iodinated contrast. 0.5 mg/mL bleomycin is used when injecting superficial skin or mucosal or lip lesions to reduce ulceration risk. Bleomycin can also be foamed using 15 units bleomycin with 2.5 mL normal saline, 2.5 mL albumin 25%, and 5 mL of air.

Sclerotherapy and Adjunctive Stasis of Efflux (STASE) Procedures

Basic Sclerotherapeutic Technique

In the "default" technique of sclerotherapy, the minimum amount of contrast is injected to confirm intraluminal position and characterize the lesion as described earlier. The saline syringe is carefully removed and then this same "in-line" port is connected to freshly created or reagitated Tessari foam between perpendicular syringes. Ports are then opened allowing communication between the "in-line" foam syringe and the lesion. The highly compressible foam stores pressure within the syringe so only light, regular, pulsation/vibration of the sclerosant-containing syringe is necessary for the sclerosant to slowly progress into the low-volume tubing into the lesion. At this point, one starts low frame-rate DSA at 0.5 frames per second (1 frame every other second) in a "negative roadmap" sclerotherapy technique to slowly observe "white" (negative) sclerosant emanate from the access point slowly increasing in area displacing "dark" (positive) contrast peripherally deeper into the lesion. It is very important to observe that both the region of sclerosant as well as the "front" of dark contrast progress normally only into intraluminal space (Fig. 6).

If there is evidence of extravasation, the access site should be promptly abandoned. Gentle sclerosant administration should continue for as long as the volume of the malformation is being filled or until origins of draining veins are identified. Often the outflow vein(s), if small or of lower flow will begin to sclerose/contract and one can resume sclerosant administration after a pause of one to 3 minutes. The draining vein(s) or other channels within the malformation proper will begin to thrombose and pressurize and allow new channels and regions of the venous malformation to then fill with sclerosant from the same access point. As the lesion fills, there can be a degree of "whiteout" near the access point than can strain one's confidence in the maintenance of intraluminal position during sclerotherapy. As a remedy, one can easily switch the stopcock from sclerosant to contrast for 0.5 cc volume and then back to sclerosant effectively pushing contrast as a "tracer" that is sandwiched between sclerosant boluses not affecting the efficacy of sclerosant (Fig. 7).

The transit of agent can be simultaneously, and in when desirable, exclusively observed under ultrasound. One hopes to identify intensely echogenic sclerosant slowly progressing throughout the lesion. Dirty shadowing from within a superficial region of the venous malformation when a deeper component has been carefully accessed is confirmation of satisfactory permeation throughout the lesion (Fig. 8).

Once a particular access point has been maximized, assuming maximum allowable dose has not been exceeded, one should cap and leave the access in situ to prevent leakage and then move on to a second access point in a geographically distinct untreated portion of the lesion to perform similar maneuvers. It is important to remember that the lesion can become increasingly firm and swollen during and after sclerotherapy at any given site and therefore should be frequently monitored by palpation throughout the procedure. Continued therapy in an already "tense" lesion can increase the risk of significant postprocedure pain or skin impairment and if deeper, possibly compartment syndrome or tissue necrosis. One must also observe for skin changes of blanching or untoward erythema that should prompt cessation of further injection and heightened observation post procedure. One must always bear in mind that sclerotherapy is largely elective and should be staged to reduce risk of complication.

On occasion, one encounters a scenario where (i) the lesions is of low volume, irreversibly fills with contrast, and denies admission of sclerosant into the lesion, (ii) a portion of the lesion in communication with the access point is under greater pressure and does not accept sclerosant, or (iii) the lesion has a low threshold for extravasation, for example, finer architecture if placed under the usual elevated pressures of scleroembolic therapy. In these cases, a second access site is placed at some distance from the original therapeutic access point to allow decompression of a portion or all of the venous malformation and enable one to essentially "irrigate" the lesion with the therapeutic agent under lower pressure (Fig. 9).[48]

In situations where the luminal architecture is exquisitely fine, delicate, stromal rich or where maintaining access for any length of time is tenuous, one may consider the most of simple of access using a 25- to 27-guage needle or butterfly needle connected directly to a small syringe containing an agent such as bleomycin 0.5-1.0 units per mL solution of 1:1 normal saline to contrast for "positive roadmap" sclerotherapy. Additionally, nonfoamed or "neat" 1 to 3% sodium tetradecyl sulfate can be administered under such circumstances. Conedbeam CT has been described as effective for access of lesions in tenuous locations (Fig. 10).[49]

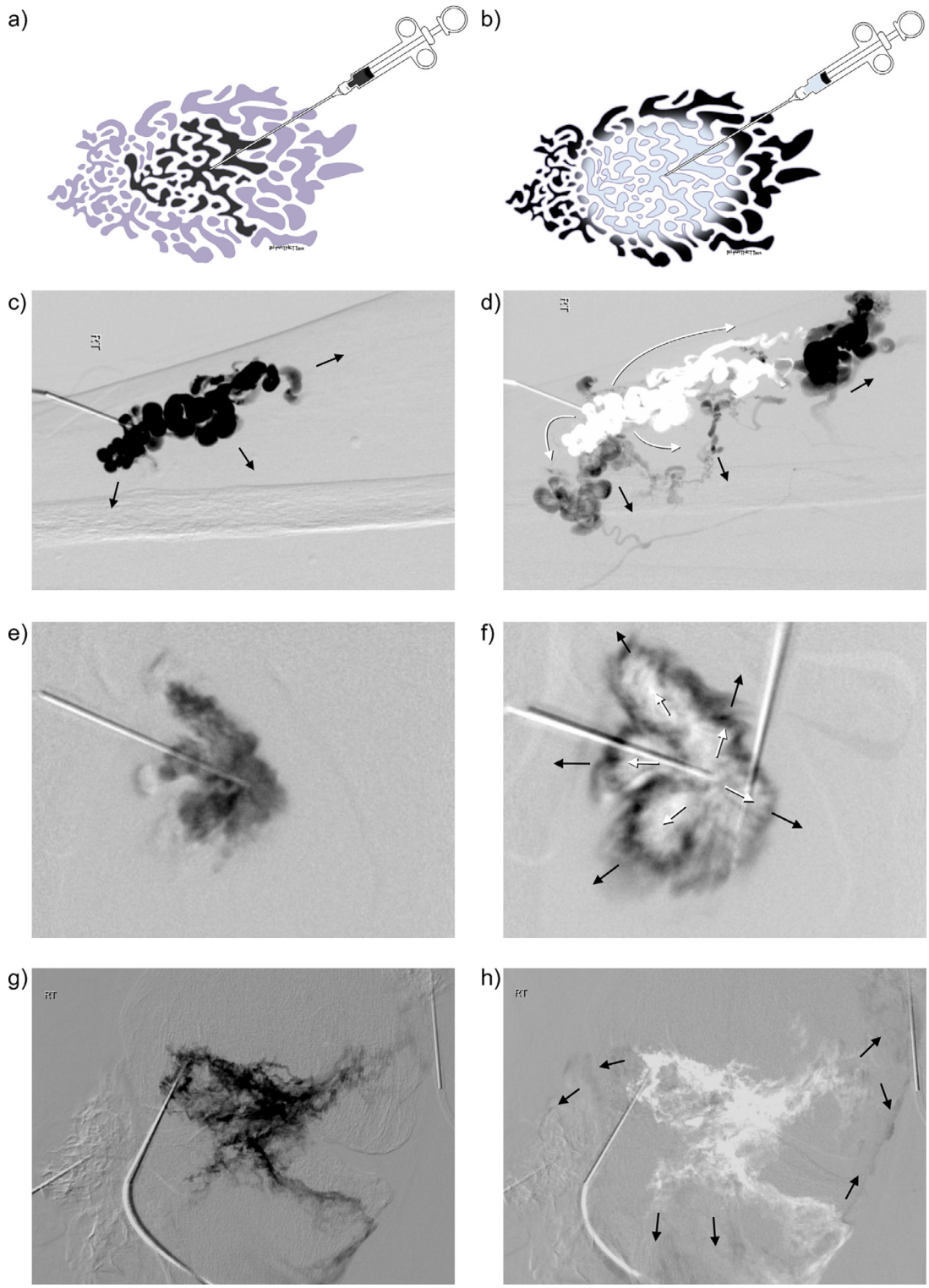

Figure 6 Contrast displacement technique of sclerotherapy in venous malformations. (a) The minimum amount of contrast (black) is injected into the venous malformation to confirm intraluminal position and characterize the lesion. (b) Sclerosant is then administered (light blue) to displace the contrast (black) deeper and more peripherally into the lesion. (c) Initial contrast injection within a lower calf venous malformation as it dissipates outward (black arrows). (d) "Negative roadmap" sclerotherapy technique demonstrates "white" (negative) sclerosant emanating from the access point (white arrows) displacing "dark" (positive) contrast peripherally deeper into the lesion (black arrows). (e) Initial contrast phlebogram of a Type I venous malformation near the obturator foramen, (f) Contrast front within the lesion (black arrows) displaced peripherally by incoming negative sclerosant (white arrows), (g) Mid-case contrast injection at one of multiple access points within a diffuse multicentric venous malformation of the knee, (h) Near complete sclerotherapeutic penetration (white) with displacement of faintly identified contrast progressing into other regions of the lesion (black arrows).

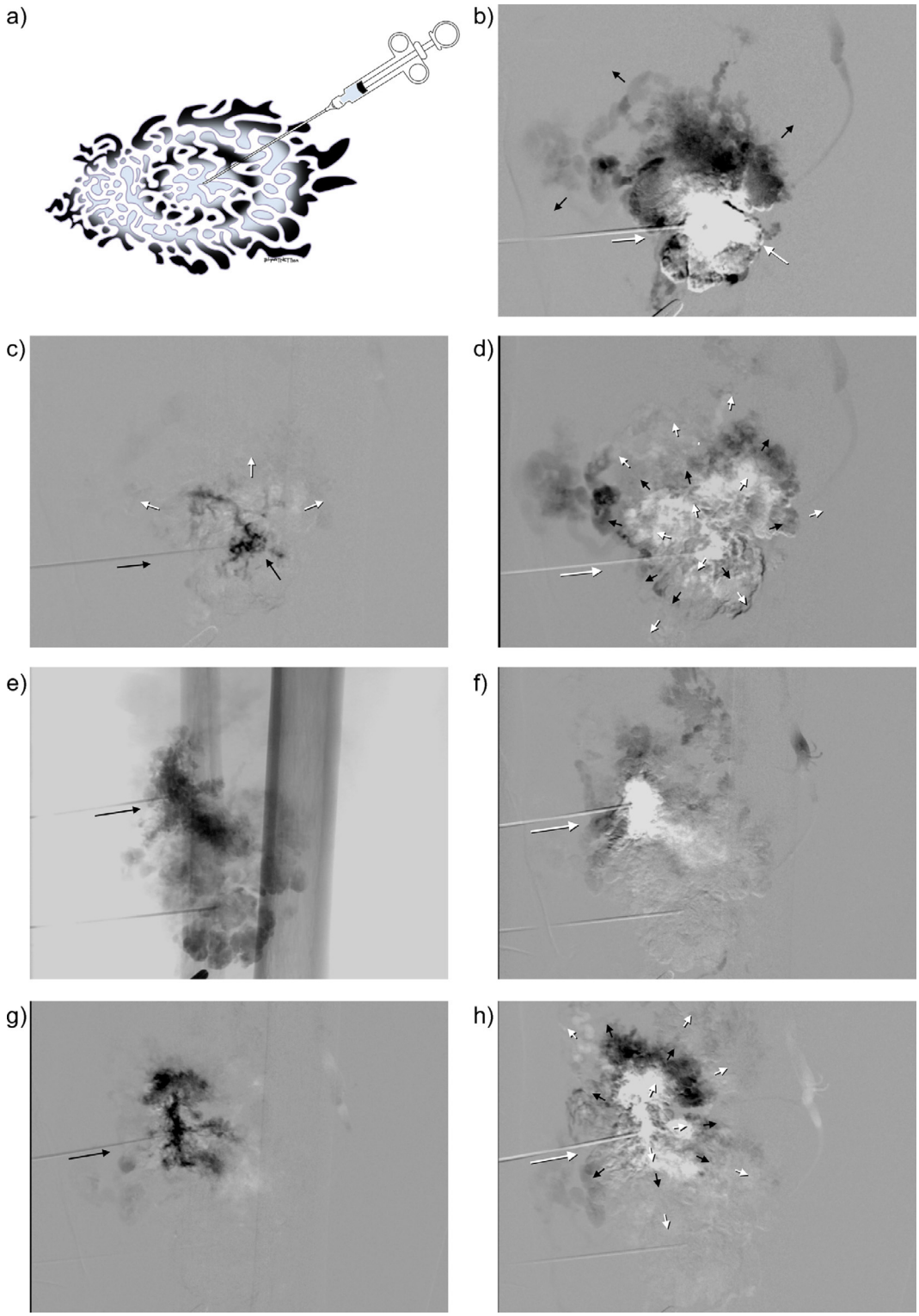

Figure 7 "Tracer" technique using intermittent contrast administration during sclerotherapy. (a) Small "tracer" bolus of contrast administered mid-sclerotherapy resulting in a "ring" of contrast (black) between concentric rings of sclerosant (light blue) within the venous malformation. (b) First dose of sclerosant administered into a large complex venous malformation resulting in a "whiteout" appearance near the first access point (white arrows) with peripheral displacement of contrast within the lesion (black arrows). (c) "Tracer" contrast administered into the lesion (black arrows) with peripheral displacement of previous sclerosant (white arrows), (d) A second dose of sclerosant centrally displaces the tracer ring of contrast to mid-lesion (black arrows) located between both the first (peripheral) and second (central) doses of sclerosant (white arrows). (e) Contrast is administered at a second, more cranial access site (black arrow). (f) "Whiteout" appearance of first dose of sclerosant administered at second access site (white arrow), (g) "Tracer" contrast administered (black arrow), (h) "Tracer" ring of contrast (black arrows) displaced between subsequent second dose of sclerosant centrally and first dose peripherally (white arrows).

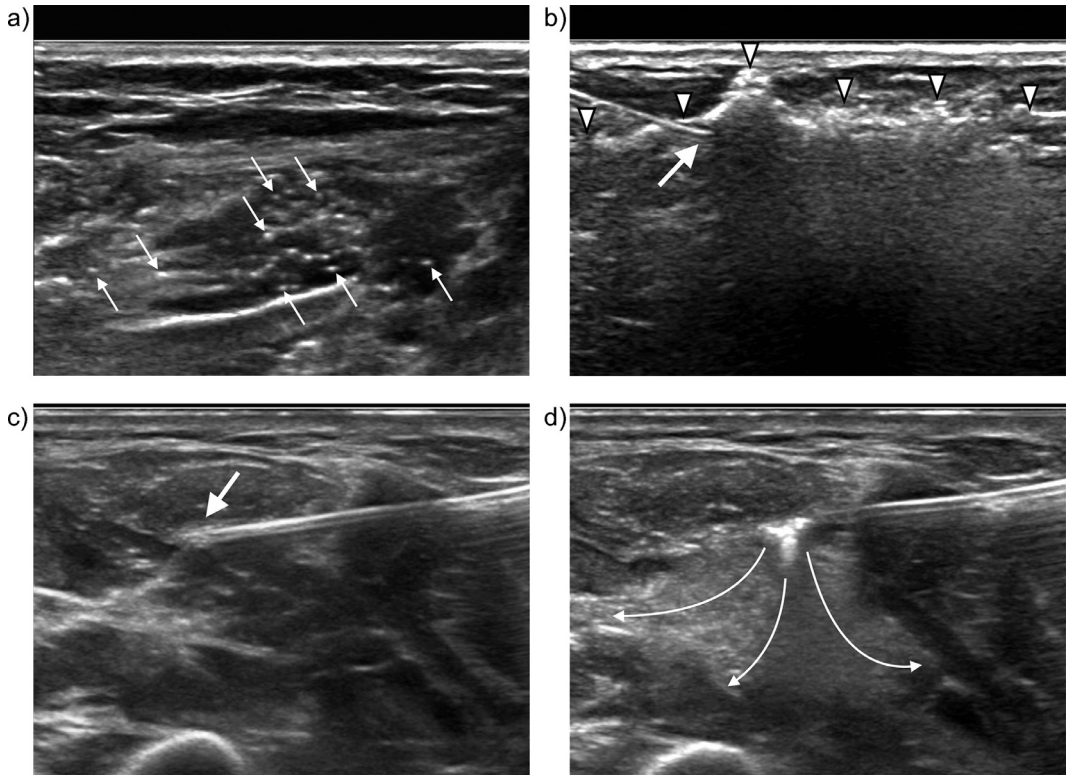

Figure 8 Ultrasound visualization during sclerotherapy. (a) Early administration of sodium tetradecyl sulfate sclerofoam reveals innumerable echogenic reflectors (thin white arrows) within vascular spaces caused by foam bubbles. (b) Access needle (white arrow) depositing sclerofoam causing intense superficial reflection with deeper diffuse dirty shadowing (white arrowheads), (c) Needle access into a vascular space within a forearm venous malformation (white arrow), (d) Polidocanol foam administration revealing diffuse and homogeneous echogenicity as it permeates the lesion (curved arrows).

Nonsclerotherapeutic Glue Embolization

Venous malformations, particularly of the head and neck, and especially near the orbit present a unique subset of percutaneous and surgical challenges. Staged sclerotherapy, even with bleomycin, can be complicated by damage to adjacent critical structures from direct toxicity or delayed inflammation.[50,51] Surgery for venous malformations in the head and neck often leaves residual malformation. After wound healing, reattempt at resection of the now decentralized lesion in scar can be even more challenging than the original surgery.[52] A combined purely embolic and surgical approach has been developed whereby the venous malformation is directly embolization with n−butyl cyanoacrylate (n-BCA) which permeates throughout the lesion.[53] An acute inflammatory reaction ensues soon after embolization creating a clear line of demarcation between the venous malformation and normal tissue facilitating complete and immediate resection with lower morbidity and recurrence rate.[52]

The lesion can be accessed with a 21- to 25-guage needle for pre-embolization phlebography to determine flow dynamics/rate of venous efflux. Glue is mixed with ethiodized oil 1:1 ratio in higher outflow and 1:4 ratio in lower outflow conditions. A venting needle similar to that described previously can be used to assist in achieving better penetration into the lesions and avoid extravasated glue or lesion rupture (Fig. 11).

STASE Using Temporary Extralesional Occlusive Techniques

One of the leading causes of technical and clinical failure in percutaneous therapy for venous malformations is an inability to safely maintain sclerosant within the confines of the lesion for sufficient length of time and concentration because of uncontrolled rapid venous efflux from the lesion. This can lead to nontarget distal embolization, deep venous thrombosis, and pulmonary embolus, not to mention other potentially severe physiologic sequalae. If one is to have any meaningful chance at success, adjunctive temporary or permanent efflux restriction techniques must be employed.

The simplest STASE – temporary occlusion technique merely involves sustained compression of the venous outflow with either a tourniquet, inflatable cuff, or focal manual compression with a clamp and gauze.[54,7] Although more labor-intensive, manual compression is preferred as pressure can be better adjusted real-time in a very focal manner during and after injection. Of course, this technique can only be used if the venous structure in question is sufficiently superficial and accessible. If one must use tourniquets or cuffs, extreme vigilance during administration is required. Intravascular pressure during sclerotherapy with an overly tight cuff can exceed local tissue pressure which can lead to transcapillary reflux of sclerosant or embolics into local arteriolar/arterial systems leading to nerve injury or tissue necrosis.[8] Before

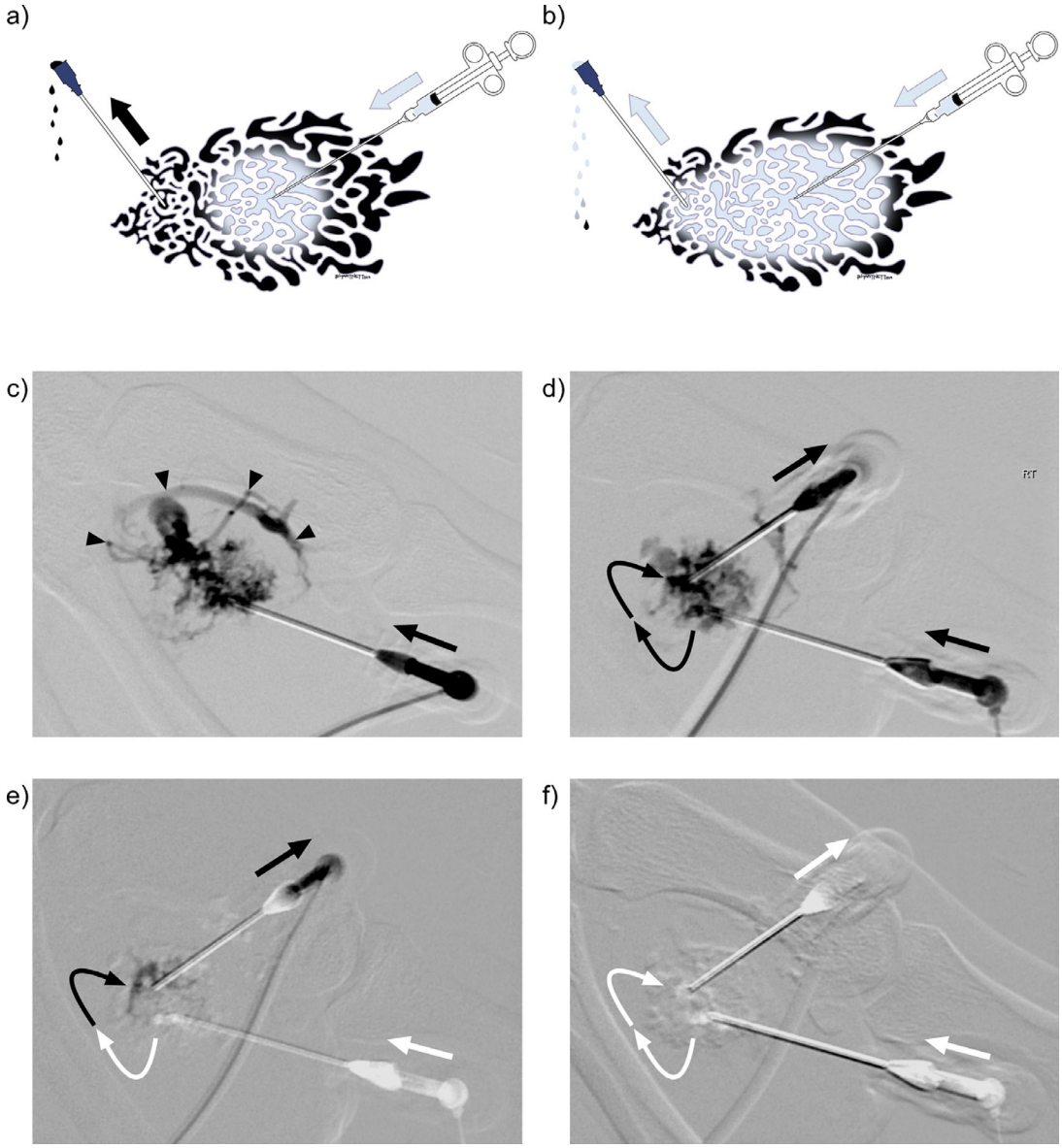

Figure 9 Two-needle irrigation technique of sclerotherapy. a) During sclerosant administration (light blue arrow) within a low volume lesion, a second needle can be placed as a "vent" allowing previous phlebographic contrast to exit (black arrow) decompressing the intraluminal compartment. (b) With decompression, continued contrast injection (right blue arrow) pushes the final portions of contrast out the venting needle, allowing deeper sclerosant penetration and irrigation of the lesion as it exits the venting needle (left blue arrow). (c) Phlebogram of very low-volume left hand venous malformation (black arrow) with access requiring tourniquets resulting in reflux/efflux into adjacent arterial/venous structures (arrowheads), (d) After placement of second venting needle, contrast is able to pass through the venous malformation (curved black arrows) and exit the lesion (upper straight black arrow). (e) Sclerosant is administered (straight white arrow), enters the lesion (curved white arrow), displaces the phlebographic contrast (curved black arrow) and decompresses by way of the second venting needle (straight black arrow), (f) Sclerotherapy administration continues (lower straight white arrow), irrigating the lesion (curved white arrow), and exits the venting needle (upper straight white arrow).

administration, it is recommended that one first test the system purely with contrast to evaluate if the application of compression is effective in halting venous efflux from the lesion as any number of previously-hidden accessory venous outflow pathways can easily be recruited (Fig. 12).

Another temporary occlusion technique involves the inflation of a balloon(s) within the venous outflow of the lesion during and after administration of sclerosant. Not all venous malformations are suitable for temporary balloon outflow occlusion technique as there must be at most only one or 2 veins that are both in relatively close proximity to the malformation and are also functioning as the final single common pathway draining the lesion before entering the inviolable deep venous system. To assess if this is feasible, one can perform "test compression" phlebography from the given intralesional access point while focally compressing the observed draining vein in question and then identifying (i) that the vein *can* be compressed adequately, (ii) that multiple

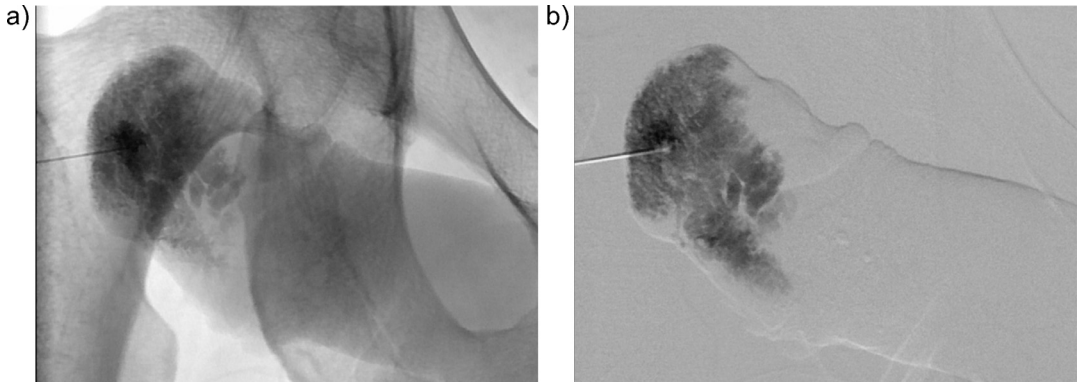

Figure 10 Bleomycin sclerotherapy under positive contrast technique. (a) Nonsubtracted image of bleomycin 1.0 mg/mL 1:1 contrast: Saline administered into fine reticular spaces of a superficial and deep venous malformation of the penis as an example of positive roadmap technique, (b) digital subtracted image of same case further demonstrating positive contrast technique.

other collateral venous drainage pathways are *not* recruited, and (iii) that there is significantly improved penetration and distribution of contrast within the substance of the venous malformation. If these criteria are met, continued contrast injection and or real-time ultrasound guidance can be used to puncture the outflow vein with a 21-guage needle and secure 0.018" wire access under Seldinger technique. Delivery of a balloon requires placement of a sheath, however, the target draining vein is often deep, perpendicular, and/or mobile and may also be in spasm, all of which can make transitioning to an appropriate vascular sheath challenging. These demands are best met with advancement of radial-type access sheaths that have been designed to provide the most atraumatic, smoothly transitioned profile of dilator/sheath assembly that also fits over a 0.018-0.021 wire system. Several manufacturers currently offer these strong yet flexible sheaths ranging from 7 to 23 cm and 4 to 7 French. A balloon should be chosen to match the outflow vein diameter.

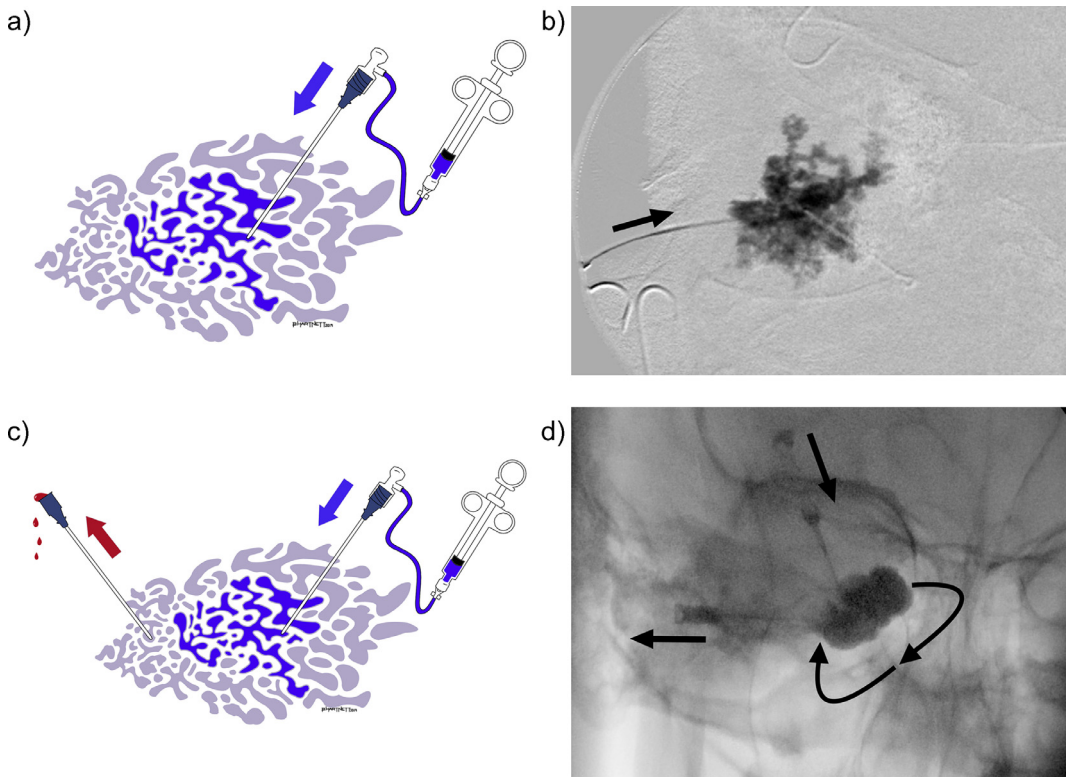

Figure 11 Glue embolization of venous malformations. (a) Glue administration (dark blue arrow) filling the vascular alone without sclerosant administration, (b) N-butyl-2 cyanoacrylate glue administration (black arrow) into an orbital venous malformation intraoperatively prior to surgical resection, (c) Better glue penetration into the venous malformation can be achieved by placing a second needle that allows venting or decompression of blood (red arrow) displaced by glue administration from first access needle (blue arrow). (d) Glue administration into intraorbital venous malformation (vertical needle), permeating lesion (curved arrows), enhanced by decompression of displaced blood via horizontal venting needle.

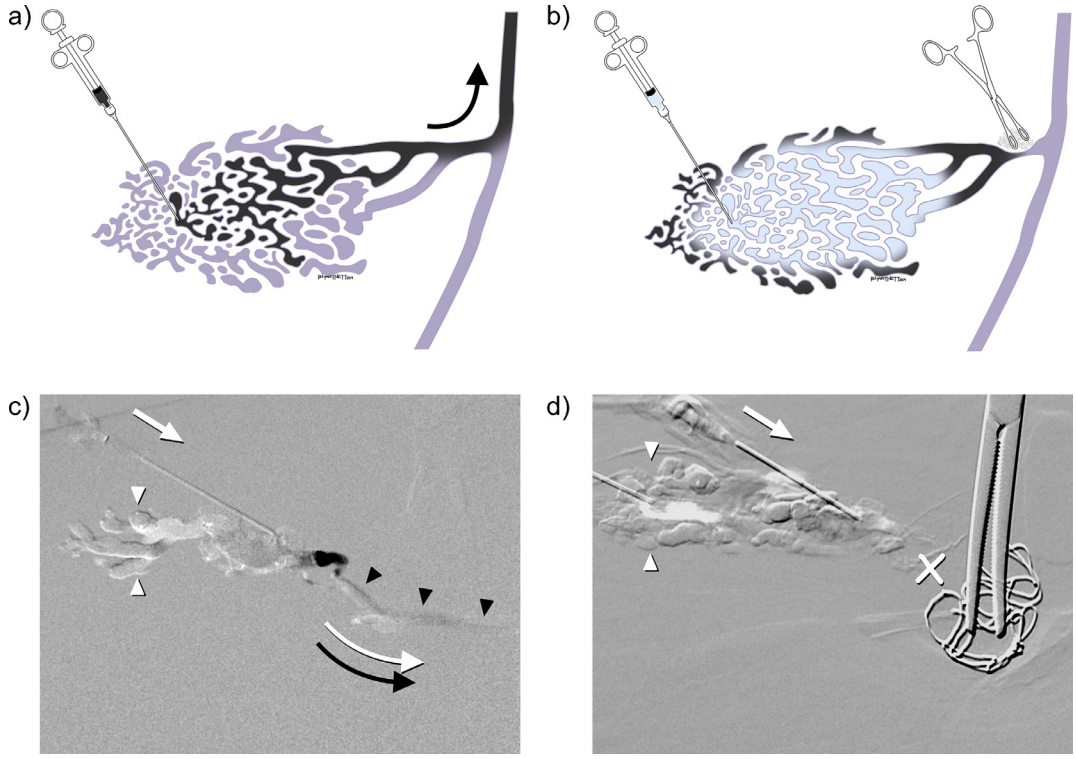

Figure 12 STASE employing focal and extralesional external compression. (a) Phlebographic injection demonstrating rapid efflux of contrast into normal deep veins and insufficient filling of the substance of the venous malformation to allow sclerotherapy, (b) STASE with external compression of the venous outflow with clamp/gauze, halting efflux, and allowing greater penetration of sclerosant into the malformation (light blue), (c) Injection of foam sclerosant (white arrow) into an incompletely filled venous malformation (white arrow heads) due to rapid venous efflux of contrast and sclerosant (back and white curved arrows) through an outflow vein (back arrowheads), (d) STASE employing external compression with clamp/gauze completely occluding venous efflux (white "x") during sclerofoam injection (white arrow) allowing significantly improved penetration into the venous malformation (white arrowheads).

It is desirable to have a sheath whose inner luminal diameter is at least one French size greater than the shaft of the balloon or other introduced devices to allow an additional port of access for either contrast or sclerosant administration. If a balloon size requires a larger sheath, firmer 0.035 wires can be used to facilitate further sheath exchanges.

Once the balloon is gently inflated, phlebography can then be performed either from the original access point within the venous malformation substance proper, or retrogradely from the end-hole of the access sheath. Once appropriate closure of outflow and improved contrast opacification of the venous malformation has been confirmed without collateral recruitment, one can finally administer the sclerosant using a negative roadmap contrast displacement technique. To maximize distribution, one can inject from the original access point and/or retrogradely from the end-hole of the venous outflow sheath and/or an entirely newly placed access site elsewhere within the lesion. The balloon should remain inflated for sufficient time to allow a sclerotherapeutic effect before slow deflation. This technique should not be used in high-volume lesions with large draining outflow veins as there is the possibility of overly-rapid evacuation of sclerosant or thromboemboli upon balloon deflation. In these cases, one should consider more permanent outflow occlusion techniques (Fig. 13).

STASE Using Permanent Extralesional or Focal Outflow Occlusion Techniques

The identical set-up can be used for permanent outflow occlusion techniques whereby the venous outflow is closed using coils instead of an occlusion balloon. As with temporary occlusion techniques, the occlusion site must be "tested" with contrast injection under conditions of either compression or better still, temporary balloon occlusion to assess if there is satisfactory occlusion resulting in improved opacification of the lesion without outflow collateralization. If so, coil deployment in the dominant abnormal outflow vein can proceed. One must be particularly cautious with coil size selection and deployment because (i) the target vein may be artifactually smaller due to spasm, (ii) veins are compliant capacitance structures that can increase in size and with position, and local metabolic demand, (iii) the target vessel may be intramuscular or in an area subject to repetitive motion, (iv) veins can become rapidly larger as one proceeds centrally in the embolization segment, and (v) coils must be deployed within the abnormal outflow vein as centrally as possible, that is, up to but not crossing/interfering with a preserved normal inflow vein as to not leave a large static column of blood that can than thrombose. This can then propagate

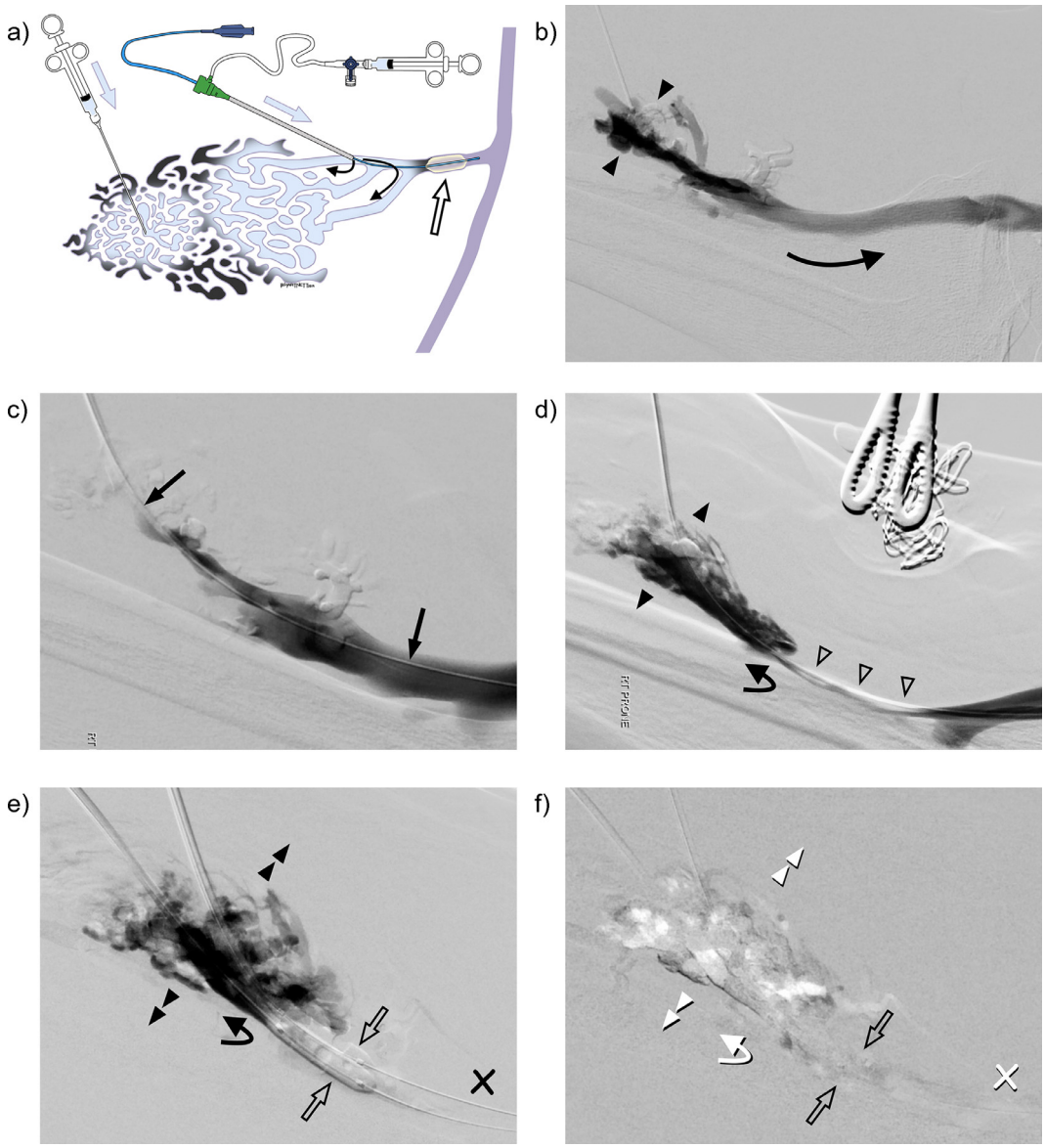

Figure 13 STASE employing extralesional temporary balloon occlusion. (a) Coaxial sheath access achieved directly to the venous outflow through which a balloon is advanced and inflated in the dominant drainage vessel (open black arrow). Sclerosant (light blue) can then be administered through the sheath (light blue arrow) which will then reflux (curved black arrows) and permeate into the lesion. Additional access points into the venous malformation can be used for further distribution of sclerosant (syringe site) which will have longer "dwell time" because of stasis of venous efflux. (b) Direct access phlebogram of a lower leg venous malformation that is underfilled (black arrowheads) due to rapid efflux through Type III venous drainage (curved black arrow), (c) passage of a wire from the malformation to the venous outflow (straight black arrow), (d) "Test compression" phlebography using external clamp/gauze that effaces and occludes venous outflow (open arrowheads) resulting in reflux (curved arrow) into the venous malformation which is much better filled (black arrowheads), (e) Final pre-STASE phlebogram with dual balloon inflation in dual vein outflow (open black arrows) resulting in reflux into the lesion, much better lesion filling (double black arrowheads) and no filling of distal deep veins (black "x"), (f) Sclerotherapeutic phase of STASE with dual balloon outflow occlusion (open arrows) refluxing sclerosant (white) into a well-filled venous malformation (double white arrowheads) and no visualization of deep vein sclerosant (white "x").

leading to deep venous thrombosis or embolize and cause pulmonary embolus. We advocate choosing an appropriately oversized firm detachable framing coil for at least the initial coil placement (Fig. 14).

Access to the outflow venous system for balloon or coil occlusion can also be achieved transvenously via retrograde means. Aside from requiring a separate puncture site distant from the treatment area in question, this route is less desirable as one must navigate venous valves and often confusing, tortuous, venous anatomy.

nBCA glue can also be deployed by way of coaxial catheters through the vascular sheath directly into the dominant venous outflow to achieve permanent outflow occlusion to assist sclerotherapy. Coaxial catheter/microcatheter technique is advised so

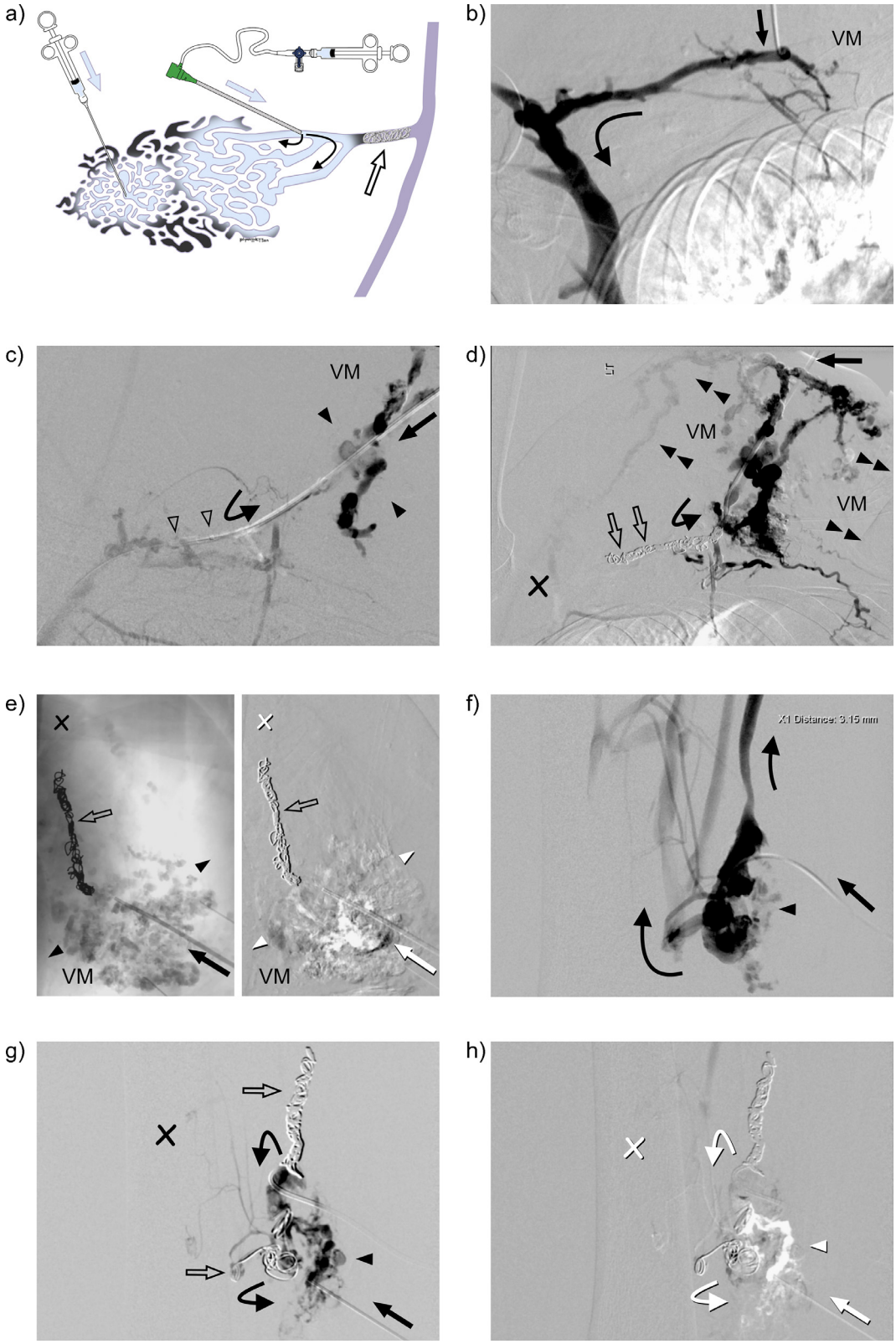

Figure 14 STASE employing permanent coil occlusion. (a) Coaxial sheath and delivery catheter access achieved directly to the venous outflow through which occlusive coils are deployed in the dominant drainage vessel (open black arrow). Sclerosant (light blue) can then be administered through the sheath (light blue arrow) which will then reflux (curved black arrows) and permeate into the lesion. Additional access points into the venous malformation can be used for further distribution of sclerosant (syringe site) which will have longer "dwell time" because of stasis of venous efflux. (b) CASE 1: Patient with very large venous malformation of the left chest wall with large draining veins like a source of previous pulmonary emboli. Direct puncture (black arrow) and contrast phlebogram of an extremely large (and underfilled) venous malformation (VM) within the left lateral chest wall with rapid efflux from a large draining vein into the left axillary subclavian venous system (large curved arrow), (c) "Test balloon occlusion" phlebogram into venous

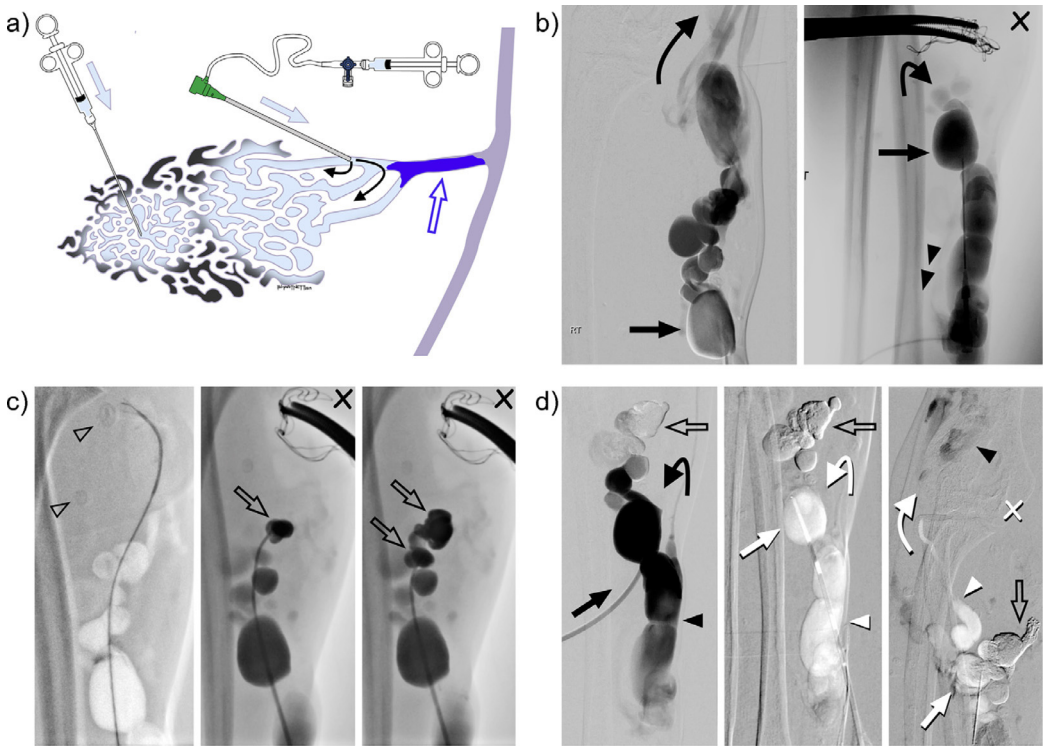

Figure 15 STASE employing focal permanent glue occlusion. (a) Coaxial sheath and delivery catheter access to the venous outflow through which glue has been administered in the dominant drainage vessel (open dark blue arrow). Sclerosant (light blue) can then be administered through the sheath (light blue arrow) which will then reflux (curved black arrows) and permeate into the lesion. (b) Left image: Access for phlebogram (black straight arrow) revealing a forearm venous malformation consisting of large tubular dysplastic veins (Type IV) with rapid venous efflux into the deep veins of the upper arm (curved black arrow), Right image: "Test compression" phlebography with clamp/gauze reveals reflux (small curved arrow) into the venous malformation which is better filled (black arrowheads) with no outflow into the deep veins (black "x"), c) Left image: Catheter access through venous outflow. Note phleboliths (hollow black arrowheads). Center image: Initiation of glue administration (hollow black arrow) during external clamp/gauze compression stopping efflux to deep veins (black "x"), Right image: Later in glue administration (hollow black arrows), (d) Presclerotherapeutic contrast (black straight arrow) demonstrating glue (hollow arrow) stopping and refluxing (curved arrow) contrast into the Type IV venous malformation, Center image: Administration of sclerosant (white straight arrow) similarly confined to venous malformation by the presence of glue at the outflow (curved white arrow and white arrowhead), Right image: Later second access site for sclerotherapy administration (straight white arrow) nearer to glue (hollow black arrow) reveals further penetration of sclerosant into additional parts of the venous malformation nearer the elbow (white arrowhead) and continued transit cranially within the malformation (curved white arrow) displacing contrast into additional regions of malformation to be treated above the elbow (black arrowhead).

that any residual glue adherent to the administration catheter can easily be sheared upon catheter removal if necessary while still maintaining vascular access. A higher glue to ethiodized oil ratio is recommended as a higher viscosity will lessen the risk of central embolization. Outflow control with local compression, tourniquets or inflatable cuffs can further increase the margin of safety during glue administration (Fig. 15).

malformation (black straight arrow) reveals that even partial occlusion of outflow vein with a balloon (open arrowheads) leads to reflux (curved arrow) and better filling of the venous malformation (black arrowheads) and lessened central opacification. (d) Coil occlusion of the venous outflow (open black arrows) leads to reflux (curved arrow) and better opacification/penetration (double black arrowheads) into the venous malformation (VM), (e) Left image: Non-subtracted phlebogram (black arrow) reveals more complete opacification (black arrowheads) of the venous malformation (VM) via multiple access points after venous outflow coiling (open arrows) without significant central vein opacification, right image: Sclerotherapy administration (white arrow) leading to excellent penetration into the lesion (white arrowheads) via multiple access points. (f) CASE 2: Direct puncture (black straight arrow) phlebogram of a leg venous a small but painful venous malformation (black arrowhead) revealing rapid efflux of contrast via multiple communicating veins to the deep system (curved arrows) (g) Coil occlusion of venous outflow at 2 sites (open black arrows) results in reflux of contrast (curved arrows) into the lesion that is better opacified (black arrowhead) on phlebographic injection (black arrow) without deep vein filling (black "x"), (h) STASE showing administered white sclerosant (white arrow) refluxed from the coiled outflow (curved arrows) to persist in the lesion (white arrowhead).

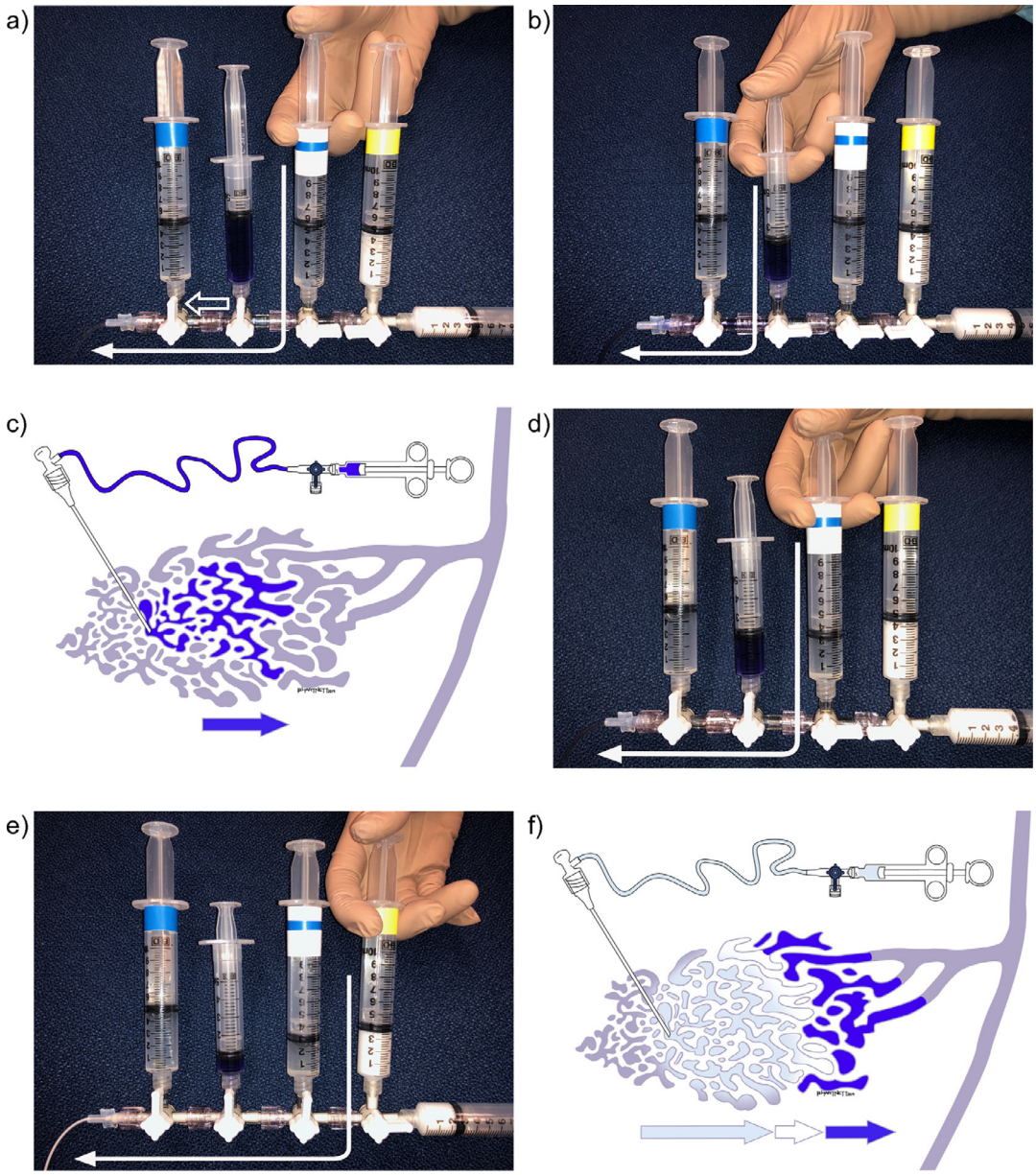

Figure 16 STASE employing glue for intralesional outflow reduction. (a) At the completion of phlebography, the saline aspiration syringe is removed from the standard phlebographic assembly leaving the orthogonal the contrast syringe (blue band). To the vacant port (hollow white arrow) is attached 3 additional stopcocks each in series with one orthogonal syringe of glue (syringe with dark purple liquid), 5% dextrose in water, (D5W, blue and white band syringe), and 2 orthogonal sclerofoam syringes (yellow bands). Stopcocks are opened and D5W is infused in the line (sold white arrow) to the lesion. (b) The D5W port is left unchanged, the glue port is opened to the lesion and administered (solid white arrow), (c) Lesion illustration demonstrating glue diffusing into the venous malformation (dark blue) and schematic representation of glue entering lesion (solid dark blue arrow), (d) a small quantity of D5W is then administered to "clear the line" (solid white arrow) of adhesive, (e) this is immediately followed by the administration of freshly agitated sclerosant (solid white arrow), (f) Illustration demonstrating the resulting glue within the venous malformation (dark blue) being displaced by a combined front of minimal D5W (white) with majority of sclerosant (light blue). Schematic representation of sclerosant (light blue arrow) displacing D5W forward (hollow white arrow) in turn displacing glue forward (dark blue arrow) within the lesion in the direction of outflow.

STASE Using Intralesional or Diffuse Outflow Reduction

Whereas the previous discussions have dealt with technical variations on *extralesional* venous outflow control to assist sclerotherapy, the embolic-occlusive characteristics of nBCA glue also allow it to assist sclerotherapy through *perilesional* and/or *intralesional* venous outflow control. To achieve this, the substance of the venous malformation proper is accessed in routine fashion with a needle/low-volume connector/3-way stopcock/saline/contrast syringe set-up. Contrast phlebography is performed noting lesion morphology and presumed greater than desired rate of venous outflow. The saline port is then detached. To

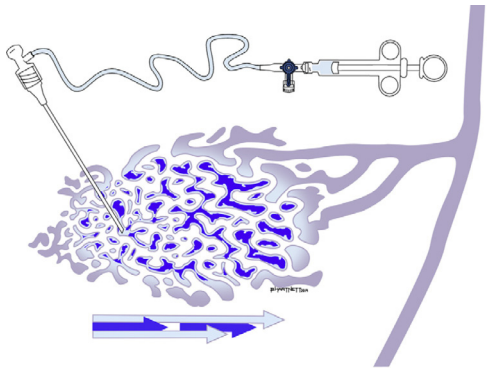

Figure 17 STASE using intralesional glue administration for volume and flow reduction. (a) Glue (dark blue) is administered into the lesion in dilute form for the purpose of occupying volume and slowing rate of flow within the lesion. Sclerosant (light blue) is then administered and moves slowly to occupy space within the intraluminal compartment of the lesion not occupied by glue. Schematic representation of sclerosant (light blue arrows) moving around and through partially glued venous malformation lumen (dark blue arrows) to exert its effect. Sclerotherapy can be performed at multiple access sites.

prevent multiple Luer Lock exchanges and risks needle dislodgement, one may attach to the vacant saline port, in series, three-way stopcocks containing (i) the appropriate concentration of glue embolic in a syringe, (ii) D5W, (iii) 2 orthogonal sclerofoam syringes. The stopcock port to contrast is closed. The port to D5W is opened to the patient and the line is gently flushed clear of residual blood or contrast with D5W. The glue port is the opened to the patient and glue is then immediately administered to distribute within the lesion to the desired point. The stopcock port to glue is immediately closed and the low volume line is cleared of glue with a small quantity of D5W. The D5W stopcock port is then closed and the freshly agitated sclerosant is immediately administered to push the front of D5W and final remaining glue forward peripherally and toward the venous outflow. In more stable access, process can also be performed more simply by exchanging syringes at the hub of the connector tubing. Distribution within the lesion is observed throughout the process, ensuring that administration is halted if one identifies glue or sclerosant passing over-deeply into the venous outflow. If there is occlusion of the system at any point, one should stop the injection and immediately remove the needle. If there is insufficient distribution of sclerosant within the lesion, a separate access point can be made and additional sclerotherapy alone in combination with the same or other outflow occlusion technique can be performed. If glue is to be used again, one must use fresh syringes of agent and a new apparatus (Fig. 16).

In addition to slowing flow, glue can also first be delivered intralesionally more diffusely in a staged manner with the intent of occupying a much more significant proportion of the intravascular volume of the lesion, which also has the result of lowering flow. The sclerosant is then administered into this environment and achieves greater concentration by encountering a lower overall lesional dilutional volume and greater wall contact/dwell time to exert its effects through lower flow rates. In this scenario, one can targeting the glued lesion with sclerosant at multiple sites if necessary (Fig. 17).

All STASE techniques are part of a continuum and can be employed in various combinations within the same case (Fig. 18).

Completion of the Procedure

At the completion of the procedure, all needles are left in situ for a period of time to allow the agent to take effect and avoid extravasation. The lesion can be aspirated if there is concern for distal embolization upon deflation of temporary outflow occlusion. The site is cleansed, and a light removable dressing is applied to allow inspection of the site while in recovery. More cavitary lesions can have a compression dressing applied to better oppose inflamed vascular walls and encourage sclerotic versus thrombotic closure.[54] Similarly the site should be elevated if possible.

The site should be inspected for signs of blanching, "duskiness", erythema, or blistering which could be signs of impending skin necrosis. Local pulses should be inspected, and a perfunctory neurologic assessment should be performed when appropriate.[8] All findings should be documented. Continued inspection should continue at regular intervals while in hospital to assess skin, neurovascular, and muscular integrity and signs of DVT.

While still in the case room, the patient may benefit from IV ketorolac at the completion of the procedure. Sustained IV hydration is essential. Postprocedure while in recovery, analgesics and anti-inflammatories are given and are based on the lesion size, location, and type of sclerosant. Small lesions with more benign sclerosants often only need over-the-counter non-steroidal anti-inflammatory (NSAID) coverage and mild narcotic analgesia. Most treated patients can be discharged the same day or the within 24 hours with instructions for elevation and rest of the affected area. More significant lesions or aggressive therapy may require patient controlled analgesia for 24 hours, IV steroids, and in hospital admission for one to 3 days with discharge on NSAIDS and narcotic analgesia for several days to 2 weeks. As described earlier, if LIC/coagulopathy is present, LMWH may be indicated, in consultation with a hematologist, for 14 days or until ambulatory.

Clinical Follow-up

Barring complications, the patient can be contacted by telephone for periprocedural follow up at one-month post intervention. For all but the smallest venous malformations anticipating single-session therapy, most patients should be scheduled for 2 to 3 staged procedures separated by one to 3-month intervals. Because maximal effect of sclerotherapy occurs at least 2 months after intervention, an in-person consultation with the patient should not occur until 3 months after their last procedure when the need for additional therapy is suspected and not until 6 months where completion of therapy is anticipated. Coscheduling ultrasound with follow-up is often very helpful and revealing. Because the interventional radiologist is usually treating patient symptoms and not the lesion *per se*,

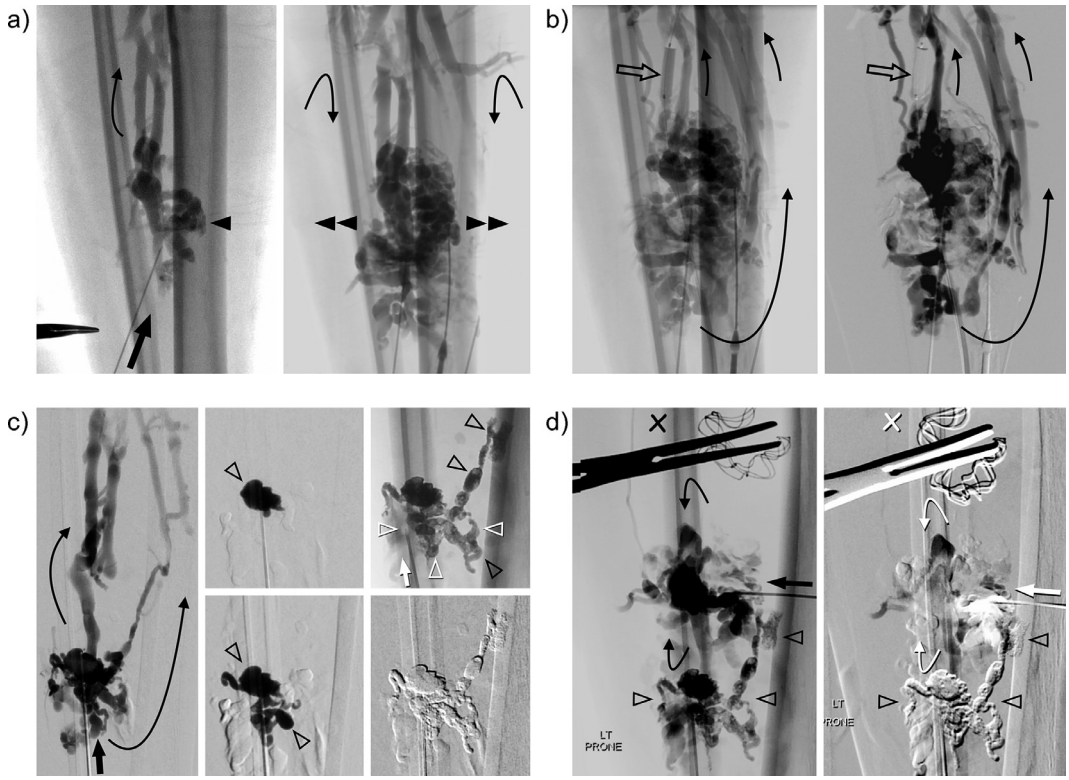

Figure 18 Combination of STASE techniques in the treatment of a venous malformation. (a) Left image: Access for phlebography (straight black arrow) reveals only minimal opacification of a calf venous malformation (black arrowhead) due to rapid venous efflux (curved arrow) into trifurcation veins. Right image: Phlebography during above-knee cuff compression reveals reflux (curved arrows) more completely opacified venous malformations (black double arrowheads), (b) Left image: Nonsubtracted phlebogram during temporary "test occlusion" with a balloon (hollow black arrow) at one of 2 expected dominant draining veins reveals recruited venous efflux via many more collateral venous structures particularly from the inferior portion of the venous malformation (curved arrows), Right image: Same image under digital subtraction, (c) Left image: Phlebogram from access to the inferior substance venous malformation leading to the venous outflow described previously prior to glue/sclerosant administration. Center images upper and lower: Administration of glue into the venous malformation (hollow black arrowhead). Right images, upper and lower: Nonsubtracted and subtracted images respectively, demonstrating administration of sclerosant (straight white arrow) penetrating the venous malformation (hollow white arrowheads) and displacing glue forward deeper into the venous malformation and also into the proximal venous efflux (hollow black arrowheads), (d) Left image: Phlebography at new site (straight black arrow) during clamp/gauze compression above and glue occlusion in the lower malformation/lower outflow (hollow black arrowheads) leads to reflux (curved arrows) and retention of contrast within malformation and no deep vein filling ("x), Right image: Sclerotherapy administration (straight white arrow) with similar retention of sclerosant within the lesion (white curved arrows) and not passage into deep veins ("x").

routine follow up MR is *not* needed to confirm findings of involution if the lesion has been rendered asymptomatic. However, there are circumstances where establishment of new baseline may be necessary. MR is probably best utilized in the re-evaluation of a persistently symptomatic venous malformation by the allowing the differentiation between treated and persisting components within the lesion that will direct future intervention.[4,7] If a lesion is fully treated, the patient can be discharged from the interventional radiologists care with patient reassurance they need only contact the interventional radiology service or their referent to reactivate their care.

Complication Management

Complications from sclerotherapy range from minor to severe which and are dependent on lesion location, morphology, size, and sclerosant/technique chosen. Erythema, tenderness, swelling, and pain are to be expected to variable degree.

If the lesion is closer to the skin, one must be aware of the possibility of skin blanching, "duskiness," and induration which can progress to skin blistering or frank skin necrosis. This later complication is rare and at our instituting should prompt consultation with plastic surgery who is best able to evaluate extent and severity of injury and then initiate and coordinate outpatient follow up with appropriate topical medication and dressings. The need for debridement is exceedingly rare and should be avoided wherever possible.[11]

Temporary or permanent nerve impairment is a major complication that is fortunately very low even with more toxic sclerosants (<1%). Nerve impairment due to direct-contact neurotoxicity can be suspected, particularly with stronger sclerosants, when it occurs in the hyperacute and

acute setting. More delayed or gradual nerve impairment may be due to sclerotherapy-induced local tissue swelling and elevation of tissue pressure which can progress onto compartment syndrome. The differentiation between these 2 etiologies can be challenging particularly if physical examination findings are confounded by the patient coming out of general anesthesia or regional nerve-blockade. In any case, if compartment syndrome is suspected, immediate surgical consultation is mandated. In hospital or outpatient steroids may relieve lesser degrees swelling and persistent nerve injury may necessitate rehabilitation physiotherapy.

Contracture formation can occur, particularly within deep or intramuscular venous malformations, so informing the patient to anticipate stiffness and encourage movement of the involved limb as soon as possible after several days is very important. For patents with preprocedure contracture or those with ongoing post procedure contracture symptoms, a physiotherapist consolation and prescribed regimen should be planned and in advance on those cases deemed highest risk.

Hemoglobinuria can occur with some sclerosants and adequate hydration is important pre and postprocedure. As renal injury can ensue, monitoring of fluid balance and urine output is critical.

Hematologic issues of DIC and venous thromboembolism must be considered before and immediately after every case. As discussed earlier, thromboprophylaxis must be considered in appropriate cases. If one is concerned regarding the possibility of DVT either clinically or because of concerns regarding overly central sclerosant delivery, Duplex ultrasonography is recommended while still in hospital.

Bleomycin specific complications include fever, flu-like symptoms, skin tingling, hyperpigmentation, flagellate rash pulmonary hypersensitivity and pulmonary toxicity/fibrosis.[40] Hyperpigmentation can occur in a few hours or as late as 2 months and may occur in regions of skin scratching or adhesive placement and removal, however, may also be idiosyncratic and due to hypersensitivity. Judicious use of adhesives perprocedurally may be helpful in reducing local hyperpigmentation. Pulmonary complications and dosing have already been discussed under "Choice and Preparation of Therapeutic Agents." There is debate on the utility and duration of surveillance of pulmonary function and chest films post therapy, however, any detected pulmonary phenomenon, acute or delayed must receive prompt respirology consultation.

Outcomes

As stated earlier, measurement of success for any intervention should be based on the level of improvement in patient presenting symptoms and improvement in function both physically and psychologically, and not solely by imaging criteria. Although reported outcomes for percutaneous intervention in venous malformations are based on a wide range of patient ages, lesion types, chosen sclerosant(s), techniques, types of center, and length of follow-up, general trends can be extrapolated. Of all treated patients, a significant percentage of patients experienced some level improvement in symptoms of pain (76%-89%), swelling (58%-84%), functional improvement (41%-80%), bleeding (70%), and cosmetic deformity (35%-59%), with the majority in each of these categories reporting that there was moderate to marked improvement after sclerotherapy.[55-59]

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