# Computer Evaluation of Tracheal Forced Expiratory Noise Time for Bronchial Obstruction Diagnostics

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***Abbreviations***

*FVC – forced vital capacity*

*FVC% - ratio of FVC to predicted value of this parameter in percents*

*VC – vital capacity*

*$FEV_1$ – forced expiratory volume in 1 sec*

*$FEV_1$% - ratio of $FEV_1$ to predicted value of this parameter in percents*

*PEF – peak expiratory flow*

*FET – forced expiratory time*

*$FET_s$ – spirometric forced expiratory time*

*$FET_{as}$ – auscultative forced expiratory time*

*$FET_a$ – tracheal forced expiratory noise time*

*ROC-curve – receiver operating curve*

***Abstract*- Computer analysis of respiratory noises provides a precise estimation of acoustic forced expiratory noises time ($FET_a$). The objective is to analyze $FET_a$ diagnostic capability in revealing bronchial obstruction. A group of patients with bronchial asthma (BA) involved 50 males (16-24 years). Selection criteria: (a) diminution of $FEV_1$/FVC (VC) relation; (b) bronchodilator response to salbutamol; (c) diurnal variability of PEF. A group of 52 healthy volunteers were recruited as the control one. Spirometry and forced expiratory tracheal noises recording were sequentially accomplished for each person. $FET_a$ values were estimated by means of developed semiautomated procedure, including bandpass filtration (200–2000 Hz), waveform envelope calculation with accumulation period of 0.01 sec, measurement of $FET_a$ at 0.5% level from the peak value of the waveform. The value of $FET_a$ was significantly larger in BA patients group than in control one. Based on ROC-analysis the cutoff point $FET_a$ > 1.86 s was chosen as a sign of bronchial obstruction. Areas under ROC-curves of $FET_a$ and baseline spirometric index $FEV_1$/FVC (VC) did not differ significantly. The mean intrasubject variability of $FET_a$ constituted 8.3% in the control group. Thus $FET_a$ is a reasonably sensitive, specific and quite repeatable test of bronchial obstruction in young men.**

***Keywords- Computer Analysis; Respiratory Noises; Forced Exhalation; Signal Processing; Expiratory Time; Bronchial Obstruction***

## I. INTRODUCTION

The concept of using the time of forced exhalation (FE) to recognize bronchial obstruction is not new. An increase in FE time (FET) due to bronchial obstruction was noticed approximately fifty years ago [24]. The diagnostic capabilities of both auscultated FET ($FET_{as}$) and spirometric FET ($FET_s$) have been studied. However contradictory results are reported. According to MacDonald, et al [13], a high variability in both $FET_{as}$ and $FET_s$ were observed. According to [26] longer $FET_s$ were associated with better spirometric performance. Men had on average longer $FET_s$ than women [7]. Authors [9] suggested that a standardized protocol may minimize FET intrasubject variability. However, they concluded that $FET_{as}$ should not be used as a diagnostic tool because of its low specificity. Others proposed that $FET_{as}$ could be used at a patient's bedside for diagnosing respiratory obstruction when spirometry was not available, the test being effective only for persons older than 60 years [25]. It should be noted that these studies were performed using subjects with a wide range of ages, which, in the absence of standards for $FET_{as}$, may cause some bias.

Computer analysis of respiratory sounds is considered to be a promising method for testing the state of the human respiratory system [18]. Digital spectral processing of forced expiratory wheezes was used to discriminate between patients with bronchial obstruction (bronchial asthma) and those that were healthy [6]. It is evident that computer analysis of respiratory noises provides a precise estimation of time parameters such as FE acoustic noises duration ($FET_a$), being the object-measured analog of $FET_{as}$. In studies [20, 21], $FET_a$ of FE tracheal noises showed promise in recognizing hidden bronchial obstruction (spirometry negative asthma-like symptoms). However the first step in assessing the diagnostic power of $FET_a$ should be evaluating its ability to diagnose bronchial obstruction revealed by spirometry. Since $FET_a$ correlated significantly with FVC, $FEV_1$/FVC [20], being dependent on gender and age [4, 7], we decided to use homogenous in gender and age sample for the first step of $FET_a$ diagnostic possibility estimation. Therefore, the objective of our study is a comparative analysis of the computer assessed $FET_a$ in FE tracheal noises among a homogenous sample of young healthy males and young male patients with bronchial asthma as a model of bronchial obstruction.

## II. METHODS

### A. Patients

Fifty males (range 16-24 years) from the Vladivostok

Allergo-Respiratory Center (Russia) with high probability of bronchial asthma (BA) newly revealed according to [14] by independent pulmonary physician were included. There were 21 smokers (7 ex-smokers, 14 current). None of the BA patients included in the group had taken anti-inflammatory therapy yet. Inclusion criteria were:

- diminution of $FEV_1/FVC$ (or $FEV_1/VC$, if VC>FVC) relation < the lower limit of the normal range (LLN), calculated by Hankinson et al., 1999 [22];
- or normal baseline spirometry but a bronchodilator response to salbutamol (an increase of $FEV_1 \geq 12\%$ of the pre-bronhodilator value);
- or normal baseline spirometry and negative bronhodilator responce but a diurnal variability of PEF > 20% [23].

A group of 52 healthy students from the Vladivostok institutions of higher education, similar in age, sex, anthropometric parameters to the BA group, were selected. There were 22 smokers (8 ex-smokers, 14 current). The investigation was carried out during their yearly physical examinations. Each subject was asked to complete a questionnaire regarding his prior history of lung disease and risk factors. Those who were included in the control group did not complain of their health status. On examination, spirometry and chest X-ray no pulmonary and cardiac pathology were identified. None had severe pneumonia, tuberculosis, chronic lung diseases, chronic disorders of the upper respiratory tract, and atopy in their past medical histories, or been ill with acute respiratory infections a month before the examination. No one in the control group was a family member of a BA patient, or worked with occupational hazards.

Subjects' characteristics are shown in Table Ⅰ. All subjects gave informed consent to take part in this study. The study was approved by the ethical committee of Medical Division of Far Eastern Branch of Russian Academy of Sciences.

TABLE I CHARACTERISTICS OF BRONCHIAL ASTHMA PATIENTS AND CONTROL SUBJECTS*

| Characteristic | Control Group n=52 | Bronchial Asthma Group n=50 | p Value |
|---|---|---|---|
| Age, yr | 18.5;17.0;19.0 | 18.0;17.0;19.0 | NS |
| Height, m | 1.79;1.75;1.83 | 1.79;1.76;1.83 | NS |
| Weight, kg | 67.5;63.0;72.5 | 65.0;59.0;78.0 | NS |
| Smoking status of ever smokers | n=22 | n=21 | NS |
| Cigarettes/day | 7.5;3.0;10.0 | 8.0;6.0;10.0 | NS |
| Duration of smoking, yrs | 2.0;1.0;3.0 | 2.0;1.0;3.0 | NS |

* Data are the median; lower quartile; upper quartile, NS means p>0.05.

### *B. Procedures*

Recording FE tracheal noises was performed with sitting subjects. A sensor was placed on each subject's right larynx area inwardly from the anterior edge of his sternocleidomastoid muscle; a clamp was applied on his nose. The sensor was applied close to the soft tissues by the stethoscopic head, and the subject himself held the box with his hand. They performed a forced expiratory maneuver from the position of maximal inspiration. The subjects held their breath for 0.5-1 seconds between inspiration and expiration. In order to carry out the maneuver properly, a maximum sharp and maximum complete expiration were required. Each subject first trained and practiced the maneuver. An experienced PFT physician monitored the FE performance. At least three well-performed attempts were recorded.

The sensor [10] has a midget electret microphone (W62A) with an ebonite stethoscopic head having a conical chamber with 20 mm at its base diameter and 5 mm in depth (an opening angle of $120^o$). We made a capillary channel (diameter 0.75 mm, length = 2.5 mm) in the chamber bottom. To introduce signals through the microphone input of the computer sound card, the PPhT software was used [10]. Measurement of $FET_a$ for each recorded file was taken by using a specially developed algorithm. According to this algorithm, filtration is carried out in a frequency band of 200 - 2000 Hz (Kaiser Windowed Direct-form Finite Impulse Response (FIR) filter), the FE waveform envelope is constructed doubly in the forward and opposite directions by moving average method with an accumulation period of 0.01 sec. Then the peak amplitude (A) of the envelope is calculated. At a threshold level L = 0.005 A, the times of beginning $T_1$ and ending $T_2$ of FE noise process are measured by envelope when moving from the peak to the left and to the right. Time $T_1$ is fixed by the program quite reliably (Fig. 1-A). While timing the ending ($T_2$), the first one of feasible solution roots (Fig. 1-A) is determined by the program although a skilled operator often can tell that noise process is still in progress. To eliminate this effect, a semiautomated procedure is used in which the program calculates consequently all roots of the equation L = 0.005 A automatically. However the operator, displacing the cursor interactively along the calculated solution roots on the plot (Fig. 1-B – Fig. 1-D) next by next, has a chance of selecting the root that corresponds to the ending of noise process. In this case to exclude the operator's subjectivity as far as possible, we stated the rule of choice of the last solution root before «a big jump of the cursor». In fact, as the ending of a slowly decreasing noise process is approached, time displacements of the right cursor reduce progressively in travel on selecting the next root (Fig. 1-B – Fig. 1-C). The subsequent sharp increase in time displacement of the right cursor (approximately by an order greater than previous displacements) points to a stable decrease of friendly signal below the threshold level L, and we named it figuratively *a Big Jump of the Cursor* (Fig. 1-D). Meanwhile it should be noted that approximately 94% of estimates made during analysis of the sample engaged the first $T_2$ root, evaluated automatically without any manual adjustment. Since $T_1$, $T_2$ have been measured automatically or semiautomatically, the program automatically calculates the duration of tracheal noises ($FET_a$) by the difference of measured times $T_2 - T_1$. The maximal individual $FET_a$ from

3 well-done attempts was used for further analysis [20].

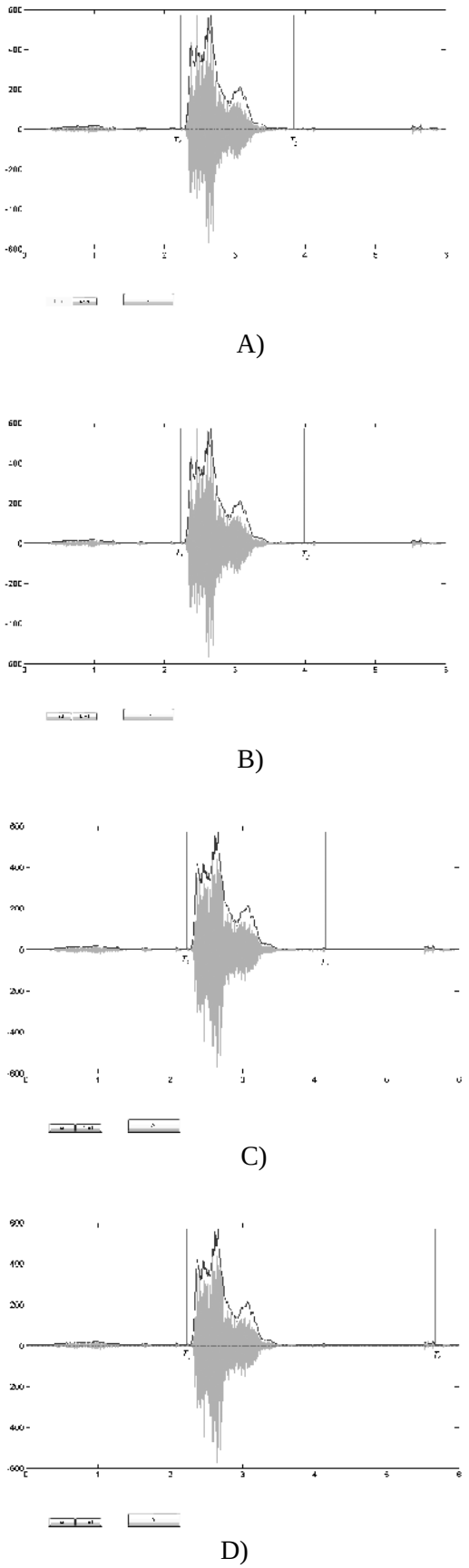

Fig. 1 Time Series diagram of tracheal forced expiratory noises, showing $FET_a = T_2 – T_1$ measuring procedure:

solid line – signal waveform envelope; dashed line – original signal carrier;

$T_1$ – time of FE noises beginning; $T_2$ – time of FE noises ending;

time (s) on the X-axis; relative amplitude (%) on the Y-axis;

A) the first solution root of $T_2$, $FET_a$ = 1.605 s;

B) the second solution root of $T_2$, $FET_a$ = 1.763 s, $FET_a$ increment (right cursor displacement from the last $T_2$ value) is 0.159 s;

C) the third solution root of $T_2$, $FET_a$ = 1.919 s, $FET_a$ increment (right cursor displacement from the last $T_2$ value) is 0.156 s;

D) the fourth solution root of $T_2$, $FET_a$ = 3.440 s, $FET_a$ increment (right cursor displacement from the last $T_2$ value) is 1.521 s

Spirometry was performed by a standard procedure [16]. Short acting $\beta_2$ agonists were not allowed within 8 h before the test. Long-acting $\beta_2$ agonists were stopped at least 12 h before the test. We selected the best of three attempts by the greatest sum of $FEV_1$+FVC. By utilizing this method, the FVC, $FEV_1$, and $FEV_1$/FVC (VC) were determined for each subject, whereas $FET_s$ was determined by the maximum of these three attempts. The predicted values of Hankinson et al. (1999) [22] were used because they overlap with all subjects' ages. Baseline spirometry analysis was determined by software [22]. Spirometry was carried out by a computer spirometer SPIRO USB (MicroMedical Ltd., UK), which had a turbine flow transducer. ATS/ERS criteria for acceptability [16] were used.

All measurements were repeated 20 minutes after 200 µg of salbutamol was administered by a metered dose inhaler connected to a spacer. An increase in $FEV_1$ by ≥12 % of the pre-bronhodilator value was regarded as a significant bronchodilator response.

Monitoring PEF (home peak flow monitoring) with the help of an electronic Asthma-Monitor (Erich Jaeger Gmbh, Würzburg, Germany) was performed for 2 weeks in all patients with normal baseline spirometry and negative bronchodilator response. Only patients which performed measuring sessions not less than 3 times per day during 2 weeks and showed variability of PEF > 20% were included in the patient sample [23].

It is noteworthy that the tracheal noises and spirometry were recorded in different FE attempts as according to [17] the interaction of expiratory airflow with flow meter armature may result in the occurrence of adventitious noises, changing $FET_a$ value determined on trachea.

### *C. Statistics*

Descriptive statistics was used to evaluate each group. The significance of parameter differences between groups was determined by the two-sided t-test for independent samples with normal distribution of variants, and by the Mann-Whitney U-test for independent samples with non normal distribution, respectively. The association of attributes was estimated by the Spearman rank correlation coefficient. The significance of differences between correlation coefficients and the difference between proportions were determined by the one-sided t-test (Statistica, StatSoft Inc.).

To estimate the repeatability of the $FET_a$ parameter, the following approach was used. As mentioned above, each subject performed a few attempts of the FE maneuver, no less than three of them being registered if correctly executed. A sample average $M(FET_a)$ and standard deviation $SD(FET_a)$ were calculated for these three attempts of each subject. Next, we computed an individual (for each subject) coefficient of variation $CV(FET_a) = SD(FET_a)/M(FET_a)$, and averaged it by all subjects of the control group $M(CV(FET_a))$.

$FET_a$ characteristics as a diagnostic test (sensitivity and specificity) and comparison of $FET_a$, $FEV_1/FVC$ (VC), and $FET_s$ areas under ROC curve were calculated in MedCalc version 9.2.1.0 (MedCalcSoftware) program.

## III. RESULTS

Both groups did not differ in age, height and body mass (Table Ⅰ). Significant differences between these groups were revealed both in acoustic variable $FET_a$ and in all analyzed spirometry indexes (Table Ⅱ). The value of $FET_a$ and $FET_s$ proved to be significantly larger in patients with BA compared to healthy controls ($p<0.0001$). Moreover significant distinctions between $FET_a$ and $FET_s$ ($p<0.0001$) were revealed both in the healthy group and in the group of BA patients.

TABLE II ACOUSTIC AND SPIROMETRIC DATA OF BRONCHIAL ASTHMA PATIENTS AND CONTROL SUBJECTS*

| Parameter | Control Group n=52 | Bronchial Asthma Group n=50 | p Value |
|---|---|---|---|
| $FET_a$, s | 1.46;1.17;1.64 | 2.45;1.92;2.86 | p < 0.0001 |
| FVC, l | 5.4;5.05;5.82 | 4.65;4.28;5.4 | p < 0.0001 |
| FVC% | 108.5;101;117.5 | 89.0;79.3;97.5 | p < 0.0001 |
| $FEV_1$, l | 4.76;4.47;5.06 | 3.41;2.99;3.92 | p < 0.0001 |
| $FEV_1$% | 111;102;119 | 76.7;65.8;85.3 | p < 0.0001 |
| $FEV_1/FVC$ | 86.8;83.5;92.6 | 71.3;66.3;77.4 | p < 0.0001 |
| $FET_s$, s | 2.65;2.21;3.09 | 3.44;2.58;4.72 | p < 0.0001 |

*Data are presented as median; lower quartile; upper quartile.

Changes of base-line spirometric index $FEV_1/FVC$ (VC) were observed in 39 of 50 BA patients. Eight of 11 patients with normal baseline spirometry showed a positive response to salbutamol, and in 3 more subjects a diurnal variability of PEF of more than 20% was observed. These 11 patients were regarded as having mild bronchial obstruction. The other 39 patients were arranged according to the severity of bronchial obstruction as determined by $FFV_1$% [19].

We estimated the ability of $FET_a$ acoustic parameter to differentiate between BA patients and healthy subjects in this sample. Based on ROC-analysis (Fig.2), the value of $FET_a$ = 1.86 s closest to the left top of the "Sensitivity – 100-Specificity" plot (maximum likelihood ratio) was chosen as a cutoff point. Thus, $FET_a > 1.86$ s was thought to be a sign of bronchial obstruction. With this threshold, the sensitivity of $FET_a$ test was 82%, and the specificity was 94.2%.

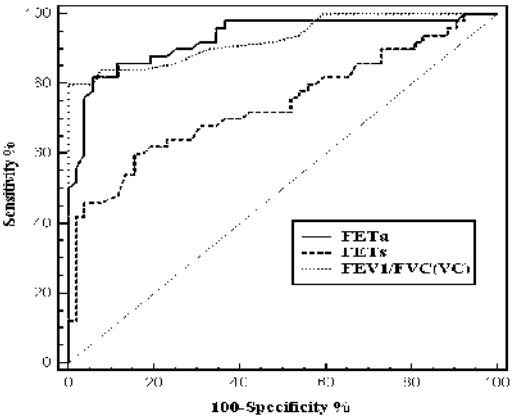


Fig. 2 Receiver operating characteristic (ROC) curves for the $FET_a$, $FET_s$, $FEV_1/FVC$(VC):

- area under curve of $FET_a$ is 0.93 (95%CI 0.86 to 0.97),

- area under curve of $FEV_1/FVC$(VC) is 0.93 (95%CI 0.86 to 0.97),

- area under curve of $FET_s$ is 0.73 (95%CI 0.64 to 0.82)

Sensitivity of $FEV_1/FVC$ (VC) < the LLN was 78% with specificity being 100%. Sensitivities between $FET_a$ and $FEV_1/FVC$ (VC) did not differ ($p=0.22$). The specificity of $FEV_1/FVC$ (VC) seemed to be slightly above ($p=0.041$).

As the relation between sensitivity and specificity of the test depends on a selected threshold and can vary according to the problem in view, it is advisable to compare the areas under the ROC curve (AUC) of the analyzed parameters (Fig. 2). There are no significant differences between the AUC of $FET_a$ and $FEV_1/FVC$ (VC) ($p=0.98$). However, there is significant difference between the AUC of $FET_s$ on the one hand and that of $FET_a$ on the other hand ($p < 0.001$).

The mean intrasubject variability of $FET_a$ parameter in the control group was: $M(CV(FET_a)) = 8.3\%$.

The interrelation of FE tracheal noise time and spirometric parameters in the groups was analyzed. In BA patients a significant correlation of $FET_a$ and $FEV_1$ ($r = -0.38$, $p=0.007$), $FEV_1$% ($r = -0.48$, $p=0.0004$), $FEV_1/FVC$ ($r = -0.65$, $p<0.000001$), and $FET_s$ ($r = 0.65$, $p<0.000001$) were found. In healthy persons, a correlation between $FET_a$ and $FEV_1/FVC$ ($r = -0.71$, $p<0.000001$), FVC ($r = 0.38$, $p=0.005$), FVC% ($r = 0.35$, $p=0.01$), and $FET_s$ ($r = 0.34$, $p = 0.002$) were found as well.

## IV. DISCUSSION

It should be noted that our $FET_a$ values can't be directly compared with $FET_{as}$ values previously measured. The main acoustic reason to such situation is that human ear is more sensitive to signal in surrounding noise than our computer procedure, which limits noise process duration by 0.5% level from the maximum of envelope (not reaching noise level usually). While $FET_a$ and $FET_s$ are correlated, $FET_a$ is significantly shorter than $FET_s$ (in healthy sample $FET_a/FET_s = 55.5 \pm 14.3$ %, in BA patient sample

$FET_a/FET_s$ = 73.3 ± 22.1 %). Thus there is a systematic bias between $FET_a$ and $FET_s$ and $FET_s$ values can't be directly compared with our $FET_a$.

Althoughour $FET_a$ can't be directly compared with $FET_{as}$ and $FET_s$ of other authors, qualitive analogy between these indexes is possible. In our study, the $FET_a$ in BA patients was significantly greater than in control subjects. Let us compare this result to the data of previous FET studies.

The relationship between an increase in $FET_{as}$ (as well as $FET_s$) and bronchial obstruction has been observed previously.

Rosenblatt and Stein (1962) [24] found that $FET_{as}$ was accurate in identifying both individuals with clinically relevant obstructive pulmonary disease and those without such disease. Lal et al. (1964) [12], having selected $FET_{as}$ cutoff point as 5 s, yielded a sensitivity of 87% and a specificity of 100%.

Regarding $FET_s$, McFadden and Linden (1972) [15] and Cochrane et al. (1974) [3] assumed that this parameter could be a reflection of small airways obstructions in persons with normal spirometry. Burki and Dent (1976) [2] concluded that a simple measurement of the $FVC/FET_s$ can be an adequate screening test to estimate the function of small airways at normal $FEV_1/FVC$ ratio. In the study of Kainu et al. (2008) [4] the mean $FET_s$ in healthy non-smokers was 9.8 (9.2-10.4) s with shorter exhalation time commonly seen in young adults.

MacDonald et al. (1975) [13] reported that both $FET_{as}$ and $FET_s$ have a high intrasubject variability (CV of $FET_{as}$ was 25%; CV of $FET_s$ was 21.4%). At the same time Kern and Patel (1991) [9] believed that performing the FE maneuver can be standardized, thereby decreasing the intrasubject variability of $FET_{as}$. Nevertheless, the basic limitation of using the $FET_{as}$ as a lung function test, these authors point out that the parameter has a very low specificity (44%), and does not improve when the cutoff point is manipulated. In the recent studies focused on $FET_s$ CV was 14.8% [25] and 11.3% [8].

In our homogeneous group of young healthy males, the $M(CV(FET_a))$ = 8.3%. The value suggests an intrasubject variability of the parameter under study. The subject's ability of performing the maneuver consistently and a probable operator's error when evaluating the $FET_a$ possibly account for this variability.

As for operational characteristics, the sensitivity and specificity of the $FET_a$ test with a cutoff point of 1.86 s appeared to be comparable with that of baseline spirometric index $FEV_1/FVC$ (VC) in our investigation of young male BA patients and healthy subjects of the same age and sex. Furthermore, the value of $FET_a$ specificity that was obtained seems to be much higher than the fixed $FET_{as}$ value [9], where a specificity of 44% (at a cutoff point of 6 s) was achieved in a wide range of ages.

Schapira et al. (1993) [26] concluded that it was appropriate to use the $FET_{as}$ in elderly patients (over 60 years) at their bedside when spirometry was inaccessible. Our results indicate that the use of $FET_a$ is effective with young men.

Lal et al. (1964) [12] reported a good correlation between the $FET_{as}$ and the spirographic indexes that represented bronchial obstruction ($FEV_1/FVC$). We also found a significant correlation between $FET_a$ and $FEV_1/FVC$, and $FEV_1$ and $FEV_1$% in BA patients. Along with studies [12, 13], we revealed a significant correlation between $FET_a$ and $FET_s$ but only in asthma patients. A substantially weaker correlation in healthy subjects was found. Furthermore, significant distinctions between these parameters were seen in both groups. It was not surprising. According to model [11] $FET_a$ in healthy individuals is determined by an expiratory resistance of the central airways (in the phase of functional expiratory stenosis). Nevertheless, in cases of bronchial obstruction, there are some distributed local areas of increased airflow resistance (local obstruction) in the respiratory system, not only in the central zone. Here, an additional noise generation may occur in more distant airway branches. This is especially the case with FE wheezes observed at the end of the maneuver. Hence, $FET_a$ will account for more noise generation time, compared with the time predicted from a normal individual with only resistance of the central airways [11]. However local areas of increased airflow resistance (local low flow bronchial obstruction) may have minor influence on flow-volume parameters measured at the mouth and consequently $FET_s$. Thus $FET_a$ may be more sensitive to local bronchial obstruction than $FET_s$. This thesis is supported by the significant distinction between the diagnostic power (AUC) of $FET_a$ and $FET_s$. Thus, $FET_a$ and $FET_s$ (at least, at separate recordings) are related but not completely interchangeable parameters.

Probably, the discrepancy of the diagnostic efficiency obtained before with respect to evaluating the $FET_{as}$ and $FET_s$ in various ages is caused by the absence of standards. Although it had been noticed the correlation of $FET_s$ and age [1, 2, 5], all subsequent investigations were carried out using samples of subjects' with a wide range of ages, with no correction made for this factor. Conceivably, other factors might influence the forced expiratory time too; including those that can be easily estimated and measured, for example, sex and anthropometric parameters. In general terms, the $FET_a$ seems to be specific to every healthy subject [20].

## V. CONCLUSION

Thus, our investigation has shown that $FET_a$ of FE tracheal noises is a reasonably sensitive sign of bronchial obstruction in young male BA patients, having spirometric deviations. The sensitivity and specificity of the $FET_a$ test are comparable with baseline spirometry, and it's repeatability in the control group is also quite acceptable. More importantly, the $FET_a$ test completely excludes a danger of intersubject respiratory infection, thus making

bronchial obstruction screening possible even in a field conditions including military or emergency situations especially in developing countries.

New studies are needed to define normal $FET_a$ values in females and different ages as well as assessing the capabilities of the $FET_a$ test to reveal hidden bronchial obstructions, particularly in spirometry negative BA patients.

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