New surgical options to improve the quality of life of amputees

Norbert Kang

Alexander Woollard

Wojciech Konczalik

Abstract

Although the loss of any part or all of a limb remains devastating, there are now many new surgical options to improve the quality of life of an amputee that clinicians should be aware of. These options include composite tissue (allograft) transplantation as well as new surgical techniques for symptom improvement and to allow patients to achieve a better outcome after prosthetic reconstruction. The emphasis of this article will be on symptom improvement and prosthetic reconstruction.

Keywords Composite tissue allograft transplantation; implanted muscle electrodes; myoelectric devices; osseointegration; prosthetic reconstruction; sensory feedback; targeted muscle reinnervation

Aetiology and epidemiology

Major limb amputations (above the wrist or ankle) are relatively common. In the UK, approximately 6000 new lower limb amputees are registered for treatment with disablement centres each year. Similarly, 300 new upper limb amputees are registered. The actual number of amputees is likely to be much higher than this. However, many amputees are elderly, diabetic or multiply disabled and never reach the point at which they can consider any form of reconstruction. For example, the mortality rate at 1 year after amputation for peripheral vascular disease is 48%. Therefore, a major limb amputation in this population can be regarded as a pre-morbid event. Nationwide, the population prevalence is approximately 26 per 100,000. Most amputations are the result of vascular disease (50%) but trauma is a close second (45%), usually in younger, fitter patients. Congenital limb disorders and tumours account for most of the remainder.

Injury pattern and selection of patients

Most amputees do not have a choice about the level of their amputation. This is decided by whatever disease process resulted in the amputation. Moreover, the presence of additional disease or injury may then limit their ability to undergo one or other of the options which are available to improve the quality of their lives.

For example, patients with peripheral vascular disease often have vascular problems affecting other organ systems — especially the heart. This may limit their ability to tolerate an attempt at prosthetic reconstruction since the energy required to move the prosthesis may exceed their cardiac capacity. For example, after transfemoral amputation, the energy requirements to move the prosthesis are estimated at 75—100% higher than baseline. Patients may experience angina or claudication pain when trying to ambulate with a prosthesis which means that these amputees become bed or wheelchair bound.

Equally, not every amputee is a candidate for composite tissue transplantation. The physical and psychological demands imposed by this type of surgery are considerable and continue for the life of the transplant. Patients undergoing this type of surgery must be compliant with taking potentially life-span reducing, life-long immunosuppressive treatments — for life.

Pathways for rehabilitation and subsequent reconstruction are already well established in the UK, with patients very much at the centre of the process.

In this way, patients seeking surgical relief become self-selecting. Surgeons should see themselves as facilitators for a part of this pathway since the decision on the best option for reconstruction is a truly multidisciplinary effort requiring the participation of rehabilitation physicians, psychologists, prosthetists, orthotists, physiotherapists and immunologists. Although this article is written for surgeons, surgery often forms only a very small part of the process of reconstruction.

Composite tissue allograft (CTA) transplantation

Composite tissue allograft (CTA) transplantation is now a viable option for reconstruction after amputation in the upper limb. However, as yet, there have been very few reports of surgeons using this approach for lower limb amputations. The main difficulties include:

- The paucity of suitable donor limbs.
- Life-long immunosuppression — and all its associated side-effects.
- Poor functional outcomes for patients undergoing CTA for above elbow amputations - outcomes are similar to those of a skilled prosthetic user.
- Selecting patients with an appropriate psychological profile.
- Cost of CTA compared with prosthetic reconstruction over the lifetime of the patient.

Recently, Shore has reviewed the techniques, advantages and disadvantages of CTA in the upper limb.[1]

Surgery for symptom improvement and to improve interaction with a prosthesis

Every amputee is unique, and each patient will have unique requirements. However, there are common themes. In general, the functional requirements are higher in the upper limb compared to the lower limb. Moreover, the importance of cosmesis in the upper limb cannot be over-stated. For some patients, this may be their only requirement because the functional value of upper

***Norbert Kang** MBBS MD FRCS(Plast) is a Consultant Plastic Surgeon at the Royal Free Hospital, London, UK. Conflicts of interest: none declared.*

***Alexander Woollard** BM BSc PhD FRCS(Plast) is a Consultant Plastic and Reconstructive Surgeon at the Royal Free Hospital, London, UK. Conflicts of interest: none declared.*

***Wojciech Konczalik** MBBS MRCS is a Plastic Surgery Registrar at the Royal Free Hospital, London, UK. Conflicts of interest: none declared.*

Please cite this article as: Kang N et al., New surgical options to improve the quality of life of amputees, Surgery, https://doi.org/10.1016/j.mpsur.2019.02.007

limb prosthetics can be so poor that many patients prefer to do without a prosthesis altogether.

The common themes are:

- pain
- attachment of the prosthesis to the patient or residual limb
- control of the prosthesis.

Surgery for pain control

Many (but by no means all) amputees experience pain in their residual limb. This can come to dominate their lives affecting their ability to benefit from a prosthetic reconstruction and making them dependent on (largely ineffective) opiate medications. The pain arises from multiple sources:

- neuromas
- phantom limb pain
- scar tissue/unstable soft-tissues
- heterotopic bone formation;
- claudication pain.

Neuromas

Traditional approaches to control neuroma pain have relied on the principle of excision and burying of the free nerve end in muscle or bone or use of end-to-end coaptation to try and reduce regrowth of the neuroma[2–4] (Figure 1). These procedures produce immediate relief, but the recurrence rate is high (approaching 60%) and the pain may recur within just a few months as a new neuroma reforms at the end of the nerve stump.[5] From the perspective of peripheral nerve physiology these approaches can never arrest the production of a new neuroma and the aim is to simply cushion the new neuroma in a less symptomatic location. In every case, the re-buried nerve ends will simply continue to sprout as they seek potential reinnervation targets. A better alternative for neuroma control is to provide end-organ targets that give neurotrophic feedback to the free axons and down-regulate their regrowth. There are two methods to achieve this: *RPNI* (regenerative peripheral nerve interfaces) and *TMR* (targeted muscle reinnervation).

Targeted muscle reinnervation surgery (TMR): Kuiken and Dumanian first described TMR surgery in 2007 as a method for achieving improved control of an upper limb prosthesis.[6] TMR involves connecting the free ends of the major nerves in a stump to redundant muscles in the stump. The nerve ends then grow through to the motor end plates in the target muscle. When this happens, any efferent signals that would have been transmitted to the amputated parts now result in contractions of the reinnervated muscle. For example, after transhumeral amputation, the stumps of the median, ulnar and radial nerves are left free at the end of the stump and form neuromas which may become painful. During TMR surgery (Figure 2), the median nerve stump is (typically) connected to the medial head of biceps while the lateral head of biceps is left connected to the musculocutaneous nerve (i.e. the normal source of innervation to both heads of biceps). Now, when the patient imagines flexing their elbow, the lateral head of biceps contracts as normal. However, when the patient imagines performing functions to do with the median nerve downstream (e.g. finger flexion) the medial head of biceps contracts. In other words, the reinnervated muscles now act as biological amplifiers of the signals travelling down the nerve stumps. Moreover, the activation of the reinnervated muscles is intuitive. There are no trick movements or special training required. The patient thinks their hand is still there and imagines moving it and a real muscle contracts accordingly. By performing TMR surgery, it was hoped that it would be possible to increase the number of myoelectric activation points under voluntary (i.e. intuitive) control. This would allow amputees to control more complex multiaxial, myoelectric, prosthetic limbs without the cognitive burden (i.e. intense training) required using conventional myoelectric prosthetic limbs.[7] Kuiken and his team achieved this aim but then noticed a fortuitous but unexpected outcome of the procedure. Many of the patients reported that their neuroma pain disappeared, and/or their phantom limb pain (PLP) improved.[8,9] It has been our own experience that most, if not all, of our patients having this treatment are able to discard (or at least reduce) their pain medications (especially

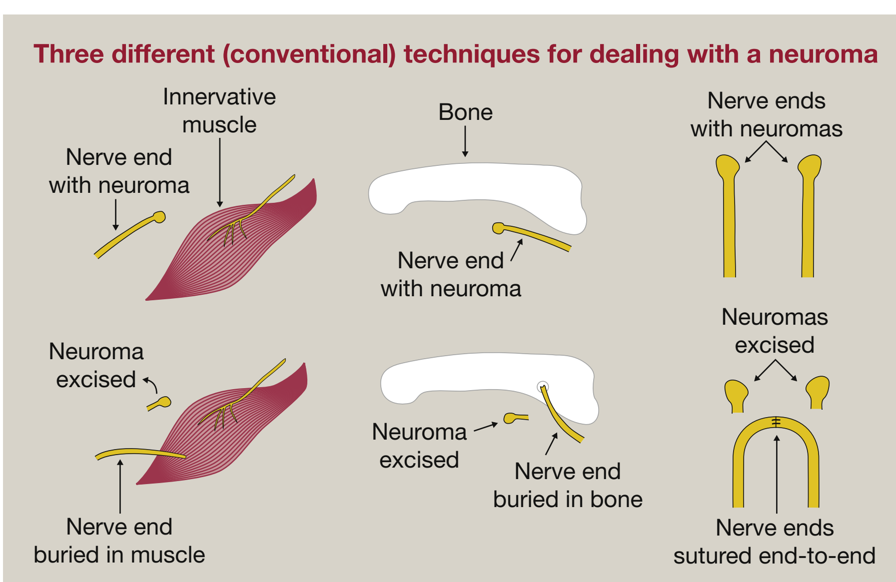
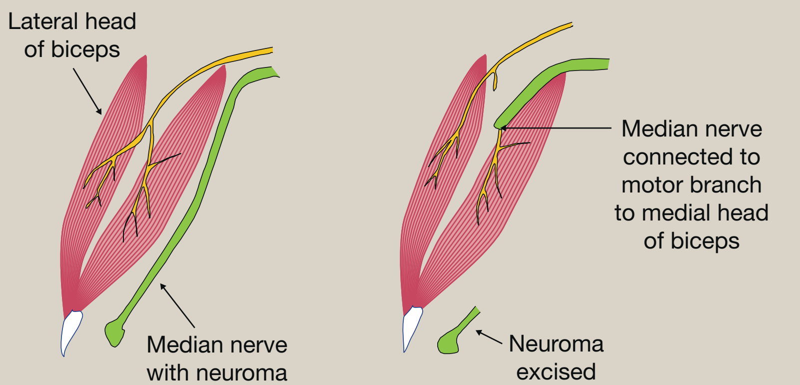


Figure 1

Please cite this article as: Kang N et al., New surgical options to improve the quality of life of amputees, Surgery, https://doi.org/10.1016/j.mpsur.2019.02.007

TMR surgery showing median nerve stump being transferred to motor branch to medial head of biceps



There is (normally) a large size mismatch between the median nerve and the motor branch to biceps

Figure 2

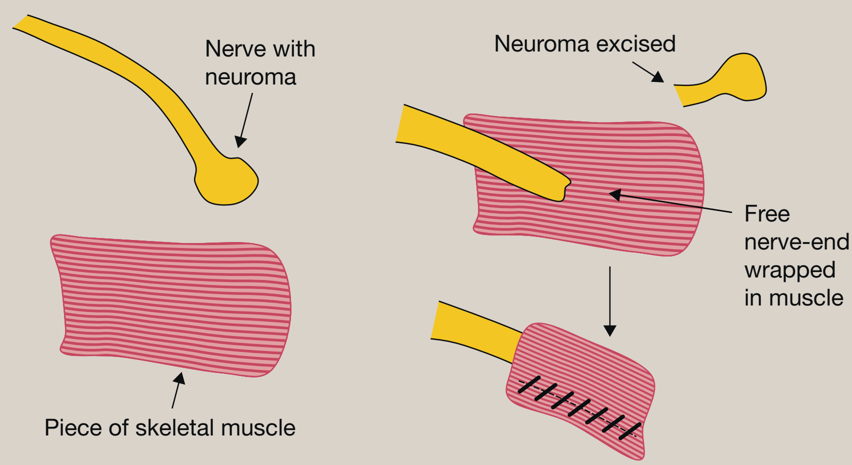
gabapentin) for the first time since their amputation. Obviously, this has major implications in terms of opiate dependence and the overall pharmacological cost of amputation.

Since then TMR surgery has become a routine method for controlling both neuroma-related and PLP. Long-term outcomes are still awaited but early studies (personal correspondence with G Dumanian) suggest that TMR surgery is an effective treatment in both upper and lower limb amputees and is even more effective when performed primarily at the time of amputation. We now believe that TMR can and should be performed for symptom control, even when there is no expectation that the patient will be provided with a complex (and costly), multiaxial, prosthetic limb. It seems that providing the free axons in the nerve stumps with a target end organ, even if the target is inappropriate, is able to suppress the formation of a sensitive neuroma and also provides feedback to the central nervous system to reduce symptoms of PLP (see below).[8] For example, the median nerve is mixed, carrying both sensory and motor axons. Yet, TMR is still able to prevent recurrence of a neuroma.

Regenerative peripheral nerve interface (RPNI): one of the major difficulties with TMR surgery is the need to have a muscle with an intact nerve supply (and therefore functioning motor end plates) to act as a target end organ for reinnervation. Cederna has therefore taken a different approach (Figure 3).[10] Although he agrees that there is a need to provide the free nerve ends with a target to prevent neuroma formation, he feels that it is unnecessary to use an entire vascularized muscle as the target. Instead, he has described RPNI in which small (3 × 2 × 2 cm) chunks of devascularized skeletal muscle are wrapped around the free nerve ends. These free muscle grafts acquire a new blood supply from the surrounding tissue bed and the vasa nervorum of the free nerve ends. The muscle grafts then provide the regrowing axons with a suitable target organ to reinnervate. His studies have shown that the size of the grafts is critical. Too small, and there is not sufficient muscle to provide a target for the nerves. Too large and the grafts will not be able to acquire a blood supply from the surrounding tissue and will undergo necrosis resulting in a mass of scar around the nerve stump — leading to reformation of a painful neuroma.[11]

How do TMR and RPNI compare?: the core principle common to both RPNI and TMR is the use of a denervated muscle target. It is crucial that the target muscle should have been disconnected from its original nerve supply since the new axons reinnervating the muscle will never be able to compete with any existing innervation.[12] With TMR, the muscle retains its normal blood supply and the reinnervating nerve is channelled into the existing motor end-plate zone through its original nerve. In some instances, the muscle selected as a target will have multiple, natural, sources of innervation (e.g. pectoralis major which is supplied by the medial and lateral pectoral nerves). In this situation, each muscle can be split into several reinnervation zones, providing several, separate, muscle targets (Figure 4). Target muscles can also be transferred into the vicinity of a stump, either as pedicled or free-functioning muscle transfers. In contrast, the muscle grafts used for RPNI have no dedicated blood or nerve supply (Figure 5) and yet achieve a similar purpose to TMR surgery because the grafts are automatically denervated when they are harvested. Therefore, RPNI is sometimes described as a *mini-TMR*. Once revascularized, the muscle grafts provoke de novo formation of motor end plates. Cederna has argued that using RPNI allows a reconstructive surgeon to provide a virtually infinite number of muscle targets for the peripheral nerve stumps. Moreover, RPNI surgery is potentially less invasive and destructive (i.e. there is no need to denervate entire, normally innervated muscles). Both techniques are still new, but we believe that time will show that these two approaches are complimentary and can be used according to the individual clinical scenario.

Please cite this article as: Kang N et al., New surgical options to improve the quality of life of amputees, Surgery, https://doi.org/10.1016/j.mpsur.2019.02.007



A nerve end with a neuroma is treated by excision of the neuroma and wrapping the free end of the nerve in a piece of skeletal muscle. The nerve fibres grow into the muscle provoking the formation of new motor end plates.

Figure 3

Phantom limb pain

Phantom limb sensation (PLS) affects all amputees. However, disabling PLP (i.e. patients with PLS that is abnormal or perceived as painful) only occurs in 5–10% of patients and can be debilitating. PLP typically occurs in attacks that vary with intensity and frequency. They mimic the normal sensations in the missing part, but these sensations are distorted in terms of their quality and intensity. The pain is often described as a feeling of 'squeezing', 'cramping', 'burning' or 'crushing' in the absent limb. Traditional treatments are notoriously poor at controlling these symptoms and currently the mainstay of treatment is to modulate these sensations using agents such as gabapentin, pregabalin and amitriptyline, coupled to long-term opioids or transcutaneous electrical nerve stimulation (TENS). Other treatments such as physiotherapy, hypnotherapy, acupuncture and mirror therapy can sometimes be as effective as drug therapy. More recently, the Swedish group under Ortiz has been developing an augmented reality system for the treatment of PLP. This system allows patients to operate a virtual limb on a computer screen. Finally, direct skeletal fixation of a prosthetic limb can also be effective. At their core, all of these different modalities work for the same reason (see below).

How does TMR and RPNI produce symptom relief in amputees?: neuromas always form at the end of an amputated nerve. However, they only become painful if the threshold for stimulation is set abnormally low. The best way to imagine what is happening is to consider what you do when you see a friend on the other side of a crowded room. You shout out their name. No response. So, you shout louder. Still no response. So, you shout as loudly as you can. A painful neuroma is shouting out for feedback from the muscle, tendon, joints, bone and skin in the missing parts. It will never get this feedback, so it stays permanently sensitive.

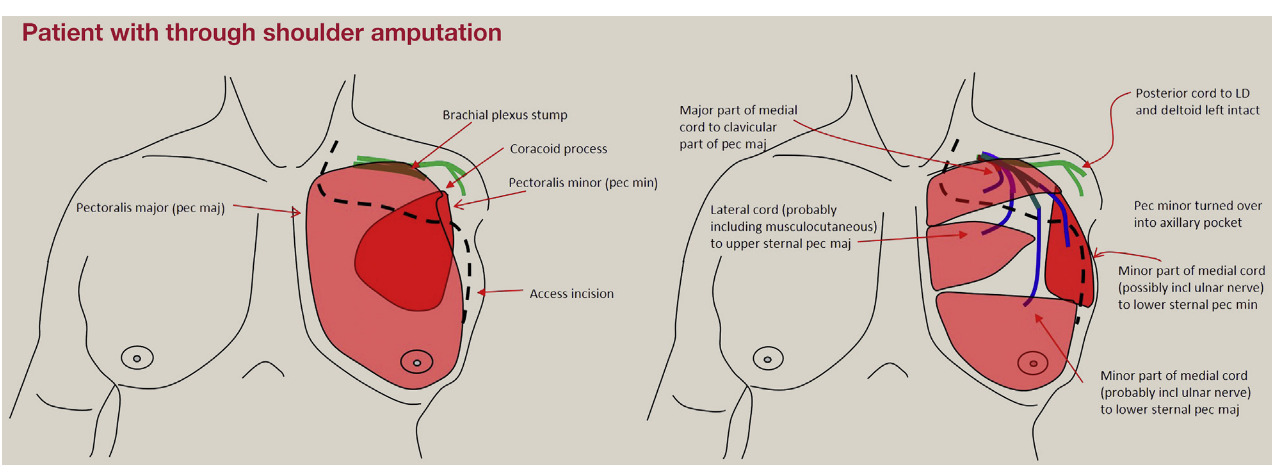


Figure 4

Please cite this article as: Kang N et al., New surgical options to improve the quality of life of amputees, Surgery, https://doi.org/10.1016/j.mpsur.2019.02.007

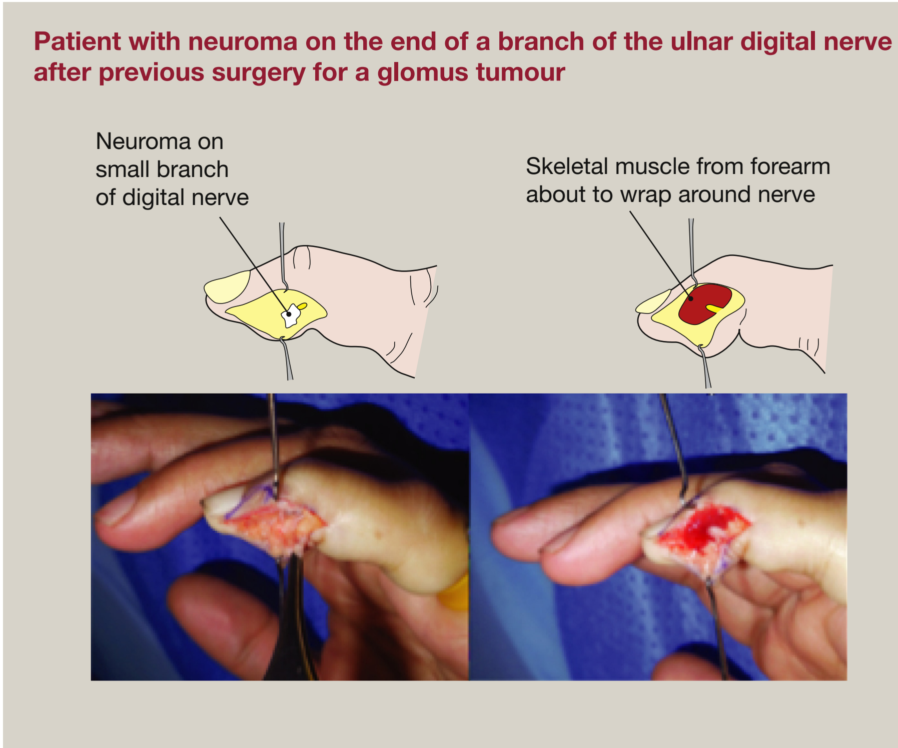


Figure 5

TMR and RPNI surgery both provide feedback to the peripheral nerves allowing the stimulation threshold to return to normal. Certainly, nerve morphology after TMR is closer to normal compared with non-amputated controls. Currently, we do not know the form of the feedback, which may be electrical or trophic or both. However, crucially, the same feedback which results in relief from the neuroma pain is probably responsible for relief from the symptoms of PLP. Although, the pattern of relief is somewhat different.

After TMR or RPNI surgery there is immediate relief from neuroma pain because the neuroma is disconnected and there is a (normal) temporary reduction in nerve transmission after injury. In contrast, symptoms of PLP tend to increase immediately after surgery. This may last for 3–6 months during which patients report an increased requirement for their neuromodulators or opiates. However, after this, symptoms of PLP reduce dramatically, often over the course of days or weeks. Patients describe suddenly not feeling the need for their pain medications — akin to the flicking of a switch. This seems to correspond with the return of the first clinically detectable evidence of voluntary control over the reinnervated muscles. We believe that the sudden reduction in symptoms of PLP relates to the restoration of central feedback from the free nerve ends as they make connections with end motor targets and receive neurotrophic support from the target muscles.

We believe that it is the restoration of feedback to the central nervous system that explains how TMR, RPNI or other interventions such as osseointegration, mirror therapy and augmented reality are able to relieve the symptoms of PLP (Figure 6). In essence, what these treatments do is to trick the brain into believing that the absent limb is still present and (importantly) is normal so that the sensations received by the brain are also normal.

The use of TMR and RPNI for PLP is still new, and we are currently running a randomized control trial to evaluate the long-term effects. However, the data that are available seem to suggest

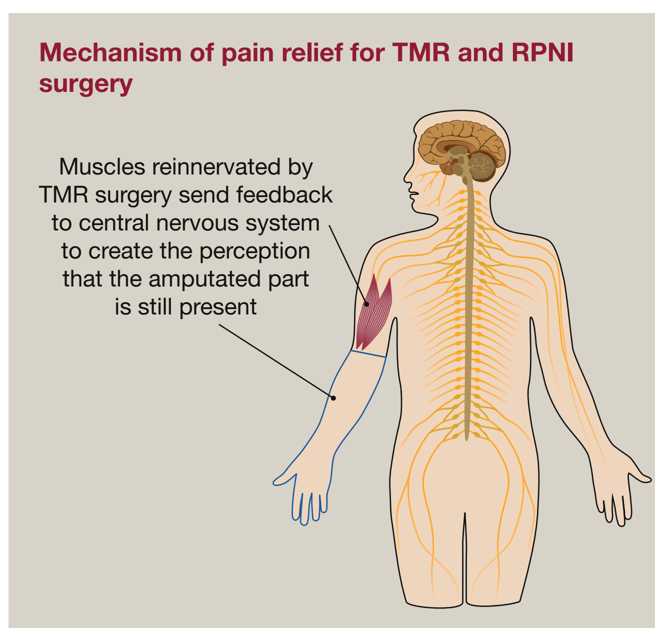


Figure 6

Please cite this article as: Kang N et al., New surgical options to improve the quality of life of amputees, Surgery, https://doi.org/10.1016/j.mpsur.2019.02.007

that this surgical approach is likely to become the standard of care in the future.

Other sources of pain for amputees

New surgical techniques to address pain arising from the nerve stumps is a particular emphasis of this article. However, there are many other potential sources of pain and discomfort for the amputee which are amenable to new treatments and surgical techniques. These include:

- folliculitis
- unstable scars and skin grafts
- heterotopic bone and
- claudication pain.

Folliculitis: especially in lower limb amputees, the presence of hair follicles within the silicone or neoprene sock used as a liner for the prosthetic socket can result in irritation and persistent episodes of folliculitis (Figure 7). This can be debilitating and requires regular disuse of the prosthesis and occasional courses of antibiotics. The best solution is to remove the hairs through the regular use of depilatory cream or waxing which are superior to shaving which tends to irritate the skin. However, this does require the patient to get into a regular routine of hair removal as part of their skin care regime. Therefore, laser hair removal may be a more effective, semi-permanent approach. However, this does still necessitate multiple treatments to achieve adequate destruction of the hair follicles.

Figure 7 A patient with hidradenitis suppurativa behind his knee which started as repeated episodes of folliculitis. Once established, this can only be dealt with surgically. Alternatively, patients may need to consider osseointegration as an alternative method of securing their prosthesis.

Scars and unstable skin grafts: although scars cannot be removed, they can be revised or moved while areas of unstable skin graft can be serially excised. This surgery can shift the load bearing area away from any troublesome scars which are of course often insensate. Where the tissues are beyond simple manipulation, tissue expansion can be used, or new, sensate tissues imported to the stump using pedicled flaps or free-tissue transfer. Often, these composite tissue transfers can bring a muscle into the stump which can act as an additional target for TMR.

Heterotopic ossification (HO): is the formation of new bone in an area of trauma. It is more common (65%) in high-energy injuries such as blast injury. Traumatic amputations are often high energy in nature. New bone can form at the free end of the residual bone, or de novo in the soft tissues (Figure 8). Where it does form, it can create a painful pressure point resulting in ulceration of the overlying skin making it difficult or uncomfortable to use a prosthesis. There is no clear mechanism to explain the formation of HO. Theories include a reaction to the level of force the tissues have been exposed to or bony fragments that have been seeded into the soft-tissues at the time of injury. However, in our opinion, the most likely culprit is fragments of the damaged periosteum scattered within the wound bed in a manner akin to the way in which buried fragments of dermis can later result in the formation of inclusion cysts.

If HO becomes troublesome, it can be resected during stump revision. This can be twinned with a soft tissue revision. However, HO can often wrap itself around vital structures such as nerves or main vessels which can make it impossible to entirely remove. The chance of a recurrence of the HO after surgical excision is less than 5%.

Claudication pain: this is caused by a mismatch between the oxygen demands of the soft tissues and the ability of the vascular network to supply those demands. It is especially prevalent in the patient group who suffer from peripheral vascular disease (PVD) or diabetes and (of course) in smokers. In some patients it is possible to improve the 'inflow' to the limb through angioplasty or bypass. It is also possible to optimize blood flow through the use of vasodilators, improvements in cardiac output and through smoking cessation.

As previously described, an amputation in those with PVD or poor cardiac function can be a pre-morbid event. Importantly, peripheral vascular disease was previously considered as a contraindication for the use of bone-anchors after amputation. That view is beginning to change since recent studies have suggested that use of a bone-anchor can actually enhance survival after amputation in this group of patients by increasing mobility and exercise tolerance.[13]

Attachment

There is evidence of patients surviving after limb amputation in ancient Egypt and even Neolithic Europe (4700–4900 BC). While the earliest evidence of prosthetic use is harder to establish, it is inconceivable that mankind's ingenuity would not have resulted in attempts to improve on the poor function left by the loss of a limb.

Please cite this article as: Kang N et al., New surgical options to improve the quality of life of amputees, Surgery, https://doi.org/10.1016/j.mpsur.2019.02.007

Figure 8 Two examples of HO at the free end of the residual bone after above knee and above elbow amputation. In both cases, amputation occurred after a high energy impact.

Any prosthesis requires an interface between the soft tissues and the prosthesis. Paré first described the use of a socket in 1525 and very little has changed in the basic design of the socket since then. In all cases, the aim of the socket is to create a rigid point of attachment for a prosthetic limb. In addition, to be effective at transmitting the forces in the residual limb to the prosthesis, the socket needs to create a rigid cylinder/cone of soft-tissue around the residual bone. The tighter the fit, the more rigid the soft-tissues and the more effective the socket will be at transferring energy from the residual limb to the prosthesis. Unfortunately, the tighter the fit, the greater the discomfort and the greater the risk of developing problems with painful ulceration of the skin of the stump. The problems are multiplied if the patient has painful neuromas in the stump which are being squashed and moved around within the socket. Moreover, the way in which the forces are transmitted from the residual limb to the prosthesis is abnormal. For example, an above knee amputee effectively 'sits' in their socket, bearing weight on their ischial tuberosity and inferior pubic ramus. Therefore, the walking gait of an above knee amputee using a standard prosthesis is always abnormal creating abnormal loads on the spine and contralateral normal limb. Finally, sockets are difficult to don and doff. To simplify this process, most amputees use a closely-fitting liner over their stump. This is typically made of silicone or neoprene, neither of which are breathable. So, amputees have to put up with sweating and hygiene issues.

A better way of attaching a prosthesis is to use a metallic bone-anchor which is inserted into the free end of the bone in the residual limb (Figure 9). Part of the bone-anchor projects through the skin and this allows a prosthesis to be attached directly to the residual skeleton. Direct skeletal fixation of a prosthesis offers multiple advantages over a standard, socket-fitted prosthesis including:

- Avoidance of discomfort from the socket.
- Avoidance of ulceration and chaffing from the socket.
- Greater ease of donning and doffing a prosthesis — especially for amputees with very short residual limbs.
- Near normal movements of the residual joint (e.g. hip or shoulder) which is not encased or restricted by a socket.
- Reduced effort of ambulation and better control of the prosthesis.
- More normal walking gait because loads are carried by the skeleton as for a normal limb.
- Greater prosthesis use — because it is more comfortable.
- Osseoperception — which is probably responsible for relief of PLP pain through central feedback.
- Avoidance of the need for repeated fitting of a socket — typically patients need to have a new socket fitted once a year due to volume changes in their stump.

Figure 9 Left: Transfemoral amputee using a standard, socket. Middle: Transfemoral patient with prosthesis attached using an OPL bone-anchor. Right: Transfemoral amputee with prothesis attached using an OPL bone-anchor.

Please cite this article as: Kang N et al., New surgical options to improve the quality of life of amputees, Surgery, https://doi.org/10.1016/j.mpsur.2019.02.007

Worldwide, there are many different types of bone-anchor systems currently in use (Figure 10). However, the two which are most widely used are those devised by Branemark (OPRA system)[14] and Al-Muderis (OPL system).[15] In all cases, bone-anchors rely on the principle of osseointegration to prevent the implant from loosening and moving once placed within the residual bone.

Osseointegration is a biological phenomenon that allows a metal implant inserted into the bone to become inseparably fused with the human skeleton (Figure 11). To achieve success, there are features common to all the implant systems which are in routine use:

- The implants are made of titanium since this is the material that most reliably achieves osseointegration.
- Osseointegration creates a seal between the bone and the implant reducing the risk of infection ascending deep into the bone.
- The skin-implant interface is immobilized with respect to the metal-work. This stops the skin edge from behaving as if it is a healing edge as it rubs up against the metal surface. Immobilization of the skin is achieved by thinning the skin and creating the circumstances which allow it to become adherent to the periosteum/bone at the point at which the transcutaneous part of the bone-anchor comes through the skin.

Rates of serious bone infection are very low with these implants — similar to standard orthopaedic joint replacement surgery. In contrast, superficial infections are common but are generally limited to the soft-tissues at the skin-implant interface. In most cases, infections can be easily managed with antibiotics.

The bone-anchor allows the bony residuum to be placed into normal anatomical alignment (when the prosthesis is attached, Figure 12). Direct skeletal fixation also allows for feedback from the prosthesis through a phenomenon called ‘osseoperception’. We believe that it is the feedback that is created by osseoperception that accounts for the relief from PLP described by many bone-anchor users. With an osseointegrated implant, users can sense the thickness of the carpet, whether they are walking on grass, or sand, or concrete. They begin to trust their prosthetic leg.

Figure 11 Titanium bone-anchor removed from a thumb after 3 years, showing the tight interface between the bone and the implant. The bone has “flowed” through the interstices of the implant and cannot be easily removed.

Osseointegration is such a secure method for fixing an implant into bone that it also allows us to place implants in seemingly unfavourable residual bone. For example, bone lengths which are very short (10 cm) or strangely shaped. To do this, 3D printing is used to custom-build implants to fit the bone. The implants can also be created to allow surgeons to use traditional methods for bony fixation such as plates and screws. Importantly, bone-anchors can be placed into the femur, tibia, humerus, radius, ulna and the hand.

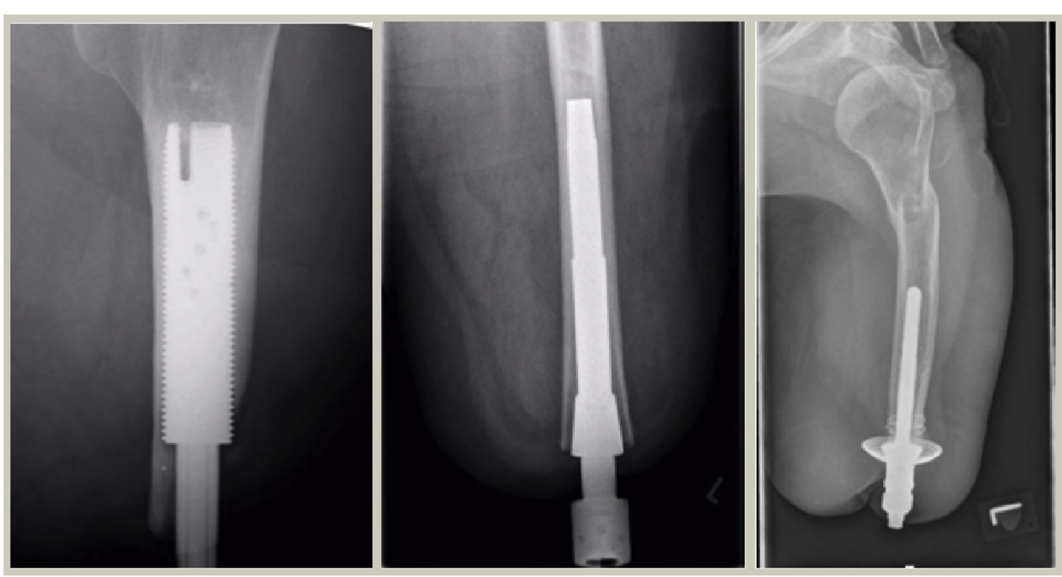


Figure 10 Three different types of bone-anchor. Left: an OPRA implant (Sweden). Middle: an OPL implant (Australia). Right: an ITAP implant (UK).

Please cite this article as: Kang N et al., New surgical options to improve the quality of life of amputees, Surgery, https://doi.org/10.1016/j.mpsur.2019.02.007

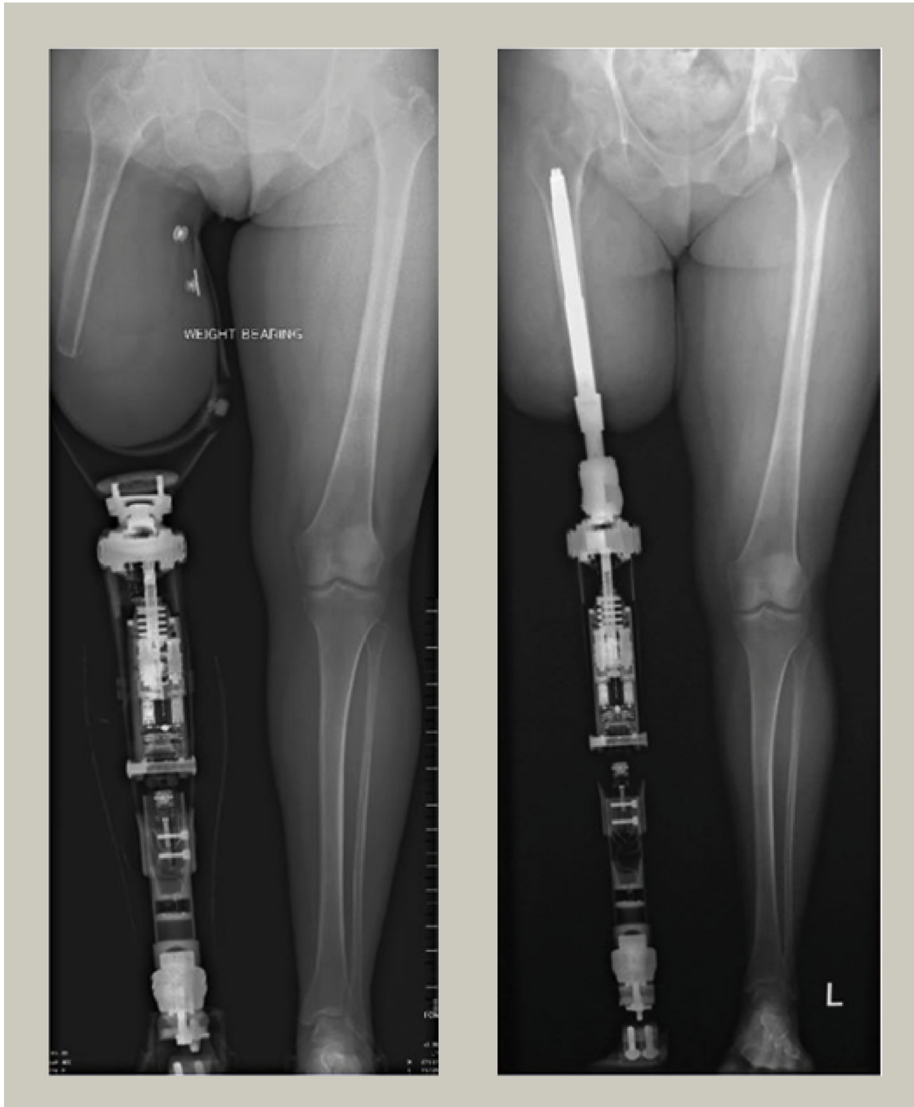


Figure 12 Transfemoral amputee before and after insertion of an OPL implant into the residuum of her right femur. The x-rays clearly show the improvement in the alignment of the residual femur with the bone-anchor in place. **(**Images courtesy of Professor Munjed Al-Muderis.)

Control

The success of a prosthesis can be measured in many ways. Donning and doffing times are measures of how easy it is for a patient to put on or take off their device. If it takes a long time for a patient to 'get up and go', or if wearing a prosthesis is inconvenient in any way, then the patient is not likely to use it. Finally, the anxiety or embarrassment surrounding the potential for malfunction of a prosthesis in a public space is immense. For example, when the stump begins to sweat, the vacuum seal may be lost, resulting in the socket rotating or disconnecting from the stump.

Therefore, it is control over the prosthesis which is arguably where the magic happens. Osseointegration surgery allows patients to gain reliable control over their prosthesis and returns many of them to a reasonably close approximation of a normal walking gait. However, improvements in the ability to control a prosthesis are particularly important in the upper limb. Currently, up to 45% of upper limb prosthetic users stop using their prosthesis because the functional benefits of a standard, socket-fitted prosthesis are so poor.

Traditional upper limb prosthetics rely on static adjuncts such as hooks, claws or a cosmetic anlage. For function, standard upper limb prosthetics are mechanically operated using cables and straps attached to the shoulder girdle or contralateral arm (Figure 13). This type of prosthesis has a long history of evolution and skilled users are able to achieve remarkable levels of function with such a device. Moreover, they have the advantages of simplicity, low cost, ease of repair and the ability to produce very graded movements. Importantly, they never run out of power at awkward moments.

Unfortunately, many amputees find the cables and straps inconvenient and uncomfortable. Donning and doffing the prosthesis can be awkward and embarrassing — especially for women. Moreover, the movements can only be produced by carrying out non-intuitive movements (e.g. shrugging your shoulders to move the elbow) and these movements are

Please cite this article as: Kang N et al., New surgical options to improve the quality of life of amputees, Surgery, https://doi.org/10.1016/j.mpsur.2019.02.007

Figure 13 Above elbow amputee using a hybrid limb. The shoulder straps are used to operate the elbow joint by shrugging his shoulders. The bulge in the upper arm houses the electronics for a myoelectric activation point to operate flexion and extension of his hand.

produced sequentially. For example, the elbow can be activated by shrugging the shoulders but once the elbow is in the correct position, it must then be locked, and the pulley mechanism has to be switched to the hand to allow the cable and straps to operate any hand movements. This is cumbersome and slow compared with a normal upper limb. Finally, the only feedback on whether a task has been successfully completed is visual.

To address some of these issues, many upper limb amputees have turned to myoelectric prosthetics which avoid the need for cables and straps. To control the prosthesis, electrodes are placed onto the skin overlying muscles in the residual limb or shoulder region. The electrodes detect the millivolt discharges created when these muscles contract and these are then amplified by electronics in the prosthesis to act as on/off signals which control small electric motors in the artificial limb.

Conventional myoelectric prosthetics are limited by:

- The low number of activation points in most residual limbs.
- The poor reliability of the surface electrodes.
- The difficulty of attaching a prosthetic limb to the amputation stump which contributes to the poor reliability of the surface electrodes.
- Lack of tactile feedback from the prosthesis.

For example, for a transhumeral amputee, there may be only two myoelectric activation points — biceps and triceps. The patient has to painstakingly learn to use these two signals to control the myriad different potential functions of a prosthetic limb (e.g. opening and closing a hand, rotating the wrist and flexing and extending the elbow). Trying to do this with just two control points means having to either manually toggle a switch in the prosthesis to alter what functions the biceps and triceps signals are applied to. Alternatively, the user learns to use trick movements such as co-contractions of the muscles to instruct the microprocessor in the prosthesis to cycle through to a different set of pre-programmed movements. Either way, none of these movements is smooth, simultaneous or intuitive. The cognitive burden imposed on amputees means that many patients simply never learn how to use their myoelectric prosthesis effectively.

The recent introduction of TMR (and possibly RPNI) surgery, has changed this situation irrevocably. With TMR surgery, it is now possible to rearrange the entire anatomy of the peripheral nervous system in the residual limb to produce multiple myoelectric activation points (see Figure 4). Importantly, these activation points are now under intuitive and simultaneous control (see section on TMR surgery above).

In practice, the actual number of activation points depends on the number of target muscles available in the residual limb and the number of donor nerves which can be transferred. These vary depending on the nature of the injury/amputation. Signal fidelity is also a problem. Movement of the residual limb within a rigid socket, changes in the shape of the stump or excessive sweating can interfere with signal detection resulting in loss of function, or worse, unpredictable function. Signal fidelity can be improved by putting the electrode array into a form-fitting sleeve rather than a rigid socket while suspending the prosthetic limb from an osseointegrated bone-anchor.[16] However, you only have to drop one glass in public to lose faith in the entire value of the prosthetic limb.

To avoid problems with signal fidelity, the next logical step is to implant the electrodes directly into or onto the surface of the reinnervated muscle.[17] This creates the challenge of devising a way of transmitting the signals picked up by the electrodes, to the prosthetic arm. Experimental attempts to do this using conventional electrode cables passed through the skin leads to problems with infection and breakage of the cables after just a few weeks. A better solution is to pass the cables through a more rigid connection such as an osseointegrated implant creating a sort of ‘USB-port’ for the prosthetic limb.[18] Alternatively, a wireless/Bluetooth system could be used, although there are pros and cons to both approaches. The hardwire option (through a bone-anchor) allows for more faithful signal transmission[19] (Figure 14). However, there is always the possibility of infection ascending along the path of the electrode cables from the bone-anchor. It is also unsuitable for patients who do not wish to have or are unsuitable for a bone-anchor. In contrast, a wireless system can be used in any patient and allows the bone-anchor and the electrode systems to be altered/upgraded independently should there be problems with one or the other. In either case, we are rapidly moving towards a ‘plug-and-play’ approach whereby a prosthetic limb can be easily donned and functions intuitively immediately it is attached to the user.

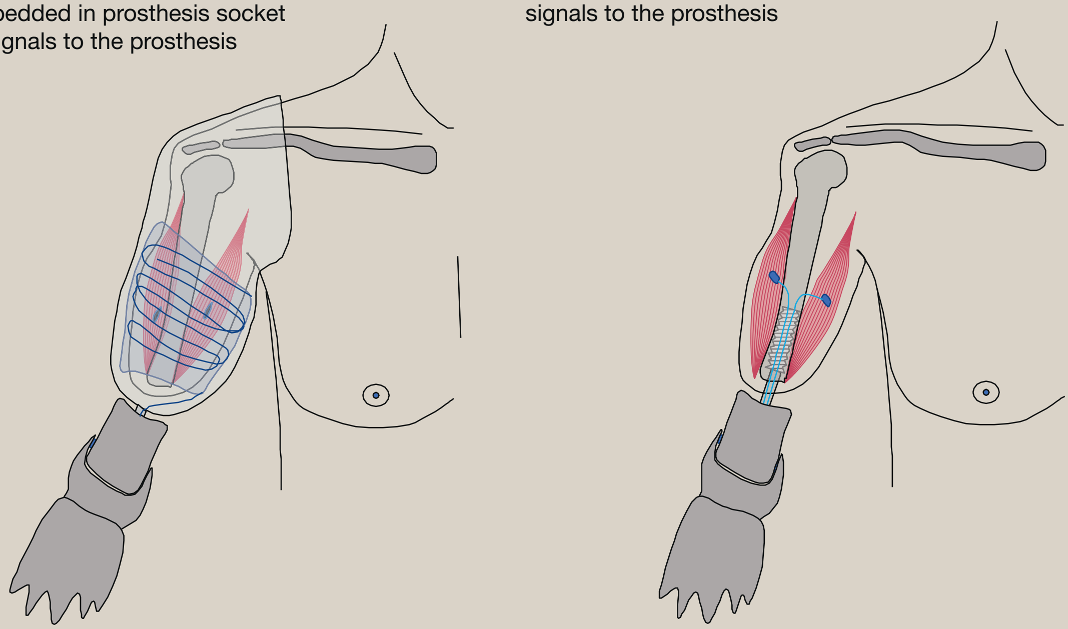
The combination of RPNI surgery and implanted electrodes may be another game changer as it has the potential to create even more myoelectric activation points. However, detecting the electrical signals from the contracting muscle grafts through the skin is impossible, since the amplitude of the electrical discharges is so small. Instead, Cederna is working towards creating

Please cite this article as: Kang N et al., New surgical options to improve the quality of life of amputees, Surgery, https://doi.org/10.1016/j.mpsur.2019.02.007

Examples of two different approaches for achieving greater signal fidelity from EMG signals to control a prosthetic limb

Implanted muscle electrodes (IMES)
- Electrodes inside biceps and triceps
- RF coil around stump to power electrodes and detect EMG signals
- Coil embedded in prosthesis socket sends signals to the prosthesis

Human-Machine Gateway
- Electrodes on epimysium of biceps and triceps
- Cables pass through bone and into bone-anchor
- OPRA bone-anchor used as conduit to send signals to the prosthesis



On the left, the EMG signals are picked up by implanting IMES directly into the muscles. The IMES are powered by wrapping a radio frequency (RF) coil around the amputation stump. The EMG signals generated are picked up by the same RF coil which is embedded in the prothesis socket. Although signal fidelity is improved, there are still problems related to the use of a socket, such as restrictions in the movement of the proximal joint. On the right, the Human-Machine-Gateway allows the signals from muscle surface (epimysial) electrodes to be passed through a bone-anchor (OPRA system) directly into the prosthesis. Therefore, the bone-anchor provides the means for both attachment and control of a prosthesis.

Figure 14

a system whereby muscle electrodes are implanted at the same time that the grafts are wrapped around the free nerve ends. Early studies in a rat model suggest that this approach works, creating the possibility of generating not just a few extra activation points (as with TMR) but many more than current prosthetic technology can cope with.

Most myoelectric control systems aim to create a single signal from a single muscle. Although TMR and RPNI have the potential to create multiple activation points, the use of complex pattern recognition software has the potential to increase the number of activation signals exponentially, without the need to surgically create more activation points. For example, arithmetically, it should be possible to create as many as 24 different combinations taking four separate activation points created through TMR or RPNI surgery. From the patient's perspective, all that has to happen is for them to learn that certain combinations of muscle contraction result in a particular movement of the prosthetic limb. Although this is not 'intuitive' in the strictest sense, many patients find pattern recognition systems much easier to use than straight, one-to-one control systems.

So far, the emphasis has been on trying to improve motor (i.e. efferent) control of a prosthetic limb. However, regular prosthetic users report that one of the greatest difficulties they encounter is the absence of tactile feedback from the limb. To know what the limb is doing, they must visualize the movements of the prosthetic limb directly. Use of a bone-anchor as a method of attachment automatically generates feedback through osseoperception but this is not sufficient to allow a user to discriminate between holding an egg or holding a wrench without direct visual confirmation. Therefore, one of the most interesting recent developments is the observation that patients undergoing TMR surgery often experience sensory recovery in the amputation stump (i.e. afferent recovery).[20–22] Some months after surgery, they report being able to 'feel' the amputated parts in the skin overlying the re-innervated muscles. For this to happen, some form of connection must be made between the sensory end organs in the skin and the sensory nerves passing into the reinnervated muscles. Whatever the mechanism, the phenomenon is consistent and has been used to provide patients with sensory feedback.

An alternative way of providing sensory feedback is through direct stimulation of the nerves using electrodes implanted in or on the nerve stumps combined with muscle electrodes to control the prosthesis. At the time of writing this article, the use of TMR

Please cite this article as: Kang N et al., New surgical options to improve the quality of life of amputees, Surgery, https://doi.org/10.1016/j.mpsur.2019.02.007

surgery combined with implanted muscle electrodes and bone-anchor technology has been used in five patients. Ortiz has created this system around the Swedish OPRA bone-anchored implant which he describes as an 'osseointegrated human-machine gateway'.[19] This system includes cuff electrodes placed around the peripheral nerves which can be stimulated to produce crude and proportional sensation. When the cuff electrodes are stimulated, patients report feeling a slight buzz (like haptic feedback from a smartphone) corresponding to different anatomical locations in the missing limbs. This is sufficient to allow them to grasp an egg without breaking it — even with their eyes shut.

Summary

There have been tremendous advances in what is technologically and surgically possible in the last few decades. Partly, this has been stimulated by the recent conflicts the Western powers have undertaken and the large numbers of amputees that this has produced. Coupled to this is our ever-ageing population suffering the Western ills of diabetes and peripheral vascular disease which continue to increase the number of elective amputations performed, year on year. Fortunately, the prospect of being able to replace an absent limb with a fully functioning, intuitively controlled prosthesis with full sensory feedback is becoming increasingly likely. Patients who once languished in pain, unable to use their prostheses due to socket problems, now have new options to consider. We are continuing to develop a panoply of technologies and surgical techniques to salvage the quality of life for amputees in which the use of osseointegrated implants combined with implanted electrodes and TMR or RPNI surgery will almost certainly become the gold standard.

The clinical arguments have been made and the health economics are rapidly becoming clear. We have the potential to restore amputees to become fully functioning members of society, no longer dependent on medication and able to return to most of their former activities of daily living. It is an exciting time to be a surgeon in this field. ◆

REFERENCES

1 Shores JT, Brandacher G, Lee WP. Hand and upper extremity transplantation: an update of outcomes in the worldwide experience. *Plast Reconstr Surg* 2015; **135:** 351e—60.

2 MacKinnon S, Dellon DA. Surgery of the peripheral nerve. New York: Thieme, 1988; 74—8.

3 Dellon AL, Mackinnon SE, Pestronk A. Implantation of sensory nerve into muscle: preliminary clinical and experimental observations on neuroma formation. *Ann Plast Surg* 1984; **12:** 30—40.

4 Dellon AL, Mackinnon SE. Treatment of the painful neuroma by neuroma resection and muscle implantation. *Plast Reconstr Surg* 1986; **77:** 427—38.

5 Pet MA, Ko JH, Friedly JL, Smith DG. Traction neurectomy for treatment of painful residual limb neuroma in lower extremity amputees. *J Orthop Trauma* 2015; **29:** e321—5.

6 Kuiken TA, Miller LA, Lipschutz RD, et al. Targeted reinnervation for enhanced prosthetic arm function in a woman with a proximal amputation: a case study. *Lancet (London, England)* 2007; **369:** 371—80.

7 Kuiken T. Targeted reinnervation for improved prosthetic function. *Phys Med Rehabil Clin* 2006; **17:** 1—13.

8 Souza JM, Cheesborough JE, Ko JH, Cho MS, Kuiken TA, Dumanian GA. Targeted muscle reinnervation: a novel approach to postamputation neuroma pain. *Clin Orthop Relat Res* 2014; **472:** 2984—90.

9 Kim PS, Ko JH, O'Shaughnessy KK, Kuiken TA, Pohlmeyer EA, Dumanian GA. The effects of targeted muscle reinnervation on neuromas in a rabbit rectus abdominis flap model. *J Hand Surg* 2012; **37:** 1609—16.

10 Kung TA, Bueno RA, Alkhalefah GK, Langhals NB, Urbanchek MG, Cederna PS. Innovations in prosthetic interfaces for the upper extremity. *Plast Reconstr Surg* 2013; **132:** 1515—23.

11 Woo SL, Kung TA, Brown DL, Leonard JA, Kelly BM, Cederna PS. Regenerative peripheral nerve interfaces for the treatment of postamputation neuroma pain: a pilot study. *Plastic Reconstruct Surg Glob Open* 2016; **4:** e1038.

12 Thompson W, Jansen JK. The extent of sprouting of remaining motor units in partly denervated immature and adult rat soleus muscle. *Neuroscience* 1977; **2:** 523—35.

13 Leijendekkers RA, van Hinte G, Frölke JP, van de Meent H, Nijhuis-van der Sanden MWG, Staal JB. Comparison of bone-anchored prostheses and socket prostheses for patients with a lower extremity amputation: a systematic review. *Disabil Rehabil* 2017; **39:** 1045—58.

14 Hagberg K, Branemark R, Gunterberg B, Rydevik B. Osseointegrated trans-femoral amputation prostheses: prospective results of general and condition-specific quality of life in 18 patients at 2-year follow-up. *Prosthet Orthot Int* 2008; **32:** 29—41.

15 Muderis MA, Tetsworth K, Khemka A, et al. The Osseointegration Group of Australia Accelerated Protocol (OGAAP-1) for two-stage osseointegrated reconstruction of amputated limbs. *Bone Jt J* 2016; **98-b:** 952—60.

16 Daly W. Clinical application of roll-on sleeves for myoelectrically controlled transradial and transhumeral prostheses. *JPO J Prosthetics Orthot* 2000; **12:** 88—91.

17 Troyk PR, DeMichele GA, Kerns DA, Weir RF. IMES: an implantable myoelectric sensor. *Conf Proc IEEE Eng Med Biol Soc* 2007; **2007:** 1730—3.

18 Al-Ajam Y, Lancashire H, Pendegrass C, et al. The use of a bone-anchored device as a hard-wired conduit for transmitting EMG signals from implanted muscle electrodes. *IEEE Trans Biomed Eng* 2013; **60:** 1654—9.

19 Ortiz-Catalan M, Hakansson B, Branemark R. An osseointegrated human-machine gateway for long-term sensory feedback and motor control of artificial limbs. *Sci Transl Med* 2014; **6:** 257re6.

20 Serino A, Akselrod M, Salomon R, et al. Upper limb cortical maps in amputees with targeted muscle and sensory reinnervation. *Brain J Neurol* 2017; **140:** 2993—3011.

21 Yao J, Chen A, Kuiken T, Carmona C, Dewald J. Sensory cortical re-mapping following upper-limb amputation and subsequent targeted reinnervation: a case report. *NeuroImage Clinical* 2015; **8:** 329—36.

22 Hebert JS, Olson JL, Morhart MJ, et al. Novel targeted sensory reinnervation technique to restore functional hand sensation after transhumeral amputation. *IEEE Trans Neural Syst Rehabil Eng Publ IEEE Eng Med Biol Soc* 2014; **22:** 765—73.

Please cite this article as: Kang N et al., New surgical options to improve the quality of life of amputees, Surgery, https://doi.org/10.1016/j.mpsur.2019.02.007