Selected Readings in Plastic Surgery

Volume 10, Number 5, Part 2 2005

MICROSURGERY: FREE TISSUE TRANSFER AND REPLANTATION

John R Griffin MD
and
James F Thornton MD

SOUTHWESTERN
THE UNIVERSITY OF TEXAS
SOUTHWESTERN MEDICAL CENTER
AT DALLAS

BAYLOR UNIVERSITY
MEDICAL CENTER
An Affiliate of the
Baylor Health Care System

MICROSURGERY: FREE TISSUE TRANSFER AND REPLANTATION

John R Griffin MD and James F Thornton MD

HISTORY

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

In 1960 Jacobson and coworkers,[6] working with laboratory animals, reported microsurgical anastomoses with 100% patency in carotid arteries as small as 1.4mm diameter. In 1965 Jacobson[7] was able to suture vessels 1mm diam with 100% patency in laboratory animals. Jacobson emphasized the importance of avoiding intimal trauma and precise intima–intima reapproximation. In 1966 Green and colleagues[8] used 9-0 nylon suture on rat aortas (avg 1.3mm diam) and vena cavas (avg 2.7mm diam) and reported anastomotic patency in 37/40 animals at 21d. Acland[9] in 1972 published a series showing 95% patency in anastomosed rat superficial epigastric arteries. Since Smith's[10] and Cobbett's[11] reviews of microsurgical instruments and techniques, suture technology has progressed to 50mcm needles with 12-0 suture.

In 1962 Malt and McKhann[12] described the first successful clinical replantations in 2 patients who had arm amputations. In 1963 Chinese surgeons successfully reattached a patient's hand amputated at the wrist. The radial and ulnar arteries were anastomosed using short links of 2.5mm diam polyethylene tubes.[13] Kleinert and Kasdan[14] in 1963 described their experience with digital amputations and near amputations. They were unable to replant digits successfully, but did revascularize near-amputated digits. They used loupe magnification and stressed the importance of using vein grafts if the vessel anastomosis was under tension.

In 1964 Nakayama and associates[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 3–4mm diam. Sixteen patients had a functional esophagus on follow-up of at least 1y.

Two separate articles in the mid-1960s described the successful experimental replantation of rabbit ears and rhesus monkey digits.[16,17] Komatsu and Tamai[18] used a surgical microscope to do the first successful replantation of a completely amputated digit in 1968. That same year Krizek and associates[19] reported the first successful series of experimental free-flap transfers in a dog model. Also in 1968 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. Also in 1971 McLean and Buncke[22] transferred the omentum to the scalp via microvascular anastomoses. In 1973 Daniel and Taylor[23] and O'Brien and associates[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, to >90% today (Table 1). Khouri's[25] survey of 9 microsurgeons "clearly indicates that operative experience is the single most critical factor related to improved success rates. . . . A major determinant of success or failure is therefore operator related and, in a broader sense, technical."

TABLE 1
Free Flap Success Rate and Learning Curve

Center/Author	Experience	Success Rate
Serafin (1980)	First 25 cases	72%
	Last 25 cases	96%
Godina (1986)	First 100 cases	74%
	Last 100 cases	96%
Harashina (1988)	First 3 years	75%
	Last 5 years	97%
Buncke (1989)	First 3 years	83%
	Last 3 years	97%
Shaw (1989)	First 100 cases	91%
	Last 100 cases	97%

(Data from Khouri RK: Avoiding free flap failure. Clin Plast Surg 19:773, 1992.)

O'Brien[26] reviews the strides made in microvascular surgery during the 1970s and '80s and looks to the future for new applications of microsurgery. Several new areas of microsurgical interest have evolved over the last 15 years. In 2000 Whitworthm and Pickford[27] 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 still being discovered.

The first human-to-human hand transplants were performed 17 years ago.[28] Today plastic and orthopedic surgeons express concern about this procedure and raise the issues of poor sensory return, acute or chronic rejection, systemic complications of immunosuppressive therapy, and loss of the transplant.[29]

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 appears to be as effective as the operating microscope in certain cases. Free flap selection in specific defects is becoming more standardized, and technologic 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 should understand the mechanisms of vessel injury, repair, and regeneration; should be familiar with the processes of vasospasm and thrombosis and their pharmacologic 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 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 and associates[30] effectively showed the 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" was seen with partial-thickness bites of the vessel wall than with properly placed full-thickness sutures. In a separate study using SEM, Harashina and colleagues[31] noted no difference in patency (94%) of 1mm 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.[31] Approximately 1–2 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 will not progress to fibrin deposition and thrombosis if it is not exposed to the media and the lumen is not injured. Over the next 24–72 hours the platelets gradually disappear. Platelets show little affinity for exposed surfaces of sutures within the vessel lumen.[30,31] 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 is in the first 3–5 days.[32,33]

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 7–10 days. With damage of the underlying subendothelial structures, media and adventitia, there is regeneration of damaged epithelium by migration and differentiation of myoendothelial cells from the cut vessel ends.[34] The remaining layers of the vessel wall regenerate via proliferation of fibroblasts with collagen deposition and myointimal thickening at the anastomotic site.[35] The elastic and muscular elements of the vessel wall fail to regenerate to the same degree as the endothelium, and these 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 the vessel walls. Simple dissection and exposure of vessels from their beds was shown by Margic[36] 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 may result in endothelial damage and platelet aggregation if the current passes too close to the branch origin. Caffee and Ward[37] described the safe and effective use of bipolar electrocautery in small vessels: the side branch must be treated with electrocautery at the lowest setting possible to achieve coagulation and 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. *All exposed vessels should be kept in a moist environment to prevent desiccation.* Prolonged vasospasm can also cause endothelial sloughing, and vessels experimentally subjected to vasospasm for >2h lose most of their endothelial layer.[30]

Topical lidocaine is often used in microvascular surgery to prevent vasospasm. The safe maximum dose of lidocaine for topical application has not been established. Johnstone and coworkers[38] report using 4% lidocaine in doses of up to 2000mg 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 these patients was 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 ≤750mg in the average adult patient. Ohta and others[39] showed experimentally that xylocaine 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.[40] Weinstein and colleagues[30] note that curved or angled clips cause more damage than flat clips. Closing pressures of vascular clips should remain <30gm/mm^2 to minimize damage to vessels.[41] O'Brien and coworkers[5] discuss the currently available clamps and clamp approximators and give examples of each.

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 intersuture distances may result in endothelial gaps, distortion, constriction, and exposed intimal flaps. Loosely tied sutures may expose subendothelial elements to the bloodstream and allow excessive anastomotic bleeding and subsequent platelet plug formation. Too many sutures or sutures tied too tightly can trigger endothelial slough.[30] 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.[30,31]

Chow and colleagues[42] 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[43] used SEM to evaluate microanastomoses in rats at intervals ranging from 1 hour to 21 days after anastomosis. Their findings paralleled those of Weinstein and colleagues[30]—that is, there was intimal loss below the site of clamp pressure and medial necrosis at the anastomosis proper. Despite these changes the patency rate was 100%, indicating that some tissue damage is tolerated without untoward consequences.

Lidman and Daniel[44] 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.

The Clotting Mechanism

Johnson[45] details 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.[46] 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 ADP, calcium ions, and serotonin.[47] The secreted ADP, 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.[48]

Multiple steps in the clotting mechanism have been manipulated pharmacologically with the aim of reducing platelet aggregation and release.[49] Johnson and Barker[50] discuss 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[51,52] and to hamper the conversion of fibrinogen to fibrin.[53] Greenberg, Masem, and May[54] showed in a rabbit model that low-dose heparin infusion significantly prevented anastomotic occlusion for 72h after surgery in the arterial inversion model.

Khouri and coworkers[55] studied the effect of heparin on rat femoral artery anastomoses and noted that a single bolus dose of heparin given before blood flow was reestablished inhibited thrombus formation by preventing the conversion of fibrinogen to fibrin. Treatment with dazmagrel, a selective thromboxane synthetase and platelet aggregation inhibitor, was only partly successful in improving patency rate at the anastomoses. In other words, fibrin could still form an occlusive thrombus even in the absence of aggregating platelets. The authors conclude that, at least in their model, fibrin mesh deposition contributed more to the pathogenesis of thrombotic occlusion of traumatized arteries than platelet aggregation. The incidence of hematomas in the animals treated with heparin was 12.5% (3/24).

In the clinic heparin is given by direct continuous infusion to save free flaps.[56] Some surgeons feel that heparin does not improve patency in uncomplicated repairs and that the risk of bleeding outweighs its potential benefit as an anticoagulant.[45,50] Perhaps paradoxically, the slow oozing that will accompany 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 in doses of 0.1mM (equivalent to one 325mg tablet), *aspirin* inhibits initial platelet aggregation at the anastomotic site. This action was believed 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.[57] Newly created anastomoses show a loss of endothelium for several millimeters from the suture line,[58] and the mechanism for prostacyclin production was thought to be absent. Contrary to previous expectations, Restifo and colleagues[59] found a clear increase in prostacyclin production at the anastomosis; they speculated that perhaps 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. The authors conclude that "the thrombogenic tendency of the anastomosis was not explained by a decrease in this antithrombotic agent." Prostacyclin itself as a topical agent in microvascular surgery is not effective.[60]

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.[49,50,61,62] Multiple experimental studies have shown that dextran improves microvascular patency.[63–68] A study in the rabbit model by Rothkopf and coworkers[62] showed patency of microanastomoses and arterial inversion grafts at 7d to be 85% in the dextran group and 48% in controls. Clinically a 10% solution of dextran-40 is usually given as a loading dose of 40–50mL, followed by continuous intravenous infusion of 25–50mL/h. Because of reports of allergic reactions to dextran,[50] a test dose should be administered first. Dextran can also cause bleeding and subsequent vessel occlusion problems, similar to heparin. There are also reports of acute renal failure secondary to dextran use.[69]

Proteolytic enzymes such as *streptokinase* and *urokinase* are being evaluated as lytic agents in thrombosed vessels and may find a place in the prevention of microvascular thrombosis, especially in traumatized vessels.[70,71] 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.[72–75] Goldberg and associates[70] report salvage of 6/7 thrombosed free flap vessels by infusion of streptokinase or urokinase. A subflap hematoma developed postoperatively in only 1 case.

Tissue plasminogen activator (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, but in the presence of high amounts of fibrin there is a shift in the activator-inhibitor complex and tPA, plasminogen, and plasmin are released, with consequent fibrinolysis.[71,76] Levy[77] 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[78] reported salvage of a free flap with a 15-minute infusion of high-dose tPA and concomitant heparin. Arnljots and colleagues[71] significantly improved patency of traumatized microvessels with low-dose tPA infusion for 2 hours. Romano[79] showed statistically significant improvement in patency rates of microanastomoses in animals treated with low-dose tPA infusion over 48 hours. Stassen and coworkers[80] report 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 anticoagulants along with fibrinolytic therapy in microsurgery.[50,75,81] The next horizon in manipulating the clotting mechanism to prevent microvascular thrombosis is through monoclonal antibody regulation of platelet aggregation. Gold and coworkers[82] 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 and associates[83] suggest another strategy for salvage of thrombosed microvascular anastomoses. The authors argue for anastomotic resection and replacement of thrombosed veins with vein grafts, together with systemic heparin administration. In the rat femoral vein model there was a high rate of recanalization when this protocol was followed.

Davies[84] surveyed the practice of anticoagulation in clinical microvascular surgery. On the basis of responses he received from 73 centers in 22 countries, Davies[84] was able to document equal success rates (89%) for *free flaps* performed with anticoagulation (691) and without anticoagulation (134). For *limb replantation* the overall success rate was lower with anticoagulation (76%) than without anticoagulation (89%). Veravuthipakorn and Veravuthipakorn[85] report very good results using no antithrombotics in free flaps nor in replants.

In light of the information currently available regarding the benefits of anticoagulation in microsurgery, the following conclusions seem warranted:

1. There are no definite indications for anticoagulation or antifibrinolytic therapy when mechani-

cal and vascular factors are optimal, eg, during elective free flap transfers.

2. When there is evidence of thrombosis in the 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 may be indicated in clinical situations where mechanical or metabolic factors are not favorable and cannot be improved.

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.[86] Mammalian skeletal muscle is much less tolerant to ischemia than skin.[87,88] Irreversible damage to the microcirculation of skeletal muscle in man begins at around 6 hours.[87] As documented by NMR spectroscopic studies,[89] 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.[90] In peripheral nerves the neuromuscular junctions are most sensitive to ischemia.[91]

Cooling prolongs tolerance to ischemia in all types of tissues.[90–98] Muscle and fat cells show a marked increase in histologic changes with duration of cold ischemia, while skin and small vessels remain relatively free of abnormality after circulation is restored to the tissue.[97] Donski and associates[97] studied the effect of cooling on the survival of free groin flaps in the rabbit: 86% of flaps that were cooled for 1–3d survived. Anderl[99] stored a human groin flap for 24h and reported complete flap survival; in the rat, maximum ischemia time was 6h at normal body temperatures and 48h if cooled.[96] Reus[98] suggests rewarming of arterial flaps before circulation is reestablished to ensure adequate blood flow during the ensuing hyperemic period.

Takayanagi and Tsukie[100] report survival of at least the skin portion of a latissimus dorsi musculocutaneous free flap after 15–17h of cold ischemia. May and colleagues[95] note 100% survival of rabbit free flaps at 4h of normothermic ischemia, decreasing to 80% at 8h. Berggren and coworkers[90] showed complete survival of bone grafts preserved in Collins-Terasaki solution at 5°C after 25h of ischemia provided that the medullary nutrient blood supply was later reconstituted. Chinese investigators successfully replanted limbs in animals after 108h of cold ischemia.[94] Baek and Kim[101] report successful replantation of 2 fingers after 42h of warm ischemia. Walkinshaw[102] showed that proximal bowel segments are more resistant to warm ischemia than distal small bowel segments and suggested using proximal bowel for free transfer.

From a review of the literature, we have compiled the following estimates of tissue tolerance to ischemia (Table 2):

TABLE 2
Ischemic Tolerance of Various Tissues

Tissue	Warm	Cold
skin and subcutaneous tissue	4–6h	up to 12h
muscle	<2h	8h
bone	<3h	24h

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 and associates[103] noted that some ischemic organs failed to reperfuse after their blood supply had been reestablished, and 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 following 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 and associates[95] investigated no-reflow in denervated free epigastric flaps in the rabbit, which closely approximates the clinical situation. The authors demonstrated mild obstruction to blood flow as early as 1h postischemia, increasing in severity and degree at 8h and 12h. Histologic changes were reversible at 4h and 8h but became incontrovertible at 12h, culminating in death of the flaps.

Zdeblick and others[104] studied the no-reflow effect in replanted rat hind limbs. Predictors of no-reflow were *(a)* an increased number of red blood cell aggregates 5min after replantation and *(b)* changes in tissue pH persisting for >1h post-replantation. Clearance of H^+ and lactate is associated with improved flow. Their findings support the concept of ongoing arterial obstruction, AV shunting, and altered thrombogenic fibrinolytic system as the mechanism of the no-reflow phenomenon.

Jacobs and colleagues[105] noted an inversely proportional relationship between warm ischemia time and fibrinolytic activity. The greatest drop in fibrinolysis occurred at 0–6h of warm ischemia. Suval and others[106,107] showed that changes in microvascular permeability occur during reperfusion after 30min or 2h of ischemia. The first manifestations of tissue damage in reperfusion injury are due to leukocytic and endothelial cell interactions. No-reflow occurred in 30% of the muscle tissue regardless of ischemia time.

Russell and colleagues[108] and Manson and coworkers[109] discuss 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—that is, the muscle flap or replanted limb grows in size upon reperfusion. This effect makes fasciotomies prudent in most cases and mandatory in all but those with the shortest ischemia times. The swelling may 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 is essentially immediate and very little inflammatory response ensues. Areas of muscle that have slight ischemic damage will therefore generate few inflammatory mediators upon reperfusion. For instance, muscle flaps that are appropriately cooled or flaps that were reperfused in under 1h will generate much less inflammation than muscle which was not cooled or that was exposed to longer ischemia times. Intermediate zones in replanted muscle or transferred muscle flaps after 2+h of warm ischemia produce high levels of inflammatory mediators and eventually show the worst cell damage. Thus in a replanted limb certain areas will suffer more than others, and surgeons may choose to be more liberal with anticoagulants when ischemia is prolonged. In the short term anticoagulants serve to decrease inflammation associated with the clotting cascade and potentially help salvage these watershed areas of significant but reversible ischemia.[110]

Several authors have shown the effect of thrombolytic agents in reversing ischemic changes in human and rat myocardium.[66,72] Others report salvage of flaps in the clinical situation upon administration of thrombolytic drugs when the no-reflow phenomenon was probably in effect.[70,73,111] Nonsteroidal antiinflammatory agents inhibit cyclooxygenase and block the effects of thromboxane A_2, such as vasoconstriction and microvascular thrombus formation. Douglas and associates[112] showed that ibuprofen-treated flaps survive longer periods of ischemia. These flaps had accelerated fluorescein uptake that suggested reversal of thrombosis and vasoconstriction. Feng and colleagues[113] postulated that the ratio of vasoconstricting to vasodilating prostaglandins may be responsible for the microcirculatory changes that result in the no-reflow phenomenon. Schmid-Schonbein,[114] on the other hand, states that capillary plugging by granulocytes appears to be the mechanism underlying no-reflow.

The actual *number* of platelets in the circulation may not affect microvascular patency in routine microsurgery cases. Kuo and colleagues[115] 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.[116] 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, occasionally free flaps experience a slow, progressive, and partial death that is potentially reversible. Weinzweig and Gonzalez[116] report their experience with 10 patients in whom free flap failure was not an all-or-none phenomenon. The authors discuss their experience with these failing flaps and state that with dressing changes, judicious debridement, and skin grafts or other local flaps the dying flaps can often 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, Bruner, and Pelzer[117] offer concise and useful principles for organization of and preparation for microsurgery.

Magnification

Daniel and Terzis[118] recount the evolution of operative magnification. Hoerenz,[119–121] Nunley,[122] and O'Brien and others[5] comprehensively review the operating microscope. Shenaq, Klebuc, and Vargo[123] recount an 8-year experience with loupe magnification for free tissue transfer. Of 251 free tissue transfers performed during this time using a 5.5X 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 surgeries done under the 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 advocate use of loupe magnification for microvascular anastomosis of vessels ≤1.0mm diam. Unlike the operating microscope, loupes are cost effective, portable, and free the operator's position.

Serletti and colleagues[124] compared loupe vs microscope visualization in a series of 200 free flaps. This was a retrospective review with an inherent bias, since at the time of flap transfer the choice of magnification was influenced by the size of 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 in children and in vessels ≤1.5mm diam. Despite the presence of bias, the findings support the use of loupe magnification for selected microsurgical cases in the hands of experienced microsurgeons.

Ross and coworkers[125] looked at the results of a large series of free flaps transferred to the head and neck with the aid of loupe vs the microscope. Similar complications were recorded in the two groups and shorter operating times in the loupe group.

Microsurgical instruments should be few in number and high in quality. Acland[126] and O'Brien[5] list the essential instruments for any microsurgical setup and their proper use.

Number of Sutures

The number of sutures used in the anastomosis is critical: too few and there may be excessive bleeding and thrombus formation; 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 and associates[127] studied the relationship between the number of sutures and the strength of a microvascular anastomosis in rat femoral vessels. They determined that an 8-suture anastomosis most closely paralleled the control state in this animal model. Zhang and colleagues[128,129] report excellent patency in rat femoral vessels using a 4-stitch sleeve anastomosis. They also describe a 3-suture sleeve technique.

Type of Sutures

Both absorbable and nonabsorbable sutures have been used for microanastomosis. Mii and coworkers[130] demonstrated faster and smoother endothelial regeneration with polyglycolic acid absorbable material than with nonabsorbable suture. Thiede et al[131] showed no increased aneurysm or pseudoaneurysm formation and no vascular ruptures due to decreased mechanical endurance with polyglycolic acid or polyglactin sutures. Chen, Seaber, and Urbaniak[132] used interrupted, nonabsorbable suture technique for anastomosis in young rat femoral arteries. The vessels were later examined when the rats were adults and had gained weight. There was evidence of growth at the anastomotic sites without stenosis or hyperplasia. The authors concluded that the use of interrupted, nonabsorbable suture technique in small vessels that are expected to grow over time is safe in rats and may be safe in children requiring microvascular surgery. Currently most practitioners use nonabsorbable (prolene or nylon) sutures in their clinical cases.

Anastomotic Technique: Interrupted, Continuous, Sleeve, and Adhesives

Techniques of microvascular anastomosis with interrupted sutures are modified from Carrel's[3] triangulation method. Daniel and Terzis[118] illustrate the basic microsurgical anastomotic techniques in their text. Mechanical factors in a given clinical setting sometimes dictate a 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.

A variety of methods have been described for microvascular anastomosis. Simple *interrupted* full-thickness sutures are preferred and the standard to which all new anastomotic techniques are compared.

Anastomoses performed with *continuous sutures* are no different from interrupted sutures in patency rates and blood velocity profiles,[133,134] only much faster.[135,136] Patency rates in the rabbit are 92% arterial and 84% venous. In the rat carotid artery Firsching et al[137] showed 100% patency at 2–4mo with continuous sutures. The main argument against the use of continuous suture is that it may narrow the caliber of the vessel lumen.[136] Suture entrapment in vessel clamps and suture breakage have also been reported.[138] Cordeiro[139] reported his experience with continuous suture anastomosis in 200 consecutive free flaps. His success rate was similar to that of other large series with interrupted sutures. In contrast, Chase and Schwartz[140] report better results with simple interrupted sutures than with continuous sutures.

Chen and Chiu[141] described a spiral interrupted suture technique that combines elements of the continuous and interrupted suture techniques. The authors note 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[142] described a refined continuous suture technique and report a 14d patency rate of 85% in the rat femoral artery, compared with 80% patency for interrupted sutures. In their opinion the overriding advantage of the continuous technique is that it cuts in half the anastomotic time.

The *sleeve* technique originally described by Lauritzen[143,144] is said to be faster and simpler to perform, and suture placement causes less trauma to the vessels. Lauritzen[144] describes his precise technique and notes that endothelialization of the anastomosis takes 1 week, or half the time needed by conventional suture anastomoses. Clinically the telescoped technique is hampered by difficulty in anastomosing veins and other vessels of various diameters. Duminy,[145] however, altered the technique and showed a high patency rate as well as easier anastomosis of different-sized vessels.

Krag and Holck[146] 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[147] demonstrated 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 and colleagues[5] confirmed Sully's findings and do not recommend sleeve anastomosis because of its overall lower patency rate.

Turan and colleagues[148] 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 to their 4-suture everted, fish-mouthed anastomoses. The patency and anastomotic complication rates were similar in the groups. The time needed for anastomosis was shorter with the everted technique.

Early experimental studies of vascular repairs using synthetic adhesives yielded less than satisfactory results.[149,150] Occasionally the adhesive penetrated into the vessel lumen and caused instant thrombosis. In 1977 Matras[151] 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,[152] a coupling technique,[153] and the sleeve method,[154] with variable results. Despite similar patency rates to conventional anastomoses,[155,156] fibrinogen adhesive is not as versatile as suturing and may 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

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 as to the type of repair. A difference of 2:1 or less may be handled by gently dilating the smaller vessel and not dilating the larger one.[157] 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.[158]

One must be extremely wary of a significant mismatch when performing end-to-end venous anastomosis.[159] 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 done.

Godina[160] 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 choice for lower extremity free flaps. In contrast, Samaha[161] 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 demonstrate a difference in patency rates between end-to-end and end-to-side techniques when repairing vessels of similar diameter.[162] When size-discrepant vessels are involved, end-to side venous repairs have proved to be significantly better.[163] The dynamics of flow in end-to-side arterial repairs are favorable.[164,165]

In 1978 Lauritzen[166] described the sleeve anastomosis or end-in-end anastomosis, an invaginating technique with far fewer sutures than the end-to-end method. Experimental studies show patency rates similar to those achieved with conventional end-to-end sutures plus significant time savings and minimal intimal trauma.[143–147,166,167] Nakayama et al[168] reported 15 free flap transfers using sleeve vascular anastomoses with only 1 failure. They suggest that this technique is best indicated if a favourable size discrepancy between donor and recipient vessels exists (small caliber upstream end to large caliber downstream end).

The sleeve technique has not been widely adopted by surgeons due to reports of stenosis, thrombus,[169,170] and aneurysm formation.[171] In the clinical setting many factors influence the choice of microvascular anastomotic technique. 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, the end-to-side technique is preferred.

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[172] in 1973 suggested reducing the number of sutures during microanastomosis by means of a saran wrap cuff, and Tschoff[173] in 1975 used a lyophilized dural cuff for the same purpose. Harris[174] reported a basic autogenous cuff technique consisting of six sutures. Modifications involving fewer sutures,[175,176] fat wraps,[177] polythene cuffs,[178] silicone rubber cuffs,[179] external absorbable splints,[180] intravascular stents,[181] and metallic circles[182] have been described.

Cuff techniques produce patency rates similar to those achieved with manual sutures while reducing operative time and suture-induced trauma in experimental models.[174–177] However, most of these techniques are difficult to implement, open up new problems, and very few have been applied clinically.[183]

Connectors have been proposed to facilitate microvascular anastomoses and improve reliability. The first ring device was introduced in 1962 by Nakayama.[184] In 1979 Ostrup and Berggren[185] introduced a modification of this device (Unilink) that subsequently evolved into the 3M microvascular anastomotic *coupler*. Clinical series of vessels anastomosed with the mechanical device have shown equal or greater patency rates and faster anastomosis of either normal or irradiated vesselss.[186–188] Histologic studies show the same healing process whether the anastomosis was done with conventional sutures or mechanically.[189] At 16 weeks postrepair, coupled anastomoses are 50% stronger than sutured vessels.[190] Biodegradable ring devices do not seem to have any advantage over nonabsorbable devices[191] and may cause thrombosis due to the inflammatory response to the ring during absorption.[187]

Most authors find mechanical coupling devices especially useful for end-to-end anastomosis in veins and soft arteries.[187,188] The applicability of these devices in thick-walled arteries, in vessels with diameters <1.0mm, or for end-to-side anastomosis is less convincing and at this point appears limited.[188,192]

Zeebregts and coworkers[193] compared standard suture technique to VCS nonpenetrating clips and Unilink rings. The authors noted excellent patency with all three methods. The devices can reduce anastomotic time in experienced hands.

Cope and colleagues[194] report the successful use of a microvascular *stapling device* that can be used for end-to-side anastomoses as well as end-to-end. In general, disadvantages of stapling techniques include: 1) the necessity to mobilize the vessel in order 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 there is discrepancy in vessel size; 5) limited availability of the apparatus.

Shennib and associates[195] studied the use of an *automatic vascular suturing device* in a pig model. The average anastomotic time was 22 minutes with 7-0 suture; patency rates were good. Devices like these may 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.

Laser Anastomosis

Laser-assisted microvascular anastomoses have been evaluated in various experimental models and in a few clinical series. The patency rates obtained compare favorably with those obtained 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 have been used, including those emitted by the carbon dioxide,[196,197] argon,[198] neodymium:YAG,[199] KPT,[200] and diode[201] lasers. The adjunctive use of photosensitizing dyes makes low-energy discharges possible and minimizes collateral tissue damage.[202]

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.[203] The tissue-welding phenomenon may be due simply to heat generated by the laser energy or may be wavelength-dependent.

To date, laser assisted microvascular anastomosis is considered investigational. Difficulties with aneurysm formation[204] and low breaking and tensile strength in the early postoperative period[205] as well as 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 appear 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, and some of these will be 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 also be continuous and applicable to many different kinds of flaps.

The Doppler ultrasound flowmeter is the most common means for gauging circulation after free-tissue transfer.[206] 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 and associates[207] find the laser Doppler unable to predict future clinical events and 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[208] describes the experimental evolution and clinical application of an implantable thermocouple to monitor patency of the microvascular pedicle.

Acland's[209] surface temperature measurements have proven most useful for monitoring replanted digits, but Kaufman and colleagues[210] found that, in muscle free flaps, temperature monitoring is labile, easily changed by environmental manipulation, and as such is unreliable in assessing the vascular status.

Khouri and Shaw[211] present 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 a microvascular thrombosis. There were 17 false-positive readings. Khouri and Shaw detected 52 thrombosed flaps using surface temperature monitoring and were able to salvage 45 of these free flaps by reexploration.[211]

In his discussion of this paper, Jones[212] notes that he has discontinued the use of surface temperature monitoring in replantation and toe-to-thumb transfers and currently uses the pulse oxymeter instead. Jones also feels 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 these can be clinically monitored more easily by means of capillary refill and Doppler probes.

Jones and Gupta[213] expand upon this topic and report 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[214] describe direct monitoring of microvascular anastomoses with an implantable ultrasonic Doppler probe. These authors as well as Swartz and colleagues[215] note that the Doppler probe can recognize and distinguish between arterial and venous occlusion, and in so doing is more reliable than a thermocouple probe. Venous occlusion may be difficult to detect by Doppler probe, especially in large muscle flaps.[215] Fernando, Young, and Logan[216] implant a laser Doppler probe directly into muscle or subcutaneous tissue distal to the vascular pedicle. The Doppler recordings correlate with blood flow in the flap, and arterial compromise is readily detected. Rothkopf and colleagues[217] assess patency rates of microvascular anastomoses in the upper extremity by color Doppler ultrasonographic imaging.

Whitney and colleagues[218] report significantly higher salvage rates (85.7%) 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 (55.5%). The overall accuracy of quantitative fluorometry in their 23-transplant, 8-year experience was 91.3%.

Jones, Glassford, and Hillman[219] described remote monitoring of free flaps with telephonic transmission of photoplethysmographic waveforms, which theoretically would facilitate surveillance of the flap by the operating surgeon.

Currently there is no consensus on which method is most effective for monitoring free tissue transfers.[220] Replants and toe-to-thumb transfers can be effectively monitored by pulse oxymetry, while free flaps are often monitored with Doppler hand-held pencil probes for several days after surgery, along with clinical observation.[220] The implantable venous Doppler is used by many modern microsurgeons. Some clinicians evaluate perfusion by clinical examination alone.

THE INFLUENCE OF PATIENT FACTORS

Tobacco Use

Cigarette smoking has been shown to affect cutaneous blood flow,[221] wound healing,[221,222] and survival of pedicled flaps.[223,224] The overall effect of byproducts of cigarette smoke is to produce a thrombogenic state through their action on the dermal microvasculature, blood constituents, and vasoconstricting prostaglandins.

Nolan,[224] Gu,[225] and van Adrichem[226] 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.[227–229] Arnez[230] reported no difference in flap loss or vascular thrombosis rates in smokers compared with nonsmokers in 50 free TRAM flap breast reconstructions. Reus[231] reported no difference in anastomotic patency or overall survival of 162 free flaps whether the patients smoked or not. Buncke[229] reviewed 963 free tissue transfers and showed no statistically significant difference in vessel patency, flap survival, or reoperation rate between cigarette smokers and nonsmokers. Smokers did show a higher incidence of healing complications at the flap interface and at the donor-site wound.[229,231]

Cigarette smoking seems to adversely affect the outcome of digital replantation surgery. Van Adrichem[232] demonstrated that tobacco smoking decreases microcirculatory blood flow in replanted digits compared with healthy digits. Buncke[229] observed that 80–90% of smokers ultimately lose their replanted digits if they smoke in the 2mo before or after surgery. He does not believe that smoking is an absolute contraindication to digital replantation, but states 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 other areas in the body and is more sensitive to the vasoconstrictive effects of nicotine.

Patient Age

Parry and colleagues[233] report 96% success with free tissue transfer in children. Canales and associates[234] echo these findings in 106 pediatric patients operated on between 1973 and 1989. Their success rate (93% in the last 5 years reported) and complications in children were similar to those obtained in their adult cases. No growth-related complications were noted at either the recipient or donor sites.

Yucel and coworkers[235] reported no significant vessel spasm and a 95% overall success rate in 20 pediatric free flaps. Clarke et al[236] reported a 99% flap survival rate in pediatric microvascular cases despite frequent but manageable complications. Vessel spasm was not a significant problem. Duteille, Lim, and Dautel[237] reported excellent results in 22 pediatric free flaps. They believe children have a greater risk of vasospasm that is compounded by the small vessel size, and recommend 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 can also undergo successful free tissue transfers.[238] Chick and coworkers[238] noted a successful outcome in 30/31 free flaps transferred in patients >65y. The wound healing complications were the same in the over-65 and under-65 groups. The authors conclude 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[239] reported successful free tissue transfer in 93/94 flaps performed in patients aged 50–79y, for a free-flap viability rate of 99%. Complications were primarily nonsurgical and averaged 30%. Mortality was 5.4%.

Serletti and colleagues[240] reported a free flap series in elderly patients (avg age 72y). 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 itself 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, but age alone should not deter the experienced microsurgeon.

Systemic Disease

Banis and others[241] have shown that microsurgery can be a valuable tool in the salvage of ischemic lower extremities from atherosclerosis of diabetic microangiopathy. Karp and coworkers[242] reported their experience with 21 free flaps in 19 diabetic patients and documented only 1 flap loss, with all patients able to ambulate on their flaps. Nevertheless, 5/19 original patients needed eventual amputation at 6–37mo.

Moran and colleagues[243] reviewed a large number of flaps comprising their 10 year experience with free flaps in the context of lower extremity peripheral vascular disease. Perioperative mortality was 5%; 5-year flap survival was 77%; limb salvage, 63%; and patient 5-year survival, 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 PVD as a comorbidity must be weighed when considering free flaps in this patient population.

Moran's group[244] also identified patients with renal insufficiency who underwent free tissue transfer. More than PVD, renal disease appears to be a stronger predictor of reconstructive failure and major medical complications, including death; 52% of these patients suffered major morbidity or mortality in postop 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 *Selected Readings in Plastic Surgery* Volume 10, Number 5, Part 1.

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 diameter to match as closely as possible the caliber of the recipient vessel(s). Autogenous vein grafts are reversed for spanning intraarterial gaps and placed directionally for bridging intravenous gaps.

The histologic changes that take place in vein grafts after placement in the arterial system have been well described in the literature.[245,246] Mitchell and coworkers[247] studied the long-term fate of microvenous autografts. The patency of intraarterial vein grafts was 98%; of intravenous vein grafts, 100%. Intraarterial vein grafts were modified by the ingrowth of smooth muscle cells from the recipient artery, and this influx of smooth muscle cells created a neointima that thickened the walls of the vein graft considerably. In contrast, intravenous vein grafts maintained normal vein morphology. There was an unexplained loss in length of the grafts of approximately 30%, which led to the recommendation that vein grafts should be 35% longer than the measured gap.

Despite the success with autogenous vein grafts, experimental investigation of synthetic materials to replace small vessels continues.[248–253] The most common materials tested for this purpose are fibrous *polyurethane* (PU) and microporous or expanded *polytetrafluoroethylene* (PTFE).

Hess[253] and O'Brien and associates[252] review 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 about long-term patency rates. Shen and colleagues[254] note significant thrombosis and occlusion when 2mm expanded PTFE grafts are used in low-flow free flaps in the rabbit.

Van der Lei and Wildevuur[255] reported poor neoendothelialization in PTFE grafts although patency was high in the high-flow, short-segment grafts. Samuels and coworkers,[256] on the other hand, noted that short-segment PTFE microvascular grafts were covered with a layer of endothelium, and reported a long-term patency rate of 80% and no evidence of excessive neointimal hyperplasia.

Yeh and others[257] describe the use of *human umbilical artery grafts* as a microvascular substitute. Although early patency of the grafts was good, with time there was significant degeneration of the vessel walls. Subsequently Roberts and colleagues[258] reported that the technique of glutaraldehyde tanning of human chorionic veins appeared 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.[259–261] Other series, both experimental[262,263] and clinical,[264–269] show high flap success rates and low morbidity in irradiated beds.

Mulholland[265] compared free flap survival rates in 226 irradiated and 108 nonirradiated head and neck reconstructions and reported similar failure rates for both groups. Reece[266] reviewed 66 elderly cancer patients who underwent tumor resection and free tissue transfer after previous radiotherapy. He found no significant differences for flap failure or wound healing problems when compared to a similar group who had not received radiotherapy. Similarly Bengston[267] and Schusterman[268] showed in large clinical series that prior radiotherapy do not predispose to a higher rate of acute free flap loss or wound complications. Kroll[269] 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[270] suggests that more caution should be exercised in performing free flap transfer in patients with an irradiated recipient bed.

Guelincks[271] proposes 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 (eg, 10-0 nylon sutures swaged on 70mcm 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 over two 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 quite readily adopt in the treatment of their patients. As of this writing, free flaps 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 a high risk of failure—such as in irradiated fields,[265] elderly patients,[238,239] or those with occlusive peripheral vascular disease from generalized arteriosclerosis or diabetes mellitus.[241] Shestak and Jones[239] reported successful free tissue transfer in 93/94 flaps in patients aged 50–79 years, for a free flap viability rate of 99%. Complications were primarily nonsurgical and averaged 30%. Mortality was 5.4%. Chick and colleagues[238] noted successful free flap transfers in 30/31 patients >65y. The wound healing complications were the same as in a younger cohort. The authors conclude 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[270] 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 due to technical factors. Khouri[270] discusses the reasons why free flaps fail and suggests ways to avoid them. In his extensive review most free flaps were performed for posttraumatic indications and to treat extremity defects, and this is where 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[270] stresses that one should always seek the vascular pedicle of largest diameter among the options of donor tissue for a given situation, since failures are high when small-diameter pedicles are used, especially if <1mm. It should also be remembered that published descriptions of a flap do not always mirror the clinical situation, and alternative sources of donor tissue should always be kept in mind. In an excellent review, Pederson[272] details the principles behind free tissue transfer in the upper extremity.

Skin, Fascia and Perforator Flaps

The **free groin flap** was the first flap to be successfully transferred by direct microvascular anastomoses, yet it is rarely used in free tissue transfers today 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**,[273–276] particularly in head and neck reconstruction. Other reliable options are the **scapular**,[277–279] p**arascapular**,[280] **lateral arm**,[281] and **dorsalis pedis** free flaps.[282,283]

Free fascial transfers are useful in reconstructions where thin, well-vascularized cover is needed or to provide for unrestricted gliding of tendons in the hand. The free **temporoparietalis (TP) fascial** flap has a consistent vascular anatomy and a pedicle of fairly large caliber.[284–286] The TP fascial flap is a versatile flap with many applications. The free fascial forearm[287] and scapular flaps[280,288] offer similar versatility whenever thin, well-vascularized cover is desired.

The **anterolateral thigh flap** is becoming increasingly popular among experienced microsurgeons for many applications.[289,290] It offers hardy yet thin skin and fascia. It can be deepithelialized or harvested directly as a fascia-fat flap. The donor site can usually be closed primarily. Donor site complications are not absent, however. Many patients, perhaps a majority, will notice some sensation loss at the lateral thigh postoperatively. Some patients may notice thigh weakness due to the dissection through the vastus and/or rectus femoris. Larger flaps that require skin grafts to close the donor site may be associated with stiffness on hip motion or knee flexion from scar adherence of the graft to muscle fascia.[291]

The blood supply of the anterolateral thigh flap can either be from septocutaneous and intermuscular perforators or via direct intramuscular perforators. Strictly speaking, 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 proper to term the flap a fasciocutaneous free flap. This is a semantic distinction that adds little to our understanding of flap elevation: The surgeon follows the perforators down to their source regardless of the path they take. Celik and colleagues[292] describe technical pearls for anterolateral thigh flap harvest, including preservation of a fascial cuff around the pedicle during dissection.

On rare occasions the surgeon will explore the flap and find no dominant or workable artery and vein to the flap. Some time is wasted and the surgeon is frustrated. Wei and Celik[293] provide an excellent review of the principles and application of perforator flaps.

The future of flap harvest may involve variations of the new **"free style"** free flap concept**.** Mardini, Tsai and Wei[294] use 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 using 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.[295–297]

The **DIEP, SGAP,**[298] and **SIEA** flaps are all being used for breast reconstruction. The results and donor morbidities of these flaps are being compared to those of free TRAM and pedicled TRAM flaps. Large series of successful breast reconstructions with DIEP flaps have been published in recent years.[299,300] The DIEP flap may be as cost-effective as the free TRAM flap in this scenario.[301]

Chevray[302] compared SIEA and DIEP flaps to each other and to TRAM flaps. Operative times were similar. The author notes the advantage of no violation of the abdominal wall when the SIEA is used. Unfortunately the SIEA pedicle is often absent or not substantial enough for flap transfer. When the vessel is present and usable, it is frequently small and has a short pedicle. In the end, hospital stays were shorter in the SIEA group in Chevray's report. The SIEA flap is considered safe only for hemiflaps, whereas the DIEP and free TRAM flaps have reliable flow across the abdominal midline.

We acknowledge the drawbacks of SIEA transfer—the hemiflap limitation, the small vessel size with short pedicle, and the time spent intraoperatively looking for SIEAs when they may not be present—and question the effectiveness of SIEA exploration in general. Perhaps primary DIEP exploration may ultimately be safer for the patient and yield better results. Since 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

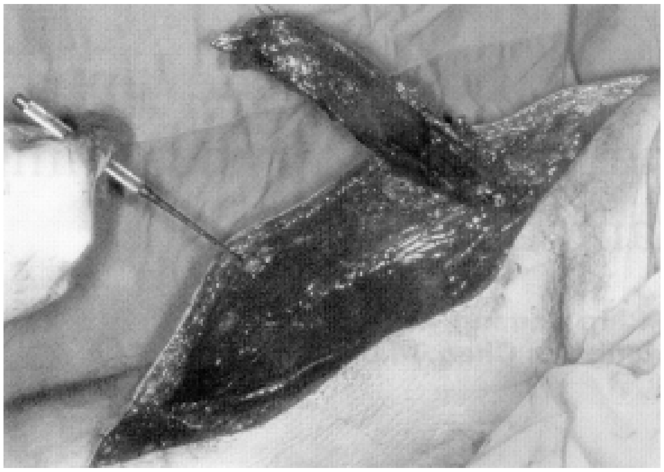
In 1970 Tamai[303] first reported free transplantation of vascularized skeletal muscle with his account of a rectus femoris muscle transfer in dogs. At biopsy 5 months later there were almost normal muscle fibers and motor nerve action potentials. Harii, Ohmori, and Torii[304] transferred the gracilis muscle in 1973 for facial reanimation in a patient with long standing Bell's palsy. At about the same time a surgical team in China[305] transferred the lateral portion of the pectoralis major muscle to the forearm to replace finger flexor musculature destroyed in a Volkmann's contracture. Ikuta[306] repeated this operation in 1976.

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 done to bring bulk and soft-tissue cover in traumatic losses or osteomyelitis. The most common muscle flaps are the latissimus dorsi and rectus abdominis muscle flaps, which have the advantage of reliable, large-caliber, and long vascular pedicles. Donor site morbidity is relatively low with either of these muscle flaps. Salgado and colleagues[307] report an alternative method for harvesting the rectus muscle via a Pfannenstiel incision. This approach may have the advantage of a more esthetic donor scar.

The concept of transplanting a tissue unit composed of skin and muscle for reconstruction originated with Tanzini, who in 1906 used the latissimus dorsi musculocutaneous flap to build a breast mound. Tanzini's work was initially accepted, subsequently ignored, and then forgotten for three generations. McCraw[308] rediscovered Tanzini's concept when he transferred a number of free musculocutaneous flaps in dogs, and this led to his landmark work on human island musculocutaneous flaps.[309] Most of the independent musculocutaneous territories described by McCraw[309] are potential sources of free flaps, and numerous others have since been identified and successfully transferred. Maxwell[310] lists several musculocutaneous free flaps and describes their history and anatomy. Maxwell credits Fujino and associates[311] in 1975 with the first clinical free transfer of a musculocutaneous unit; this was a deepithelialized gluteus maximus flap used for reconstruction in a patient with an aplastic breast.

Functional free muscle transfer is done to replace lost muscle and tendon-unit function. Functional muscle has particular application in restoration of finger flexion and extension in cases of severe post-traumatic loss or Volkmann's ischemic contracture and for facial reanimation. Both topics are covered extensively in *SRPS* issues dealing with facial nerve disorders[312] and hand surgery.[313,314] In an interesting report, Lin and coworkers[315] describe use of the soleus, latissimus, gracilis, and rectus femoris muscles in **functional free muscle transplantation** (FFMT) to restore finger flexion and extension and in the repair of biceps defects to provide functional elbow flexion and lifting power (Fig 1). It is worth noting that in this series the youngest patient was 16 years old. The authors report 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, while the range of muscle contraction is a factor of fiber length. The available donor muscle's neuronal mesh 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



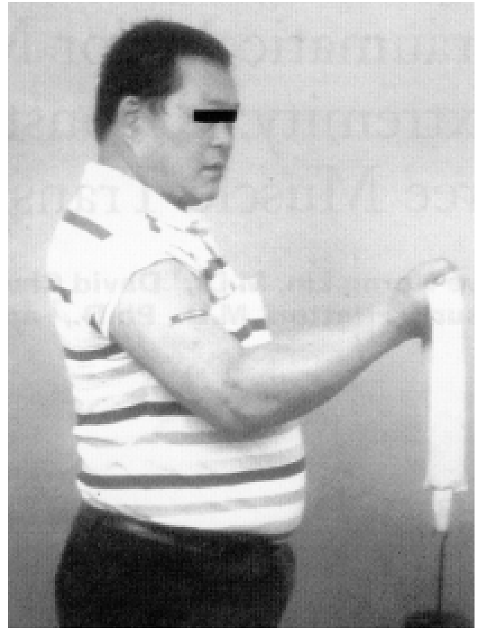
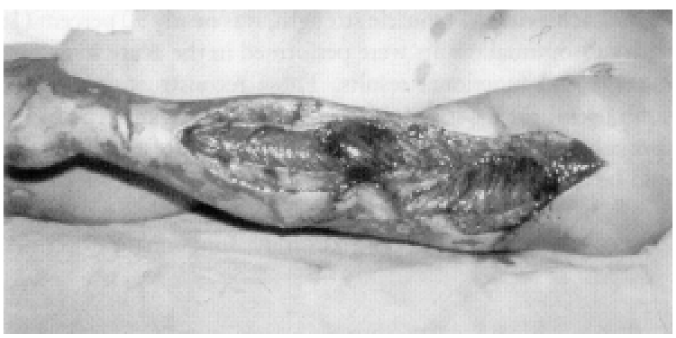
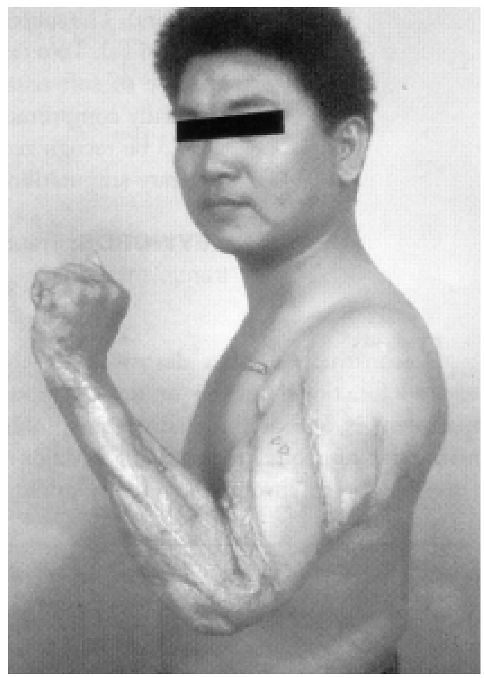


Fig 1. *Above, (A)* A roller caused proximal avulsion of the biceps muscle, nerve, and blood vessels. *(B)* Two years after gracilis FFMT the patient has M4 muscle strength and elbow flexion through 110 degrees. *Below, (A)* Electrical burn with necrosis of the elbow flexor muscles. A LDMC flap was used for cover and a gracilis FFMT for elbow flexion a year later. *(B)* Two years after last surgery, the patient has M4 muscle power and elbow range of motion of 120 degrees. *(Reprinted with permission from Lin SH, Chuang DCC, Hattori Y, Chen HC: Traumatic major muscle loss in the upper extremity: Reconstruction using functioning free muscle transplantation. J Reconstr Microsurg 20(3):227, 2004.)*





inset of the functional gracilis muscle is generally straightforward in experienced hands. Several papers detail the operative technique of gracilis harvest and anatomic variations of the muscle.[316–318] Lin and colleagues[319] harvest the gracilis through a shorter incision without the endoscope.

Functional free muscle transplantation involves the transfer of skeletal muscle by microvascular anastomoses as well as 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 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 and associates[320] demonstrated 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.

Several authors[321–325] have stressed the importance of reestablishing correct resting tension of muscle transplants. Small decreases in resting muscle tension may markedly reduce the power and amplitude of a contracture.

On average, muscle transplants have significantly less functional recovery than controls, although 100% of the control maximum tetanic tension is noted in several transplanted muscles.[326] Kuzon and colleagues[326] conclude that intraoperative ischemia *does not* affect functional recovery of a free muscle transfer, and the observed variability in functional outcome must be due to other, still undetermined factors.

Osseous and Osteocutaneous Free Flaps

Free osteocutaneous flaps evolved from the need for both vascularized skin and bone in some reconstructions. Ostrup and Fredrickson[327] pioneered the free transfer of vascularized bone in 1974. Shortly thereafter Taylor et al[328] and O'Brien[329] were instrumental in defining the advantages, risks, and limitations of the technique. Buncke and coworkers[330] transferred a free rib osteocutaneous flap to the lower leg for tibial pseudarthrosis in 1977. That same year Serafin and associates[331] used a rib osteocutaneous free flap for mandibular reconstruction.

Table 3 lists some common sources of vascularized bone and cites early reports of microsurgical transfer of the respective flaps.[327,328,332–341]

Vascularized bone autografts, whether endochondral or membranous in origin, have proved superior to nonvascularized bone grafts with regard to early incorporation, bone hypertrophy, mechanical strength to failure, and osseous mass retention.[342,343] 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.[344]

TABLE 3
Free Osseous and Osteocutaneous Transfers

Bone Source	Author (Year)
Rib (periosteal supply, ant.)	McKee (1978)
	Ariyan (1978)
Rib (nutrient supply, post.)	Ostrup (1974)
	Daniel (1977)
Fibula	Taylor (1975)
Iliac crest	Taylor (1978)
	Taylor (1979)
Second metatarsal	O'Brien (1979)
Radius	Biemer (1983)
Calvarium	Cutting (1984)
Scapula	dos Santos (1980)
	Urbaniak (1982)

Trauma and irradiation hamper bone healing in conventional nonvascularized bone grafts,[345] while vascularized bone grafts seem to tolerate irradiation of the recipient bed better.[346] Moreover, vascularized bone grafts appear to heal more rapidly even in the presence of an infected wound.[347,348] In short, the technique of vascularized free bone grafts is the standard against which emergent technologies—such as the Ilizarov distraction osteogenesis—must be measured. See Lower Extremity Reconstruction in *SRPS* for a more detailed discussion of bony reconstruction in the lower extremity.[349]

Berggren, Weiland, and Dorfman[350] 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 and associates[351] summarize the benefits and limitations of both approaches. Georgescu and Ivan[352] demonstrate successful use of the **serratus-rib** composite free flap for upper and lower extremity reconstruction.

Taylor[353] 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. The author[344] recommends free fibular grafts to repair bony defects >8cm, whereas ilium (straightened by an osteotomy) or fibula may be used for defects 6–8cm. Defects <6cm long can be repaired by conventional nonvascularized bone grafts. This data is mainly applicable to mandible defects; there may be variability in other osseous defects. Taylor has since described various techniques of harvesting vascularized fibular grafts and has proposed helpful refinements. Hidalgo[354,355] has published an extensive experience with free fibular transfers in mandibular reconstruction.

Many practitioners feel it is prudent to perform bilateral lower extremity angiography prior to fibula harvest in order to rule out peronea magna. Peronea magna is an anatomic variation where the peroneal artery is dominant and provides significant arterial flow to the foot along with the posterior tibial artery. In this variant the anterior tibial artery is hypoplastic or nonexistent. Harvesting the fibula in this scenario can leave the individual with a single-vessel-foot or worse. Angiography carries its own risks, however, including renal failure, contrast allergy, bleeding, and pseudoaneurysm of the cannulated access artery. As imaging technology improves, our reliance on angiography will likely wane. MRA and CT angiography are becoming useful tools (Fig 2).[356]

Taylor[335] also described the free transfer of vascularized **ilium** on the deep circumflex iliac vessels. The author later expanded the applications of the technique and suggested further surgical refinements.[336,357] Shenaq[358] reported less morbidity with the classic iliac crest free flap when using the inner cortex of the bone, but a recent study[359] disputes that conclusion. Mialhe and Brice[360] report a posterior iliac crest osteomusculocutaneous free flap that is based on a superficial branch of the superior gluteal artery.

Free Flaps of Viscera and Omentum

Microvascular transfers of bowel segments, primarily of the **proximal jejunum**, enjoy wide popularity for reconstruction in the oral cavity, pharynx, and cervical esophagus.[361–367]

The **greater omentum** is an excellent source of donor tissue and has been transferred by microanastomoses for multiple reconstructive problems in the past.[368,369] 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, one interesting idea has arisen where 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—see the *SRPS* issue on Lower Extremity Reconstruction.[349]

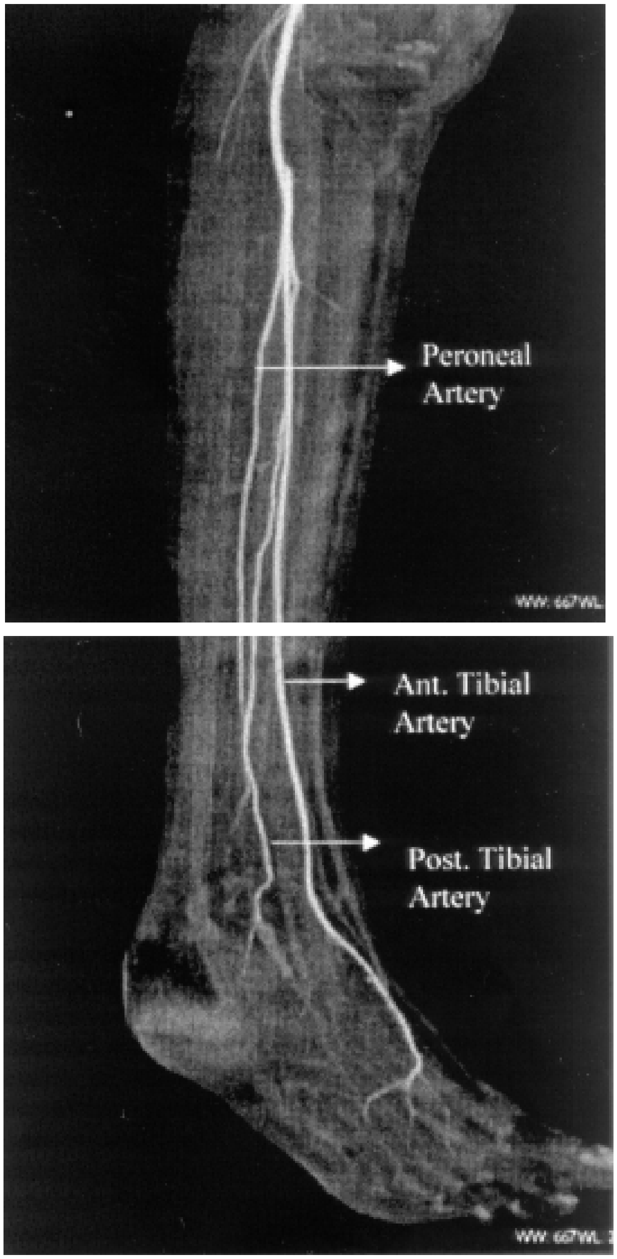
REPLANTATION

The first end-to-end anastomosis between vessels of disjoined parts was performed by Murphy[1] in 1896. A few years later the German surgeon Hoepfner[370] successfully replanted limbs in dogs. Working independently during the first years of the century, Charles Guthrie[2] and Alexis Carrel[3] transplanted kidneys, blood vessels, and composite tissues in lambs and dogs. In 1902 Carrel[3] demonstrated experimentally the feasibility of limb replantation, although his heterotransplant ultimately failed. Ten years later Carrel[3] received the Nobel Prize for his contribution to the science of vascular anastomosis and organ transplantation.

Nylen[4] and Holmgren[5] first described use of a microscope in 1921 during surgery for otosclerosis. In 1950 Barraquer and Perritt[371] sutured a human cornea under an operating microscope.

Kleinert[372] used vessel repair techniques to revascularize near-complete severed limbs in 1959. Malt and McLehman[373] replanted the arm of a 12-year-old boy who had suffered an above-elbow amputation in 1962. Also in 1962 Kleinert and Kasdan[374] performed the first revascularization of human digits, and in 1965 Tamai and Komatsu[375] 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 common-



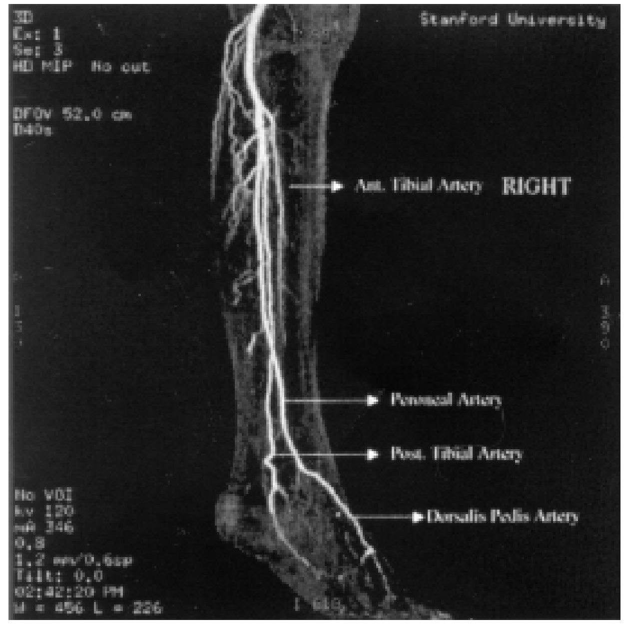


Fig 2. *Above,* Normal three-vessel runoff in lower extremity. *Above right,* CT angiogram demonstrating peroneal artery as dominant blood supply to the foot. Anterior tibial artery is occluded in proximal leg, and peroneal artery supplies dorsalis pedis artery. *(Reprinted with permission from Karanas YL, Antony A, Rubin G, Chang J: Preoperative CT angiography for free fibula transfer. Microsurgery 24(2):125, 2004.)*

place. Today the feasibility of human limb replantation is no longer in question. The reader is referred to an excellent article by Kleinert et al[376] for a history of replantation as well as an overview of popular techniques.

Arm and Forearm Replants

Upper extremity replantation has evolved rapidly since Malt and McKhann's[12] report. Survival rates have improved significantly over the last 30 years, and currently the ultimate success of a replantation attempt is judged by functional as well as cosmetic parameters.

Unlike distal amputations, the proximal limb has a large muscle mass that renders it vulnerable to ischemic degeneration and nerve injuries carry a high risk of loss of function. Review articles by Morrison and associates,[377] Wilson et al,[378] O'Brien,[379] and Whitney et al[380] offer different perspectives on the subject of major limb replantation.

In the rat, muscle necrosis and permanent breakdown of biochemical systems occur within 4h of ischemia.[381] In man, muscle necrosis has been documented after only 2½ hours of tourniquet ischemia.[382] Metabolic parameters correlate with histologic evidence of extensive cellular damage. With increasing ischemic times, the histologic appearance does not return to normal even after perfusion is restored. Cooling theoretically prolongs the safe ischemic period, although Muramatsu and coworkers[383] noted that even when cooled, muscle enzymes (CPK, SGOT) continued to leak out of the replanted dog hind limb after 6h of ischemia.

Nunley and others[384] described the technique of arterial and venous shunting as an aid to revascularization or replantation after upper limb injuries. The shunt allows adequate time for thorough debridement, appropriate bony stabilization, and identification of anatomic structures. The authors conclude that the AV shunt has 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 demonstrated in limb replantation.[329,385] Usui and others[386] and Smith and colleagues[387] note some benefit from fluorocarbon perfusion of amputated extremities, with less alteration of lactate, pH, and CPK levels. This improvement is offset by loss of capillary endothelium and increased edema.

Fukui and others[388] describe their experience with continuous postoperative infusion of urokinase, prostaglandin E, heparin, and low molecular weight dextran. In the 13 cases reported there were no instances of arterial thrombosis, and the authors note significant differences in platelet count, fibrinogen, and AT III in the patients receiving the drug infusion compared with controls.

Indications and Contraindications

Meyer and colleagues[389] state 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 >6h.[378] The following are universal contraindications to replantation:[378]

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

Functional Recovery

Return of function in forearm replantations depends largely on two factors: (a) the degree of nerve regeneration, and (b) the hand rehabilitation program.[390] Russell and associates[391] report their results in upper limb replantation and revascularization. The most frequent complication of surgery was infection (29%) compounded by inadequate debridement, which led to 4 failures. Nonunion occurred in 13% and intrinsic muscle function was weak or absent in all patients. Excellent or good results were noted in 8/19 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 conclude that the potential for functional recovery is proportional to the amount of viable tissue remaining.

Hand and Digit Replants

Weiland and coworkers[392] chart the progress of digital and hand replantation efforts at their institution over a 7-year period. Survival of the replanted limbs rose from 32% in 1970, to 69% to 74% in 1975, to better than 90% in 1976. As survival of the replanted extremity climbed, clinical emphasis shifted to considerations of long-term functional result.

Strauch and colleagues[393] offer an excellent review of the problems and complications encountered in replantation surgery in the hand. Waikakul and colleagues[394] report a large series of over 1000 digital replantations in which the functional results were generally good, with a replant viability rate of 93%. Zone 2 replants had the worst outcome.

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[329,395,396]
- 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 (FDS) tendon insertion
- single-digit amputations distal to the FDS insertion
- ring finger avulsion injuries

Level and Type of Injury

Tsai, McCabe, and Maki[397] describe their technique for replantation of the fingertip at the level of the DIP joint or distally. They noted a 69% survival rate and 25% of patients had 2-point discrimination <5mm. Clean, minimally crushed amputations yield the best results after replantation.[329] Avulsion injuries, severely contaminated wounds, and amputations with multiple levels of injury are secondary choices for replantation.[376,396,398] 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 instance, may not revascularize the flexor tendons and PIP joint.[376] Microsurgical repair in cases where the entire finger has been degloved does not result in good function.[391,396]

Ring avulsions are a special case. In 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 that sharp injuries with regards to recovery of range of motion.[399] Adani and colleagues[400] report acceptable results in complete ring avulsion replants.

Age

O'Brien[329] states that any limb amputation in a child merits an attempt at replantation so long as the part is not severely crushed. Kleinert et al[376,396] feel that age alone is not a contraindication to replantation, but it must be considered in the decision. Microsurgical repair of the tiny vessels of infants makes the operation technically difficult; on the other hand, functional return after replantation of digits in small children is often quite 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[376,396] believes that 12+h of warm ischemia is a relative contraindication to digital replantation, although survival of the replanted part has been documented after as long as 42h of warm ischemia.[101] Prompt cooling of the amputated digit to 4°C prolongs the acceptable ischemic period to approximately 24h, with a good chance of complete survival and full functional return.

Patient Selection

A patient's occupation, economic and social status, nationality, mental health and cooperativeness must all be taken into account when deciding whether to attempt replantation or not.[401]

Single-Digit Amputations

Urbaniak[402] is a proponent of replantation in single-digit amputations distal to the superficialis insertion if there is no crush injury. Tamai[395] also replants single digits when local wound conditions are favorable and if the patient desires the procedure, but his recommendation is influenced by the fact that in Japan patients who are missing a finger may be labeled as gangsters and may not be able to get a job.

May and colleagues[403] documented excellent survival and good esthetic results in a series of 24 digits replanted distal to the PIP joint, which prompts them to advocate the procedure in selected cases. Wilson et al[378] suggest a role for single-digit replantation when adjacent fingers are severely injured and the cut is clean. Waikakul and others[394] also advocate single-digit replantation.

Kleinert[376,396] discourages single-digit replantation although his own results with it have been impressive. O'Brien[329] weighs the merits of single-digit replantation based on patient sex, occupation, and expected functional result. Jones, Schenck and Chesney[404] 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 about 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 once healed, and secondary procedures are often needed. In addition, replanted digits may require further soft-tissue coverage. Ross and colleagues[399] reported the best range of motion in zone 1 and zone 5 replants. Interestingly, 2-tendon replanted digits had better range of motion than 1-tendon fingers. Early motion protocols were advocated. Yu and coworkers[405] reviewed 79 replanted digits in which a total of 102 secondary procedures were performed. 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 described in the lower extremity,[406] scalp,[407–410] ear,[411–415] penis,[416,417] testes,[417] scrotum,[417,418] upper and lower lips,[419,420] tongue,[421] nose,[422] and face–scalp composite.[423]

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 and associates[407] discuss 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.[424] Omentum is also an excellent option for scalp salvage.

Ademoglu and colleagues[425] discuss whether amputated great toes should be replanted. Even though load distribution is altered, the gait is not significantly affected and the authors stop short of recommending great toe replantation. Kutz and others[406] state that lower extremity replantation may be indicated in distal, clean, sharp amputations in young patients. For a more extensive discussion on lower extremity replantation, see the *SRPS* issue on Lower Extremity Reconstruction.[349]

Mutimer, Banis, and Upton[412] report successful microsurgical reattachment of totally amputated ears. Turpin[413] describes the evolving technique for successful ear replantation. The author notes that vein grafts are usually required and that postoperative venous congestion is a frequent problem. Turpin suggests that all patients should receive heparin anticoagulation, and medicinal leeches or frequent abrasion may be necessary to control venous congestion.[413]

Operative Technique

The surgical principles of microvascular repair have been previously discussed. When performing a 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 surgeon's preference. A common approach involves the following steps:

- preoperative patient evaluation and preparation
- identification of structures in amputated part
- identification of structures in the amputation stump
- bone shortening (minimal) and bony fixation
- arterial repair (with or without recirculation)
- venous repair
- muscle-tendon unit repair
- nerve repair
- skin closure or soft-tissue cover[395,426]

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,[427] a single intramedullary K-wire,[428] interosseous wiring,[429] intramedullary screws,[393] or bone plates and external fixation devices. Arata and colleagues[430] describe 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 and colleagues[431] describe 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 and colleagues[432] report 92% of normal growth in epiphyses transferred either by replantation or free tissue transfer. Bowen and others[433,434] report on the vascularity and feasibility of growth plate transfer, and note that both epiphyseal and metaphyseal circulations must be revascularized in order to obtain adequate growth and structural integrity. Chen and coworkers[435] report 29 vascularized toe joint transfers to hand and finger joints with good results. The outcomes of these joint flaps must be compared with arthrodesis and well-functioning metallic or Silastic arthroplasties. Certainly in some complex hand joint injuries, a vascularized toe joint may 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 <20% of cases.[426] The ideal is two or three venous repairs per finger, but this may be impossible in distal amputations, amputations in children, injuries that have a severe dorsal component, or in postreplant venous thrombosis.

Vein grafts are routine practice when the vessel ends are short or if there is tension at the anastomosis. Mitchell and coworkers[436] studied avulsion injuries in rat limb arteries and veins. As seen through the operating microscope, the damage to the vessels averaged 0.8cm from the rupture site, and serial histologic examination revealed significant injury for up to 4cm. Arteries were more severely damaged than veins, especially at bifurcation points, and distal injuries were worse and more frequent than proximal ones.

Buncke and associates[437] review the applications and long-term results of vein grafts in replantation surgery.

Arteriovenous Fistulas

Working in the rabbit ear replantation model, Nichter and colleagues[438] created an efferent AV fistula by anastomosing a distal artery to a proximal vein. Heparin in Ringer's lactate is frequently used to flush the vessel ends before and during anastomosis.[329] Topical application of lidocaine or papaverine may relieve and sometimes avoid vasospasm during the dissection.[329]

Nerve Repair or Graft

Twenty-five years after its publication, Terzis's[439] excellent review of microneural repair techniques is still valid. Nerve grafting in replantation surgery is an option when primary approximation is still impossible after adequate debridement. Donor nerves may be harvested from other amputated and unreplanted parts;[395] simple epineural technique is usually best. If both ends of the nerves being sutured are well-vascularized, complete reinnervation is expected. Schultes and associates[440] compared vascularized versus nonvascularized nerve graft transfers in a rat model, and found significant histologic differences, with less fibrosis and myelin degeneration in vascularized grafts.

Heparin

Gordon and others[441] report a 71.4% 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.[442–448] Leeches are typically applied to the area of anastomosis to relieve venous congestion in flaps or in appendages through vasodilation and vascular decompression.[448] The key to the benefit of leeches lies with hirudin, a selective thrombin inhibitor that leeches secrete and which they inject into the host tissue as they feed on the host's blood.

Anthony and colleagues[445] 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 there was continued bleeding from the bite sites as a result of the injected hirudin.

Prophylactic antibiotics are usually recommended when leeches are used because of reports of infection with *Aeromonas hydrophila,*[446] which is often insensitive to ampicillin and cephalothins but consistently sensitive to ciprofloxacin, tetracycline, and trimethoprim-sulfamethoxasole.[447] Oral antibiotic coverage with one of these drugs is recommended when using leeches.

The reader is referred to an article by Valauri[448] describing the technical aspects and clinical applications of medicinal leeches in microsurgery.

Tissue Expansion

As described by various authors,[449–453] 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 and coworkers[454] correlated sensory recovery of replanted parts with arterial pulse pressure, and concluded that two-point discrimination reached normal levels (<6mm) 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.

Chen and others[455] categorize 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. Grade IV patients (4%) have negligible function of their replanted limb.

Matsuda and colleagues[456] report effective recovery of pinch, grasp, and sensation in 60% of their replants. Schlenker, Kleinert, and Tsai[397] found 2-point discrimination of <10mm in only 9 of 20 replanted thumbs. The average active range of motion for the IP joint was 35% of normal and for the MP joint, 29%. Most patients were able to return to work after a mean interval of 7mo.

Tamai's[426] results in 293 upper extremity replants are listed in Table 4.

Table 5 lists the limb survival results of replantation surgery as reported by some of the major centers.[392–395,402,457–460]

Alternatives to Replantation — Salvage Procedures

For failed digital replants and amputations that cannot be replanted at the time of injury, toe-to-finger or toe-to-thumb transplants can restore at least partial function. Leung[461] and Frykman[462] describe the technique and functional results of these transfers.

The field of toe-to-hand transfers continues to be refined. Williamson and colleagues,[463] Yu and Huang,[464] and Chung and Kotsis[465] report adequate reconstruction with toe transfers after multiple finger loss. The rate of return to work was satisfactory. In their review, Wei, Jain, and Chen[466] discuss technical refinements and donor site considerations and illustrate excellent functional and esthetic results.

Wei's group[467] also reported limited sensory recovery after toe-to-finger transfer, perhaps curtailed at the outset by the relatively low density of sensory receptors in toe glabrous skin. As determined by patient questionnaire, toe transfers to the hand produced minimal lower limb morbidity in Chung and Wei's[468] series. Beyaert and col-

TABLE 4
Functional Results in 181 Replantations

Replantation	Excellent		Good		Fair		Poor	
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%)
	65/181	(36%)	65/181	(36%)	28/181	(15%)	23/181	(13%)
			(72%)					

(Data from Tamai S: Twenty years' experience of limb replantation—Review of 293 upper extremity replants. J Hand Surg 7:549, 1982.)

TABLE 4
Clinical Results of Replantation

Author (Year)	No. Complete (% viable)	No. Incomplete (% viable)
Sixth People's Hosp (1975)	320 (54)	53 (57)
Weiland (pre-1976)	86 (39)	
(-1976)	50 (90)	
Tamai (1978)	102 (86)	61 (93)
Urbaniak (1979)	107 (82)	80 (94)
Hamilton (1980)	83 (65)	77 (84)
Schlenker (1980)	51 (71)	13 (77)
Kleinert (1980)	243 (49)	347 (70)

leagues[469] noted some disturbance of gait after second toe transfer in children.

In order to decrease the time of disability, potentially ameliorate soft-tissue cover problems, and facilitate earlier return to work, many surgeons have advocated earlier toe-to-hand transfers in nonreplantable digit loss. Yim, Wei, and Lin[470] compared outcomes of "primary" toe-to-hand transfers to delayed transfers. Primary transfers are defined as those performed in the acute period or within a mean 7d of injury. There were no significant differences 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.

In conclusion, *there is no apparent medical or surgical reason to wait several months for toe-to-hand transfer,* 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 may not be psychologically ready for primary toe transfer in the early posttrauma period, while others may benefit from an earlier return of hand function and no additional hospitalizations.

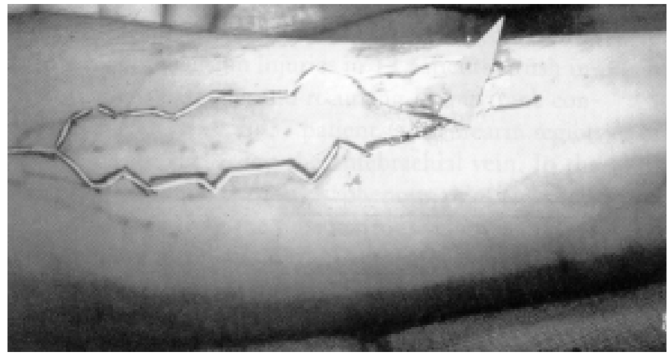
Sometimes the digit is replantable but an associated soft-tissue defect cannot be satisfactorily addressed by local flaps or grafts. There may be also some avulsion and devascularization injuries that need additional soft-tissue coverage. A recent article by De Lorenzi and coworkers[471] recounts their experience with arterialized venous free flaps in these problems. These flaps, like full-thickness skin grafts, are thin, supple, and can be tailored precisely to fit the defect and Brunner's lines (Fig 3). An insightful discussion and informative review of arterialized venous flaps by Brooks[472] accompanies their paper.

Hand Transplant/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 demonstrated 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.[28]

Jones[473] updated the status of limb allograft transplantation in 2002. In general, immunosuppression has been well tolerated in human recipients, although there is still considerable risk of posttransplant diabetes as well as chronic infections. Transplanted hands show good mechanical motor function but poor sensory return. Patients need to be followed long term to fully assess if the risk was worth the reward, as many organ transplants have half lives <10y.

Should hand amputees put their long-term health at risk for a hand allograft that may fail long before the patient's expected death? What psychological trauma may ensue for a patient that regains use of a hand for several years, only to lose it again to chronic rejection? The prospect for a second allograft of course exists. Given 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.



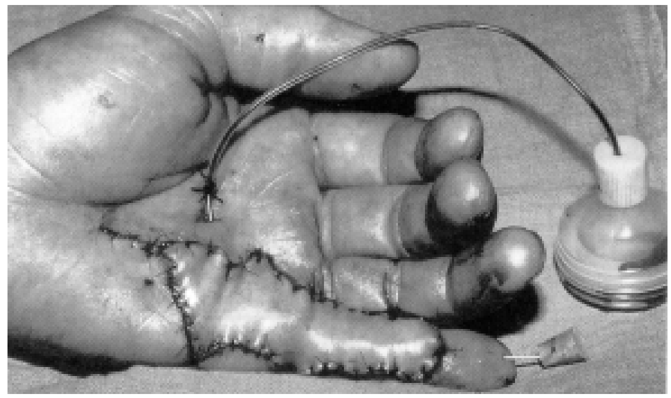


Fig 3. *Above,* Tissue defect after excision of recurrent Dupuytren's. *Above right,* Indicating excision of the venous free flap from the lower arm. *Below right,* Clinical results after 1 week; venous stasis in the arterialized venous flap is normal. *(Reprinted with permission from De Lorenzi F, Hulst RRWJvd, Dunnen WFAd, et al: Arterialized venous free flaps for soft-tissue reconstruction of digits: a 40-case series. J Reconstr Microsurg 18(7):569, 2002.)*

BIBLIOGRAPHY

1. Murphy JB: Resection of arteries and veins injured in continuity: End-to-end suture: Experimental and clinical research. *Med Rec 51:73, 1897.*
2. Guthrie CC: Some physiologic aspects of blood vessel surgery. *JAMA 51:1658, 1908.*
3. Carrel A: The operative technique of vascular anastomoses and the transplantation of viscera. *Med Lyon 98:859, 1902. (English translation in Clin Orthop 29:3, 1963).*
4. Nylen CO: The otomicroscope and microsurgery, 1921-1971. *Acta Otolaryngol 73:453, 1972.*
5. O'Brien BM, Morrison WA, Gumley GJ: Principles and Techniques of Microvascular Surgery. *IN: McCarthy JG (ed), **Plastic Surgery.** Philadelphia, WB Saunders, 1990. Vol 1, Ch 12, pp 412-473.*
6. Jacobson JH, Miller DB, Suarez E: Microvascular surgery: A new horizon in coronary artery surgery. *Circulation 22:767, 1960.*
7. Jacobson JH, Katsumura T: Small vein reconstruction. *J Cardiovasc Surg 6:157, 1965.*
8. Green GE, Som ML, Wolff WI: Experimental microvascular suture anastomosis. *Circulation (Suppl) 23:1, 1966.*
9. Acland RD: Prevention of thrombosis in microvascular surgery by the use of magnesium sulfate. *Br J Plast Surg 37:227, 1966.*
10. Smith JW: Microsurgery: Review of the literature and discussion of microtechniques. *Plast Reconstr Surg 37:227, 1966.*
11. Cobbett JR: Microvascular surgery. *Surg Clin North Am 47:521, 1967.*
12. Malt RA, McKhann CF: Replantation of severed arms. *JAMA 189:716, 1964.*
13. Gallico GG III: Replantation and Revascularization of the Upper Extremity. *IN: McCarthy JG (ed), **Plastic Surgery.** Philadelphia, WB Saunders, 1990. Vol 7, Ch 93, pp 4355-4383.*
14. Kleinert HE, Kasdan ML: Salvage of devascularized upper extremities, including studies on small vessel anastomosis. *Clin Orthop 29:29, 1963.*
15. Nakayama K et al: Experience with free autografts of the bowel with a new venous anastomosis apparatus. *Surgery 55:796, 1964.*
16. Buncke HJ Jr, Schulz WP: Experimental digital amputation and reimplantation. *Plast Reconstr Surg 36:62, 1965.*
17. Buncke HJ Jr, Schulz WP: Total ear reimplantation in the rabbit utilising microminiature vascular anstomoses. *Br J Plast Surg 19:15, 1966.*
18. Komatsu S, Tamai S: Successful replantation of a completely cut-off thumb. *Plast Reconstr Surg 42:374, 1968.*

19. Krizek TJ et al: Experimental transplantation of composite grafts by microsurgical vascular anstomoses. *Plast Reconstr Surg 36:538, 1965.*
20. Cobbett JR: Free digital transfer. Report of a case of transfer of a great toe to replace an amputated thumb. *J Bone Joint Surg 51B:677, 1969.*
21. Antia NH, Buch VI: Transfer of an abdominal dermo-fat graft by direct anastomosis of blood vessels. *Br J Plast Surg 24:15, 1971.*
22. McLean DH, Buncke HJ: Autotransplant of omentum to a large scalp defect with microsurgical revascularization. *Plast Reconstr Surg 49:268, 1972.*
23. Daniel RK, Taylor GI: Distant transfer of an island flap by microvascular anastomoses. A clinical technique. *Plast Reconstr Surg 52:111, 1973.*
24. O'Brien BM et al: Successful transfer of a large island flap from the groin to the foot by microvascular anastomoses. *Plast Reconstr Surg 52:271, 1973.*
25. Khouri RK: Avoiding free flap failure. *Clin Plast Surg 19:773, 1992.*
26. O'Brien BMcC: The role of microsurgery in modern surgery. *Ann Plast Surg 24:258, 1990.*
27. Whitworthm IH, Pickford MA: The first toe-to-hand transfer: a thirty-year follow-up. *J Hand Surg 25B(6):608, 2000.*
28. Lee WP, Mathes DW: Hand transplantation: pertinent data and future outlook. *J Hand Surg 24A(5):906, 1999.*
29. Jones NF: Concerns about human hand transplantation in the 21st century. *J Hand Surg 27A(5):771, 2002.*
30. Weinstein PR, Mehdorn HM, Szabo Z: Microsurgical anastomosis: Vessel injury, regeneration, and repair. *In: Serafin D, Buncke HJ Jr,* ***Microsurgical Composite Tissue Transplantation.*** *St Louis, CV Mosby, 1979, Ch 9, pp 111-144.*
31. Harashina T, Fujino T, Watanabe S: The intimal healing of microvascular anastomoses. *Plast Reconstr Surg 58:608, 1976.*
32. Ketchum LD et al: Experimental use of pluronic F68 in microvascular surgery. *Plast Reconstr Surg 53:288, 1974.*
33. Hayhurst JW, O'Brien BM: Experimental study of microvascular technique, patency rates, and related factors. *Br J Plast Surg 28:128, 1975.*
34. Ts'Ao C: Myointimal cells as a possible source of replacement for endothelial cells in the rabbit. *Circ Res 23:671, 1968.*
35. Lidman D, Lyczakowski T, Daniel RK: The morphology and patency of arterial and venous microvascular anastomoses throughout the first postoperative year. A histological study. *Scand J Plast Reconstr Surg 18:187, 1984.*
36. Margic K: Early changes in dissected small vessels: Experimental study on rat arteries and veins. *Plast Reconstr Surg 75:375, 1985.*
37. Caffee HH, Ward D: Bipolar coagulation in microvascular surgery. *Plast Reconstr Surg 78:374, 1986.*
38. Johnstone RE, Wax MK, Bishop DJ, Chafin JB: Large doses of topical lidocaine during microvascular surgery are not associated with toxic blood concentrations. *Anesthesiology 82:593, 1995.*
39. Ohta I et al: Topical use of xylocaine for relieving vasospasm: effect of concentration. *J Reconstr Microsurg 7:205, 1991.*
40. Gertz SD, Rennels ML, Nelson E: Endothelial cell ischemic injury: Protective effect of heparin or aspirin assessed by scanning electron microscopy. *Stroke 6:357, 1975.*
41. Acland RD: Microvascular anastomosis: A device for holding stay sutures and a new vascular clamp. *Surgery 75:185, 1974.*
42. Chow SP, Huang CD, Chan CW: Microvascular anastomosis of arteries under tension. *Br J Plast Surg 35:82, 1982.*
43. Acland RD, Trachtenberg L: The histopathology of small arteries following experimental microvascular anastomosis. *Plast Reconstr Surg 60:868, 1977.*
44. Lidman D, Daniel RK: Evaluation of clinical microvascular anastomosis: Reasons for failure. *Ann Plast Surg 6:215, 1981.*
45. Johnson PC: Platelet-mediated thrombosis in microvascular surgery: new knowledge and strategies. *Plast Reconstr Surg 86:359, 1990.*
46. Spate TH, Gaynor E: Vascular endothelial damage and thrombosis. *Adv Cardiol 4:147, 1969.*
47. Tangelder GJ et al: Blood platelets: An overview. *J Reconstr Microsurg 5:167, 1989.*
48. Chang WHJ, Petry JJ: Platelets, prostaglandins, and patency in microvascular surgery. *J Microsurg 2:27, 1980.*
49. Ketchum LD: Pharmacological alterations in the clotting mechanism: Use in microvascular surgery. *J Hand Surg 3:407, 1978.*
50. Johnson PC, Barker JH: Thrombosis and antithrombotic therapy in microvascular surgery. *Clin Plast Surg 19:799, 1992.*
51. Danese CA, Haimov M: Inhibition of experimental arterial thrombosis in dogs with platelet deaggregating agents. *Surgery 70:927, 1971.*
52. Rhee RY et al: Low dose heparin therapy: In vitro verification of antithrombotic effect. *J Vasc Surg 14:628, 1991.*
53. Rosenberg RD: Actions and interactions of antithrombin and heparin. *N Engl J Med 292:146, 1975.*
54. Greenberg BM, Masem M, May JW Jr: Therapeutic value of intravenous heparin in microvascular surgery: An experimental vascular thrombosis study. *Plast Reconstr Surg 82:463, 1988.*
55. Khouri RK et al: Thrombosis of microvascular anastomoses in traumatized vessels: Fibrin versus platelets. *Plast Reconstr Surg 86:110, 1990.*
56. May JW Jr, Rothkopf DM: Salvage of a failing microvascular free muscle flap by direct continuous intravascular infusion of heparin: A case report. *Plast Reconstr Surg 83:1045, 1989.*
57. Seuter F: Inhibition of platelet aggregation by acetylsalicylic acid and other inhibitors. *Haemostatis 5:85, 1976.*
58. Acland RD, Trachtenberg L: The histopathology of small arteries following experimental microvascular anastomoses. *Plast Reconstr Surg 59:868, 1977.*
59. Restifo RJ, Dumanian GA, Garrett KO, et al: Prostacyclin production at the human microvascular anastomosis: its effect on initial platelet deposition. *Plast Reconstr Surg 97:784, 1996.*
60. Salemark L et al: Adverse effects of topical prostacyclin application in microvascular surgery: An experimental study. *J Reconstr Microsurg 7:27, 1991.*
61. Battle J et al: Effect of Dextran on factor VIII/von Willebrand factor structure and function. *Thromb Haemost 54:697, 1985.*

62. Rothkopf DM et al: The effect of Dextran on microvascular thrombosis in an experimental rabbit model. *Plast Reconstr Surg 92:511, 1993.*
63. Bygdeman S, Tangen D: Effect of dextran on collagen-induced platelet aggregation in vitro. *Thromb Res 6:109, 1975.*
64. Eldor A, Weksler B: Heparin and dextran sulfate antagonized PGI_2_ inhibition of platelet aggregation. *Thromb Res 16:617, 1979.*
65. Wiman D, Ostrup LT, Enestrom S: The effect of dextran on the incidence of thrombosis in microvenous Nakayama ring pin anastomoses. *Scand J Plast Reconstr Surg 13:263, 1979.*
66. Wieslander JB et al: Effect of dextran 70 and saline on thrombus formation following arteriotomy and intimectomy in small arteries. *Microsurgery 7:168, 1986.*
67. Wieslander JB et al: The influence of dextran and saline solution upon platelet behavior after microarterial anastomosis. *Surg Gynecol Obstet 163:256, 1986.*
68. Wolfort S et al: The beneficial effect of dextran on anastomotic patency and flap survival in a strongly thrombogenic model. *J Reconstr Microsurg 8:375, 1992.*
69. Tsang RK, Mok JS, Poon YS, van Hasselt A: Acute renal failure in a healthy young adult after dextran 40 infusion for external-ear reattachment surgery. *Br J Plast Surg 53(8):701, 2000.*
70. Goldberg JA, Pederson WC, Barwick WJ: Salvage of free tissue transfers using thrombolytic agents. *J Reconstr Microsurg 5:351, 1989.*
71. Arnljots B et al: Prevention of microvascular thrombosis with low-dose tissue plasminogen activator. *Plast Reconstr Surg 90:281, 1992.*
72. Puckett CL, Misholy H, Reinisch JF: The effects of streptokinase on ischemic flaps. *J Hand Surg 8:101, 1983.*
73. Lipton HA, Jupiter JB: Streptokinase salvage of a free-tissue transfer: Case report and review of the literature. *Plast Reconstr Surg 79:977, 1987.*
74. Cange S et al: Streptokinase in the management of limb arterial thrombosis following free-flap surgery. *Plast Reconstr Surg 79:974, 1987.*
75. Maeda M et al: Continuous local intraarterial infusion of antithrombotic agents for epigastric flap transfer in rabbit. *J Reconstr Microsurg 6:261, 1990.*
76. Hergrueter CA et al: Human recombinant tissue type plasminogen activator and its effect on microvascular thrombosis in the rabbit. *Plast Reconstr Surg 81:418, 1988.*
77. Levy EA et al: A comparison of human recombinant tissue-type plasminogen activator and urokinase in microsurgical thrombolysis in the rat. *J Reconstr Microsurg 7:209, 1991.*
78. Fudem GM, Walton RL: Microvascular thrombolysis to salvage a free flap using human recombinant tissue plasminogen activator. *J Reconstr Microsurg 5:231, 1989.*
79. Romano JE, Biel MA: Maintaining long-term vessel patency in microvascular surgery using tissue-type plasminogen activator. *Otolaryngol Head Neck Surg 105:391, 1991.*
80. Stassen JM, Lü G, Andréen O, et al: Intraoperative thrombolytic treatment of microarterial occlusion by selective rt-PA infusion. *Plast Reconstr Surg 96:1215, 1995.*
81. Rapoport S et al: Aggressive postoperative pharmacotherapy for vascular compromise of replanted digits. *AJR 144:1065, 1985.*
82. Gold HK et al: Pharmacodynamic study of $F(ab')_2$ fragments of murine monoclonal antibody 7E3 directed against human platelet glycoprotein IIb/IIIa in patients with unstable angina pectoris. *J Clin Invest 86:651, 1990.*
83. Lan M et al: Microvascular salvage procedures with adjuvant antithrombotic therapy for restitution of patency in a rat model. *J Reconstr Microsurg 8:201, 1992.*
84. Davies DM: A world survey of anticoagulation practice in clinical microvascular surgery. *Br J Plast Surg 35:96, 1982.*
85. Veravuthipakorn L, Veravuthipakorn A: Microsurgical free flap and replantation without antithrombotic agents. *J Med Assoc Thai 87(6):665, 2004.*
86. Serafin D et al: Transcutaneous PO_2_ monitoring for assessing viability and predicting survival of skin flaps: experimental and clinical correlations. *J Microsurg 2:165, 1981.*
87. Eriksson E, Anderson WA, Replogle RL: Effects of prolonged ischemia on muscle microcirculation in the cat. *Surg Forum 25:254, 1974.*
88. Thomason PR, Matzke HA: Effects of ischemia on the hind limb of the rat. *Am J Phys Med 54:113, 1975.*
89. Wolff K-D, Stiller D: Ischemia tolerance of free-muscle flaps: An NMR-spectroscopic study in the rat. *Plast Reconstr Surg 91:485, 1993.*
90. Berggren A, Weiland AJ, Dorfman H: The effects of prolonged ischemia time on osteocyte and osteoblast survival in composite bone grafts revascularized by microvascular anastomoses. *Plast Reconstr Surg 69:290, 1982.*
91. Lundborg G: Ischemic nerve injury. *Scand J Plast Reconstr Surg (Suppl) 6:3, 1970.*
92. Medins G, Laufman H: Hypothermia in mesenteric arterial and venous occlusions. *Ann Surg 148:747, 1958.*
93. Hayhurst JW et al: Experimental digital replantation after prolonged cooling. *Hand 6:134, 1974.*
94. American Replantation Mission to China: Replantation surgery in China. *Plast Reconstr Surg 52:176, 1973.*
95. May JW Jr et al: The no-reflow phenomenon in experimental free flaps. *Plast Reconstr Surg 61:256, 1978.*
96. Cooley DC, Hansen FC, Dellon AL: The effect of temperature on tolerance to ischemia in experimental free flaps. *J Microsurg 3:11, 1981.*
97. Donski PK et al: The effects of cooling on experimental free flap survival. *Br J Plast Surg 33:353, 1980.*
98. Reus WF, Schlenker JD: Comparison of blood flow after warm and cool ischemia in island flaps: latissimus dorsi myocutaneous and epigastric flaps in the dog. *Ann Plast Surg 10:130, 1983.*
99. Anderl H: Storage of a free groin flap. *Chir Plast 4:42, 1977.*
100. Takayanagi S, Tsukie T: Survival of a myocutaneous free flap after prolonged ischemia. A case report. *J Microsurg 2:296, 1981.*
101. Baek S-M, Kim S-S: Successful digital replantation after 42 hours of warm ischemia. *J Reconstr Microsurg 8:455, 1992.*
102. Walkinshaw M et al: Ischemic injury to enteric free flaps: An experimental study in the dog. *Plast Reconstr Surg 81:939, 1988.*

103. Ames A III et al: Cerebral ischemia: II. The no-reflow phenomenon. *Am J Pathol 52:437, 1968.*
104. Zdeblick TA, Shaffer JW, Field GA: An ischemia-induced model of revascularization failure of replanted limbs. *J Hand Surg 10A:125, 1985.*
105. Jacobs GR, Reinisch JF, Puckett CL: Microvascular fibrinolysis after ischemia: its relation to vascular patency and tissue survival. *Plast Reconstr Surg 68:737, 1981.*
106. Suval WD et al: Assessment of ischemia reperfusion injury in skeletal muscle by macromolecular clearance. *J Surg Res 42:550, 1987.*
107. Suval WD et al: Microvascular transport and endothelial cell alterations preceding skeletal muscle damage in ischemia and reperfusion injury. *Am J Surg 154:211, 1987.*
108. Russell RC et al: Reperfusion injury and oxygen free radicals: A review. *J Reconstr Microsurg 5:79, 1989.*
109. Manson PN et al: The role of oxygen-free radicals in ischemic tissue injury in island skin flaps. *Ann Surg 198:87, 1983.*
110. Blaisdel FW: The patholophysiology of skeletal muscle ischemia and the reperfusion syndrome: a review. *Cardiovasc Surg 10(6):620, 2002.*
111. Schubert W et al: Use of streptokinase for the salvage of a free flap: Case report and review of the use of thrombolytic therapy. *Microsurgery 8:117, 1987.*
112. Douglas B et al: Beneficial effects of ibuprofen on experimental microvascular free flaps: Pharmacologic alteration of the no-reflow phenomenon. *Plast Reconstr Surg 79:366, 1987.*
113. Feng L-J et al: Vasoactive prostaglandins in the impending no-reflow state: Evidence for a primary disturbance in microvascular tone. *Plast Reconstr Surg 81:755, 1988.*
114. Schmid-Schonbein GW: Capillary plugging by granulocytes and the no-reflow phenomenon in the microcirculation. *Fed Proc 46:2397, 1987.*
115. Kuo YR, et al: Reactive thrombocytosis without endothelial damage does not affect the microvascular anastomotic patency. *Ann Plast Surg 50(1):57, 2003.*
116. Weinzweig N, Gonzalez M: Free tissue failure is *not* an all-or-none phenomenon. *Plast Reconstr Surg 96:648, 1995.*
117. Germann G, Bruner S, Pelzer M: Structure and organization of a microsurgically oriented plastic surgery unit. *Microsurgery 24(2):95, 2004.*
118. Daniel RK, Terzis JK: ***Reconstructive Microsurgery.*** *Boston, Little Brown, 1977.*
119. Hoerenz P: The operating microscope. I. Optical principles, illumination systems, and support systems. *J Microsurg 1:364, 1980.*
120. Hoerenz P: The operating microscope. II. Individual parts, handling, assembling, focusing, and balancing. *J Microsurg 1:419, 1980.*
121. Hoerenz P: The operating microscope. III. Accessories. *J Microsurg 2:22, 1980.*
122. Nunley JA: Microscopes and microinstruments. *Hand Clin 1:197, 1985.*
123. Shenaq SM, Klebuc MJA, Vargo D: Free-tissue transfer with the aid of loupe magnification: experience with 251 procedures. *Plast Reconstr Surg 95:261, 1995.*
124. Serletti JM, Deuber MA, Guidera PM, et al: Comparison of the operating microscope and loupes for free microvascular tissue transfer. *Plast Reconstr Surg 95(2):270, 1995.*
125. Ross DA, Ariyan S, Restifo R, Sasaki CT: Use of the operating microscope and loupes for head and neck free microvascular tissue transfer: a retrospective comparison. *Arch Otolaryngol Head Neck Surg 129(2):189, 2003.*
126. Acland RD: Instrumentation for microsurgery. *Orthop Clin North Am 8:281, 1977.*
127. Colen LB, Gonzales FP, Buncke HJ Jr: The relationship between the number of sutures and the strength of microvascular anastomoses. *Plast Reconstr Surg 64:325, 1979.*
128. Zhang L, Moskovitz M, Baron DA, Siebert JW: Different types of sleeve anatomosis. *J Reconstr Microsurg 11(6):461, 1995.*
129. Zhang L, et al: New four-stitch sleeve anastomosis: an experimental study in rats with reports of clinical use. *Microsurgery 17(6):291, 1996.*
130. Mii Y, et al: Microvascular anastomosis with absorbable and nonabsorbable sutures: A comparative study in rats. *J Microsurg 2:42, 1980.*
131. Thiede A, et al: Absorbable and nonabsorbable sutures in microsurgery: Standardized comparable studies in rats. *J Microsurg 1:216, 1979.*
132. Chen LE, Seaber AV, Urbaniak JR: Microvascular anastomoses in growing vessels: a long-term evaluation of nonabsorbable suture materials. J Reconstr Microsurg 9(3):183, 1993.
133. Lee BY, Thoden WR, Brancato RF, et al: Comparison of continuous and interrupted suture techniques in microvascular anastomosis. *Surg Gynecol Obstet 155(3):353, 1982.*
134. Wheatley MJ, Mathes SJ, Hassett C: Comparison of continuous and interrupted suture techniques in microvascular end-to-side anastomosis. *J Reconstr Microsurg 2(2):93, 1986.*
135. Peerless SJ; Gamache FW Jr; Hunter IG: Continuous suture method for microvascular anastomosis: technical note. *Neurosurgery 8(6):695, 1981.*
136. Schlechter B; Guyuron B: A comparison of different suture techniques for microvascular anastomosis. *Ann Plast Surg 33(1):28, 1994.*
137. Firsching R et al: Continuous and interrupted suture technique in microsurgical end-to-end anastomosis. *Microsurgery 5:80, 1984.*
138. Hamilton RB, O'Brien BM: An experimental study of microvascular patency using a continuous suture technique. *Br J Plast Surg 32:153, 1979.*
139. Cordeiro PG; Santamaria E: Experience with the continuous suture microvascular anastomosis in 200 consecutive free flaps. *Ann Plast Surg 40(1):1, 1998.*
140. Chase MD, Schwartz SI: Consistent patency of 1.5 millimeter arterial anastomoses. *Surg Forum 13:220, 1962.*
141. Chen L, Chiu DTW: Spiral interrupted suturing technique for microvascular anastomosis: A comparative study. *Microsurgery 7:72, 1986.*
142. Man D, Acland RD: Continuous-suture technique in microvascular end-to-end anastomosis. *J Microsurg 2:238, 1981.*
143. Lauritzen C, Hansson HA: Microvascular repair after the sleeve anastomosis. An ultrastructural study in the rat femoral vessels. *Scand J Plast Reconstr Surg 14:65, 1980.*
144. Lauritzen CG: The sleeve anastomosis revisited. *Ann Plast Surg 13:145, 1984.*

145. Duminy FJ: A new microvascular "sleeve" anastomosis. *J Surg Res 46:189, 1989*.
146. Krag C, Holck SS: Microvascular anastomosis: A comparison of the end-to-end and the telescoped technique in rats. *J Microsurg 2:3, 1980*.
147. Sully L et al: An experimental study of the sleeve technique in microarterial anastomoses. *Plast Reconstr Surg 70:186, 1982*.
148. Turan T, Ozcelik D, Kuran I, et al: Eversion with four sutures: an easy, fast, and reliable technique for microvascular anastomosis. *Plast Reconstr Surg 107(2):463, 2001*.
149. Hafner CD, Fogarty TJ, Cranley JJ: Nonsuture anastomosis of small arteries using a tissue adhesive. *Surg Forum 11: 417, 1963*.
150. Jacobsen JH, Moody RA, Kusserow BK, et al: The tissue response to a plastic adhesive used in combination with microsurgical technique in reconstruction of small arteries. *Surgery 60:379, 1966*.
151. Matras H, Chiari FM, Kletter G, Dinges HP: Zur klebung von mikrogefabanastomosen (Eine experimentelle studie). *In: Schmid E, Widmaier W, and Reichert H (Eds),* ***Weiderherstellung von Form und Funktion Organischer Einheiten.*** *Stuttgart, Georg Thieme Verlag, 1977, p 357*.
152. Aksik IA, Kikut RP, Apshkalne DL: Extraintracranial anastomosis performed by means of biological gluing materials: experimental and clinical study. *Microsurgery 7:2, 1986*.
153. Sagi A, Yu HL, Ferder M, et al: "No suture" microanastomosis using Vicryl rings and fibrin adhesive system: an unsuccesful attempt. *Plast Reconstr Surg 79:776, 1987*.
154. Park SH et al: A new microvascular anastomosis by using a sleeve method and tissue adhesive. *J Korean Soc Plast Reconstr Surg 13:1, 1986*.
155. Bowen CV, Leach DH, Crosby NL, Reynolds R: Microvascular anastomoses: a comparative study of fibrinogen adhesive and interrupted suture techniques. *Plast Reconstr Surg 97:792, 1996*.
156. Isogai N, Cooley BG, Kamiishi H: Clinical outcome of digital replantation using the fibrin glue-assisted microvascular anastomosis technique. *J Hand Surg 21B:573, 1996*.
157. Biemer E: Vein grafts in microvascular surgery. *Br J Plast Surg 30:197, 1977*.
158. Brener BJ, Raines JK, Darling RC: The end-to-end anastomosis of blood vessels of different diameters. *Surg Gynecol Obstet 138:249, 1974*.
159. Sindo ML, Nalbone VP: Clinical vessel anastomosis in head and neck free tissue transfer. *Facial Plast Surg 12:9, 1996*.
160. Godina M: Preferential use of end-to-side arterial anastomoses in free flap transfers. *Plast Reconstr Surg 64(5):673, 1979*.
161. Samaha FJ, Oliva A, Buncke GM, et al: A clinical study of end-to-end versus end-to-side techniques for microvascular anastomosis. *Plast Reconstr Surg 99:1109, 1997*.
162. Albertengo JB, Rodriguez A, Buncke HJ, Hall EJ: A comparative study of flap survival rates in end-to-end and end-to-side microvascular anastomosis. *Plast Reconstr Surg 67(2):194, 1981*.
163. Bas L, May JW Jr, Handren J, Fallon J: End-to-end versus end-to-side microvascular anastomosis patency in experimental venous repairs. *Plast Reconstr Surg 77(3):442, 1986*.
164. Lazzarini-Robertson AA: Hemodynamic principles and end-to-side microvascular anastomosis. *Surg Gynecol Obstet 147:339, 1978*.
165. Nam DA, Roberts TL, Acland RD: An experimental study of end-to-side microvascular anastomosis. *Surg Gynecol Obstet 147(3):339, 1978*.
166. Lauritzen C. A new and easier way to anastomose microvessels: an experimental study in rats. *Scand J Plast Reconstr Surg 14:65, 1980*.
167. Zhang L, Tuchler RE, Shaw WW, Siebert JW: A new technique for microvascular sleeve anastomosis. *Microsurgery 12:321, 1991*.
168. Nakayama Y, Soeda S, Iino T, Uchida A: Is the sleeve anastomosis a risky technique? *Br J Plast Surg 40:288, 1987*.
169. Sully L, Nightingale M, O'Brian B, Hurley J: An experimental study of the sleeve technique in microarterial anastomoses. *Plast Reconstr Surg 70:186, 1982*.
170. Wieslander JB, Mecklenburg CV, Aberg M: Endothelialization after end-to-end and end-in-end (sleeve) microarterial anastomoses. *Scand J Plast Reconstr Surg 18:193, 1984*.
171. Kanaujia RR, Hoi KI, Miyamoto Y, et al: Further technical considerations of the sleeve microanastomosis. *Plast Reconstr Surg 81:725, 1988*.
172. McLean DH, Buncke HJ: Use of the Saran wrap cuff in microsurgical arterial repairs. *Plast Reconstr Surg 51:624, 1973*.
173. Tschoff HM: Small artery anastomosis, using a cuff of dura mater and a tissue adhesive. *Plast Reconstr Surg 55:606, 1973*.
174. Harris GD, Finseth F, Buncke HJ: The microvascular anastomotic autogenous cuff. *Br J Plast Surg 34:50, 1981*.
175. Merrel JC, Zook EG, Russell RC: Cuffing techniques in microarterial surgery. *J Hand Surg 9A:76, 1984*.
176. Kanaujia RR: Micro-arterial anastomosis using only two sutures and an autogenous cuff. *J Hand Surg 13B:44, 1988*.
177. Hung LK, Au K, Ho YF: Comparative study of artery cuff and fat wrap in microvascular anastomosis in the rat. *Br J Plast Surg 41:278, 1988*.
178. Coleman DJ, Timmons MJ: Non-suture external cuff techniques for microvascular anastomosis. *Br J Plast Surg 42:550, 1989*.
179. Deshmukh GR, Yang Y, Tellis VA, Gerst PH: A simple cuff-suture technique for microvascular anastomosis. *J Reconstr Microsurg 8:491, 1992*.
180. Yamagata S, Handa H, Taki W, et al: Experimental non suture microvascular anastomosis using a soluble PVA tube and plastic adhesive. *J Microsurg 1:208, 1979*.
181. Mikaelson C, Arnbjornsson E.: Nonsuture end-to-end microvascular anastomosis using intravascular stents. *Ann Chir Gynaecol 85:36, 1996*.
182. Karamürsel S, Kayikcioglu A, Safak T, et al: A new technique for microvascular anastomosis: External metallic circle. *Plast Reconstr Surg 104:1059, 1999*.
183. Robbins TH: Microvascular anastomosis: vascular cuff technique. *Plast Reconstr Surg 87:567, 1991*.
184. Nakayama K, Tamiya T, Yamamoto K, et al: A simple new apparatus for small vessel anastomosis (free autograft of the sigmoid included). *Surgery 52:918, 1962*.

185. Ostrup LT, Berggren A: The Unilink instrument system for fast and safe microvascular anastomosis. *Ann Plast Surg 17:521, 1986*.
186. Ragnarsson R, Berggren A, Klintenberg C, et al: Microvascular anastomoses in irradiated vessels: a comparison between the Unilink system and sutures. *Plast Reconstr Surg 85:412, 1990*.
187. Berggren A, Ostrup LT, Ragnarsson R: Clinical experience with the Unilink/3M Precise microvascular anastomotic device. *Scand J Plast Reconstr Surg 27:35, 1993*.
188. Ahn CY, Shaw WW, Berns S, Markowitz BL: Clinical experience with the 3M microvascular coupling anastomotic device in 100 free-tissue transfers. *Plast Reconstr Surg 93:1481, 1994*.
189. Blair WF, Morecraft RJ, Steyers CM, et al: A microvascular anastomotic device: II. A histologic study in arteries and veins. *Microsurgery 10:29, 1989*.
190. Gilbert RW, Ragnarsson R, Berggren H, et al: Strength of microvascular anastomoses: comparison between the Unilink anastomotic system and sutures. *Microsurgery 10:40, 1989*.
191. Joji S, Muneshige H, Ikuta Y: Experimental study of mechanical microvascular anastomosis with new biodegradable ring device. *Br J Plast Surg 52:559, 1999*.
192. Ragnarsson R, Berggren A, Ostrup LT: Long-term evaluation of the Unilink anastomotic system: a study with light and scanning electron microscopy. *Scand J Plast Reconstr Hand Surg 26:167, 1993*.
193. Cope C, Lee K, Stern H, Pennington D: Use of the vascular closure staple clip applier for microvascular anastomosis in free-flap surgery. *Plast Reconstr Surg 106(1):107, 2000*.
194. Zeebregts C, Acosta R, Bolander L, et al: Clinical experience with non-penetrating vascular clips in free-flap reconstructions. *Br J Plast Surg 55(2):105, 2002*.
195. Shennib H, Korkola SJ, Bousette N, Giaid A: An automated interrupted suturing device for coronary artery bypass grafting: automated coronary anastomosis. *Ann Thorac Surg 70(3):1046, 2000*.
196. Vale BH, Frenkel A, Trenka-Benthin S, Matlaga BF: Microsurgical anastomosis of rat carotid arteries with the CO_2 laser. *Plast Reconstr Surg 77:759, 1986*.
197. Fried MP, Moll ER: Microvascular anastomoses. An evaluation of laser-assisted technique. *Arch Otolaryngol Head Neck Surg 113:968, 1987*.
198. Krueger RR, Almquist EE: Argon laser coagulation of blood for the anastomosis of small vessels. *Lasers Surg Med 5:55, 1985*.
199. Jain KK, Gorisch W: Repair of small blood vessels with the neodymium-YAG laser: a preliminary report. *Surgery 85:684, 1979*.
200. Samonte BR, Fried MP: Laser-assisted microvascular anastomosis using CO_2 and KPT/532 lasers. *Lasers Surg Med 11:511, 1991*.
201. Unno N, Sakaguchi S, Koyano K: Microvascular anastomosis using a new diode laser system with a contact probe. *Lasers Surg Med 9:160, 1989*.
202. Chuck RS, Oz MC, Delohery TM, et al: Dye-enhanced laser tissue welding. *Lasers Surg Med 9:471, 1989*.
203. Schober R, Ulrich F, Sander T, et al: Laser-induced alteration of collagen substructure allows microsurgical tissue welding. *Science 232:1421, 1986*.
204. Flemming AF, Colles MJ, Guillianotti R, et al: Laser-assisted microvascular anastomosis of arteries and veins: laser tissue welding. *Br J Plast Surg 41:378 1988*.
205. Kiyoshige Y: CO_2 laser assisted microvascular anastomosis: first clinical trials. *J Reconstr Microsurg 7:61, 1991*.
206. Solomon GA, Yaremchuk MJ, Manson PN: Doppler ultrasound surface monitoring of both arterial and venous flow in clinical free tissue transfer. *J Reconstr Microsurg 3:39, 1986*.
207. Walkinshaw M, et al: Clinical evaluation of laser doppler blood flow measurements in free flaps. *Ann Plast Surg 18:212, 1987*.
208. May JW, et al: Removable thermocouple probe microvascular patency monitor: an experimental and clinical study. *Plast Reconstr Surg 72:366, 1983*.
209. Acland RD: Discussion of DH Harrison, M Girling, and G Mott, "Experience in monitoring the circulation in free-flap transfers". *Plast Recontr Surg 68:554, 1981*.
210. Kaufman T, et al: Is experimental muscle flap temperature a reliable indicator of its viability? *Ann Plast Surg 19:34, 1987*.
211. Khouri RK, Shaw WW: Monitoring of free flaps with surface-temperature recordings: Is it reliable? *Plast Reconstr Surg 89:495, 1992*.
212. Jones NF: Discussion of "Monitoring of free flaps with surface-temperature recordings: Is it reliable?" by RK Khouri and WW Shaw. *Plast Reconstr Surg 89:500, 1992*.
213. Jones NF, Gupta R: Postoperative monitoring of pediatric toe-to-hand transfers with differential pulse oximetry. *J Hand Surg 26A(3):525, 2001*.
214. Roberts JO, Jones BM: Direct anastomotic assessment for postoperative microvascular monitoring. *Ann Plast Surg 19:219, 1987*.
215. Swartz WM, et al: Direct monitoring of microvascular anastomoses with the 20-MHz ultrasonic doppler probe: An experimental and clinical study. *Plast Reconstr Surg 81:149, 1988*.
216. Fernando B, Young VL, Logan SE: Miniature implantable laser doppler probe monitoring of free tissue transfer. *Ann Plast Surg 20:434, 1988*.
217. Rothkopf DM, et al: Radial and ulnar artery repairs: Assessing patency rates with color Doppler ultrasonographic imaging. *J Hand Surg 18A:626, 1993*.
218. Whitney TM, et al: Improved salvage of complicated microvascular transplants monitored with quantitative fluorometry. *Plast Reconstr Surg 90:105, 1992*.
219. Jones JW, Glassford EJ, Hillman WCJ: Remote monitoring of free flaps with telephonic transmission of photoplethysmograph waveforms. *J Reconstr Microsurg 5:141, 1989*.
220. Jones NF: Intraoperative and postoperative monitoring of microsurgical free tissue transfers. *Clin Plast Surg 19:783, 1992*.
221. Reus WF, Robson MC, Zachary L, Heggers JP: Acute effects of tobacco smoking on blood flow in the cutaneous microcirculation. *Br J Plast Surg 37:213, 1984*.
222. Siana JE, Rex S, Gottrup F: The effect of cigarette smoking on wound healing. *Scand J Plast Reconstr Surg 23:207, 1989*.
223. Lawrence WT, Murphy RC, Robson MC, Heggers JP: The detrimental effect of cigarette smoking on flap survival: an experimental study in the rat. *Br J Plast Surg 37:216, 1984*.

224. Nolan J, Jenkins RA, Kurihara K, Schultz RC: The acute effects of cigarette smoke exposure on experimental skin flaps. *Plast Reconstr Surg 75:544, 1985*.
225. Gu YD, Zhang GM, Li FG, Jiang JF: Clinical and experimental studies of cigarette smoking in microvascular tissue transfers. *Microsurgery 14:391, 1993*.
226. van Adrichem LNA, Hoegen R, Hovius SER, et al: The effect of cigarette smoking on the survival of free vascularized and pedicled epigastric flaps in the rats. *Plast Reconstr Surg 97:86, 1996*.
227. Rao VK, Morrison WA, O'Brien BM: Effect of nicotine on blood flow and patency of experimental microvascular anastomosis. *Ann Plast Surg 11:206, 1983*.
228. Yaffe B, Cushin BJ, Strauch B: Effect of cigarette smoking on experimental microvascular anastomosis. *Microsurgery 5:70, 1984*.
229. Chang LD, Buncke G, Slezak S, Buncke HJ: Cigarette smoking, plastic surgery, and microsurgery. *J Reconstr Microsurgery 12:467, 1996*.
230. Arnez ZM, Bajec J, Bardsley AF, et al: Experience with 50 free TRAM flap breast reconstructions. *Plast Reconstr Surg 87:470, 1991*.
231. Reus WF, Colen LB, Straker DJ: Tobacco smoking and complications in elective microsurgery. *Plast Reconstr Surg 89:490, 1992*.
232. van Adrichem LNA, Hovius SE, van Strik R, et al: The acute effect of cigarette smoking on the microcirculation of a replanted digit. *J Hand Surg 17A:230, 1992*.
233. Parry SW, Toth BA, Elliott LF: Microvascular free-tissue transfer in children. *Plast Reconstr Surg 81:838, 1985*.
234. Canales F, et al: Microvascular tissue transfer in paediatric patients: analysis of 106 cases. *Br J Plast Surg 44:423, 1991*.
235. Yucel A, Aydin Y, Yazar S, et al: Elective free-tissue transfer in pediatric patients. *J Reconstr Microsurg 17(1):27, 2001*.
236. Clarke HM, Upton J, Zuker RM, Manktelow RT: Pediatric free tissue transfer: an evaluation of 99 cases. *Can J Surg 36(6):525, 1993*.
237. Duteille F, Lim A, Dautel G: Free flap coverage of upper and lower limb tissue defects in children: a series of 22 patients. *Ann Plast Surg 50(4):344, 2003*.
238. Chick LR, et al: Free flaps in the elderly. *Plast Reconstr Surg 90:87, 1992*.
239. Shestak KC, Jones NF: Microsurgical free-tissue transfer in the elderly patient. *Plast Reconstr Surg 88:259, 1991*.
240. Serletti JM, Higgins JP, Moran S, Orlando GS: Factors affecting outcome in free-tissue transfer in the elderly. *Plast Reconstr Surg 106(1):66, 2000*.
241. Banis JC Jr, et al: Microsurgical adjuncts in salvage of the ischemic and diabetic lower extremity. *Clin Plast Surg 19:881, 1992*.
242. Karp NS, Kasabian AK, Siebert JW, et al: Microvascular free-flap salvage of the diabetic foot: a 5-year experience. *Plast Reconstr Surg 94:834, 1994*.
243. Moran SL, Illig KA, Green RM, Serlettii JM: Free-tissue transfer in patients with peripheral vascular disease: a 10-year experience. *Plast Reconstr Surg 109(3):999, 2002*.
244. Moran SL, Salgado CJ, Serletti JM: Free tissue transfer in patients with renal disease. *Plast Reconstr Surg 113(7):2006, 2004*.
245. Larson RM, et al: Structural and biochemical alterations in canine venous autografts. *J Surg Res 25:380, 1978*.
246. Biemer E, et al: Autologous vein grafts as artery replacement in microsurgery. An experimental study of micro- and macromorphologic changes 3 weeks to 12 months postoperatively. *Handchirurgie 13:108, 1981*.
247. Mitchell GM, et al: The long-term fate of microvenous autografts. *Plast Reconstr Surg 82:473, 1988*.
248. Young PH, Yasargil MG: Use of small-diameter synthetic grafts in carotid bypasses in rats. *J Microsurg 3:3, 1981*.
249. Tizian C: Patency rates in microvascular prostheses: An experimental study. *Br J Plast Surg 34:72, 1981*.
250. Watanabe K: Microarterial prostheses of expanded polytetrafluoroethylene. *J Microsurg 2:11, 1980*.
251. Hess F: History of (micro) vascular surgery and the development of small-caliber blood vessel prostheses (with some notes on patency rates and re-endothelialization). *Microsurgery 6:59, 1985*.
252. O'Brien CJ, et al: One millimetre polytetrafluoroethylene (Gore-Tex) as a microvascular prosthesis: Technique and early patency. *Aust NZ J Surg 54:469, 1984*.
253. Hess F, et al: Evaluation of the patency rate of fibrous microvascular polyurethane prostheses after implantation in the rat aorta. *Microsurgery 4:178, 1983*.
254. Shen T-Y, et al: The use of long synthetic microvascular grafts to vascularise free flaps in rabbits. *Br J Plast Surg 41:305, 1988*.
255. van der Lei B, Wildevuur CRH: Microvascular polytetrafluoroethylene prostheses: The cellular events of healing and prostacyclin production. *Plast Reconstr Surg 81:735, 1988*.
256. Samuels RM, et al: Long-term histological changes in 1 millimeter polytetrafluoroethylene (Gore-tex) prosthetic arterial grafts. *Microsurgery 10:274, 1989*.
257. Yeh H-S, et al: Human umbilical artery for microvascular grafting—Experimental study in the rat. *J Neurosurg 61:737, 1984*.
258. Roberts AHN, et al: Glutaraldehyde-tanned microvascular grafts. *Br J Plast Surg 42:429, 1989*.
259. Tan E, O'Brien BM, Brennen M: Free flap transfer in rabbits using irradiated recipient vessels. *Br J Plast Surg 31:121, 1978*.
260. Watson JS: Experimental microvascular anastomosis in radiated vessels: a study of the patency rate and the histopathology of healing. *Plast Reconstr Surg 63:525, 1979*.
261. Krag C, De Rose G, Lyczakowski T, et al: Free flaps and irradiated recipient vessels: an experimental study in rabbits. *Br J Plast Surg 35:328, 1982*.
262. Ragnarsson R, Berggren A, Klintenberg C, Ostrup L: Microvascular anastomoses in irradiated vessels: a comparison between the Unilink system and sutures. *Plast Reconstr Surg 85:412, 1990*.
263. Aitasalo K, Aro HT, Virolainen P, Virolainen E: Healing of microvascular free skin flaps in irradiated recipient tissue beds. *Am J Surg 164:662, 1992*.
264. Kiener JL, Hoffman WY, Mathes SJ: Influence of radiotherapy on microvascular reconstruction in the head and neck region. *Am J Surg 162:404, 1991*.
265. Mulholland S, Boyd B, McCabe S, et al: Recipient vessels in head and neck microsurgery: radiation effect and vessel access. *Plast Reconstr Surg 92:628, 1993*.
266. Reece GP, Schusterman MA, Miller MJ, et al: Morbidity associated with free-tissue transfer after radiotherapy and chemotherapy in elderly cancer patients. *J Reconstr Microsurgery 10:375, 1994*.

267. Bengston BP, Schusterman MA, Baldwin BJ, et al: The influence of prior radiotherapy on the development of postoperative complications and success of free tissue transfers in head and neck cancer reconstruction. *Am J Surg 166:326, 1993*.
268. Schusterman MA, Miller MJ, Reece GP, et al: A single center's experience with 308 free flaps for repair of head and neck cancer defects. *Plast Reconstr Surg 93:472, 1994*.
269. Kroll SS, Schustermann MA, Reece GP, et al: Choice of flap and incidence of free flap success. *Plast Reconstr Surg 98:459, 1996*.
270. Khouri RK, Cooley BC, Kunselman MA, et al. A prospective study of microvascular free-flap surgery and outcome. *Plast Reconstr 102:711, 1998*.
271. Guelincks PJ: Scanning electron microscopy of irradiated recipient blood vessels in head and neck free flaps. *Plast Reconstr Surg 74:217, 1984*.
272. Pederson WC: Upper extremity microsurgery. *Plast Reconstr Surg 107(6):1524, 2001*.
273. Soutar DS et al: The radial forearm flap: A versatile method for intraoral reconstruction. *Br J Plast Surg 36:1, 1983*.
274. Matthews RN et al: Radial forearm flap for floor of mouth reconstruction. *Br J Surg 72:561, 1985*.
275. Soutar DS, McGregor IA: The radial forearm flap in intraoral reconstruction: The experience of 60 consecutive cases. *Plast Reconstr Surg 78:1, 1986*.
276. Takato T et al: Oral and pharyngeal reconstruction using the free forearm flap. *Arch Otolaryngol Head Neck Surg 113:873, 1987*.
277. Gilbert A, Teot L: The free scapular flap. *Plast Reconstr Surg 69:601, 1982*.
278. Urbaniak JR, et al: The vascularized cutaneous scapular flap. *Plast Reconstr Surg 69:772, 1982*.
279. Barwick WJ, Goodkin DJ, Serafin D: The free scapular flap. *Plast Reconstr Surg 69:779, 1982*.
280. Nassif TN et al: The parascapular flap: A new cutaneous microsurgical free flap. *Plast Reconstr Surg 69:591, 1982*.
281. Sullivan MJ, Carroll WR, Kuriloff DB: Lateral arm free flap in head and neck reconstruction. *Arch Otolaryngol Head Neck Surg 118:1095, 1992*.
282. O'Brien BM et al: Microvascular osteocutaneous transfer using the groin flap and iliac crest, the dorsalis pedis flaps and second metatarsal. *Br J Plast Surg 32:188, 1979*.
283. Zuker RM, Manktelow RT: The dorsalis pedis free flap: Technique of elevation, foot closure, and flap application. *Plast Reconstr Surg 77:93, 1986*.
284. Hing DN, Buncke HJ, Alpert BS: Use of the temporoparietal free fascial flap in the upper extremity. *Plast Reconstr Surg 81:534, 1988*.
285. Kaplan IB, Gilbert DA, Terzis JK: The vascularized fascia of the scalp. *J Reconstr Microsurg 5:1989*.
286. Carstens MH, et al: Clinical applications of the subgaleal fascia. *Plast Reconstr Surg 87:615, 1991*.
287. Ismail TIA: The free fascial forearm flap. *Microsurgery 10:155, 1989*.
288. Jin Y-T, Cao H-P, Chang T-S: Clinical application of the free scapular fascial flap. *Ann Plast Surg 23:170, 1989*.
289. Wei FC, Jain V, Celik N, et al: Have we found an ideal soft-tissue flap? An experience with 672 anterolateral thigh flaps. *Plast Reconstr Surg 109(7):2219, 2002*.
290. Chen HC, Tang YB. Anterolateral thigh flap: an ideal soft tissue flap. *Clin Plast Surg 30(3):383, 2003*.
291. Kimata Y, Uchiyama K, Ebihara S, et al: Anterolateral thigh flap donor-site complications and morbidity. *Plast Reconstr Surg 106(3):584, 2000*.
292. Celik N, Wei FC, Lin CH, et al: Technique and strategy in anterolateral thigh perforator flap surgery, based on an analysis of 15 complete and partial failures in 439 cases. *Plast Reconstr Surg 109(7):2211, 2002*.
293. Wei FC, Celik N: Perforator flap entity. *Clin Plast Surg 30:325, 2003*.
294. Mardini S, Tsai FC, Wei FC: The thigh as a model for free style free flaps. *Clin Plast Surg 30(3):473, 2003*.
295. Kim JT, Koo BS, Kim SK: The thin latissimus dorsi perforator-based free flap for resurfacing. *Plast Reconstr Surg 107(2):374, 2001*.
296. Chen SL, Chen TM, Wang HJ: Free thoracodorsal artery perforator flap in extremity reconstruction: 12 cases. *Br J Plast Surg 57:525, 2004*.
297. Blondeel PN, Van Landuyt K, Hamdi M, Monstrey SJ: Soft tissue reconstruction with the superior gluteal artery perforator flap. Clin Plast Surg 30(3):371, 2003.
298. Guerra AB, Metzinger SE, Bidros RS, et al: Breast reconstruction with gluteal artery perforator (GAP) flaps: a critical analysis of 142 cases. *Ann Plast Surg 52(2):118, 2004*.
299. Chevray PM: Breast reconstruction with superficial inferior epigastric artery flaps: a prospective comparison with TRAM and DIEP flaps. *Plast Reconstr Surg 114(5):1077, 2004*.
300. Gill PS, Hunt JP, Guerra AB, et al: A 10-year retrospective review of 758 DIEP flaps for breast reconstruction. *Plast Reconstr Surg 113(4):1153, 2004*.
301. Hamdi M, Blondeel P, Van Landuyt K, et al: Bilateral autogenous breast reconstruction using perforator free flaps: a single center's experience. *Plast Reconstr Surg 114(1): 83, 2004*.
302. Thoma A, Veltri K, Khuthaila D, et al: Comparison of the deep inferior epigastric perforator flap and free transverse rectus abdominis myocutaneous flap in postmastectomy reconstruction: a cost-effectiveness analysis. *Plast Reconstr Surg 113(6):1650, 2004*.
303. Tamai S: Free muscle transplants in dogs with microsurgical neurovascular anastomoses. *Plast Reconstr Surg 46:219, 1970*.
304. Harii K, Ohmori K, Torii S: Free gracilis muscle transplantation with microneurovascular anastomoses for the treatment of facial paralysis. *Plast Reconstr Surg 57:133, 1976*.
305. Sixth People's Hospital, Shanghai: Free muscle transplantation by microsurgical neurovascular anastomoses. *Chin Med J (Engl) 2:47, 1976*.
306. Ikuta Y, Kubo T, Tsuge K: Free muscle transplantation by microsurgical technique to treat severe Volkmann's contracture. *Plast Reconstr Surg 58:407, 1976*.
307. Salgado CJ, Orlando GS, Herceg S, Serletti JM: Pfannenstiel incision as an alternative approach for harvesting the rectus abdominis muscle for free-tissue transfer. *Plast Reconstr Surg 105(4):1330, 2000*.
308. McCraw JB, Dibbell DG: Experimental definition of independent myocutaneous vascular territories. *Plast Reconstr Surg 60:212, 1977*.
309. McCraw JB, Dibbell DG, Carraway JH: Clinical definition of independent myocutaneous vascular territories. *Plast Reconstr Surg 60:341, 1977*.

310. Maxwell GP: Musculocutaneous free flaps. *Clin Plast Surg 7:111, 1980.*
311. Fujino T, Harashina T, Aoyagi F: Reconstruction for aplasia of the breast and pectoral region by microvascular transfer of a free flap from the buttock. *Plast Reconstr Surg 56:178, 1975.*
312 Anderson RG: Facial nerve disorders and surgery. *Selected Read Plast Surg 9(20), 2001.*
313. Masson JA: Hand III: Flexor tendons. *Selected Read Plast Surg 9(34), 2003.*
314. Masson JA: Hand IV: Extensor tendons, Dupuytren's disease, and rheumatoid arthritis. *Selected Read Plast Surg 9(35), 2003.*
315. Lin SH, Chuang DC, Hattori Y, Chen HC: Traumatic major muscle loss in the upper extremity: reconstruction using functioning free muscle transplantation. *J Reconstr Microsurg 20(3):227, 2004.*
316. Cavadas PC, Sanz-Gimenez-Rico JR, Landin L, Martinez-Soriano F: Segmental gracilis free flap based on secondary pedicles: anatomical study and clinical series. *Plast Reconstr Surg 114(3):684, 2004.*
317. Hasen KV, Gallegos ML, Dumanian GA: Extended approach to the vascular pedicle of the gracilis muscle flap: anatomical and clinical study. *Plast Reconstr Surg 111(7):2203, 2003.*
318. Lasso JM, Rosado J, Perez Luengo E, et al: Gracilis flap: a variation of the main vascular pedicle (letter). *Plast Reconstr Surg 114(2):597, 2004.*
319. Lin PY, Kuo YR, Kueh NS, Jeng SF: Refinement of minimally invasive harvest of gracilis muscle flap without endoscopic assistance. *J Reconstr Microsurg 19(8):537, 2003.*
320. Terzis JK et al: Recovery of function in free muscle transplants using microneurovascular anastomoses. *J Hand Surg 3:37, 1978.*
321. Harii K: Microneurovascular free muscle transplantation for reanimation of facial paralysis. *Clin Plast Surg 6:361, 1979.*
322. Manktelow RT, McKee NH: Free muscle transplantation to provide active finger flexion. *J Hand Surg 3:416, 1978.*
323. Manktelow RT: Muscle transplantation. *In: Serafin D, Buncke HJ Jr (eds),* ***Microsurgical Composite Tissue Transplantation.*** *St Louis, CV Mosby, 1979, Ch 26, pp 369-390.*
324. Manktelow RT, Zuker RM, McKee NH: Functioning free muscle transplantation. *J Hand Surg 9A:32, 1984.*
325. Frey M: The importance of the correct resting tension in muscle transplantation. Experimental and clinical aspects. *Plast Reconstr Surg 71:510, 1983.*
326. Kuzon WM Jr et al: The effect of intraoperative ischemia on the recovery of contractile function after free muscle transfer. *J Hand Surg 13A:263, 1988.*
327. Ostrup LT, Fredrickson JM: Distant transfer of a free living bone graft by microvascular anastomoses. *Plast Reconstr Surg 54:274, 1974.*
328. Taylor GI, Miller GDH, Ham FJ: The free vascularized bone graft: A clinical extension of microvascular techniques. *Plast Reconstr Surg 55:533, 1975.*
329. O'Brien BM (Ed): ***Microvascular Reconstructive Surgery.*** *New York, Churchill Livingstone, 1977.*
330. Buncke HJ Jr et al: Free osteocutaneous flap from a rib to the tibia. *Plast Reconstr Surg 59:799, 1977.*
331. Serafin D, Villarreal-Rios A, Georgiade NG: A rib-containing free flap to reconstruct mandibular defects. *Br J Plast Surg 30:263, 1977.*
332. McKee DM: Microvascular bone transplantation. *Clin Plast Surg 5:283, 1978.*
333. Ariyan S, Finseth FJ: The anterior chest approach for obtaining free osteocutaneous rib grafts. *Plast Reconstr Surg 62:676, 1978.*
334. Daniel RK: Free rib transfer by microvascular anastomoses (Letter). *Plast Reconstr Surg 59:737, 1977.*
335. Taylor GI, Watson N: One-stage repair of compound leg defects with free, revascularized flaps of groin skin and iliac bone. *Plast Reconstr Surg 61:494, 1978.*
336. Taylor GI, Townsend P, Corlett R: Superiority of the deep circumflex iliac vessels as the supply for free groin flaps. Clinical work. *Plast Reconstr Surg 64:745, 1979.*
337. O'Brien BMcC et al: Microvascular osteocutaneous transfer using the groin flap and iliac crest and the dorsalis pedis flap and second metatarsal. *Br J Plast Surg 32:188, 1979.*
338. Biemer E, Stock W: Total thumb reconstruction: A one-stage reconstruction using an osteocutaneous forearm flap. *Br J Plast Surg 36:52, 1983.*
339. Cutting CB, McCarthy JG, Berenstein A: Blood supply of the upper craniofacial skeleton: The search for a composite calvarial bone flap. *Plast Reconstr Surg 74:603, 1984.*
340. Dos Santos LF: Retalho escapular: Um novo retalho livre microcirurgico. *Rev bras Cir 70:133, 1980.*
341. Urbaniak JR: The vascularized cutaneous scapular flap. *Plast Reconstr Surg 69:772, 1982.*
342. Weiland AJ: Bone grafts: A radiologic, histologic, and biomechanical model comparing autografts, allografts, and free vascularized bone grafts. *Plast Reconstr Surg 74:368, 1984.*
343. Canalis RF: A method for the assessment of osteoneogenesis in experimental bone grafts. *Arch Otolaryngol 107:482, 1981.*
344. Taylor GI: The current status of free vascularized bone grafts. *Clin Plast Surg 10:185, 1983.*
345. Albrektsson T: The healing of autologous bone grafts after varying degrees of surgical trauma. *J Bone Joint Surg 62B:403, 1980.*
346. Ostrup L, Fredrickson J: Reconstruction of mandibular defects after radiation using a free living bone graft transferred by microvascular anastomoses. Experimental study. *Plast Reconstr Surg 55:563, 1975.*
347. Brown K, Cruess R: Bone and cartilage transplantation in orthopedic surgery: a review. *J Bone Joint Surg 64A:270, 1982.*
348. Hurst L, Mirza M, Spellman W: Vascularized fibular graft for infected loss of the ulna: Case report. *J Hand Surg 7:498, 1982.*
349. Griffin JR, Thornton JF: Lower extremity reconstruction. *Selected Read Plast Surg 10(5)Part 1, 2005.*
350. Berggren A, Weiland AJ, Ostrup LT, Dorfman H: Microvascular free bone transfer with revascularization of the medullary arnd periosteal circulation or the periosteal circulation alone. A comparative experimental study. *J Bone Joint Surg Am 64(1):73, 1982.*
351. Serafin D et al: Vascularized rib-periosteal and osteocutaneous reconstruction of the maxilla and mandible: An assessment. *Plast Reconstr Surg 66:718, 1980.*
352. Georgescu AV, Ivan O: Serratus anterior–rib free flap in limb bone reconstruction. *Microsurgery 23:217, 2003.*

353. Taylor GI: Fibular transplantation. *In: Serafin D, Buncke HJ Jr (Eds),* ***Microsurgical Composite Tissue Transplantation.*** *St Louis, CV Mosby, 1979, Ch 29, pp 418-423.*
354. Hidalgo DA: Fibula free flap: A new method of mandible reconstruction. *Plast Reconstr Surg 84:71, 1989.*
355. Hidalgo DA: Aesthetic improvements in free-flap mandible reconstruction. *Plast Reconstr Surg 88:574, 1991.*
356. Karanas YL, Antony A, Rubin G, Chang J: Preoperative CT angiography for free fibula transfer. *Microsurgery 24:125, 2004.*
357. Taylor GI, Townsend P, Corlett R: Superiority of the deep circumflex iliac vessels as the supply for free groin flaps. Experimental work. *Plast Reconstr Surg 64:595, 1979.*
358. Shenaq SM: Refinements in mandibular reconstruction. *Clin Plast Surg 19:809, 1992.*
359. Mirovsky Y, Neuwirth MG: Comparison between the outer table and intracortical methods for obtaining autogenous bone graft from the iliac crest. *Spine 25(13):1722, 2000.*
360. Mialhe C, Brice M: A new compound osteomyocutaneous free flap: the posterior iliac artery flap. *Br J Plast Surg 38(1):30, 1985.*
361. Coleman JJ et al: Ten years experience with the free jejunal autograft. *Am J Surg 154:394, 1987.*
362. Seidenberg B et al: Immediate reconstruction of the cervical esophagus by a revascularized isolated jejunal segment. *Ann Surg 149:162, 1959.*
363. Jurkiewicz MJ: Vascularized intestinal graft for reconstruction of the cervical esophagus and pharynx. *Plast Reconstr Surg 36:509, 1965.*
364. Robinson DW, MacLeod A: Microvascular free jejunum transfer. *Br J Plast Surg 35:258, 1982.*
365. Tabah RJ et al: Microvascular free tissue transfer in head and neck and esophageal surgery. *Am J Surg 148:498, 1984.*
366. Gluckman JL et al: Complications associated with free jejunal graft reconstruction of the pharyngoesophagus. A multiinstitutional experience with 52 cases. *Head Neck Surg 7:200, 1985.*
367. Reece GP, Bengtson BP, Schusterman MA: Reconstruction of the pharynx and cervical esophagus using free jejunal transfer. *Clin Plast Surg 21:125, 1994.*
368. Freeman JL et al: Greater omentum used for carotid cover after pharyngolaryngoesophagectomy and gastric 'pull-up' or colonic 'swing'. *Arch Otolaryngol 108:685, 1982.*
369. Arnold PG, Irons GB: The greater omentum: Extensions in transposition and free transfer. *Plast Reconstr Surg 67:169, 1981.*
370. Hoepfner: Cited in Kleinert HE et al: Replantation. *Clin Symp 43:2, 1991.*
371. Perritt RA: Recent advances in corneal surgery. *IN: American Academy of Ophthalmology and Otolaryngology Course No. 280, 1950.*
372. Kleinert HE, Kasdan M, Romero J: Small blood vessel anastomosis for salvage of severely injured upper extremity. *J Bone Joint Surg 45A:788, 1963.*
373. Malt RA, McLehman: Cited in Kleinert HE et al: Replantation. *Clin Symp 43:2, 1991.*
374. Kleinert HE, Kasdan ML: Anastomosis of digital vessels. *J Kentucky Med Assoc 63:106, 1965.*
375. Komatsu S, Tamai S: Successful replantation of a completely cut-off thumb. Case report. *Plast Reconstr Surg 42:374, 1968.*
376. Kleinert HE et al: Replantation. *Clin Symp 43:2, 1991.*
377. Morrison WA, O'Brien BM, MacLeon AM: Major limb replantations. *Orthop Clin North Am 2:343, 1977.*
378. Wilson CS et al: Replantation of the upper extremity. *Clin Plast Surg 10:85, 1983.*
379. O'Brien BMcC: Reconstructive microsurgery of the upper extremity. *J Hand Surg 15:316, 1990.*
380. Whitney TM et al: Reconstruction of the upper extremity with multiple microvascular transplants: analysis of method, cost, and complications. *Ann Plast Surg 23:396, 1989.*
381. Eisenhardt HJ et al: Energy metabolism and histomorphological findings in replanted rat hind limbs using various conservation methods. *Microsurgery 5:61, 1984.*
382. Miller SH et al: Effects of tourniquet ischemia and postischemic edema on muscle metabolism. *J Hand Surg 4:547, 1979.*
383. Muramatsu I et al: Metabolic and histologic changes in the ischemic muscles of replanted dog legs. *Clin Orthop 196:292, 1985.*
384. Nunley JA, Koman LA, Urbaniak JR: Arterial shunting as an adjunct to major limb revascularization. *Ann Surg 193:271, 1981.*
385. Tamai S et al: Traumatic amputation of digits: The fate of remaining blood. An experimental and clinical study. *J Hand Surg 2:13, 1977.*
386. Usui M, Sakata H, Ishii S: Effect of fluorocarbon perfusion upon the preservation of amputated limbs. An experimental study. *J Bone Joint Surg 67B:473, 1985.*
387. Smith AR et al: Limb preservation in replantation surgery. *Plast Reconstr Surg 75:227, 1985.*
388. Fukui A et al: Continuous local intra-arterial infusion of anticoagulants for digit replantation and treatment of damaged arteries. *J Reconstr Microsurg 5:127, 1989.*
389. Meyer VE, Chen Z-W, Beasley RW: Basic technical considerations in reattachment surgery. *Orthop Clin North Am 12:871, 1981.*
390. Chow JA et al: Forearm replantation—Long term functional results. *Ann Plast Surg 10:15, 1983.*
391. Russell RC et al: The late functional results of upper limb revascularization and replantation. *J Hand Surg 9A:623, 1984.*
392. Weiland AJ et al: Replantation of digits and hands: Analysis of surgical techniques and functional results in 71 patients with 86 replantations. *J Hand Surg 2:1, 1977.*
393. Strauch B et al: Problems and complications encountered in replantation surgery. *Hand Clin 2:389, 1986.*
394. Waikakul S, Sakkarnkosol S, Vanadurongwan V, Unnanuntana A: Results of 1018 digital replantations in 552 patients. *Injury 31(1):33, 2000.*
395. Tamai S: Digital replantation. *Clin Plast Surg 5:195, 1978.*
396. Kleinert H, Jablon M, Tsai T: An overview of replantation and results of 347 replants in 245 patients. *J Trauma 20:390, 1980.*
397. Tsai T-M, McCabe SJ, Maki Y: A technique for replantation of the finger tip. *Microsurgery 10:1, 1989.*
398. Thomas BP, Katsarma E, Tsai TM.: Replantation of total degloving of the hand: a case report. *J Reconstr Microsurg 19(4):217, 2003.*
399. Ross DC, Manktelow RT, Wells MT, Boyd JB: Tendon function after replantation: prognostic factors and trategies to enhance total active motion. *Ann Plast Surg 51(2):141, 2003.*

400. Adani R, Marcoccio I, Castagnetti C, Tarallo L: Long-term results of replantation for complete ring avulsion amputations. *Ann Plast Surg 51(6):564, 2003*.
401. Gold AH, Lee GW: Upper extremity replantation: Current concepts and patient selection. *J Trauma 21:551, 1981*.
402. Urbaniak JR: Replantation of amputated parts: Technique, results, and indications. *In: **AAOS Symposium on Microsurgery.** St Louis, CV Mosby, 1979, pp 64-82*.
403. May JW, Toth BA, Gardner M: Digital replantation distal to the proximal interphalangeal joint. *J Hand Surg 7:161, 1982*.
404. Jones JM, Schenck RR, Chesney RB: Digital replantation and amputation—Comparison of function. *J Hand Surg 7:183, 1982*.
405. Yu JC, Shieh SJ, Lee JW, et al: Secondary procedures following digital replantation and revascularization. *Br J Plast Surg 56(2):125, 2003*.
406. Kutz JE, Jupiter JB, Tsai T-M: Lower limb replantation. A report of nine cases. *Foot and Ankle 3:17, 1983*.
407. Nahai F, Hester TR, Jurkiewicz MJ: Microsurgical replantation of the scalp. *J Trauma 25:897, 1985*.
408. Juri J, Irigaray A, Zeaiter C: Reimplantation of scalp. *Ann Plast Surg 24:354, 1990*.
409. Sakai S, Soeda S, Ishii Y: Avulsion of the scalp: Which one is the best artery for anastomosis? *Ann Plast Surg 24:350, 1990*.
410. Arashiro K, Ohtsuka H, Ohtani K, et al: Entire scalp replantation: case report and review of the literature. *J Reconstr Microsurg 11:245, 1995*.
411. Juri J et al: Ear replantation. *Plast Reconstr Surg 80:431, 1987*.
412. Mutimer KL, Banis JC, Upton J: Microsurgical reattachment of totally amputated ears. *Plast Reconstr Surg 79:535, 1987*.
413. Turpin IM: Microsurgical replantation of the external ear. *Clin Plast Surg 17:397, 1990*.
414. Sadove RC: Successful replantation of a totally amputated ear. *Ann Plast Surg 24:366, 1990*.
415. Shelley OP, Villafane O, Watson SB: Successful partial ear replantation after prolonged ischaemia time. *Br J Plast Surg 53(1):76, 2000*.
416. Abbou CC et al: Reimplantation du penis et des deux testicules apres autoemasculation complete. *Chirurgie 105:354, 1979*.
417. Jordan GH, Gilbert DA: Management of amputation injuries of the male genitalia. *Urol Clin North Am 16:359, 1989*.
418. Tamai S, Nakamura Y, Motomiya Y: Microsurgical replantation of a completely amputated penis and scrotum. *Plast Reconstr Surg 60:287, 1977*.
419. Holtje W-J: Successful replantation of an amputated upper lip. *Plast Reconstr Surg 73:664, 1984*.
420. Schubert W et al: Use of the labial artery for replantation of the lip and chin. *Ann Plast Surg 20:256, 1988*.
421. Day TA, Tarr C, Zealear D, et al: Tongue replantation in an animal model. *Microsurgery 20(3):105, 2000*.
422. Tajima S, Ueda K, Tanaka Y: Successful replantation of a bitten-off nose by microvascular anastomosis. *Microsurgery 10:5, 1989*.
423. Wilhelmi BJ, Kang RH, Movassaghi K, et al: First successful replantation of face and scalp with single-artery repair: model for face and scalp transplantation. *Ann Plast Surg 50(5):535, 2003*.
424. Lipa JE, Butler CE: Enhancing the outcome of free latissimus dorsi muscle flap reconstruction of scalp defects. *Head Neck 26(1):46, 2004*.
425. Ademoglu Y, Ada S, Kaplan I: Should the amputations of the great toe be replanted? *Foot Ankle Int 21(8):673, 2000*.
426. Tamai S: Twenty years' experience of limb replantation: Review of 293 upper extremity replants. *J Hand Surg 7:549, 1982*.
427. Green DP, Anderson JR: Closed reduction and percutaneous pin fixation of fractured phalanges. *J Bone Joint Surg 55:1651, 1973*.
428. Urbaniak JR, Hayes MG, Bright DS: Management of bone in digital replantation: Free vascularized and composite bone grafts. *Clin Orthop 133:184, 1978*.
429. Lister G: Interosseous wiring of the digital skeleton. *J Hand Surg 3:427, 1978*.
430. Arata J, Ishikawa K, Sawabe K, et al: Osteosynthesis in digital replantation using bioabsorbable rods. *Ann Plast Surg 50(4):350, 2003*.
431. Tsai T-M et al: Immediate free vascularized joint transfer from second toe to index finger proximal interphalangeal joint: A case report. *J Hand Surg 10B:85, 1985*.
432. Nunley JA et al: Longitudinal epiphyseal growth after replantation and transplantation in children. *J Hand Surg 12A:274, 1987*.
433. Bowen CVA et al: Experimental microvascular growth plate transfers. Part I—Investigation of vascularity. *J Bone Joint Surg 70B:305, 1988*.
434. Bowen CVA, O'Brien BMcC, Gumley GJ: Experimental microvascular growth plate transfers. Part 2. Investigation of feasibility. *J Bone Joint Surg 70B:311, 1988*.
435. Chen SH, Wei FC, Chen HC, et al: Vascularized toe joint transfer to the hand. *Plast Reconstr Surg 98(7):1275, 1996*.
436. Mitchell GM et al: A study of the extent and pathology of experimental avulsion injury in rabbit arteries and veins. *Br J Plast Surg 38:278, 1985*.
437. Buncke HJ Jr, Alpert B, Shah KG: Microvascular grafting. *Clin Plast Surg 5:185, 1978*.
438. Nichter L, Haines PC, Edgerton MT: Successful replantation in the face of absent venous drainage: An experimental study. *Plast Reconstr Surg 75:686, 1985*.
439. Terzis JK: Clinical microsurgery of the peripheral nerve: The state of the art. *Clin Plast Surg 6:247, 1979*.
440. Schultes G, Gaggl A, Kleinert R, Karcher H: Vascularized versus non-vascularized nerve transfers: histologic study in rats. *J Reconstr Microsurg 17(8):637, 2001*.
441. Gordon L et al: Partial nail plate removal after digital replantation as an alternative method of venous drainage. *J Hand Surg 10A:360, 1985*.
442. Batchelor AGG, Davison P, Sully L: The salvage of congested skin flaps by the application of leeches. *Br J Plast Surg 37:358, 1984*.
443. Lim CL: Successful transfer of "free" microvascular superficial temporal artery flap with no obvious venous drainage and use of leeches for reducing venous congestion: Case report. *Microsurgery 7:87, 1986*.
444. Rao P, Bailie FB, Bailey BN: Leechmania in microsurgery. *Practitioner 229:901, 1985*.
445. Anthony JP et al: Quantitative fluorimetric effects of leeching on a replanted ear. *Microsurgery 10:167, 1989*.
446. Mercer NSG et al: Medical leeches as sources of wound infection. *Br Med J 294:937, 11 April 1987*.

447. Braga A et al: Sensitivities of Aeromonas hydrophila cultured from medicinal leeches to oral antibiotics. *J Reconstr Microsurg 6:135, 1990*.
448. Valauri FA: The use of medicinal leeches in microsurgery. *Blood Coagul Fibrinolysis 2:185, 1991*.
449. Shenaq SM: Pretransfer expansion of a sensate lateral arm free flap. *Ann Plast Surg 19:558, 1987*.
450. Hallock GG: Free flap donor site refinement using tissue expansion. *Ann Plast Surg 20:566, 1988*.
451. Leighton WD et al: Experimental pretransfer expansion of free-flap donor sites: I. Flap viability and expansion characteristics. *Plast Reconstr Surg 82:69, 1988*.
452. Leighton WD et al: Experimental pretransfer expansion of free-flap donor sites: II. Physiology, histology, and clinical correlation. *Plast Reconstr Surg 28:76, 1988*.
453. Hallock GC: Preexpansion of free flap donor sites used in reconstruction after burn injury. *J Burn Care Rehabil 16(6):646, 1995*.
454. Gelberman R et al: Digital sensibility following replantation. *J Hand Surg 3:313, 1978.*
455. Chen Z-W et al: Present indications and contraindications for replantation as reflected by long-term functional results. *Orthop Clin North Am 12(4):849, 1981*.
456. Matsuda M, Shibahara H, Kato N: Long term results of replantation of ten upper extremities. *World J Surg 2:603, 1978*.
457. Schlenker JD, Kleinert HE, Tsai TM: Methods and results of replantation following traumatic amputation of the thumb in sixty-four patients. *J Hand Surg 5:63, 1980.*
458. Shieh SJ, Chiu HY, Lee JW, Hsu HY: Evaluation of the effectiveness of sensory reeducation following digital replantation and revascularization. *Microsurgery 16:578, 1995.*
459. Sixth People's Hospital, Shanghai: Replantation of severed fingers: Clinical experience in 217 cases involving 373 severed fingers. *Chin Med J 1:184, 1975.*
460. Hamilton RB, O'Brien BM: Replantation and revascularization of digits. *Surg Gynecol Obstet 151:508, 1980.*
461. Leung PC: Thumb reconstruction using second-toe transfer. *Hand Clin 1(2):285, 1985.*
462. Frykman GK et al: Functional evaluation of the hand and foot after one-stage toe-to-hand transfer. *J Hand Surg 11A:9, 1986*.
463. Williamson JS, Manktelow RT, Kelly L, et al: Toe-to-finger transfer for post-traumatic reconstruction of the fingerless hand. *Can J Surg 44(4):275, 2001*.
464. Yu Z, Huang Y: Sixty-four cases of thumb and finger reconstruction using transplantation of the big toe skin-nail flap combined with the second toe or the second and third toes. *Plast Reconstr Surg 106(2):335, 2000*.
465. Chung KC, Kotsis SV: Outcomes of multiple microvascular toe transfers for reconstruction in 2 patients with digitless hands: 2-and 4-year follow-up case reports. *J Hand Surg 27A(4):652, 2002*.
466. Wei FC, Jain V, Chen SH: Toe-to-hand transplantation. *Hand Clin 19(1):165, 2003*.
467. Wei FC, Carver N, Lee YH, et al: Sensory recovery and Meissner corpuscle number after toe-to-hand transplantation. *Plast Reconstr Surg 105(7):2405, 2000*.
468. Chung KC, Wei FC: An outcome study of thumb reconstruction using microvascular toe transfer. *J Hand Surg 25A(4):651, 2000*.
469. Beyaert C, Henry S, Dautel G, et al: Effect on balance and gait secondary to removal of the second toe for digital reconstruction: 5-year follow-up. *J Pediatr Orthop 23(1):60, 2003*.
470. Yim KK, Wei FC, Lin CH: A comparison between primary and secondary toe-to-hand transplantation. *Plast Reconstr Surg 114(1):107, 2004*.
471. De Lorenzi F, van der Hulst RR, den Dunnen WF, et al: Arterialized venous free flaps for soft-tissue reconstruction of digits: a 40-case series. *J Reconstr Microsurg 18(7):569, 2002*.
472. Brooks D: Invited discussion of De Lorenzi F et al, Arterialized venous free flaps for soft-tissue reconstruction of digits: a 40-case series. *J Reconstr Microsurg 18(7):575, 2002*.
473. Jones NF: Concerns about human hand transplantation in the 21st century. *J Hand Surg 27A(5):771, 2002.*

Selected Readings in Plastic Surgery

PUBLISHER

Selected Readings in Plastic Surgery
411 North Washington, Suite 6900
Dallas, Texas 75246-1777
(214) 824-0154 FAX (214) 824-0463
srps@swbell.net

INFORMATION FOR SUBSCRIBERS

A SELECTED READINGS IN PLASTIC SURGERY (ISSN 0739-5523) volume consists of 30 numbers, issued approximately 15 times per year. A subscription entitles you to receive 15 numbers, so to obtain an entire volume, you must subscribe for 2 consecutive years.

ANNUAL SUBSCRIPTION RATES*:* A 15-issue subscription is $300 US. CDs of volume 9, numbers 1-20 and 21-40, are also available for $300 each. CME quizzes are $60 for 15 issues. Modules (please inquire) are $200 each. International subscribers, add $50 to the above. Single issues are $40 US, $50 non-US. Binders with tabs are available for domestic shipping only at $20 each. We accept payment by check (US funds), purchase order, or VISA/MasterCard charge. Please allow 8 to 10 weeks for receipt of your first issue.

SHIPPING

We mail 8 times a year, two issues per mailing. Claims for lost copies will be honored for 3 months after publication for domestic subscribers and 6 months for subscribers outside the U.S. Please note that all sales are final – no returns will be accepted.

BACK ISSUES

To obtain back issues you may write to us at 411 North Washington, Suite 6900, Dallas TX 75246; e-mail *srps@swbell.net*; or fax 214-824-0463. Please inquire about availability and price before placing your order. Prepayment or credit card information must accompany all requests.

ISSN 0739-5523

Printed on recycled paper using soy-based ink; 100% recyclable.

SOUTHWESTERN
THE UNIVERSITY OF TEXAS
SOUTHWESTERN MEDICAL CENTER
AT DALLAS

BAYLOR UNIVERSITY MEDICAL CENTER
An Affiliate of the Baylor Health Care System