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A consecutive series of targeted muscle reinnervation (TMR) cases for relief of neuroma and phantom limb pain: UK perspective

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KEYWORDS
Targeted muscle reinnervation;
Neuroma pain;
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Amputation;
Surgical complications

Summary *Background:* Studies have suggested that targeted muscle reinnervation (TMR) can improve symptoms of neuroma pain (NP) and phantom limb pain (PLP) in patients.
Objectives: Our primary objective was to measure changes in NP and PLP levels following TMR surgery at 4-time points (baseline, 3, 6- and 12-months postoperatively). Secondary aims included identification of the character and rate of any surgical complications and patients' satisfaction with TMR.
Methods: A retrospective review of outcomes of 36 patients who underwent TMR surgery to treat intractable NP and/or PLP after major amputation of an upper (UL) or lower limb (LL) at a single centre in London, UK over 7 years. The surgical techniques, complications, and satisfaction with TMR are described.
Results: Forty TMR procedures were performed on 36 patients. Thirty patients had complete data for NP and PLP levels at all pre-defined time points. Significant improvements ($p<0.01$) in both types of pain were observed for both upper and LL amputees. However, there were varying patterns of recovery. For example, UL amputees experienced worsening of PLP in the first few months post-operatively whereas surgical complications were more common in LL cases. Patients were overwhelmingly satisfied with the improvements in their symptoms (90%).
Conclusions: TMR surgery appeared to relieve both NP and PLP although the retrospective nature of this study limits the strength of this conclusion. However, complication rates were

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high, and it is crucial for surgeons and patients to fully understand the course and outcomes of this novel surgery prior to undertaking treatment.

Introduction

Neuroma pain (NP) and phantom limb pain (PLP) are often similar in quality (e.g., paraesthesiae) but differ in terms of location, intensity, or trigger factors.[1] Characteristically, NP occurs when a trigger point (i.e., a neuroma) is disturbed by palpation or pressure, and the unpleasant paraesthesiae are then localised to the area of the amputation and/or the injured nerve end.[2] Although PLP is often perceived as paraesthesia, these symptoms are felt in the parts of the limb that are now absent and may accompany the feelings of pressure or crushing of these same parts.[3]

Targeted Muscle Reinnervation (TMR) provides a simultaneous solution for both NP and PLP because the new muscle targets provide local feedback to the end of the nerve, preventing regrowth of the neuromas, and distant feedback to the CNS to address the PLP.[4-6] From a patient's perspective, TMR surgery is seductively simple. However, from a surgeon's perspective, achieving these goals requires knowledge, surgical skills, and working practices that are not currently widely available.

This paper describes the outcomes from treatment of a consecutive series of TMR patients treated by a single centre in London, UK over 7 years (2013-2020). The main objective was to determine the therapeutic effects of TMR on intractable NP and PLP in a heterogeneous group of upper and lower limb amputees looking at changes in pain levels over time, after surgery. Intractable pain was defined as pain that could not be managed by pharmacological or other means. The key secondary aim was to identify and characterise the surgical complications. An additional secondary aim was to determine patients' satisfaction with the procedure.

Methods

We performed a retrospective review of all amputees with NP and/or PLP treated with TMR between October 2013 and February 2020 at the Royal Free Hospital, London, United Kingdom. Data were collected from patient records and telephone interviews, especially during the COVID-19 pandemic. It is our normal practice to record pain levels using an 11-point Numerical Rating scale (NRS) at the first clinic appointment (i.e., baseline). Using the NRS, pain levels were then recorded at 4-time points (baseline, 3 months, 6 months, and 12 months) after surgery. Pain levels were documented as an average of the NP and PLP experienced within the last week. Information on pain medications, surgical complications, and overall satisfaction rate following surgery was also collected. The preliminary assessment of patients took place at least one week before the TMR surgery with follow-up appointments at 3, 6, and 12 months in either the out-patient clinics or via telephone—conducted by a member of the team. In cases with a surgical complication, patients were seen as needed by the operating surgeon(s).

Surgical technique

TMR, developed by Todd Kuiken and Gregory Dumanian, has been described in detail.[7-9] In all cases, we made extensive use of intraoperative nerve stimulation. With this in mind, muscle relaxants were used sparingly at induction and were quickly reversed once the surgery was underway. We also avoided using local anaesthetics in the vicinity of the likely muscle targets, to avoid misinterpretation of muscle activity. Finally, tourniquets were avoided because hypoxia of the target muscles quickly led to fatigue of muscle contractions which also made interpretation of the nerve stimulator results difficult.

Upper limb (UL)

Most of our UL patients are either through-shoulder or transhumeral amputees. TMR surgery for shoulder amputations is often technically very challenging due to the short length of the donor's nerves, decreased number of suitable muscle targets, dense scarring related to the initial injury/amputation, and the possible desire to create suitable myoelectric activation points for a prosthesis. [10] Our preferred approach is to divide the pectoralis major muscle into three separate neurovascular territories, creating three separate targets for a donor nerve (**Figure 1**). We often use pectoralis minor as a target but then detach the muscle from the chest wall and rotate it into a subcutaneous position in the axillary area. In contrast, amputations at the transhumeral level allow greater flexibility in terms of the number and location of nerve transfers because of the larger number of potential targets and the longer peripheral nerve stumps (**Figure 2**).

Lower limb (LL)

Most of our LL patients are either above or below-knee amputees. TMR surgery in this group is generally technically simple and performed entirely for either NP and/or PLP. For above-knee amputees, the commonest site of troublesome neuroma pain is the sciatic nerve. For this group, the sciatic nerve is split into two components (common peroneal and posterior tibial) which are coapted to motor branches of either the biceps femoris or semitendinosus/semimembranosus muscles (**Figure 3**). For below-knee amputees, the commonest site of troublesome neuroma pain is the common peroneal or posterior tibial nerves.

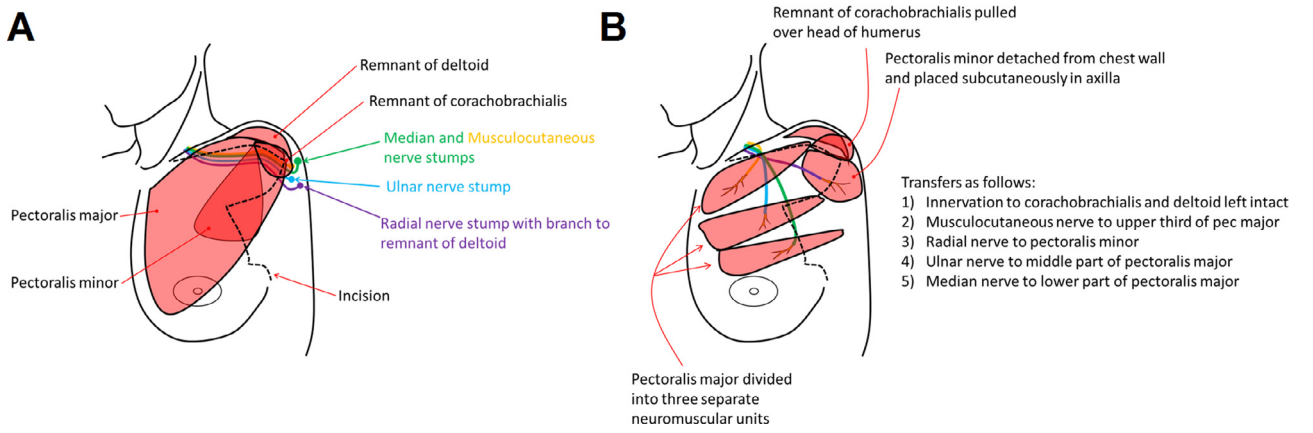

Figure 1 Typical nerve transfers performed in patients with a shoulder disarticulation/high transhumeral amputation. **1A:** Pre-operative identification of the stumps of the median, ulnar, radial, and musculocutaneous nerves based on the patients' reports of paraesthesia in the expected nerve territories - on palpation of their neuromas. **1B**: Nerve transfers performed during the TMR procedure. Division of the pectoralis major muscle into three neuromuscular units which are used as targets for the musculocutaneous, ulnar, and median nerves.

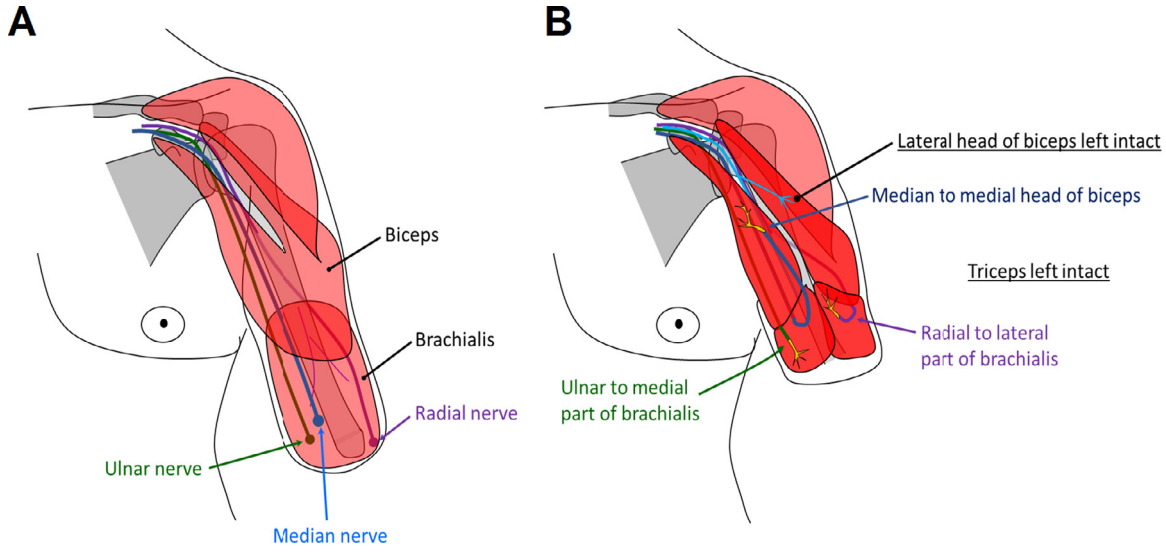

Figure 2 Typical nerve transfers performed in patients with a transhumeral amputation. **2A:** Pre-operative identification of the stumps of the radial, median and ulnar nerves based on the patients' reports of paraesthesia in the expected nerve territories - on palpation of their neuromas. **2B**: Nerve transfers performed during the TMR procedure. From a neuromuscular perspective, when present, the brachialis can be separated into two separate parts (medial and lateral) providing two additional targets for a nerve transfer.

All transfers are performed in the popliteal fossa leaving the distal neuromas untouched. For the common peroneal nerve, we regard the pure sensory and mixed motor components of the nerve as a single entity and (typically) coapt both parts to the motor branch of the lateral head of the gastrocnemius. The posterior tibial nerve is usually transferred to either the motor branch of the soleus muscle or to the medial head of the gastrocnemius (Figure 4).

Pain assessment

During each follow-up appointment and/or phone call, patients were asked to describe two average pain levels (i.e., one for neuroma-related pain and the other for phantom limb pain) experienced within the preceding week using the 11-point numerical rating scale (where 0 meant "no pain" and 10 indicated "the worst imaginable pain"). NP was defined as pain located within the stump, elicited by tapping directly onto the nerve end or following direct application of pressure over the neuroma. Furthermore, NP was recorded as present if patients described "sharp", "shooting", or "electric shock-like pain" arising from these specific sites in the residual limb. In contrast, PLP was defined as being present if the patient reported pain in the amputated parts of the limb which was described as either "burning"," stabbing", "crushing", "throbbing", or "cramping". Patients simply being aware of their amputated parts were recorded as phantom limb sensation only.

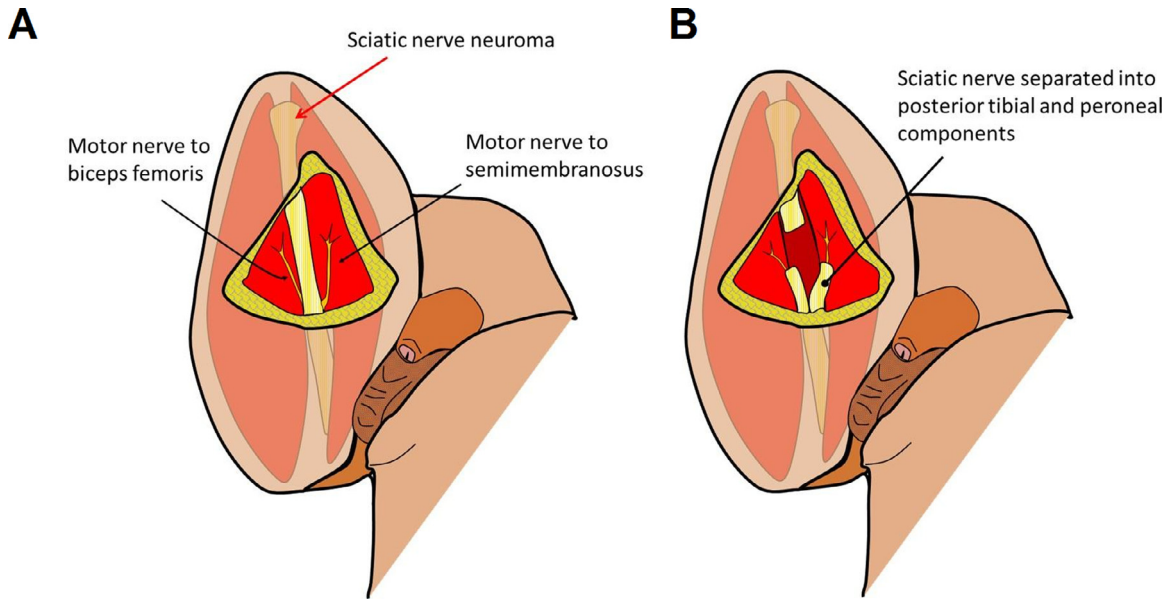

Figure 3 Typical nerve transfers performed for an above-knee amputee with a sciatic nerve neuroma. **4A**: Identification of the sciatic nerve (and sometimes the neuroma) through a longitudinal posterior thigh incision. **4B**: Nerve transfers performed – usually leaving the distal neuroma untouched.

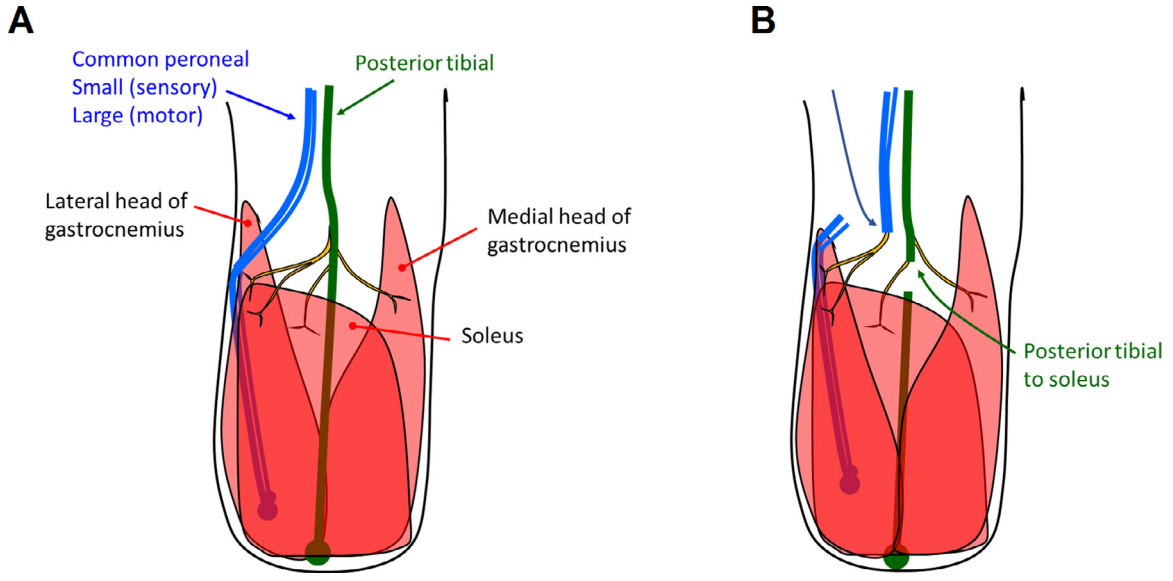

Figure 4 Typical nerve transfers performed for a below-knee amputee with common peroneal and posterior tibial neuromas. **5A**: Typical anatomy encountered in the popliteal fossa before the transfer of the nerves. **5B**: Nerve transfers performed to treat neuromas of these two nerves – usually leaving the distal neuromas untouched.

Statistical analysis

Statistical analysis was performed using IBM SPSS Statistics for Windows, version 26 (IBM Corp., Armonk, N.Y., USA). Based on previously described methodologies [5,11], a paired student T-test was performed to assess mean change in PLP and NP levels 12 months post-TMR surgery in LL and UL groups. Changes in medication were analysed using Wilcoxon signed-rank test, with tablet dosages treated as ordinal data. Medication data was collected from hospital electronic patient records and confirmed via telephone interviews when possible. Cases with missing data were excluded from the analysis and annotated as appropriate.

Results

Baseline characteristics collected from the records included age, gender, ASA score at the time of surgery, the reason for amputation, TMR indication, duration from amputation to TMR, level of limb amputation, as well as follow-up time (**Table 1** and **Table 2**). A total of 40 TMR procedures were

Table 1 Baseline characteristics. Standard deviation (SD) – where appropriate.

Variable	No.	Percentage (%)
Number of patients	36	100
Total number of TMR cases	40	100
Re-do TMR	4	10
Mean age (years)	49 (12.40)	
Male	27	75
Female	9	25
Mean ASA score	2.33 (0.66)	
Mean time duration from amputation to TMR (years)	10.99 (11.36)	
Mean follow-up (weeks, n=38)	85.21 (57.94)	
Median follow-up duration (weeks, n=38)	52	
Latest follow-up appointment (n=38)		
3 months	1	3
6 months	2	5
12 months	1	3
18 months	18	47
24 months	11	29
24 months +	5	13
Data pertaining to limb amputation		
Level of amputation	n=40	
Lower limb	29	73
Trans-femoral	6	15
Trans-tibial	23	58
Upper limb	11	28
Shoulder disarticulation	2	5
Trans-humeral	8	20
Trans-radial	1	3
Time since amputation to TMR (n=40)		
Less than 1 year	4	10
1-4 years	14	35
5-9 years	7	18
10-14 years	3	8
>15 years	12	30

Table 2 Reasons for amputation and indications for TMR in the cohort.

Variable	No.	Percentage (%)
Reason for amputation (n=36)		
Trauma	23	64
Peripheral vascular disease	3	8
Tumour	2	6
Infection	3	8
Unknown	5	14
TMR indications (n=40)		
Neuroma-related pain & phantom limb pain	35	88
Neuroma pain	2	5
Phantom limb pain	3	8

performed on 36 patients, of which 4 were revision TMR procedures – mostly for the unmasking of neuroma pain.

The mean age at the time of surgery was 49 ([range] = 23-75, [SD] =12.40) with 75% of patients being male. (Table 1). The average ASA score was 2.33 ([SD] =0.66) and the mean duration from amputation to TMR was 10.99 (SD=11.36) years. The predominant cause of amputation was trauma (Table 2). Most cases had a follow-up period of >18 months (47%).

The majority of cases were LL amputees (n=29) with transtibial amputations being the most frequent presentation. Amongst UL patients, transhumeral amputation was the most common (73%). The main indications for TMR included unsuccessful pharmacological management of phantom limb and/or neuroma-related stump pain. Unsuccessful management was defined as the inability to alleviate pain with opioids, non-opioid analgesics, or adjuvant treatments (e.g., mirror therapy). Two surgeries (5%) were per-

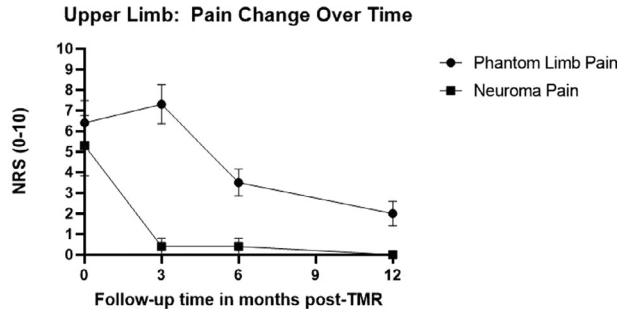

Figure 5 UL amputees: Change in NP and PLP pain levels over 12 months after TMR surgery. Each data point represents the mean of the NRS for the cohort at that time point. Error bars denote the standard error of the mean (SEM).

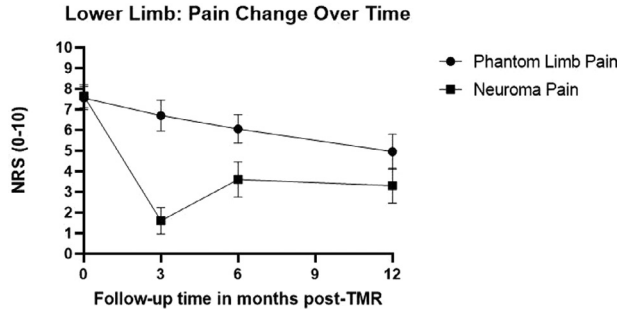

Figure 6 LL amputees: Change in NP and PLP pain levels over 12 months after TMR surgery. Each data point represents the mean of the NRS for the cohort at that time point. Error bars denote the standard error of the mean (SEM).

formed to prepare patients for use of a specialised myoelectric prosthesis.

Pain outcomes

Of the 36 patients who underwent TMR surgery, 28 patients had complete records (78%) of their pain levels at each of the 4 pre-defined time points. Therefore, the pain data analysed refer to a total of 30 procedures performed since 2 of the LL patients also underwent a second TMR procedure.

In UL patients (n=10), NP decreased from 5.30 ([SD] = 4.62) at baseline to 0.4 ([SD] =1.27) at 3- and 6-months post-operatively with complete resolution at 12 months in all patients (Figure 5). With respect to PLP, a slight increase was noted at 3 months from 6.40 ([SD] = 3.40) to 7.30 ([SD]=3.02) with a subsequent decrease to 3.50 ([SD]=2.06) at 6 months and stabilisation at 2.0 ([SD]=1.89) one-year post-TMR (Figure 5). Of these patients, 1 eventually became PLP-free and 5 reported only mild pain (NRS between 1 and 3) by the 12-month timepoint.

Following LL TMR procedures, NP initially decreased from a baseline of 7.65 ([SD]=2.50) to 1.60 ([SD]=2.84) at 3 months (n=20). Subsequently, pain levels increased to an average of 3.60 ([SD]=3.78) at 6 months and decreased to 3.30 ([SD]=3.77) at 12 months postoperatively (Figure 6). Out of 20 surgeries performed, 10 resulted in full NP resolution while two patients continued to experience mild residual pain. In terms of PLP, there was a gradual decrease from 7.55 ([SD] =2.54) mean baseline level to 6.70 ([SD]=3.36) at the 3-month time point to 6.05 ([SD]=3.1) at 6 months, finally settling at 4.95 ([SD]=3.81) at 12 months (Figure 6). Of these patients, four patients reported full resolution of their PLP at 12 months, and three noted marked decreases of pain to minimal levels (NRS between 1 and 3).

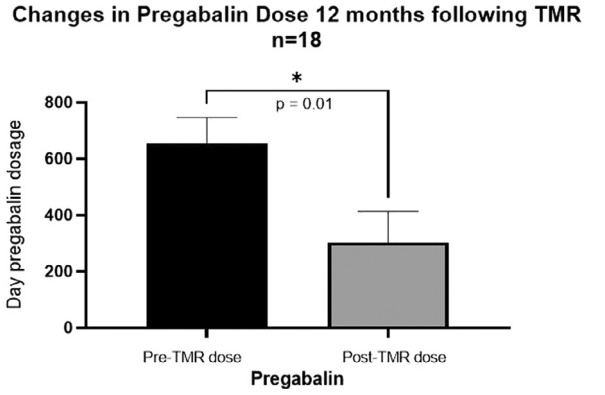

Figure 7 Mean change in pregabalin use comparing baseline and 12 months after TMR surgery. Error bars denote the standard error of the mean (SEM).

Table 3 summarizes the changes in pain 12 months post-surgery. For UL patients, TMR resulted in an average change of -5.3 and -4.4 in NP and PLP, respectively. Smaller improvements were noted in LL patients with the mean change being -4.35 and -2.6 for NP and PLP, respectively. All results were statistically significant.

Medications

The most frequently prescribed analgesics included pregabalin, gabapentin, paracetamol with codeine, morphine, and tramadol. Pregabalin was the single most commonly prescribed medication in this cohort. Therefore, we elected to study changes in the use of this drug to highlight changes in medication usage over the 12 months of follow-up after surgery. Only 18 patient records included full dosing information at baseline and 12 months post-operatively. Out of these, 4 patients were UL amputees and 14 were LL amputees. Importantly, these data showed that 9 out of 18 patients discontinued pregabalin after one year (3 UL and 6 LL patients). On average, we noted a 352 mg reduction in daily intake over the 12 months of follow-up. Given that tablet dosing is discrete data, a Wilcoxon signed rank test was performed, which found the change to be statistically significant with a $p < 0.01$ (Figure 7).

Surgical complications

Forty-six complications occurred in 28 out of 40 TMR procedures performed (70% of procedures), with 13 patients (36% of 36 patients) experiencing more than one complication as a result of their procedure. Complications occurred in 23 LL procedures (79%) and 5 UL procedures (45%), meaning that LL amputees were 1.76 times more likely to de-

Table 3 Mean change in numerical rating score (NRS) for NP and PLP at 12 months after TMR surgery in both upper and lower limb patients. Paired Student's T-tests were performed to determine the significance of any changes in mean pain levels comparing baseline and 12 months after surgery. * denotes a statistically significant value ($p < 0.05$)

Mean change in NP and PLP from baseline at 12 months after TMR surgery			
Upper Limb Patients			
Variable	Mean change (SD)	95% CI	p-value
Neuroma pain (n=10)	5.30 (4.62)	8.61, 2.00	0.006*
Phantom limb pain (n=10)	4.40 (4.03)	7.29, 1.52	0.007*
Lower Limb Patients			
Neuroma-related pain (n=20)	4.35 (4.53)	6.47, 2.228	<0.0001*
Phantom Limb Pain (n=20)	2.60 (3.98)	4.46, 0.74	0.009*

Table 4 Surgical complications associated with TMR procedure. Note: more than one complication developed in 13 of 36 patients.

Complication Type (n=46)	No. of complications occurring in upper limb cases	No. of complications occurring in lower limb cases	Sum of complications	Percentage of complications (%/n=46)
Unmasking of neuromas	0	12	12	26
Infection	4	7	11	24
Bursa	0	6	6	13
Paraesthesia	1	4	5	11
Wound dehiscence	1	3	4	9
Hematoma	1	2	3	7
Ulceration	0	2	2	4
Seroma	1	1	2	4
Lymphatic discharge	0	1	1	2

velop any sort of complication following surgery than UL patients. The most common complication amongst UL patients was a post-operative wound infection which was most often managed with a 5-day course of oral antimicrobials (usually co-amoxiclav). In contrast, the commonest complication amongst LL patients was the unmasking of a pre-existing neuroma. Unmasking occurred in 41% of LL patients but did not occur at all in UL patients. Typically, symptoms of unmasking became apparent within a few weeks of surgery, and four patients required an additional TMR procedure. Other common complications included surgical site infections, (inflamed) bursa formation, paraesthesia, and wound dehiscence. Table 4 summarizes the nature of the complications.

Satisfaction with TMR surgery

Twenty-two patients' notes (61%, 9 UL and 13 LL patients) contained data on their satisfaction following surgery, as well as information on their willingness to consider a prophylactic TMR if this option had been presented to them at the time of amputation (Table 5). Importantly, 91% of these responses indicated overall satisfaction with the procedure at the 12-month post-op visit (9 UL and 11 LL patients). However, out of 22 patients, only 50% (6 UL, 5 LL patients) felt they would have agreed to a prophylactic (preventive) TMR procedure

Discussion

Overall, most of our patients experienced some relief from their symptoms of NP and PLP after TMR. This effect was sustained at 12-months follow-up. Our results appear to confirm the outcomes of previous studies which have highlighted the effectiveness of TMR in achieving predictable, reproducible, and durable relief from both NP and PLP.[5,6,9,12] Specifically, all of our UL patients experienced complete resolution of their NP and a 69% reduction in PLP by 12 months after surgery. Importantly, 60% experienced either complete resolution or had only mild PLP symptoms at 12 months follow-up. In contrast, our LL patients experienced a 57% reduction in NP at 12 months with only 50% experiencing complete resolution of their NP pain at 12 months. Over the same period, the LL patients only experienced a 34% reduction in their PLP with only 35% experiencing either full resolution or only mild PLP at 12 months follow-up. Although less impressive than in the UL, the importance of the pain relief achieved for both groups is reflected in the significant reduction in routine use of pregabalin, over the 12 months after surgery. This hints at the potential for a massive saving in the drug budget for amputees with NP and PLP, following a single surgical intervention.

Despite the generally positive outcomes, our UL patients experienced a noticeable (albeit temporary) worsening of PLP. This contrasts with the experience of our LL patients who experienced a gradual decline in PLP over time. In the UL, we suspect that this increase was due to a more com-

Table 5 Patient-reported outcomes relating to their satisfaction with TMR surgery for pain alleviation.

Question	Yes	%, n=22	No	%, n=22	Undecided	%, n=22	Unknown	%, n=36	Total	%, n=36
Satisfaction with outcomes after TMR surgery (n=22)	20	91	2	9	-	-	14	39	22	61
Would agree to TMR at the time of amputation (n=22)	11	50	2	9	9	41	14	39	22	61

plete loss of feedback to the CNS and this might reflect the more extensive suite of nerve transfers that is usually performed compared with LL amputees where we (typically) only transferred one or two nerves. This worsening settled within 4-6 weeks but it is consistent with the results from Kuiken et al. who also described this type of exacerbation.[13] Differences in the extent of the nerve transfers performed might explain the differences we observed in the degree of resolution of NP and PLP comparing the upper and LL. We speculate that carrying out a larger number of nerve transfers in the LL in the future might address the higher rate of the unmasking of neuromas that we observed, and this might have knock-on effects in achieving a more complete resolution of PLP. However, we think that performing the TMR procedure at a much more proximal level (e.g., mid-thigh for a below-knee amputee) is unlikely to be helpful and runs the risk of creating problems with permanently anesthetic areas of skin in the stump which may then be prone to ulceration when they wear a prosthesis. Our experience has also taught us to modify the advice we give to patients before surgery describing TMR more as a pain-reducing but not pain abolishing procedure.

The overall surgical complication rate was high and nearly 70% of the cohort were affected by a complication of some kind. This was not described or highlighted in previous studies of TMR. We speculated that the development of complications had a common aetiology since they often developed at the same time.[14,15] Specifically, we now think that they were the result of a degree of insensitivity (denervation) of the residual limb caused by TMR making the patients prone to self-injuring themselves during the critical first few weeks after surgery. Excessive early mobilization and prosthesis use resulted in ischaemic pressure on the healing soft tissues.[16,17] and might explain the lower complication rate we observed in the UL compared to the LL patients. To address this issue, we now recommend that patients do not wear their prostheses for at least six weeks after surgery in the LL and longer if there is any delay to wound healing.

The most frequently reported complication amongst our LL amputees was the development of further neuroma pain in the weeks/months after the TMR surgery – especially amongst the transtibial amputees. We have called this phenomenon “unmasking” because patients often recall that these neuromas were present before surgery but felt that they were not as big a concern as the common peroneal or posterior tibial neuromas which were the subject of the initial TMR procedure. However, once the main neuromas have been dealt with, the NP arising from these lesser neuromas swells in importance, sometimes becoming as debilitating as the original problem. In most cases, unmasking was related to smaller cutaneous nerves such as the saphenous, sural, or lateral cutaneous (thigh) nerves or terminal branches of the femoral nerve, especially for above-knee amputees. We speculated that unmasking was more significant in the LL because of the need to use a soft-tissue compressing, neuroma-provoking socket which might explain the complete absence of this problem in the UL.[18] To deal with the unmasking, we had to re-explore the residual limb and perform a further TMR procedure in four cases, using muscle targets that were unused at the original procedure. We combined this with a regenerative peripheral nerve interface (RPNI) approach, as described by Cederna in two cases.[19,20] Since identifying this problem, we have become more careful in our initial examination of the residual limb and now perform a TMR or RPNI procedure for these smaller cutaneous nerves at the initial procedure instead of focusing on just the obvious common peroneal and posterior tibial neuromas - even when the patients do not complain specifically about these neuromas.

Despite the large spectrum of complications, and their high frequency, overall, most of our patients appeared to have been satisfied with the outcomes of their surgery (90% were satisfied). Unfortunately, sample bias could not be excluded as patients who might not obtain satisfactory results have been less keen to return for follow-up, although we did not see any positive evidence for this. Equally, patients with a good response to treatment might have felt that it was not necessary to return for each post-operative consultation, leading to further loss of data.[21] Importantly, only 50% of patients would have agreed to a prophylactic (preventative) TMR procedure at the time of the initial amputation. We have speculated that the high complication rate may have tempered their enthusiasm for supporting this recommendation (even though all complications eventually settled). However, the full reasons for this hesitancy were not evaluated in this study. Moreover, it is worth noting that not every patient with a nerve injury or amputation experiences disabling neuroma pain or increased post-op pain.[22,23] Therefore, using TMR surgery prophylactically means that we could end up treating patients who were never going to develop significant NP or PLP in the first place. This is a particular concern because of the potential economic burden that may be created by making a wholesale recommendation to perform TMR surgery in every patient who undergoes an amputation in comparison to simpler (potentially

cheaper) solutions with a long track record of success in treating NP such as burying the nerve ends into deeper sites as advocated by Dellon and Aszmann.[24] We could not make an economic analysis for this study but hope to do so in the future.

The main limitations of this study are its retrospective nature, relatively small sample size, lack of a control group, and absence of a standardized patient-reported outcome measure. Although our study appears to corroborate the effectiveness of TMR for the treatment of NP and PLP which has been noted in previous studies, we acknowledge the difficulty in reaching such a firm conclusion given the limitations of our methodology. However, surprisingly, the side-effect profile of TMR has not been previously described. This experience has helped us to understand the limits of the TMR procedure and to refine our surgical technique. Finally, we used an NRS to monitor pain levels because of its simplicity, reproducibility[25], and (patients') ease of understanding compared to a visual analogue scale (VAS).[26] Importantly, it allowed us to collect information by telephone.[26] However, we are conscious of the shortcomings of using an NRS as the predominant outcome measure for this study and are currently conducting a multi-institutional randomized controlled clinical trial to produce more robust data to support our current observations. This includes the use of standardised, patient-reported outcome measures for pain perception, mood, and quality of life to demonstrate the value of TMR surgery in these areas, alongside the reduction in pain medication.

Conclusions

TMR has the potential to transform the lives of amputees with intractable NP and PLP allowing a large proportion of this patient group to lead lives that are relatively free of the debilitating side-effects of chronic pain and multiple drug use. This is true, especially for UL amputees where the beneficial effects on NP and PLP are sometimes close to miraculous, but also in the LL. Further studies, including randomized clinical trials, are needed to fully support these conclusions.

Ethics approval

The study was discussed with the Royal Free Hospital R&D Department before commencement. It was the view of the Hospital Institutional Review Board that no Human Research Ethics Committee approval was required, due to the retrospective nature of the study - provided all patients gave their express written consent to publish the data collected from their existing records.

Consent for publication

All patients whose data are presented in this study gave their informed, written consent for publication of their clinical outcomes.

Funding

No funding was obtained for the completion of this study.

Data availability statement

The data supporting the findings of this study are available from DM upon reasonable request.

Declaration of Competing Interest

The authors declare that they have no conflicts of interest and received no funding support or inducements for any aspect of this study. All the conclusions are the authors' own and are drawn solely from the data presented.

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