

# Surgical management for chronic pain

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## Abstract

Chronic pain in the UK affects up to 43% of the population. The consequences include physical and psychological distress, loss of function, employment, family and social strain and increased utilization of healthcare services. Modern pain management services operate across primary, secondary and tertiary care and incorporate general practitioners, psychologists, physiotherapists, pharmacists, specialist nurses, pain physicians and surgeons. This allows for a coordinated approach to chronic pain, engaging the patient in a structured pathway from conservative measures, through to surgery if necessary. Surgical interventions have been utilized effectively throughout the 20<sup>th</sup> century for the treatment of a variety of conditions, some of which are now effectively managed with improved pharmacological approaches or novel neuromodulation techniques. Ablative procedures that aim to permanently interrupt the pain pathway still represent the final solution for some conditions, particularly those with cancer associated pain; however, the search for less invasive, less risky measures continues. This is stimulated by an increased understanding of the neurobiology of pain transmission and the physiological changes which occur in persistent pain.

**Keywords** Ablation; chronic pain; neuromodulation; surgery

## Definitions

The International Association for the Study of Pain (IASP) defines pain as ‘An unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage.’ Persistent pain is generally considered to be that lasting longer than 3 months. Chronic pain can be considered as persistent pain where negative psychological or social sequelae have occurred due to the disease. These can include a reliance on pharmacological methods of treatment, loss or reduction in employment, social isolation, depression, anxiety and a preoccupation with pain-associated loss of physical function.

Chronic pain is not included in the International Classification of Disease (ICD)-10, but will be in ICD-11, which will make a distinction between chronic primary and chronic secondary pain. Primary pain includes those conditions without a better explanation by another diagnosis of chronic pain, such as chronic widespread pain, primary headache, and irritable bowel

syndrome. Secondary pain is characterised by identification of a distinct cause such as cancer, surgery, persistent inflammation of the joints or viscera, or disease of the somatosensory nervous system (neuropathic pain).

## Introduction

The prevalence of all forms of chronic pain in the UK is estimated to be around 43% and climbing. Moderate to severely limiting pain affects almost 8 million people, which is comparable to other European data. This includes high-functioning patients and the 16% of patients who experience suicidal ideations. There is a consistently higher figure in females and a steady increase in prevalence with age, reaching up to 62% in the over 75 year olds, which is only likely to increase given the changing population distribution.<sup>1</sup>

Figures between 11.2% and 16.5% are suggested for chronic widespread pain sufferers, including fibromyalgia, where surgical treatments are not usually successful, and chronic neuropathic pain, between 8 and 10%. The economic consequences are enormous, costing the UK over 12.3 billion for back pain alone, and using far more primary care resources compared to non-sufferers.<sup>1</sup>

Surgery for chronic pain has changed significantly over the last century. Commonly, procedures were reserved for the management of patients with incurable cancer only and involved nerve ablation, to permanently interrupt the pain signal. Advances in our understanding of pharmacology has allowed satisfactory conservative management of even patients with severe disease. Neuromodulation techniques have offered alternatives in the treatment pathway of chronic pain for both malignant and benign pathology.

A distinction between surgery for cancer and non-cancer pain is often helpful, as a different approach is required to allow identification of appropriate patients in each group. With an increase in the scope of chronic pain services and dedicated multidisciplinary teams focussed on management rather than cure, the role for surgery in non-cancer pain is continually changing. The recent emphasis on avoiding opiates for management of chronic non-malignant pain may have the potential to change the landscape further in the future.

Management of symptomatology towards the end of life falls under the jurisdiction of both primary and palliative care services, with hospice care providing a level of comfort that makes surgery unnecessary in the majority of patients. Surgery does still have an important role to play in those considered for interventional therapy. Neuromodulation techniques may be an acceptable compromise between invasive intervention and potential serious consequences.

## The pain pathway

The sequence for the perception and response to pain (nociception) can be divided into four broad areas: transduction, conduction, transmission, modulation and perception.

1. Transduction starts with the activation of a peripheral pain receptor (nociceptor) by noxious chemical, thermal or mechanical stimuli and the transformation of this into an action potential.

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- Conduction involves the propagation of the signal along afferent sensory fibres, via cell bodies in the dorsal root ganglion, to terminate in the dorsal horn of the spinal cord. The speed of transmission is dependent on whether it travels via small unmyelinated C-fibres (slower) or large myelinated A-delta-fibres (faster). Signals from larger A-beta fibre mechanoreceptors can also travel with these signals and are thought to have a role in modulation of pain in the spinal cord.
- Transmission involves the release of pro-nociceptive substances such as glutamate, substance-p and calcitonin-gene-related-peptide (CGRP) causing activation of interneurons and second order neurons. Activation generates a second action potential which travels via long tracts to various parts of the brainstem and cortex.
- Perception of pain is produced by a combination of inputs from multiple areas of the cortex and midbrain. This 'pain matrix' consists of areas associated with temporal/discriminative perception such as the somatosensory and insular cortices, and affective/emotional areas such as the amygdala and anterior cingulate cortex (ACC). This combination provides information about intensity and placement while integrating previous experiences to assign salience to the stimulus. The thalamus plays a central role in co-ordinating this response (Figure 1).

The pathway for pain from the body is via the lateral spinothalamic tract (LST) lying in the superficial anterolateral quadrant of the spinal cord. This transmits pain, temperature and itch sensation from the contralateral side of the body. Similarly to the dorsal horn it is arranged somatotopically with cranial structures located anteriorly and projects to the thalamus where it synapses on one of a number of nuclei. The craniofacial region transmits sensory information through the trigeminal nerve via the Gasserian ganglion to sensory nuclei in the pons region of the brainstem.

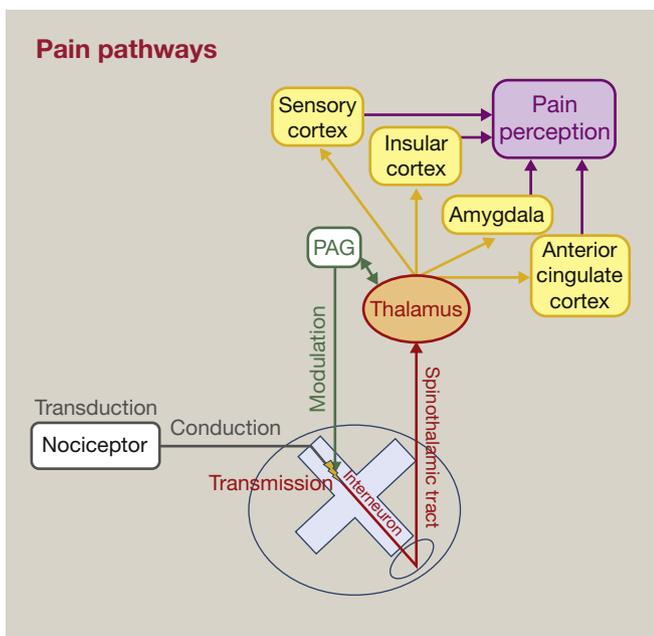


Figure 1

Modulation can be achieved by decreasing neurotransmitter release from primary afferents, using medications such as opioids, or increasing the impact of descending inhibition, using medications such as anti-depressant. The same increase in descending inhibitory controls can be achieved with electrical stimulation in areas of the spinal cord and brain, namely the periaqueductal grey, nucleus raphe magnus and locus coeruleus.

## Ablative procedures (Figure 2)

### Cordotomy

Initially performed as an open surgical technique, it is now almost exclusively performed percutaneously using radio-frequency (RF) ablation of the LST. For a cervical lesion, the patient is placed in a lateral position with the unaffected side up. The needle is placed into the LST through the C1 or C2 vertebral foramen and stimulated to assess the motor and sensory responses. Adequate responses prompt a RF lesion at 80°C for 20–45 seconds. The indications include unilateral, cancer-related pain below the fourth cervical dermatome with a life-expectancy estimated at less than 12 months, however it is most commonly performed for costo-pleural syndrome due to malignant mesothelioma. An improvement in analgesia requirements of over 50% has been reported in up to 83% of patients but this is only below the level of the C4 dermatome for up to 1 year. Side effects include failure, subsequent new pain on the opposite side (mirror pain), dysaesthesia, Horner's syndrome, postural hypotension and respiratory difficulty.<sup>2</sup>

### Dorsal route entry zone (DREZ) lesion

Similar to cordotomy, DREZ lesioning involves the use of RF thermocoagulation to disrupt pain pathways. It differs from cordotomy by targeting the grey matter of the dorsal root at distinct levels, causing selective disruption of second-order neurons, and hence selective pain. The procedure is performed via a laminectomy/laminoplasty and involves insertion of a RF probe 2–3mm into the dorsal horn aiming for Rexed laminae 1–4, where 20–30 lesions per root are created at 75°C for 15 seconds.

Avulsion injuries as well as segmental pain caused by spinal cord injury are common indications for the procedure and are associated with some of the best outcomes at 70–90% pain relief. Other indications include localized compression of the brachial plexus, such as Pancoast syndrome, peripheral nerve lesions, amputations and radiation-induced plexopathy. It has also occasionally been used to treat spasticity, although the results for the latter are not as convincing.

The risks associated with the procedure include failure (particularly with poorly localized pain), ipsilateral weakness due to damage of the corticospinal tract, sensory ataxia due to damage of the dorsal columns, or loss of sensation with or without associated dysaesthesia. Occasionally it can cause loss of bladder control. Despite these it remains an important line of treatment in some conditions.

### Midline myelotomy

Midline myelotomy was developed to interrupt fibres of the LST tract as they decussate, potentially negating the need for bilateral cordotomies. It has been suggested that the division of the

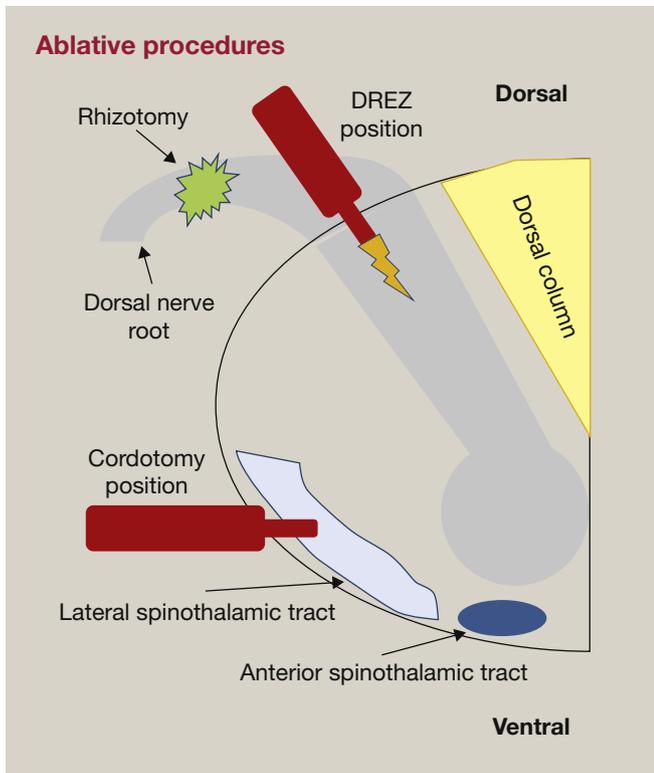


Figure 2

midline commissure is linked to disruption of pain pathways in the dorsal columns. Modern techniques crush a small section of the midline tissue and have produced excellent pain relief in conditions such as pelvic, gastric, hepatobiliary and pancreatic cancer pain.

#### Dorsal rhizotomy/ganglionectomy

Similar to DREZ, dorsal rhizotomy, or ganglionectomy, aims to disrupt the passage of afferent pain signals, this time through selective dissection of the dorsal nerve root or ganglion respectively. Potentially, this preserves distal axons and minimises neuroma formation. Rhizotomy is performed via a laminectomy, while the dorsal root ganglion can be reached via intervertebral foramen but requires dissection of the ventral root, which can prove difficult.

Although in theory, sensory nerves and motor nerves are separated between dorsal and ventral roots, some small, sensory fibres that enter the ventral horn to synapse in the dorsal horn. This combined with the overlap of dermatomal representation, makes prediction of success based on selectively nerve root block difficult, and the need for lesions at multiple levels more likely to be necessary for adequate analgesia.

Quoted success rates are generally variable due to the lack of standardization in both procedure and patient characteristics. Reasonable indications include intractable occipital neuralgia, with long-term success rates for excellent to moderate analgesia of 20 and 40% respectively. Ganglionectomy for monoradicular pain is less promising and is associated with an increased chance of dysaesthesia, especially with ganglionectomy, while failed back surgery syndrome is a particularly poor indication.

#### Peripheral neurectomy

Theoretically, primary denervation of a painful area could lead to a decrease in pain intensity, assuming the area is served by easily identifiable, purely sensory nerves. In reality, the mixture of motor and sensory components may lead to unintended motor deficits, which are problematic for articular pain in joints such as the knee and elbow. Pelvic pain secondary to dysmenorrhoea may be treated by presacral neurectomy, although convincing results for this are limited and it may be associated with an increase in side-effects compared to other treatment modalities.

The formation of a painful neuroma due to trauma or surgery is thought to occur in up to 60% of patients and represents a problem without agreed optimal treatment. Treatments trialled include simple excision, excision with a separate treatment of the cut end such as transposition, or formation of a cap. Studies are small; however, one meta-analysis suggested that the majority of patients will have a meaningful reduction in pain after surgery, but the superiority of one technique over another was not evident. A group with pain persisting over 2 years and more than one previous neuroma surgery, had better results with either excision and transposition of the nerve into another tissue such as muscle, bone, or excision and coverage with healthy tissue.<sup>3</sup>

#### Neuromodulation procedures

##### Spinal cord stimulation

Direct electrical stimulation of the dorsal columns was proposed as a treatment for intractable pain in the 1960s, following Wall and Melzack's gate control theory of pain. A spinal cord stimulator (SCS) consists of an electrode array and a pulse generator, which can be rechargeable or non-rechargeable. The analgesic mechanism of action is partially dependent on the level of the electrodes in the spinal column, with effects such as bronchodilatation and cardiac nervous system stabilization occurring with higher placed leads, and peripheral vasodilatation and decreased bladder spasticity occurring at lower levels. Other proposed mechanisms of action include activation of native inhibitory mechanisms, suppression of neuroimmune and sympathetic agitators of pain, and inhibition of wide dynamic range neurons in the spinal cord.<sup>4</sup>

Percutaneous placement under local anaesthesia (LA) allows for on-table testing of position. Surgical placement may require general anaesthesia as a laminotomy is required to allow adequate access to the epidural space. Stimulation patterns consist of pulse width, amplitude, and frequency, with typical figures for each of 100–500  $\mu$ s, 2–8 V and 60–100 Hz, respectively for traditional tonic stimulation. Recent advances in impulse generator patterns have suggested that alternatives such as burst stimulation (alternating high and low frequency pulses) and high-frequency stimulation (1–10 kHz) may offer superior analgesia to tonic stimulation without the uncomfortable paraesthesia.

The National Institute for Health and Care Excellence (NICE) recommends SCS as an option for adults with more than 6 months of neuropathic pain despite appropriate conventional medical management, and who have had a successful trial of stimulation as part of the assessment.<sup>5</sup> The most common indication for SCS is leg pain secondary to failed back surgery syndrome (FBSS), where patients experience new or persistent pain

despite technically successful spinal surgery, and where improvements in pain relief, satisfaction and opiate requirements have been demonstrated during the trial. Axial back pain is notoriously difficult to treat with currently available technology, but efforts are being made to improve the efficacy in this area. Complex regional pain syndrome, particularly type 1, where there is no direct evidence of nerve damage, is also considered an effective use of SCS.

SCS has also been shown to be an effective treatment for chronic ischaemic leg pain and avoidance of amputation for appropriate patients, but is not currently recommended unless in the context of research. Similarly in Europe, SCS is used more extensively as a treatment for refractory angina pectoris, but the studies that demonstrate similar efficacy to coronary artery bypass grafting are small so it is not recommended in the UK. Alternative areas where SCS may be effective include chronic spasticity pain associated with multiple sclerosis or Parkinson's disease, chronic pelvic pain and bladder dysfunction.

### Deep brain stimulation

Analgesia by stimulating areas of the brain directly responsible for pain processing represents an attractive prospect for those patients with disease unresponsive to conservative management. NICE guidance recommends it should only be used in patients with refractory chronic pain syndromes where other treatments have failed to control symptoms (excluding headache.)

There are three main targets for stimulation. These are: the ventral posterolateral and ventral posteromedial nucleus of the thalamus, the periventricular and periaqueductal grey matter surrounding the third ventricle, and rostral anterior cingulate cortex (ACC) posterior to the anterior horns of the lateral ventricles. Stimulation of the posterior hypothalamus has also been attempted for cluster headache when occipital nerve stimulation has failed. The ACC represents a promising area of treatment for those with a substantial affective component, as well as a variety of pain conditions such as FBSS, persistent post-stroke pain, spinal cord injury and those in whom electrical neuromodulation has failed. Indeed, targeting the affective component directly, may be part of the solution for a number of patients with no potential satisfactory treatment options.

Motor cortex stimulation (MCS) is a less invasive stimulation modality where electrodes are placed on the motor cortex and connected to an impulse generator, similar to DBS and SCS. Despite small studies, success rates of up to 76% have been reported for neuropathic facial pain and post-stroke pain. The greatest success appears to be with facial pain, trigeminal neuropathic pain and complex regional pain syndrome (CPRS), with less reliable improvements found in hemibody post-stroke pain and post-herpetic neuralgia. MCS is also potentially safer than DBS, but differences in success rates may reflect study design more than a true effect difference. It seems likely both procedures will have a place in future treatment pathways, ideally guided by functional imaging techniques to guide stimulation placements.

### Intrathecal drug delivery

The UK currently licences morphine, baclofen and ziconotide for intrathecal drug delivery (ITDD), although other medications are used extensively during anaesthesia for short-term pain relief.

ITDD allows drugs to be delivered directly to the dorsal horn receptor sites, therefore requiring much smaller doses with fewer medication side effects. These potential benefits make it an attractive treatment option and, although convincing evidence is lacking for chronic non-cancer pain, there is good evidence for use in cancer pain.<sup>6</sup>

The system consists of a catheter, which can be external or tunnelled, and an infusion pump, which can be either external or fully implanted. Externalized systems are usually reserved for patients with limited life expectancy as they offer a quick, cheap method of delivering high doses, but come with a significantly increased risk of infection. Numerous infusion regimes exist, including fixed-rate, variable-rate and patient-administered bolus dosing. The choice is a balance between flexibility of drug delivery against reduced battery life and more frequent pump refills.

The problems associated with ITDD systems are significant and limit the application from widespread use. Complications include infection, particularly of the pump pocket and meninges, CSF leak, drug leakage, catheter displacement or occlusion, and intrathecal granuloma formation. Granulomas adjacent to the catheter tip are more common with morphine and hydromorphone, particularly at higher concentrations and low flow rates. MRI compatibility is also an issue.

## Decompression procedures

### Microvascular decompression for trigeminal neuralgia

The International Association for the Study of Pain (IASP) defines trigeminal neuralgia (TN) as 'a unilateral painful disorder that is characterized by brief electric shock-like pains, is abrupt in onset and termination, and is limited to the distribution of one of more divisions of the trigeminal nerve'. This is further subclassified by cause: either microvascular compression at the brainstem root entry zone or by a lesion other than vascular compression (e.g. multiple sclerosis, MS). It occurs most often in the fifth decade, is twice as likely in females and has an annual incidence in the UK of 26/100,000.<sup>7</sup>

Damage to the nerve root and loss of myelin is thought to be involved in the pathogenesis, either through direct vascular compression or the deposition of MS associated plaques. TN is a clinical diagnosis and should be differentiated from other disorders such as trigeminal autonomic cephalgia, temporomandibular joint disorder, intracranial tumours and infection of structures supplied by the trigeminal nerve. Investigations should be used to exclude sinister causes, and MRI tomographic angiography can help to identify suitable candidates for surgical intervention.

Initial management involves a trial of carbamazepine or oxcarbazepine followed by other anti-neuropathic agents if these fail. Psychological interventions within an MDT service is often helpful. Surgical management can be considered at multiple points along the sensory pathway, becoming more invasive as the nerve root is approached. Superficial neurolysis of the distal branches can be attempted in frail patients; however, results are usually short-lived and carry a risk of dysaesthesia formation. Ablation of the Gasserian ganglion using either radiofrequency heating, chemical destruction or balloon compression can be performed, all bypassing a needle percutaneously into the foramen ovale. Generally, these methods provide relief for anywhere

up to five years in 50% of patients but the risk of *anaesthesia dolorosa* or other dysaesthesias is high.

Surgery to the posterior fossa for TN can involve one of two main procedures. Microvascular decompression (MVD) requires a craniotomy and aims to place a Teflon felt between the nerve root and any vessels (such as the superior cerebellar artery) causing compression. Success rates are initially excellent at 80–90%, but suffer from a relapse rate of 30–40%. Alternatively, gamma knife surgery uses focussed radiation to the trigeminal nerve root and can sometimes be performed in patients who are not suitable for MVD. Nerve root division is no longer used routinely.

## Decompression

### Peripheral nerve entrapment

Anatomical peculiarities at several places can lead to nerves entrapment. This may develop over time, be present dynamically during certain movements, presenting with pain or with painless muscle weakness or sensory disturbance. Areas such as the carpal tunnel and cubital tunnel, and the piriformis muscle or inguinal ligament are common places for entrapment, but many of the larger named nerves are prone to compression at some point along their course. The outcomes from decompression of peripheral nerves are excellent and should be considered early in the treatment pathway where an obvious cause can be found.

### Spinal surgery for pain

Low back pain in the UK is the largest cause of years lived with disability and one of the most common reasons for work absence. It represents a huge physical as well as psychological burden. The cause is often difficult to identify definitively and poor correlation exists between disease severity demonstrated on imaging and reported symptoms. A large proportion of back or neck pain resolves with advice, simple analgesia and adequate healing time, yet surgical interventions account for a large proportion of healthcare spending.

When pain persists and is refractory to conservative measures, the patient is at risk of developing associated symptoms of chronic pain, including persistent medication use despite a lack of efficacy, psychological decline, and increasing adoption of the sick role. Surgery is likely to be most effective where pain is persistent and significantly troublesome to warrant risks, but where these associated elements of chronic pain, have not yet developed. For those with persistent pain, risk stratification tools such as the STarTBack can be used to assess the likelihood of successful recovery, and highlight patients in whom increased MDT input may be required.<sup>8</sup>

### Spinal decompression

Spinal decompression can be performed for one of two main indications, nerve root compression or spinal canal stenosis causing cord or cauda equina compression. Current NICE guidance allows for the consideration of nerve root decompression for people with either clinical or radiological sciatica, where conservative measures have failed.<sup>5</sup> Release of the affected nerve can be an easy and effective solution in certain circumstances.

One of the most common reasons to perform decompression is intervertebral disc herniation. This involves herniation of the nucleus pulposus through a defect in the annulus, which can either be contained by the posterior longitudinal ligament or present as a free entity in the spinal canal. It often occurs in conjunction with abnormalities of the bony as well as ligamentous structures and causes pain or neurological deficit either through direct compression of adjacent structures or indirectly through inflammatory-mediated swelling. Herniation is more common at regions of greater articulation (L4-S1 and C5-7), accounts for around 5% of all low back pain problems and is the most common cause of radicular pain. The diagnosis can be made reliably by MRI or CT myelography but as suggested by NICE guidance, acute spinal pain without red flags requires imaging only when in specialist settings and likely to change management.

Spinal cord stenosis can be caused by degenerative bony disease, hypertrophy of surrounding structures or a congenitally narrow aperture. It presents with inducible leg weakness and pain on exertion, which is relieved quickly by rest and flexion of the lumbar spine. Cauda equina compression can produce dysfunction of the intestinal and pelvic organs and represent a surgical emergency. Cervical stenosis impacts the spinal cord directly causing myelopathy, upper motor neurone symptoms of upper and lower limbs, and gait disturbance.

Standard surgical treatment can involve decompressive laminectomies, often with foraminotomies, fusion/stabilization or interspinous spacer insertion. A Cochrane review of 2016 concluded that there was no evidence for superiority of any of the surgical procedures but did note a higher rate of major complications in those patients receiving fusion surgery. A separate review noted a side-effect rate between 10% and 24% for surgery and no reported side-effects with conservative management and highlighted the importance of careful patient consent.<sup>9</sup>

## Conclusion

The arsenal with which we can combat chronic pain is growing, but unfortunately so is our estimation of the prevalence. Multidisciplinary approaches have evolved to provide a treatment pathway for patients without the option of surgical interventions but there remains a proportion who will benefit from more invasive procedures. Pharmacology will undoubtedly be part of the solution, but the possibility that minimally invasive, neuromodulatory procedures provide is a low risk, high reward treatment with applicability in both cancer and chronic non-cancer pain.

Surgery will continue to have a place in certain conditions such as TN and hopefully, through improvements in patient selection, the proportion of patients benefitting from intervention will increase and those unlikely to benefit guided towards a non-surgical approach. More research is required in all areas of pain medicine, specifically that aiming to illuminate the best treatment among the myriad options available and how it compares to best conservative management. For now, maintaining communication between all those involved in the management of chronic pain remains the avenue likely to yield the best results. ◆

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