

# Repetitive Transcranial Magnetic Stimulation (rTMS) of the Motor Cortex has the Potential to be used as a Supplementary Therapy for the Relief of Cancer Pain in Patients who are Nearing the End of their Lives

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## Abstract

Individuals who have advanced stage cancer often experience discomfort that is challenging to alleviate. Administering high doses of pain medication may not be sufficient to alleviate their pain or may result in undesirable side effects, such as drowsiness. In this study, we present the first case where a patient's pelvic discomfort was significantly reduced by a series of five sessions of repetitive transcranial magnetic stimulation (rTMS) of the motor cortex. This led to an improvement in the quality of death for the patient and allowed for a reduction in medical care required.

**Keywords:** Palliative care; Refractory pain; Cancer pain; End of life; Repetitive transcranial Magnetic stimulation

## Introduction

A significant majority of cancer patients experience chronic pain [1]. This pain can be nociceptive and often requires opioid analgesics for treatment [2]. Alternatively, neuropathic pain may require anticonvulsant or antidepressant medication [3, 4]. In many cases, the pain is mixed in nature and can be challenging to manage during the terminal phase of cancer due to the need for high-dose medication combinations [5]. Unfortunately, the use of these medications can result in sleepiness and lower the quality of life for the patient at the end of their life [6]. In this study, we discuss a patient whose pelvic discomfort was effectively managed through a course of five sessions of repeated transcranial magnetic stimulation. This treatment resulted in a significant reduction in the need for analgesic medications, as evidenced by the Medication Quantification Scale (MQS) [7] score, and allowed the patient to regain a normal level of awareness. As a result, the patient was able to get married in a dignified setting before passing away, as she had desired.

## Clinical Case Report

In August 2020, a 23-year-old patient experienced multiple episodes of haematochezia and was subsequently diagnosed with adenocarcinoma of the rectum. In February 2021, after undergoing radiation and abdominopelvic excision, the patient was treated with chemotherapy. However, despite this therapy, local disease progression was observed, and in October 2022, peritoneal carcinomatosis with liver and lung metastases was discovered. As the patient's condition deteriorated, she experienced increasing abdominal and pelvic discomfort, partly due to the nociceptive pain caused by the tumor's compression. Initially, oral morphine was used to manage this pain at a dosage of 40 mg per day, which was later increased to 200 mg after four months. Additionally, the patient experienced neuropathic pain resulting from the surgery and radiation, with a DN4 score of 7/11 [8-10].

A 23-year-old patient was diagnosed with rectal adenocarcinoma in August 2020 after experiencing haematochezia. Chemotherapy was initiated in February 2021, but the patient showed local disease progression, which led to peritoneal carcinomatosis with liver and lung metastases in October 2022. Despite receiving oral morphine for nociceptive pain, as well as pregabalin and intravenous amitriptyline

for neuropathic pain, the patient's pain level, assessed by the Numerical Rating Scale (NRS), remained high, ranging from 8 to 10, and was associated with intellectual slowness and tiredness. The patient also received antidepressant, anxiolytic, and psychological therapies. The patient wished to have a traditional wedding ceremony, but it seemed unfeasible if the medication dosages and side effects could not be reduced. The use of ketamine and intrathecal morphine were unsuccessful in reducing pain or opioid dosages, and surgery had to be stopped after 10 days. The Medication Quantification Scale (MQS) score was 126 when determining therapeutic dosages. The patient was admitted to the Palliative Care Unit of the Federative Pain-Palliative and Supportive Care Center in December 2022.

Based on previous success in treating refractory pelvic and perineal pain with motor cortex stimulation by rTMS, it was recommended for this patient. The right motor cortex area corresponding to the perineal region was stimulated for 20 minutes with the following settings: 80% of the resting motor threshold in 20 trains of 10 seconds each at 10 Hz, with a 50-second inter-train interval (2000 stimuli). The patient experienced a significant reduction in discomfort in the days after the first session of rTMS. Medication was reduced by about 50%, as evidenced by a drop in the MQS score to 96 and subsequently to 56. The patient was able to return to almost normal levels of alertness and clarity throughout the day and was even able to start walking again. Her anxiety and depressive symptoms also decreased. Four more rTMS sessions were conducted to maintain this improvement, and the patient was able to have the wedding she had envisioned [11-15]. Her death, which occurred six weeks later due to intestinal blockage, was ultimately caused by the disease's progression.

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**Received:** 28-Feb-2023, Manuscript No. jpcm-23-91907; **Editor assigned:** 02-Mar-2023, PreQC No. jpcm-23-91907(PQ); **Reviewed:** 16-Mar-2023, QC No. jpcm-23-91907; **Revised:** 21-Mar-2023, Manuscript No. jpcm-23-91907(R); **Published:** 28-Mar-2023, DOI: 10.4172/2165-7386.1000509

**Citation:** Denis C (2023) Repetitive Transcranial Magnetic Stimulation (rTMS) of the Motor Cortex has the Potential to be used as a Supplementary Therapy for the Relief of Cancer Pain in Patients who are Nearing the End of their Lives. J Palliat Care Med 13: 509.

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## Discussion

Persistent or end-of-life cancer-related pain can be a challenging issue to manage effectively. In many cases, high doses of analgesics and co-analgesics are necessary to control both neuropathic and nociceptive components of the pain. Opioids at WHO step 3 are often used to manage nociceptive pain, with oral, parenteral, or intrathecal administration being available options. However, even with these treatments, some patients continue to experience nociceptive pain that is mostly resistant to morphine, and some patients experience side effects despite continuing treatment. Similarly, some types of neuropathic pain may require large doses of anticonvulsants and antidepressants, which can cause severe sleepiness and further reduce the patient's quality of life. In terminal patients suffering from mixed pain, the combination of several classes of treatment with the potentiation of their individual side effects often leads to significant sleepiness and a noticeable decrease in quality of life. Consequently, it can become extremely difficult or even impossible to pursue personal or family projects under such circumstances.

Noninvasive brain stimulation using rTMS is a new approach to pain management. In our previous study, we found that motor cortex stimulation through rTMS had a positive effect on non-cancer pelvic pain. Using rTMS as adjuvant therapy within a multidisciplinary treatment program offered by palliative care units can be a potentially beneficial strategy with a favorable benefit-to-risk balance. Studies have shown that rTMS is effective in treating depression and chronic pain, particularly of neuropathic origin. The precentral motor cortex is the focus of treatment for chronic pain rather than somatosensory cortical regions. Despite the initial skepticism, several studies have demonstrated the effectiveness and mechanisms of action of invasive and noninvasive motor cortex stimulation, highlighting the importance of this target. The side effects of rTMS are usually mild and infrequent [16-19].

In addition, it has been observed that unilateral stimulation can be effective in relieving bilateral or midline pain, as seen in the current case. The dorsolateral prefrontal cortex is a common target for rTMS treatment of depression [20]. A previous study on chronic pain patients who received motor cortex stimulation reported simultaneous improvements in pain and depression, which is the emotional component of pain. This combined effect can be beneficial for patients at the end of life. In the case described, the patient was able to regain a sufficient level of alertness, clarity, and motivation to complete a challenging task at the end of her life, which was to organize her wedding, thanks to a series of five rTMS treatments given over a week.

## Conclusion

To aid in the management of cancer pain in terminally ill patients, noninvasive brain stimulation using rTMS can be used as an additional treatment option. This therapy has the potential to improve various pain components, including the emotional side of pain such as depression. Additionally, by reducing the need for high doses of pain medications, rTMS can decrease the severity of side effects, ultimately leading to an improved quality of life for the patient.

## Acknowledgement:

Not applicable.

## Conflict of Interest:

Author declares no conflict of interest.

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