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Variations in Respiratory Sounds in Relation to Fluid Accumulation in the Upper Airways

Azadeh Yadollahi[1], Frank Rudzicz[2], Aman Montazeri[3], and T. Douglas Bradley[4]

Abstract— **Obstructive sleep apnea (OSA) is a common disorder due to recurrent collapse of the upper airway (UA) during sleep that increases the risk for several cardiovascular diseases. Recently, we showed that nocturnal fluid accumulation in the neck can narrow the UA and predispose to OSA. Our goal is to develop non-invasive methods to study the pathogenesis of OSA and the factors that increase the risks of developing it. Respiratory sound analysis is a simple and non-invasive way to study variations in the properties of the UA. In this study we examine whether such analysis can be used to estimate the amount of neck fluid volume and whether fluid accumulation in the neck alters the properties of these sounds.**

Our acoustic features include estimates of formants, pitch, energy, duration, zero crossing rate, average power, Mel frequency power, Mel cepstral coefficients, skewness, and kurtosis across segments of sleep. Our results show that while all acoustic features vary significantly among subjects, only the variations in respiratory sound energy, power, duration, pitch, and formants varied significantly over time. Decreases in energy and power over time accompany increases in neck fluid volume which may indicate narrowing of UA and consequently an increased risk of OSA. Finally, simple discriminant analysis was used to estimate broad classes of neck fluid volume from acoustic features with an accuracy of 75%. These results suggest that acoustic analysis of respiratory sounds might be used to assess the role of fluid accumulation in the neck on the pathogenesis of OSA.

I. Introduction

Obstructive sleep apnea (OSA) is a common disorder that increases cardiovascular morbidity and mortality [1, 2]. Although OSA occurs due to the partial or complete collapse of the upper airway (UA) during sleep, the underlying mechanisms for this collapse are not fully understood. Recently, we showed that sedentary living causes fluid accumulation in the legs during the day some of which can be displaced rostrally into the neck when moving from the upright to the recumbent position at bedtime. Therefore, developing non-invasive techniques to monitor fluid accumulation in the neck might improve our understanding of the pathogenesis of OSA and how to implement treatments to counteract this effect.

Overnight fluid shif from the legs into the neck could cause distension of the neck veins and/or edema of the peripharyngeal soft tissue and facilitate UA obstruction. In previous studies, we applied lower-body positive pressure (LBPP) via inflatable trousers to awake individuals to simulate nocturnal fluid displacement out of the legs. We demonstrated that fluid shift out of the legs to the neck narrowed the UA and increased its resistance to airflow in healthy non-obese subjects [3]. Fluid displacement also increased UA collapsibility in healthy men while awake [4]. We have also shown that during the night, the volume of fluid displaced from the legs is strongly related to the degree of overnight increase in neck circumference and severity of OSA in non-obese otherwise healthy men, men with heart failure, end-stage renal disease, and patients with hypertension [5-7].

Respiratory sounds analysis is a simple and non–invasive technique to study the pathophysiology of the UA and has been widely used for investigation of UA obstruction [8-13]. In previous studies, we showed that tracheal sound analysis can reflect variations in the anatomy and physiology of the UA in individuals with or without OSA [14, 15]. Furthermore, we applied LBPP to healthy awake individuals and simultaneously recorded UA resistance and respiratory sounds with a microphone in front of the nose. Our results demonstrated that variations in UA resistance in association with fluid accumulation in the neck change acoustic properties of respiratory sounds such as formants and energy [16].

In this study we recorded tracheal respiratory sounds and neck fluid volume in healthy awake individuals while lying down in the supine position. The goal of this study is to examine the variations in tracheal sound features in relation to fluid accumulation in the neck and to investigate whether tracheal sound analysis can be used to monitor fluid accumulation in the neck.

II. Method

A. Data

Data for this study were recorded from 10 healthy awake subjects (5 men, 5 women) aged 33.2 ± 8.5, with a mean body mass index (BMI) of 23.9 ± 4.0, and no history of sleep or respiratory disorders. Subjects were recruited by advertisement with no restriction on sex, age or BMI. Subjects lay supine for 90 minutes while neck fluid volume (NFV), leg fluid volume (LFV) and tracheal respiratory sounds were recorded simultaneously. However in this study, we only investigated the relationship between NFV and tracheal respiratory sound. NFV was recorded using bioelectrical impedance which is a non-invasive, well validated, and highly reproducible technique to measure fluid volume of tissues [17]. In this method, two electrodes inject high

[1]A. Yadollahi is with the Institute of Biomaterial and Biomedical Engineering, University of Toronto, Canada, and Sleep Lab, Toronto Rehabilitation Institute. e-mail: azadeh.yadollahi@uhn.ca

[2]F. Rudzicz is with Toronto Rehabilitation Institute and the Department of Computer Science, University of Toronto, Canada, email: frank@cs.toronto.edu

[3]A. Montazeri is with the Toronto Rehabilitation Institute, email: aman.montazeri@uhn.ca

[4]TD. Bradley is with the Department of Medicine, University of Toronto, Canada, and Sleep Lab, Toronto Rehabilitation Institute, email: douglas.bradley@utoronto.ca

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frequency (50 kHz), low amplitude (400 μA) current into the tissues and two sensing electrodes measure bioelectrical impedance which is inversely related to the amount of fluid in the tissue. For NFV, sensing electrodes were placed on the right side of the neck: one below the right ear and one at the base of the neck; injecting electrodes were placed one inch away from the sensing electrodes. Tracheal respiratory sounds were recorded by a Sony microphone embedded in a chamber (diameter of 6 mm) and attached to the suprasternal notch of the subject with double-sided tape. Tracheal sounds were low-pass filtered with the cut-off frequency of 5 kHz. Both NFV and tracheal sounds were digitized and recorded simultaneously with a sampling rate of 12.5 kHz (MP150, Biopac Systems).

B. Feature Extraction

Tracheal sound was bandpass filtered in the frequency range of $[30 - 3000]Hz$ to remove the low- and high-frequency noises, such as motion artifacts. For every subject, 4 segments of data (2 minutes each) at the beginning (T_0), between 20-30 minutes (T_{30}), between 50-60 minutes (T_{60}), and at the end of recording (T_{90}) were selected by an expert and the inspiratory breath cycles void of noise were marked manually. For each inspiratory breath cycle, several features in the temporal and spectral domains were extracted. Temporal features include duration (**Dur**), average energy (**Eng**), skewness (**Skew**), kurtosis (**Kurt**), the ratio between voiced and unvoiced segments of breath sound ($\boldsymbol{R_{VUV}}$), and zero crossing rate (**ZCR**, normalized by the duration) of the inspiratory breath cycle. The spectral features include average power ($\boldsymbol{P_{Avg}}$) in various frequency bands ([30-100] Hz, [100-450] Hz, [450-600] Hz, [600-800] Hz, [800-1200] Hz, [1200-2000] Hz and [2000-3000] Hz), pitch (**Pitch**), Mel-Power (**MelPwr**), Mel-Cepstrum coefficients (**MelCeps**), and the first three formants (**F1**, **F2**, **F3**) of the inspiratory breath cycle.

C. Fluid Volume Estimation

Bioelectrical impedance of the tissue is inversely related to the amount of fluid in tissue. In this study we continuously recorded impedance ($\mathbf{I_N}$) and phase (θ) of the neck's bioelectrical impedance and calculated neck resistance ($\mathbf{R_N} = I_N \times \cos(\theta)$) and reactance ($\mathbf{X_N} = I_N \times \sin(\theta)$). NFV was estimated as [18]:

$$NFV = \rho L^2 / R_N, \tag{1}$$

where ρ is the blood's resistivity, L is neck's length in cm and R_N is neck's resistance in Ω.

D. Statistical Data Analysis

In order to determine the effects of time, of individual subject characteristics, and of the interaction between these variables, we perform multi-way analyses of variance (ANOVAs) on each acoustic feature. We then perform Pearson correlation analysis between the bioelectrical impedance driven variables (I_N, θ, R_N, X_N and NFV) and the acoustic variables to measure relationships between variations in the NFV and acoustic features of tracheal respiratory sounds. We then apply several regression analyses to investigate how well acoustic features can predict variations in NFV. This includes multilinear regression of the observations of NFV given the acoustic data reduced to two dimensions according to the first two principal components, plus an interaction term between these dimensions (i.e., their pairwise product). The first two principal components of the acoustic data account for 90.52% and 5.40% of the variance, respectively, as determined by the eigenvalues of the covariance matrix of the acoustics.

In the last analysis, we examine five standard discriminant functions on randomized partitions of the data using 10-fold cross validation. The five discriminant functions are:

- **linear** The linear method fits a multivariate Gaussian to each class, with a pooled estimate of covariance.
- **diag.** The diagonal method fits a multivariate Gaussian to each class, with a diagonal covariance matrix estimate.
- **quad.** The quadratic method fits multivariate Gaussians with covariance estimates stratified by class.
- **dquad** The diagonal quadratic method is similar to the quadratic method, but with a diagonal covariance matrix estimate.
- **mahal.** Uses Mahalanobis distances with stratified covariance estimates.

In all cases, we split the NFV data into three classes whose boundaries are determined empirically and whose prior probabilities are learned automatically during training. The three classes used in discriminant analysis are NFV values below 350 ml, above 450 ml, and between these two boundaries.

III. Results

Figure 1 shows variations in leg and neck impedances and fluid volumes over time for a typical subject. As seen in Fig. 1, the leg's impedance (Fig. 1-a) increases asymptotically over time as a result of fluid moving out of the leg (Fig. 1-b). Consequently, neck impedance decreases over time (Fig. 1-c) which indicates that there is more fluid accumulating in the neck (Fig. 1-d). Similar patterns were observed in all subjects which confirms that some of the fluid displaced from the legs shifts into the neck while supine.

Table I shows the F-statistics for each acoustic variable according to variance among individuals, variance due to time (T_0, T_{30}, T_{60}, and T_{90}), and to the interaction between these two variables. Kolmogorov-Smirnov goodness-of-fit tests of normality were performed on each variable in Table I independently; each variable is normally distributed with $p < 0.001$. There is a significant amount of variance among subjects across all acoustic variables ($p < 0.05$) that may be due to the high variability of UA anatomy and physiology among individuals. R_{VUV}, Eng, Dur, ZCR, P_{Avg}, MelPwr, and formants (F_1, F_3) of tracheal breath sounds vary significantly over time. The interactions between subjects and time are significant for all features ($p < 0.001$) except for skewness and kurtosis.

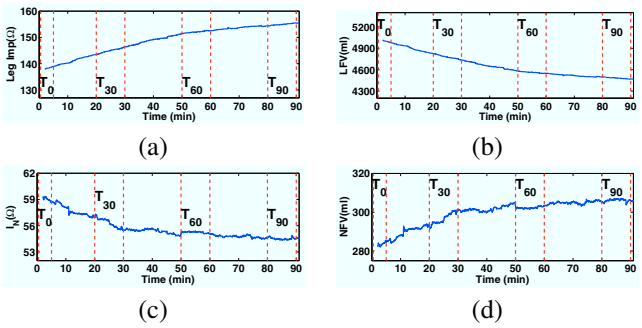

Fig. 1. Variations in leg and neck impedances and fluid volumes over time for a typical subject: a) leg impedance, b) leg fluid volume, c) neck impedance and d) neck fluid volume.

	Subject		Time		Interaction	
Feature	$F(9)$	p	$F(3)$	p	$F(27)$	p
Pitch	52.94	< 0.001	1.70	0.17	5.33	< 0.001
R_{VUV}	93.93	< 0.001	23.34	< 0.001	14.64	< 0.001
Eng	126.06	< 0.001	4.26	< 0.01	4.96	< 0.001
Dur	69.88	< 0.001	25.98	< 0.001	12.46	< 0.001
ZCR	128.79	< 0.001	44.72	< 0.001	18.78	< 0.001
P_{Avg}	203.34	< 0.001	6.60	< 0.001	8.96	< 0.001
MelPwr	68.03	< 0.001	9.67	< 0.001	11.92	< 0.001
MelCeps	65.49	< 0.001	1.10	0.35	12.17	< 0.001
Skew	2.19	< 0.05	0.37	0.78	1.08	0.36
Kurt	6.19	< 0.001	0.34	0.80	1.14	0.29
F1	47.49	< 0.001	2.72	< 0.05	12.39	< 0.001
F2	143.49	< 0.001	1.74	0.16	11.60	< 0.001
F3	191.72	< 0.001	5.05	< 0.005	11.16	< 0.001

TABLE I

RESULTS OF ANOVA ON EACH ACOUSTIC FEATURE. F-STATISTICS AND ASSOCIATED p VALUES ARE SHOWN ACCORDING TO VARIANCES DUE TO SUBJECT, TIME, AND THE INTERACTION BETWEEN THESE VARIABLES.

Of the acoustic features that vary significantly with time, R_{VUV}, Eng, ZCR, P_{Avg} and MelPwr decreased after 90 minutes. These results indicate that the overall energy of respiratory breath sounds decrease over time. Since energy of respiratory breath sounds is related to the respiratory flow rate, the results suggest a decrease in respiratory flow rate over time. On the other hand, the duration of respiratory cycle increases over time which could be a mechanism to increase the total breathing volume.

Table II shows the Pearson correlation coefficients, r, between the bio-impedance/fluid variables and the acoustic variables. While there are no strong correlations (i.e., $|r| > 0.5$), neck impedance (I_N, θ and resistance R_N) have medium correlations (i.e., $0.1 < |r| \leq 0.5$) with each of F2, F3, and Eng acoustic measures, as NFV has with ZCR. Each of these 10 correlations are significant at $p < 0.00001$.

Since the aim is to use these acoustic measures to predict NFV, this analysis suggests that ZCR could be a useful feature for this task. Although here we assume an independence between the acoustic variables, that will not be the case during automated classification where acoustic measures will be combined. Furthermore, the relationship between several acoustic variables and NFV were not significant, including R_{VUV} ($p = 0.225$), Eng ($p = 0.518$), Dur ($p = 0.354$),

r	I_N	θ	R_N	X_N	NFV
F1	-0.174	0.269	-0.181	0.084	0.116
F2	$\mathbf{-0.341}$	**0.393**	$\mathbf{-0.348}$	-0.030	0.243
F3	$\mathbf{-0.356}$	**0.418**	$\mathbf{-0.364}$	-0.012	0.185
Pitch	0.174	-0.197	0.178	0.004	-0.093
$\boldsymbol{R_{VUV}}$	0.091	-0.100	0.094	-0.026	0.044
Eng	**0.357**	$\mathbf{-0.318}$	**0.360**	0.125	-0.0262
Dur	0.181	-0.211	0.185	-0.005	-0.034
ZCR	-0.243	0.297	-0.247	-0.072	**0.389**
$\boldsymbol{P_{Avg}}$	0.255	-0.162	0.256	0.130	0.104
MelPwr	0.168	-0.029	0.165	0.161	0.233
MelCeps	0.151	-0.126	0.151	0.122	-0.030
Skew	-0.044	0.024	-0.043	-0.043	-0.025
Kurt	0.140	-0.124	0.141	0.061	0.023

TABLE II

PEARSON CORRELATION COEFFICIENTS, r, BETWEEN THE BIO-IMPEDANCE/FLUID VARIABLES AND THE ACOUSTIC VARIABLES. *Medium* CORRELATIONS ARE IN **bold**.

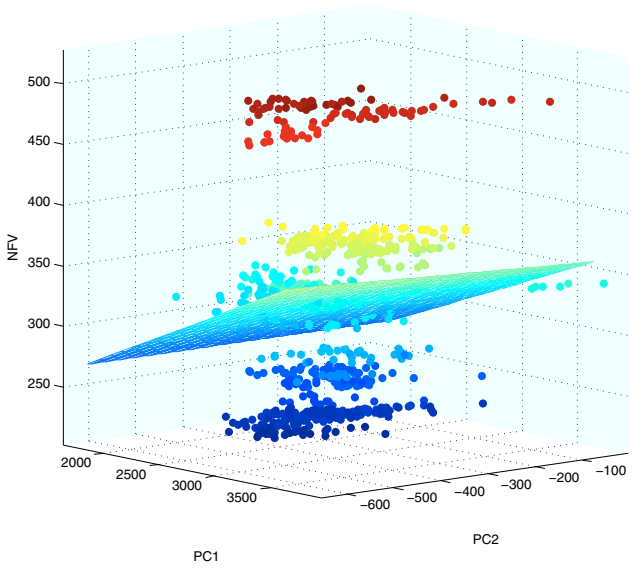

Fig. 2. Multilinear regression of NFV given the associated acoustic data reduced according to the first and second principal components.

MelCeps ($p = 0.413$), Skew ($p = 0.503$), and Kurt ($p = 0.531$), suggesting at least that more data are required before the utility of these independent variables can be determined.

Multilinear regression of NFV given all acoustic predictor variables results in an R^2 goodness-of-fit statistic of 0.4221, and an F-statistic of 41.4047 ($p < 0.00001$). On the other hand, although the first two principal components (PC1 and PC2) represent more than 95% of variations in the data space, the restricted multilinear regression between NFV and PC1 and PC2 gives an R^2 goodness-of-fit statistic of 0.0447 , and an F-statistic of 11.6587 ($p < 0.00001$). The insufficiency of this reduced space in predicting NFV can be visualized in Figure 2 where the especially high volumes of neck fluid are not adequately predicted.

The results of discriminant analysis are shown in Table III according to the average (μ) accuracy across folds, along with the variance (σ). All approaches are significantly better than a uniform probability baseline at the 99.9% level of

Model type	Accuracy μ (%)	σ
linear	75.3	0.1314
diag.	64.5	0.2457
quad.	68.9	0.1700
dquad.	50.3	0.2807
mahal.	77.6	0.2086

TABLE III

AVERAGE (μ) AND STANDARD DEVIATION (σ) OF THE ACCURACY OF DISCRIMINANT ANALYSIS FOR ESTIMATING NFV FROM ACOUSTIC VARIABLES.

confidence.

IV. DISCUSSION

In this study, we investigated the application of respiratory sound analysis to monitor fluid accumulation in the UA. We recorded tracheal respiratory sounds and bio-electric impedance of the neck over time. Our results showed that with an increase in NFV, several acoustic features associated with tracheal sound energy decreased over time. One possible explanation for this phenomenon is that it may represent narrowing and partial obstruction of the UA over time as a result of fluid accumulation in the neck that decreases upper airway patency, airflow and sound intensity. Interestingly, the duration of the respiratory cycle increases over time which could be a mechanism to compensate for the decrease in breathing flow rate or increased airflow resistance, and to adjust the total breathing volume.

The results of the present study provide a reasonable estimate of NFV from tracheal sound analysis (accuracy of 75%). We are currently investigating non-linear regression algorithms, additional features of tracheal sound, and alternative more sophisticated classification algorithms including various discriminative training methods to improve estimation accuracy. Also, considering the high variation of acoustic features among subjects, we intend to examine adaptive algorithms that can modify the statistical parameters of a general population model to be more attuned to individual characteristics, such as maximum likelihood linear regression and maximum a posteriori estimation. These results can be used to develop simple and non-invasive acoustic techniques to monitor fluid accumulation in the neck and its role on the pathogenesis of OSA in a wide range of patients, specially those with fluid retaining conditions.

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