NICE advice

Differential target multiplexed spinal cord stimulation for chronic lower back and leg pain

Medtech innovation briefing
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Summary

- The **technology** described in this briefing is differential target multiplexed spinal cord stimulation (DTM SCS). It is used for people with chronic, intractable, lower back and leg pain.
- The **innovative aspects** are that it uses multiple stimulation signals targeting 6 different anatomical locations on the spinal cord, designed to provide superior pain relief to conventional spinal cord stimulation.
- The intended **place in therapy** would be as an alternative to traditional spinal cord stimulation in adults with chronic, intractable, lower back and leg pain.
- The **main points from the evidence** summarised in this briefing are from 5 studies (1 randomised controlled trial, 1 prospective feasibility study, 1 case series and 2 case reports) including a total of 87 people who had treatment with DTM SCS. They show that DTM SCS is more effective than traditional spinal cord stimulation.

- **Key uncertainties** around the evidence are that there is only 1 randomised study with a control group and none of the evidence comes from the NHS.
- **Experts advised** that DTM SCS is a minor innovative variation of traditional spinal cord stimulation, which could however, provide pain relief and improvements in quality of life to people. They also noted that few patients with chronic intractable pain currently receive spinal cord stimulation.
- The **cost** of DTM SCS therapy is £18,246 per person (excluding VAT). This includes the cost of an implantable neurostimulator and 2 percutaneous leads but does not include the cost of a trial phase or the procedure costs associated with implantation. The trial phase costs £2,170 and the surgical implantation procedure costs £6,564.

The technology

Differential target multiplexed spinal cord stimulation (DTM SCS; Medtronic) is a novel spinal cord stimulation therapy for people with chronic, intractable, lower back pain and leg pain. It is based on a proprietary algorithm that is programmed into the Intellis neurostimulator.

The algorithm delivers 3 therapy options with each option consisting of 4 stimulation signals (1 base signal and 3 prime signals). The base and prime signals differ from each other in frequency, pulse width, charge balancing and amplitude, and differentially target 2 anatomical locations in a person's spinal cord. This means that in total the multiplexed signals of the DTM SCS algorithm target 6 anatomical locations. The amplitudes for the base and prime signals at each of the 6 anatomical targets can be adjusted to suit the person's pain needs.

The DTM SCS therapy system consists of:

- an implantable neurostimulator (Intellis)
- percutaneous or surgical leads (Vectris)
- an external wireless stimulator used for testing during trial and implantation
- a clinician programmer
- a patient programmer and recharger.

Innovations

DTM SCS represents a novel spinal cord stimulation waveform that targets multiple anatomical locations using multiple electrical signals. Pre-clinical studies suggest that DTM SCS better modulates glial and neuronal gene expression back towards a non-pain state when compared with low- or high-frequency spinal cord stimulation (Vallejo et al. 2020).

The system components also have several innovative features. This includes the extended battery life of the Intellis neurostimulator which is powered by overdrive battery technology (provides up to 95% battery capacity at 9 years). The system also provides wireless programming and Snapshot reporting that allows objective monitoring of the person's progress. It also includes other features such as AdaptiveStim technology which automatically adjusts therapy as a person moves and SureScan MRI technology to allow full body MRI scanning under specific conditions.

Current care pathway

People presenting with chronic pain are usually assessed by a multidisciplinary team experienced in managing chronic pain. Treatment offered is based on the presentation and severity of pain and includes pharmacological and non-pharmacological options. Pharmacological treatment options include non-steroidal anti-inflammatory medicines, tricyclic antidepressants, antiseizure medicines, analgesics and opioids. Non-pharmacological treatment options include physiotherapy, psychological therapy and spinal cord stimulation. Spinal cord stimulation is recommended by NICE for adults who have chronic neuropathic pain (for at least 6 months) and have had a successful spinal cord stimulation trial.

The following publications have been identified as relevant to this care pathway:

- NICE's guideline on neuropathic pain in adults: pharmacological management in non-specialist settings
- NICE's guideline on chronic pain (primary and secondary) in over 16s: assessment of all chronic pain and management of chronic primary pain
- NICE's guideline on low back pain and sciatica in over 16s: assessment and management

- NICE's technology appraisal guidance on spinal cord stimulation for chronic pain of neuropathic or ischaemic origin
- NICE's medical technologies guidance on Senza spinal cord stimulation system for delivering HF10 therapy to treat chronic neuropathic pain
- NICE's medtech innovation briefing on Evoke Spinal Cord Stimulator for managing chronic neuropathic or ischaemic pain.

Population, setting and intended user

DTM SCS therapy is intended to be used for adults experiencing chronic lower back and leg pain, including unilateral pain.

Treatment would be managed by a multidisciplinary team with experience in neuromodulation. The Intellis neurostimulator and percutaneous or surgical leads would be implanted by specialist pain consultants or surgeons in an operating theatre. Stimulation settings can be adjusted by clinicians or the person using the therapy to suit individual pain needs using an external programmer.

Costs

Technology costs

The cost of DTM SCS therapy is £18,246 (excluding VAT) and includes the cost of:

- the implantable neurostimulator (Intellis): £15,046 (excluding VAT), including a 9-year limited device warranty
- 2 percutaneous leads (Vectris): £3,200 (excluding VAT).

There are additional costs for the trial phase and the surgical procedure. The trial phase costs £2,170, which includes the cost of a trial lead (£1,200) and the cost of an external trial battery (£970). The cost of the surgical procedure is £6,564 (average NHS reference costs 2019 to 2020 for Healthcare Resource Group [HRG] codes AB12Z for insertion of neurostimulator and AB14Z for insertion of neurostimulator electrodes). Spinal cord stimulation devices are NHS England, high-cost tariff-excluded devices (HCTED).

Costs of standard care

NICE's technology appraisal guidance on spinal cord stimulation for chronic pain of neuropathic or ischaemic origin describes spinal cord stimulation devices (including stimulator, controller and charger, but excluding leads) as ranging from £6,858 to £13,289. The cost of leads ranges from £928 to £1,804 for surgical implantation and £1,065 to £1,158 for percutaneous implantation. However, these costs were last reviewed in 2013. NICE's medical technologies guidance on Senza spinal cord stimulation system for delivering HF10 therapy to treat chronic neuropathic pain reports more recent costs:

- Senza costs £16,648 (including electrodes, leads, implantable pulse generator, remote control and battery charger).
- Non-rechargeable spinal cord stimulation system costs £11,281 (95% CI £8,888 to £14,516), with a lifespan of 4 years.
- Rechargeable spinal cord stimulation system costs £17,422 (95% CI £13,726 to £22,418).

An updated version of the Senza spinal cord stimulation system is now available, called Senza Omnia (2500). Costs may be higher than those listed above. Experts noted that the device costs listed here may have changed since the time of the NICE publication.

Resource consequences

DTM SCS therapy on Intellis has been launched in the UK and is currently being used in 9 NHS hospitals. DTM SCS would be used as an alternative to conventional spinal cord stimulation devices and the care pathway would remain unchanged. The costs for DTM SCS therapy are within the range of conventional spinal cord stimulation systems currently available in the NHS. Training of healthcare professionals on the Intellis system and DTM SCS is provided by the company.

Regulatory information

Differential target multiplexed spinal cord stimulation (DTM SCS) therapy is delivered using Medtronic's Intellis platform. The Intellis system is a CE marked Class III medical device.

The following manufacturer field safety notices or medical device alerts for this technology

have been identified:

- Medicines and Healthcare products Regulatory Agency Field Safety Notice for Intellis (2020/012/018/291/008). This alert was for the Intellis Software Application version 1.3.80 that could not reset invalid memory correctly. The users were requested to update to version 1.3.130.
- Medicines and Healthcare products Regulatory Agency Field Safety Notice for the Intellis recharger (2021/003/026/487/007). This alert was for the potential unintended heating of the Intellis Model 97755 Recharger. Clinicians were requested to reinforce care and maintenance guidelines with all users, who were also requested to contact their Medtronic representative if their recharger was visibly damaged.

Equality considerations

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

People likely to benefit from this technology may have disabilities caused by issues with mobility if their condition has a substantial and long-term negative effect on the ability to do normal daily activities. Disability is a protected characteristic under the Equality Act 2010.

Clinical and technical evidence

A literature search was carried out for this briefing in accordance with the interim process and methods statement for medtech innovation briefings. This briefing includes the most relevant or best available published evidence relating to the clinical effectiveness of the technology. Further information about how the evidence for this briefing was selected is available on request by contacting mibs@nice.org.uk.

Published evidence

Five studies are summarised in this briefing, reporting on 87 people who had treatment with differential target multiplexed spinal cord stimulation (DTM SCS). These include 1 randomised controlled trial, 1 prospective feasibility study, a case series and 2 case

reports.

The clinical evidence and its strengths and limitations is summarised in the overall assessment of the evidence.

Overall assessment of the evidence

Studies evaluating the clinical utility of DTM SCS are of variable methodological quality, but all show that DTM SCS is effective in reducing chronic back and leg pain. The highest methodological quality evidence comes from a recent randomised controlled trial (Stimgenics Open-Label, Post Market Study [SGX-SCS-RCT]) done in the USA (Fishman et al. 2021a). This trial provides direct evidence for the clinical superiority of DTM SCS compared with traditional spinal cord stimulation. Interim analyses from SGX-SCS-RCT have been reported in 3 abstracts (Fishman et al. 2020a, Fishman et al. 2020b and Vallejo et al. 2021). The results reported in the trial are the only ones that provide evidence for medium-term effectiveness (1 year).

There is some heterogeneity in the patient populations of the 2 prospective studies, which makes the evidence less generalisable. Additionally, the comparator in all studies is traditional (low-frequency) spinal cord stimulation (currently considered standard care). However, other modalities such as high-density or high dose, burst, 10-kHz high-frequency therapy, and closed-loop spinal cord stimulation exist (Provenzano et al. 2021). There is no comparative evidence on DTM SCS against any of those.

Fishman et al. (2021a)

Study size, design and location

A randomised controlled trial assessing the effectiveness of spinal cord stimulation for treating chronic lower back pain (LBP) and leg pain (LP) in 128 people in the US.

Intervention and comparator

DTM SCS compared with traditional spinal cord stimulation.

Key outcomes

At 3 months, an LBP responder rate of 80.1% with DTM SCS was superior to 51.2% with traditional spinal cord stimulation (p=0.0010). The mean LBP reduction (5.36 cm) with DTM SCS was greater than the reduction (3.37 cm) with traditional spinal cord stimulation (p<0.0001), based on the 10-cm visual analogue scale (VAS). Similar results were reported for LP, with mean reductions in LP VAS of 5.29 cm with DTM SCS and 4.76 cm with traditional spinal cord stimulation (not statistically significant).

Strengths and limitations

The results were robust to sensitivity analyses (an analysis with a modified intention-to-treat population [completer's analysis], tipping point analyses and additional opioid use). The clinical utility observed at 3 months was sustained at 6 and 12 months; however, attrition rates were higher for the traditional spinal cord stimulation group. This trial was not blinded because of the nature of the programs. Some of the study authors declared financial or non-financial interests with the company.

Fishman et al. (2020c)

Study size, design and location

A prospective, open-label, feasibility study evaluating the effectiveness of DTM SCS during a trial period (4 days plus or minus 1 day) in 20 people in the US.

Intervention and comparator

Change in LBP relative to baseline after a trial period with traditional spinal cord stimulation followed by a trial period with DTM SCS.

Key outcomes

The mean baseline numeric pain rating scale (NRS) score was 7.4 (0: no pain, 10: extremely severe pain). Significant relief in back pain was observed for both treatments, with significantly better response with DTM SCS. At the end of the trial period, people reported a reduction in their mean NRS score from baseline to 4.2 (p<0.001) after traditional spinal cord stimulation and to 2.4 (p<0.001) after DTM SCS.

Strengths and limitations

This was the first study to provide evidence for the effectiveness of the technology in treating chronic pain. The duration of the trial periods was very short and does not allow estimations of the long-term effectiveness. The duration of the trial periods was also based on clinician's decision only. Some of the study authors declared financial or non-financial interests with the company.

Gunduz et al. (2021)

Study size, design and location

A case series reporting on pain intensity in 3 people with chronic refractory back pain and no prior operation who had DTM SCS in Germany.

Intervention and comparator

Pain intensity pre-intervention and 3 months post-intervention.

Key outcomes

Pain intensity was documented using an NRS (0: no pain, 10: extremely severe pain). Preoperative mean NRS was 8.5 (range 7 to 9). Postoperative NRS was 2.6 (range 1 to 5) after 3 months.

Strengths and limitations

The study provides some limited evidence for the technology's effectiveness in people with chronic refractory back pain and no prior surgery, for whom the scientific literature is less abundant. The study is presented in abstract format only, so is limited in detail.

Brown et al. (2021)

Study size, design and location

A case report of a person with failed back surgery syndrome, right-sided meralgia paresthetica and lower abdominal wall neuralgia who had DTM SCS in the US.

Intervention and comparator

Pain intensity pre- and post-intervention.

Key outcomes

Pain intensity was documented using an NRS (0: no pain, 10: extremely severe pain). Pain intensity decreased from 8 pre-procedure to 3 immediately post-procedure, reaching stable relief of 80% throughout the following 4 days.

Strengths and limitations

The study is presented in abstract format only so is limited in detail and it is difficult to assess the quality and reliability of its results. It reports on a single case.

Fishman et al. (2021b)

Study size, design and location

A case report of a person with adult degenerative scoliosis who had DTM SCS in the US. The person had a single cervical electrode placed at C2.

Intervention and comparator

Pain intensity pre- and post-intervention.

Key outcomes

Pain intensity was documented using an NRS (0: no pain, 10: extremely severe pain). The overall pain score reduced by 42% from 7 to 4. A 75% subjective pain relief of neck pain, thoracic pain, lumbar pain and bilateral lower extremity pain was reported during the trial.

Strengths and limitations

This study provides evidence for the technology's effectiveness in a population for which there is limited evidence. However, the study is presented in abstract format only so is limited in detail. It reports on a single case. Some of the study authors may have financial or non-financial interests with the company.

Sustainability

The company claims that the small size and long battery life of the device may lead to sustainability benefits. There is no published evidence to support these claims.

Recent and ongoing studies

- A post-market, observational clinical study to evaluate the effects of differential target multiplexed DTM SCS programming in treating intractable chronic upper extremity limb pain. ClinicalTrials.gov identifier: NCT04466111. Status: active but not recruiting, no results published. Indication: chronic, intractable pain of the upper limb. Device: Intellis neurostimulator with DTM SCS. Last update: 18 April 2022. Country: US.

- DTM-LE spinal cord stimulation (SCS) study. ClinicalTrials.gov identifier: NCT04601454. Status: active but not recruiting, no results published. Indication: chronic pain. Device: Intellis neurostimulator with DTM SCS. Last update: 3 May 2022. Country: US.

- Open-label, post-market study: study the effects of differential target multiplexed spinal cord stimulation (DTM SCS) programs in treating intractable chronic back pain in subjects without prior history of spine surgery. ClinicalTrials.gov identifier: NCT04571242. Status: active but not recruiting, no results published. Indication: chronic back pain. Device: Intellis neurostimulator with DTM SCS. Last update: 2 June 2022. Country: US.

- The UPGRADE Study: real world outcomes of differential target multiplexed (DTM SCS) stimulation in existing and new Medtronic implants. ClinicalTrials.gov identifier: NCT04725838. Status: recruiting. Indication: chronic back pain. Device: Intellis neurostimulator with DTM SCS. Estimated study completion date: 29 January 2025. Country: US.

- Differential target multiplexed spinal cord stimulation: a multicenter cohort study. ClinicalTrials.gov identifier: NCT05068011. Status: recruiting. Indication: chronic, intractable pain of the upper limb related to the cervical spine or neuropathic arm pain. Device: Intellis neurostimulator with DTM SCS. Estimated study completion date: March 2024. Country: Belgium.

- Impact of the SCS with different waveforms over the quality of life (SCS-Quality). ClinicalTrials.gov identifier: NCT04244669. Status: recruiting. Indication: failed back surgery syndrome. Device: Intellis neurostimulator with DTM SCS. Estimated study completion date: July 2023. Country: Spain.
- Comparison of spinal cord stimulation in combination with standard pain treatment versus standard pain treatment only in patients with intractable chronic back pain without previous history of spine surgery. Trials identifier: ISRCTN10663814. Status: active, no longer recruiting. Indication: intractable chronic back pain. Device: Intellis neurostimulator with DTM SCS. Estimated study completion date: March 2024. Countries: Spain, Belgium, Netherlands and Germany.

Expert comments

Comments on this technology were invited from clinical experts working in the field and relevant patient organisations. The comments received are individual opinions and do not represent NICE's view.

All 3 experts were familiar with the technology and 1 had used it before. This expert was also involved in research related to the technology.

Level of innovation

All of the experts were familiar with spinal cord stimulation and all agreed that differential target multiplexed spinal cord stimulation (DTM SCS) is a minor variation of traditional spinal cord stimulation. The experts disagreed about whether DTM SCS can replace conventional spinal cord stimulation. The experts who felt it could replace standard care acknowledged its additional programming options. All experts were familiar with alternative spinal cord stimulation approaches, but none were aware of any technologies with the same mechanism of action (simultaneously targeting multiple targets in the spinal cord).

Potential patient impact

The experts agreed that the patient benefits include better pain relief and therefore improved quality of life. One expert estimated that about 100 to 300 people per year would be eligible for DTM SCS. The other 2 experts disagreed about the proportion of people

who would be eligible for an intervention with the technology. One expert said that only 30% of the people who currently access spinal cord stimulation would be eligible for this therapy, whereas the other stated 100%. One expert expressed concern that despite NICE guidelines, less than 1% of people with intractable neuropathic pain have spinal cord stimulation.

Potential system impact

All 3 experts thought that the costs of using DTM SCS would be about the same as for conventional spinal cord stimulation. They also considered that there would be no need for a change in existing facilities in order to accommodate DTM SCS. All experts thought that training would be needed for the clinicians and hospital nurses only in relation to using and programming the external programmer. The experts estimated that a minority of specialised hospitals would be carrying out the procedure.

General comments

The experts felt that there are no safety concerns specific to DTM SCS that would be different from those for standard spinal cord stimulation. All experts suggested that research with outcome measures such as EQ-5D and SF36 would be beneficial. Two experts acknowledged that the UK has a National Neuromodulation Registry, where all people having spinal cord stimulation should be entered. Another expert noted that there is an unequal spread of manufacturer devices used in different hospitals despite equal efficacy and costing. They attributed this to clinician preferences of certain devices and companies.

Expert commentators

The following clinicians contributed to this briefing:

- Dr Craig Montgomery, consultant in pain medicine and anaesthesia, Leeds Teaching Hospitals NHS Trust. Did not declare any interests.
- Mr Girish Vajramani, consultant neurosurgeon, University Hospital Southampton NHS Foundation Trust. Did not declare any interests.

- Dr Ashish Gulve, consultant in pain medicine, The James Cook University Hospital. Declared direct financial interests with both the notifying company and companies with competitor products.

Development of this briefing

This briefing was developed by NICE. The interim process and methods statement for medtech innovation briefings sets out the process NICE uses to select topics, and how the briefings are developed, quality-assured and approved for publication.

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