NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Interventional procedures consultation document

Targeted muscle reinnervation for managing limb amputation pain

When a portion of an arm or a leg is surgically removed (limb amputation), nerves at the end of the limb are cut. This often results in persisting limb pains of 2 types: residual limb pain often resulting from nerve endings forming painful benign tumours, or phantom limb pain felt in the removed part of the limb. These pains can be difficult to treat with standard pain relief and sometimes do not go away even with treatment. Targeted muscle reinnervation involves rerouting the nerves that were cut, by attaching them to other nerves in nearby muscles (reinnervation). The aim of the procedure is to manage pain after limb amputation.

NICE is looking at targeted muscle reinnervation for managing limb amputation pain.

NICE's interventional procedures advisory committee met to consider the evidence and the opinions of professional experts with knowledge of the procedure.

This document contains the draft guidance for consultation. Your views are welcome, particularly:

- comments on the draft recommendations
- information about factual inaccuracies
- additional relevant evidence, with references if possible.

NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others.

This is not NICE's final guidance on this procedure. The draft guidance may change after this consultation.

After consultation ends, the committee will:

- meet again to consider the consultation comments, review the evidence and make appropriate changes to the draft guidance

- prepare a second draft, which will go through a resolution process before the final guidance is agreed.

Please note that we reserve the right to summarise and edit comments received during consultation or not to publish them at all if, in the reasonable opinion of NICE, there are a lot of comments or if publishing the comments would be unlawful or otherwise inappropriate.

Closing date for comments: 21 February 2025

Target date for publication of guidance: June 2025

1 Draft recommendations

To treat intractable pain that develops after limb amputation

1.1 Targeted muscle reinnervation can be used in the NHS while more evidence is generated to treat intractable pain that develops after limb amputation. It can only be used with special arrangements for clinical governance, consent, and audit or research.

1.2 Healthcare professionals wanting to do targeted muscle reinnervation to treat intractable pain that develops after limb amputation should:

- Inform the clinical governance leads in their healthcare organisation.
- Ensure that people (and their families and carers as appropriate) understand the procedure's safety and efficacy, and any uncertainties about these.
- Take account of NICE's advice on shared decision making, including NICE's information for the public.
- Audit and review clinical outcomes of everyone having the procedure. The main efficacy and safety outcomes identified in this guidance can be entered into NICE's interventional procedure outcomes audit tool (for use at local discretion).
- Discuss the outcomes of the procedure during their annual appraisal to reflect, learn and improve.

1.3 Healthcare organisations should:

- Ensure systems are in place that support clinicians to collect and report data on outcomes and safety for everyone having this procedure.
- Regularly review data on outcomes and safety for this procedure.

To prevent intractable pain from developing after limb amputation

1.4 More research is needed on targeted muscle reinnervation before it can be used in the NHS to prevent intractable pain from developing after limb amputation.

1.5 This procedure should only be done as part of a formal research study and a research ethics committee needs to have approved its use.

What research is needed

1.6 More research, preferably randomised controlled trials, is needed on:

- patient selection
- details of the technique used
- the need for reintervention
- short- and long-term outcomes, including effects on pain and quality of life.

Why the committee made these recommendations

Evidence on this procedure shows it can reduce pain that develops after limb amputation and there are no major safety concerns. But, there is a lack of high-quality evidence. The evidence includes procedures that were done after amputation to treat pain and at the same time as amputation to prevent pain from developing.

Intractable pain is pain that does not go away, even with treatment. This can have a substantial impact on quality of life and there are few treatment options. So, this procedure can be used with special arrangements to treat intractable pain that develops after limb amputation.

It is unclear who would benefit from the procedure when it is used at the same time as amputation to prevent intractable pain from developing. More evidence is needed on patient selection before the procedure is used in this population.

2 The condition, current treatments, unmet need and procedure

The condition

2.1 A limb may need to be amputated for a variety of reasons, including peripheral vascular disease, infection, trauma and cancer. When the limb is amputated, nerves at the end of the residual limb are cut. This can cause 2 types of persisting limb pain: residual limb pain (often resulting from nerve endings forming painful neuromas) or phantom limb pain sensed in the removed part of the limb. Pain can persist for many years after the amputation. It can have a substantial effect on quality of life and its management can be challenging.

Current treatments

2.2 Medicines that may be used to help relieve persisting limb pain after amputation include:

- non-steroidal anti-inflammatory drugs such as ibuprofen
- antiepileptics such as pregabalin or gabapentin
- antidepressants that are used to treat nerve pain such as amitriptyline or nortriptyline
- opioids such as codeine or morphine
- corticosteroid or local anaesthetic injections.

2.3 Surgical options for treating a painful neuroma include:

- removal of the damaged nervous tissue (neurolysis)

- transposition of the neuroma away from the exposed painful region into a suitable tissue
- repair and reconstruction of the damaged nerve to make the nerve fibres regenerate into the distal nerve end with the possibility to regain function.

Unmet need

2.4 Chronic pain after amputation is common and can be difficult to manage. It can be debilitating, with a negative impact on quality of life and preventing mobilisation on prosthetic limbs. Conventional surgical treatments for painful neuromas include excising and burying the nerve endings in muscle, but the neuroma can reoccur.

The procedure

2.5 Targeted muscle reinnervation (TMR) is a procedure that redirects nerves severed by amputation to new muscle targets. The aim is to reduce residual limb pain or phantom limb pain. It also aims to reduce chronic pain that has not responded to conventional treatments (intractable pain), without the risk of neuroma recurrence. The procedure can be done at the time of initial amputation to prevent pain developing or secondarily to treat pain that has developed after amputation.

2.6 The procedure is done under general anaesthetic. There are 3 main steps: preparation of the donor nerve, identification of a motor branch to the targeted muscle, and finally, nerve coaptation. The major mixed motor and sensory nerves proximal to the amputation site are identified. A nerve stimulator is used to show the motor and sensory nerve branches within, and these are traced distally towards the stump. Motor nerve branches to muscles that are not functional after the amputation are identified and divided, and the involved sensory nerves are then coapted to these motor branches using 8-0 or 9-0 nylon sutures under magnification. It has

been hypothesised that the nerve endings stop causing pain once they have found an alternative muscle, because their physiology is restored.

2.7 Regenerative peripheral nerve interface is another technique that involves innervation of denervated muscle. The severed nerve is dissected longitudinally into its main fascicles, which are then implanted into free muscle grafts. It might be done instead of TMR if no suitable muscle target is available. It is sometimes done at the same time as TMR, if multiple nerves are involved.

3 Committee considerations

The evidence

3.1 NICE did a rapid review of the published literature on the efficacy and safety of this procedure. This comprised a comprehensive literature search and detailed review of the evidence from 10 sources, which was discussed by the committee. The evidence included 1 systematic review, 1 randomised controlled trial (also included in the systematic review), 1 retrospective propensity score-matched study, 1 prospective case series (also included in the systematic review) and 6 retrospective case series or cohort studies (1 of which was also included in the systematic review). It is presented in the summary of key evidence section in the interventional procedures overview. Other relevant literature is in the appendix of the overview.

3.2 The professional experts and the committee considered the key efficacy outcomes to be: reduction in pain and improved quality of life.

3.3 The professional experts and the committee considered the key safety outcomes to be: pain, bleeding, infection and reoperation.

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3.4 Patient commentary was sought but none was received.

Committee comments

3.5 The committee was informed that the procedure may have different benefits in upper and lower limbs. It may help use of a prosthesis in upper limbs.

3.6 The committee was informed that the procedure may unmask a neuroma in another nerve and another operation may be needed.

3.7 The committee was informed that this procedure should be done by surgeons experienced in nerve surgery.

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Chair, interventional procedures advisory committee
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