



## Correspondence

## Keep calm and beam on? Unmet needs in radiotherapy and deep brain stimulation



## Introduction

Deep brain stimulation (DBS) of the subthalamic nucleus (STN) and globus pallidus internus (GPI) was approved in 2002 as a treatment option for Parkinson's disease (PD), although it had been in use since the 1980s. Since then, more than 160,000 patients worldwide have received DBS, and as the incidence of PD is rising sharply, the number of people with PD who have undergone DBS will also increase. Importantly, an additional effect of longevity (related in part to deployment of advanced treatments for PD [1]), the likelihood increases of encountering a co-occurrence of cancer in patients treated with DBS. This will create specific challenges, including the consideration of radiotherapy and diagnostic MRI artefacts interfering with radiotherapy planning, malfunctioning of the pulse generator or other parts of the DBS device due to ionising effects or electromagnetic interference, and cerebral temperature-related tissue damage.

According to the World Health Organization, breast and lung cancers are among the top three most common cancers. Their localization may interfere with the DBS system, especially with pulse generators that are placed in a subcutaneous pocket in the infraclavicular region. This is illustrated by a patient with PD who previously underwent DBS and developed breast cancer, and in whom the pulse generator was relocated to the anterior abdominal wall in order to prevent interference with preoperative imaging, surgery itself, and radiotherapy [2]. Special care should be taken to prevent possible malignant DBS withdrawal syndrome associated with acute cessation or failure of the DBS device [2,3]. To date, only five case reports have been published on the co-occurrence of cancer in PD patients with DBS [2,4–7] (Table 1), but here we focus on the occurrence of brain metastases or primary cerebral tumours in patients who have been treated with DBS as this may pose problems for radiotherapy planning and interferes with functioning of the DBS leads.

Proper pulse generator functioning can be affected by radiation, either due to the direct or diffuse effects of ionizing radiation or electromagnetic interferences produced by linear accelerators. Concerns regarding the irradiation of (parts of) the DBS device includes (1) malfunction and (2) failure of the device, mainly related to ionising effect or electromagnetic interference. Regarding the potential risk of temperature related malfunction of leads and surrounding tissue damage, in cardiac pacemakers reports, device dysfunction was observed in only 3% of patients [8]. The dose of the radiation therapy appears to have only a limited effect on the risk of malfunction occurring, as some malfunctions were observed at radiation doses as low as 0,3 Gy [8]. After radiation therapy, device failure occurs in about 2.5% of patients with pacemakers and 6.8% of patients with cardiac defibrillators [8].

Based on the above, in the case of patients who underwent DBS, general recommendations should be to turn off the device shortly

before radiotherapy and the DBS device should be turned back on as soon as possible. During radiotherapy, the neurostimulator should be shielded to limit the extent of damage, although the extension leads are generally not damaged by radiation. Should the pulse generator be exposed to a cumulative dose of 5 Gy or more it will need to be checked for any malfunction. The latter should take into account the latest update of user and/or physician manuals of the manufacturer. Nonetheless, it appears that radiotherapy can be safely performed in patients who previously underwent DBS without malfunction of the pacemaker or the DBS leads, although the radiation tolerance dose for the same medical device models varied widely in published DBS reports [4–7]. Comprehensive tests need to be performed to establish safety and tolerability thresholds for DBS. It has been suggested limiting the maximum dose of radiation to 2 Gy in case of implanted medical devices, although later reports show that higher doses of radiation were also safe, even up to 60 Gy [7].

In summary, despite the lack of structured studies, radiation therapy was safely delivered in all reported patients with DBS devices without any untoward effects regarding malfunction of the pulse generators or leads. It is recommended to implement multidisciplinary care to avoid unnecessary delays in the treatment plan, and standardised procedures and clear guidelines should be developed to prevent device-related problems and delays in treatment. Moreover, it is advised that guidance is sought with DBS manufacturers and consult device-specific guidelines regarding radiation therapy. Further efforts should be made to undertake structured research looking into the safety and feasibility of radiotherapy in patients with an implanted DBS device.

## Declaration of competing interest

The authors declare that there is no conflict of interest regarding this work.

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**Table 1**

Overview of case reports on radiation therapy and cancer surgery in patients who previously underwent deep brain stimulation.

Author, (year)	Type of neoplasms	Gy	Number of fractions	Dose to the DBS device [Gy]	Patients outcome
Mazdai (2005) [4]	Squamous cell cancer	66	33	7.5	No AE related to DBS and radiotherapy.
Borkenhagen (2013) [7]	Lung cancer	66	33	Mean 5.53 Max 48.12	No AE related to DBS and radiotherapy
Guy (2014) [6]	Brain metastasis	21	3	Electrodes < 1 Pulse generator < 0.01	No AE related to DBS and radiotherapy
Kotecha (2016) [5]	Brain metastasis	30	10	Mean 28 Max 33	No AE related to DBS and radiotherapy
Son (2018) [2]	Breast carcinoma	–	–	–	Surgery was performed safely after relocation of the pacemaker

**Parkinson Vereniging.**

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