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MICROSURGERY

Kailash Narasimhan, MD
John R. Griffin, MD
James F. Thornton, MD

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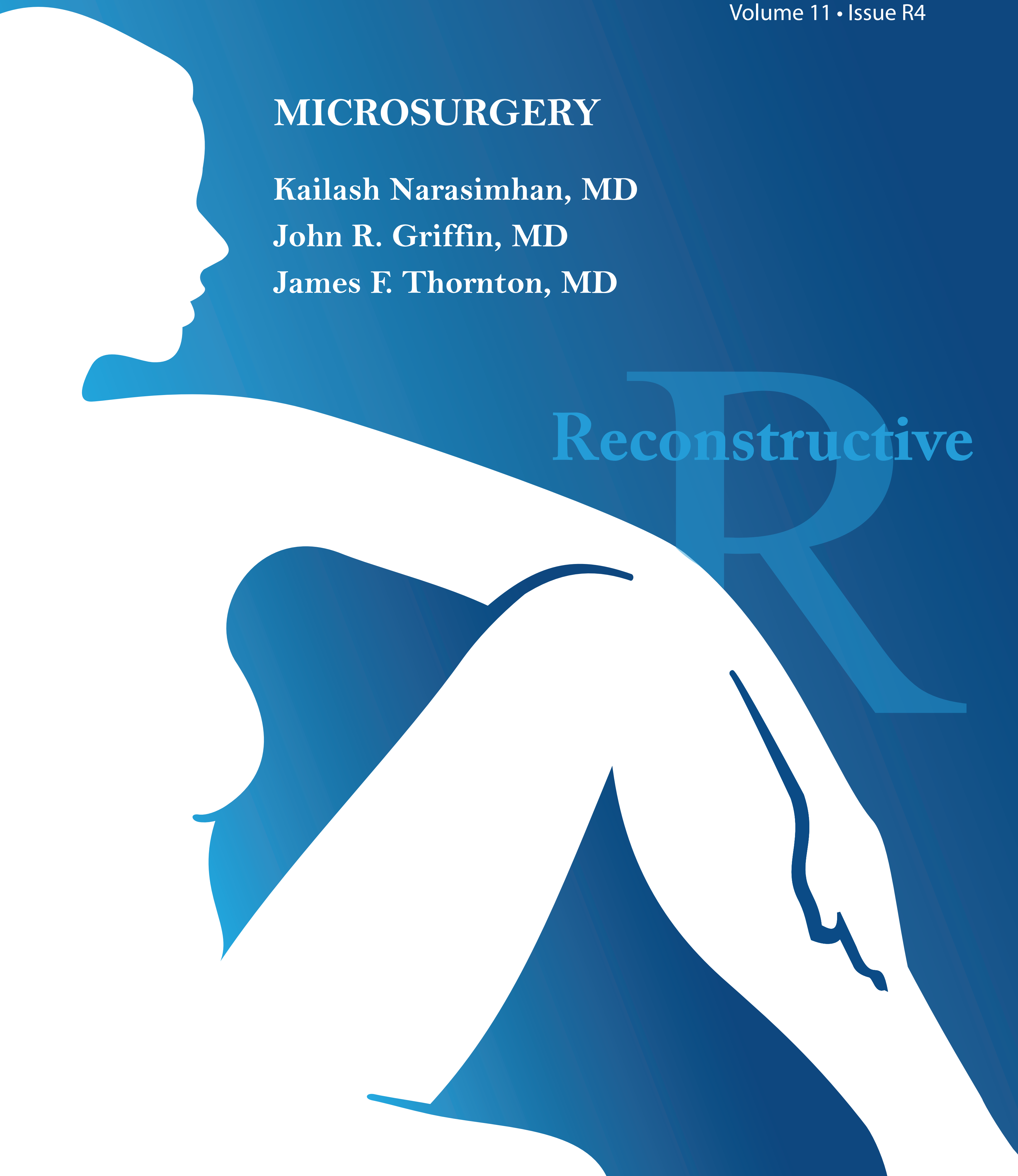

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Business Office
P.O. Box 36466
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info@SRPS.org

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MICROSURGERY

Kailash Narasimhan, MD*

John R. Griffin, MD†

James F. Thornton, MD*

*University of Texas Southwestern Medical Center at Dallas, Dallas, Texas

†Private Practice, San Mateo, California

HISTORY

In the late 1890s and early 1900s, surgeons began approximating blood vessels, both in laboratory animals and in human patients, without the aid of magnification.[1,2] In 1902, Carrel[3] described the technique of triangulation for blood vessel anastomosis and advocated end-to-side anastomosis for blood vessels of disparate size. Nylén[4] first used a monocular operating microscope for human eardrum surgery in 1921. Soon after, as reported by Mudry,[5] Holmgren used a stereoscopic microscope for otolaryngological procedures.

In 1960, Jacobson et al.[6] working with laboratory animals, reported microsurgical anastomoses with 100% patency in carotid arteries as small as 1.4 mm in diameter. In 1965, Jacobson and Katsumura[7] were able to suture 1-mm-diameter vessels with 100% patency in laboratory animals. The authors emphasized the importance of avoiding intimal trauma and precise intima-intima reapproximation. In 1966, Green et al.[8] used 9-0 nylon suture on rat aortae (average diameter, 1.3 mm) and vena cavae (average diameter, 2.7 mm) and reported anastomotic patency in 37 of 40 animals at 21 days. Acland,[9] in 1972, presented a series that showed 95% patency in anastomosed rat superficial epigastric arteries. Since the reviews of microsurgical instrumentation and techniques presented by Smith[10] and Cobbett[11] in the 1960s, suture technology has progressed to 50-µm needles with 12-0 suture.

Per Gallico,[12] in 1963, surgeons in China successfully reattached a patient's hand that had been amputated at the wrist. The radial and ulnar arteries were anastomosed with short links of 2.5-mm-diameter polyethylene tubes. Also in 1963, Kleinert and Kasdan[13] described their experience with digital amputations and near-amputations. The authors were unable to successfully replant digits but did revascularize nearly amputated digits. They used loupe magnification and emphasized the importance of using vein grafts if vessel anastomosis was under tension. In 1964, Malt and McKhann[14] described the first successful clinical replantations in two patients who had undergone arm amputations.

Also in 1964, Nakayama et al.[15] reported what is most likely the first clinical series of free tissue microsurgical transfers. The authors brought vascularized intestinal segments to the neck for cervical esophageal reconstruction in 21 patients. The intestinal segments were attached by direct microvascular anastomoses in vessels that were 3 to 4 mm in diameter. Sixteen patients had a functional esophagus at follow-up of at least 1 year.

Two separate articles published in the mid-1960s described the successful experimental replantation of rabbit ears and rhesus monkey digits.[16,17] In 1965, Krizek et al.[18] reported the first successful series of experimental free flap transfers in a dog model. In 1968, Komatsu and Tamai[19] used a surgical microscope to aid in the first successful replantation of a completely amputated digit. In 1969, Cobbett[20] transferred a great toe to the hand.

In 1971, Antia and Buch[21] reported successful free transfer of a superficial epigastric artery skin flap to the face. The authors anastomosed the superficial epigastric artery and vein to the common carotid artery and internal jugular vein to repair a cheek defect. In 1972, McLean and Buncke[22] transferred the omentum to the scalp via microvascular anastomoses. In 1973, Daniel and Taylor[23] and O'Brien et al.[24] independently reported the free tissue transfer of groin flaps for lower extremity reconstruction.

Since the beginning of clinical microvascular surgery in the early 1970s, donor sites for free tissue transfer have multiplied and microsurgical tools and techniques have been expanded and refined. As microsurgery became more prevalent and experience with free tissue transfer mounted, the success rates of microvascular procedures also climbed. Current success rates are higher than 90% (Table 1).[25–31] Khouri[32] presented a survey of nine microsurgeons and reported that operative experience is the most critical factor related to improved success rates.

In 1990, O'Brien[33] reviewed the strides made in microvascular surgery during the 1970s and 1980s and looked to the future for new applications of microsurgery. New areas of microsurgical interest have evolved during the last 21 years. In 2000, Whitworthm and Pickford[34] reported good results at 30 years for the patient with the first toe-to-thumb transfer. Clinicians continue to refine techniques for salvage of severely injured upper extremities, including the scenario of failed replantation. Functional free muscle transfer is an active area of research, with new applications being discovered. Recently, functional free gracilis has been described as being reinnervated by the nerve to the supinator for reconstruction of the thumb and finger extension in patients with C7–T1 brachial plexus root avulsion.[35]

Currently, new studies indicate the long-term sequelae involved with upper limb transplantation. Jensen et al.[36] noted that although most patients who undergo hand transplant achieve improved social, functional, cosmetic, and sensory outcomes, measurements of quality of life are limited. Chang and Mathes[37] reported that although more than 65 hand transplants have been performed and favorable outcomes have been reported, to achieved optimal outcomes, the transplant must be performed at a dedicated center that facilitates integration of multiple specialists, ethicists, pharmacists, and rehabilitation professionals.

As the results of surgery became more predictable and the number of available free flaps grew, efforts shifted to minimizing donor site morbidity. Clinical applications and choices of perforator flaps continue to change. In the hands of experienced operators, loupe magnification now seems to be as effective as the operating microscope in certain cases. Free flap selection for specific defects is becoming more standardized, and technological innovations in anastomotic techniques and devices hold promise for the future of microsurgery.

BASIC SCIENCE CONCEPTS IN MICROSURGERY

In addition to possessing the appropriate technical skills, the microvascular surgeon needs to understand the mechanisms of vessel injury, repair, and regeneration; be familiar with the processes of vasospasm and thrombosis and their pharmacological control; and be aware of the effects of ischemia and hypoxia on revascularized tissue.

Vessel Injury and Regeneration

Microvascular anastomoses inevitably disturb the endothelium and subendothelium of the vessel walls. Exposure of the underlying subendothelium to the bloodstream results in platelet aggregation, which is

TABLE 1

Free Flap Success Rate and Learning Curve

Study	Experience	Success Rate (%)
Serafin, 1980[25]	First 25 cases	72
	Last 25 cases	96
Godina, 1986[26]	First 100 cases	74
	Last 100 cases	96
Harashina, 1988[27]	First 3 years	75
	Last 5 years	97
Khouri and Shaw, 1989[29]	First 100 cases	91
	Last 100 cases	97
Canales et al., 1991[28]	First 3 years	83
	Last 3 years	97
Selber et al., 2012[30]	Review of nearly 5,000 cases (4,965)	99
Holom et al., 2013[31]	Review 143 head and neck cases	92

the first step in the formation of a thrombotic plug.

Among the multiple connective tissue components of the blood vessel wall, collagen stimulates the greatest amount of platelet clumping. Weinstein et al.[38] effectively showed blood vessel injury and repair processes through scanning electron microscopy (SEM) of anastomoses. Full-thickness sutures that afforded intimal continuity provoked the least amount of anastomotic bleeding and platelet aggregates. "Far worse damage" occurred with partial-thickness bites of the vessel wall than with properly placed full-thickness sutures. In a separate study using SEM, Harashina et al.[39] noted no difference in patency (94%) of 1-mm-diameter rat femoral vessels anastomosed with either adventitial or full-thickness sutures.

During healing of the vessel wall, a pseudointima forms within the first 5 days.[39] Approximately 1 to 2 weeks after injury, new endothelium covers the anastomotic site. At the time of anastomosis, a layer of platelet covers the denuded endothelium of the vessel wall. This layer of platelet cells does not progress to fibrin deposition and thrombosis if it is not exposed to the media and the lumen is not injured. During the next 24 to 72 hours, the platelets gradually disappear. Platelets show little affinity for exposed surfaces of sutures within the vessel lumen.[38,39] The disappearance of platelets within the lumen and the formation of pseudointima correlate well with previous clinical and experimental observations and lead to the conclusion that the critical period of thrombus formation in the anastomosis occurs during the first 3 to 5 days.[40,41]

The mechanism of endothelial regeneration depends on the presence or absence of mechanical injury to the subendothelial structures. If the endothelial layer alone is damaged, it is reconstituted from surrounding cells and regeneration is complete in 7 to 10 days. With damage of the underlying subendothelial structures, media and adventitia, regeneration of damaged epithelium occurs by migration and differentiation of myoendothelial cells from the cut vessel ends.[42] The remaining layers of the vessel wall regenerate via proliferation of fibroblasts with collagen deposition and myointimal thickening at the anastomotic site.[43] The elastic and muscular elements of the vessel wall fail to regenerate to the same degree as the endothelium, and the layers do not return to their preinjury state.

These findings led to an emphasis on gentle dissection of all vessels and careful controlled placement of sutures through vessel walls. Simple dissection and exposure of vessels from their beds was shown by Margić[44] to result in significant endothelial loss, although the vessels maintained flow. Also, to avoid damage to vessels during dissection, side branches should be tied or coagulated using bipolar electrocoagulation. Improper bipolar coagulation can result in endothelial damage and platelet aggregation if the current passes too close to the branch origin. Caffee and Ward[45] described the safe and effective use of bipolar electrocautery in small vessels. The authors reported that the side branch must be treated with electrocautery at the lowest setting possible to achieve coagulation and that this must be done well away from its junction with the main vessel.

Special attention should be given to small vessels, which if desiccated can lose their endothelial cell layer and trigger diffuse platelet aggregation. It is important that all exposed vessels be kept in a moist environment to prevent desiccation. Prolonged vasospasm can also cause endothelial sloughing, and vessels experimentally subjected to vasospasm for longer than 2 hours lose most of their endothelial layer.[38]

Topical lidocaine often is used in microvascular surgery to prevent vasospasm. The safe maximum dose of lidocaine for topical application has not been established. Johnstone et al.[46] reported using 4% lidocaine in doses of up to 2000 mg with no adverse effects. The anesthetic was applied topically to arteries and veins being anastomosed during free tissue transfer. The measured serum concentrations of the drug in the study patients were well below toxic levels, suggesting that most of the topically applied lidocaine is not fully absorbed. Nevertheless, the standard pharmacology references list the maximum safe dose of injectable lidocaine as ≤500 mg for the average adult patient. Ohta et al.[47] showed experimentally that Xylocaine (AstraZeneca, Wilmington, DE) has its optimum spasmolytic and antispasmodic effects at a concentration of 20%. Clinically, 2% lidocaine also has a beneficial effect on moist vessels.

Injury to the endothelium from microvascular clips is directly related to clip pressure.[48] Weinstein et al.[38] noted that curved or angled clips cause more damage than do flat clips. Closing pressures of vascular clips should remain <30 gm/mm^2 to minimize damage to vessels.[49] O'Brien et al.[50] presented a discussion of the currently available clamps and clamp approximators and provided examples of each. El-Shazly[51] described a new double transverse microvascular clamp that can be applied simultaneously as one clamp to both the artery and the vein, allowing anastomosis to be performed more easily by rendering the working environment less crowded.

The most significant damage to vessel walls is from needle and suture penetration and technique of placement. Large needles and obliquely placed sutures cause major endothelial lacerations, exposing subendothelium and inducing platelet aggregation. Repeat needle puncture for suture placement produces large platelet plugs at bleeding sites.

Unequal inter-suture distances can result in endothelial gaps, distortion, constriction, and exposed intimal flaps. Loosely tied sutures can expose subendothelial elements to the bloodstream and allow excessive anastomotic bleeding and subsequent platelet plug formation. Too many sutures or sutures that are tied too tightly can trigger endothelial slough.[38] Excessive trauma to vessel walls, undue tension on suture lines, and loosely approximated sutures can produce medial discontinuity and result in pseudoaneurysms or aneurysms at the anastomotic site.[38,39]

Chow et al.[52] subjected microanastomoses in the animal model to various levels of tension and found a greater tolerance for microanastomotic tension than had been previously surmised. Acland and Trachtenberg[53] used SEM to evaluate microanastomoses in rats at intervals ranging from 1 hour to 21 days after anastomosis. Their findings paralleled those of Weinstein et al.[38] in that intimal loss occurred below the site of clamp pressure and medial necrosis occurred at the anastomosis proper. Despite the noted changes, the patency rate was 100%, indicating that some tissue damage is tolerated without untoward consequences.

Lidman and Daniel[54] investigated the reasons why clinical microvascular anastomoses failed and found that anastomoses performed in the zone of injury were most often implicated. Another common problem leading to surgical failure was external compression of the anastomosis by hematoma.

Clotting Mechanism

Johnson[55] detailed the biochemical and physical aspects of the process of platelet-mediated thrombosis in vessels. Platelets do not adhere to undamaged, healthy intimal surfaces, but when the intima is injured in any fashion, exposed collagen triggers platelet adhesion to the vessel surfaces.[56] Once these platelets are activated by collagen, platelet granules are released, which in turn attract more platelets—a process known as *aggregation*. The activated platelets have stimulated receptor sites to which fibrinogen adheres, and fibrinogen then forms proteinaceous bridges between platelets. As platelets become activated, they also promote the change of fibrinogen to fibrin. The fibrin in turn promotes “red clot” and further strengthens the growing clot.

Platelets contain two types of granules: alpha granules and dense granules. Alpha granules contain von Willebrand factor and fibrinogen. Dense granules contain adenosine diphosphate, calcium ions, and serotonin.[57] The secreted adenosine diphosphate, calcium, fibrinogen, and von Willebrand factor all contribute to ongoing recruitment of platelets, which eventually reach a critical mass that can cause thrombus formation by either occluding the vessel or initiating the classic extrinsic pathway of coagulation.[58]

Multiple steps in the clotting mechanism have been manipulated pharmacologically with the aim of reducing platelet aggregation and release.[59] Johnson and Barker[60] presented a discussion of current antithrombotic therapy in microvascular surgery. Heparin has been used for years as an anticoagulant. Heparin acts primarily to increase the action of antithrombin-3, which inactivates thrombin. Heparin has also been shown to decrease platelet adhesion[61,62] and to hamper the conversion of fibrinogen to fibrin.[63] Greenberg et al.[64] showed in a rabbit model that low-dose heparin infusion significantly prevented anastomotic occlusion for 72 hours after surgery in the arterial inversion model. A recent review presented by Froemel et al.[65] indicates that no consensus has been reached regarding which prophylactic antithrombotic agents can be routinely used. Current regimens continue to use aspirin, heparin, and colloids (dextran). Good surgical technique, however, remains one of the best prophylactics.

Khouri et al.[66] studied the effect of heparin on rat femoral artery anastomoses and noted that a single bolus dose of heparin administered before blood flow was reestablished inhibited thrombus formation by preventing the conversion of fibrinogen to fibrin. Treatment with dazmegrel, a selective thromboxane synthetase and platelet aggregation inhibitor, was only partly successful in improving the patency rate at the anastomoses. Fibrin could still form an occlusive thrombus even in the absence of aggregating platelets. The authors concluded that at least in their model, fibrin mesh deposition contributed more to the pathogenesis of thrombotic occlusion of traumatized arteries than did platelet aggregation. The incidence of hematomas in the animals treated with heparin was 12.5% (three of 24 rats).

In the clinic, heparin is administered by direct continuous infusion to save free flaps.[67] Some surgeons think that heparin does not improve patency in cases of uncomplicated repairs and that the associated risk of bleeding outweighs the potential benefit of heparin as an anticoagulant.[55,60] Perhaps paradoxically, the slow oozing that accompanies injudicious heparin use in free flaps can result in large clots around the small vessels, ultimately causing occlusion and thrombosis of outflow or inflow. For this reason, heparin infusion is used sparingly by most microsurgeons.

When administered intraoperatively at a dose of 325 mg, aspirin inhibits initial platelet aggregation at the anastomotic site. This action was thought to be mediated by the endothelial cyclooxygenase pathway with subsequent blockage of thromboxane A_2. Even at low doses, however, aspirin inhibits release of prostacyclin, a potent vasodilator and platelet inhibitor.[68] Newly created anastomoses show a loss of endothelium for several millimeters from the suture line,[53] and the mechanism for prostacyclin production was thought to be absent. Contrary to previous expectations, Restifo et al.[69] found a clear increase in prostacyclin production at the anastomosis. The authors speculated that the rising levels of prostacyclin stemmed from smooth muscle or fibroblasts in the subendothelium or from an up-regulation of prostacyclin synthetase triggered by cytokines released after vessel injury. They concluded that the thrombogenic tendency of the anastomosis was not explained by a decrease in the antithrombotic agent. Prostacyclin itself as a topical agent in microvascular surgery is not effective.[70]

Dextran is a polysaccharide that is clinically available in molecular weights of 40,000 (dextran-40) and 70,000 (dextran-70). Dextran was first used as a volume expander but was later found to have numerous effects on the microvascular clotting scheme, with both antiplatelet and antifibrin functions. Several pathways have been theorized for the observed decrease in platelet adhesion noted after dextran administration, including elevated negative electric charge on platelets and inactivation of von Willebrand factor, a major contributor to platelet aggregation and adhesion to vessel wall collagen.[59,60,71,72] Multiple experimental studies have shown that dextran improves microvascular patency.[73–78] A study in the rabbit model by Rothkopf et al.[72] showed patency of microanastomoses and arterial inversion grafts at 7 days to be 85% in the dextran group and 48% in the control group. Clinically, a 10% solution of dextran-40 usually is administered as a loading dose of 40 to 50 mL; a continuous infusion of 25 to 50 mL/h is then intravenously administered. Because of reports of allergic reactions to dextran,[60] a test dose should be administered first. Dextran can also cause bleeding and subsequent vessel occlusion problems, similar to heparin. Acute renal failure occurring secondary to dextran use has also been reported.[79]

Proteolytic enzymes such as streptokinase and urokinase are being evaluated as lytic agents in thrombosed vessels and might find a place in the prevention of microvascular thrombosis, especially in traumatized vessels.[80,81] Streptokinase was administered to four patients and urokinase to two, resulting in a 100% success rate. Streptokinase is produced by group C beta-hemolytic streptococci, and urokinase is produced by human kidney cells. Both can convert plasminogen into plasmin, a highly specific fibrinolytic enzyme.[82–85] Goldberg et al.[80] presented a report of the salvage of six of seven thrombosed free flap vessels by infusion of streptokinase or urokinase. A sub-flap hematoma developed postoperatively in one of the six cases. Currently, these enzymes are used in the salvage of flaps and not for preventive purposes. Trussler et al.[86] used catheter-directed thrombolysis with tissue plasminogen activator (tPA) to salvage two free flaps.

tPA is produced by human vascular endothelium and is responsible for activating plasminogen, the inactive precursor to plasmin. Apparently, tPA is rapidly bound by specific inhibitors. However, in the presence of high amounts of fibrin, a shift occurs in the activator-inhibitor complex and tPA, plasminogen, and plasmin are released, with consequent fibrinolysis.[81,87] Levy et al.[88] compared the effects of urokinase and tPA in the rat model and found no statistical difference between the two substances with respect to lysis of microsurgical thrombosis. In 1989, Fudem and Walton[89] reported salvage of a free flap with a 15-minute infusion of high-dose tPA and concomitant heparin. Arnljots et al.[81] significantly improved patency of traumatized microvessels with low-dose tPA infusion for 2 hours. Romano and Biel[90] showed statistically significant improvement in patency rates of microanastomoses in animals treated with low-dose tPA infusion over 48 hours. Stassen et al.[91] reported successful dissolution of arterial thrombosis with selective infusion of recombinant tPA during digital revascularization. Selective infusion reduces the risk of systemic complications from tPA administration.

Several authors stress the importance of using anti-coagulants along with fibrinolytic therapy in microsurgery.[60,85,92] The next horizon in manipulating the clotting mechanism to prevent microvascular thrombosis is through monoclonal antibody regulation of platelet aggregation. Gold et al.[93] showed profound inhibition of platelet function in humans after administration of murine monoclonal antibodies directed against human platelet glycoprotein IIb/IIIa receptor, which mediates platelet aggregation and contributes to thromboembolic disorders.

Lan et al.[94] suggested another strategy for salvage of thrombosed microvascular anastomoses. The authors argued for anastomotic resection and replacement of thrombosed veins with vein grafts, together with systemic heparin administration. In the rat femoral vein model, a high rate of recanalization was noted when this protocol was implemented.

Davies[95] surveyed the practice of anticoagulation in clinical microvascular surgery. On the basis of responses he received from 73 centers in 22 countries, the author was able to document equal success rates (89%) for free flap procedures performed with anticoagulation (691 cases) and without anticoagulation (134 cases). For limb replantation, the overall success rate was lower with anticoagulation (76%) than without anticoagulation (89%). Veravuthipakorn and Veravuthipakorn[96] reported very good results achieved when using no antithrombotics in free flaps or in replants. Considering the information that is currently available regarding the benefits of anticoagulation in microsurgery, the following conclusions seem warranted:

1. Indications have not been defined for anticoagulation or antifibrinolytic therapy when mechanical and vascular factors are optimal (e.g., during elective free flap transfers).
2. When evidence of thrombosis is present in postoperative microvascular anastomosis, flap reexploration and treatment with fibrinolytic therapy and anticoagulation seem prudent. Flap reexploration is the essential step.
3. Anticoagulation or fibrinolytic therapy might be indicated in clinical situations in which mechanical or metabolic factors are not favorable and cannot be improved.

In general, the standard treatment for threatened flaps is reexploration. Trussler et al.[97] reported the cases of two patients who presented with late occlusions to their free flaps, one at postoperative day 6 and the other at postoperative day 12. Both patients underwent flap salvage with highly selective catheter-directed thrombolysis. This option deserves further study, especially in select cases of delayed or late pedicle thrombosis in free flaps.

Tissue Response to Ischemia and Hypoxia

The transfer of tissues by microvascular anastomoses requires a period of tolerance to ischemia by the donor tissue. Skin and subcutaneous tissue are relatively resistant to the effects of anoxia, and intracellular pH changes are reversible for up to 24 hours.[98] Mammalian skeletal muscle is much less tolerant to ischemia than is skin.[99,100] Irreversible damage to the microcirculation of skeletal muscle in man begins at approximately 6 hours.[99] As documented by nuclear magnetic resonance spectroscopic studies,[101] irreversible damage to energy metabolism occurs after 4 hours of ischemia.

In contrast, connective tissue rich in fibroblasts, chondroblasts, or osteoblasts is relatively resistant to prolonged hypoxia.[102] In peripheral nerves, the neuromuscular junctions are most sensitive to ischemia.[103]

Cooling prolongs tolerance to ischemia in all types of tissues.[102–110] Muscle and fat cells show a marked increase in histological changes with duration of cold ischemia, whereas skin and small vessels remain relatively free of abnormality after circulation is restored to the tissue.[109] Donski et al.[109] studied the effect of cooling on the survival of free groin flaps in the rabbit: 86% of flaps that were cooled for 1 to 3 days survived. Anderl[111] stored a human groin flap for 24 hours and reported complete flap survival; in the rat, maximum ischemia time was 6 hours at normal body temperatures and 48 hours if cooled.[108] Reus and Schlenker[110] suggested rewarming of arterial flaps before circulation is reestablished to ensure adequate blood flow during the ensuing hyperemic period.

Takayanagi and Tsukie[112] reported survival of at least the skin portion of a latissimus dorsi musculocutaneous free flap after 15 to 17 hours of cold ischemia. May et al.[107] noted 100% survival of rabbit free flaps at 4 hours of normothermic ischemia, decreasing to 80% at 8 hours. Berggren et al.[102] showed complete survival of bone grafts preserved in Collins-Terasaki solution at 5°C after 25 hours of ischemia, provided that the medullary nutrient blood supply was later reconstituted. Chinese investigators successfully replanted limbs in animals after 108 hours of cold ischemia.[106] Baek and Kim[113] reported successful replantation of two fingers after 42 hours of warm ischemia. Walkinshaw et al.[114] showed that proximal bowel segments are more resistant to warm ischemia than are distal small bowel segments and suggested using proximal bowel for free transfer. Based on a review of the literature, we have compiled estimates of tissue tolerance to ischemia, which we present in Table 2.[115–117]

Reperfusion Injury and the No-Reflow Effect

Success in the clinical setting often depends on the response of the vascular endothelium to ischemia. While studying the effects of ischemia on rabbit brains in 1968, Ames et al.[118] noted that some ischemic organs failed to reperfuse after their blood supply had been reestablished. The authors called this the *no-reflow phenomenon*.

The mechanism of no-reflow is thought to involve cellular swelling in the vascular endothelium with subsequent intravascular platelet aggregation and leakage of intravascular fluid into the interstitial space. This hypothesis correlates well with clinical observations of excellent blood flow immediately after anastomosis that decreases shortly after the no-reflow phenomenon takes effect, at which point the low-flow state triggers intravascular thrombosis and flap ischemia.

May et al.[107] investigated no-reflow in denervated free epigastric flaps in the rabbit, which closely approximates the clinical situation. The authors observed mild obstruction to blood flow as early as 1 hour after ischemia, increasing in severity at 8 and 12 hours. Histological changes were reversible at 4 and 8 hours but became incontrovertible at 12 hours, culminating in death of the flaps.

Zdeblick et al.[119] studied the no-reflow effect in replanted rat hind limbs. Predictors of no-reflow were an increased number of red blood cell aggregates 5 minutes after replantation and changes in tissue pH values persisting for longer than 1 hour after replantation. Clearance of H^+ and lactate is associated with improved flow. The authors' findings support the concept of ongoing arterial obstruction, arteriovenous shunting, and an altered thrombogenic fibrinolytic system as the mechanisms of the no-reflow phenomenon.

Jacobs et al.[120] noted an inversely proportional relationship between warm ischemia time and fibrinolytic activity. The greatest decrease in fibrinolysis occurred at 0 to 6 hours of warm ischemia. Suval et al.[121,122] showed that changes in microvascular permeability occur during reperfusion after 30 minutes or 2 hours of ischemia. The first manifestations of tissue damage in reperfusion injury are caused by leukocytic and endothelial cell

TABLE 2

Ischemic Tolerance of Various Tissues

Tissue	Warm (h)	Cold (h)
Skin and subcutaneous tissue[115]	4–6	≤10
Muscle[116]	<2	8
Bone[117]	<3	24

interactions. No-reflow occurred in 30% of the muscle tissue regardless of ischemia time.

Russell et al.[123] and Manson et al.[124] presented discussions of the mechanisms of ischemia-induced injury to cells and the role of oxygen free radicals in the reperfusion of ischemic tissue. Reperfusion of muscle is followed by a local response and an inflammatory response. The local response consists of swelling (i.e., the muscle flap or replanted limb grows in size at the time of reperfusion). Therefore, fasciotomies are prudent in most cases and mandatory in all except those with the shortest ischemia times. The swelling might also be evident in buried muscle flaps.

The inflammatory response parallels ischemia time up until cell death begins to occur. When cell death is diffuse, such as after very long ischemia times, the no-reflow phenomenon is essentially immediate and very little inflammatory response ensues. Areas of muscle that have slight ischemic damage will therefore generate few inflammatory mediators at the time of reperfusion. For instance, muscle flaps that are appropriately cooled and flaps that were reperfused in less than 1 hour generate much less inflammation than does muscle that was not cooled or was exposed to longer ischemia times. Intermediate zones in replanted muscle or transferred muscle flaps after 2 or more hours of warm ischemia produce high levels of inflammatory mediators and eventually show the worst cell damage. Thus, in a replanted limb, certain areas suffer more than do other areas, and surgeons might choose to be more liberal with anti-coagulants when ischemia is prolonged. In the short term, anticoagulants serve to decrease inflammation associated with the clotting cascade and potentially help salvage the watershed areas of significant but reversible ischemia.[125]

Several authors[76,82] have shown the effect of thrombolytic agents in reversing ischemic changes in human and rat myocardium. Others[80,83,126] have reported salvage of flaps in the clinical situation with the administration of thrombolytic drugs when the no-reflow phenomenon was likely in effect. Nonsteroidal anti-inflammatory agents inhibit cyclo-oxygenase and block the effects of thromboxane A_2, such as vasoconstriction and microvascular thrombus formation. Douglas et al.[127] showed that ibuprofen-treated flaps survive longer periods of ischemia. The ibuprofen-treated flaps had accelerated fluorescein uptake that suggested reversal of thrombosis and vasoconstriction. Feng et al.[128] postulated that the ratio of vasoconstricting to vasodilating prostaglandins might be responsible for the microcirculatory changes that result in the no-reflow phenomenon. Schmid-Schönbein,[129] on the other hand, stated that capillary plugging by granulocytes seems to be the mechanism underlying no-reflow.

The actual number of platelets in the circulation might not affect microvascular patency in routine microsurgery cases. Kuo et al.[130] studied microanastomoses in splenectomized rats with thrombocytosis versus rats with normal platelet counts and found similar patency rates.

In summary, the common denominator in failure of microvascular anastomoses is endothelial disruption with exposure of subendothelial collagen-containing surfaces to which platelets adhere.[131] If platelet aggregation reaches a certain mass, it will trigger fibrin deposition that leads to vasospasm, stenosis, and eventual thrombosis of the vessel. As the blood flow rate through the anastomosis falls below a critical level, the flap fails. When this happens in enough of the watershed areas, it can propagate to other potentially salvageable but nevertheless vulnerable areas of the muscle.

Free flap failure is not necessarily an all-or-none phenomenon. Although thrombosis at the arterial or venous anastomosis with cessation of blood flow to a flap often results in complete flap loss, free flaps occasionally experience a slow, progressive, and partial death that is potentially reversible. Weinzweig and Gonzalez[131] reported their experience with 10 patients in whom free flap failure was not an all-or-none phenomenon. The authors discussed their experience with these failing flaps and stated that with dressing changes, judicious débridement, and skin grafts or other local flaps, the dying flaps often can be salvaged without resorting to other free tissue transfer.

TECHNICAL FACTORS

Many factors contribute to the success of a microvascular procedure. Among technical variables are instruments and sutures used for the anastomosis and the technique of anastomosis. Other miscellaneous considerations influencing the outcome of free tissue transfer are the choice of donor and recipient vasculature, whether the anastomosis is performed outside the "zone of injury," technical expertise of the surgeon, and patient history of tobacco smoking. One of the most important prerequisites for success in microsurgery is organization. The operating room, staff, and equipment must be well prepared for microsurgery. The surgeons must be organized in their planning and execution, and the hospital unit itself must be organized. Postoperative care is as important as all the steps that come before the recovery room. Germann et al.[132] offered concise and useful principles for organization of and preparation for microsurgery.

Magnification

Daniel and Terzis[133] recounted the evolution of operative magnification. Hoerenz,[134–136] Nunley,[137] and O'Brien et al.[50] comprehensively reviewed the operating microscope. Shenaq et al.[138] recounted an 8-year experience with loupe magnification for free tissue transfer. Among 251 free tissue transfers performed during the time of the study period using a 5.5× loupe, 97.2% were successful. The partial flap necrosis rate was 1.2%, and the revision rate for anastomoses was 8.3%, which compares well with surgery performed with the guidance of an operating microscope. The most favorable results were achieved with free flaps (98.5% success) and toe-to-hand transfers (96.4% success). Digital replantation was less successful (79.2% success). The authors supported the use of loupes for vessels ≥1.0 mm in diameter. Loupes are cost-effective and portable, and they free the operator's position.

Serletti et al.[139] compared loupe versus microscope visualization in a series of 200 free flaps. The authors conducted a retrospective review with an inherent bias in that at the time of flap transfer, the choice of magnification was influenced by the size of the vessels encountered, the anatomic area of surgery, and patient factors. In general, the authors chose loupe magnification for adult head and neck and breast reconstruction. The microscope was used more often for children and for vessels ≤1.5 mm in diameter. The findings support the use of loupe magnification for selected microsurgical cases in the hands of experienced microsurgeons.

Ross et al.[140] assessed the results of a large series of free flaps transferred to the head and neck with the aid of loupe versus the microscope. Similar complications occurred in the two groups, and shorter operating times were required in the loupe group.

Head-mounted magnification devices that have more power and field of vision than do standard loupes are being developed. Chiummariello et al.[141] reported their experience with the Varioscope M5 (Life Optics, Chicago, IL) device. The authors remarked that the device offers increased freedom of movement over the operating microscope. Another potential advantage is variable magnification range. Devices such as this continue to be explored. They have not yet supplanted the operating microscope for most surgeons.

Microsurgical instruments should be few in number and high in quality. Acland[142] and O'Brien et al.[50] listed the essential instruments for any microsurgical setup and their proper use. The instruments include magnification loupes of at least 2.5 or a microscope with 200 to 250 focal length, jewelers' forceps, microscissors, a vessel dilator, a needle holder, irrigation, cellulose sponges, microscopic hemoclips, and Merocel (Medtronic, Minneapolis, MN).

Number of Sutures

The number of sutures used in the anastomosis is critical: too few and excessive bleeding and thrombus formation can occur; too many and the increased damage to the endothelium risks intravascular thrombosis. The goal is to achieve a well-approximated, sealed, nonbleeding union with a minimum number of sutures.

Colen et al.[143] studied the relationship between the number of sutures and the strength of a microvascular anastomosis in rat femoral vessels. The authors determined that an eight-suture anastomosis most closely paralleled the control state in this animal model. Zhang et al.[144,145] reported achieving excellent patency in rat femoral vessels when using a four-stitch sleeve anastomosis. The authors also described a three-suture sleeve technique.

Type of Sutures

Both absorbable and nonabsorbable sutures have been used for microanastomosis. Mii et al.[146] noted faster and smoother endothelial regeneration with polyglycolic acid absorbable material than with nonabsorbable suture. Thiede et al.[147] showed no increased aneurysm or pseudoaneurysm formation and no vascular ruptures caused by decreased mechanical endurance with polyglycolic acid or polyglactin sutures. Chen et al.[148] used an interrupted, non-absorbable suture technique for anastomosis in young rat femoral arteries. The vessels were later examined when the rats were adults and had gained weight. Evidence indicated growth at the anastomotic sites without stenosis or hyperplasia. The authors concluded that the use of an interrupted, non-absorbable suture technique in small vessels that are expected to grow over time is safe in rats and might be safe in children requiring microvascular surgery. Currently, most practitioners use non-absorbable (Prolene [Ethicon, Somerville, NJ] or nylon) sutures in their clinical cases.

Anastomotic Techniques: Interrupted, Continuous, Sleeve, and Adhesive

Techniques of microvascular anastomosis with interrupted sutures have been modified from the triangulation method presented by Carrel.[3] Daniel and Terzis[133] illustrated the basic microsurgical anastomotic techniques in their text. Mechanical factors in certain clinical settings sometimes dictate departure from or modification of the conventional triangulation or bicentric angulation methods, but patency rates must not suffer in the process. The surgeon's expertise and time required for the anastomosis should be considered when formulating the operative plan.

Various methods have been described for microvascular anastomosis. Simple interrupted full-thickness sutures are preferred and are the standard with which all new anastomotic techniques are compared.

Anastomoses performed with continuous sutures are no different from those performed with interrupted sutures regarding patency rates and blood velocity profiles,[149,150] but they can be performed much faster.[151,152] Patency rates in the rabbit are 92% arterial and 84% venous. In the rat carotid artery, Firsching et al.[153] showed 100% patency at 2 to 4 months with continuous sutures. The main argument against the use of continuous suture is that it can narrow the caliber of the vessel lumen.[152] Suture entrapment in vessel clamps and suture breakage have also been reported.[154] Cordeiro and Santamaria[155] reported their experience with continuous suture anastomosis in 200 consecutive free flaps. The authors' success rate was similar to that of other large series that used interrupted sutures. In contrast, Chase and Schwartz[156] reported better results with simple interrupted sutures than with continuous sutures.

Chen and Chiu[157] described a spiral interrupted suture technique that combines elements of the continuous and interrupted suture techniques. The authors noted that the technique is faster than a simple interrupted suture but is frequently associated with a purse-string-like constriction of end-to-end venous anastomoses.

Man and Acland[158] described a refined continuous suture technique and reported a 14-day patency rate of 85% in the rat femoral artery, compared with 80% patency for interrupted sutures. The authors suggested that the overriding advantage of the continuous technique is that it decreases the anastomotic time by half.

The sleeve technique originally described by Lauritzen[159] and Lauritzen and Hansson[160] is said to be faster and simpler to perform, and suture placement causes less trauma to the vessels. Lauritzen[159] described a precise technique and noted that endothelialization of the anastomosis takes 1 week, or half the time needed with conventional suture anastomoses. Clinically, the telescoped technique is hampered by difficulty in anastomosing veins and other vessels of various diameters. Duminy,[161] however, altered the technique and achieved a high patency rate and easier anastomosis of different-sized vessels.

Krag and Holck[162] compared the telescoped anastomotic technique with the traditional end-to-end method in the femoral arteries and veins of rats. They found less risk of late thrombus deposition with the sleeve technique (13% versus 41%), although the patency rates at 1 week were the same (88%). Sully et al.[163] reported a lower patency rate (84%) with the telescoping technique compared with the conventional interrupted suture technique (98%) in the rat femoral artery model. O'Brien et al.[50] confirmed the findings presented by Sulley et al. and did not recommend sleeve anastomosis because of its overall lower patency rate.

Turan et al.[164] extended the concept of fish-mouthing the vessel ends and applied it to microsurgery. In a controlled animal study, the authors compared traditional interrupted anastomoses with their four-suture everted, fish-mouthed anastomoses. The patency and anastomotic complication rates were similar in the two groups. The time needed for anastomosis was shorter with the everted technique.

Early experimental studies of vascular repairs with synthetic adhesives yielded less than satisfactory results.[165,166] Occasionally, the adhesive penetrated into the vessel lumen and caused instant thrombosis. In 1977, Matras et al.[167] proposed the use of fibrin tubes for vascular end-to-end anastomosis. Other authors have used fibrinogen adhesive to augment techniques such as conventional suture anastomosis,[168] a coupling technique,[169] and the sleeve method,[170] with variable results. Despite patency rates similar to those achieved with conventional anastomoses,[171,172] fibrinogen adhesive is not as versatile as suturing and might not be applicable to end-to-end anastomoses or anastomoses in which the vessels are of different caliber.

End-to-End, End-to-Side, and End-in-End Sleeves and Arteriovenous Loops

End-to-end vessel anastomosis is most common in microvascular surgery. When a size discrepancy exists between the donor and recipient vessels, a decision must be made regarding the type of repair. A difference of 2:1 or less can be handled by gently dilating the smaller vessel and not dilating the larger one.[173] Another option in dealing with vessel size discrepancy is to cut the end of the smaller vessel at a slightly oblique angle to increase its diameter.[174]

One must be extremely wary of a significant mismatch when performing end-to-end venous anastomosis.[175] If the discrepancy is such that the anastomosis would be compromised, end-to-side anastomosis should be considered. If a limb or appendage depends on only a single vessel for perfusion, an end-to-side repair must also be performed.

Godina[176] reported his clinical experience with microvascular transplantation and showed a higher failure rate with end-to-end anastomoses. He subsequently proclaimed the end-to-side technique as his preferred choice for lower extremity free flaps. In contrast, Samaha et al.[177] found no statistical differences in the patency rates in 1051 consecutive tissue transplants as long as good clinical judgment was used in the choice of recipient vessels.

Animal experiments have failed to show a difference in patency rates between end-to-end and end-to-side techniques when repairing vessels of similar diameter.[178] When size-discrepant vessels are involved, end-to-side venous repairs have proved to be significantly better.[179] The dynamics of flow in end-to-side arterial repairs are favorable.[180,181]

In 1978, Lauritzen[182] described the sleeve anastomosis or end-in-end anastomosis, an invaginating technique with far fewer sutures than those required for the end-to-end method. Experimental studies showed patency rates similar to those achieved with conventional end-to-end sutures plus significant time savings and minimal intimal trauma.[159–163,182,183] Nakayama et al.[184] presented a report of 15 free flap transfers using sleeve vascular anastomoses, with only one failure occurring. The authors suggested that this technique is best indicated if a favorable size discrepancy exists between donor and recipient vessels (small caliber upstream end to large caliber downstream end).

The sleeve technique has not been widely adopted by surgeons because of reports of stenosis.[163,185,186] The choice of technique should be secondary to the choice of recipient vessels. In single-vessel limbs and when anastomosing vessels of considerable size mismatch, thrombus, and aneurysm formation, the end-to-side technique is preferred.

Another option to consider when recipient vessels are compromised is the arteriovenous loop. This technique is particularly useful when the zone of injury is difficult to determine, in severe trauma, and in irradiated zones. The loops can be immediate or delayed. With this technique, one creates an extension of the arterial pedicle with a looped vein graft. The flap or replanted tissue is supplied via end-to-side anastomoses off the loop. Revisions are facilitated as long as the loop remains patent. Cavadas[187] described his experience with 56 arteriovenous loops in the upper and lower extremities (Fig. 1). The author achieved excellent success rates.

Figure 1. Long arteriovenous loop can be constructed using the contralateral saphenous vein graft connected proximally to the popliteal artery and distally to the ipsilateral in situ saphenous vein at the malleolar region. This construct is especially useful in diabetic patients. (*Reprinted with permission from Cavadas.[187]*)

Cuffs, Couplers, Staplers, and Automatic Suturing Devices

The use of cuffs and stents to simplify and expedite microvascular anastomoses has been touted as an alternative to conventional methods. McLean and Buncke,[188] in 1973, suggested reducing the number of sutures during microanastomosis by means of a Saran Wrap (S. C. Johnson & Son) cuff. Tschoff,[189] in 1975, used a lyophilized dural cuff for the same purpose. Harris et al.[190] presented a basic autogenous cuff technique consisting of six sutures. Modifications involving fewer sutures,[191,192] fat wraps,[193] polythene cuffs,[194] silicone rubber cuffs,[195] external absorbable splints,[196] stents,[197] intravascular stents,[198] and metallic circles[199] in experimental models have been described. However, most of these techniques are difficult to implement and present new problems, and very few have been applied clinically.[200]

Connectors have been proposed to facilitate microvascular anastomoses and improve reliability. The first ring device was introduced in 1962 by Nakayama et al.[201] In 1986, Ostrup and Berggren[202] introduced a modification of this device (called *Unilink*) that subsequently evolved into the microvascular anastomotic coupler manufactured by 3M (Saint Paul, MN). Clinical series of vessels anastomosed with the mechanical device have shown equal or greater patency rates and faster anastomosis of either normal or irradiated vessels.[203–205] Histological studies showed the same healing process whether the anastomosis was performed with conventional sutures or mechanically.[206] At 16 weeks after repair, coupled anastomoses are 50% stronger than are sutured vessels.[207] Biodegradable ring devices do not seem to have any advantage over nonabsorbable devices[208] and might cause thrombosis because of the inflammatory response to the ring during absorption.[204]

Some authors[204,205] find mechanical coupling devices to be especially useful for end-to-end anastomosis in veins and soft arteries. The applicability of these devices in thick-walled arteries, in vessels with diameters <1.0 mm, and for end-to-side anastomosis is less convincing and seems limited.[205,209]

Zeebregts et al.[210] compared a standard suture technique with nonpenetrating vascular closure staple clips and with Unilink rings. The authors noted excellent patency with all three methods. The devices can reduce anastomotic time in experienced hands.

Cope et al.[211] reported the successful use of a microvascular stapling device that can be used for end-to-side and end-to-end anastomoses. In general, the disadvantages of stapling techniques include the following: 1) the necessity to mobilize the vessels to evert them; 2) shortening of the vessel through loss of the everted cuff; 3) the need to precisely match the bushing size with the vessel; 4) less flexibility in "tailoring" the anastomosis when discrepancy in vessel size is present; and 5) limited availability of the apparatus.

Shennib et al.[212] studied the use of an automatic vascular suturing device in a pig model. The average anastomotic time was 22 minutes with 7-0 suture, and patency rates were good. Devices such as these might find future applications in microvascular surgery. Of course, they will provide a benefit only if they serve to shorten operating time, improve patency rates, and/or make the anastomosis technically easier. Arterial coupling devices have been used in more recent studies. In a recent study by Spector et al.,[213] in 80 flaps (including DIEP, TRAM, and superior gluteal flaps), arterial coupling was used and resulted in a 100% success rate. The authors concluded that although not commonly used, in properly selected patients, coupling the artery can prove expeditious and improve efficiency.

Laser Anastomosis

Laser-assisted microvascular anastomoses have been evaluated.[214,215] The associated patency rates compare favorably with those achieved with conventional manual sutures and have the advantage of shorter operative times, limited endothelial trauma with small thrombogenic risk, and no suture material to trigger a foreign-body reaction.

A wide range of laser wavelengths has been used, including those emitted by carbon dioxide,[216,217] argon,[218] neodymium-doped yttrium aluminium garnet,[219] potassium titanyl phosphate,[220] and diode[221] lasers. The adjunctive use of photosensitizing dyes makes low-energy discharges possible and minimizes collateral tissue damage.[222]

The mechanism of tissue fusion through laser energy is still undefined. The initial strength of such a bond depends on physical factors (collagen coiling and crosslinking and coagulum formation) rather than biological processes such as inflammation and healing.[223] The tissue-welding phenomenon might be caused by heat generated by the laser energy or might be wavelength-dependent.

To date, laser-assisted microvascular anastomosis is considered to be investigational. Difficulties with aneurysm formation,[224] low breaking and tensile strength during the early postoperative period,[225] and the cumbersome size and high maintenance cost of conventional lasers have delayed full acceptance into clinical practice. On the other hand, miniature diode lasers with fiberoptic delivery systems and selective photo-welding techniques seem promising to the future of microsurgery.

MONITORING PERFUSION

Salvage of a failing free flap requires timely recognition of inadequate flow and prompt intervention to correct the problem. To be effective, clinical assessment of skin color, temperature, and capillary refill must be performed by a knowledgeable and experienced observer. Other, more sophisticated methods of evaluating circulation after free tissue transfer have been proposed. Some are reviewed below.

Devices to monitor blood flow in flaps should be relatively inexpensive, highly reliable, and simple to operate and interpret. The monitoring technique should be continuous and applicable to many kinds of flaps.

The Doppler ultrasound flowmeter is the most common means for gauging circulation after free tissue transfer.[226] It can be used to monitor both arterial and venous blood flow in flaps. The laser Doppler has the additional advantage that it can continuously record the microcirculatory flow in all types of cutaneous and musculocutaneous free flaps and replanted limbs. Nevertheless, Walkinshaw et al.[227] found the laser Doppler to be unable to predict future clinical events and to be no more accurate than clinical assessment in pointing to the need for clinical intervention.

Temperature monitoring is a widely used measure of flap circulation. May et al.[228] described the experimental evolution and clinical application of an implantable thermocouple to monitor patency of the microvascular pedicle.

The surface temperature measurements presented by Acland[229] have proven most useful for monitoring replanted digits. However, Kaufman et al.[230] found that, in muscle free flaps, temperature monitoring is labile and easily changed by environmental manipulation and as such is unreliable in assessing the vascular status.

Khouri and Shaw[231] presented their series of 600 consecutive free flaps monitored by surface temperature recordings. They specifically monitored the difference in temperature between the flap and a control site on the patient's normal skin. After 10,000 temperature readings, the authors found only one temperature difference >1.8°C that failed to show microvascular thrombosis. Seventeen readings were false-positive. Khouri and Shaw detected 52 thrombosed flaps using surface temperature monitoring and were able to salvage 45 of the free flaps by reexploration.

In a discussion of the article by Khouri and Shaw,[231] Jones[232] noted that he had discontinued the use of surface temperature monitoring in replantation and toe-to-thumb transfers and preferred using the pulse oximeter instead. Jones also noted that differential surface temperature monitoring is not sufficiently sensitive to monitor free muscle flaps covered with split-thickness skin grafts. In his opinion, the only clinical applicability of surface temperature recordings is in skin or skin island flaps, and even those can be clinically monitored more easily by means of capillary refill and Doppler probes.

Jones and Gupta[233] expanded on the topic and reported efficacy of differential oximetry to assess perfusion in pediatric toe-to-hand transfers. Continuous pulse oximetry of a normal digit is the baseline reference.

Roberts and Jones[234] described direct monitoring of microvascular anastomoses with an implantable ultrasonic Doppler probe. Those authors and Swartz et al.[235] noted that the Doppler probe can recognize and distinguish between arterial and venous occlusion and that in doing so, it is more reliable than a thermocouple probe. Venous occlusion can be difficult to detect by Doppler probe, especially in large muscle flaps.[235] Fernando et al.[236] implanted a laser Doppler probe directly into muscle or subcutaneous tissue distal to the vascular pedicle. The Doppler recordings correlated with blood flow in the flap, and arterial compromise was readily detected. Rothkopf et al.[237] assessed the patency rates of microvascular anastomoses in the upper extremity by using color Doppler ultrasonographic imaging.

Whitney et al.[238] reported significantly higher salvage rates (86%) of transplanted toes and cutaneous flaps that were reexplored based on quantitative fluorometry findings compared with similar microvascular transplants that were not monitored with fluorescein (56%). The overall accuracy of quantitative fluorometry in their 8-year experience with 23 transplants was 91%. Jones et al.[239] described remote monitoring of free flaps with telephonic transmission of photoplethysmographic waveforms, which theoretically would facilitate surveillance of the flap by the operating surgeon.

Based on type and location of vascularized tissue, monitoring of flaps and anastomoses should be individualized.[240] Replants and toe-to-thumb transfers can be effectively monitored by pulse oximetry, whereas free flaps often are monitored with Doppler handheld pencil probes for several days after surgery, along with clinical observation.[240] The implantable venous Doppler probe is used by many modern microsurgeons. Some clinicians evaluate perfusion by clinical examination alone.

INFLUENCE OF PATIENT FACTORS

Tobacco Use

Cigarette smoking has been shown to affect cutaneous blood flow,[241] wound healing,[241,242] and survival of pedicled flaps.[243,244] The overall effect of byproducts of cigarette smoke is to produce a thrombogenic state through action on the dermal microvasculature, blood constituents, and vasoconstricting prostaglandins.

Nolan et al.,[244] Gu et al.,[245] and van Adrichem et al.[246] showed, in experimental studies, that smoking was detrimental to microvascular surgery in terms of delayed anastomotic healing and free flap failure. Surprisingly, large clinical series and some experimental studies have failed to show any damaging effects of cigarette smoking on free tissue transfers.[247–249] Arnez et al.[250] reported no difference in flap loss or vascular thrombosis rates in smokers compared with nonsmokers in 50 free transverse rectus abdominus muscle (TRAM) flap breast reconstructions. Reus et al.[251] reported no difference in anastomotic patency or overall survival of 162 free flaps in smokers and non-smokers. Chang et al.[249] reviewed 963 free tissue transfers and showed no statistically significant difference in vessel patency, flap survival, or reoperation rate between smokers and nonsmokers. Smokers did show a higher incidence of healing complications at the flap interface and at the donor site wound.[249,251]

Cigarette smoking seems to adversely affect the outcome of digital replantation surgery. van Adrichem et al.[252] showed that tobacco smoking decreases microcirculatory blood flow in replanted digits compared with healthy digits. Chang et al.[249] observed that 80% to 90% of smokers ultimately lose their replanted digits if they smoke during the 2 months before or after surgery. Smoking is not an absolute contraindication to digital replantation according to Buncke who stated that it is imperative for patients not to smoke postoperatively. The reason why cigarette smoking has a greater adverse effect on digital replantations than on free flaps is unclear. Digital blood flow is under much stronger vasomotor control than are other areas in the body and is more sensitive to the vasoconstrictive effects of nicotine.

Patient Age

Parry et al.[253] reported a 96% success rate with free tissue transfer in children. Canales et al.[29] echoed the findings in 106 pediatric patients operated on between 1973 and 1989. Their success rate (93% in the last 5 years reported) and complications were similar in their pediatric and adult patients. No growth-related complications were noted at either the recipient or donor sites.

Yücel et al.[254] reported no significant vessel spasm and a 95% overall success rate in 20 pediatric free flaps. Clarke et al.[255] reported a 99% flap survival rate in pediatric microvascular cases despite frequent but manageable complications. Vessel spasm was not a significant problem. Duteille et al.[256] reported achieving excellent results with 22 pediatric free flaps. The authors noted that children have a greater risk of vasospasm that is compounded by small vessel size and recommended great care with vessel dissection. Regional and local anesthesia is used to enhance vessel dilation, and fat cells are left around the vessels. Lidocaine 2% is used around the vessels at the time of anastomosis.

Patients older than 65 years can also undergo successful free tissue transfers.[257] Chick et al.[257] noted a successful outcome in 30 of 31 free flaps transferred in patients older than 65 years. The complications associated with wound healing were the same in the 65 and older group and in the the younger-than-65 group. The authors concluded that age alone is not a factor in success or failure of free flaps when preexisting medical conditions are factored out of the equation. Advanced age alone was not a factor in morbidity or mortality from the microsurgical procedure.

Shestak and Jones[258] reported successful free tissue transfer in 93 of 94 flap procedures performed in patients who were 50 to 79 years old, for a free flap viability rate of 99%. Fourteen (15%) major surgical complications and 13 (14%) substantial postoperative medical problems occurred. The mortality rate was 5.4%.

Serletti et al.[259] reported a series of free flaps in elderly patients (average age, 72 years). Success rates were excellent and in line with other age groups. The higher rate of medical complications was associated with patient comorbidities but not with age as an independent factor. Complications also increased as operative times increased. Higher rates of reconstructive failure were noted in cases of attempted limb salvage in patients with peripheral vascular disease.

To summarize, comorbidities and type of reconstruction must be taken into account when evaluating elderly patients for free tissue transfer. However, patient age should not deter the experienced microsurgeon.

Systemic Disease

Banis et al.[260] showed that microsurgery can be a valuable tool in the salvage of ischemic lower extremities from atherosclerosis of diabetic microangiopathy. Karp et al.[261] reported their experience with 21 free flaps in 19 diabetic patients and documented only one flap loss, with all patients able to ambulate on their flaps. Nevertheless, five of 19 original patients needed eventual amputation at 6 to 37 months after surgery.

Moran et al.[262] reviewed a large number of flaps comprising their 10-year experience with free flaps in the context of lower extremity peripheral vascular disease. The perioperative mortality rate was 5%; 5-year flap survival rate was 77%; limb salvage rate was 63%; and patient 5-year survival rate was 67%. Clearly, peripheral vascular disease is a significant risk factor for any long surgery. It is also a known risk factor for early death. Many of the amputations and patient deaths had nothing to do with the free tissue transfer, but peripheral vascular disease as a comorbidity must be weighed when considering free flaps in this patient population.

Moran et al.[263] also identified patients with renal insufficiency who underwent free tissue transfer. Renal disease seems to be a stronger predictor than peripheral vascular disease of reconstructive failure and major medical complications, including death. Fifty-two percent of the patients in the study by Moran et al. suffered major morbidity or mortality during postoperative year 1. Among those who survived the first year, reconstruction was successful in 55%.

For a more complete review of peripheral vascular disease, renal disease, and other comorbidities in reconstructive microsurgery of the lower extremity, the reader is referred to the Lower Extremity Reconstruction issue of *Selected Readings in Plastic Surgery*.[264]

MICROVASCULAR GRAFTS AND PROSTHESES

When it is not possible to repair a vessel by anastomosing the cut ends, such as in cases of traumatic loss or when additional vessel resection is needed, grafts of autogenous veins are the most common substitute circulatory conduit used in humans. Vein grafts are readily available and can be harvested in predetermined lengths and diameters to match as closely as possible the caliber of the recipient vessel(s). Autogenous vein grafts are reversed for spanning intra-arterial gaps and placed directionally for bridging intravenous gaps.

The histological changes that take place in vein grafts after placement in the arterial system have been well described in the literature.[265,266] Mitchell et al.[267] studied the long-term fate of microvenous autografts. The patency of intra-arterial vein grafts was 98%. The patency of intravenous vein grafts was 100%. Intra-arterial vein grafts were modified by the ingrowth of smooth muscle cells from the recipient artery, and the influx of smooth muscle cells created a neointima that considerably thickened the walls of the vein graft. In contrast, intravenous vein grafts maintained normal vein morphology. An unexplained loss in length of the grafts of approximately 30% occurred, which led to the recommendation that vein grafts should be 35% longer than the measured gap.

Despite the success achieved with autogenous vein grafts, experimental investigation of synthetic materials to replace small vessels continues.[268–273] The most common materials tested for this purpose are fibrous polyurethane and microporous or expanded polytetrafluoroethylene (PTFE).

O'Brien et al.[271] and Hess et al.[272,273] presented reviews of the experimental results obtained with PTFE microvascular prostheses. In some series, the early patency rates were adequate, but in time, neointimal hyperplasia and subsequent anastomotic narrowing were noted and led to concern regarding long-term patency rates. Shen et al.[274] noted significant thrombosis and occlusion when 2-mm expanded PTFE grafts were used in low-flow free flaps in rabbits.

van der Lei and Wildevuur[275] reported poor neoendothelialization in PTFE grafts, although patency was high in the high-flow, short-segment grafts. Samuels et al.,[276] on the other hand, noted that short-segment PTFE microvascular grafts were covered with a layer of endothelium. The authors reported a long-term patency rate of 80% and no evidence of excessive neointimal hyperplasia.

Yeh et al.[277] described the use of human umbilical artery grafts as a microvascular substitute. Although early patency of the grafts was good, with time, marked degeneration of the vessel walls occurred. Subsequently, Roberts et al.[278] reported that the technique of glutaraldehyde tanning of human chorionic veins seemed to be responsible for the low patency rate of the grafts, rather than fibrosis from the immunological reaction.

MICROANASTOMOSES OF IRRADIATED VESSELS

Radiotherapy is known to impair wound healing by decreasing the number of blood vessels in tissue by progressive thrombosis, resulting in tissue ischemia; by decreasing fibroblast proliferation and production of collagen; and by destroying epithelial cells. Patency in experimental microvascular anastomoses performed after irradiation has been highly variable. Earlier studies showed that it is significantly lower than in nonirradiated vessels.[279–281] Other series, both experimental[203,282] and clinical,[283–288] showed high flap success rates and low morbidity in irradiated beds.

Mulholland et al.[284] compared free flap survival rates in 226 irradiated and 108 nonirradiated head and neck reconstructions and reported similar failure rates for both groups. Reece et al.[285] presented a report of 66 elderly cancer patients who underwent tumor resection and free tissue transfer after previous radiotherapy. The authors found no significant differences for flap failure or wound healing problems when compared with a similar group of patients who had not received radiotherapy. Similarly, Bengston et al.[286] and Schusterman et al.[287] showed, in large clinical series, that previous radiotherapy does not predispose patients to a higher rate of acute free flap loss or wound complications. Kroll et al.[288] reviewed 854 consecutive free flaps and concluded that previous irradiation had no significant effect on flap failure rates. A prospective survey of 493 free flaps by the International Microvascular Research Group[289] suggested that more caution should be exercised in performing free flap transfer in patients with an irradiated recipient bed.

Guelinckx et al.[290] proposed the following guidelines for anastomosis of irradiated recipient vessels:

- limit dissection of recipient vessels to reduce manipulation and injury
- restrict electrocoagulation of arterial side branches
- use small-gauge needles and suture materials (e.g., 10-0 nylon sutures swaged on 70-mm needles)
- pass the microneedle from inside to outside to minimize intramural dissection and injury
- shorten the period of vessel cross-clamping to minimize stasis and microthrombi
- flush vessels with a heparinized solution during the anastomosis and before restoring blood flow

FREE FLAPS

It has been more than 2 decades since the first reports of human composite tissue transfers by microvascular anastomoses. Twenty-five years ago, free tissue transfer was in the hands of a few pioneers; 20 years ago, free tissue transfer was primarily practiced at university centers. Today, free tissue transfer is fully entrenched as a technique that nonacademic private practitioners readily adopt in the treatment of their patients. Free flaps currently are being performed at an ever-increasing rate and for ever-expanding indications.

Microsurgical procedures are now used with confidence in situations that were previously thought to present high risk of failure, such as in irradiated fields,[284] elderly patients,[257,258] and those with occlusive peripheral vascular disease from generalized arteriosclerosis or diabetes mellitus.[260] Shestak and Jones[258] reported successful free tissue transfer in 93 of 94 flaps in patients who were 50 to 79 years old, for a free flap viability rate of 99%. Complications were primarily nonsurgical and averaged 30%. Mortality was 5.4%. Chick et al.[257] noted successful free flap transfers in 30 of 31 patients who were older than 65 years. The wound healing complications were the same as in a younger cohort. The authors concluded that age alone is not a factor in the success or failure of free tissue transfers when preexisting medical conditions are factored out of the equation.

The reported success rates of microvascular transfers rose as experience with the procedures mounted. Approximately 10 years ago, success rates were in the 90% to 94% range, with 10% incidence of thrombosis. In the survey by Khouri et al.,[289] encompassing data from nine microsurgical centers, the combined success rate of microvascular flap transfers was 98.8%, and only 3.7% of flaps were reexplored for thrombosis. Moreover, an esthetic final result is what most plastic surgeons currently strive for and expect from microvascular surgery, not just simply a cover for the wound.

Failure of free tissue transfers is most often caused by technical factors. Khouri et al.[289] presented a discussion of the reasons why free flaps fail and suggested ways to avoid them. In the authors' extensive review, most free flap procedures were performed for posttraumatic indications and to treat extremity defects, cases in which the overwhelming majority of complications occurred. Apparently, the magnitude of the traumatic insult is the single most important factor influencing the subsequent development of microvascular thrombosis. Khouri et al emphasized that one should always seek the vascular pedicle of largest diameter, considering failures are more likely when small-diameter pedicles are used, especially diameters <1 mm. Published descriptions of a flap do not always mirror the individual clinical situation. Therefore, alternative sources of donor tissue should always be kept in mind. In an excellent review, Pederson[291] detailed the principles of free tissue transfer in the upper extremity (Figs. 2–4).

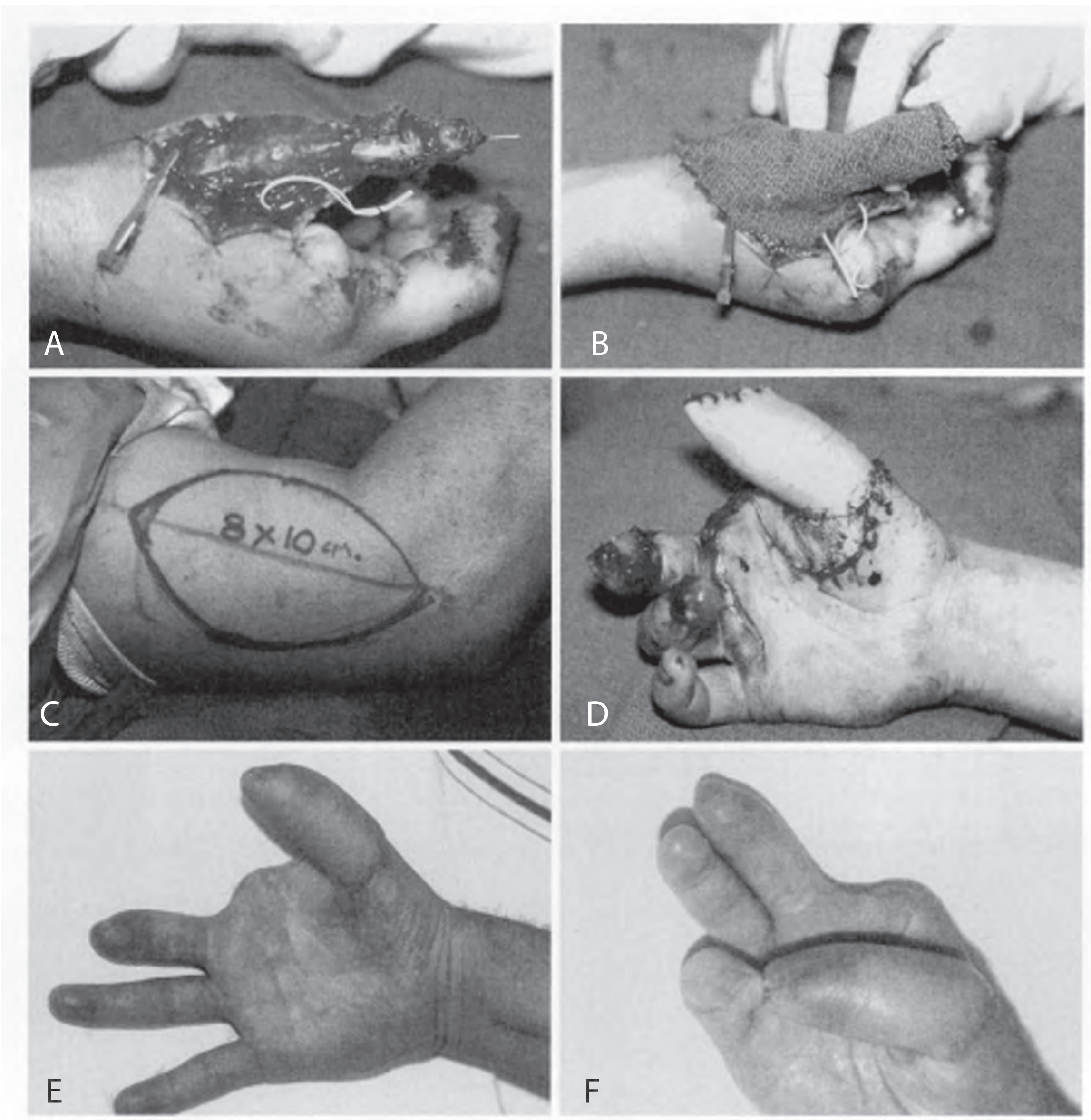


Figure 2. *A*, Degloving injury to the thumb of a 23-year-old man. *B*, Cloth is used for template for lateral arm flap. *C*, Flap is marked on lateral upper arm. *D*, Flap is placed. Seam is placed dorsally with anastomosis of lateral cutaneous nerve of the arm to the ulnar digital nerve of the thumb. *E*, Results at 8 months postoperatively. Protective sensation had returned. *F*, Flexion at 8 months postoperatively. (*Reprinted with permission from Pederson.[291]*)

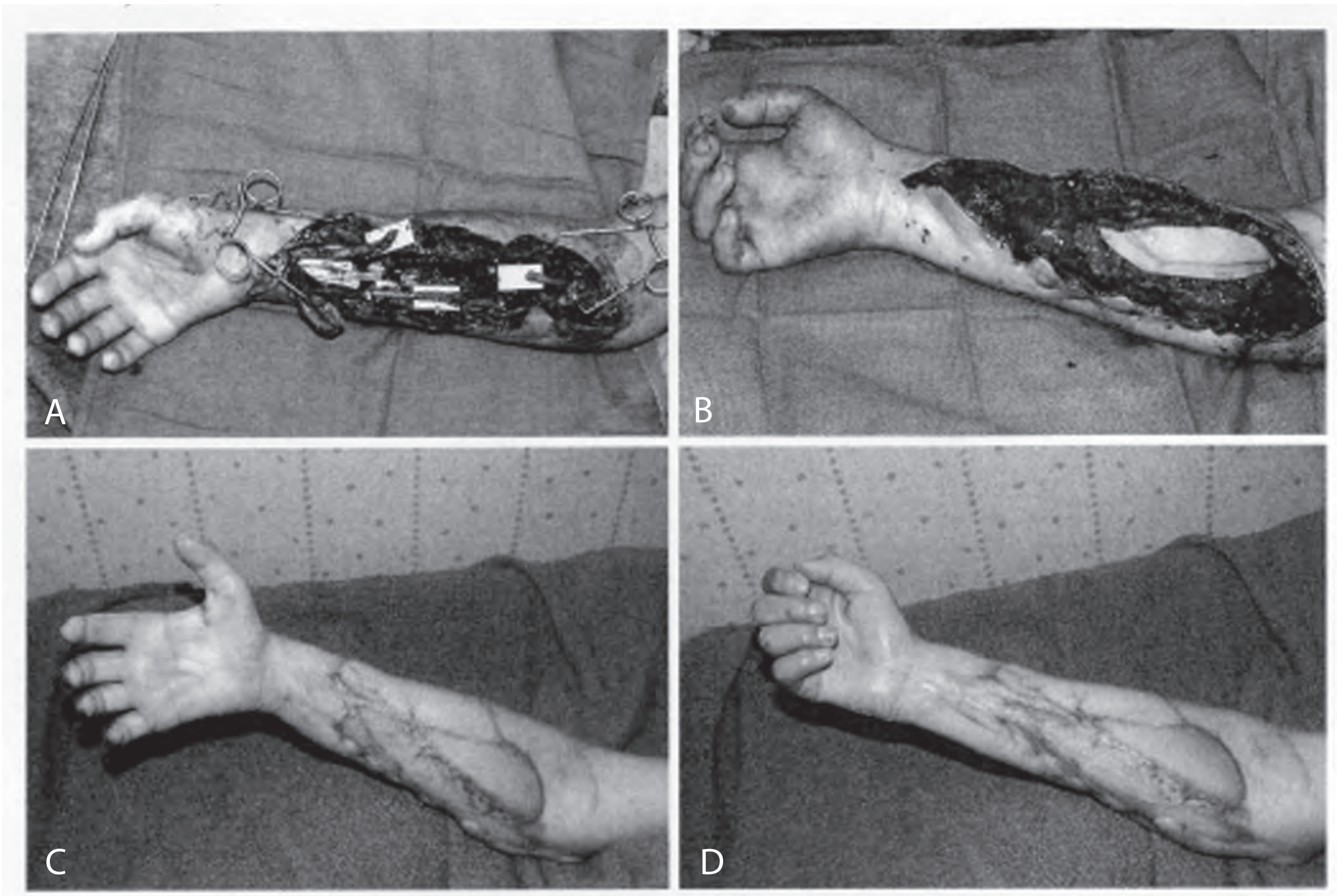


Figure 3. *A*, Intraoperative view of the forearm of a 12-year-old boy after a propeller injury. Note the disrupted median nerve. *B*, Intraoperative view after innervated gracilis transfer. Skin paddle for monitoring is over proximal muscle. *C*, Extension at 8 months postoperatively. *D*, Flexion at 8 months postoperatively. (*Reprinted with permission from Pederson.*[291])

Figure 4. Great toe wrap-around flap in a case of partial thumb amputation. Patient is shown 1 year after great toe wrap-around reconstruction of the left thumb. (*Reprinted with permission from Pederson.*[291])

Skin, Fascia, and Perforator Flaps

The free groin flap was the first flap to be successfully transferred by direct microvascular anastomoses. Currently, it rarely is used in free tissue transfers because of the anatomic variability of the donor vascular pedicle. One of the most common and versatile skin flaps for microvascular transfer is the radial forearm flap,[292–295] particularly in head and neck reconstruction. Other reliable options are the scapular,[296–298] parascapular,[299] lateral arm,[300] and dorsalis pedis free flaps.[301,302]

Free fascial transfers are useful in reconstructions for which thin, well-vascularized cover is needed and to provide for gliding of tendons in the hand. The free temporoparietalis (TP) fascial flap has a consistent vascular anatomy and a pedicle of fairly large caliber.[303–305] The TP fascial flap is a versatile flap with many applications. The free fascial forearm[306] and scapular flaps[299,307] offer similar versatility for thin, well-vascularized tissue.

The anterolateral thigh (ALT) flap has become a major workhorse in numerous anatomic regions, including extremity, head and neck, and perineal reconstruction (Figs. 5 and 6).[308,309] It offers hardy yet thin skin and fascia. It can be deepithelialized or harvested directly as a fascia-fat flap. The donor site often can be closed primarily. Donor site complications are not absent, however. Many patients notice some sensation loss at the lateral thigh postoperatively. Some patients notice thigh weakness caused by the dissection through the vastus and/or rectus femoris. Flaps that require skin grafts to close the donor site might be associated with stiffness during hip motion or knee flexion because of scar adherence of the graft to muscle fascia.[310] Engel et al.[311] advocated the use of the ALT flap at their center as the first choice free flap for multiple applications. Rodriguez et al.[312] presented a report of multiple ALT flaps used for trauma reconstruction and described similar virtues regarding the ALT.

Novak et al.[313] compared the donor site morbidity of the ALT flap with that of the radial forearm flap. Interestingly, the radial forearm flap donor site seemed to generate more cold intolerance and possibly had a poorer cosmetic appearance.

The blood supply of the ALT flap can be from septocutaneous and intermuscular perforators or from direct intramuscular perforators. If the flap is harvested and found to have muscular perforators, it is termed a *perforator flap proper*. If the blood supply arrives via septal vessel, it is probably more correct to term the flap a *fasciocutaneous free flap*. This is a semantic distinction that adds little to our understanding of flap elevation in that the surgeon follows the perforators down to their source regardless of the path they take. Celik et al.[314] described technical pearls for ALT flap harvest, including preservation of a fascial cuff around the pedicle during dissection (Fig. 7). The authors concluded, "with increasing knowledge of perforator flap entity and refinements of surgical techniques, the anterolateral thigh perforator flap reconstruction can be as reliable as other types of cutaneous flaps."

On rare occasions, the surgeon explores the flap and finds no dominant or workable artery and vein to the flap. Some time is wasted, and the surgeon is frustrated. Wei and Celik[315] provided an excellent review of the principles and application of perforator flaps and relevant anatomy. Work continues to help delineate perforator flap dissection for specific dermatomes.[316] Better understanding of the cutaneous patterns of perforator locations will likely help surgeons to select, tailor, and successfully dissect these flaps (Fig. 8).[317]

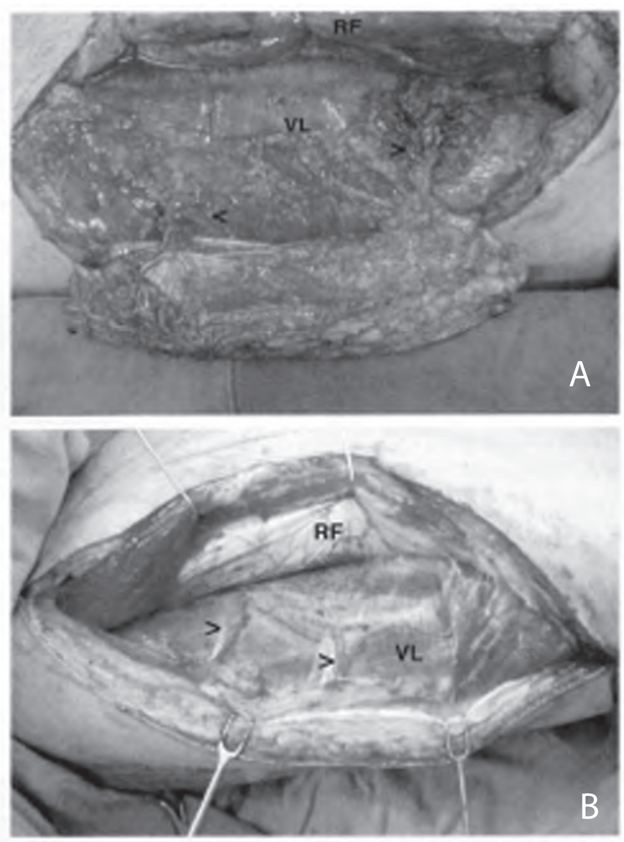


Figure 5. *A*, Intramuscular dissection of a perforator through vastus lateralis muscle to anterolateral thigh flap. *Arrowheads* indicate musculocutaneous perforator. *B*, Septocutaneous vessels to anterolateral thigh flap. *Arrowheads* indicate septocutaneous vessel. *RF*, rectus femoris; *VL*, vastus lateralis. (*Reprinted with permission from Pederson.[291]*)

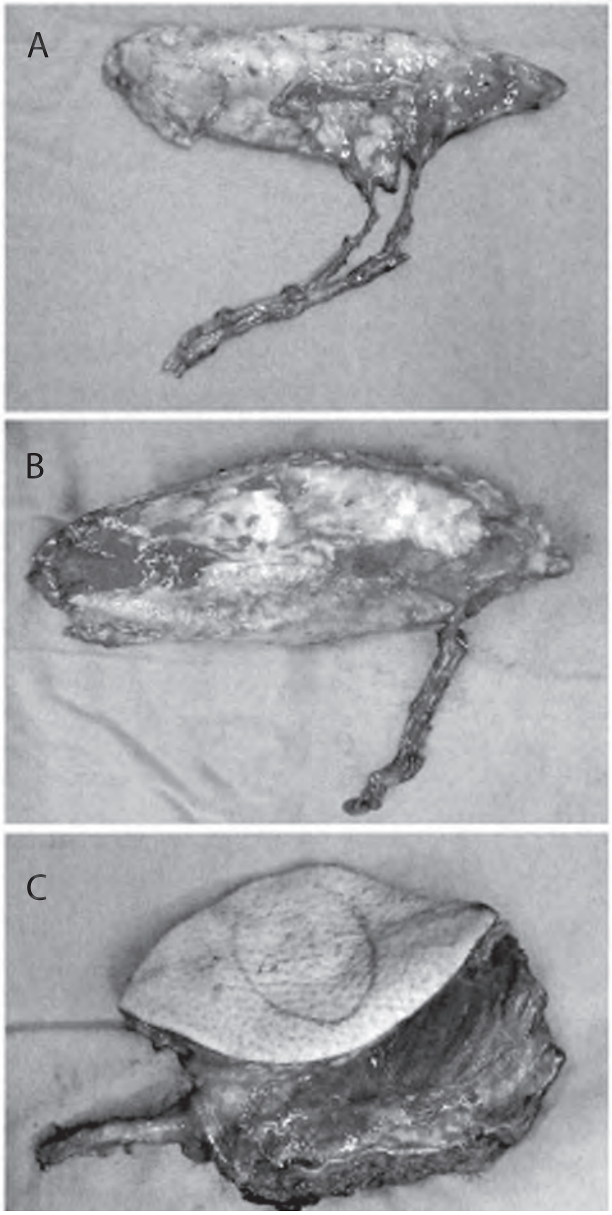


Figure 6. *A*, Cutaneous anterolateral thigh flap dissected suprafascially. *B*, Fasciocutaneous anterolateral thigh flap. *C*, Musculocutaneous anterolateral thigh flap with part of vastus lateralis muscle. (*Reprinted with permission from Pederson.*[291])

The future of flap harvest might include the new "free style" free flap concept. Mardini et al.[318] used color Doppler to guide harvest of free style free flaps from many areas around the body. The thigh is being used as the model donor site for flaps with this retrograde technique. Other perforator flaps and perforator-type flaps are being used with increasing frequency. Perforator variants are being derived from the thoracodorsal system and the gluteal vessels.[319–321] Kim et al.[319] described a thin latissimus dorsi perforator-based flap (Figs. 9–11).

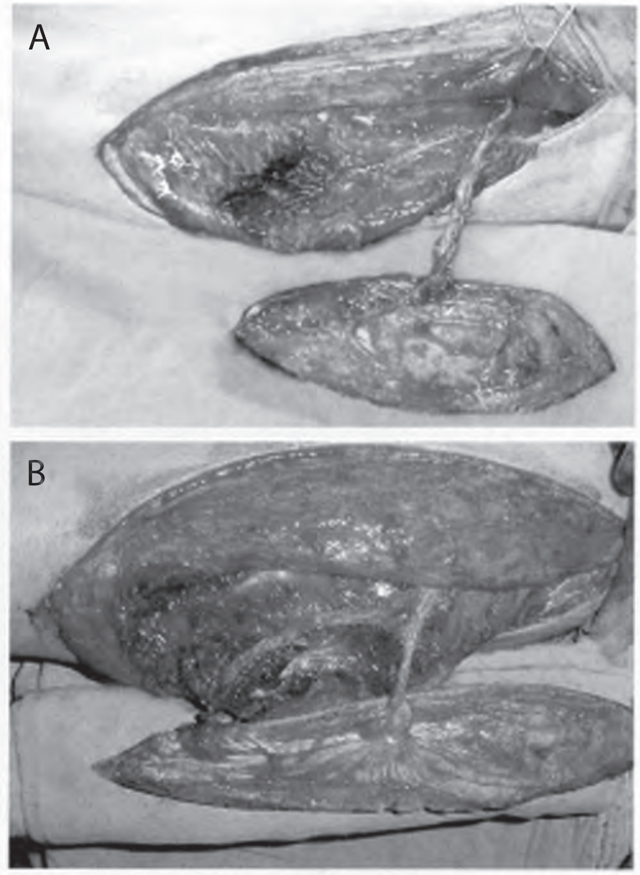


Figure 7. *A*, Anterolateral thigh musculocutaneous perforator flap. One musculocutaneous perforator dissected free from the vastus lateralis. *B*, Dissection of two intramuscular perforators. (*Reprinted with permission from Celik et al.*[314])

The deep inferior epigastric perforator (DIEP), superior gluteal artery perforator,[322] superficial inferior epigastric artery (SIEA), and gracilis flaps are all being used for breast reconstruction. The results and donor morbidities associated with these flaps are being compared with those associated with free TRAM and pedicled TRAM flaps. Large series of successful breast reconstructions with SIEA and DIEP flaps have been published in recent years.[323,324] The DIEP flap might be as cost-effective as the free TRAM flap in this scenario.[325]

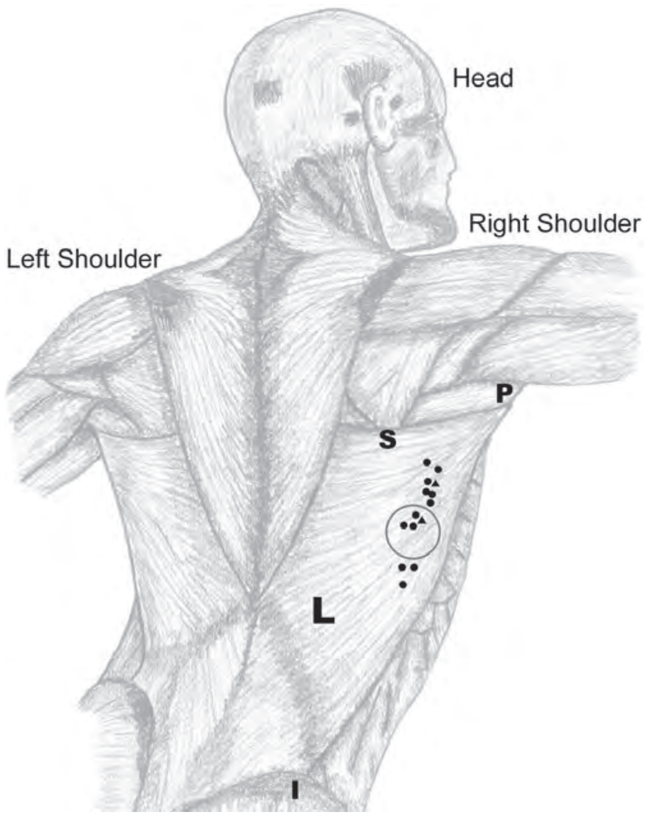


Figure 8. Locations of the 16 skin perforators. *Circle* represents 3-cm-diameter circle that is centered on the first anatomic landmark. Each *black dot* represents one skin perforator, and each *black triangle* represents two skin perforators. *P*, posterior axillary fold; *S*, scapular tip; *L*, latissimus dorsi muscle; *I*, iliac crest. (*Reprinted with permission from Lin et al.*[317])

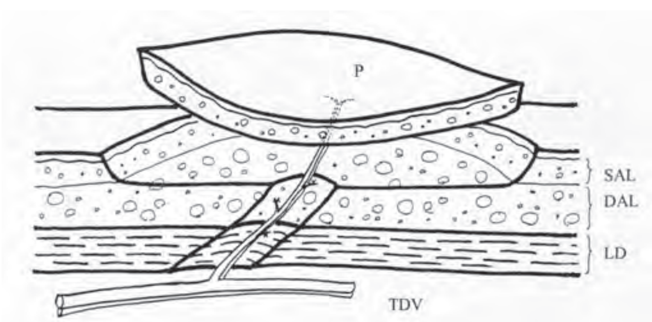


Figure 9. Illustration shows cross-section of thin latissimus dorsi perforator-based flap and dissection plane through superficial fascial layer. *SAL*, superficial adipose layer; *DAL*, deep adipose layer; *LD*, latissimus dorsi muscle; *TDV*, thoracodorsal vessels. (*Reprinted with permission from Kim et al.*[319])

Chevray[323] compared SIEA and DIEP flaps with each other and with TRAM flaps. Operative times were similar. The author noted the advantage of non-violation of the abdominal wall when the SIEA is used. Unfortunately, the SIEA pedicle often is absent or not substantial enough for flap transfer. When the vessel is present and usable, it frequently is small and has a short pedicle. Hospital stays were slightly shorter in the SIEA group.

The SIEA flap generally is considered safe, primarily for hemi-flaps, whereas the DIEP and free TRAM flaps generally have reliable flow across the abdominal midline. SIEA transfer has drawbacks, which are the hemi-flap size limitation, the small vessel size with short pedicle, and time spent intraoperatively looking for SIEA when they might not be present. Occasionally, however, one side of the lower abdominal skin is SIEA-dominant, with respect to arterial and venous flow, or just venous outflow. For this reason, we advocate looking at the SIEA and superficial inferior epigastric vein on all patients before performing DIEP dissection.

If blood flow, pedicle length, and adequate harvest size are available for an SIEA, the patient has the advantage of not having to undergo abdominal fascial opening and muscle dissection. Considering that both DIEP and SIEA flap transfers purport to have decreased abdominal wall morbidity relative to the free TRAM, further studies comparing these flaps will be instructive.

Muscle and Musculocutaneous Free Flaps

In 1970, Tamai[326] first reported free transplantation of vascularized skeletal muscle with his account of a rectus femoris muscle transfer in dogs. At biopsy 5 months later, muscle fibers and motor nerve action potentials were almost normal. Harii et al.[327] transferred the gracilis muscle, in 1973, for facial reanimation in a patient with long-standing Bell palsy. At about the same time, a surgical team in China[328] transferred the lateral portion of the pectoralis major muscle to the forearm to replace the finger flexor musculature destroyed in a Volkmann contracture. Ikuta et al.[329] repeated this operation in 1976.

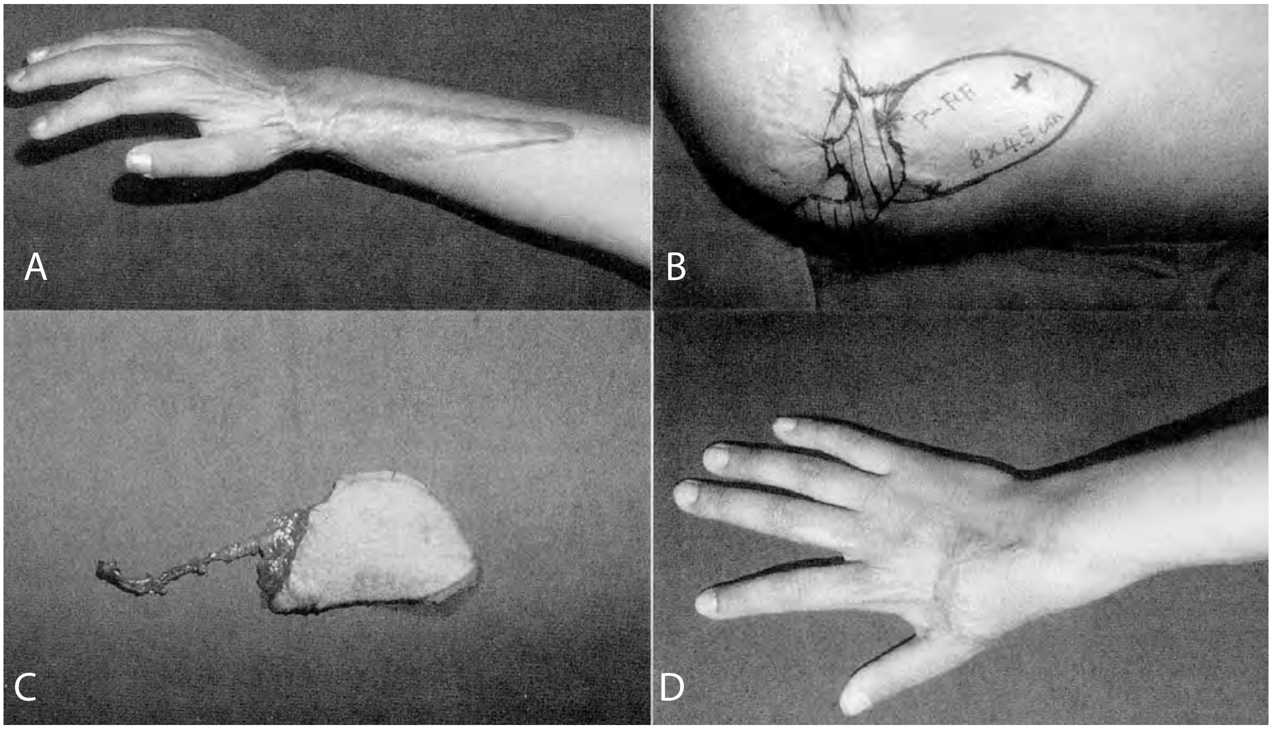
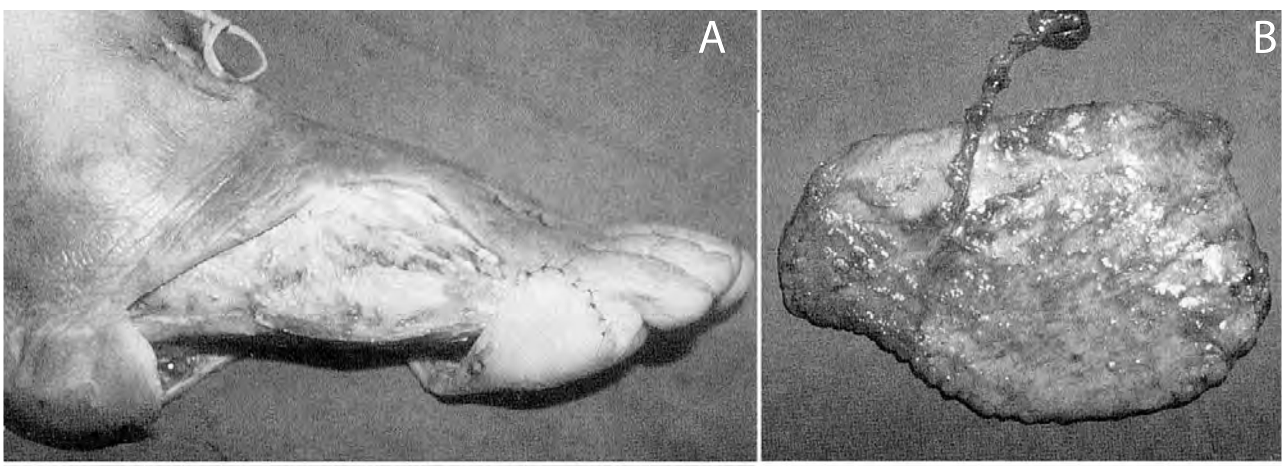


Figure 10. *A*, Post-burn scar contracture on the right wrist of a 5-year-old girl creates limited range of motion. *B*, Thin 8 × 4.5 cm latissimus dorsi perforator-based free flap was designed on the patient's back near the scars. *C*, Flap with pedicles that were dissected to the main muscular branch under the muscle to gain proper vein diameter for anastomosis. Underlying muscle was not included in this flap. *D*, Postoperative results. (*Reprinted with permission from Kim et al.*[319])



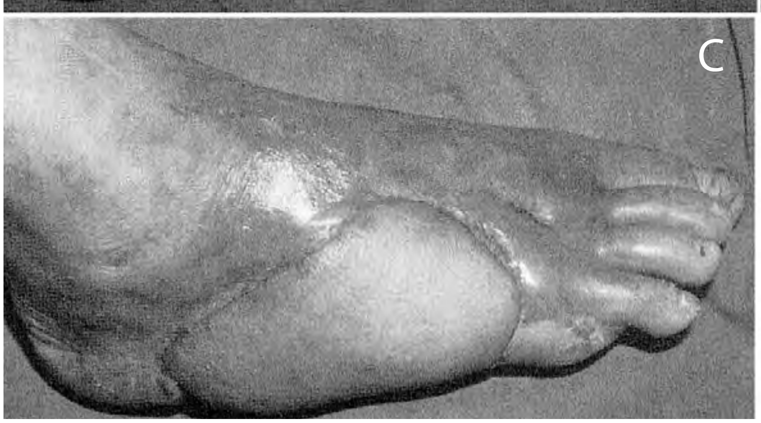


Figure 11. *A*, Diabetic, cellulitic foot of a 53-year-old man has extensive defect after undergoing débridement. *B*, Thin 20 × 10 cm latissimus dorsi perforator-based free flap containing thin superficial adipose layer was elevated for covering the defects in the foot dorsum, lateral foot, and plantar areas. *C*, Appearance at 1 month postoperatively. (*Reprinted with permission from Kim et al.*[319])

Today, the transfer of skeletal muscle as a free flap is a common operation in plastic surgery. The vast majority of these free muscle transfers are performed to provide bulk and soft-tissue coverage in cases of traumatic losses or osteomyelitis. The most common muscle flaps are the latissimus dorsi and rectus abdominis muscle flaps, which offer the advantages of reliable, large-caliber, long vascular pedicles and relatively low donor site morbidity. Salgado et al.[330] reported an alternative method for harvesting the rectus muscle via a Pfannenstiel incision. This approach might offer the advantage of a more esthetic donor scar. Other refinements have evolved out of consideration for donor site morbidity caused by muscle harvest. Brooks and Buntic[331] and Buntic et al.[332] reported their first 100 cases of partial superior latissimus flaps and partial medial rectus flaps. The authors noted that the partial latissimus preserves function of the bulk of the muscle, as the motor nerve, or the relevant portion, is preserved. The partial rectus preserves lateral muscle function (Fig. 12).[332]

The concept of transplanting a tissue unit composed of skin and muscle for reconstruction originated with Tanzini[333] who, in 1906, used the latissimus dorsi musculocutaneous flap to build a breast mound. The work conducted by Tanzini was initially accepted, subsequently ignored, and then forgotten for three generations. McCraw and Dibbell[334] rediscovered the concept originated by Tanzini when they transferred a number of free musculocutaneous flaps in dogs, which led to their landmark work on human island musculocutaneous flaps.[335] Most of the independent musculocutaneous territories described by McCraw et al.[335] are potential sources of free flaps, and numerous others have since been identified and successfully transferred.

Maxwell[336] listed several musculocutaneous free flaps and described their history and anatomy. Maxwell credited Fujino et al.[337] with the first clinical free transfer of a musculocutaneous unit, in 1975; this was a deepithelialized gluteus maximus flap used for reconstruction in a patient with an aplastic breast.

Functional free muscle transfer is performed to replace lost muscle and tendon-unit function. Functional muscle has particular application in restoration of finger flexion and extension in cases of severe posttraumatic loss or Volkmann ischemic contracture and for facial reanimation. Both topics are covered extensively in *Selected Readings in Plastic Surgery* issues dealing with facial nerve disorders[338] and hand surgery.[339,340] In an interesting report, Lin et al.[341] described use of the soleus, latissimus, gracilis, and rectus femoris muscles in functional free muscle transplantation to restore finger flexion and extension and in the repair of biceps defects to provide functional elbow flexion and lifting power. It is worth noting that in that series, the youngest patient was 16 years old. The authors reported M4 return of function in most of their transfers.

Selection of a donor muscle for transplantation must be based on the functional requirements of the patient and the dynamic characteristics of the muscle. The working strength of a skeletal muscle is directly proportional to the cross-sectional area of the contracting muscle fibers, whereas the range of muscle contraction is a factor of fiber length. The neuronal mesh of the available donor muscle should match the anatomy of the recipient nerve branch as much as possible. Many muscles have been tried, but the gracilis muscle is emerging as the clinical favorite for many applications. Harvest and inset of the functional gracilis muscle is generally straightforward in experienced hands. Several articles detail the operative technique of gracilis harvest and anatomic variations of the muscle (Figs. 13–16).[342–344] Hasen et al.[343] described wide elevation of the adductor longus on both sides of the vascular pedicle (Figs. 17 and 18). Lin et al.[345] harvested the gracilis through a shorter incision without the endoscope.

Functional free muscle transplantation involves the transfer of skeletal muscle by microvascular anastomoses and reinnervation by microsurgical technique, suturing an undamaged motor nerve in the recipient site to the motor nerve in the transplanted muscle. The ultimate success of a free innervated muscle transfer depends not only on survival of the muscle but also on function of the part. Histologically, muscle fibers that are not reinnervated gradually degenerate and are eventually replaced by fat cells. The question of whether muscle fibers survive in their original state and are reinnervated or whether they first degenerate and subsequently regenerate remains unanswered.

Many factors are important to the outcome of any procedure: effective tenotomy in reestablishing proper muscle resting tension, amount and quality of donor nerve tissue and of the anastomosis, quality of donor and recipient vasculature, and other anatomic conditions at the recipient site. In a rabbit rectus femoris muscle model, Terzis et al.[346] showed that despite 100% patency of the anastomosis, maximum working capacity after reimplantation was only one-fourth of normal. Still, revascularized free muscle transplants can be expected to at least partially replace the function of lost muscles in various areas.

Some authors[347–351] have emphasized the importance of reestablishing correct resting tension of muscle transplants. Small decreases in resting muscle tension can markedly reduce the power and amplitude of a contracture. A recent article[352] advocates the importance of early passive motion for these functional transfers in the upper extremity. Doi et al.[352] reported that early motion might help with excursion and prevent adhesions.

On average, muscle transplants have significantly less functional recovery than do controls, although 100% of the control maximum tetanic tension has been noted in several transplanted muscles.[353] A study by Kuzon et al.[353] involved orthotopically replanting gracili on 15 dogs and comparing twitch, tension, and maximal tetanic contraction with contralateral leg gracilis controls. In several individual replants, 100% of control maximal tetanic tension was observed. Kuzon et al. concluded that intraoperative ischemia, if less than 4 hours, does not affect functional recovery of a free muscle transfer and that the observed variability in functional outcome must be caused by other, still undetermined, factors.

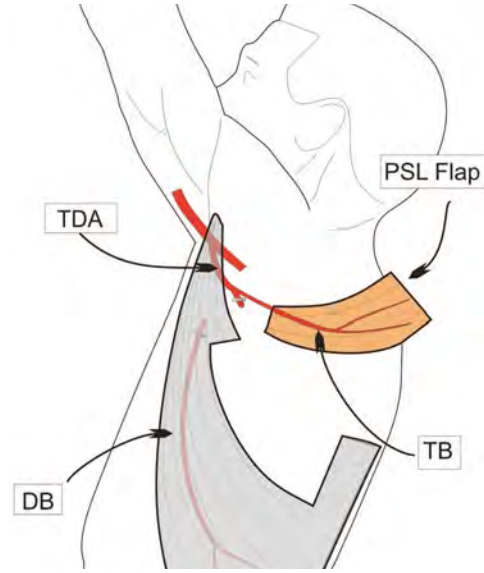


Figure 12. Illustration shows the partial superior latissimus flap (*PSL Flap*) isolated on the transverse arterial branch of the latissimus muscle. Additional pedicle length is gained by harvest of the thoracodorsal artery (*TDA*) and vein, with or without the subscapular system. Lateral descending branch (*DB*) has been ligated. Flap is harvested with the transverse branch (*TB*) of the artery and the transverse nerve branch that accompanies it. Remaining latissimus muscle is innervated by the intact descending branch of the thoracodorsal nerve (not pictured). Vascularity of the remaining muscle is preserved through intercostal perforators and perforators of the thoracolumbar fascia. (*Reprinted with permission from Buntic et al.[332]*)

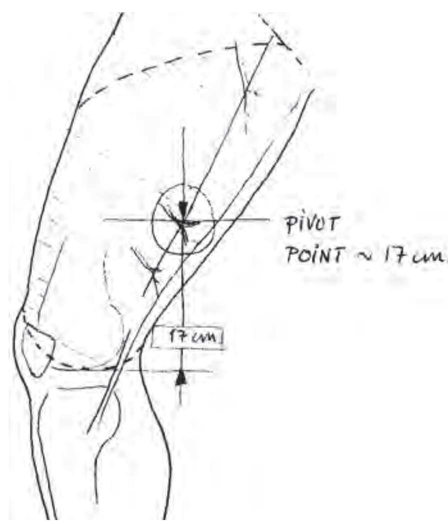


Figure 13. Potential arc of rotation of the distally based gracilis pedicles flap based on the proximal secondary pedicle. Distal to the patella, the reach of the flap depends on the exact location of the proximal secondary pedicle and might not be reliable. (*Reprinted with permission from Cavadas et al.[342]*)

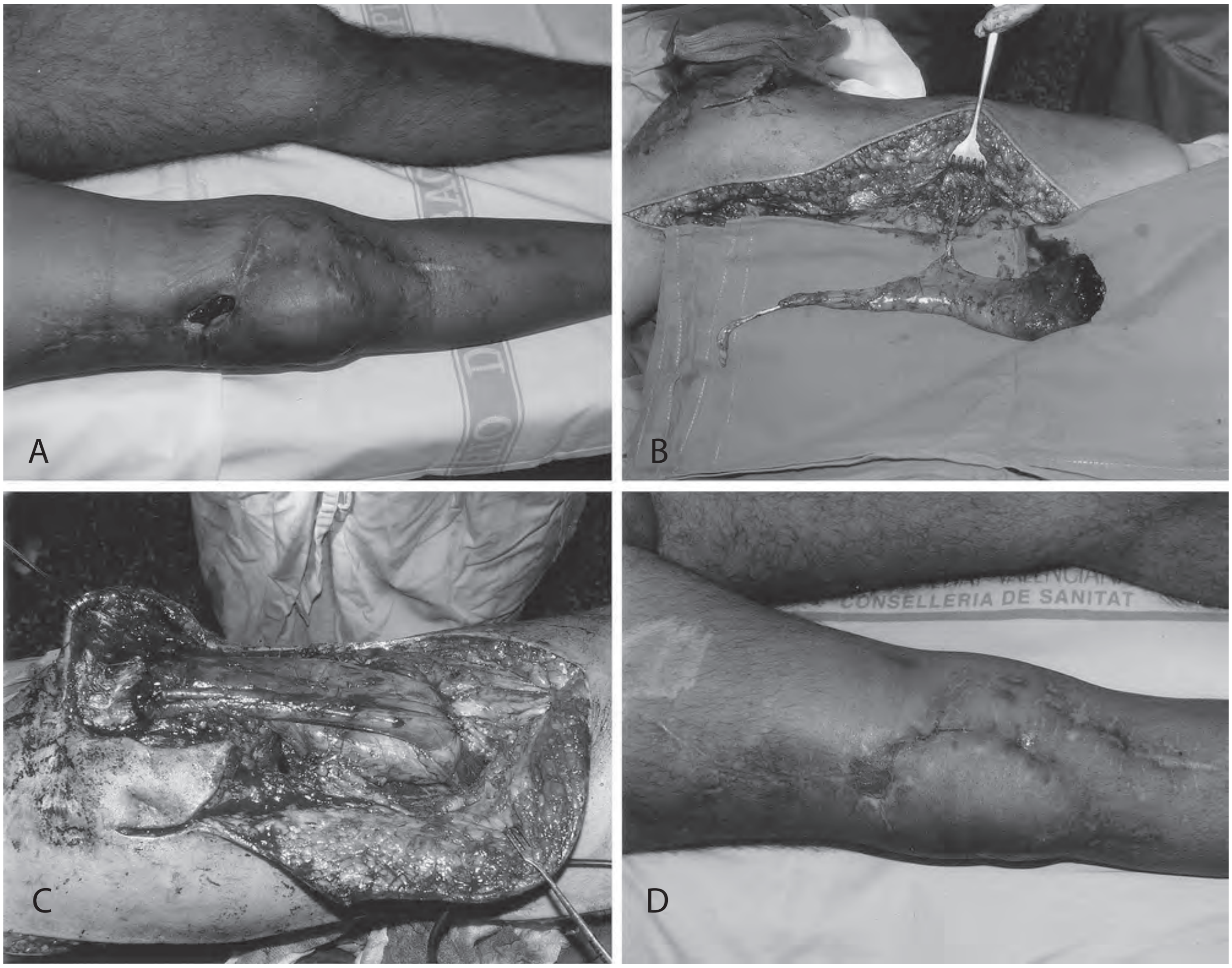


Figure 14. Pedicled reverse gracilis muscle flap. *A*, Chronic infected suprapatellar defect with missing quadricipital tendon. *B*, Ipsilateral gracilis muscle is dissected based on the proximal secondary pedicle. *C*, Muscle is turned over to allow access to the patella and reconstruction of the quadricipital tendon. *D*, Result after skin grafting of the muscle. (*Reprinted with permission from Cavadas et al.*[342])

Osseous and Osteocutaneous Free Flaps

Free osteocutaneous flaps evolved from the need for both vascularized skin and bone in some reconstructions. Ostrup and Fredrickson[354] pioneered the free transfer of vascularized bone in 1974. Shortly thereafter, Taylor et al.[355] and O'Brien[356] were instrumental in defining the advantages, risks, and limitations of the technique. Buncke et al.[357] transferred a free rib osteocutaneous flap to the lower leg for tibial pseudarthrosis in 1977. That same year, Serafin et al.[358] used a rib osteocutaneous free flap for mandibular reconstruction.

Several authors have listed rib, fibula, iliac crest, second metatarsal, radius, calvaria, and scapula as common sources of vascularized bone and have cited early reports of microsurgical transfer of the respective flaps.[297,301,354,355,359–366] Vascularized bone autografts have been shown to be superior to nonvascularized bone grafts regarding early incorporation, bone hypertrophy, mechanical strength to failure, and osseous mass retention.[367,368] The rate of graft union is affected not only by the graft itself but also by the condition of the recipient bone ends. When bone defects are large or the recipient bed is poorly vascularized, clinical evidence suggests that osteocyte survival is greater in free vascularized bone grafts.[369]

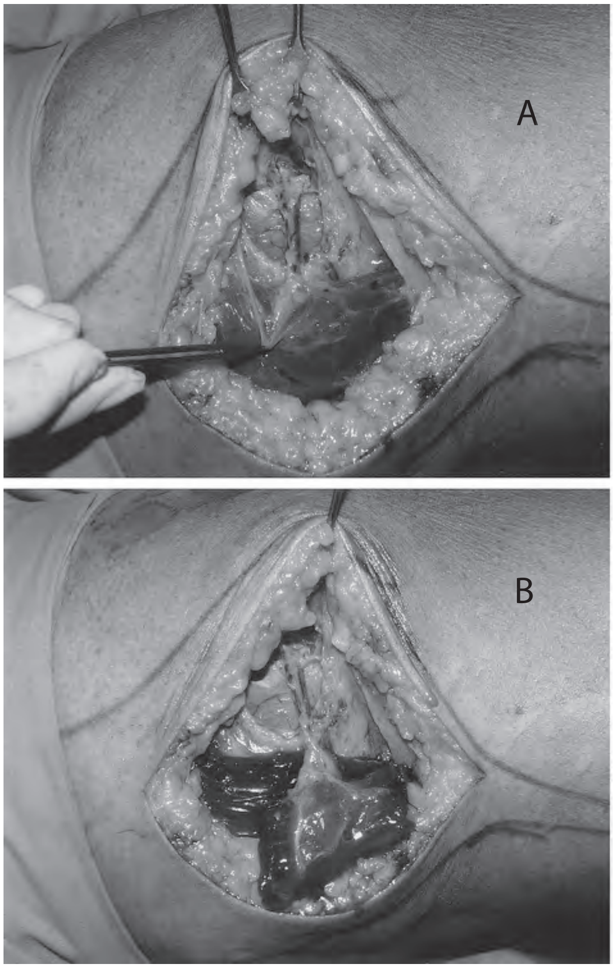


Figure 15. *A*, Intraoperative view of dissected proximal secondary pedicle up to its origin from the superficial femoral vessels. *B*, Intraoperative view of segmental gracilis flap fully dissected and ready for free transfer. The gracilis muscle has not been divided. (*Reprinted with permission from Cavadas et al.*[342])

Trauma and irradiation hamper bone healing in conventional nonvascularized bone grafts,[370] whereas vascularized bone grafts seem to better tolerate irradiation of the recipient bed.[371] Moreover, vascularized bone grafts seem to heal more rapidly, even in the presence of an infected wound.[372,373] In short, the technique of vascularized free bone grafts is the standard against which emergent technologies, such as Ilizarov distraction osteogenesis, must be measured. See the *Selected Readings in Plastic Surgery* Lower Extremity Reconstruction issue[264] for a more detailed discussion of bony reconstruction in the lower extremity.

Berggren et al.[374] compared medullary and periosteally supplied costal grafts in dogs. Grafts that were revascularized through their periosteal vessels showed less resorption, albeit with some marrow necrosis and partial loss of osteocytes. Grafts with both medullary and periosteal blood supply survived completely but were partially resorbed with time. Both types of grafts healed to their recipient site equally well.

Vascularized rib grafts can be harvested either via an anterior approach, preserving periosteal blood supply, or posteriorly, conserving primarily medullary blood supply. Serafin et al.[375] summarized the benefits and limitations of both approaches. Georgescu and Ivan[376] showed successful use of the serratus-rib composite free flap for upper and lower extremity reconstruction.

In 1979, Taylor[377] was the first to report transfer of a free vascularized graft of fibular bone beneath a previously implanted groin flap for repair of a tibial defect. In 1983, the author[369] recommended free fibular grafts to repair bony defects >8 cm, whereas ilium (straightened by an osteotomy) or fibula can be used for defects 6 to 8 cm. Defects <6 cm long can be repaired by conventional nonvascularized bone grafts. These data are mainly applicable to mandible defects; other osseous defects might have variability. Taylor[369] also described various techniques of harvesting vascularized fibular grafts and has proposed helpful refinements. Most recently, Taylor[378] described a novel technique of free vascularized fibula flap reconstruction of the clavicle combined with biceps tendon for repair of the coronoid ligaments and plate stabilization of the acromioclavicular joint (Fig. 19). Hidalgo[379,380] reported extensive experience with free fibular transfers in mandibular reconstruction.

Many practitioners think it is prudent to perform bilateral lower extremity angiography before fibula harvest to rule out peronea magna. Peronea magna is an anatomic variation with which the peroneal artery is dominant and provides significant arterial flow to the foot along with the posterior tibial artery. With this variant, the anterior tibial artery is hypoplastic or nonexistent. Harvesting

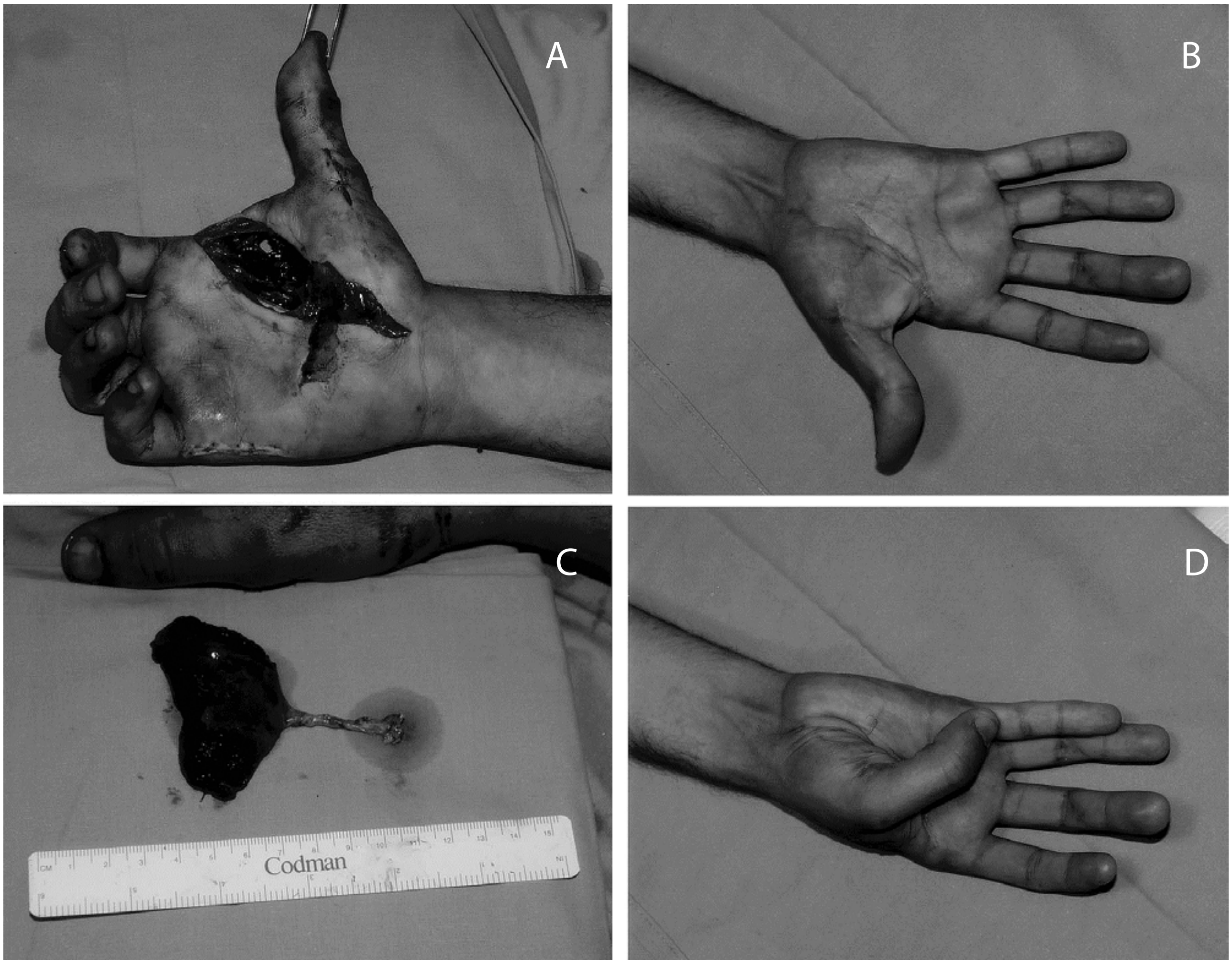


Figure 16. *A*, Crush injury of the first web of the right (dominant) hand in a 22-year-old man. *B*, All nonviable muscles underwent débridement. The resultant defect was filled with a segmental gracilis free transfer based on the proximal secondary pedicle and revascularized to the radial vessels. *C*, Absence of adduction retraction. *D*, Good opposition because of the remaining abductor pollicis brevis muscle. (*Reprinted with permission from Cavadas et al.*[342])

the fibula in such a case can leave the patient with a single-vessel-foot or worse. Angiography has its own associated risks, however, including renal failure, contrast material allergy, bleeding, and pseudoaneurysm of the cannulated access artery. As imaging technology improves, our reliance on angiography will likely wane. Magnetic resonance angiography and computed tomographic angiography are useful tools.[381] Duymaz et al.[382] noted that computed tomographic angiography has provided excellent visualization of the lower extremity and can be used for planning purposes in cases of free tissue reconstruction of the lower extremity (Fig. 20).

Taylor and Watson[362] described the free transfer of vascularized ilium on the deep circumflex iliac vessels. Taylor et al.[363,383] later expanded the applications of the technique and suggested further surgical refinements. Shenaq[384] reported less morbidity with the classic iliac crest free flap when using the inner cortex of the bone, but a study by Mirovsky and Neuwirth[385] disputed that conclusion. Mialhe and Brice[386] presented a report of a posterior iliac crest osteomusculocutaneous free flap that is based on a superficial branch of the superior gluteal artery.

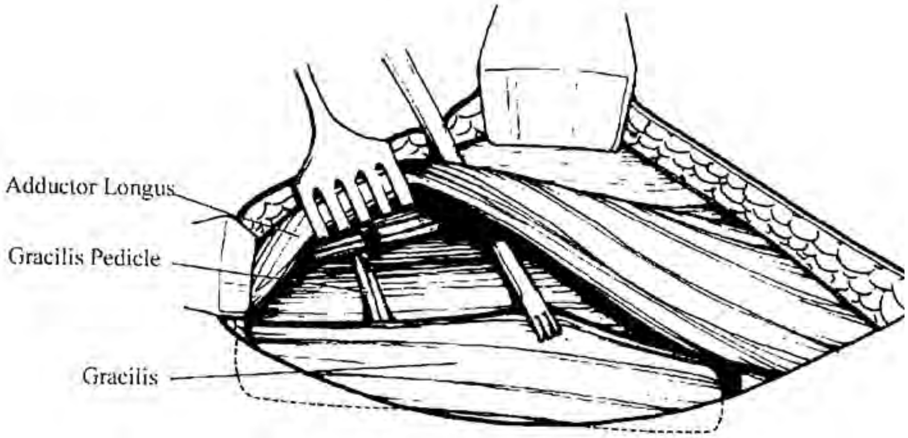


Figure 17. Illustration shows that after division of the intramuscular branches to the adductor longus muscle, the gracilis muscle is divided distally and proximally and the adductor longus muscle is mobilized on both sides of the pedicle. (*Reprinted with permission from Hasen et al.*[343])

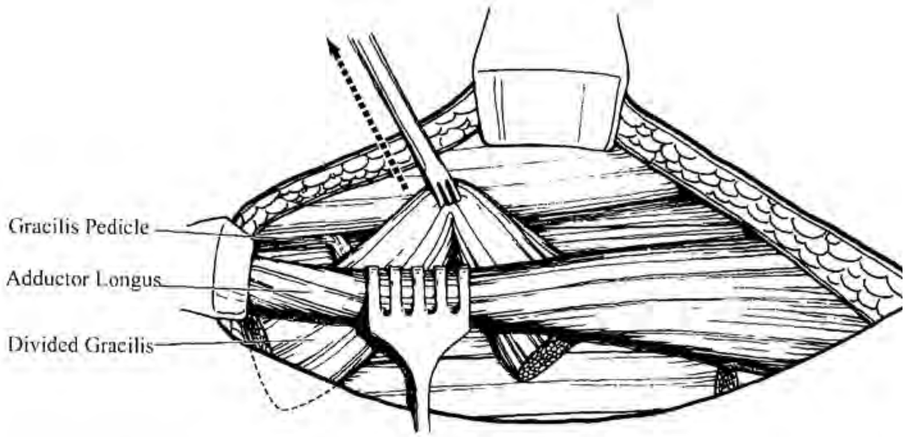


Figure 18. Illustration shows passage of the gracilis muscle into the space created between the adductor longus and sartorius muscles for final proximal pedicle dissection. (*Reprinted with permission from Hasen et al.*[343])

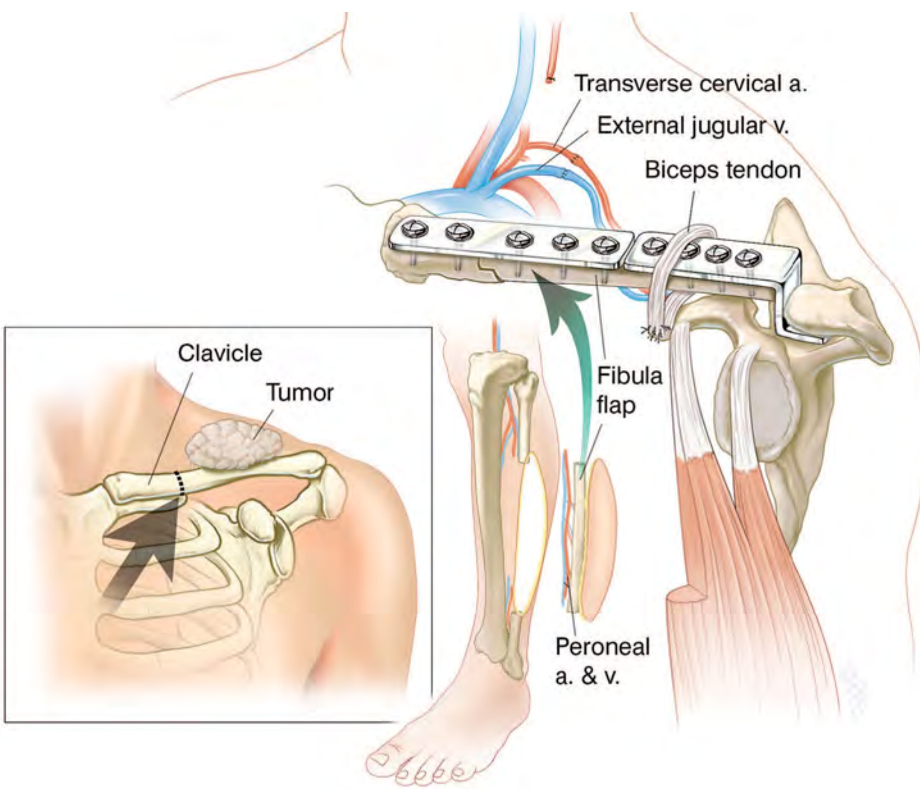


Figure 19. Patient is a 42-year-old man with a 5-cm recurrent dermatofibrosarcoma adherent to the periosteum of the lateral third of the left clavicle shown by magnetic resonance imaging 9 years after initial resection. *Left inset*, Wide tumor excision with 3-cm skin margins and 9.5 cm of the clavicle was performed sparing adjacent neurovascular structures and a ligamentous acromioclavicular joint cuff. *Arrow* indicates the site of the bone section. *Center inset*, Left osseocutaneous fibular flap was raised on the peroneal vessels and was transferred. *a. & v.*, artery and vein. *Right image*, In a separate operation, the acromioclavicular joint dislocation was reduced and held by fixing the modified clavicular plate with unicortical screws and positioning the hook beneath the acromion laterally. *a.*, artery; *v.*, vein. (*Reprinted with permission from Taylor et al.*[378])

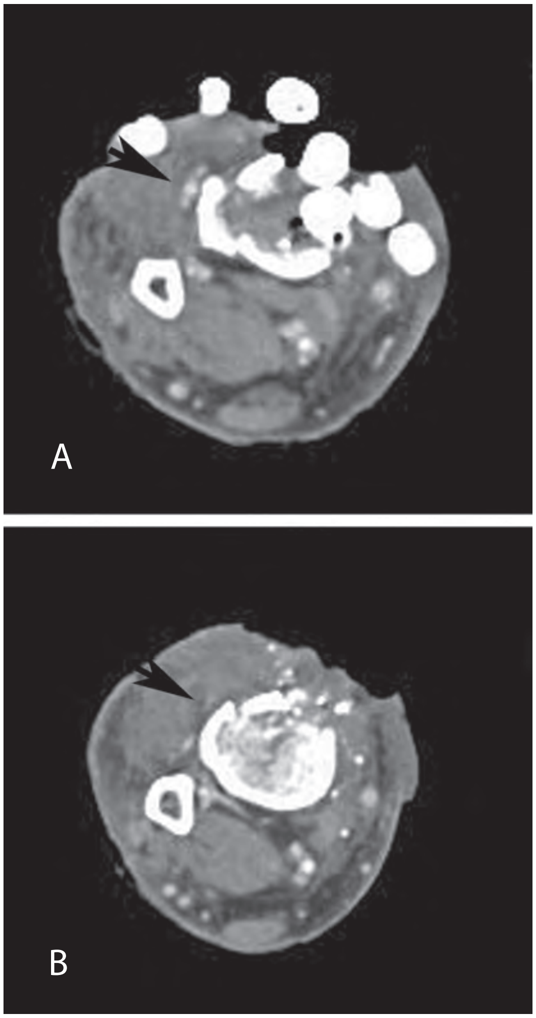


Figure 20. Computed tomographic angiography scans of a 54-year-old man with a comminuted tibial fracture and anterior soft-tissue defect over the right leg. *A*, Patent anterior tibial arterial and venous comitantes at the proximal margin of the injury site (*arrow*) are shown. *B*, Image obtained 4 cm distal to the image shown in *A* shows occlusion of anterior tibial vessels, evidenced by the absence of contrast (*arrow*). (*Reprinted with permission from Duymaz et al.*[382])

Free Flaps of Viscera and Omentum

Microvascular transfers of bowel segments, primarily of the proximal jejunum, are widely used for reconstruction in the oral cavity, pharynx, and cervical esophagus.[387–393] The greater omentum is an excellent source of donor tissue and has been transferred by microanastomoses for multiple reconstructive problems in the past.[394,395] Today, because of the increasing abundance of other free tissue options and the need for laparotomy to harvest the omentum, its popularity has waned considerably. Nevertheless, after latissimus, and latissimus-serratus, the omentum remains a reliable option for large scalp defect reconstruction. In addition, the omentum can be used for wound coverage in the lower extremity, and the gastroepiploic system is used simultaneously for lower limb revascularization in the context of peripheral vascular disease and ischemic wounds.[264]

REPLANTATION

The first end-to-end anastomosis between vessels of disjoined parts was performed by Murphy[1] in 1896. According to Kleinert et al.,[396] a few years later, the German surgeon Hoepfner successfully replanted limbs in dogs. Working independently during the first years of the century, Guthrie[2] and Carrel[3] transplanted kidneys, blood vessels, and composite tissues in lambs and dogs. In 1902, Carrel experimentally showed the feasibility of limb replantation, although his heterotransplant ultimately failed. Ten years later, the author received the Nobel Prize for his contribution to the science of vascular anastomosis and organ transplantation.

In 1921, Nylén and Holmgren first described the use of a microscope during surgery for otosclerosis.[4] In 1950, Perritt[397] sutured a human cornea under an operating microscope.

Malt and McKhann[14] replanted the arm of a 12-year-old boy who had suffered an above-elbow amputation in 1962. In 1963, Kleinert et al.[398] presented a report on vessel repair techniques to revascularize near-complete severed limbs. In 1965, Kleinert and Kasdan[399] reported the first revascularization of human digits and Komatsu and Tamai[19] performed the world's first replantation of a human digit.

As the 20th century progressed, surgeons attempted to operate on increasingly finer structures of the body, and reports of successful reattachment of severed extremities became commonplace. Today, the feasibility of human limb replantation is no longer in question. The reader is referred to an excellent article by Kleinert et al.[400] for a history of replantation and an overview of popular techniques.

Arm and Forearm Replants

Upper extremity replantation has evolved rapidly since the report presented by Malt and McKhann.[14] Survival rates have improved significantly during the last 30 years, and the ultimate success of a replantation attempt is now judged by functional and cosmetic parameters.

Unlike distal amputations, the proximal limb has a large muscle mass that renders it vulnerable to ischemic degeneration. Nerve injuries to the proximal limb are associated with a high risk of loss of function. Review articles by Morrison et al.,[401] Wilson et al.,[402] O'Brien,[403] and Whitney et al.[404] offer different perspectives on the subject of major limb replantation.

In the rat, muscle necrosis and permanent breakdown of biochemical systems occur within 4 hours of ischemia.[405] In man, muscle necrosis has been documented after only 2.5 hours of tourniquet ischemia.[406] Metabolic parameters correlate with histological evidence of extensive cellular damage. With increasing ischemic times, the histological appearance does not return to normal even after perfusion is restored. Cooling theoretically prolongs the safe ischemic period, although Muramatsu et al.[407] noted that even when cooled, muscle enzymes (creatine kinase, serum glutamic-oxalacetic transaminase) continued to leak out of the replanted dog hind limb after 6 hours of ischemia.

Nunley et al.[408] described the technique of arterial and venous shunting as an aid to rapidly perfuse the upper limb during lengthy replantation operations. The shunt allows adequate time for thorough débridement, appropriate bony stabilization, and identification of anatomic structures. The authors concluded that the arteriovenous shunt improved their operative technique without jeopardizing muscle viability.

The value of tissue perfusion in replantation, although proven for many years in major organ transplants, has not been conclusively shown in limb replantation.[356,409] Usui et al.[410] and Smith et al.[411] noted some benefit from fluorocarbon perfusion of amputated extremities, with less alteration of lactate, pH, and creatine kinase levels. This improvement was offset by loss of capillary endothelium and increased edema.

Fukui et al.[412] described their experience with continuous postoperative infusion of urokinase, prostaglandin E, heparin, and low-molecular-weight dextran. In the 13 cases reported, no instances of arterial thrombosis occurred, and the authors noted significant differences in platelet count, fibrinogen, and antithrombin III in the patients receiving the drug infusion compared with the control group.

Indications and Contraindications

Meyer et al.[413] stated that patients with amputations proximal to the wrist joint but close to it are good candidates for replantation, as evidenced by Chen grade I or II recovery in 80%. In general, upper extremities amputated proximal to the midforearm should not be replanted if the warm ischemia time is longer than 6 hours.[402] The following are universal contraindications to replantation:[402]

- concomitant life-threatening injury
- multiple segmental injuries in the amputated part
- severe crushing or avulsion of the tissues
- extreme contamination
- inhibiting systemic illness (e.g., small-vessel disease, diabetes mellitus)
- previous surgery or trauma to the amputated part precluding replantation

Functional Recovery

Return of function in cases of forearm replantations depends largely on two factors: the degree of nerve regeneration and the hand rehabilitation program.[414]

Russell et al.[415] reported their results in cases of upper limb replantation and revascularization. The most frequent complication of surgery was infection (29%) compounded by inadequate débridement, which led to four failures. Nonunion occurred in 13%, and intrinsic muscle function was weak or absent in all patients. Excellent or good results were noted in eight of 19 patients; all had clean, guillotine-type distal amputations or incomplete proximal amputations with intact nerves. Fair and poor results were associated with crush or avulsion injuries. The authors concluded that the potential for functional recovery is proportional to the amount of viable tissue remaining.

Hand and Digit Replants

Weiland et al.[416] charted the progress of digital and hand replantation efforts at their institution over a 7-year period. Survival of the replanted limbs increased from 32% in 1970, to 74% in 1975, to more than 90% in 1976. As survival of the replanted extremity climbed, clinical emphasis shifted to considerations of long-term functional results.

Strauch et al.[417] offered an excellent review of the problems and complications encountered in replantation surgery in the hand. Waikakul et al.[418] presented a large series of more than 1000 digital replantations for which the functional results were generally good, with a replant viability rate of 93%. Zone 2 replants experienced the worst outcomes.

Indications and Contraindications

All other criteria being favorable, few surgeons would argue against replantation in the following circumstances:

- multiple finger amputations
- thumb amputations
- complete amputations of the hand at the palm or wrist[356,419,420]
- all amputations in children

Replantation is controversial in the following clinical situations:

- loss of a single digit other than the thumb, especially the index and small fingers, even when the amputation level is proximal to the flexor digitorum superficialis tendon insertion
- single-digit amputations distal to the digitorum superficialis insertion
- ring finger avulsion injuries

Level and Type of Injury

Tsai et al.[421] described their technique for replantation of the fingertip at the level of the distal interphalangeal joint or distally. They noted a 69% survival rate, and 25% of patients had 2-point discrimination <5 mm. Clean, minimally crushed amputations yield the best results after replantation.[356] Avulsion injuries, severely contaminated wounds, and amputations with multiple levels of injury are secondary choices for replantation.[409,420,422] The severity of the damage often necessitates dissection of a large area to escape the zone of injury, and repair of injuries such as ring avulsions, for example, might not revascularize the flexor tendons and proximal interphalangeal (PIP) joint.[400] Microsurgical repair in cases in which the entire finger has been degloved does not result in good function.[415,420]

Ring avulsions are a special case. With ring avulsions, the zone of injury varies by level and by actual severity of the soft-tissue injury and devascularization. In general, avulsion injuries fare significantly worse than do sharp injuries regarding recovery of range of motion.[423] Adani et al.[424] reported achieving acceptable results after complete ring avulsion replants.

Patient Age

O'Brien[356] stated that any limb amputation in a child merits an attempt at replantation as long as the part is not severely crushed. Kleinert et al.[400,420] stated that age alone is not a contraindication to replantation but that it must be considered in the decision-making process. Microsurgical repair of the tiny vessels of infants renders the operation technically difficult; on the other hand, functional return after replantation of digits in small children often is good. Useful functional recovery cannot be expected with any reliability in the elderly. Thus, any attempt at replantation should be carefully weighed against the potential systemic insult from the anesthesia and operation.

Length of Warm Ischemia Time

Kleinert et al.[400,420] asserted that >12 hours of warm ischemia is a relative contraindication to digital replantation, although survival of the replanted part has been documented after as long as 42 hours of warm ischemia.[113] Prompt cooling of the amputated digit to 4°C prolongs the acceptable ischemic period to approximately 24 hours, with a good chance of complete survival and full functional return.

Patient Selection

A patient's occupation, economic and social statuses, nationality, mental health, and cooperativeness must all be taken into account when deciding whether to attempt replantation.[425] Patients in occupations such as manual labor might value gross motor skills and strength with rapid recovery, as opposed to a violinist who values manual dexterity and fine motor skills. Economics is important because some patients need to return to work sooner and cannot sacrifice the time and expense to undergo the rigorous rehabilitation required after digital or extremity replantation.

Single-Digit Amputations

Urbaniak[426] is a proponent of replantation in single-digit amputations distal to the superficialis insertion if no crush injury is present. Tamai[419] also replants single digits when local wound conditions are favorable and if the patient desires the procedure. However, his recommendation is influenced in that a person in Japan who is missing a finger can be labeled as a gangster and might not be able to get a job.

May et al.[427] documented excellent survival and good aesthetic results in a series of 24 digits replanted distal to the PIP joint, which prompted them to advocate the procedure in selected cases. Wilson et al.[402] suggested a role for single-digit replantation when adjacent fingers are severely injured and the cut is clean. Waikakul et al.[418] also advocated single-digit replantation. Kleinert et al.[400,420] discouraged single-digit replantation, although the results he has achieved with the procedure have been impressive. O'Brien[356] weighed the merits of single-digit replantation based on patient sex, occupation, and expected functional result. Jones et al.[428] compared hand function in patients who had received single-digit replants and those who had been amputated and concluded that there is little functional need to replant a single digit except the thumb. Ultimately, the discussion regarding single-digit replantation in adults remains a philosophical one, and each surgeon must come to his or her own conclusion based on the situation at hand.

Secondary Procedures

Most replanted digits that include at least one joint in the replanted part experience significant stiffness after healing, and secondary procedures often are needed. In addition, replanted digits might require further soft-tissue coverage. Ross et al.[423] reported the best range of motion in zone 1 and zone 5 replants. Interestingly, two-tendon replanted digits had better range of motion than did one-tendon fingers. Early motion protocols were advocated. Yu et al.[429] reviewed 79 replanted digits that underwent a total of 102 secondary procedures. Flexor tenolysis was used often with good results.

Replants of Miscellaneous Body Parts

Although the vast majority of reported surgical reattachments are in the upper extremity, successful replants have been achieved in the lower extremity,[430] scalp,[431–434] ear,[435–439] penis,[440,441] testes,[441] scrotum,[441,442] upper and lower lips,[443,444] tongue,[445] nose,[446] and face-scalp composite.[447]

Scalp replantation is one of the most critical problems the plastic surgeon can encounter. Despite appropriate efforts in experienced hands, scalp replants do not always survive nor are the parts always replantable to begin with. Nahai et al.[431] presented a discussion of the appropriate management of extensive scalp avulsions. Should replantation be deemed too risky, the latissimus and the combined latissimus-serratus free flaps are excellent salvage options for subtotal and total scalp avulsions.[448] Omentum is also an excellent option for scalp salvage.

Ademoğlu et al.[449] discussed whether amputated great toes should be replanted. Even though load distribution is altered after amputation of a great toe, the gait is not significantly affected. The authors stopped short of recommending great toe replantation. A more recent study by Lin et al.[450] showed that great toe replantation should be restricted to traumatic amputations in children and incomplete amputations in adults. This is especially true at the level proximal to the interphalangeal joint. Complete amputation of the great toe with injuries of the lateral toes portends a poor prognosis for the survival of replanted toes. Kutz et al.[430] stated that lower extremity replantation might be indicated in cases of distal, clean, sharp amputations in young patients. For a more extensive discussion on lower extremity replantation, see the *Selected Readings in Plastic Surgery* Lower Extremity Reconstruction issue.[264]

Mutimer et al.[436] reported successful microsurgical reattachment of totally amputated ears. Turpin[437] described the evolving technique for successful ear replantation. The author noted that vein grafts usually are required and that postoperative venous congestion is a frequent problem. Turpin suggested that all patients should receive heparin anticoagulation and noted that medicinal leeches or frequent abrasion might be necessary to control venous congestion.

Operative Technique

The surgical principles of microvascular repair have been previously discussed. When performing replantation, one must be particularly careful to place the anastomoses outside the zone of injury and to incorporate only undamaged vessel ends. Excessive shortening of replanted parts results in muscle-tendon imbalance and dysfunction.

The operative sequence for replantation varies according to the clinical situation and preference of the surgeon. A common approach involves the following steps:

- preoperative patient evaluation and preparation
- identification of structures in amputated part
- identification of structures in amputation stump
- bone shortening (minimal) and bony fixation
- arterial repair (with or without recirculation)
- venous repair
- muscle-tendon unit repair
- nerve repair[419,451]
- skin closure or soft-tissue coverage

Adjuncts to Microvascular Anastomoses in Replantation

Internal Fixation

Internal fixation techniques allow early mobilization while maintaining bony stability. Fixation can be accomplished with crossed K-wires,[452] a single intramedullary K-wire,[453] interosseous wiring,[454] intramedullary screws,[417] or bone plates and external fixation devices. Arata et al.[455] described the use of absorbable poly-L-lactide rods in digit replants. No nonunions were noted. The type of fixation used is based on considerations of fragment stability, early mobilization, patient reliability and compliance, and surgeon's preference.

Free Vascularized Joint Transfers

Tsai et al.[456] described the immediate free transfer of a second toe joint for replacement of an index finger PIP joint at the time of replantation when other methods of bony stabilization were unsatisfactory. Nunley et al.[457] reported 92% of normal growth in epiphyses transferred either by replantation or free tissue transfer. Bowen et al.[458,459] presented a report of the vascularity and feasibility of growth plate transfer and noted that both epiphyseal and metaphyseal circulations must be revascularized to obtain adequate growth and structural integrity. Chen et al.[460] reported performing 29 vascularized toe joint transfers to hand and finger joints and achieving good results. The outcomes of these joint flaps must be compared with arthrodesis and well-functioning metallic or Silastic (Dow Corning Corporation, Midland, MI) arthroplasties. With some complex hand joint injuries, a vascularized toe joint might be preferred to these other options.

Vein Grafts

Most replantation attempts fail because of venous insufficiency. In the absence of venous repair, replantation is successful in fewer than 20% of cases.[451] The ideal is two or three venous repairs per finger, but this might be impossible in cases of distal amputations, amputations in children, injuries that have severe dorsal components, or post-replant venous thrombosis.

Vein grafts are routinely performed when the vessel ends are short and when tension at the anastomosis is present. Mitchell et al.[461] studied avulsion injuries in rat limb arteries and veins. As seen through the operating microscope, the damage to the vessels averaged 0.8 cm from the rupture site, and serial histological examination revealed marked injury for up to 4 cm. Arteries were more severely damaged than were veins, especially at bifurcation points. Distal injuries were worse and more frequent than proximal injuries. Buncke et al.[462] reviewed the applications and long-term results of vein grafts in replantation surgery.

Arteriovenous Fistulae

Working in the rabbit ear replantation model, Nichter et al.[463] created an efferent arteriovenous fistula by anastomosing a distal artery to a proximal vein. Heparin in Ringer solution frequently is used to flush the vessel ends before and during anastomosis.[356] Topical application of lidocaine or papaverine can relieve and sometimes avoid vasospasm during the dissection.[356]

Nerve Repair or Graft

Twenty-five years after its publication, the excellent review of microneural repair techniques presented by Terzis[464] is still valid. Nerve grafting in replantation surgery is an option when primary approximation is still impossible after adequate débridement. Donor nerves can be harvested from other amputated and non-replanted parts;[419] a simple epineural technique usually is best. If both ends of the nerves being sutured are well vascularized, complete reinnervation is expected. Schultes et al.[465] compared vascularized versus nonvascularized nerve graft transfers in a rat model and found significant histological differences, with less fibrosis and myelin degeneration in vascularized grafts.

Heparin

Gordon et al.[466] reported a 71% clinical success rate in digital replantation without venous anastomoses by systemic infusion of heparin and removal of the nail plate.

Leeches

Multiple reports confirm the usefulness of medicinal leeches in salvaging failing flaps or replants.[467–473]

Leeches typically are applied to the area of anastomosis to relieve venous congestion in flaps or in appendages through vasodilation and vascular decompression.[473] The key to the benefit of leeches lies with hirudin, a selective thrombin inhibitor that leeches secrete and inject into the host tissue as they feed on the host's blood.

Anthony et al.[470] used quantitative fluorometry to study the effects of leeches on a replanted ear. The authors noted immediate benefits from leeching, namely evacuation of the pooled blood and relief of venous congestion. Later, bleeding continued from the bite sites as a result of the injected hirudin.

Prophylactic antibiotics usually are recommended when leeches are used because of reports of infection with *Aeromonas hydrophila*,[471] which often is insensitive to ampicillin and cephalothin but consistently sensitive to ciprofloxacin, tetracycline, and trimethoprim-sulfamethoxazole.[472] Oral administration of one of these drugs is recommended when using leeches. The reader is referred to an article by Valauri[473] that describes the technical aspects and clinical applications of medicinal leeches in microsurgery.

Tissue Expansion

As described by various authors,[474–478] free flaps can be modified in size and contour by using tissue expanders before transfer.

Analysis of Results

There are as many different standards for evaluating functional recovery after replantation as there are reporting surgeons. Gelberman et al.[479] correlated sensory recovery of replanted parts with arterial pulse pressure and concluded that two-point discrimination reached normal levels (<6 mm) only when pulse pressure in the replanted digit was at least 86% of normal, as measured by the contralateral digit. Two-point discrimination was worse in replanted digits than in isolated nerve injuries.

Zhong-Wei et al.[480] categorized the various functional results obtained in their series as ranging from grade I to grade IV. Patients who achieve grade I return (34%) are able to resume their original work and have at least 60% range of motion. Patients with grade IV functional results (4%) have negligible function of their replanted limbs.

Matsuda et al.[481] reported achieving effective recovery of pinch, grasp, and sensation in 60% of their replants. Schlenker et al.[482] found 2-point discrimination of <10 mm in only nine of 20 replanted thumbs. The average active range of motion for the interphalangeal joint was 35% of normal and for the metacarpophalangeal joint was 29%. Most patients were able to return to work after a mean interval of 7 months.

The results presented by Tamai[451] in a report of 293 upper extremity replants are listed in Table 3. Excellent or good results were achieved in 72% of the cases. Table 4 lists limb survival results after replantation surgery as reported by some major centers.[416,419,420,426,482–484]

Alternatives to Replantation: Salvage Procedures

For failed digital replants and non-replantable injuries, toe-to-hand transplants can restore function. Leung[485] and Frykman et al.[486] described the technique and functional results of these transfers.

The field of toe-to-hand transfers continues to be refined. Williamson et al.[487] Yu and Huang,[488] and Chung and Kotsis[489] reported achieving adequate reconstruction with toe transfers after multiple-finger loss. The rate of return to work was satisfactory. In their review, Wei et al.[490] discussed technical refinements and donor site considerations. They reported excellent functional and aesthetic results.

Buncke et al.[491] reported their accumulated experience of 40 years of toe-to-thumb reconstruction. The authors reviewed their technical refinements and results. Emphasis was placed on low donor site morbidity and excellent functional results.

Wei et al.[492] also reported limited sensory recovery after toe-to-finger transfer, perhaps curtailed

TABLE 3

Functional Results after 181* Upper Extremity Replants[451]

Replant	Excellent		Good		Fair		Poor	
	n	%	n	%	n	%	n	%
Arm	0/5	0	1/5	20	3/5	60	1/5	20
Forearm	2/10	20	3/10	30	2/10	20	3/10	30
Hand	3/14	20	6/14	43	3/14	20	2/14	14
Digit	60/152	39	55/152	36	20/152	13	17/152	11
Total	65/181	36	65/181	36	28/181	15	23/181	13

*181 of 293 replants were followed for more than 1 year and are thus included in the table.

TABLE 4

Clinical Results after Replantation

Study	Number Complete (% Viable)	Number Incomplete (% Viable)
Sixth People's Hospital, 1975[483]	320 (54)	53 (57)
Weiland, before 1976[416]	86 (39)	N/A
Weiland, 1976[416]	50 (90)	N/A
Tamai, 1978[419]	102 (86)	61 (93)
Urbaniak, 1979[426]	107 (82)	80 (94)
Hamilton et al., 1980[484]	83 (65)	77 (84)
Kleinert et al., 1980[420]	243 (49)	347 (70)
Schlenker et al., 1980[482]	51 (71)	13 (77)

at the outset by the relatively low density of sensory receptors in toe glabrous skin. The authors described their method of pulp reduction (Fig. 21). As determined by patient questionnaire, toe transfers to the hand produced minimal lower limb morbidity in a series presented by Chung and Wei.[493] Beyaert et al.[494] noted some disturbance of gait after second toe transfer in children.

To decrease the time of disability, potentially ameliorate soft-tissue coverage problems, and facilitate earlier return to work, many surgeons have advocated earlier toe-to-hand transfers in cases of non-replantable digit loss. Yim et al.[495] compared outcomes of "primary" toe-to-hand transfers with those of delayed transfers. Primary transfers are defined as those performed during the acute period or within a mean 7 days after injury. No significant differences were shown in intraoperative difficulty, early technical outcome, or early functional results. Primary reconstruction seemed to require fewer secondary procedures, such as tenolysis, but the difference was not statistically significant.

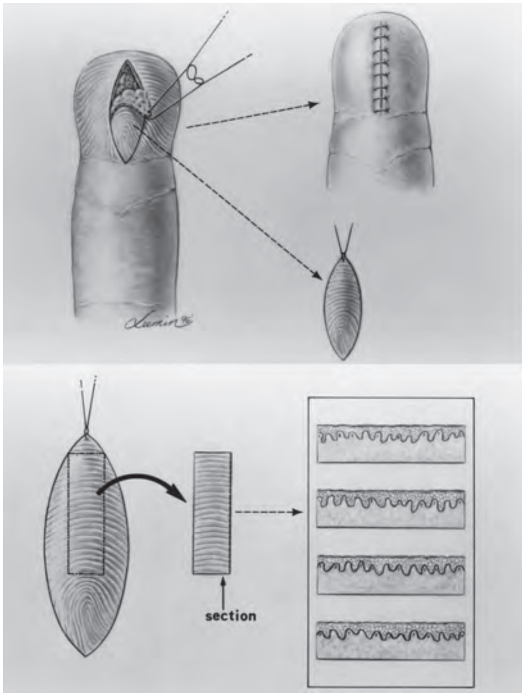


Figure 21. Toe-to-hand transplantation after traumatic digit loss. *A*, Pulp reduction was performed at least 9 months after toe transplantation. Palmar surface of a transplanted digit is shown with the ellipse of skin excised and marked with a suture before fixation. *B*, Preparations of sections. Oblong piece of tissue was obtained from the distal part of the pulp reduction specimen, embedded in paraffin, and sectioned transverse to the epidermal ridges. Every fifth section was mounted and stained with Masson trichrome (30 sections per specimen). (*Reprinted with permission from Wei et al.*[492])

In conclusion, no medical or surgical reason to wait several months for toe-to-hand transfer is apparent, particularly when the thumb needs functional reconstruction. On the other hand, the need for urgency in this setting has yet to be defined. A person who has just lost a thumb is in a particularly vulnerable emotional state, and it would be rash to attach a sense of urgency to what is essentially an elective reconstruction. Some patients might not be psychologically ready for primary toe transfer during the early posttraumatic period, whereas others might benefit from an earlier return of hand function and no additional hospitalizations.

It is sometimes the case that the digit is replantable but an associated soft-tissue defect cannot be satisfactorily addressed by local flaps or grafts. Some avulsion and devascularization injuries might need additional soft-tissue coverage. A 2002 article by De Lorenzi et al.[496] recounted the authors' experience with arterialized venous free flaps in such cases. These flaps, like full-thickness skin grafts, are thin and supple and can be tailored to precisely fit the defect and Brunner lines. An insightful discussion and informative review of arterialized venous flaps was presented by Brooks.[497]

Hand Transplant and Composite Tissue Transfer

Transplantation of composite tissue allografts, such as the hand, offers immense potential in reconstructive surgery. Experimental studies of limb transplantation in rodents have shown the efficacy of combination therapy using multiple immunosuppressants. By 2002, 14 human hand transplants had been performed. A review of the current replantation literature forecasts significant functional return after hand transplantation, provided patient selection is appropriate and allograft rejection can be prevented.[37]

Jones[498] updated the status of limb allograft transplantation in 2002. In general, immunosuppression has been well tolerated in human recipients, although considerable risk of posttransplant diabetes and chronic infections still exists. Transplanted hands show good mechanical motor function but poor sensory return. Patients need to be followed for the long term to fully assess whether the risk was worth the reward, as many organ transplants have half-lives shorter than 10 years.

It needs to be considered whether hand amputees should put their long-term health at risk for a hand allograft that might fail long before the patient's expected death. Psychological trauma might ensue for a patient who regains use of a hand for several years only to lose it again to chronic rejection. The prospect for a second allograft exists. Considering the long-term potential for organ failure, opportunistic infection, allograft rejection, and malignancy resulting from long-term immunosuppression, the risk:benefit ratio of hand transplantation must be carefully weighed.

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