Bioimpedance Harmonic Analysis as a Diagnostic Tool to Assess Regional Circulation and Neural Activity

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Abstract. The novel technique based on harmonic analysis of bioimpedance microvariations with original hard- and software complex incorporating a high-resolution impedance converter was used to assess the neural activity and circulation in human urinary bladder and penis in patients with pelvic pain, erectile dysfunction, and overactive bladder. The therapeutic effects of shock wave therapy and Botulinum toxin detrusor injections were evaluated quantitatively according to the spectral peaks at low 0.1 Hz frequency (M for Mayer wave), respiratory (R) and cardiac (C) rhythms with their harmonics. Enhanced baseline regional neural activity identified according to M and R peaks was found to be presumably sympathetic in pelvic pain patients, and parasympathetic – in patients with overactive bladder. Total pulsatile activity and pulsatile resonances found in the bladder as well as in the penile spectrum characterised regional circulation and vascular tone. The abnormal spectral parameters characteristic of the patients with genitourinary diseases shifted to the norm in the cases of efficient therapy. Bioimpedance harmonic analysis seems to be a potent tool to assess regional peculiarities of circulatory and autonomic nervous activity in the course of patient treatment.

1. Introduction
The most diseases of genitourinary system are manifested by the disorders in blood flow and neural control. While specific methods are employed to individually evaluate any of these pathogenic factors, no method is available to assess simultaneously the changes in regional circulation and neural activity. Pelvic pain (PP) and overactive bladder (OAB) are complex syndromes involving sympathetic and parasympathetic disorders. However, there are no methods to obtain quantitative description of these painful and disturbing syndromes to objectively evaluate the treatment results.

In this study, we demonstrated the possibilities of the novel method based on the bioimpedance harmonic analysis to assess regional neural and vascular activity in human genitourinary organs during some genitourinary diseases and their treatment.

2. Study design
Regional circulatory and neural activities in the minor pelvic organs were assessed by bioimpedance harmonic analysis (BHA) in patients with pelvic pain (PP), overactive bladder (OAB) syndromes, and erectile dysfunction (ED) prior to and after the treatment.

2.1. Patient groups, examination, and treatment
All patients included in the study were divided into groups according to clinical diagnosis, therapeutic modality, and examined organ.
Patients with chronic PP \((n=16)\), ED \((n=6)\), and Peyronie disease \((n=6)\) received the course of shockwave therapy (SWT). To assess regional circulatory and neural activity, two Ag-Ag/Cl electrodes 0.4 mm in diameter were applied to the patient’s penis for measuring penile electric activity. To measure vesical impedance, the electrodes were applied to the front abdominal wall in projection of urinary bladder. The patients were examined prior to SWT as well as during and after the course of treatment (5-10 procedures).

In the patients with documented OAB \((n=8)\), vesical impedance measurements were performed prior to and on day 1-4 after Botulinum toxin (BT) injections into vesical wall and sphincter.

Healthy human voluntaries composed two control groups examined with vesical \((n=6)\) and penile \((n=16)\) BHA.

2.2. Method and calculations

Two silver wire electrodes were covered with a narrow gauze bandage soaked in physiological saline, applied to penis or to the front abdominal wall in projection of urinary bladder, and connected to the impedance converter in bipolar electrode mode. The rhythmic variations of the vesical or penile impedance were recorded, processed, and automatically analyzed with fast Fourier transform implemented in an original software-hardware system (‘Biola’, Russia).

Calculations were performed as follows. A record of variable component (figure 1, A) was cut into 12.8 or 25.6-sec fragments containing 2048 or 4096 points. FFT was calculated with Hanning windows (figure 1, B, C). The bioimpedance variations were analyzed in the frequency band of 0.05-15.0 Hz. The periodicities in small variations of vesical and penile bioimpedance included the major spectrum peaks at the frequencies of heart beats (C), respiration (R), and Mayer (M) wave (0.1 Hz). The magnitude of selected peaks was calculated as ‘efficient impedance’ being equal to the square root of the sum of squared amplitudes of all individual spectrum components comprising these peaks.

This procedure reflects the fact that any ‘smooth’ peak in digital Fourier transform consists of a number of several sinusoidal components. Total pulsatile activity (TPA) was calculated as effective impedance on the basis of cardiac C-peak and its harmonics with the epoch of 12.8 sec (2048 points) according to the formula:

\[
TPA = \sqrt{C_1^2 + C_2^2 + C_3^2 + \ldots}
\]

Neural activity (NA) was calculated as effective impedance corresponding to the frequency band encompassing M and R peaks measured with the epoch of 25.6 sec (4096 points). Mayer to respiratory peak ratio (M/R) was calculated to characterize the regional sympathetic-parasympathetic balance.
3. Results

Recordings of variable component of the urinary bladder impedance made it possible to observe the bioimpedance oscillations of vascular and respiratory origin (figure 1, A). The low-frequency peak M was conventionally termed as ‘Mayer wave’. Oscillations of arterial pressure at this frequency range are supposed to reflect the neural vasomotor sympathetic activity [1]. The respiration-related oscillations were usually presented with respiratory R-peak and its harmonics. The pulse-induced variations were reflected by one or several cardiac harmonics C1, C2, …, Cn. The harmonic spectra of vesical and penile bioimpedance were characterized with high M- and R- peaks, which were several times greater than the cardiac harmonics. This fact is interpreted as indication on the neurogenic nature of M and R rhythmic bioimpedance variations in these organs. Moreover, our experimental studies supported the idea that M-peak reflects sympathetic activity, while R-peak is an indicator of parasympathetic regional activity [2].

The parameter NA was elevated in vesical and penile spectra compared to the norm in patients with pelvic pain syndrome evidencing to enhanced neurogenic activity in minor pelvic organs. The increased neurogenic activity was presumably sympathetic, as revealed by elevated M/R ratio. SWT diminished the pain syndrome by decreasing NA in both organs, while M/R ratio decreased and approximated to the normal values thereby evidencing moderation of sympathetic activity.

Table 1. Parameters of bioimpedance analysis in patient groups.

| Patient groups       | NA (mOhm) | M/R   | TPA (mOhm) |
|----------------------|-----------|-------|------------|
| Bladder, pelvic pain | 359.2±70.9| 0.65±0.27 | 24.0±3.1   |
| After SWT            | 106.4±18.6| 0.21±0.04 | 14.2±2.4   |
| Overactive bladder   | 238.9±102.6| 0.16±0.05 | 16.6±4.4   |
| After BT treatment   | 250.6±188.2| 0.32±0.09 | 37.8±21.3  |
| Normal bladder       | 126.6±43.0| 0.21±0.06 | 13.9±1.2   |
| Penis, pelvic pain   | 31.4±12.7 | 1.93±0.44 | 16.6±5.5   |
| After SWT            | 12.7±5.0  | 0.99±0.37 | 4.2±1.7    |
| Penis, ED            | 43.6±16.5 | 1.85±0.76 | 6.72±3.29  |
| After SWT            | 28.5±10.6 | 1.18±0.07 | 6.08±1.20  |
| Penis, ED+Peyronie   | 32.6±12.2 | 1.12±0.10 | 6.92±1.52  |
| After SWT            | 29.4±7.1  | 1.41±0.51 | 5.96±0.88  |
| Normal penis         | 16.0±0.8  | 0.61±0.11 | 4.6±0.8    |

The abnormally elevated NA parameter was documented in patients with OAB. In these patients, an enhanced neurogenic activity was probably determined by the parasympathetic component as evidenced by diminished M/R ratio. The neurogenic activity remained enhanced in BT-treated bladder with M/R ratio shifted in favor of sympathetic activity.

In patients with pelvic pain, TPA was significantly elevated in comparison with the normal value. After SWT, it diminished significantly in both examined organs. In these patients, the changes in TPA were paralleled with a decrease of sympathetic activity suggesting the potency of SWT to dramatically moderate the painful syndrome due to depression of the regional neural activity. Moreover, TPA diminished due to disappearance of resonant harmonics in successfully treated patients (figure 2, a).

In patients with OAB, TPA and sympathetic activity increased after BT treatment. The elevation of pulsatile activity resulted from a 2.5-fold increase of fundamental C1-harmonic (31.1 vs 12.2 mOhm), while the resonant harmonics decreased in these patients (figure 2, b) probably evidencing the changes in viscoelastic properties of the vesical arteries.

BHA helped to delineate the diagnostics of the pathologic features of ED, and to provide objective information on therapeutic efficacy. The elevated parameter NA in patients with ED decreased after SWT in the group of patients with ED only, but it did not change in the patients with ED complicated by Peyronie disease. The M/R ratio diminished slightly in patients with ED, although, it increased in
the group “ED+Peyronie”. Analysis of the changes in C harmonics in the above groups showed that the resonant harmonics successfully disappeared in the group “ED” (figure 2, c), while they remained pronouncedly elevated in the group “ED+Peyronie” (figure 2, d).

![Figure 2. Percent changes in C-harmonics in the bladder (circles) and penis (triangles) impedance spectra before (I- solid lines) and after (II- dotted lines) treatment of the patients with a) pelvic pain; b) OAB syndrome; c) ED; and d) ED+Peyronie disease.](image)

Thus, BHA can be routinely used prior to therapy for comprehensive diagnostics of the functional disorders on the basis of quantitative physiologic indices; moreover, it can assess the early and long-term effects of selected treatment modality.

4. Conclusions
The study showed that BHA can be an informative tool to assess regional neural and circulatory status in diverse pathologies. Moreover, this method gives the objective data on therapeutic efficacy.

The increased neurogenic activity in minor pelvic organs of the patients with pelvic pain originated mostly from enhanced sympathetic component, while in the patients with overactive bladder, it resulted from augmented parasympathetic component. In patients with pelvic pain and erectile dysfunction, circulation disorders were characterized by elevated total pulsatile activity in the bladder and penile impedance spectra. Large pulsatile resonances attested to the changes in viscoelastic properties of the arteries probably indicated abnormalities in vascular conditions.

Physiotherapy employing the focused shock waves seems to have a considerable advantage in treatment of the patients with chronic pelvic pain due to moderating abnormally enhanced regional sympathetic activity. In the patients with overactive bladder, Botulinum toxin treatment shifted regional sympathetic-parasympathetic balance in favor of sympathetic activity. A high fundamental cardiac harmonic with moderate pulsatile resonances indicate the healthy status of regional circulation in all examined patients and attest to efficacy of the corresponding treatment.

References
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