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Addressing common orthopaedic calamities with microsurgical solutions

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ABSTRACT

Reconstructive microsurgery has been an essential aspect of orthopaedic surgery and extremity reconstruction since the introduction of the operating microscope in the mid-20th century. The reconstructive ladder ranges from simple healing by secondary intention to complex procedures such as free tissue transfer and vascularized composite allotransplantation. As orthopaedic surgery has evolved over the past 60 years, so too have the reconstructive microsurgical skills that are often needed to address common orthopaedic surgery problems. In this article, we will discuss a variety of complex orthopaedic surgery scenarios ranging from trauma to infection to tumor resection as well as the spectrum of microsurgical solutions that can aid in their management.

Introduction

It has been more than a half century since Susumo Tamai MD reported on the world's first thumb replantation [1]. Tamai- an Orthopaedic Surgeon was encouraged by the late Harry Buncke MD to report the case during a microsurgery conference organized by Berish Strauch MD that took place in New York. At that time, reconstructive microsurgery was in its infancy, and the concepts of microsurgical repair of vessels and nerves were confined to traumatic conditions affecting the hand and upper extremity. In 1973 G. Ian Taylor MD reported on the world's first free tissue transfer, which was for lower extremity reconstruction following an open fracture [2,3]. The ability to perform microsurgery in the form of arterial, venous, and lymphatic anastomoses as well as neural coaptation has allowed for the growth of autogenous tissue transplantation, allotransplantation, and replantation, which have all had profound impact on the field of Orthopaedic Surgery and has facilitated advanced care in every Orthopaedic specialty in adults and children.

Replantation

Many of the early advances in microsurgery developed from interests in limb and digit replantation. Since these early days, there have been many refinements and modifications described in the treatment of patients requiring replantation. In particular, one advance has been in the field of supermicrosurgery, defined as microsurgery in less than 0.8mm vessels, which has allowed the replantation of distal fingertips to become a reality [4]. As the digital arteries divide at the level of the distal transverse palmar arch just distal to the flexor digitorum profundus tendon insertion, they routinely decrease in size from 0.8mm to as small as 0.3mm in the radiating branches, necessitating the use of supermicrosurgery when considering replantation of parts distal to this division point. Although the need for distal fingertip reattachment has been debated in the literature, it should be considered in children, young women, and patients with certain occupations, such as musicians [5]. Additionally, multiple studies and systematic reviews have demonstrated high distal finger replant survival rates and good functional outcomes, including high rates of nail salvage, fingertip sensibility, range of motion, and preservation of length and aesthetic appearance [6,7].

Aside from supermicrosurgery, other innovations that have advanced the care of patients with complex hand and upper extremity trauma include venous flowthrough flaps, filet flaps, ectopic banking, and heterotopic procedures. Venous flaps were first described by Nakayama et al in 1981 and consist of a vein with its

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overlying skin [8]. Due to their thin pliable nature, venous flaps have become an important tool when treating complex hand injuries requiring both revascularization as well as soft tissue coverage [9]. In a systematic review of venous flaps used for traumatic hand injuries, the forearm was the most common donor site, most flaps were supplied with an arterial inflow, and the majority (79.6%) of flaps healed well without issue [10]. Other small flaps that can be used for dysvascular digits requiring soft tissue coverage include the second toe plantar free flap, thenar free flap (radial artery perforator free flap), hypothenar perforator free flap (fourth common digital artery perforator flap) [11], as well as a pedicled digital artery flap from an adjacent finger [12]. In cases of multi-digit injury in which some digits are unreplantable and other digits require soft tissue coverage as well as revascularization, consideration should be given to the microvascular finger fillet flap, which utilizes the "spare parts" from the non-salvageable digit(s) [13]. Similarly, amputated parts can sometimes be replanted in a heterotopic position to improve function and aesthetics, such as the use of pollicization in the case of concurrent nonreplantable thumb amputation and index finger injury/amputation [14]. Another concept important in the management of complex hand trauma is the process of ectopic banking. First described by Godina in 1986 [15], ectopic banking refers to the temporary banking of an amputated part away from the zone of injury. It can be helpful in situations in which an amputation or devascularizing injury would only be immediately reconstructible if radical debridement were performed on the day of injury, thereby resulting in the debridement of vital structures important in the function and aesthetics of the ultimate reconstruction [16,17]. Additionally, ectopic banking has been described in cases where multi-system trauma patients are too hemodynamically unstable on the day of injury to undergo a standard replantation procedure, which has a longer operative time compared to ectopic banking, which only addresses the skin and vasculature [18]. Over time, as ectopic banking has evolved as a technique, there have been discussions regarding the details of the procedure, including surgical indications, preoperative counseling, ideal banking location, ideal banking duration, and management of the amputation stump soft tissue and arterial inflow [16,19]. While some of these questions are still up for debate, ectopic banking continues to be an important tool in the toolbox of the reconstructive extremity surgeon.

Vascularized composite allotransplantation (VCA)

Hand transplant

Vascularized composite allotransplantation was reported by Gilbert as early as 1964 (20). Although the procedure was a technical success, immunosuppression was in its infancy at the time and acute rejection necessitated the amputation of the transplanted hands at 3 weeks post-operatively. However, this set the stage for future success in the field of hand transplant, which was reinvigorated when the world's first successful hand transplant was performed by Dubernard et al in 1998 [20,21]. Since then, over 85 hand transplants have been successfully performed around the world, including bilateral hand transplants in both adults and children [22–24]. Functional outcomes have been overall positive thus far but there are many areas of research that require continued investigation and discussion, including indications for surgery, the ethical implication of placing a healthy patient on life-long immunosuppression, the impact of anatomic level of transplantation on post-transplant function, immunosuppression protocols, and neural regeneration and reinnervation of the transplanted part [24–33].

One particular topic of discussion has been hand transplantation in the pediatric population. The world's first bilateral pediatric hand transplant was performed in 2015 in an 8-year-old child who had previously suffered from staphylococcal sepsis at age two years, resulting in quadrimembral amputation and kidney failure, for which he underwent a living-related kidney transplant at age four years. While his procedure was a technical success with the help of extensive preoperative planning and 3D modeling [34,35], his post-hand transplant course has also answered a number of questions in pediatric VCA, including the demonstration of good function above what was able to be obtained preoperatively through adaptive learning [36], the ability of the transplanted limbs to grow with the child [37], and the ability of the brain to re-organize its somatotopic maps after the restoration of sensory input from the transplanted limb [38]. However, when looking at the ethics of hand transplantation in children, one must consider the risks of lifelong immunosuppression in the pediatric population and the higher likelihood of negative side effects given their overall longer life expectancy. While advances in immunosuppression and prostheses may swing the pendulum, the current recommendation for hand transplantation in children leans towards patients requiring bilateral transplants, preferably already on immunosuppression, who would derive a large functional gain from hand transplant compared to current prosthetics and autologous reconstructive options [39,40].

The ultimate functionality of the transplanted hand depends on reinnervation, which determines sensibility as well as movement of the distal parts. Using her clinical and basic science knowledge of peripheral nerve regeneration, MacKinnon et al has described multiple surgical and non-surgical strategies for optimizing nerve regeneration after hand transplant [41], including the use of FK-506, augmentation of Schwann cell support, and optimization of surgical technique. FK-506, also known as tacrolimus, is a calcineurin phosphatase inhibitor that is typically part of the immunosuppression regimen following allotransplantation. While its immunosuppressive effects are primarily due to inhibition of the activation of T-cell proliferation, it has also been noted to enhance peripheral nerve regeneration after injury and in isograft and allograft models through calcineurin-independent pathways [41,42]. FK-506 has been shown to increase the number of regenerated nerve fibers, stimulate chronically axotomized motor neurons, and protect neural cells from ischemia and block neuronal apoptosis [41,42]. MacKinnon et al recommend pre-loading the transplant recipient with FK-506 in order to induce the most therapeutically regenerative environment at the time of transplant and to continue FK-506 as part of the post-operative immunosuppression regimen while the transplanted extremity is undergoing reinnervation. Aside from FK-506, Schwann cell augmentation with TGF-β or supplementation with autologous cultured or stem cell-derived Schwann cells is another method of supporting reinnervation after hand transplant [43], although these pathways require further investigation before implementation *in vivo*. Finally, nerve regeneration after hand transplant can be positively influenced by optimal surgical techniques at the time of transplant. For example, the motor and sensory fascicles of the ulnar nerve should be topographically mapped and aligned. Release of potential entrapment points and distal nerve transfers (such as distal anterior interosseous nerve to recurrent branch of the median nerve) have also been advocated for in the literature [41].

Beyond hand transplantation

Aside from hand transplant, VCA also has other implications for the field of orthopaedic surgery. Although amputees with lower extremity prostheses generally have higher satisfaction compared to amputees with upper extremity prostheses, a recent study found that 43% of lower extremity amputees would be interested in being evaluated for lower extremity transplant [44]. The primary reasons for interest in allotransplantation included the possible restoration of functional knee and/or ankle movement as well as the restoration of limb sensibility. While there has been some discussion of the pros and cons of lower extremity allotransplantation [45], there have only been a few successful cases reported in the literature. One case involved unilateral lower limb allotransplantation in ischiopagus conjoined twins joined at the pelvis, therefore avoiding the need for postoperative immunosuppression [46]. Another case involved bilateral above-knee transplantation of lower extremities in a 21-year-old man, who was able to recover some aspects of both knee and ankle motion and was able to achieve ambulation with assistance but ultimately developed primary central nervous system post-transplant lymphoproliferative disease (CNS PTLD) requiring cessation of immunosuppression and amputation of his transplanted lower extremities [47–49]. One other type of VCA in its infancy is vascularized elbow allotransplantation, which has been demonstrated to be technically feasible in a rat as well as a human cadaveric study [50,51].

There are many advances yet to be made in the field of VCA as it pertains to orthopaedic surgery. Regardless of type of VCA, the decision to operate should always be based on a careful consideration of risks and benefits for each individual patient. Additionally, surgical planning and preoperative counseling should always include the possibility of VCA failure and salvage options should be kept at hand should the patient subsequently require an amputation of their transplant [52]. In summary, VCA holds significant promise in the treatment of orthopaedic patients, and further innovation in the field depends on interest on the part of the surgeon as well as the public and patients [53].

The orthoplastic approach to limb salvage

First coined by the senior author (LSL) in the 1990s, the orthoplastic approach to limb salvage refers to the collaborative efforts of orthopaedic surgeons and plastic surgeons in extremity reconstruction after trauma, tumor resection, or any variety of pathologies. The orthopaedic surgeon strives to achieve stable bony fixation while the plastic surgeon must be able to provide stable soft tissue coverage, since both are required for functional and aesthetic extremity reconstruction. The two specialties are complementary, and must have a good mutual understanding of the other's role and objectives in order to coordinate the best care for the patient [54].

First and foremost, in cases of traumatic open fractures, the wound must be adequately debrided, sometimes requiring multiple trips to the operating room to achieve a clean wound bed. There also needs to be a discussion regarding the type of fixation (internal vs external) required from the orthopedic perspective, with forethought given to the required soft tissue access needed for reconstruction. For example, anterior pins in the leg are typically superior to medial or lateral pins, which may preclude vascular access for either local or free flaps. The plastic surgeon should be available to assess the soft tissue options either at the time of bony fixation or shortly thereafter, and timely soft tissue coverage should be obtained [55,56]. Additionally, by tapping into both orthopaedic and plastic surgical expertise, the orthoplastic approach is helpful in determining whether an extremity is best treated with limb salvage or amputation and can help guide patient decision-making.

Pediatric lower extremity vascular injures

Despite advances in orthopedic surgery and vascular surgery, lower extremity Gustillo IIIC injuries in the pediatric population remain a challenge for pediatric trauma centers. While vascular surgeons are routinely on call for adult trauma centers and play a key role in the management of IIIC level injuries in the adult patient, there are typically no pediatric vascular surgeons available at most pediatric trauma centers given its relevant nonexistence as a surgical field. However, concurrent orthopedic and vascular injuries threatening limb perfusion do occur in children and when not managed appropriately, can lead to significant morbidity including decreased function and amputation [57]. Additionally, pediatric vascular injury presents an added challenge due to the small caliber of vessels involved and often require unique microsurgical expertise in order to perform microvascular anastomoses, vein grafting, and arterial repair. Gans et al [58] described the implementation of a lower extremity vascular trauma (LEVT) protocol that includes around-the-clock coverage by microsurgery-trained surgeons and outlines the treatment algorithm for pediatric IIIC injuries, including when to involve different subspecialty teams such as trauma surgery, orthopedic surgery, and microsurgery (Fig. 1). In their series of 22 patients, Gans et al found that implementation of the LEVT protocol resulted in a decrease in preoperative vascular radiographic studies and quicker time to definitive vascular care [58]. Although this single-institution report is promising, further work needs to be done in order to standardize the treatment of pediatric IIIC injuries and to establish a reliable protocol for addressing limb-threatening vascular injuries in the pediatric population (Fig. 2).

Free vascularized bone and composite tissue transfer

There are many indications for the use of free vascularized bone grafts (FVBG) in orthopaedic surgery, including segmental bone defects secondary to trauma, tumor, and infection. Commonly used FVBG include the fibula, medial femoral condyle or trochlea flap, and less frequently, fibular epiphyseal transfers in children. A common composite tissue transfer is the toe to hand transfer.

Fibula flap

The free fibula flap was first described by Ian Taylor in 1975 [59], and has since become one of the most frequently utilized FVBG for a variety of reconstructive efforts, including segmental defects of the upper and lower extremity as well as the craniofacial skeleton. Its popularity stems from its relatively large size and length, acceptable donor site morbidity, and reliable anatomy and dissection. The fibula can be harvested as an osseous flap, osteocutaneous flap, or an osteomyocutaneous flap if the gastrocnemius and/or soleus is taken as well [60]. The vascular pedicle is the peroneal artery, which typically has a large caliber ranging from 1.5 to 4mm in diameter and is accompanied by two veins. The shorter pedicle length can be increased by dissecting it free of the proximal fibula and harvesting the distal bone for reconstruction [60].

The free vascularized fibula graft (FVFG) has come to play an important role in the reconstruction of large spinal defects and for the treatment of failed spinal fusion. Erdmann et al described four cases of spinal osteomyelitis and nonunion following thoracic and lumbar spinal fusion treated with hardware removal and FVFG with subsequent infection clearance and bony union [61]. Similarly, numerous studies have described the utility of FVFG for the reconstruction of spinal defects due to tumor resection, radiation, osteomyelitis, and/or failed arthrodesis with good success [62–65] (Fig. 3). Mericli et al found that compared to patients who underwent spinal tumor resection and reconstruction with nonvascularized bone graft and alloplastic cage, the patients who underwent spinal tumor resection with FVFG reconstruction achieved higher rates and quicker time to bony union postoperatively [66]. Vrints et al also discussed the merits of FVFG reconstruction and avoiding hardware placement, thereby allowing for increased accuracy of

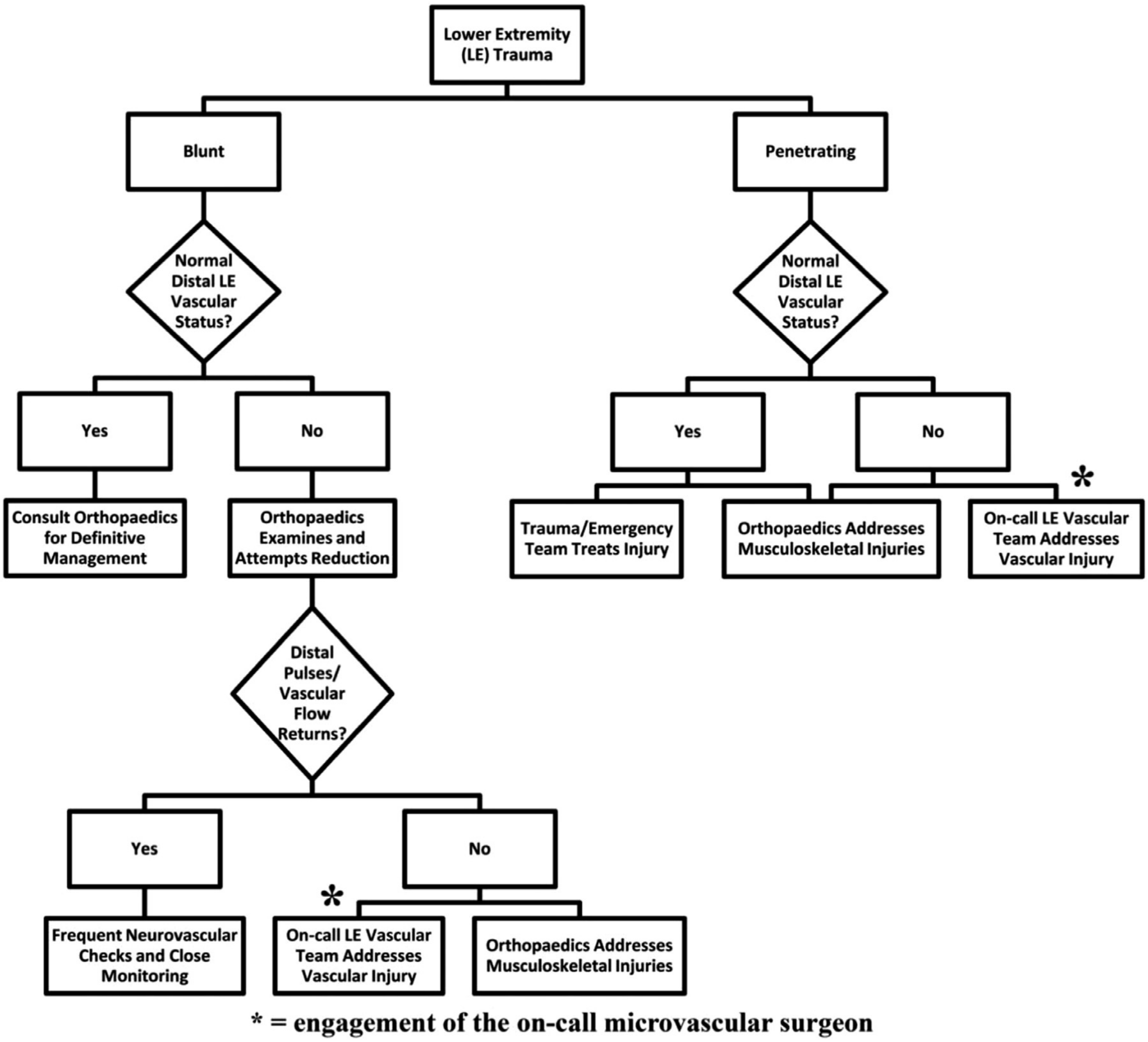

Fig. 1. Pediatric lower extremity trauma combined musculoskeletal and vascular injury protocol (Reprinted with permission from Gans et al. A lower extremity musculoskeletal and vascular trauma protocol in a children's hospital may improve treatment response times and appropriate microvascular coverage. Journal of Orthopaedic Trauma. 2015).

post-resection radiation therapy [67]. One essential technical consideration when performing spinal reconstruction with FVFG is the selection of recipient vessels, which is highly dependent on the anatomical level and surgical approach. While there are a plethora of recipient vessels in the cervical region, the thoracolumbar region can present a challenge with possible recipients being intercostal vessels, lumbar vessels, inferior mesenteric vessels, iliac vessels, the aorta (end to side with or without greater saphenous vein patch), among others [61,68,69]. Success of this complex reconstructive endeavor relies on careful preoperative planning as well as interdisciplinary communication between the orthopedic and reconstructive surgeon.

In addition to spinal reconstruction, the FVFG is also used in the treatment of hip osteonecrosis in both adults and children [70]. Osteonecrosis of the femoral head occurs when bone death progresses to articular incongruity and osteoarthritis, resulting in the need for total hip arthroplasty (THA). Many procedures have been described to delay this pathologic progression, including core decompression, nonvascularized bone grafts, porous tantalum implant placement, and osteotomies, but these have been shown to have limited efficacy and predictability [70]. One surgical intervention involves decompression, excision of necrotic bone, and placement of a FVFG, which simultaneously brings in bone with osteoinductive potential and aids in revascularization. Eward et al investigated the use of the FVFG for pre-collapse osteonecrosis of the femoral head and found that 75% of patients had a surviving graft for at least ten years postoperatively and only 40% converted to THA at a mean of eight years postop [71]. Similarly, Bertrand et al demonstrated that FVFG can be used for the treatment of avascular necrosis after slipped capital femoral epiphysis with 90% of patients maintaining their native hip for eight years postop [72]. Garrigues et al investigated the use of FVFGs for osteonecrosis that resulted from hip dislocation in 35 young patient, of which seven required THA at an average of 45 months postop [73]. A systematic review performed by Ligh et al included 166 hips and found a mean graft survival before THA of 5.2 years [74]. Overall, FVFGs tend to be more beneficial for younger patients with less severe femoral head osteonecrosis [75]. Contraindications to this procedure include joint space narrowing and acetabular involvement.

Medial femoral condyle (MFC)

First described as a pedicled reverse-flow osteoperiosteal flap by Masquelet and Hertel [76,77], the MFC has become a versatile FVBG with a variety of applications in both upper and lower extremity reconstruction. One of the reasons the MFC is so versatile

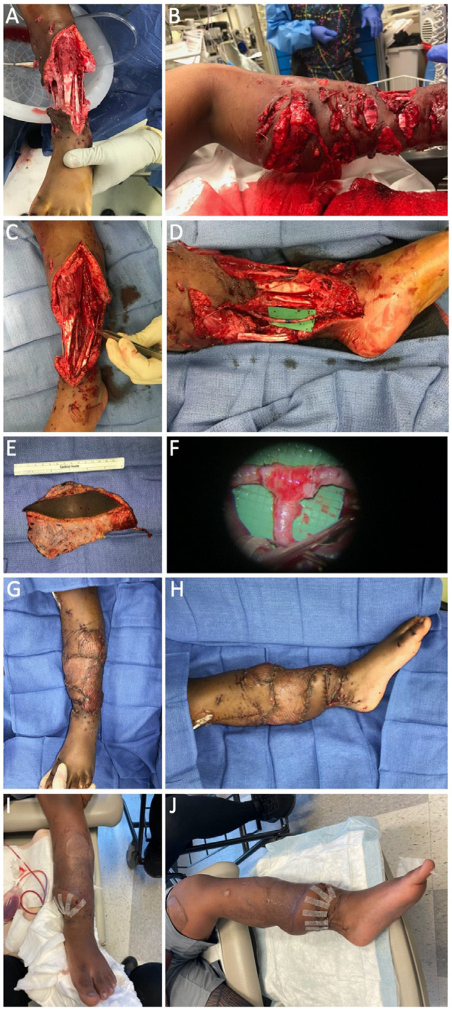

Fig. 2. Seven-year-old male whose left lower extremity was mauled by a pit bull and was devascularized on presentation (A and B). He underwent emergent revascularization with a reversed saphenous vein graft for reconstruction of the anterior tibial artery and posterior tibial artery (C and D). This was followed by soft tissue coverage with a free myocutaneous latissimus dorsi flap connected to the posterior tibial artery in flow-through fashion as well as split thickness skin grafts (E–H). Follow up at 2.5 years demonstrates stable soft tissue coverage and good aesthetic contour after debulking of the flap (I and J).

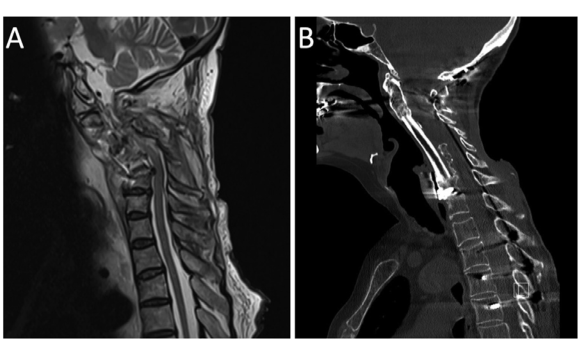

Fig. 3. Sixty-one-year-old woman with a history of cervical stenosis who underwent C4 corpectomy and anterior C3-C5 discectomy and fusion followed by C2-T2 posterior fusion three months later presents with worsening upper extremity weakness. Pre-operative MRI demonstrates a prevertebral collection and collapse of the C5 vertebral body (A). She underwent serial washout and antibiotic treatment followed by a staged procedure: (1) occipital-T5 fusion with tricortical allograft and BMP plus halo vest placement, and subsequently (2) C3-C6 corpectomy with a free fibula autograft fusion. Her one-year postoperative CT scan demonstrates a stable construct with osseous incorporation of the vascularized fibula graft (B).

is that the blood supply to this donor area is both plentiful and consistent [78]. Yamamoto et al studied this arterial supply in a cadaveric model, which demonstrated that the descending genicular artery was present 89% of the time and could be found branching from the superficial femoral artery approximately 13.7cm proximal to the articular surface. Meanwhile, the superior medial genicular artery was present 100% of the time which allows it to be a backup but its disadvantage is a shorter pedicle length, branching only an average of 5.2cm proximal to the articular cartilage [79]. A described variation of the MFC is the medial femoral trochlea osteochondral flap (MFT), which is used when there is a need for concurrent cartilage transfer. The MFC/MFT donor site morbidity has been studied, with overall low incidence of complications, with the most common being chronic knee pain and sensory changes, which are more evident in MFT donor sites vs MFC donor sites [80].

The MFC has been extensively described for the treatment of hand and wrist pathologies. While it first gained popularity as a thin pliable corticoperiosteal wafer for the treatment of small nonunions of the hand such as scaphoid nonunions with proximal pole avascular necrosis, it has now expanded in indications to include the treatment of hand and wrist conditions such as kienbock's disease, capitate avascular necrosis, failed radiolunate arthrodesis, and multiple metacarpal defects [81–88] Its use has also been described for more proximal upper extremity nonunions including resistant nonunions of the distal radius, forearm, humerus, and clavicle [88–90]. In cases requiring osteochondral grafting, the MFT has been described for scaphoid and lunate reconstruction [91,92].

In addition to upper extremity reconstruction, the MFC and MFT can also play an important role in reconstruction of the foot. VBGs such as the MFC and MFT are typically indicated when conventional bone grafting fails or the defect is too large for conventional bone grafting. Haddock et al studied five patients who underwent MFC for talar avascular necrosis, talar nonunion, or navicular avascular necrosis and found a 100% flap survival rate, with all five patients achieving union and full weight bearing status [93]. Other case reports similarly support the use of the MFC in the treatment of navicular avascular necrosis [94,95]. A randomized control trial investigating the use of core decompression with cancellous bone graft vs core decompression with MFC in the treatment of talar osteochondral lesions found that the MFC group demonstrated better pain relief and improved physical function as well as a decreased rate of partial malperfusion as assessed on MRI at 12 months of follow up [96].

Epiphyseal transfer

A major challenge of reconstructing bony defects in children is when growth plates are involved and failure to address this can result in growth limitations and limb-length discrepancies. Multiple authors have described the free vascularized transfer of the fibular epiphysis in children as a means of reconstructing bony defects of the upper and lower extremity that also allows for continued growth potential [97–101]. Morsy et al [102] performed an anatomic cadaver study and found that the proximal fibula can be transferred on either the anterior tibial artery or the inferior lateral genicular artery and recommended against the use of the peroneal artery alone. However, Kurlander et al [98] performed a systematic review of vascularized fibular epiphyseal transfer for pediatric extremity reconstruction and found that the most commonly utilized pedicle was the anterior tibial artery (64%) followed by the peroneal artery (23%). All 62 cases in the systematic review reported growth based on xray with a full growth rate of 63% for patients undergoing upper extremity reconstruction and 56% for patients undergoing lower extremity reconstruction, with "full growth" being defined as having open growth plates at last follow up. Similarly, Shammas et al [99] calculated an approximate 0.54cm/year of growth following fibular epiphyseal transfer for reconstruction of the proximal humerus in a series of four patients. However, in their systematic review, Kurlander et al also found an 8% rate of permanent foot drop due to the intimate relationship between the anterior tibial artery and the peroneal nerve and also noted an overall high rate of complications and revision surgery. Nonetheless, given the paucity of other bony reconstructive options that also maintain growth potential in children, the vascularized fibular epiphyseal transfer remains an important tool in the reconstructive armamentarium.

Toe to hand transfer

Composite transfer of a toe for thumb reconstruction was one of the earliest described elective microsurgery procedures and set the foundation for free tissue transfer [103]. Given that the thumb accounts for up to 50% of hand function, reconstruction of the thumb is imperative in restoring hand function in cases of trauma or congenital abnormalities. While toe to thumb transfer was initially popularized for thumb reconstruction following traumatic amputation, technical refinements have increased its indication to include treatment of multiple finger amputations aside from the thumb, dystrophic nails, pulp loss, arthritic joints, as well as congenital malformations such as hypoplastic thumb [104–109]. Variations on the technique include the great toe flap, second toe flap, toe pulp flap, and wrap-around toe flap, and with selection depending on each patient's reconstructive needs. In the majority of cases, the dominant blood supply is the first dorsal metatarsal artery, but in a small portion of the population, the plantar artery can be dominant [110]. Innervation of the toe is from the plantar digital nerves and branches of the deep or superficial peroneal nerves. Overall satisfaction following toe to hand transfers is high, with patients who underwent toe to hand transfers for thumb amputation scoring higher on the Michigan Hand Outcomes Questionnaire for overall function, activities of daily living, and aesthetic outcome compared to patients suffering from thumb amputation without reconstruction [104,111]

Aesthetic limb resurfacing

The majority of post-traumatic extremity reconstruction is focused on function, but there has been a growing interest in aesthetic resurfacing of extremities after trauma. Jeon et al [112] presented a series of 14 patients who underwent free flap surgery for the primary purpose of improving aesthetics. They were able to achieve both subjective improvement in patient satisfaction based on survey data as well as objective improvement in aesthetic outcome, as evaluated by independent graders of pre-operative and post-operative photos. Integral to their success was the utilization of perforator flaps (TDAP and DIEP) that were judiciously thinned through the removal of deep subcutaneous fat as well as excision of some areas of the superficial fascial system and part of the superficial subcutaneous fat layer away from the perforators, allowing them to achieve favorable aesthetic results with only a 27% rate of secondary revision procedures. Seth et al [113] also described their technique for raising super-thin and suprafascial anterolateral thigh (ALT) flaps for extremity reconstruction with contour improvement. While the major focus of the primary reconstruction may not be aesthetics, a significant proportion of patients ultimately desire secondary revisions for aesthetic purposes. In a recent case series by Nelson et al [114], 21% of lower extremity free flap patients desired secondary revisions, with the most commonly performed procedures being flap debulking via direct excision, scar revision, and suction-assisted lipectomy. As extremity reconstruction evolves, there is no doubt that increased emphasis will be placed on the ultimate aesthetic outcome of the reconstruction and therefore, it may be helpful to incorporate aesthetic goals into the initial reconstructive plan for each patient.

Solutions for peripheral nerve injuries

Ninkovic procedure for peroneal nerve injury

Microsurgical techniques can be useful in the treatment of peroneal nerve injuries, which are the most common nerve injuries of the lower extremity. In the setting of an acute open injury, surgical exploration with primary repair or repair with nerve grafting is recommended. However, if the acute intervention fails or if the patient is not assessed in a timely manner, there may be irreversible degeneration of the muscles of the anterior compartment, leading to foot drop. In these cases, there are a variety of surgical techniques described to address the foot drop, including arthrodesis, posterior tibial tendon transfers via the circumtibial or interosseous pathway, or the posterior tibial muscle bridle transfer, but all of these transfers depend on the use of an antagonistic muscle to restore ankle dorsiflexion. As an alternative, Ninković et al described a neurotized transfer of the lateral head of the gastrocnemius, consisting of simultaneous transposition of the lateral head of the gastrocnemius muscle to the tendons of the tibialis anterior and a deep peroneal nerve to tibial nerve transfer [115]. By performing a concurrent nerve transfer from the proximal uninjured end of the deep peroneal nerve to the distal tibial nerve supplying the lateral head of the gastrocnemius, the end result is a neurotized muscle that can be voluntarily contracted to aid with ambulation. Several studies in the literature have demonstrated excellent overall results with this technique in the treatment of patients with chronic peroneal nerve injury and foot drop [115–117].

Free functional muscle transfer for brachial plexus injuries

Free functioning muscle transfers (FFMT) involve transplantation of a vascularized and innervated muscle to an area of the body lacking functional musculature, such as following brachial plexus injury as well as extensive direct trauma, infection requiring wide debridement, ischemic contracture, or tumor resection. In particular, for brachial plexus injuries, FFMT is indicated for delayed presentation, failure of previous nerve and/or tendon transfers, lack of donor nerves, and/or complete C5-T1 postganglionic injuries [118]. In cases of complete brachial plexus injury, the primary goals of reconstruction are elbow flexion followed by finger flexion and finger extension [119]. Options for donor muscles include the gracilis, latissimus dorsi, rectus femoris, and vastus lateralis, with the gracilis being the most popular at many institutions due to its low donor site morbidity, ease of dissection, and reliable blood supply from the medial femoral circumflex system and innervation from the anterior branch of the obturator nerve. Free functional gracilis transfer has been described for the treatment of brachial plexus injuries in both adults and children [120,121]. Estrella et al [122] performed a retrospective review of 42 adult patients who underwent gracilis flaps for the restoration of elbow flexion and found a 90% flap success rate with 88% of patients achieving at least M3/5 muscle strength postoperatively. In a larger series, Silva et al [123] reported on a series of 87 adult patients, of which 65% achieved at least M3 strength following surgery; interestingly, they utilized a variety of donor nerves, including spinal accessory, intercostal, median nerve fascicles, ulnar nerve fascicles, and phrenic nerve. Along with the studies in adult patients, there have also been some studies looking at pediatric brachial plexus injuries and FFMT, but the results are somewhat more mixed. El-gammal et al

[124] described a series of 18 children suffering from late obstetric brachial plexus palsy who underwent free gracilis flap at a mean age of 102.5 months. They were able to achieve improvements in both active elbow flexion as well as active finger flexion with a concurrent decrease in passive elbow ROM. However, only 17% achieved a grade 3 (useful hand) on the Raimondi hand scale. Likewise, Chim et al [125] reported on 12 children who underwent free functional gracilis transfers for the treatment of traumatic brachial plexus injury and demonstrated overall good outcomes, but did caution regarding the possibility of elbow flexion contracture as children grow. Overall, there is no consensus on the ideal donor nerve, with multiple studies utilizing a variety of donor nerves, including spinal accessory nerve (SAN), intercostal, median nerve fascicles, ulnar nerve fascicles, and phrenic nerve, with no significant difference between SAN and ulnar nerve [126] as well as between SAN and intercostal nerves [127]. Finally, there have been a number of modifications and additions to the FFMT technique for treatment of brachial plexus injury, including adding a nerve transfer at the time of FFMT [128] and doing a double FFMT for the restoration of multiple joint motions [129].

Restoring shoulder function with nerve transfers

Shoulder function is essential to overall upper extremity function and the ability to perform activities of daily living. A number of nerve transfers have been described for restoring shoulder motion, each with its own surgical indication depending on the extent of nerve injuries [130]. For isolated axillary nerve injuries, a common transfer is the nerve to the long head of the triceps to the anterior branch of the axillary nerve, which has been shown in multiple studies to improve shoulder abduction postoperatively [131]. It can also be combined with the spinal accessory to suprascapular nerve transfer for C5-C6 nerve root injuries or concurrent axillary and suprascapular nerve injuries in order to restore both shoulder abduction and external rotation [132,133]. Interestingly, in their technique paper, Colbert et al [133] advocated for the use of the nerve to the medial head of the triceps (as opposed to the lateral head of the triceps) due to its ease of exposure, longer length, and no requirement for intramuscular dissection. In cases of winged scapula, a thoracodorsal nerve to long thoracic nerve can be performed. In C5-C7 root injury, the triceps are weakened and therefore cannot provide a donor nerve to the axillary nerve or long thoracic nerve, so intercostal nerves can serve as an important alternative donor nerve; spinal accessory to suprascapular nerve transfer can also be performed for these patients. In addition to success in adult patients, nerve transfers have also been successfully performed for neonatal brachial plexus injuries [134,135]. It is important to be familiar with the anatomy and depending on the exact location and extent of nerve injury, various combinations of nerve transfers can be helpful for each specific situation [136–138].

Microsurgical treatment of lymphedema

Lymphedema is a chronic condition caused by impairment of lymphatic fluid drainage, resulting in edema, cellulitis, and over time, irreversible fibrosis. It can either be congenital or as a result of secondary mechanical obstruction of lymphatic drainage, oftentimes due to surgical lymphadenectomies in the setting of oncologic resection [139]. Non-operative treatment options for patients with early lymphedema include compressive garments and manual decongestive therapy but require patient compliance and are not ultimately curative. Operative treatments have also been described with many of the earlier procedures focusing on surgical resection, but these resulted in high morbidity and therefore are generally reserved for the most advanced and debilitating cases [139]. Suction assisted lipectomy can also be used as an adjunctive, less morbid debulking procedure. However, more recent focus has been on restoring lymphatic flow, rely upon microsurgical skills, and include lymphovenous anastomosis (LVA) and vascularized lymph node transfer (VLNT). LVA consists of diverting obstructed lymphatic fluid into the venous system through a surgically created anastomosis between lymphatic channels and veins. A systematic review of LVA performed by Scaglioni et al [139] looking at 18 studies found significant variation in surgical technique but demonstrated symptomatic relief in 50-100% of patients, overall good reduction in limb circumference measurements as well as reduction in number of cellulitis episodes. Drobot et al [140] performed a retrospective review of 70 patients who underwent LVA for either primary or secondary lymphedema and demonstrated a 35% decrease in upper limb volume and 25.5% decrease in lower limb volume at 9 months post-operatively. Higher volume reductions were seen for early-stage lymphedema vs late-stage lymphedema, which was not unexpected since LVA relies on the presence of healthy, non-sclerotic lymphatic channels. Of note, the vast majority of subdermal vessels used for LVA are less than 1mm in caliber, necessitating experience in supermicrosurgery in order to successfully perform this procedure.

Another operative procedure for the treatment of lymphedema is vascularized lymph node transfer (VLNT), which involves the transfer of lymph nodes and their blood supply to the affected limb [141]. While LVA is most effective in early lymphedema before lymph vessels become sclerotic, VLNT can be efficacious in more advanced cases of lymphedema because it does not rely on the native lymphatic channels. The exact physiology of how the transferred lymph nodes facilitate lymphatic drainage is still somewhat unclear. In a systematic review of VLNT performed in 2016, Scaglioni et al [142] found 24 studies with 271 cases of VLNT. The most common lymph node donor site was the inguinal region followed by the lateral thoracic lymph nodes, which were found to be the least effective with the highest complication rates. Overall, however, benefits of VLNT were reported in both early and advanced lymphedema. VLNT has been described for treatment of congenital lymphedema [143,144] and post-surgical lymphedema [145] and has been used in combination with LVA as well [146].

Non-healing lower extremity wounds

Limb salvage in patient with peripheral vascular disease and diabetes

Diabetic foot ulcers (DFUs) can be a source of significant morbidity and mortality in patients with diabetes mellitus. Their development stems from a combination of macrovascular and microvascular insults as well as peripheral neuropathy [147], and lack of treatment can lead to limb and life-threatening infections. While up to two thirds of small superficial DFUs can be treated conservatively with local wound care, the remaining one third of DFUs will require operative debridement, leading to subsequent exposure of vital structures such as tendon and/or bone [148]. The combination of critical limb ischemia (CLI) and DFUs in the diabetic patient presents a particularly significant reconstructive challenge. Successful treatment of this patient population requires a multidisciplinary team that includes a nutritionist, wound care specialist, endocrinologist, podiatrist, orthopedist, vascular surgeon, and reconstructive microsurgeon [149]. Multiple studies have described the benefits of a combination approach that includes revascularization (endovascular vs open bypass) as well as free flap coverage of large DFUs, either in a simultaneous or staged fashion [147,150,151]. Randon et al reported a 55.8% three year amputation-free survival rate [150], while Chang et al reported a 68% five year amputation-free survival rate for patients who underwent revascularization and free flap reconstruction [151]. Additionally, Hong et al demonstrated an increase in five year overall survival in patients who underwent free flap reconstruction of their DFUs (86.8%) compared to patients who underwent above the ankle amputation (41.4%) [152]. Despite the benefits of microvascular free tissue transfer for the treatment of DFUs, there is still a significant risk of amputation and functional impairment following attempted limb salvage; this was demonstrated by Lu et al, who reported on a series of 29 patients, seven of which required below-knee amputation at a mean time of 8 months following free tissue transfer [153]. Therefore, patients should be counseled appropriately during the initial discussion with the reconstructive surgeon. Finally, a technical consideration in free flap reconstruction is the selection of recipient vessels in a patient who has concurrent CLI; as such, Lee et al advocated for the use of end-to-side anastomoses so as to not disrupt distal flow to the limb [154].

Limb salvage in patient with osteomyelitis

Lower extremity wounds with underlying osteomyelitis are some of the most difficult challenges faced by the orthopedic surgeon. While acute osteomyelitis can sometimes be treated successful with antibiotics alone, chronic osteomyelitis typically needs to be addressed with a combination of surgical debridement, soft tissue coverage, and antibiotic therapy [155]. The Cierny-Mader classification is a useful classification system emphasizing anatomy of the bony infection and physiology of the host and can be used to guide optimal treatment [156]. There has been some debate regarding the prevention of osteomyelitis in the patient with an acute open fracture. Marko Godina advocated for the early coverage of open fractures within 72 hours of injury in order to prevent infection and osteomyelitis [17]. While the advent of negative pressure wound therapy (NPWT) has revolutionized care of this patient population, there is still some evidence that definitive soft tissue coverage should be performed within seven days of injury in order to decrease risk of infection [157]. However, the timing of soft tissue coverage also depends on the capabilities of the trauma facility and should strike a balance between early coverage and taking the time to create a thorough operative plan and ensure that the appropriate personnel are available [158]. In addition to prevention, there has also been debate regarding the optimal treatment of osteomyelitis requiring debridement and free tissue transfer for coverage. Although there has been some historical and anecdotal bias towards the use of muscle flaps for treatment of infection, recent studies have demonstrated no significant difference in osteomyelitis recurrence between muscle flaps and fasciocutaneous flaps, with the latter also having the benefit of improved aesthetics and possibly decreased donor site morbidity [159–163]. However, if osteomyelitis does recur following free tissue transfer, there is an increased risk for flap failure and eventual amputation [164].

Radiation-induced nonunions

Radiation therapy is used in the treatment of a number of malignancies and is known to have deleterious effects on the surrounding tissues, including bone. Its pathologic effect on bone is secondary to direct cellular damage as well as radiation-induced vascular injury. Important factors that influence the ultimate effect of radiation on bone include the total radiation dose, the dose per fraction, the total volume of radiated tissue, and the treatment schedule [165]. Radiation injury to non-critical bones such as the clavicle can often be treated with debridement and/or resection. However, radiation injury that leads to pathologic fracture or nonunion of critical bony structures needs to be addressed with surgical fixation and supplemental nonvascularized or vascularized bone grafting. Multiple studies have described the use of the free vascularized fibula graft (FVFG) for treatment of radiation-induced nonunions of the humerus, femur, and fibula with postoperative union rates ranging from 78-100% [166–168]. Additionally, MFC flaps have also been described for the treatment of upper extremity nonunions and clavicular nonunions [169,170].

Fig. 4. Forty-six-year-old female who underwent right total ankle replacement complicated by wound breakdown, osteomyelitis, and hardware exposure (A). She underwent limb salvage with hardware removal, antibiotic spacer placement, and soft tissue coverage with a free lateral arm flap. She ultimately healed well and was able to undergo spacer removal and revision total ankle arthroplasty (B).

Complications around the knee and ankle

Soft tissue coverage of the knee

Soft tissue defects around the knee can result from a variety of etiologies, ranging from trauma, to oncologic resection, to hardware complications following total knee arthroplasty. Many of these cases can be managed with local pedicled flaps such as the workhorse gastrocnemius flap or the more recently described free style perforator flap [171,172]. However, when wounds are too large and complex or when local options have failed, free tissue transfer should be considered. There are a number of recipient vessels around the knee, including the anterior tibial, posterior tibial, peroneal, popliteal, geniculate, sural, profunda femoral, superficial femoral, descending branch of the lateral femoral circumflex, among others [171,173]. Louer et al looked at 34 cases of free flap coverage for knee reconstruction and described a 97% flap survival rate and 88% lower extremity salvage rate [174]. Many different free flaps have been used successfully for knee salvage, including but not limited to the latissimus dorsi, gracilis, scapula, rectus abdominis, and fibula, with an overall high rate of flap survival and limb salvage [175,176]. However, the functional outcomes following free tissue transfer for knee salvage described in recent literature are somewhat less promising in this typically complex patient cohort and require further investigation [171,177].

Soft tissue coverage of the ankle

The distal leg and ankle is an area of tenuous blood supply that makes healing following trauma or elective surgery more difficult. There has been some success in using skin grafts, Integra, as well as local flaps for coverage of these wounds, with popular options being the reverse sural flap, peroneus brevis flap, and propeller flaps [178–180]. However, there remains a role for free tissue transfer in cases of large and complex defects as well as for robust and reliable coverage of underlying hardware (Fig. 4). A number of studies have highlighted the success of free tissue transfer for ankle coverage [181]. Cunningham et al examined 2065 patients who underwent total ankle arthroplasty, and found that 1.4% of patients required flap coverage, 68% of which were free flaps and 32%

of which were local flaps [182]. Risk factors for needing flap coverage include older age, higher comorbidity index, diabetes mellitus, and pulmonary disease. The most commonly used free flap in their case series was the radial forearm flap. Functional outcomes were promising, with 75% of flap patients presenting with a stable plantigrade foot at 1.5 years follow up.

Limb salvage following oncologic resection

Large defects of the upper and lower extremity can occur following tumor extirpation, and often require free tissue transfer for successful reconstruction and limb salvage [183,184] A systematic review by Lucattelli et al investigated the use of free flap reconstruction in 17 studies and 132 sarcoma patients [185]. They described a number of different free flaps used in the reconstruction of upper extremity sarcoma defects including the latissimus dorsi, gastrocnemius, tensor fascia lata, anterolateral thigh, gracilis, rectus abdominis, and superficial circumflex iliac perforator flap, and found a near 100% flap success rate. Additionally, they found that multimodal treatment with surgery, chemotherapy, and/or radiation was relatively common in this patient population. Specifically, of the patients who required radiation therapy, 57% received it as a neoadjuvant therapy, thereby making locally-based reconstruction difficult and necessitating the import of healthy non-radiated tissue in the form of a free flap. Penna et al reported on a cohort of 33 patients who underwent free flap reconstruction following upper and lower extremity soft tissue sarcoma resection and found a 97% flap survival rate and 97% limb salvage rate [186]. An investigation of soft tissue sarcoma patients who underwent free flap reconstruction versus those who did not require free flap reconstruction revealed that the free flap group tended to have higher tumor grades and have a history of neoadjuvant chemotherapy and/or radiation [187]. The specifics of each reconstructive effort should be tailored to the individual patient's needs, and may include skin, muscle, fascia, nerve, and/or blood vessels. For example, Stranix et al described the transfer of functional composite thigh flaps which included fasciocutaneous tissue along with sensory nerve, plicated iliotibial band, and motorized vastus lateralis [188]. Finally, it has been suggested that the option of free flap reconstruction may influence management of the primary tumor resection, allowing for adequate resection margins and decrease rates of local recurrence [187,189].

Conclusion

Microsurgery has and will continue to play an integral role in the advancement of orthopedic surgery. Specifically, microsurgical tools can be used to address many of the complex orthopaedic issues related to oncologic resection, infection, and trauma in both adults and children. Continued interdisciplinary collaboration must continue in order to advance both orthopaedic and microsurgery and will result in better outcomes for all patients.

Declarations of Competing Interest

None

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None

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