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Radiation therapy in patients with implanted deep brain stimulation

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ABSTRACT

Background. As deep brain stimulation (DBS) and radiation therapy (RT) have become established treatments for movement disorders and malignancies respectively, patients being treated with both simultaneously are becoming more frequent.

Objectives. Literature regarding the safety of RT in patients with implanted DBS is scarce, and there are no clear guidelines on how to manage them.

Methods. We present a follow-up of two Parkinson's Disease (PD) patients with DBS undergoing RT in the context of previous literature.

Results. No adverse events nor malfunctioning of the DBS system were observed. This was in line with previous reports.

Conclusions. Since there are no clear safety guidelines for RT in DBS patients, it is important to document experience in this field. A combined approach involving multidisciplinary discussions between neurosurgeons, radiotherapists, clinical oncologists and neurologists is recommended.

Key words: deep brain stimulation, radiation therapy, Parkinson's Disease, safety guidelines

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Introduction

Since DBS became an effective treatment of PD and other movement disorders, more than 150,000 devices have been implanted worldwide [1]. On the other hand, 14 million people are diagnosed with malignancies every year, and half of them will require RT in the course of their disease [2, 3]. Therefore, to consult a patient with DBS who requires RT is becoming more frequent. We looked for biomarkers of good outcome after surgery. The question of neoplastic disease in remission as an indication for potential DBS therapy in advanced PD remains unclear [4]. Unfortunately, literature on the safety of radiation therapy in patients with implanted DBS is scarce, and there are no clear guidelines on how best to manage them [5].

Methods

We followed up two PD patients with implanted DBS who required RT due to various malignancies in the context of previous reports of such a coincidence.

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VIA MEDICA

Results

Patient 1 was a 67-year-old male with a diagnosis of PD 27 years earlier. He underwent left-sided pallidotomy in 2002, with a significant improvement which lasted for about eight years, and again in 2012 at the age of 65. Due to disabling peak L-dopa dose dyskinesias and motor fluctuations, he was qualified to bilateral subthalamic nucleus deep brain stimulation (STN-DBS). Two-stage neurosurgical implantation of a St Jude Libra DBS system was done without any complications. Improvement after STN-DBS was measured with UPDRS. Improvement in UPDRS was 27% one year after surgery. Reduction of LEDD at 43% throughout a two-year observation resulted in significant improvement of dyskinesias. At the time of qualification for DBS, he was diagnosed with prostate cancer during hormonotherapy, and was stable on urological examination and biochemical markers (PSA). Nevertheless, in November 2013 local progression of the disease was diagnosed and pelvic RT with 30 Gy in 10 fractions without any complications was performed. Three months later, he was admitted to the Neurology Department due to a first-in-life incident of generalised seizures. CT brain scan showed two lesions in the left hemisphere, one of them near the DBS electrode (Fig. 1), with further local progression of cancer with metastases to retroperitoneal lymph nodes. The patient was qualified for palliative RT of the brain metastatic tumours with 6 MV photons and a dose of 20 Gy in five fractions. Estimated maximal dose for brain DBS electrodes was 21 Gy. Neurostimulation was ON during the whole RT procedure. After treatment, regression of tumours was observed in MRI. No complications for patient or the DBS system were seen for the next six months. Unfortunately, due to disease progression and urosepsis, the patient died in May 2015. An autopsy was not performed.

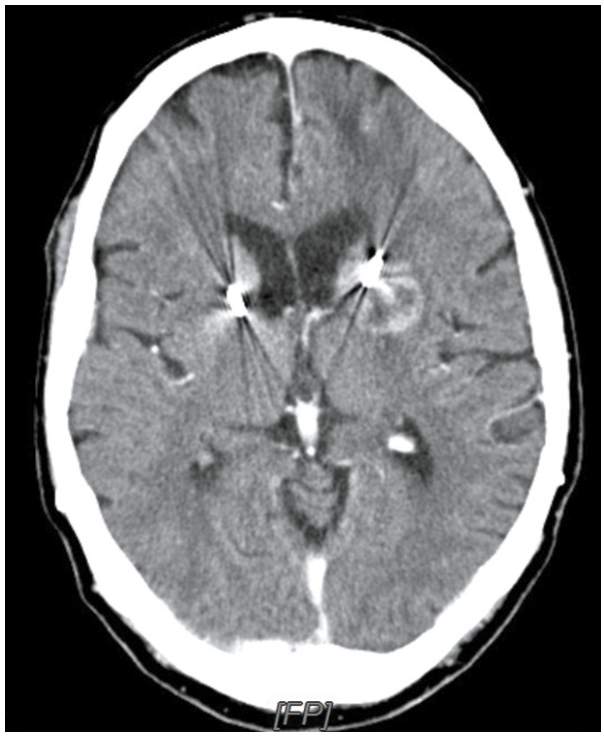

Figure 1. Two metastatic brain tumours, one near DBS electrode, in left hemisphere of Patient 1 (CT scan)

Patient 2 was a 68-year-old female who had suffered from PD for 29 years. In 2010, due to motor fluctuations and very severe peak levodopa dose dyskinesias, she was qualified for bilateral DBS-STN (Medtronic Soletra). At the time of qualification, she had a history of left-sided mastectomy due to breast cancer. At the 7 years follow up, a motor improvement in UPDRS of 40% and a reduction of LEDD of 51%, with a significant decrease of dyskinesias, were observed. In 2015, left IPG was replaced with Medtronic Activa SC. In 2016, local recurrence of breast cancer close to the IPG was diagnosed and she was qualified to RT. In September 2016, radiation therapy of the left supraclavicular and subclavian area with 15 MV photons and dose of 20 Gy in five fractions was carried out. Maximal estimated dose for left IPG was 1.7 Gy. Neurostimulation was ON during the whole RT procedure. Immediately after RT and during the last control (February 2017), no dysfunction of the DBS system was observed, with oncological remission.

Discussion

Experience of the use of RT in patients with DBS is scarce. Nutt et al. published an example of very serious consequences of diathermy for DBS [6]. Similarly, full body coil MRI might be harmful for DBS patients [7].

These arguments prompted us to seek to determine the safety guidelines for other procedures such as RT in conjunction with DBS. The leading DBS manufacturer has stated that "the DBS system may be affected by, or adversely affect,… radiation therapy." [8]. There are only two previous case reports detailing the safety of irradiation of a pulse generator device, and two reports on the safety of cranial RT in a patient with an implanted DBS. In the report by Mazdai et al. [9], a patient being treated with DBS for severe PD underwent radiation therapy to the head and neck. In this case, the estimated dose to the device was 7.5 Gy. In a similar report by Borkenhagen et al. [10], a patient with bilateral DBS devices implanted for the treatment of PD underwent radiation therapy to a left upper lung tumour directly underneath the location of the IPG. The mean dose to the device was 5.53 Gy, and the maximum dose was 48.12 Gy. Follow-up interrogation of IPG revealed no changes in its settings or evidence of malfunctioning. In both cases, the IPGs were found to be in good working order, despite receiving a radiation dose exceeding typical pacemaker tolerances (3–5 Gy) [11]. In the third case, a patient who had a DBS implanted for the treatment of severe PD underwent a course of hypofractionated radiation therapy (21 Gy in three fractions of 7 Gy per fraction delivered over seven days) for the treatment of two brain metastases using stereotactic dynamic intensity modulated arc therapy [12]. In this case, the

Table 1. Data on radiation therapy in previously reported cases and our two patients

Author and year of publication (number of pts)	Indication for DBS	DBS system	Tumour localisation (radiation dose)	Beam energy	Radiation dose for IPG	Radiation dose for electrodes	Clinical consequences
Mazdai et al. 2006 (n = 1)	PD	Medtronic	Head and neck (66 Gy — 33 frac.)	4 MV photons	7.5 Gy (total)	–	None for DBS system
Brokenhagen et al. 2014 (n = 1)	PD	Medtronic	Lung close to IPG	6MV photons	Mean 5.53 Gy Max. 48.12 Gy	NA	Three years follow-up (tumour cured). None for DBS system
Guy et al. 2014 (n = 1)	PD	–	Lung (brain metastases –21 Gy — 3 frac.)	–	< 0.01 Gy	< 1 Gy	None for DBS system
Kotecha et al. 2016 (n = 1)	Tremor	Medtronic, lead model 3389	Brain metastases (WB-RT, 30 Gy — 10 frac.)	6 MV photons	0.61 Gy (total)	Mean 28 Gy Max. 33 Gy	None for DBS system
Patient 1	PD	St. Jude Medical Libra	Brain metastases (WB-RT, 20 Gy — 5 frac.)	6 MV photons	–	Mean 9.9 Gy Max. 21 Gy	None for DBS system
Patient 2	PD	Medtronic Activa	Breast cancer (20 Gy — 5 frac.)	15 MV photons	Mean 0.6 Gy Max. 1.7 Gy	–	None for DBS system

electrodes received less than 1 Gy and the pulse generator received less than 0.01 Gy. Regarding the fourth patient, the IPG was well outside the field of radiation therapy and received a nominal dose of only 6.1 cGy/fraction (61 cGy total), but the electrodes received a maximum of 33 Gy [13]. Data from these previous four case reports and from our two patients is set out in Table 1. Much larger experience with pacemakers and implantable cardioverter defibrillators (PM/ICD) shows that patients undergoing RT with electrons or kV photons do not need supplementary device evaluations in the PM/ICD clinic. Because the impact of RT on a device depends on the beam energy rather than the total dose of radiation, it is recommended to limit photon beam energy to ≤ 10 MV when possible. The frequency of pacemaker malfunction is about 3%, and mainly consists of device resets and, exceptionally, replacements [14].

To minimise IPG exposure to RT, especially when the device is located very close to a tumour, surgical relocation of IPG using a longer extension should be considered [15]. Maintaining cardiostimulation during radiation therapy, especially for patients who also have an implanted ICD, is crucial. Similarly, in patients with movement disorders, turning off the neurostimulation makes the RT procedure impossible to perform due to involuntary movements. Thus, turning off the stimulation during RT is in fact not recommended because in the majority of reported cases IPGs were turned on, and procedures were safe. Radiotherapy is an established therapy method in oncology, so it is important to suggest that manufacturers consider a built-in 'safe RT' approach in the devices. Furthermore, we believe it would be sensible to report all cases of DBS patients undergoing RT and to create a web-based registry of such coincidences.

Conclusions

As the number of patients with DBS continues to rise, the influence of RT on those patients should be analysed. It is important to document the experience of DBS patients simultaneously receiving RT. We believe that all previously reported cases add to the argument for adopting a combined approach for patients, with multidisciplinary discussions between neurosurgeons, radiotherapists, clinical oncologists and neurologists. Drawing on the analagous experience of cardiologists in the field of implantable pulse generators, safety guidelines will be established in the future.

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Additional informed consent was obtained from all individual participants for whom identifying information is included in this article.

References

1. Ponce FA, Lozano AM. Deep brain stimulation state of the art and novel stimulation targets. Prog Brain Res. 2010; 184: 311–324, doi: 10.1016/S0079-6123(10)84016-6, indexed in Pubmed: 20887882.
2. Delaney G, Jacob S, Featherstone C, et al. The role of radiotherapy in cancer treatment: estimating optimal utilization from a review of evidence-based clinical guidelines. Cancer. 2005; 104(6): 1129–1137, doi: 10.1002/cncr.21324, indexed in Pubmed: 16080176.
3. Torre LA, Bray F, Siegel RL, et al. Global cancer statistics, 2012. CA Cancer J Clin. 2015; 65(2): 87–108, doi: 10.3322/caac.21262, indexed in Pubmed: 25651787.
4. Szlufik S, Przybyszewski A, Dutkiewicz J, et al. Evaluating reflexive saccades and UDPRS as markers of Deep Brain Stimulation and Best Medical Treatment improvements in Parkinson's disease patients: a prospective controlled study. Neurol Neurochir Pol. 2019; 53(5): 341–347, doi: 10.5603/PJNNS.a2019.0045, indexed in Pubmed: 31621890.
5. Smilowska K, Bloem BR, Esselink RAJ, et al. Keep calm and beam on? Unmet needs in radiotherapy and deep brain stimulation. Parkinsonism Relat Disord. 2020; 71: 15–16, doi: 10.1016/j.parkreldis.2020.01.005, indexed in Pubmed: 31955127.
6. Nutt JG, Anderson VC, Peacock JH, et al. DBS and diathermy interaction induces severe CNS damage. Neurology. 2001; 56(10): 1384–1386, doi: 10.1212/wnl.56.10.1384, indexed in Pubmed: 11376192.
7. Henderson JM, Tkach J, Phillips M, et al. Permanent neurological deficit related to magnetic resonance imaging in a patient with implanted deep brain stimulation electrodes for Parkinson's disease: case report. Neurosurgery. 2005; 57(5): E1063; discussion E1063, doi: 10.1227/01.neu.0000180810.16964.3e, indexed in Pubmed: 16284543.
8. Medtronic DBS Systems indications, safety, and warnings. https://www.medtronic.com/us-en/healthcare-professionals/therapies-procedures/neurological/deep-brain-stimulation/indications-safety-warnings/brief-statement-movement-disorders.html (Nov 2017).
9. Mazdai G, Stewart DP, Hounsell AR. Radical radiation therapy in a patient with head and neck cancer and severe Parkinson's disease. Clin Oncol (R Coll Radiol). 2006; 18(1): 82–84, doi: 10.1016/j.clon.2005.09.009, indexed in Pubmed: 16477925.
10. Borkenhagen JF, Morris ZS, Hoberg JR, et al. Delivery of definitive dose external beam radiation in close proximity to an implanted deep brain stimulator. Pract Radiat Oncol. 2014; 4(5): 294–297, doi: 10.1016/j.prro.2013.10.003, indexed in Pubmed: 25194097.
11. Munshi A, Agarwal JP, Pandey KC. Cancer patients with cardiac pacemakers needing radiation treatment: a systematic review. J Cancer Res Ther. 2013; 9(2): 193–198, doi: 10.4103/0973-1482.113348, indexed in Pubmed: 23771357.
12. Guy JB, Levy A, Malkoun N, et al. Preventing radiotherapy-induced side effects on deep brain stimulators: the need for a multidisciplinary management. Br J Neurosurg. 2014; 28(1): 107–109, doi: 10.3109/02688697.2013.801395, indexed in Pubmed: 23692069.
13. Kotecha R, Berriochoa CA, Murphy ES, et al. Report of whole-brain radiation therapy in a patient with an implanted deep brain stimulator: important neurosurgical considerations and radiotherapy practice principles. J Neurosurg. 2016; 124(4): 966–970, doi: 10.3171/2015.2.JNS142951, indexed in Pubmed: 26315009.
14. Zaremba T, Jakobsen AR, Søgaard M, et al. Radiotherapy in patients with pacemakers and implantable cardioverter defibrillators: a literature review. Europace. 2016; 18(4): 479–491, doi: 10.1093/europace/euv135, indexed in Pubmed: 26041870.
15. Son BC, Kim JS, Park WC, et al. Management of Pulse Generators in a Breast Cancer Patient with in Situ Subthalamic Nucleus Deep Brain Stimulation. J Neurol Surg A Cent Eur Neurosurg. 2019; 80(3): 223–227, doi: 10.1055/s-0038-1677518, indexed in Pubmed: 30708388.