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Tremor and Other Hyperkinetic Movements

Deep Brain Stimulation Case Files

Management of Elevated Therapeutic Impedances on Deep Brain Stimulation Leads

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Abstract

Clinical Vignette: A 64-year-old male with a history of essential tremor with bilateral thalamic ventralis intermedius deep brain stimulation implants had elevated therapeutic impedance values despite normal lead integrity impedances and good response to stimulation.

Clinical Dilemma: Do elevated therapeutic impedance values indicate a sign of hardware malfunction? What are the guidelines to approach deep brain stimulation hardware malfunction?

Clinical Solution: Lead integrity impedance values are a better evaluation of hardware integrity. The discrepancy between therapeutic and lead-integrity impedance values can arise when using low voltage settings.

Gaps in Knowledge: There are no established guidelines for the management of possible hardware malfunction in deep brain stimulation. The recommended approach is to distinguish between open and short circuit problems followed by an "inching" evaluation, assessing the structures from the implantable and programmable generator to the intracranial leads. Constant-current devices will deliver a more stable stimulation but the effect of their adoption is still not clear.

Expert Commentary: This case emphasizes the need for clinicians to understand fundamental differences in lead integrity and therapeutic impedance while utilizing a methodical approach in treating hardware malfunction. It highlights future avenues of investigation regarding the utility of constant current DBS technology.

Keywords: Therapeutic impedance, lead integrity impedance, deep brain stimulation, open circuit, short circuit, constant current

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Clinical vignette

A 64-year-old male with a history of essential tremor that was refractory to medication therapy had significant impairment and disability in his activities of daily living, including eating and grooming. He received bilateral thalamic ventralis intermedius (Vim) deep brain stimulation (DBS) implants. The system included Medtronic 3387 (Minneapolis, MN) leads and the Activa PC 37601 implantable and programmable generator (IPG). No surgical complications were reported. He developed an immediate microlesion effect on the right side of the body with a nearly month-long control of tremor prior to his device activation. Post activation he improved beyond the microlesion effect and he regained lost function in his activities of daily living. He reported side effects of slurring of speech and tongue numbness when the DBS was activated, and these were persistent at the setting that maximally controlled tremors. A monopolar threshold survey for benefits and side effects during programming revealed low thresholds for sensory side effects on the left but not right Vim lead (Table 1).

Despite the narrow thresholds revealed at programming for the left Vim DBS, a bipolar stimulation setting resulted in significant symptom control without side effects. Postoperative lead location and mapping

Table 1. **Summary of the Side Effect Thresholds in the Monopolar Survey for the Bilateral Vim Performed 2 Months after left Vim Implantation**

Contact Tested	Side Effect Threshold (V)	Side Effect Noted
Left Vim		
0	0.7	Tingling of right hand
1	0.7	Tingling of right fingertips
2	0.9	Tingling of right lip and first and second fingers
3	1.7	Tingling of right face and right hand with slurring of speech
Right Vim		
8	1.5	Tingling of left hand
9	1.4	Tingling of left fingertips and lips
10	2	Tingling of left lip and slurring of speech
11	3	Tingling of lips and slurring of speech

Abbreviations: Vim, Thalamic Ventralis Intermedius.

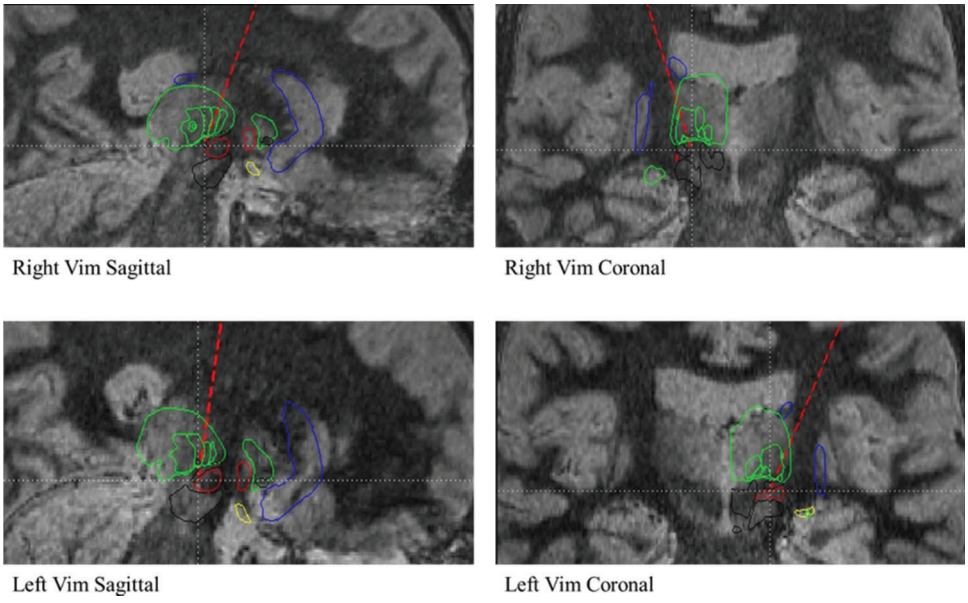

Figure 1. **Postoperative Lead Location Mapping.** The dashed red line is the location of the deep brain stimulation lead based on comouted tomography–magnetic resonance imaging fusion. The green structure the lead touches is the thalamus. The red structure beneath the thalamus is the subthalamic nucleus. Coordinates for right thalamic ventralis intermedius (Vim), 3.9 mm posterior; 12.8 mm lateral; and 2.2 mm inferior to the midcommissural point. Coordinates for left Vim, 5.7 mm posterior; 13.2 mm lateral; and 3.7 mm inferior to the midcommissural point.

revealed that the left Vim was slightly lateral to the right Vim lead (Figure 1).

Clinical dilemma

A discrepancy was observed between the measured lead integrity impedances (LIIs) and the therapeutic impedances. The LII measured at 3 V were within normal limits (Table 2). The therapeutic impedances for the left Vim lead were recorded as abnormally high (Table 2). Despite the high therapeutic impedance values, the patient had a persistent positive clinical benefit with left Vim stimulation. The bipolar configuration (2 as cathode and 3 as anode) provided an optimal benefit to side effect ratio.

Table 2. **Summary of Relevant Programming Sessions with Therapeutic Impedance Measurements**

Since Left Vim Insertion	Cathode	Anode	Voltage (V)	Pulse Width (μs)	Frequency (Hz)	Current (A)	Therapeutic Impedance (ohm)
2 months	2	3	0.8	90	180	0.186	High (>4000)
2 months	2	3	1	90	135	0.237	High
3 months	2	3	1	90	135	0.183	High
4 months	2	3	1.2	90	150	0.222	High
4 months	2	3	1.4	60	180	N/A	High
5 months	2	3	1.8	60	180	0.458	High
7 months	2	3	1.9	60	135	0.622	3154
Lead integrity impedance	C-0, 1317; C-1, 1342; C-2, 1348; C-3, 1391; 0-1, 2518; 0-2, 2813; 0-3, 2870; 1-2, 2728; 1-3, 2891; 2-3, 2667						

Abbreviations: Vim, Thalamic Ventralis Intermedius.
Initial lead integrity impedances are summarized in the last row.

Several interesting questions arise from this clinical situation. What is the difference between therapeutic impedance and LII? As the high therapeutic impedance did not limit clinical benefit in this case, do elevated therapeutic impedance values indicate a sign of hardware malfunction? What are the guidelines to approach deep brain stimulation hardware malfunction?

Clinical solution

To answer these questions, it is important to define a few terms first.

Impedance is a measure of resistance to the propagation of current in an alternating current system.[1]

LII assesses the impedances at all the different contacts at predetermined stimulation parameters (set by the DBS manufacturer): voltage $\propto$ (LII $\times$ current), Ohm's law.

LII measurements are surrogates of the electrical features of a DBS system,[2] assessing for hardware malfunction. Most LIIs usually fall in the range of 500 to 1500 ohms.[2] An increase in LII is frequently the warning sign of an open electrical circuit (e.g., connector break) and a drop is typically a sign indicating a short circuit.[2,3] The LII measurements available through the current IPGs have very good accuracy (less than 4% error).[4]

The therapeutic impedance on the other hand assesses the impedance of the system as programmed by the user and can be useful, for example for battery usage and life estimation.[1,5] The therapeutic impedance is calculated by a relatively complex equation. This equation can result in overcompensation when low voltages are utilized and it could reveal a "high" therapeutic impedance value.

In this case's DBS system (Medtronic Activa PC), a high LII is defined as a value above 40,000 ohms (when measured at 3 V), while a high therapeutic impedance is defined as a value above 4,000 ohms. In our case, the measured current associated with the optimal DBS settings was low, 0.186–0.458 A (Table 2). A careful review of Table 2 however reveals that when set at a higher voltage (1.9 V), the therapeutic impedance value (3154 ohms) gets closer to the LII. The measured current also increased (0.622 A). The therapeutic impedances are usually consistent with LII; however, this is highly dependent on the stimulation parameters used. Lower voltages can result in a discrepancy between the therapeutic impedance and LII as noted in this case. The clinician programming a DBS patient should be aware of what a "high" therapeutic impedance value may indicate, but should also test the contact at higher voltage to confirm. It is important for a practitioner to distinguish between LII and therapeutic impedances.

The other interesting observation resides in the apparent disconnect between the "high" measured therapeutic impedance and the persistent clinical benefit. A better understanding of this apparent discrepancy lies in appreciating the factors that affect impedance in DBS and the effects of DBS stimulation on tissues. The effects and side-effects of DBS result from the volume of tissue activated, which is directly related to current density.[4] The most widely used IPGs employ constant voltage stimulation.[4] A higher impedance results in a smaller volume of tissue activation while a smaller impedance results in a larger volume of tissue activation.[2,6] In this case, the higher therapeutic impedance indicates a smaller volume of tissue activation that achieved the desired clinical effect while avoiding side effects.

In light of this information and the normal LII, it was decided to continue using the programming settings with the best clinical response regardless of the therapeutic impedance values.

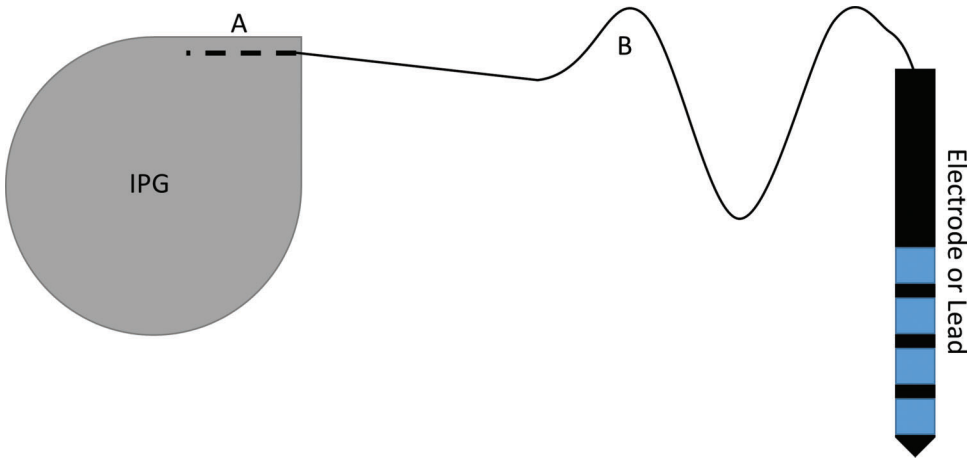

Figure 2. **Schematic Representation of the Components of the Deep Brain Stimulation Hardware.** From left to right, the implantable and programmable generator (IPG), the IPG connector block (A) by which the connection cable (B) connects to the IPG. The connection cable then connects to the electrode or lead.

Gaps in knowledge

Despite the wide use of DBS, multiple accepted practice guidelines are based on limited evidence or are the basis of current active debate. In the following sections, we will review the evidence for two uses of impedance measurements in DBS: hardware malfunction (open and short circuits) and mode of stimulation (constant voltage versus constant current).

Short circuits and open circuits in DBS

Short circuits are characterized by low impedances (usually less than 50 ohms) and high currents, and open circuits by high impedances and low currents. These can occur because of malfunction of any of the different components of the DBS hardware (Figure 2). The symptoms of such a malfunction typically include an acute decrease in benefit from DBS, though it can develop gradually mimicking a "progression" of the underlying disorder.[7]

Short circuits result from either infiltration of fluids into the connections or lead "fracture".[7] The rate of occurrence has been estimated to be approximately 2.5% per year.[7] Open circuits can result from lead "fractures" and are estimated to occur in 5% of patients and 1.8% of implanted leads.[1,8] Many of these fractures are "macroscopic" and can be readily identified by either direct palpation or radiological evaluation (X-rays and/or computed tomography scans). Sometimes open circuits are noted but there is no evidence of macroscopic abnormalities (14.3–25% of all cases).[3] Limited information is available regarding cases with a more gradual change in impedances[9] or in cases with intermittent connectivity problems.[10] There are no clear guidelines to manage cases of open and/or closed circuits, most of the published literature is based on case series.[3] Any surgical revision is associated with increased morbidity and mortality and thus developing management guidelines is important. Yang et al.[3] and Allert et al.[10] recently proposed similar guidelines to approach cases of open circuits (as well as a limited approach to short circuits). After ruling out the presence of macroscopically noted problems, they recommend attempting to reprogram with alternate usable contacts (if possible) as well as with medication changes. If this conservative approach fails, then they recommend intraoperative impedance and system connection check to try to localize the problem. If localization fails by intraoperative testing, they recommend a sequential replacement and intraoperative impedance assessment starting with the IPG and moving proximal to the lead until the source of the open circuit is identified. In some cases, extraction of the entire system is required. These proposed guidelines[3,10] rely on single-center experiences and have not been prospectively evaluated for clinical outcomes, side effects, or cost–benefit analysis.

Constant voltage versus constant current

Current density alters the volume of tissue activated, inducing the effects and side effects of DBS. The most widely used IPGs use constant voltage stimulation resulting in a change of current density with changes in impedance. LII varies over time: a gradual increase in impedance in the first 1–3 weeks following implantation and then a slower plateau over the next few months.[11,12] In the chronic phase (more than 6 months to 1 year) the LII tends to decrease gradually (rate varies significantly between studies but is less than 100 ohms a year).[12–14] The mechanism of decrease in LII chronically has not been elucidated with a possible role of brain atrophy.[13,14]

Impedance is determined by the effect of multiple factors: IPG and lead connection; the surface area of the electrode(s); the characteristics of the encapsulation layer; and the conductivity of the stimulated tissue.[2,4] The first two factors are relatively stable while the last two are more variable. Studies have shown that the encapsulation layer characteristics and tissue conductivity account for most of the impedance variability.[2,15] The thickness and conductivity of this encapsulation layer is variable between individuals and is affected by stimulation.[2,5,14] Studies have shown that active contacts have lower impedances than inactive ones.[2] Determining the conductivity of

the stimulated tissue is complex. There are conductivity differences between white and gray matter. The mean conductivity values have not been assessed following chronic DBS stimulation.[2,5] Satzer et al.[5] correlated contact location (using 7 T magnetic resonance imaging and microelectrode recording) with changes in electrode impedance in 62 patients with DBS in the subthalamic nucleus for Parkinson's disease. Lower impedances were noted in contacts located in the rostral subthalamic nucleus (consistent with previous reports).[14] Unexpectedly, gray matter impedances were higher than those measured at the border of the subthalamic nucleus (as determined by microelectrode recording and not imaging).[5] Further studies will be needed to determine the changes in the encapsulation layer and tissue conductivity and to assess longitudinally the intra- and interindividual variability with chronic stimulation.

Newer IPGs capable of constant current stimulation are currently marketed to address this variability in impedance. These systems offer a constant current density by automatically adjusting the voltage to changes in the impedance. The field of DBS in general seems to be moving toward more widespread adoption of the constant current stimulation paradigm.[4] Recent studies determined that constant current stimulation is at least non-inferior to constant voltage stimulation.[4,6,16,17] The arguments in favor of adoption include a stable current density delivery, safety, and equal effectiveness when compared with constant voltage stimulation. Preda et al.[6] and Lettieri et al.[15] studies hinted at a possible increased benefit in dystonia patients. Larger randomized studies assessing different DBS targets in various disease states will be required to determine the benefits of constant current versus constant voltage stimulation.

Expert commentary

This case highlights the need for clinicians managing DBS devices to better understand fundamental differences between the impedance that is measured to verify lead integrity versus the therapeutic impedance, which is measured at the active contact of stimulation. While the former guides a clinician in assessing the "health" of the electrical system, the latter provides information on the volume of brain tissue activated. The latter measure has also been suggested as an important measure to understand the clinical impact of DBS. The author points out the need for a methodical approach to treating hardware malfunction. This approach should include accurately assessing the origin of the issue, but the approach should also include a framework for troubleshooting problems that are more complex. Often in DBS cases, more than one issue emerges during programming and this can be confusing to an inexperienced programmer. Working through each issue one at a time is important for success; however, assessing the integrity of the DBS system is the first step to any troubleshooting algorithm. Impedance measurements may become more important to the field as we begin to examine questions regarding the use of constant current stimulation. Use of constant current technology stabilizes the amount of electrical current delivered despite impedance variability and this facilitates a smoother delivery of the electrical current. It is unknown whether the theoretical benefits of providing a more stable volume of tissue activation will translate into a meaningfully different outcome.

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