Chapter 4

Functional Lung Examination in Diagnostics of Asthma and Its Phenotypes

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Additional information is available at the end of the chapter

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Abstract

In this chapter, we review the diagnostic approach to asthma phenotypes in children using lung function testing. Various methods are reviewed and their advantages and disadvantages are discussed. Medical history and physical examination including lung auscultation is the first line examination, which may raise the suspicion on asthma. Besides the simple lung auscultation, more advanced approaches (computer analysis of breath sounds) are described. Spirometry and other classical lung function testing methods (body plethysmography, dilution techniques) are discussed with respect to their contribution to asthma diagnostics and phenotype classification. Afterward, impulse oscillometry and methods intended for patients with insufficient cooperation follows. We highlight their potential in diagnostics of early asthma stages. Measurement of exhaled nitric oxide is discussed and its potential for allergic asthma (eosinophilic inflammation) detection is assessed. In conclusion, various lung function testing methods may contribute to both setting the diagnosis of asthma itself and classification of asthma phenotypes. Their smart combination allows for more precise diagnostics and treatment of young patient with bronchial asthma.

Keywords: asthma in children, wheezing, diagnostics, phenotype, endotype classification, lung function testing, spirometry, impulse oscillometry, FeNO, lung auscultation, harmonic analysis, Fourier transform

1. Asthma phenotypes and endotypes in children

Asthma is a heterogeneous disease, usually characterized by chronic airway inflammation. It is defined by the history of respiratory symptoms such as wheeze, shortness of breath, chest tightness, and cough that vary over time and in intensity, together with variable expiratory airflow limitation [1]. Currently, asthma is considered to be a syndrome rather than one disease with common etiopathogenesis. There have been various attempts to subclassify asthma into more homogeneous groups with similar pathophysiology and clinical presentation. Such subclassification will help to improve the therapeutic approach to our patients and will offer a possibility of individualized therapy, which will increase the safety and efficacy of asthma treatment. Moreover, research in more homogeneous groups of patient will offer better insight into the pathogenesis of bronchial asthma with.

Recently, the terms asthma phenotype and endotype have been introduced. “Phenotype” is defined as a recognizable cluster of demographic, etiologic, and clinical characteristics. These are generally regarded to arise from interactions between the genotype and environmental influences. It may be described by clinical characteristics including physical, biochemical, and other variables that can be objectively measured. There is no reference to an underlying pathophysiological process. The term “endotype” is used to describe a disease subtype based on distinct pathological mechanisms [2].

A number of phenotypes and endotypes in children have been proposed, unfortunately up to now, there is no clear consensus in this field. Martinez et al. categorized wheezing during the first 6 years of childhood into three distinct groups—transient early, persistent, and late-onset wheeze. This classification is based on the presence or absence of wheezing before the age of 3 years and its persistence or incidence to age 6 years. The limitation of this approach comes from the fact that it can be set only retrospectively and thus it is of little clinical impact. Later, another classification of early wheeze has been suggested by a European Respiratory Society task force—a dichotomy based on trigger factors: episodic viral wheeze and multiple-trigger wheeze [3]. Besides the time- and symptom-based approaches, there exist many other phenotypes, which have been adopted from adults: allergic asthma, nonallergic asthma, asthma with fixed airflow limitation, asthma with obesity, and so on. They have some importance in older children (adolescents).

Although phenotype- and endotype-based approaches to asthma are of an extreme importance for research purposes and for understanding asthma itself, to date, no strong relationship has been found between specific pathological features and particular clinical patterns or treatment responses. More research is needed to understand the clinical utility of phenotypic classification in asthma.

2. Functional lung examination in asthma diagnostics

Setting a diagnosis of asthma is difficult and requires a complex approach. There exists no single test capable of setting the diagnosis without other concomitant examinations. Particular difficulties occur when conducting a confident diagnosis in children younger than 5 years. Symptoms of cough and wheeze are very common in this age and the assessment of airflow limitation is also age-restricted, all leading to difficulties with setting up the diagnosis. A probability-based approach, based on the pattern of symptoms during and between viral respiratory infections, may be helpful [1]. It allows to individually decide about the trial of controller treatment (usually inhaled corticosteroids—ICS), which may further underpin the diagnosis.

Besides the evaluation of clinical symptoms (wheeze, cough, breathlessness, activity, and social behaviour), adjunct tests may be employed as well [1]. Because of the scope of our chapter, we focus on lung function testing and exhaled nitric oxide levels.

The evaluation of airflow limitation and its reversibility is a key question in asthma-diagnostic approach. However, it must be noted that the presence of airflow limitation (even reversible after beta-agonists) does not confirm the diagnosis. Other aspects need to be taken into account when making conclusions. All the limitations of the functional examination may be deduced from this fact. A similar situation occurs in phenotype classification. In case of time-based classification of wheezing phenotypes, the early functional lung examination may assist to objectify the presence of airflow limitation and its development in time. In case of symptom-based classification, the functional examination is of smaller importance; however, it may assist in clinically uncertain situations. Endotype classification is usually based on invasive tests (e.g. endobronchial biopsies, bronchoalveolar lavage cytology, etc.). However, some tests such as exhaled nitric oxide measurement may indicate the allergic (eosinophilic) asthma endotype. To sum up, functional examination informs about the presence of airflow limitation and its reversibility, but with the exception of fractional exhaled nitric oxide (FeNO), it will only assist in phenotype classification.

3. Evaluation of bronchial obstruction by different lung function-testing methods

In this subchapter, various methods for detection of bronchial obstruction will be reviewed. We focus on tests that are routinely used in clinical settings. In addition, we discuss less available methods, which have the potential to enrich the spectrum of diagnostic tools in future. However, their clinical impact needs to be further studied.

The choice of diagnostic tool is influenced by several factors:

- sensitivity of the method with regard to bronchial obstruction, respectively asthma itself,
- specificity of the method with regard to bronchial obstruction, respectively asthma itself,
- invasiveness of the method and patient burden (e.g., need of sedation/anesthesia, radiation, etc.),
- age of the patient—depending on the ability of the child to follow up the instructions and coordinate breathing, some methods (e.g., spirometry) are available only in older children,
- availability of the method,
- time and financial demands.

When indicating an optimal diagnostic test, one should bear in mind its different characteristics and potential limitations in asthma diagnostics and phenotype classification. In a clinical setting, a combination of several methods is employed to reach a confident diagnosis.

3.1. Lung auscultation

Because of its simplicity, noninvasiveness, and wide applicability, lung auscultation is the first-line method in lung examination. This method is a part of the physical examination and is usually accompanied by aspection, palpation, and percussion. The subject of the examination is the sound effect of the air flow passing from and to the alveoli. A sit does not require special patient cooperation. This method can be applied to the whole-age spectrum of the patients. On the other hand, it has also several disadvantages. Taking the principle of the method into account, it is not possible to completely eliminate the contamination of the tracked sound signal by artifacts from the internal and external surroundings of the patient. Those signal artifacts may be of such intensity that important information gets lost. Moreover, the sensitivity of lung auscultation in the detection of bronchial obstruction is relatively low. The bronchial obstruction is not reliably recognizable if the airway lumen is reduced less than by 30–50% as compared to the healthy state. These problems can be solved in part by appropriate frequency tuning of the phonendoscope, or by processing the captured record by one of the advanced audio signal-processing methods—see subsequent subchapter. The first-mentioned adjustment is applicable in general but has only a limited effect with respect to the range of commonly observed frequencies. The second adjustment is bound to the possibility of making any record of the listening examination. Several phonendoscopes, which enable to make audio recordings, are currently available on the market. These recordings can then be played back and processed using specific software on a common PC.

Another disadvantage of lung auscultation is the considerable level of subjectivity in its evaluation. The Working Group of the European Respiratory Society and the American Thoracic Society (ERS/ATS task force) drew up a paper on the standardization of the lung sound nomenclature [4]. A library of reference auscultation findings has been created, including their interpretation [5]. Typical findings for bronchial obstruction include “wheezing” and non-constantly “prolonged expiration” (i.e., expiration phase more than two times longer than inspiration). The finding of these sound phenomena indicates the presence of bronchial obstruction with a high probability and is an indication for the beta-mimetic therapeutic test (salbutamol/albuterol). Positivity of this therapeutic test further supports the diagnosis of bronchial obstruction and indicates its reversibility. In order to obtain valid results of this test, several rules need to be followed—the application of sufficient dose of beta-mimetic (400 mg of salbutamol in the form of a “metered dose inhaler”), the correct way of application—via a “spacer” (“aerochamber”), and last but not the least, sufficient interval between the applications of beta-mimetics and the lung auscultation (15–20 min).

To conclude, lung auscultation and the detection of obstructive phenomena (wheezing, prolonged expiration) together with positive beta-mimetic test are the basic and most available diagnostic tools for bronchial obstruction.

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3.2. Spirometry

Spirometry is a test that measures how an individual inhales or exhales volumes of air as a function of time. The primary signal measured in spirometry may be volume or flow. Spirometry is highly valuable as a screening test of general respiratory health. However, on its own, spirometry does not lead clinicians directly to an etiological diagnosis. Spirometry requires cooperation between the subject and the examiner, and the results obtained will depend on technical as well as personal factors. In children, the spirometry is recommended to be performed from the age of 3–5 years depending on the child's psychomotor development (ability to follow instructions and coordinate breathing) and experiences and skills of the examiner. Naturally, the success rate of spirometry in the preschoolers is much lower than in older children.

During spirometry, several maneuvers may be performed, which will answer various clinical questions:

- forced vital capacity (FVC) and forced expiratory volume in 1-s (FEV1);maneuver—derivation of maximum effort flow-volume curve;
- slow vital capacity (sVC) and inspiratory capacity (IC) maneuver;
- peak expiratory flow (PEF);
- maximum voluntary ventilation (MVV).

Details of the previously mentioned examinations may be found in ERS/ATS document [6]. Technical demands for the devices, guidelines for quality control and reporting may be found also in previously mentioned ATS/ERS document.

3.2.1. Diagnostic use of results

In principle, there are two main types of lung diseases, the so-called obstructive and restrictive ones. Both types lead to changes in ventilation and are reflected by specific spirometric parameters.

Figure 1 shows the usual shape of the expiratory limb of the maximum effort flow-volume curve (MEFV) as well as the physiologic time-volume tracing found in healthy individuals.

In case of a restrictive disorder, the velocity of expiration is usually normal, but there is a reduction in pulmonary volumes (**Figure 2**). Both the FVC and FEV1 parameters are reduced, and their reduction is proportional leading to normal FEV1/FVC index (the so-called Tiffeneau index is within the norm for the patient's age).

Contrarily, the obstructive disorder (**Figure 3**) is characterized by a decreased expiratory velocity, and lung volumes are usually preserved. In case of severe or complicated obstruction, air trapping and hyperinflation may occur, both leading to a secondary decrease in FVC. The typical finding of obstructive ventilation disorder is therefore a reduced FEV1, FVC is normal or decreased disproportionately to FEV1, resulting in a reduction of the Tiffeneau index mentioned earlier.

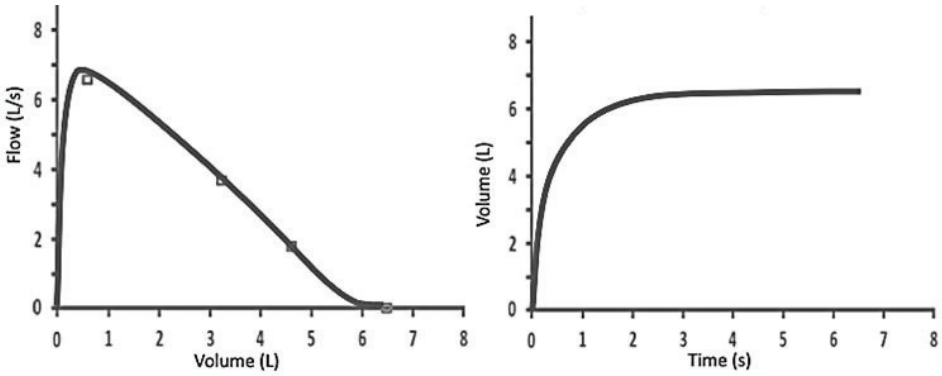

Figure 1. Typical shapes and values of breathing curves (taken from [7]).

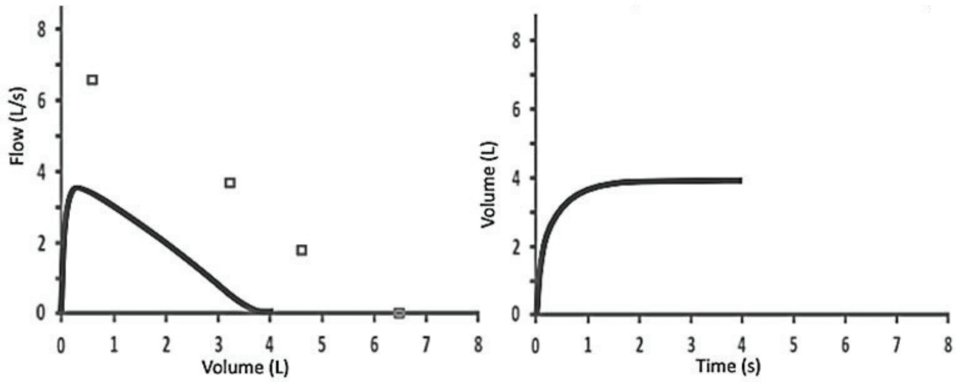

Figure 2. The effect of restriction disorder (taken from [7]).

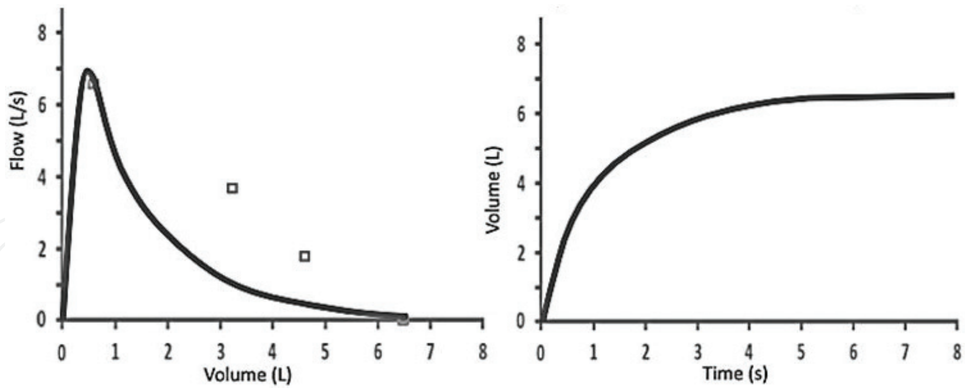

Figure 3. The effect of obstructive disorder (taken from [7]).

When interpreting the spirometry results, one should bear in mind that the complete assessment of pulmonary volumes is possible only using body plethysmography (or dilution techniques). After that, obstructive and restrictive ventilation disorders can be reliably distinguished. The optimal lung function interpretation strategy proposed by ATS/ERS task force is shown in **Figure 4**.

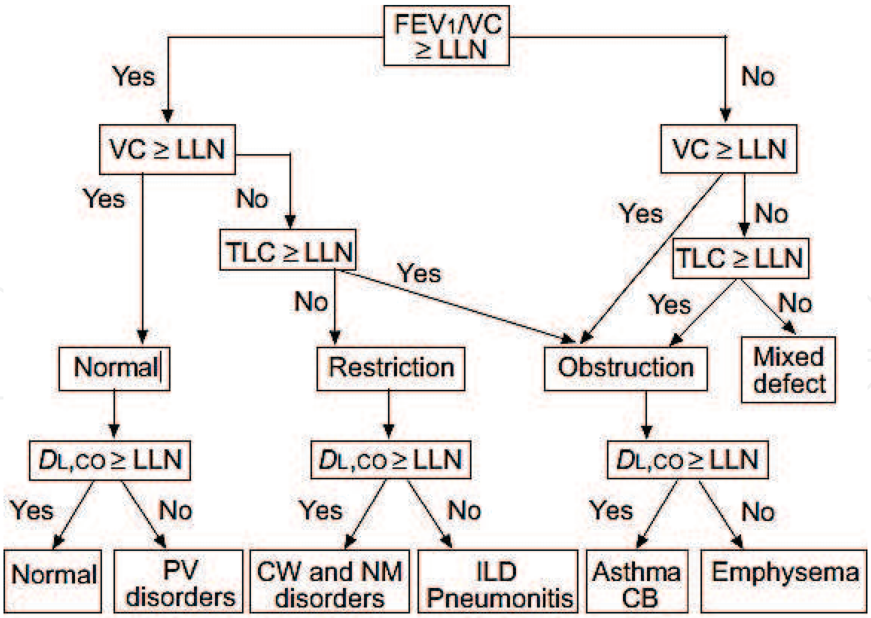

Figure 4. Algorithm for diagnostic evaluation of spirometry (taken from [8]). VC, vital capacity; LLN, lower limits of normal; FEV1, expiratory volume in 1 s; TLC, total lung capacity; $D_{L,CO}$, diffusing capacity for carbon monoxide; CW, chest wall; NM, neuromuscular; ILD, interstitial lung diseases; CB, chronic bronchitis.

As mentioned earlier, the information obtained from the simple spirometry is sufficient to raise only suspicion on the disease. The final diagnosis always needs to be confirmed by other methods (see subsequent subchapters) or by spirometry performed under specific conditions—the so-called bronchomotoric tests. They include bronchodilating test—that is, evaluation of airway obstruction after bronchodilator administration—usually beta-2-mimetics. If bronchial hyperresponsiveness needs to be evaluated, bronchoconstrictive test with direct or indirect stimuli capable of induction of bronchospasm may be used. The most commonly used bronchoprovocative stimuli include methacholine, histamine, mannitol, dry and cold cough, or physical activity.

3.3. Whole-body plethysmography

According to the definition, the whole-body plethysmography is a diagnostic method based on the measurement of volume changes of the patient's body during respiration. Applied to pulmonary function testing, it allows to determine the total pulmonary capacity (TLC) and all its components including indirectly measurable volumes. Similar to the spirometry, the results are significantly affected by conditions of measurement and their history before it. That is why it is generally not allowed to smoke, to eat heavy foods, to drink alcohol, to have an excessive physical activity, and so on, before this examination. The examination takes place in an airtight box. The patient stands or sits inside and breathes through the mouthpiece and the nose is closed by a pin. The examination proceeds in two phases (specific airway resistance measurement—performed with opened shutter and FRC measurement—inspiration and expiration against the closed shutter). A schematic derivation of the respective parameters is shown in **Figure 5**.

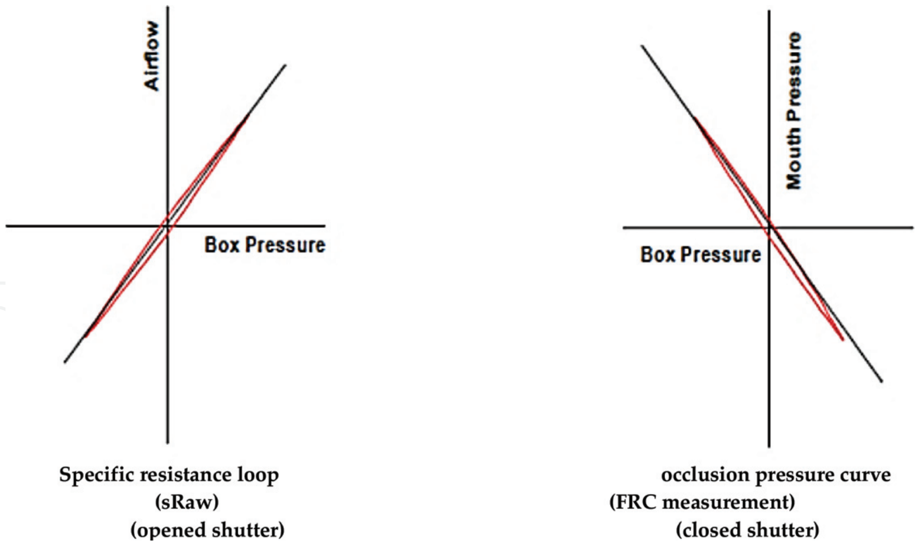

Figure 5. Output curves of plethysmography (taken from [9]).

3.3.1. Diagnostic use of results

As mentioned earlier, body plethysmography allows the evaluation of indirectly measurable pulmonary volumes and capacities—that is, residual volume (RV), functional residual capacity (FRC), and total lung capacity (TLC). They allow conducting a definitive diagnosis of restrictive lung disorder. In addition, it is possible to assess respiratory tract resistance (Raw) —important for airway obstruction assessment.

The quantification of the given parameter is performed using the inclination of the given curve/loop. The shape of specific resistance loop is also of a significant diagnostic value—it can indicate the localization of the obstruction within air passages (**Figure 6**).

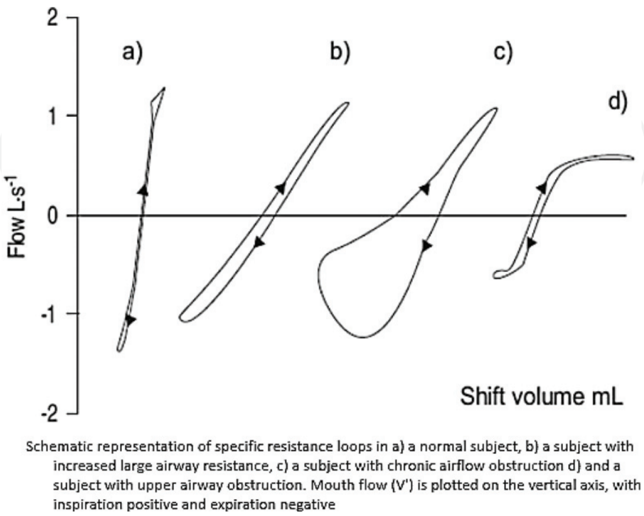

Figure 6. Typical shapes of specific resistance loops (taken from [9]). Note: the pressure in the box on the horizontal axis is replaced by the corresponding volume change of the air in the box.

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Figure 7 shows a typical finding in a healthy individual, a patient with obstructive and restrictive disorder, respectively.

3.4. Dilution techniques

Dilution techniques represent complementary method to the abovementioned functional examinations. Similar to the body plethysmography, they enable to evaluate indirectly measured volumes and pulmonary capacities (RV, FRC, and TLC). In principle, two modifications of this method are available—the closed variant using Fick's principle and the opened method (e.g., multiple-breath inert gas washout test). In the diagnostics of bronchial obstruction and asthma, these methods give only complementary information.

3.5. Impulse oscillometry

Impulse oscillometry (IOS) is one of the modifications of forced oscillation techniques (FOTs). It is a noninvasive diagnostic method which is performed during tidal breathing and is based on the superimposition of external pressure signals on the patient's tidal breathing. In a simplified way, we can say that the whole respiratory tract including air in the airway is forced by external pulses of different course in time to oscillate. The behaviour of the respiratory tract is then described by several variables (resistance, reactance, inertance, and elastance) which allow assessing mechanical properties of the respiratory tract and its components (airways, lung parenchyma, and chest wall). To get reliable results, it is necessary only to ensure a regular breath pattern (no specific breathing maneuvers are required). The examination can thus be performed in all age categories of patients.

The following parameters are evaluated when interpreting IOS results:

- respiratory tract resistance (R_{rs}) and its frequency dependence,
- respiratory tract reactivity (X_{rs}) and its frequency dependence,
- auxiliary parameters (resonant frequency—F_{res}, volume dependence of Z_{rs} impedance, and others).

The outcome of the examination gives information about the resistance of the central and peripheral airways. Further, it also gives an overview of the mechanical properties of the respiratory tract. It should be noted that basic IOS examination (i.e., without specific breathing maneuvers) does not provide any information on lung volumes.

In conclusion, IOS is a suitable method for the diagnostics of bronchial obstruction in noncooperative and poorly cooperative patients.

3.6. Fractional exhaled nitric oxide (FeNO)

Measuring the fraction of nitric oxide in exhaled breath is relatively new and promising tool assisting conventional lung function testing in asthma diagnostics and phenol/endotype classification. Nitric oxide is an important mediator with plenty of different functions; when

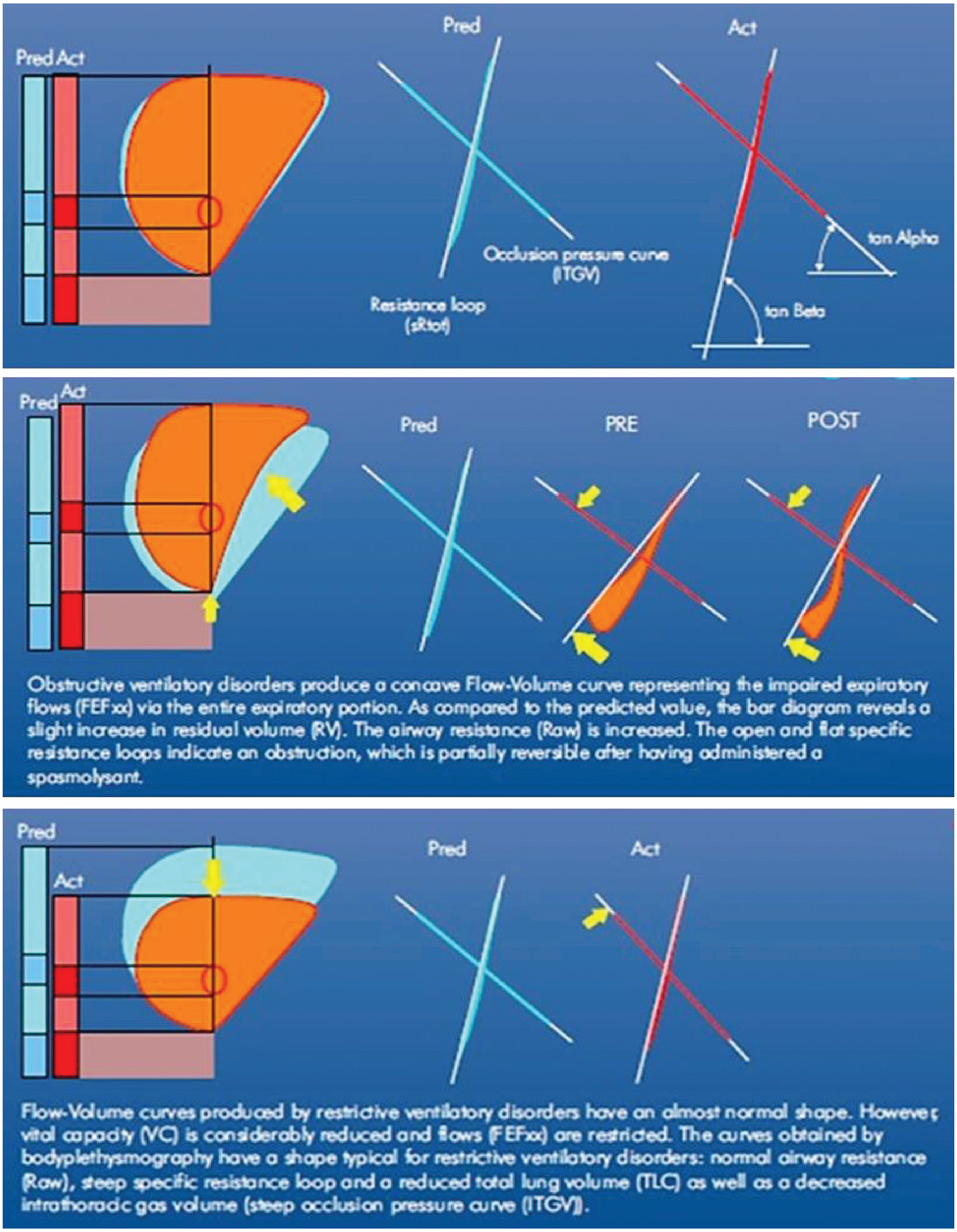

Figure 7. Typical shapes of spirometric and plethysmographic curves (taken from [9]). Note: “Pred” means predicted and “Act” means actual value or shape of the followed-up parameter.

assessed in exhaled air, it reflects the allergic airway disease, more precisely the activity of eosinophilic inflammation. While symptoms and lung function assess the pathogenetical mechanisms of allergic asthma indirectly, FeNO measurement reflects directly the activity of this inflammation. It is strongly and positively correlated with eosinophils in airway wall, bronchoalveolar lavage fluid, and induced sputum. As a noninvasive tool, it may greatly contribute to the diagnostics of allergic/eosinophilic phenotype of asthma [10].

Currently, there exist various modifications of FeNO-measuring systems including online and offline variants. Principally, there exist single- and multiple-breath approaches, both having its advantages and disadvantages. Technical aspects of these methods have been reviewed elsewhere [11]. FeNO measurements may be successfully performed in young children as well [12]. Modifications for infants are also available.

There is sufficient evidence about the usefulness of FeNO in clinical setting—especially in patients with asthma. FeNO measurements are highly correlated with eosinophilic airway inflammation, and as this type of inflammation positively responds to steroid treatment, it can guide the therapy. High levels of FeNO predict steroid responsiveness. Moreover, it can predict the relapse of asthma symptoms after steroid treatment withdrawal [13].

To conclude, we highlight the role of FeNO measurement in both asthma diagnostics and phenol/endotype classification. It may be regarded as an "inflamometer," as though this tool should be available to the pulmonologist managing asthma patients.

3.7. Lung function testing in infants, toddlers, and preschoolers

According to GINA 2017 [1], lung function testing (spirometry) is recommended for patients older than 4–5 years when setting the diagnosis of asthma and for long-time follow-up. As children younger than 3–4 years are usually not capable of performing acceptable trials of maximum effort flow-volume curve, alternative methods are used to objectify their lung function. These methods (infant pulmonary function testing—IPF) are not widely available, and their clinical impact remains unclear [14, 15]. However, based on the authors' experiences, IPF may be of a clinical benefit in the management of infants with recurrent wheeze.

Currently, there exist a number of commercially available methods assessing different aspects of lung function (**Table 1**). These methods require tidal breathing and face-mask tolerance; consequently, they are performed under light sedation (chloral hydrate). Generally, they are considered to be safe and well tolerated. Principally, it is also possible to perform bronchomotoric test in infants using various methods of IPF. Their limitations include the need of prolonged sedation (at least 30 min of quite sleep) to conclude the subsequent testing, various technical problems (no commercially available equipment for such testing), and the need of knowledge of the short-term variability of the respective parameters. In author's lung function laboratory, bronchodilator test with salbutamol is routinely performed with valuable clinical implications. To our knowledge, there is no laboratory performing bronchoconstrictive tests in infants on regular basis.

Method	Outcome	Parameter
1. Bodypletysmography	Lung volume	Functional residual capacity (FRC)
	Central airway obstruction	Airway resistance (Reff)
2. TidalBreathAnalysis	Ventilation	Minute ventilation
	Peripheral airway obstruction	Shape of the FV curve, tPTEF/tE
3. Resistance-Compliance	Mechanic properties of respiratory tract	Compliance (Crs)
		Resistance (Rrs)
4. Thoracoabdominal compression	Peripheral airway obstruction	Maximal flow at the FRC level
	Ventilatory reserve, airway collapse	Shape of the FV curve
5. Raised volume thoracoabdominal compression	Additionally to 4.: Lung volumes	Total lung capacity (TLC), vital capacity (VC)
6. Multiple breath washout test	Lung volume	Functional residual capacity (FRC)
	Ventilation inhomogeneity (most peripheral airway obstruction)	Lung clearance index (LCI)

Table 1. Summary of lung function methods intended for patients with limited cooperation and their outcome parameters.

The contribution of IPF in asthma diagnostics includes the detection of airway obstruction, its localization (peripheral or central airways), its quantification (mild, moderate, and severe) and reversibility (reaction on salbutamol). In addition, consequences of bronchial obstruction such as hyperinflation, ventilation inhomogeneity, and changes in breathing pattern may be detected as well.

4. Utilization of advanced methods for processing of audio signals

Together with the development of possibilities and availability of computer technology, the possibilities of using exact computational methods of signal processing grow both in basic research and in the field of practical problems. From a number of methods available, we prefer the harmonic analysis. The outcomes of all available methods are similar likely due to the demand for easy interpretation of results to physicians or patients. We describe the given approach on the basis of the Fourier transform analysis, where we have achieved the most convincing results so far.

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4.1. Background

The validity and reliability of outputs of the advanced sound analysis significantly increases with the quality of the input data. It is also advantageous to know what frequencies are important to look for and what their presence means from both diagnostic and technical point of view.

The most specific issue is created by pediatric patients, where the quality of respiratory sound can also be affected by the size of the patient body. Children have a distinct quality of lung sounds, which is generally attributed to acoustic transmission through smaller lungs and thinner chest walls. Acoustic measurements have shown higher median frequencies of normal lung sounds in infants than in older children and adults [16]. Scientific studies show that higher median frequencies in infants were explained by lower power at low frequencies, while the decrease in power toward higher frequencies was similar at all ages (infants, children, and adults) [17].

4.2. Physical principle of sound in the airways

The harmonic analysis is a mathematical apparatus for processing the oscillating periodic signal, which the sound also is. Sound is an oscillation of acoustic pressure, which propagates by space. The oscillation of acoustic pressure is composed of many sine oscillations characterized by various frequencies. A timbre and character of sound detectable by human ear originates from the number of oscillated frequencies. The sound composed of the integer multiples of the base frequency (the lowest frequency) with a clearly defined period is perceived as a musical tone. On the contrary, the sound including the noninteger multiples of the base frequency and without a clearly defined period is perceived as noise [18].

The respiratory sound, which is caused by airflow in airways, is sound in a frequency range from 20 to 2000 Hz and higher. However, it can still be detected at or above 2000 Hz with proper sensitive microphones in a quiet room according to our experience [16, 17, 19]. The normal lung sound spectrum is devoid of discrete peaks and is not musical [18].

One of the manifestations of asthma and other respiratory diseases is bronchial obstruction. Such a narrowing of the air passages causes a vibration and turbulence of the airflow, which results in the change of the sound manifestation of breath. This change of sound, which is manifested by the presence of wheezing and crackles, can be detected by listening using the phonendoscope. For wheezing, the frequencies in the range of 300–1000 Hz with higher amplitudes in comparison with neighboring areas are typical [20]. The duration of these areas is normally from 0.5 to 0.75 s. These searched phenomena in the respiratory sound could be emphasized using an intensive respiration caused, for example, by physical activity [20–23].

4.3. Harmonic analysis and Fourier transform

Using harmonic analysis, such a sound can be decomposed and particular frequencies of mentioned sine oscillation can be searched. Thus, the important frequencies of wheezes can be discovered too. The visualized result of the Fourier transform is called the frequency spectrum [18] and its example is shown in **Figure 8**.

Figure 8 shows the frequency spectrum of analyzed music sound in a defined time range—the horizontal axis is a frequency scale and it indicates harmonic frequencies in this sound; the vertical axis indicates an amplitude level of every frequency in the sound. The frequencies can be clearly defined in this case because the analyzed sound is a mentioned musical sound.

For illustrative interpretation of the outputs of harmonic analyzes, we have developed our own software. The software operates on the principle of mentioned Fast Fourier Transform using Matlab background and creates frequency spectra throughout the length of the analyzed recording, working with defined time intervals [22]. The length of the time intervals corresponds to the duration of wheezing approximately. For better clarity of outcomes of performed analysis, a specific suitable color scaling for frequencies in the obtained frequency spectra was applied [21, 22]. Then, every level of amplitude is defined by one concrete color (**Figure 9**).

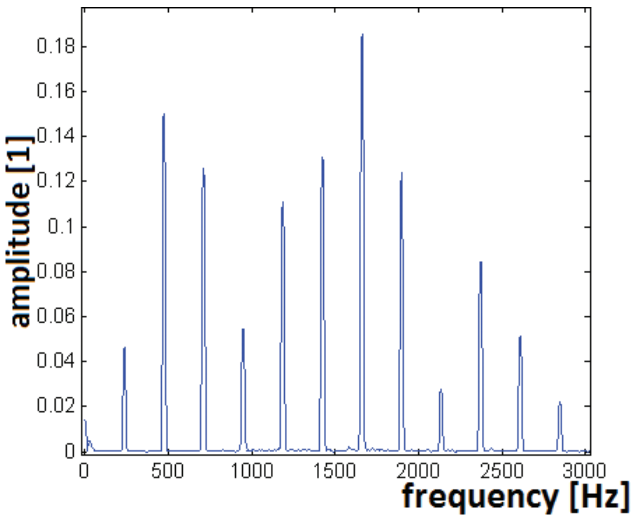

Figure 8. Illustration of frequency spectrum.

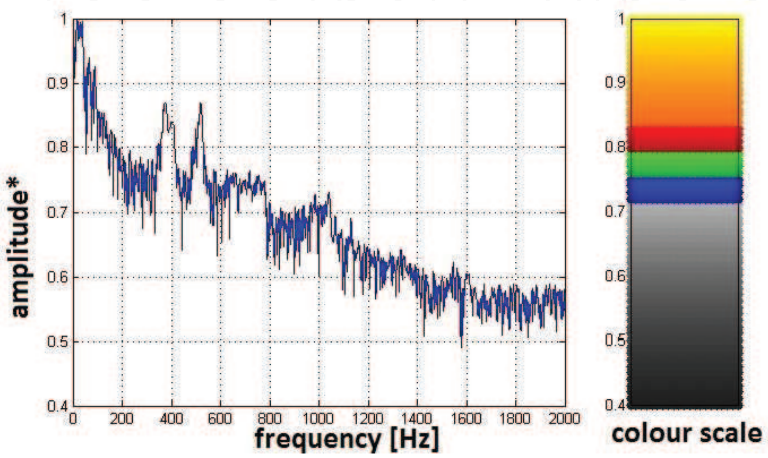

Figure 9. Color scaling of obtained frequencies. The color scale matches special colors according to values of all amplitudes.

Finally, the colored data were rearranged back to the time line of original recording (**Figure 10**).

By this approach, the oscillations of acoustic pressure are presented by the progression of the frequency spectra of the sound recording in time (**Figure 10**). Such a method of sound-recording acquisition of patients' breath, which is required for frequency spectrum creation and for the detection of wheezing in this spectrum, is completely noninvasive and without the need of cooperation of patient.

4.4. Our experimental work

While looking for a way of how to utilize the harmonic analysis in auscultation examinations most effectively, we have performed relatively large set of experiments. The main part of the work includes data collection. Based on these data, we have verified and modified the properties of our method to best suit our purpose. All audio recordings of respiratory sounds were obtained in collaboration with the Department of Pneumology in UH Motol.

The following text is focused on the part of our study, which was attended by nine volunteer patients with asthma aged from 9 to 18 years. It is a relatively homogeneous group in terms of diagnosis and clinical manifestations. In this group, it was also possible to perform the generally respected spirometric examination for subsequent result comparison.

4.4.1. Instrumentation

The usual commercially available electronic phonendoscope Littmann 3200 recording the heard respiratory sound was utilized in the study. The instrument digitizes the recording with a sampling frequency of 4000 Hz and allows the application of a specific input filtration. The

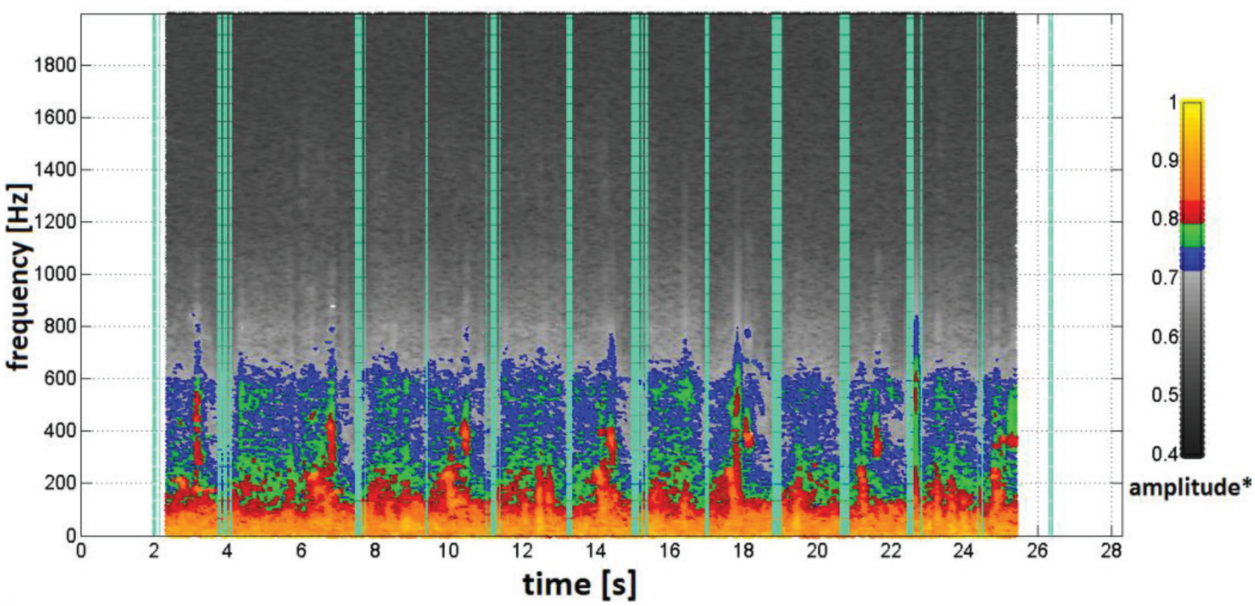

Figure 10. The frequency spectrum of sound recording of patient's breath. The pale blue vertical lines indicate moment of transitions between inspiration and expiration phase. The lines repeat in 2-s time interval. It corresponds to the length of respiratory cycle (inspiration + expiration) for ordinary human in defined age [21].

manufacturer does not provide any information about the sensitivity of the device, but guarantees that the limiting factor in the evaluation of the recordings will always be the auditory organ of the listener and not the sensitivity of the instrument.

4.4.2. Measurement protocol

The quality of respiratory sound recording is affected by location, where the sound was recorded [20, 22–24]. Probably, the best location for respiratory sound recording is on the back on paravertebral line on the right and left side (lung lobes in **Figure 11a** and **b**) and on jugulum (**Figure 11c**). The sound with frequencies up to 600 Hz goes through lung parenchyma better than the sound with frequencies over 600 Hz. These frequencies could be detected better on jugulum.

The recordings were acquired in the examination of patients during restful and deep breathing, which was induced by light physical load (10–15 squats) according to instructions and under the supervision of the attending physician.

4.5. Results

Data processing followed the procedure described in Chapter 4.3. In all patients included in our study, specific artifacts (**Figure 12**, black-circled areas) appeared in the expiration phases. In two of those cases, these artifacts were not listened by experienced physicians just as a result of their extinction within the other recorded noise. Data processed so far indicated that in asthmatic patients, there are clearly visible manifestations of the obstruction in the expiration phases in the frequency ranging from approximately 400 to 600 Hz, regardless of whether they are identifiable by listening or only through our analysis.

Even the control records of healthy volunteers are not without interest. From **Figure 13**, it is well seen that they show significantly lower level of noise compared to the asthmatic patients in all of the breathing phases.

It is worth noting that there are vertical pale blue lines indicating the transitions between inspiration and expiration. These lines were also determined automatically by applying a harmonic analysis with the use of the fact that the airflow stops at that moment [21].

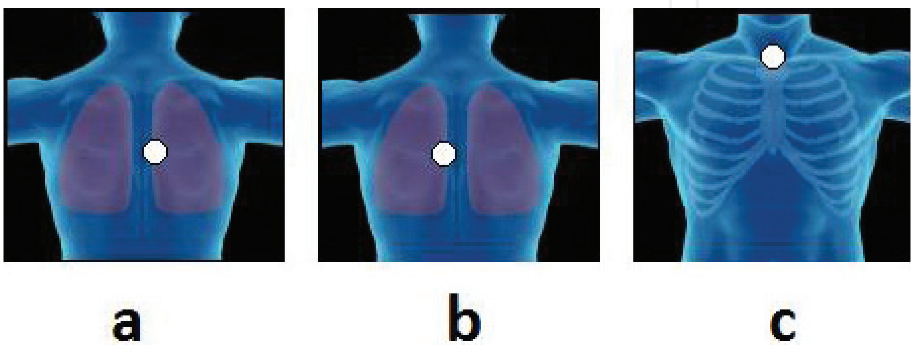

Figure 11. Locations for sound recording.

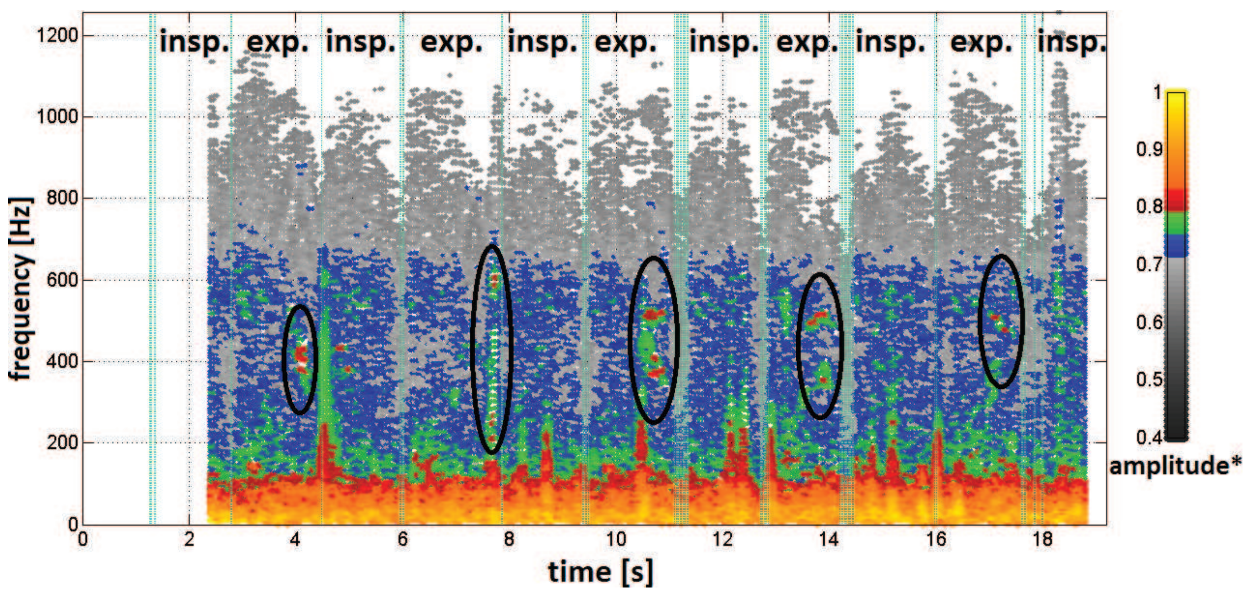

Figure 12. Development of amplitude and frequency spectrum of an asthmatic patient.

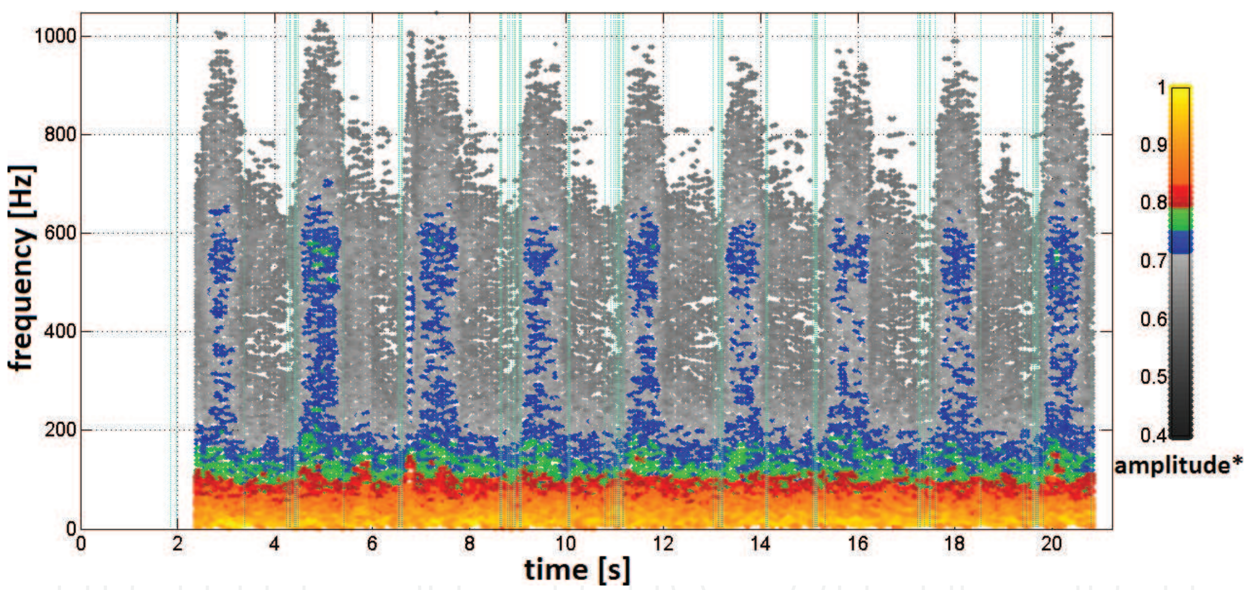

Figure 13. Development of amplitude and frequency spectrum of a healthy volunteer.

5. Conclusion

Data processed so far show that—despite the relatively simple technique used—the audio display provides valuable diagnostic information. Furthermore, using a suitable method, this information can easily be detected in the record through specific sound phenomena despite other sounds in the record. Therefore, we believe that research focused on alternative complementary methods has its importance—it can provide solutions in cases where other commonly observed methods fail or are complicated to be applied.

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