Use of targeted muscle reinnervation to reduce phantom limb pain in people with amputation

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Clinical Question: For adults with major limb amputations, does targeted muscle reinnervation (TMR) decrease the severity level of phantom limb pain (PLP) compared to non-TMR treatment?

Background: Pain management for people with major limb amputations is an ongoing concern due to the chronic nature of the condition, the current recommended treatment options, and the impact of pain on a person's quality of life. While there are several treatment options for PLP such as pharmaceutical therapies, mirror box therapy, transcutaneous electrical nerve stimulation (TENS), and virtual reality therapy, these methods have limited success[1] and often require continued management. Current pain management techniques are reactive to pain, while TMR may serve as a proactive approach to post-amputation pain experiences, such as residual limb pain, neuroma, and PLP.[2] Use of TMR to prevent PLP has the potential to significantly improve quality of life in people with limb amputations.

TMR is a surgical procedure that was first performed by Kuiken and Dumanian in 2002.[1] TMR can give the bisected motor nerve "somewhere to go, something to do" such as improving the control of myoelectric prostheses.[1] This procedure has been shown to allow more intuitive control and assist with pattern recognition technology.[3] There are two types of TMR, primary and secondary, based on the timing of TMR relative to amputation.[4] Primary TMR can be defined as concurrent TMR surgery occurring with the initial amputation procedure, while secondary TMR is after the amputation procedure has already been performed.[4] The purpose of this CAT is to determine if primary TMR can reduce the severity of PLP experienced by adults with major limb amputations.

Search Strategy:
Databases Searched: PubMed, CINAHL
Search Terms: (TMR OR "targeted muscle reinnervation") AND "phantom limb pain"
Inclusion/Exclusion Criteria: 2000- present, English

Synthesis of Results: 3 studies[1,2,5] published in 2018 investigated the impact of TMR on PLP levels compared to untreated or standard neuroma excision surgery in a total of 101 adults with major limb amputations (range 22-51 participants per study). Study designs differed among the articles, ranging from a low quality case series[5] to a high quality randomized controlled trial.[2] The majority of participants were male with lower extremity, traumatic amputations. All studies showed a reduction in the occurrence[2,5] or the severity[1,2] of PLP in patients who had TMR surgery. Two studies[1,2] used the Numerical Rating Scale (NRS) and three Patient-Reported Outcomes Measurement Information System (PROMIS) instruments: Pain Behavior, Pain Intensity, and Pain Interference. The other study[5] did not disclose the outcome measures used for reporting pain. Two[1,2] of the three studies were highly pertinent to the clinical question. One study[5] was less appropriate and generalizable due to the limited reporting of the methodology and participant characteristics. The ability to draw clinical findings was restricted by the lack of pre-amputation pain data[1,2,5] which may impact the level of post-amputation pain a person experiences. Furthermore the lack of long term follow-up[2,5] does not demonstrate the efficacy of TMR on PLP over a person's lifetime.

Clinical Message: Performing TMR during major limb amputation has been shown to decrease the severity and occurrence rate of PLP. Further investigation should include non-traumatic etiologies and longer follow-up periods.

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Evidence Table

	Dumanian (2018)[2]	**Bowen (2018)**[5]	**Valerio (2018)**[1]
Population	Number of participants: 28 (30 limbs) (15 limbs TMR, 15 limbs standard care) Ages: TMR – 39.6 y (mean), 16.5 (SD) Standard care – 45.3 y (mean), 14.6 (SD) Genders: TMR – males (12), females (2) Standard care – males (8), females (2) Causes of amputation: TMR – trauma (13), infection (2) Standard care – trauma (14), infection (1) Levels of amputation: above elbow (3), below elbow (1), above knee (10), below knee (16)	Number of participants: 22 (18 primary TMR, 4 secondary TMR) Ages: Not stated Genders: Not stated Causes of amputation: Not stated Levels of amputation: below knee (22)	Number of participants: 51 TMR, 438 untreated Ages: TMR – 18-34 y (11), 35-49 y (14), 50-59 y (14), 60+ y (12) Untreated – 18-34 y (83), 35-49 y (103), 50-59 y (114), 60+ y (138) Genders: TMR – males (30), females (21) Untreated – males (288), females (150) Causes of amputation: TMR – cancer (20), infection (5), ischemia (2), trauma (16), other (8) Untreated – cancer (22), infection (90), ischemia (43), trauma (171), other (112) Levels of amputation: TMR – shoulder disarticulation (7), above elbow (4), below elbow (4), above/through knee (18), below knee (18)
Study design	Randomized controlled trial	Case series	Cohort study
Intervention	TMR (timing unknown)	TMR (both primary and secondary)	TMR (timing unknown)
Comparison	Standard neuroma procedure	Standard amputation procedure	Standard amputation procedure
Relevant Outcome(s)	Self-reported pain levels, radiological results	Self-reported pain levels	Self-reported pain levels
Outcome Measure(s)	Numerical Rating Scale (NRS), 3 PROMIS assessments - Pain Behavior, Pain Intensity, Pain Interference, MRI scan, Neuro-Quality of Life, Orthotics Prosthetics Users Survey (OPUS)-Upper Extremity	Not stated	Numerical Rating Scale (NRS), 3 PROMIS assessments - Pain Behavior, Pain Intensity, Pain Interference
Timing of Measurement	MRIs were taken preoperatively and one year postoperatively	Unspecified administration and timing	TMR median postoperative follow-up was 330 days
Key Findings	TMR patients postoperatively: NRS: avg decrease of 3.2 at 12 months 72% no or mild PLP at 18 months Standard patients postoperatively: NRS: avg increase of 0.2 at 12 months 40% no or mild PLP at 18 months	Primary TMR patients postoperatively: 72% experienced PLP at 1 month 19% experienced PLP at 3 months 13% experienced PLP at 6 months	TMR patients postoperatively: NRS median for worst PLP of 1/10 PROMIS Pain Intensity: 36.3 PROMIS Pain Behavior: 50.1 PROMIS Pain Interference: 40.7 Untreated patients: NRS median for worst PLP of 5/10 PROMIS Pain Intensity: 48.3 PROMIS Pain Behavior: 56.6 PROMIS Pain Interference: 55.8
Key Limitations	Less generalizable due to limited amputation causes, lack of long term follow-up	Small sample size, lack of statistical analyses, lack of methodology, unstated outcome measures, possible bias due to authors reporting on their own patients, lack of long term follow-up	Data represents small period of time, selection bias between TMR and untreated patient groups, characteristic differences between patient groups

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