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Supporting gastroesophageal reflux disease diagnostics by using wavelet analysis in esophageal pH-metry

Piotr M. Tojza, Grzegorz Redlarski
Gdansk University of Technology
in Gdansk
ul. G.Narutowicza 11/12 80-233 Gdansk, Poland
Email: {poitr.tojza, grzegorz.redlarski}@pg.edu.pl

Maria Janiak
Gdansk Medical University
in Gdansk
ul. Marii Sklodowskiej-Curie 3A, 80-210 Gdansk, Poland
Email: marj@gumed.edu.pl

***Abstract*—This paper presents a new approach to computer supported esophageal pH-metry measurement analysis performed in order to diagnose gastroesophageal reflux disease. In this approach wavelet analysis was used to analyse the esophageal pH-metry course. The research was performed on three groups of pH-metry courses: whole 24-hour pH-metry course, sleep only pH-metry course and 20 minutes after the end of a meal pH-metry course. After performing a 128 level decomposition of the pH-metry course, the W_x was defined as a parameter of extreme differential. This parameter was used to distinguish patients esophageal pH-metry results and on that basis classify patients as healthy or sick. Using this method the sensitivity of 77% was achieved.**

I. Introduction

GASTROESOPHAGEAL reflux disease (GERD) is one of the most commonly diagnosed diseases of the upper gastrointestinal tract, especially among the inhabitants of developed countries [1], [2], [3], [4]. It is estimated that the symptoms occur at least once a month in 44% of American adults, about 20% of Europeans, 6.6% of Japanese and Singaporeans or 3.5% of Koreans. However, among people in Africa and some Asian countries the disease is diagnosed very rarely [2]. The impact on the occurrence and development of the disease is largely influenced by the lifestyle of inhabitants of developed countries including the type of diet, the use of stimulants (alcohol, coffee, smoking cigarettes) or stress. In addition, the symptoms of GERD may increase as a result of misalignment during sleep or during increased physical effort (eg. during exercise in the gym) [5]. Studies suggest that many people are not fully aware of having the disease, though being effected by it's developing symptoms, and reporting to the doctor only when the disease has developed [5].

Among the numerous methods of diagnosing GERD 24hour esophageal pH-metry and 24-hour pH-metry with impedance measurements are the most popular invasive diagnostic techniques. These methods are characterized by a very high percentage of correctly diagnosed patients, but their main drawback is the time needed by a specialist gastroenterologist to evaluate the results of the measurement. Analysis of 24-hour format pH and impedance is a tedious and time-consuming task, that reduces the time the physician can spend on treating other patients or performing studies [6], [7], [8], [9].

Due to the impact of GERD on the condition of the upper gastrointestinal tract, which reflects on the health and lifestyle of patients, special attention should be paid to the process of early GERD diagnosis. This is particularly important in the context of the increase in the amount of positively diagnosed inhabitants of developed countries. In view of the increasing trend in the incidence of patients affected by GERD, taking into account the time-consuming diagnostic test, it is advisable to take steps to automate the assessment process of pH and pH with impedance measurements. Automating the process of pH-impedance courses evaluation will shorten the laborious analysis allowing the physician to quickly assess the results using their knowledge and experience. In order to implement the automation assessment process of pH courses discrete wavelet analysis was used.

II. Upper gastrointestinal tract reflux diseases

The mechanism of regurgitation of the stomach to the esophagus is a physiological process that occurs naturally in the human circadian cycle [2], [10]. Excessive exposure of tissues of the esophagus to the material alleged to reflux - mainly of hydrochloric acid and pepsin is prevented by the antireflux barrier, consisting of four components: the gastro-esophageal connection (lower esophageal sphincter), a mechanism for cleaning the esophagus of hydrochloric acid - the so called acid clearance, the upper esophageal sphincter and the resistance of esophageal mucosa [9]. These mechanisms help to protect esophagus tissue against chemical reactions destroying the tissues, since the esophagus is not adapted, as is the case of the stomach or duodenum, to longer exposure to the harmful effects of gastric acid.

The pathological situation will occur when, for various reasons, the physiological mechanisms protecting the esophagus from the gastric acid fail. Given that the hydrochloric acid and pepsin are the most harmful secretions of the upper gastrointestinal tract, often such a situation leads to occurrence and development of upper gastrointestinal tract reflux

TABLE I
PARAMETERS USED TO CALCULATE THE *Total DeMeester Parameter*

Lp.	Required parameter
1	Number of reflux episodes
2	Number of long reflux episodes (longer than 5 minutes)
3	Time of the longest reflux episode
4	Time during pH < 4 in horizontal position [%]
5	Time during pH < 4 in suspine position [%]
6	Total time during which pH < 4

diseases, mainly gastroesophageal reflux disease - GERD and reflux laryngo-pharyngeal - LPR. If left untreated, pathological changes result in deterioration of the patients quality of life, and in the extreme case lead to tumour lesions that are more complicated to treat and can lead to death [2], [5], [11], [12].

III. GERD DIAGNOSTICS

GERD diagnosis is possible with the use of a number of invasive and non-invasive tests. Apart from 24-hour pH-metry and 24-hour pH-metry impedance other methods are used, such as: gastrointestinal endoscopy, radiography with a double contrast or esophageal manometry [2], [12]. Each of these methods has a number of advantages, however, their limitations result in a lower GERD detection efficiency in comparison with pH-metry with impedance measurements. Therefore esophageal pH-impedance measurement is considered to be the best and the most common invasive GERD diagnostic method. Multichannel intraluminal Impedance-pH metry (MII-pH) is now the "gold standard" in reflux disease diagnostics [2], [5], [12], [13], [14], [15], [16], [17], [18], [19].

Esophageal pH-metry can determine the pH of the contents in the esophagus. It is accepted that the exposure of the esophagus to content which pH is less than 4 is harmful. Analysis of pH courses involves determining and defining certain parameters, characteristic to GERD, based on the method described by *DeMeester* [8]. These characteristic parameters are shown in Table I.

After characteristic parameters are calculated, the Total DeMeester Count can be calculated and compared with a reference value of 14.71 [8]. If the value of the Total DeMeester Count is higher than the reference value the patient is diagnosed as sick. Unfortunately, pH-metry alone has some limitations, as it allows track only pH changes in the esophagus, but it does not allow to determine the physical state of content passing from the stomach into the esophagus. This is especially problematic, since non-acid reflux episodes cannot be detected [12]. An extensions of diagnostic capabilities can be provided by studying esophageal impedance. Esophageal impedance measurement was first described in 1991 [12] and has since gained considerable popularity in the diagnosis of diseases of the upper gastrointestinal tract. This method, however, was not the subject of this research work.

IV. WAVELET ANALYSIS

Wavelet transform is currently one of the most used signal processing technique [20]. It allows for the use of other than the sine basis function (Fourier analysis can decompose a signal into components of a sinusoidal). As a result, it is possible to decompose the analysed signal components based other shapes, which often is highly useful in the identification of the signal's characteristics. In addition, the Fourier transform allows to obtain the data only in the frequency domain, while wavelet transform can give information in both time and frequency domains. Wavelet transform of a signal is calculated according to the formula (1)

$$S_\psi(a,b) = \frac{1}{\sqrt{a}} \int_{inf}^{\inf} s(t)\psi(\frac{t-b}{a})dt \qquad (1)$$

where: a: scale parameter, b: ptranslation parameter, $s(t)$: examined signal, ψ: chosen wavelet, $S_\psi(a,b)$: wavelet coefficient and $\psi(\frac{t-b}{a})$: kernel [20].

The coefficient a in the formula (1) is responsible for the scale representation of the selected wavelets. Values between 0 and 1 cause the wavelet to be shortened, and for a value above 1 is extended. The b in the formula (1) is responsible for moving the wavelet in the time domain (for b greater than 0 the wavelet is moved to the right on the timeline). This transformation should be viewed in the context of the five most popular families of wavelets, containing the ranks of their representatives: orthogonal (*Haar, Daubechies, Symlets*, etc.), the biorthogonal (*BiorSplines, ReversBiors*, etc.), function scaling (eg. *Meyer*) without scaling function (*Morlet, Mexican hat, Gaussian*, etc.) and the type Complex (*Shanon, Gaussian Complex, Complex Morlet*, etc.). The most common representatives of each of these families usually include wavelet type *Daubechies, Taking, Meyr, Morlet, Shannon*. The set of wavelet functions used to transform the signal consists of a basic waveform and the features that are scaled and time-shifted copies of the output signal.

A. pH-metry wavelet analysis

The study aimed to develop new mechanisms to accelerate the evaluation of esophageal pH measurements by the gastroenterologist. Currently used methods of pH-metry analysis are based on strictly defined coefficients *DeMeester*. In this paper an attempt to develop an alternative evaluation method is shown, which is based on wavelet digital signal processing.

To determine the effectiveness of diagnostic method the sensitivity parameter is used. Sensitivity is one of the most commonly used parameters to assess diagnostic tests [21]. The sensitivity of the test means the number of detected ill patients compared to the total number of patients in the study group of patients.

The esophageal pH courses were subjected to wavelet analysis. The aim of the decomposition was to find and determine clear criteria to distinguish and classify different pH courses into two groups: healty and sick. Three different approaches were adopted in relation to the types of analysed pH data:

- 21-hour test results (total registration period) divided into 4-hour intervals,
- courses of 20 minutes measured from the end of meals,

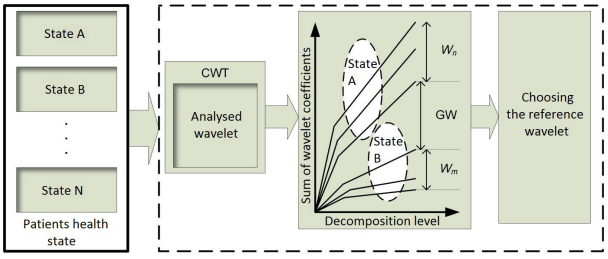

Fig. 1. The idea of wavelet decomposition of pH-metry courses.

- waveforms representing the 6 hour and 25 minute periods of sleep.

Wavelet decomposition was carried out using the five most common representatives of wavelet families *Daubechies, Taking, Meyer, Morlet, Shannon*.

B. Wavelet selection

The method of selecting wavelets for the analysis of non-stationary signals (biomedical signals) was preceded by a comprehensive analysis of the literature [22], [23], [24], [25], [26]. This analysis shows that different states of patients health (registered on pH courses) can be presented in the form of graphs, representing the sum of wavelet coefficients as a function of the level of the signals decomposition. The resulting graph shows the sum of wavelet coefficients in the form of ribbons. It was suspected that different health states will cause those ribbons to be located close to each other in a specific part of the coordinate system. In another approach it was suspected that health states could be distinguished when calculating and comparing the length between value of extreme wavelet sum coefficient, distinguished in the coordinate system. Such parameters were named W_m and W_n. Also a GW coefficient was defined as width of the gap between W_m and W_n regions. This approach is illustrated in Fig. 1, where the defined health states are: A - sick, and B - healthy.

In each case of the carried out analysis a 128 level, continuous decomposition was performed. For each level of decomposition, a series of wavelet coefficients were obtained, which then were summed. As a result a vector of dimension 1 x 128 containing sums of wavelet coefficients was obtained. This approach was used directly in the analysis of 20-minute pH courses after the end of a meal or sleep time. In the case of 21 hours pH courses, the whole course was divided into seven 4-hour episodes and subjected to decomposition separately. Eventually vectors were combined formed in one graph.

In the next step, W_x was defined and named - parameter of extreme differential, calculated using the (2) equation, that is related to maximal differential between extreme wavelet ribbons coefficients values.

$$W_x = L_{max128} - L_{min128} \tag{2}$$

where: L_{max128}: maximal value for the 128 level of decomposition and L_{min128}: minimal maximal value for the 128 level of decomposition.

To determine which of the wavelets from selected wavelet families is the best, an experiment was conducted, using a model pH course of a healthy person. In this experiment a 128 level continuous wavelet decomposition was carried out, followed by an examination - for which of the checked wavelets the difference between the extreme values W_n will be the lowest. The results of the experiment are shown in Table II. The analysis showed that in two cases - for wavelets type *Shannon Haar*, the result of the decomposition virtually precludes their further use in these studies. Very good, as expected, results were obtained for wavelets *db3, Bior* and *Morlet*. However, in the case of wavelet type *Meyer* when plotting the ribbons representing the sum of the wavelet coefficients, it turned out that the value of the designated indicators W_1, W_2 and GW are highly unsatisfactory. This issue is caused by an overlap in some of the waveforms representing health states: A and B (which in practice means the inability to distinguish them). To sum up, taking into account the previously made assumptions about the selection process, it has been shown that the most effective wavelet to decompose pH waveforms is *Morlet* wavelet type.

V. 21-HOUR PH-METRY COURSE ANALYSIS

Conducting research in the relevant field, wavelet decomposition of each registered 21-hour pH course was performed. For this purpose, each 24-hour pH course was divided into seven 4-hour intervals, and then - after the process of their decomposition - the wavelet coefficients were summed and plotted on a single graph, representing a patient exam results.

Patients results were divided into two groups: a test and a validation group. The test group consisted of patients whose Total DeMeester Count was below 50, and therefore diagnosed as healthy and/or mildly sick. The validation group included patients whose Total DeMeester Count was above 50.

In the first place the W_x coefficient was calculated for patients of the test group. The calculated values, as well as the *DeMeester* coefficients are shown in the Table III.

As a result, it was observed that in the case of healthy individuals the extreme differential coefficient W_x is equal to 336 (first case) and 557 (in second) units. The above observation can be justified by analyzing the pH courses of healthy patients, in whose case - because of the a small or marginal amount of reflux episodes - there is no frequent changes of pH during 24 hours. Therefore, the amount of wavelet components in the pH courses remain relatively low, which in turn leads to low sum of wavelet coefficients values.

For sick patients the extreme differential coefficient W_x vary from 789 to 2.327 units. High W_x values are associated with a large dynamics in pH signal changes, resulting from various kinds of components, causing significant variations in pH over a short of period of time. High values of W_x however are not directly proportional to the *DeMeester* count, which can be seen by comparing patients with D and G. The *DeMeester* count for the G patient is lower than that of patient D, while the value of the extreme differential takes a value equal to 2371, which is 250% higher than for the patient D. High *DeMeester*

TABLE II
VALUES OF MAXIMUM WIDTH OF WAVELET COEFFICIENTS W_n

Wavelet decomposition level	32			64			96			128		
Wavelet type	W1	GW	W2	W1	GW	W2	W1	GW	W2	W1	GW	W2
db3	90	191	45	392	400	118	1416	815	337	1416	815	337
bior4.4	74	163	40	325	341	100	787	434	177	1359	523	278
Meyr	-47	-29	-91	-213	-11	-31	-452	32	-68	-629	-27	-91
Morlet	46	93	27	169	235	61	379	343	102	832	283	155
Shannon	solutions ambiguous											
Haar	solutions ambiguous											

TABLE III
VALUES OF W_x PARAMETER FOR PATIENTS FROM THE TEST GROUP: WHOLE 21 HOUR PH COURSES

Patients ID	W_x parameter	Pateints diagnosis	*DeMeester* count
C	789	sick	68,0
D	924	sick	94,0
E	1417	sick	107,8
F	1477	sick	102,0
G	2327	sick	80,4
A	336	healthy	1,0
B	557	healthy	11,7

TABLE IV
VALUES OF W_x PARAMETER FOR PATIENTS FROM THE VALIDATION GROUP: WHOLE 21 HOUR PH COURSES

Patients ID	W_x parameter	Pateints diagnosis	*DeMeester* count
H	382	sick	42,0
I	973	sick	19,5
J	987	sick	43,1
K	624	sick	18,7
L	1608	sick	41,8
M	1434	sick	15,9
N	601	sick	19,4
O	1198	sick	29,5
P	647	sick	21,5

count is due to the presence of components dependent not only on pH value but also on time. Hence, in some patients high *DeMeester* count results from the presence of only one dominant pathological symptom, which determines the high value, while in other patients all or most of the symptoms are present, but manifest less frequently.

In the next stage of research, the extreme differential coefficient W_x was compared between a wider group of patients - the validation group, in order to verify the results of the analysis performed on the test group. The test results are shown in Table IV.

As can be seen in Table IV except the case of patient H, the value of W_x for all patients is above 600. Therefore, on the basis of both the above observations and the results from the test group patients, to distinguish the sick from the healthy patients, the value of W_x coefficient was set to 600 units. This allowed to achieve a 77% sensitivity. It should also be noted that the value of extreme differential of more than 1000 units always points to the case of a sick person.

TABLE V
DATA CONCERNING INDIVIDUAL PATIENTS FROM THE TEST GROUP: PH COURSES DURING SLEEP

Patients ID	Pateints diagnosis	*DeMeester* count
1	12,4	healthy
2	11,3	healthy
3	68,0	sick
4	42,0	sick
5	94,0	sick
6	19,5	sick
7	18,7	sick
8	41,8	sick
9	15,9	sick
10	19,4	sick
11	19,6	sick
12	29,5	sick
13	107,8	sick
14	102,0	sick

A. Wavelet analysis of pH-metry courses during sleep

The next stage of the research was wavelet decomposition referred to the pH courses registered during patients sleep. The purpose of this approach was to check if the plotted sum of wavelet coefficients (as a function of the decomposition level) concerning healthy and sick patients differ from each other in such a way that they can be helpful from a diagnostic point of view. As previously, a continuous 128 lv wavelet decomposition was performed after which the sum of wavelet coefficients was plotted. In contrast to earlier studies - relating to the entire pH course - this analysis was carried out for the entire time during the patients sleep, without dividing it into pieces. Therefore, in this case the W_x coefficient was not calculated, and only a single ribbon curve was plotted for each patient. As previously the patient were divided into two groups: test and validation groups. The results for the test group is shown in Table V.

Analysis of these results, shown in Fig. 2 (for the patients listed in Table V) indicates that distinguishing a clear criterion for patient assessment using wavelet analysis based on pH courses of sleep is not possible. Charts of healthy and sick patients in many cases overlap, and therefore there is no direct way to observe a border of a clear division of the plane between the healthy and the sick. Regarding these observations and the medical *DeMeestera* criteria it can be stated, that a comparison of healthy and sick patients (relating to the sleep phase), is pointless in relation to cases in which the *DeMeester* coefficient does not exceed 25.

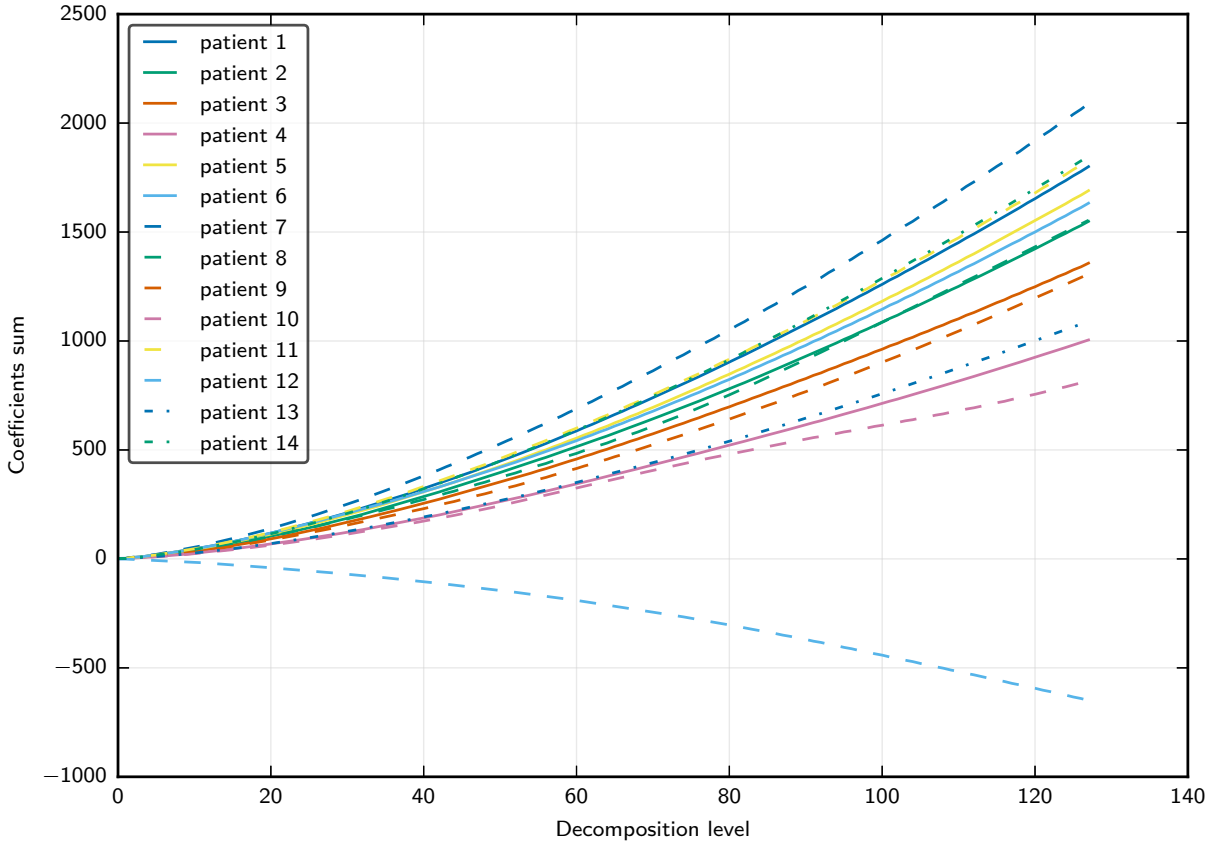

Fig. 2. Results of wavelet analysis of pH-courses during sleep

TABLE VI
VALUES OF W_x PARAMETER FOR PATIENTS FROM THE TEST GROUP: PH COURSES AFTER MEALS

Patients ID	W_x parameter	Pateints diagnosis	*DeMeester* count
A	821	sick	68,0
B	713	sick	94,5
C	1246	sick	107,8
D	887	sick	102,0
E	1303	sick	80,4
F	230	healthy	11,7
G	196	healthy	1,0

B. Wavelet analysis of pH-metry courses after meals

The basis for this approach were 20 minute fragments of pH recordings, that represented the changes in the pH after the patient stopped eating a meal. An example analysis is shown in Fig. 3. During that 20 minutes, the patients couldn't eat another meal. As previously the patients were divided into 2 groups: test and validation groups.

When analysing the results presented in Table VI it can be concluded that in the case of healthy patients extreme differential coefficient W_x achieves the lowest value in the group, whereas in the group of sick patients, the value of the coefficient is greater than 500 units. The conducted experiments did not confirm that the ribbons of wavelet coefficients sums are grouped in certain areas of the coordinate system separately for healthy and sick patients. Therefore the only clear difference between the ribbons describing healthy and sick patients is the W_x coefficient. On this basis - in order to verify the observed phenomenon, that in healthy patients the extreme differential is lower that sick patients - a threshold has been set, to discriminate those two groups of medical conditions. The threshold was set to 250 units. To verify the primary results, the threshold was applied to results obtained from the validation group. The results of these studies, together with *DeMeester* coefficients are shown in Table VII.

The results shown in Table VII lead to state that adopting a threshold of 250 units for W_x coefficient, to distinguish healthy from sick patients, is not fully satisfactory. This is due to the fact that for one of the healthy patient W_x is equal 405, although in can be noted that for this patient the *DeMeester* coefficient is 12.4, so very close to the borderline od 14.7. Moreover it can be seen that the lowest W_x was calculated for a patient whose *DeMeester* coefficient was equal 17. Therefore in the relevant group of 6 sick patients (whose *DeMeester* coefficients were higher than 20) only in 3 cases the W_x coefficient is above 400. For all sick patients, whose *DeMeester* coefficient were higher than 30 the W_x coefficient was significantly higher than 400. On this basis it can be stated that, as with the analysis of 21-hour pH courses, the

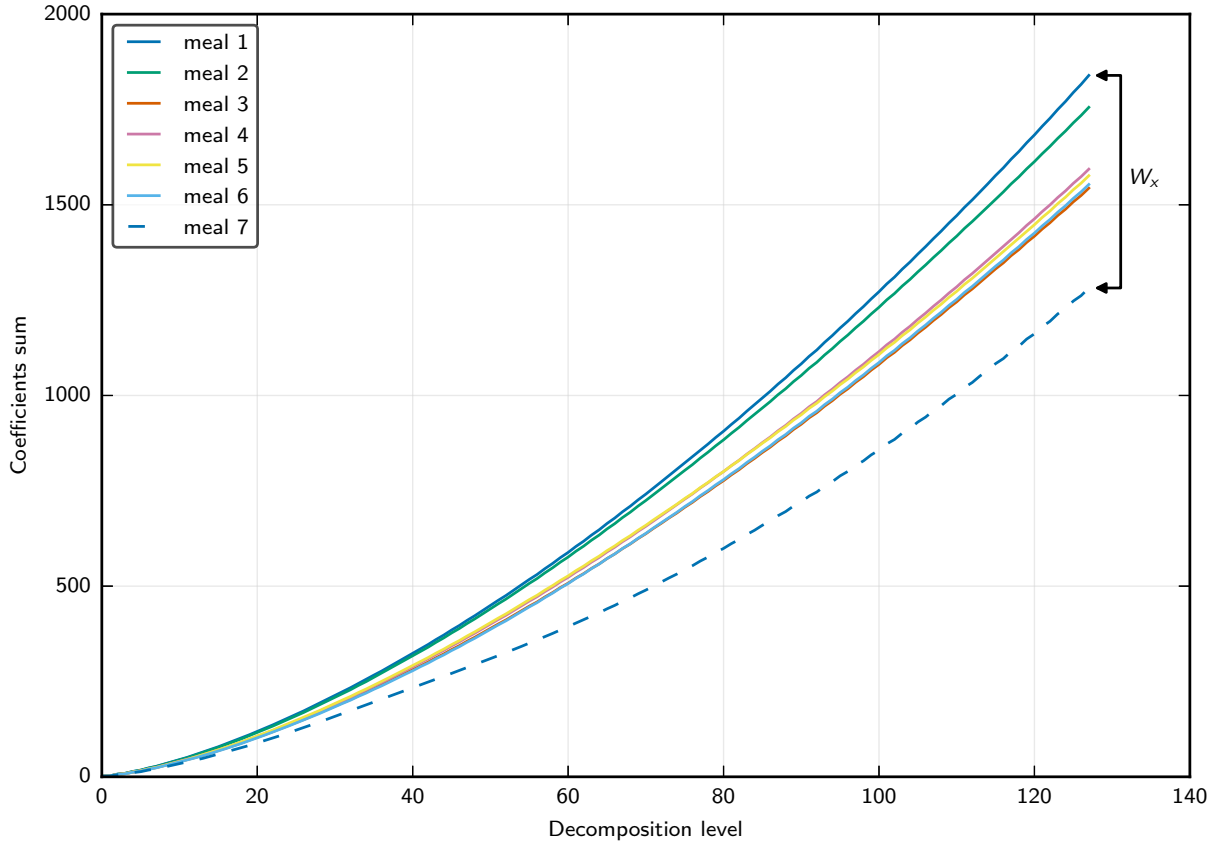

Fig. 3. An example wavelet analysis of 20 minute pH-metry courses taken after meals

TABLE VII
VALUES OF W_x PARAMETER FOR PATIENTS FROM THE VALIDATION GROUP: PH COURSES AFTER MEALS

Patients ID	W_x parameter	Pateints diagnosis	*DeMeester* count
H	405	healthy	12,4
I	821	sick	68,0
J	592	sick	42,0
K	713	sick	94,0
L	486	sick	19,5
M	266	sick	18,7
N	757	sick	41,8
O	543	sick	15,9
P	730	sick	19,4
R	385	sick	19,6
S	1988	sick	29,5
T	603	sick	107,8
U	887	sick	102,0
Q	206	sick	17,0

values of wavelet coefficients depend directly on the nature of changes in the pH course. Thus, both courses that in a short amount of time change their values quickly and courses with a small amount of fluctuation, but constant low pH value may eventually affect the resulting high value of the calculated *DeMeester* coefficient. The sensitivity in this case was 71%.

VI. CONCLUSION

Summing up the results of the research, it can be stated that: A) the method of wavelet analysis of esophageal pH courses registered during the patients sleep can not be used as a tool supporting the diagnosis of reflux diseases, B) both the method of 21-hour pH courses wavelet analysis and the 20-minute pH courses registered after meals wavelet analysis do not give fully satisfactory results, and therefore can not be used as the only method of diagnosing reflux diseases, but they can be used as an additional source of information, support the decision.

The proposed methods can be used as a preliminary assessment procedure when analysing esophageal pH courses, which would be subject to verification by a medical specialist in the course of further analysis. A particular advantage of the presented methods is that its implementation on a computer is quick, and the extreme differential W_x calculation process takes a small amount of time. This in turn leads to a fast diagnosis suggestion that is computed and available for the gastroenterologist. Significant advantages and disadvantages developed methods are shown in Table. VIII.

The conducted experiments showed that wavelet analysis can be successfully applied to evaluate esophageal pH courses in the means for supporting diagnosis of reflux diseases of the gastrointestinal tract. Further research on the methods pro-

TABLE VIII
ADVANTAGES AND DISADVANTAGES OF USING WAVELET DECOMPOSITION TO ANALYSE ESOPHAGEAL PH COURSES

W_x advantage	W_x disadvantage
use only pH courses	sensitivity level around 71% to 77%
easy to implement as a computer program	no possibility to asses the level of the reflux disease advancement
possibility to apply regardless of the pH recording equipment manufacturer	no possibility to check the number or the time of reflux episodes
possibility to fully automate the process of initial diagnostics/classification	possibility to use only as a additional, aiding tool in the diagnostics process

posed should focus primarily on determining accurate extreme differential coefficients W_x to distinguish between the results of healthy and sick patients. Moreover effort should be put on researching the dependence of the thresholds on other, not mentioned here, factors, eg. age, ancestry or general health of patients, to improve the sensitivity of the test. Research showed that improving the sensitivity of the method could be obtained by: increasing the number of patients (collected data), researching other wavelets, researching the corelation between GERD symptoms and pH data for each patient and optimizing the threshold for other specific factors in order to better adjust the threshold value to each patient (like age, sex, general health, etc). Since using wavelet decomposition is a new approach to the topic of GERD diagnostics it is difficult to state which path will lead to better results without commencing more research. Hence, with this state of knowledge, it is difficult to predict the best or optimal course of action. Therefore future work in this topic will present the latest findings in all or in the most promising of the proposed paths.

Further studies should be performed in order to apply classification algorithms to the found wavelet parameters. This can improve the sensitivity of the results as well as allow to find correlations between GERD symptoms and the pH-courses. Such algorithms were successfully applied in other similar research like [27], [28]. Such course can lead in the near future to develop a full medical computers system to aid the diagnostic process of GERD detection, that can be wildly used in the healthcare system. Such system would improve the quality of diagnosis, lower the cost of the diagnostic process and could be wildly used by medical staff. Such systems are being developed in a vast field of medical and healthcare areas: [29], [30].

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