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IMPEDANCE CHARACTERIZATION OF A DEEP BRAIN STIMULATING ELECTRODE: TRANSIENT PULSE RESPONSE

BY

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Abstract. The goal of this study was to present an analytical equation for the instantaneous electrical impedance $Z(t)$ of the electrode for the case when it is used with pulsed current of similar values with those used for clinical applications. $Z(t)$ increases with time t being proportional with $t^{0.9}$. It decreases with increasing voltage U, increasing current I and decreasing resistivity ρ. We propose an equation for $Z(t)$ for different values of I and ρ ($Z_{I,\rho}(t)$). This equation is used to calculate the patient-specific parameters of interest, *i.e.*, the voltage necessary to inject a certain current, the delivered charge, the electrical efficiency of the electrode, etc., as function of time for specific conditions. For the same applied voltage, the delivered charge and the electrical efficiency are little higher for monopolar configuration than for bipolar configuration but the difference decreases as ρ increases.

Keywords: deep brain stimulation; instantaneous electrical impedance; pulsed current.

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1. Introduction

Over the last two decades deep brain stimulation (DBS) has evolved from an experimental technology to a well-established surgical therapy for numerous disorders (Miocinovic *et al*., 2013; Shah *et al*., 2010; Hariz *et al*., 2013). Present day implantable pulse generator (IPG) units and external trial stimulators for DBS applications deliver biphasic, charge-balanced pulse-pair trains as advocated by Lilly nearly a half century ago (Lilly, 1961). The maximum amplitude and pulse width of IPG unit are 10.5 V and 450 ms. The Medtronic 3387 DBS electrode is used with pulsed voltage or pulsed current, in the range of 1-8 V (0.1–2 mA), 60–180 μs pulse width, and 100–185 pulses per second (Coffey, 2008). Optimal selection of stimulation parameters remains a challenge.

An accurate description of the DBS electrode impedance is important for *in vivo* applications (*i.e.* stimulation, electrode-tissue interface characterization, brain tissue characterization, the formation of the encapsulation layer, field potential recording, etc.) and for the development of computational models of neural recording and stimulation that aim to improve the understanding of neuro–electric interfaces and electrode design.

There is little information about the Medtronic 3387 DBS electrode impedance characterization with pulsed signal (Wei and Grill, 2009) or with pulsed signal of clinical relevance (Holsheimer *et al*., 2009). We don't have an analytical equation for the electrode impedance as function of time, current or voltage and saline resistivity. Detailed characterization of the impedance of the electrode is required for the accurate calculation of the current passing through the tissue and the charge delivered to the brain for given stimulation conditions. This may facilitate the selection of optimal stimulation parameters. The average value of the impedance reported for patients was 1200 Ω (range: 415–1999 Ω) (Coffey, 2008). As a safety feature, the programming device calculates the charge density based on a conservative impedance value of 500 Ω. No distinction is made between the electrical impedance of the brain tissue, as part of the electrode impedance, and the total impedance of the electrode which include as well the impedance of the connecting leads and of the metal-tissue interface. Consequently the voltage applied on the tissue is significantly lower than the voltage applied on the DBS electrode. The experimental measurements show that the electrode impedance is time, voltage, current and saline concentration (electrical resistivity) dependent (Wei and Grill, 2009; Lempka *et al*., 2009). Consequently it is opportune to find an analytical equation for the instantaneous impedance of the DBS electrode as function of the above parameters.

The goal of this study was to present a simple quantitative analytical model for the electrical impedance of the Medtronic 3387 DBS electrode using pulsed current of similar values with those used for *in vivo* applications. An analytical equation for the electrode impedance as function of time, current and saline resistivity is given.

2. Methods

The impedance properties for two adjacent contacts (bipolar configuration) of the Medtronic 3387 DBS electrode showed in Fig. 1*a* were measured. Two contacts were specifically used to make available two metal-saline interfaces. Thus the contribution of the impedance of the two interfaces was relevant by comparison to other contributions (*e.g.*, saline impedance and the coupling capacitance between the leads).

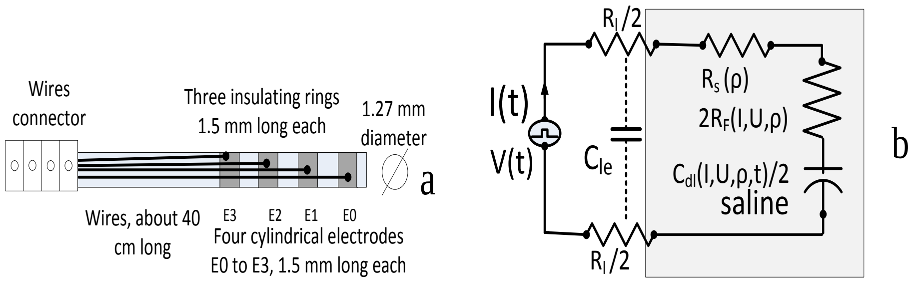

Fig. 1 – (*a*) The Medtronic 3387 electrode for deep brain stimulation; (*b*) The equivalent circuits of the DBS electrode for the case of bipolar configuration.

Measurements were performed in a tank filled with 2 l saline, placed in a Faraday cage, of different concentrations (1-9 NaCl gl^{-1}, electrical resistivity ρ from 5.025 to 0.625 Ωm) at 23ºC. The voltage transients generated by applying clinically relevant positive pulse currents (200 μs width and 20 ms repetition period, if not otherwise specified) were measured at 7 current amplitudes from 0.15 mA to 2 mA. The experimental setup was similar with that used in literature (Holsheimer *et al*., 2009). The voltages were measured using a double-beam digital oscilloscope Agilent DSOX4022A, sample interval 0.1 μs, and transferred to a computer for storage and analysis. The measurements were replicated six times at 4 min time interval, if not otherwise stated, at each amplitude level and the average data are presented. The instantaneous impedance $Z(I,\rho,t)$ was calculated as the ratio between the instantaneous voltage and the instantaneous current.

The saline impedance R_s was previously approximated (Holsheimer *et al*., 2009) with the asymptotic impedance of the DBS electrode for pulse width ≈ 0 s or as the asymptotic high frequency impedance (Wei and Grill, 2009) (the metal-electrolyte impedance was modeled as a parallel *RC* circuit). To discriminate between metal-electrolyte impedance and bulk (saline) impedance, we calculated R_s and the geometry factor (*GF*) using simulations. For bipolar configuration a 2D axisymmetric finite element models of the DBS electrode and its surrounding medium were created.

2.1. Data Analysis

The series *RC* equivalent is at the heart of the behavior of an electrode-electrolyte interface. This equivalent does not account for the very-low-frequency behavior of the interface (Geddes, 1997). Various equivalent circuits have been suggested in an effort to better reproduce the electrode-saline interface response (Geddes, 1997; Schwan, 1968; de Boer, 1978). We will use a simple electrical circuit presented in Fig. 1*b* and will show that for the experimental conditions of interest for clinical use of the DBS electrode, the experimental data can be analyzed using this model. The coupling capacitance C_{le} between the metallic leads running from the DBS electrode connector to the cylindrical contacts will be neglected. We assume that the two metal-saline interfaces have the same characteristics and the equivalent circuit reduces to (R_l + $R_S(\rho)$+2$R_F(U,I,\rho)$) in series with $C_{\mathrm{dl}}(U,I,\rho,t)/2$, where R_l is the resistance determined by the length of the metallic leads between the DBS electrode connector and the cylindrical contacts, $R_S(\rho)$the resistance of the saline, $R_F(U,I,\rho)$ the faradaic resistance at metal-saline interface, and $C_{\mathrm{dl}}(U,I,\rho,t)$ a time-dependent double layer capacitance at metal-saline interface. If $U(t)$ is the applied voltage and $I(t)$ is the current passing through the circuit, we have:

$$U(t) = I(t)(R_l + R_s(\rho) + 2R_F(I,\rho)) + \frac{2\,Q(t)}{C_{dl}\,(I,\rho,t)} \tag{1}$$

where Q(t) is the electric charge on the double layer capacitance at interface:

$$Q(t) = \int_0^t I(t)dt \tag{2}$$

For a constant-current stimulation Eq. (2) reads:

$$Q(t) = It \tag{3}$$

From Eq. (1) it results:

$$U(t) = I(R_l + R_s(\rho) + 2R_F(I,\rho)) + \frac{2\,It}{C_{dl}\,(I,\rho,t)} \tag{4}$$

We will assume that for short time the double layer capacitance increases with time as:

$$C_{dl}(t) = \ C_{dl0}t^m \tag{5}$$

where C_{dl0}, units Fs^{-m}, was a measure of the double layer capacitance at 1 second and m was a measure of the deviation from pure capacitive (m = 0) behavior. It results:

$$U(t) = I(R_l + R_s(\rho) + 2R_F(I,\rho) + \frac{2\,t^{1-m}}{C_{dl\,0}(I,\rho)}) \qquad (6)$$

and the instantaneous impedance of the DBS electrode is:

$$Z(I,\rho,\mathrm{t}) = R_l + R_s(\rho) + 2R_F(I,\rho) + \frac{2\,t^{1-m}}{C_{dl\,0}(I,\rho)} \qquad (7)$$

The experimental data obtained for values of I, ρ and t relevant for clinical applications of the DBS electrode are very well described if m = 0.1. The validity of Eq. (7) for m = 0 was verified by carrying out measurements on a lamped impedance network built from a resistors and a capacitor in series whose value has been (separately) determined by an impedance analyzer (Agilent 4294A). By fitting the experimental data to Eq. (7) the values for R and C were determined with errors below 0.3%.

3. Results

The resistance R_l of the 2×40 cm long metallic leads was measured with the contacts E1 and E2 short-circuited. It was 86.4 ± 0.3 Ω (mean value and standard deviation (SD)), comparable with the results from literature (Wei and Grill, 2009; Holsheimer *et al.*, 2009). R_s of the saline involving contacts E1 and E2 was calculated using simulations. The result for 0.9% NaCl was R_s = 108 ± 3 Ω (mean value and SD for 13 simulation at different constant currents from 0.15 mA to 2 mA. This value is higher than the asymptotic value of ≈ 88 Ω reported for pulse width ≈ 0 s (Holsheimer *et al.*, 2009). It is lower that the value (mean ± SD = 133 ± 7 Ω) estimated from the voltage transient responses to symmetrical biphasic square current pulses (Wei and Grill, 2009). From simulations for different electrical resistivity ρ from 0.625 to 10 Ωm, the geometry factor of the DBS electrode for bipolar configuration was calculated as:

$$GF = \frac{\rho}{R_s} \qquad (8)$$

The value was GF = (0.0058 ± 0.0001) m, in good agreement with the value reported in literature (Vinter *et al.*, 2009). In the case of monopolar stimulation, the IPG placed in the chest is used as reference electrode. The geometry of the connection between the head and neck, the geometry of the neck and of the connection between the neck and chest is complex and it consists of materials with very different electrical resistivity. For this reason we did not made simulations for the case of monopolar configuration and we used data from AC measurements (Neagu and Neagu, 2016). The geometry factor for monopolar configuration was estimated as *GFm* = 0.0049 m.

3.1. Constant-Current Stimulation

Fig. 2 shows the instantaneous impedance for the DBS electrode as function of time for the case of stimulation with constant-current of 0.15, 1.2 and 2 mA in 0.9% saline solution. The impedance decreases as the current increases. The experimental data have been fitted to Eq. (7) to determine $R_F(I)$ and $C_{dl0}(I)$. The fitting curves are showed by lines superimposed on the symbols in Fig. 2.

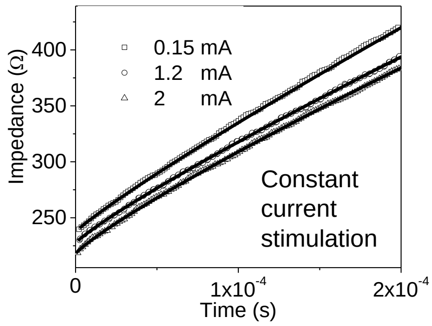

Fig. 2 – The instantaneous impedance as function of time The data have been fitted to Eq. (7) to determine $R_F(I)$ and $C_{dl0}(I)$. The fitting curves are showed by lines superimposed on the symbols.

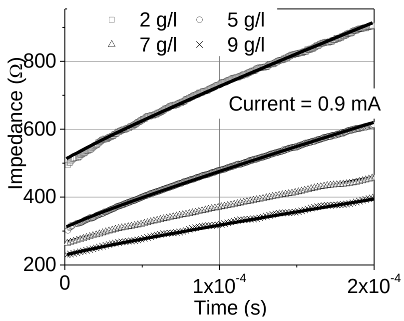

Fig. 3 – The instantaneous impedance as function of time for the DBS electrode in saline with different resistivity. The data have been fitted to Eq. (7) to determine $R_F(\rho)$ and $C_{dl0}(\rho)$.

Table 1

The Values Obtained for $R_F(I)$ and $C_{dl0}(I)$ by Fitting the Experimental Data for a Saline Resistivity ρ = 0.625 Ωm (0.9% NaCl) and Different Stimulating Currents to Eq. (7) with m = 0.1

Current, [mA]	0.15	0.34	0.68	0.9	1.2	2
R_F, [Ω]	21.4	20.4	19.7	18.8	17.3	12.9
C_{dl0}, [μFs^{-m}]	5.06	5.12	5.26	5.41	5.56	5.68

The fitting is very good, indicating that the theoretical model is appropriate. In fact, for a parallel circuit and $t \approx 0$ s R_F is shunted by C_{dl} and the impedance will be $Z(0) = R_s + R_l$ = 194.4 Ω. This value is lower than the experimental values in Fig. 2 indicating that the experimental data are not well described by a parallel equivalent circuit. Because we know R_s from simulation it results that the series circuit is appropriate to describe the experimental data.

The parameter values are presented in Table 1. As the current increases, R_F decreases and C_{dl0} increases in good agreement with data in literature (Wei and Grill, 2009; Schwan, 1968; Weinman and Mahler, 2010).

Fig. 3 shows the instantaneous impedance as function of time for the DBS electrode in saline with different resistivity of 2.631, 1.086, 0.793 and 0.625 Ωm, *i.e.*, for NaCl concentration of 2, 5, 7 and 9 gl^{-1} respectively. The data are for a current of 0.9 mA. As the saline resistivity decreases the impedance decreases. $R_s(\rho)$ was determined using Eq. (8). The experimental data have been fitted to Eq. (7) to determine $R_F(\rho)$ and $C_{dl0}(\rho)$. The fitting curves are showed by lines superimposed on the symbols in Fig 3. The fitting is very good, indicating that the theoretical model is appropriate. Parameter values are presented in Table 2.

Table 2
The Values Obtained for $R_F(\rho)$ and $C_{dl0}(\rho)$ by Fitting the Experimental Data for I = 0.9 mA and Different Saline Resistivity to Eq. (7) with m = 0.1

Resistivity, [Ωm]	5.025	2.631	1.821	1.086	0.793	0.625
R_F, [Ω]	60	44	32.9	23.3	21	17.8
C_{dl0}, [μFs^{-m}]	0.82	1.31	2.29	3.01	4.85	5.59

As the saline resistivity decreases $R_F(\rho)$ decreases and $C_{dl0}(\rho)$ increases, as expected.

4. Discussion

Data in Tables 1 to 2 will be used to obtain an analytical equation for the instantaneous impedance of the DBS electrode for experimental conditions of interest for clinical applications. This means that we will deduce an analytical equation of the instantaneous impedance $Z_{I,\rho}(t)$ for different values of the stimulation current and the electrical resistivity of the medium. Consequently, knowing I and ρ, the instantaneous impedance or other quantities related with it (*e.g.*, electrical charge delivered for certain conditions, the current injected, etc.) can be calculated.

4.1. Analytical Equation for the Instantaneous Impedance

Eq. (7) shows that in order to get an analytical equation for the instantaneous impedance we need to estimate $R_F(I,\rho)$ and $C_{dl0}(I,\rho)$. The variables I and ρ are independent variables. Taylor series is a representation of a function as an infinite sum of terms that are calculated from the values of the function's derivatives at a single point. We will expand $f(x,y)$ (*e.g.*, $R_F(x,y)$ or $C_{dl0}(x,y)$ were x is I and y is ρ), in Taylor series around a point (x_0, y_0). Because the variation range of R_F and C_{dl0} with I and ρ is low, the series will be truncated after the second term:

$$f(x, y) \approx f(x_0, y_0) + (x - x_0) f_x(x_0, y_0) + (y - y_0) f_y(x_0, y_0) + \cdots + \tag{9}$$

where f_x and f_y denote the respective partial derivatives. Data in Tables 1 and 2 will be used to obtain $f(x_0,y_0)$ and the partial derivatives as function of I and ρ.

By fitting the data in Table 1, first row, with a line $R_F(I) = a - sI$, we obtain a = (22.6 ± 0.5) Ω and s = (4623 ± 401) ΩA^{-1}. By fitting the data in Table 2, first row, with a line it results $R_F(\rho) = a + s\rho$ with a = (14.8 ±2.1) Ω and s = (9.6 ± 0.8) m^{-1}. We will choose $x = I,\ y = \rho, x_0 = I_0 = 9 \times 10^{-4}$A and $y_0 = \rho_0 = 0.625\ \Omega$m. $R_F(I_0,\rho_0)$ = (18.8 + 17.8)/2 = 18.3 Ωm and we get:

$$R_F(I, \rho) \cong 18.3 + (I - 0.0009)(-4623) + (\rho - 0.625)9.6 + \cdots + \tag{10}$$

Similarly, from data in Table 1, second row, we have $C_{dl0}(I) = a + sI$, with a = (5.05 ± 0.06)×10^{-6} $Fs^{-0.1}$ and s = (3.4 ± 0.4)×10^{-6} $Fs^{-0.1}A^{-1}$. Electrochemical impedance measurements show that specific capacitance values for bright Pt are typically in the range of 10–30 μFcm^{-2} (Franks, 2005; Morgan *et al*., 2007). Assuming that I is very low, as in the case of electrochemical impedance measurements, and t = 100 µs, from Eq. (5) we get for the specific capacitance 33.5 μFcm^{-2} (the geometrical area of a cylindrical contact is 0.06 cm^{-2}) in good agreement with data in literature (Franks, 2005; Morgan *et al*., 2007).

The variation of C_{dl0} with ρ is nonlinear and can be described assuming $C_{dl0}(\rho) = b\rho^c$ with b and c constants. By fitting the data in Table 2, second row, we obtain $C_{dl0}(\rho) = 3.65\times10^{-6}\rho^{-0.95}$. The standard error of b and c is lower than 10%. We will choose $I_0 = 9 \times 10^{-4}$A and $\rho_0 = 0.625\ \Omega$m. $C_{dl0}(I_0,\rho_0)$ = (5.41 + 5.59) ×10^{-6}/2 = 5.5×10^{-6} $Fs^{-0.1}$ and we get:

$$\begin{aligned} C_{dlo}(I, \rho) \cong\ & 5.5 \times 10^{-6} + (I - 0.0009)3.7 \times 10^{-4} + \\ & + (\rho - 0.625)(-3.47 \times 10^{-6}\rho^{-1.95}) + \cdots +. \end{aligned} \tag{11}$$

It results:

$$Z_{I\rho}(t) = R_l + \frac{\rho}{GF} + 2R_F(I, \rho) + 2\frac{t^{0.9}}{C_{dl0}(I, \rho)} \tag{12}$$

where $R_F(I,\rho)$ is given by Eq. (10) and $C_{dl0}(I,\rho)$ is given by Eq. (11). Eq. (12) allows us to calculate the instantaneous impedance for different I and different ρ. Fig. 4 shows the impedance at t = 50 µs for I in the range of 0.1- 4 mA and ρ in the range of 0.4-10 Ωm. $Z_{I\rho}(5\times10^{-5})$ varies in the range 200 to 2100 Ω. This interval is a little larger than the interval reported for patients (range: 415–1999 Ω)

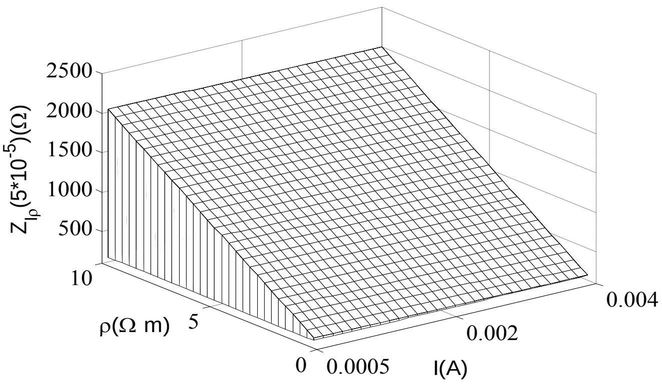

Fig. 4 – The calculated impedance at t = 50 µs for I in the range of 0.1- 4 mA and ρ in the range of 0.4-10 Ωm.

(Coffey, 2008) because the ranges for the two parameters I and ρ are larger. It is known that the safety limit of the charge density is below 30 μCcm^{-2}/ph (Coffey, 2008). For a pulse width of 100 µs the maximum safety current is 18 mA. Eq. (12) allows us to calculate the necessary voltage to inject a certain current for different ρ. The result for t = 100 µs is showed in Fig. 5 for bipolar configuration. The injected current is higher than the maximum safety limit of 18 mA only if ρ is low and U is high.

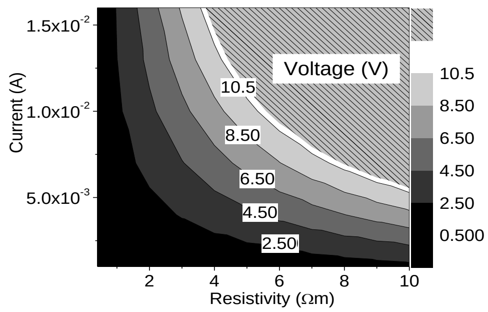

Fig. 5 – The necessary voltage to inject a certain current for different ρ and t = 100 µs.

4.2. Electrical Efficiency of the DBS Electrode

We propose that the electrical (energy) efficiency of the electrode during the stimulation process can be characterized by the ratio between the voltage drop on the saline and the voltage U_{ap} applied on the DBS electrode.

The voltage drop on saline is:

$$U_s(I, \rho, t) = IR_s(\rho) \tag{13}$$

The electrical efficiency $\eta(I,\rho,t)$ for a constant current I is:

$$\eta(I,\rho,t)=\frac{U_s(I,\rho,t)}{U_{ap}}=\frac{R_s(\rho)}{Z(I,\rho,t)} \tag{14}$$

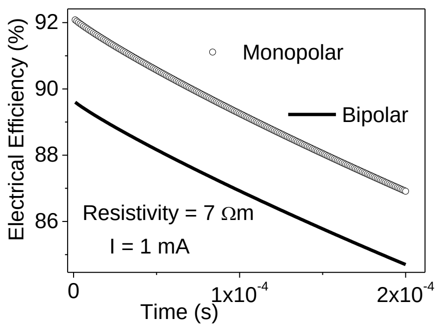

Fig. 6 – The electrical efficiency as function of time.

Eq. (14) shows how much of the applied voltage will spread in the tissue and eventually contribute to stimulation. Fig. 6 shows the electrical efficiency calculated for 1 mA and ρ = 7 Ωm. The line is for bipolar configuration and the circles for monopolar configuration. Electrical efficiency decreases as the time increases. The efficiency will decrease if other series resistances at the electrode-tissue interface are taken into account such as the encapsulation layer at the surface of the contacts or of the IPG. Finding solutions to decrease R_l, R_F and C_{dl} seems reasonable in order to increase the electrical efficiency of the DBS electrode.

4.3. Clinical Relevance of the Results

Detailed characterization of the instantaneous impedance of the DBS electrode may facilitate the selection of better stimulation parameters reducing the occurrence of side-effects. Data reported for patients in literature are not correlated with the applied voltage, the current or time. As a safety feature, the programming device calculates the charge density based on a conservative impedance value of 500 Ω. A proper knowledge of injected current and/or injected charge density is important for a better understanding of the physiological effect of the electrical stimulation.

The electrical (energy) efficiency of the electrode during the stimulation process can be calculated using Eq. (14). This will allow to find a better correlation between the voltage applied and the physiological response.

Knowing the *GF* and the tissue mean resistivity, the tissue resistance can be calculated using Eq. (8). For example, for white matter ρ = 7 Ωm (mean value) (Haueisen *et al*., 1997) and, consequently, using Eq. (8) the white matter resistance is 1209 Ω (bipolar configuration). It is significantly lower that the electrode impedance. This means that only a part of the voltage applied on the DBS electrode is applied on the nervous tissue and only this voltage is responsible for the physiological response.

In the case of monopolar configuration the high resistivity materials at the connection between head and neck, neck and the connection between neck and chest are of particular importance. Simulations shows that only 50% of the electrical impedance between the active contact and the IPG placed in the chest is determined by the brain tissue contained in a cylinder around the active contact with a radius of 12 mm and a height of 1.5 mm, in good agreement with data in literature (Walckiers *et al*., 2010). In the case of monopolar stimulation, because the resistance is spread over a large volume, an increase of the electrical efficiency does not necessarily means an increase of the volume of the activated tissue. The activation of a neuron by an extracellular stimulation is linked to the value of the double spatial derivative of the electrical potential along the fiber direction (Rattay, 1989). It is known that the use of a IPG implanted in the chest as reference electrode leads to an increase of the electrode impedance (+48%) and a reduction of the area of activated tissue (−15%) (Rattay). It is obvious that the stimulated volume is almost double in the case of bipolar configuration when higher voltage drop is expected around the two active contacts.

5. Conclusions

An analytical equation is proposed for the Medtronic 3387 DBS electrode impedance as function of time, current and saline resistivity of similar values with those used for clinical applications. This equation should be used to calculate the parameters of interest, *i.e*., the necessary voltage to inject a certain current, the delivered charge or electrical efficiency, as function of time for specific experimental conditions. This may facilitate the selection of optimal stimulation parameters. An appropriate estimation of the voltage drop on the tissue or the delivered charge is essential in the effort to understand the neuro-electric interface. At the same time a correct characterization of electrode impedance is important for a better electrode design. For the same applied current the electrical efficiency is little higher for monopolar configuration in respect with the values for bipolar configuration.

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CARACTERIZAREA IMPEDANŢEI ELECTRODULUI PENTRU STIMULARE PROFUNDĂ ÎN CREIER: RĂSPUNSUL TRANZITORIU LA IMPULS

(Rezumat)

Scopul lucrării este de a prezenta o ecuaţie pentru impedanţa instantanee $Z(t)$ a electrodului pentru cazul când este folosit cu impulsuri de curent similare ca valoare cu acelea folosite pentru aplicaţii clinice. $Z(t)$ creşte cu creşterea timpului t, fiind proporţional cu $t^{0,9}$ şi descreşte cu creşterea tensiunii U, cu creşterea curentului I şi scăderea rezistivităţii ρ. Propunem o ecuaţie pentru $Z(t)$ pentru diferite valori ale lui I şi ρ ($Z_{I,\rho}(t)$). Această ecuaţie este folosită pentru a calcula parametrii de interes pentru un anumit pacient, de exemplu, tensiunea necesară pentru a injecta un curent de o anumită valoare, sarcina injectată, randamentul electric al electrodului, etc. ca funcţie de timp pentru condiţii particulare date. Pentru o valoare dată a tensiunii aplicate, sarcina injectată şi randamentul electric sunt puţin mai mari pentru configuraţia monopolară în comparaţie cu valorile pentru configuraţia bipolară, iar diferenţa scade dacă ρ creşte.