

Respiration monitoring using a paper-based wearable humidity sensor, a step forward to clinical tests

İrfan Solak^{a,1}, Şerife Gençer^{a,1}, Beyza Yıldırım^a, Emine Öznur^b, Dooyoung Hah^a, Kutay Icoz^{a,*,2}

^a Electrical and Electronics Engineering Department, Abdullah Gül University, Kayseri 38080, Turkey

^b Department of Chest Diseases, Kayseri City Hospital, Kayseri 38080, Turkey

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ABSTRACT

Monitoring respiratory variables can provide valuable information for clinical applications and sport activities. Paper-based wearable respiration monitoring systems have great advantages and potential, they are low-cost, easily disposable, non-invasive and can provide real-time, reliable data. Despite some examples presented for exhaled breath analysis using paper-based sensors exist, none of them have been validated yet in a study involving many patients. In this work, we present a novel paper-based platform for exhaled breath sensors and validate it on 101 subjects including 41 patients to demonstrate its clinical applicability. By using the paper-based wearable capacitive sensors, we collected respiration data from different groups of people, namely, smokers, non-smokers and patients diagnosed with pneumonia, or chronic obstructive pulmonary disease (COPD). The change in humidity during inhale and exhale was converted to capacitance change and thus an electrical signal was obtained. The electrical signal was transmitted to a nearby computer and capacitance versus time data was post-processed. Four ratio parameters were defined on the recorded data; area, rate, maximum amplitude, and average maximum-minimum difference, all of which were compared between deep breathing and normal breathing. The collected data was statistically analyzed, and the humidity changes were compared among different groups. The results show that the developed sensor and the proposed analysis method can be used to detect the humidity changes in breathing, and to differentiate between smokers and non-smokers, and between non-smokers and patients with pulmonary disease.

1. Introduction

The number of individuals having a chronic respiratory disease increased almost 40% in 27 years [14], according to World Health Organization. In 2020, 22.3% of the global population used tobacco, and the recent severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has affected more than 5 million people [16]. All these significant facts motivate researchers to develop new sensor systems for detecting respiratory diseases and for monitoring respiration parameters from exhaled breath. In the last decades, paper-based sensors have drawn great interest because they are low-cost, disposable, easily accessible and can be used to measure physical, chemical and biological quantities [5]. In a recent study, paper-based wearable electrochemical sensor system was reported to detect hydrogen peroxide (H₂O₂) in

exhaled breath which is a biomarker associated with asthma and chronic obstructive pulmonary disease (COPD) [10]. The humidity and temperature measurements of exhaled breath has clinical importance [3] and the ranges of these two parameters were reported considering gender, body mass index, and age of the participants in two different sites [12]. Paper-based respiration monitoring systems are based on the hygroscopic character of the cellulose fiber (adsorption and desorption of water molecules). In [11] and [6], carbon ink was printed on a paper, and the sensor designs had interdigitated patterns to increase the sensing area. The absorption of humidity by the paper changed the dielectric constant of the capacitive sensor and thus an electrical signal was obtained. A similar study described paper-based capacitive sensor where an interdigitated sensor was fabricated by screen-printing the composite of multi-walled carbon nanotubes (MWCNT) and polydimethylsiloxane

* Corresponding author.

E-mail address: kutay.icoz@agu.edu.tr (K. Icoz).

¹ authors contributed equally

² ORCID: 0000-0002-0947-6166

(PDMS) [15]. The fabrication of the paper-based respiration sensor was further simplified by drawing the pattern with a pencil and a stencil [8]. All of these studies [6,8,15] reported breathing index, and respiration pattern of at most 10 healthy subjects, which shows that it is necessary to expand the tests for a larger group of people, using paper-based respiration monitoring system.

There have been also other studies that connected the breath humidity level to a pulmonary disease. Expiratory air humidity rates of healthy rats and rats with acute pulmonary edema were measured using a handheld commercially available sensor and significantly lower humidity rate for unhealthy rats was reported, which shows that humidity can be considered a parameter for monitoring pulmonary edema [1].

This study aimed to define new parameters obtained from the humidity changes during normal and deep breathing recorded by a pencil-drawn paper-based sensor, and to compare these parameters among four groups: smokers, non-smokers, and patients (COPD or pneumonia). To the best of our knowledge, paper-based respiration sensors have been only tested for healthy individuals so far. This study will show that measurements from a paper-based respiration sensor can be used to discern different groups of subjects which is a step forward to clinical tests. The statistical analysis revealed that significant difference can be detected using the paper-based respiration sensor.

2. Materials and methods

2.1. Stencil fabrication

To standardize the sensor drawing, a stencil (Fig. 1) was produced from polymethyl methacrylate (PMMA). The pattern was created in CorelDRAW (Corel Corporation, Ottawa, Ontario, Canada) and the 2-mm-thick PMMA sheets were cut by using an Epilog Model 10,000, 30 Watts laser cutter (Epilog Laser, Golden, Colorado, USA).

2.2. Sensor fabrication

To find the optimum paper for sensor fabrication, we tested 7 different types of papers which are commercially available and easily accessible. Among these 7 different types, ISOLAB weighing paper (Ref: I.037.33.001) showed the best repeatability in terms of capacitance change when exposed to the same humidity level. Different types of

pencils were also tested and a 2B pencil was determined as one of the best options. A sensor pattern was drawn on the paper using the stencil and the pencil (Fig. 1).

2.3. Head mask design

To standardize the measurements, a head mask was designed by using computer-aided design (CAD) tools, and then, fabricated by 3D printing. The complete mask is shown in Fig. 2. The paper sensor was placed in the sensor holder, and an Arduino Nano board in the forehead chamber. The height of the sensor holder can be adjusted for each subject.

2.4. Electronic components

The paper-based sensor was connected to analog input pins of the Arduino Nano as it was used as a capacitance meter. The capacitance value, C was determined by using the time constant $\tau = RC$ of the circuit where R is the resistance of the connections. The measured data was transferred to a nearby computer using Bluetooth module of the Arduino and processed in MATLAB®.

2.5. Sensor characterization

The paper-based sensor was characterized, and tested for dynamic response, stability, reproducibility, and repeatability. Table 1 represents the rise time and fall time from respiration patterns of a nonsmoker, smoker, and patient. A descriptive pattern is shown in Fig. 3a.

As seen from the respiration pattern each subject was asked to perform normal breathing (one minute) and deep breathing (one minute) while capacitive changes were observed continuously. To examine the applicability of the sensor to different people, a same sensor was tested with two different healthy subjects at different times (Fig. 3b). Although one of the main advantages of the paper-based systems is being low-cost and thus being disposable, we tested the shelf life and long-term usage of the sensor. For this, a sensor was tested after 3 months of production and no significant change was observed. Fig. 3c shows repeatability of the sensor by recording normal breathing of a subject for 3 min. Nose breathing and mouth breathing were also compared (Fig. 3d-e) and it was observed that recording from mouth has

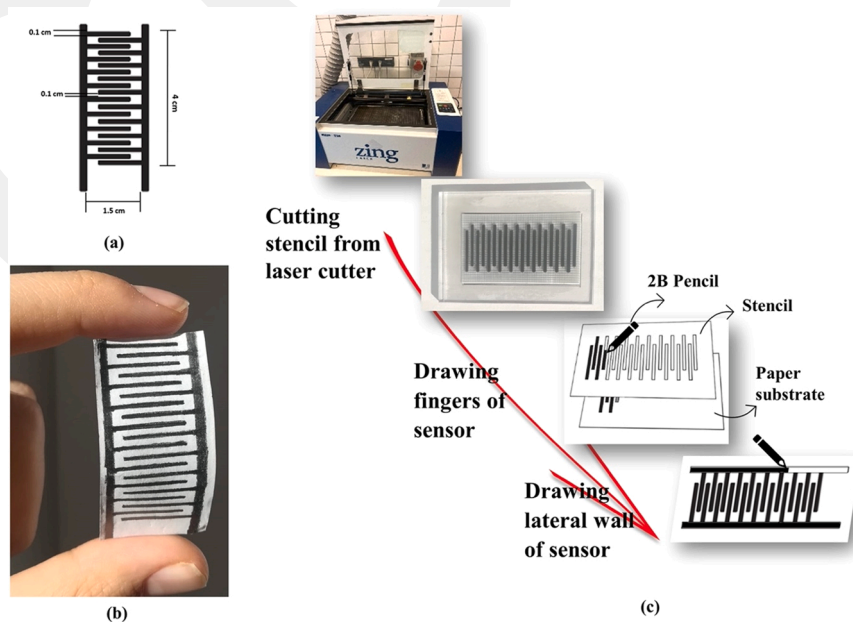


Fig. 1. Schematic illustration of the fabrication of a paper-based sensor by drawing with a pencil a) Physical dimensions b) Photograph of the paper sensor c) Fabrication steps.

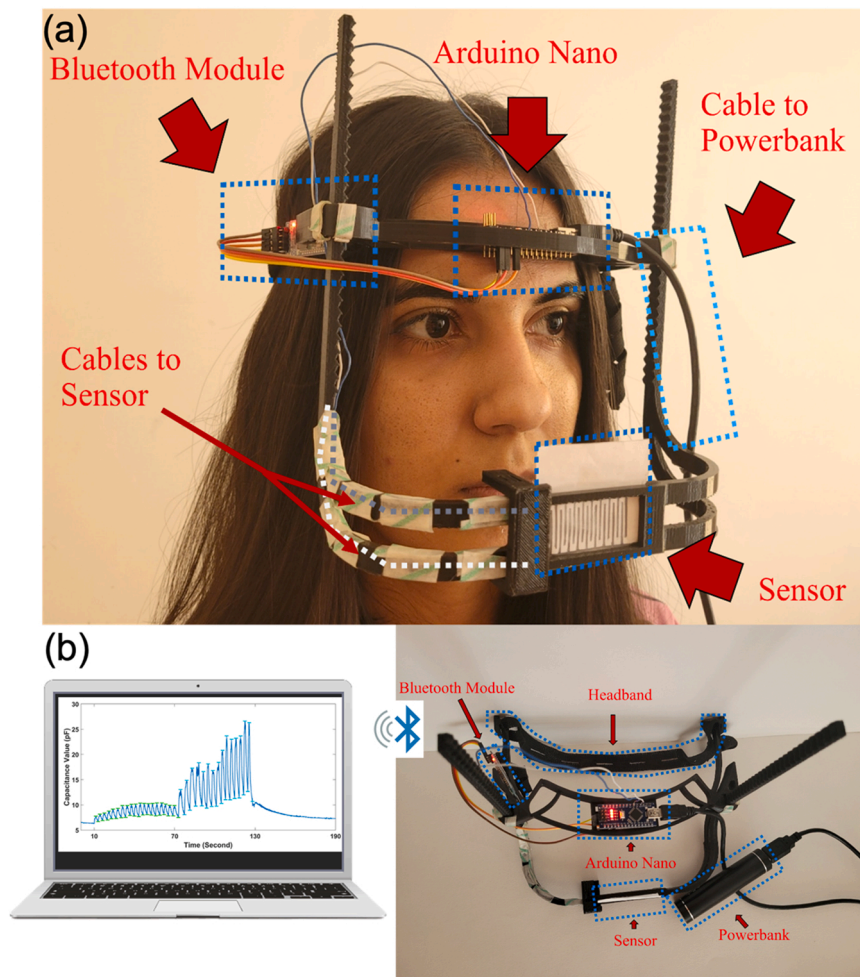


Fig. 2. a) A subject wearing the head mask including the paper-sensor. b) Photograph of the top view of the head mask and the components.

Table 1
Sensors dynamic response of sensors.

Groups	Normal Breathing		Deep Breathing	
	Rise Time (s)	Fall Time (s)	Rise Time (s)	Fall Time (s)
Nonsmoker	0.35	1.06	0.47	1.79
Smoker	0.66	1.21	0.78	1.51
Patient	0.53	1.17	0.76	0.98

higher capacitive changes. All these characterization tests showed that the distance between mouth and sensor is important, paper-based sensor can produce repeatable results, the sensor has reproducible response.

2.6. Data collection and statistical analysis

The wearable system was used to collect expiratory air humidity data from 30 individuals who smoke regularly, 30 individuals who do not smoke, and 41 patients; who are diagnosed with COPD (20 subjects) or Pneumonia (21 subjects) (Table 2). We collected the data in normal environments (for patients: hospital rooms, for smoker/non-smoker university classrooms), not in a strictly controlled environment. The data were collected in April, May, June, and October of 2022. The windows of the rooms/classrooms were closed not to have any air flow and room temperature and humidity were not altered other than the standard values. The standard hospital rooms were set to 24 °C and 30% humidity. The parameters were calculated from the normal and deep breathing patterns of the subjects. The obtained data was first tested for normal distribution, and then, t-test (for normal distribution) or Mann

Whitney test (for non-normal distribution) were applied using SPSS 28.0.1.1 (IBM) to determine statistical significance at $P < 0.05$.

3. Results

3.1. Breathing patterns

All recordings started after a 10-second waiting period during which the stability of electrical connections was checked. Then subjects in this study were asked to breath normally for 1 min and deeply for another 1 min. The adsorption and desorption of moisture by the cellulose paper during the breathing resulted in capacitance variations. A record of a typical capacitance measurement is shown in Fig. 4. Normal breathing caused capacitance variations between 6 and 10 pF whereas deep breathing caused variations between 6 and 25 pF.

In the similar works reported earlier [6,8,15], the paper-based sensor was used to monitor respiration during light and vigorous exercise, and breathing index was calculated for each subject. In our study, since we could not ask patients to do exercise, we recorded capacitance variations during normal breathing and deep breathing, instead. We defined multiple parameters which were calculated from the recorded signals.

3.2. Multiparameter analysis of respiration

To obtain parameters from the respiration patterns including normal and deep breathing, we first focused on ratio parameters to compare the subject groups of smokers, nonsmokers, and patients (Fig. 5).

The first parameter is the ratio of areas (Fig. 5a), which was defined

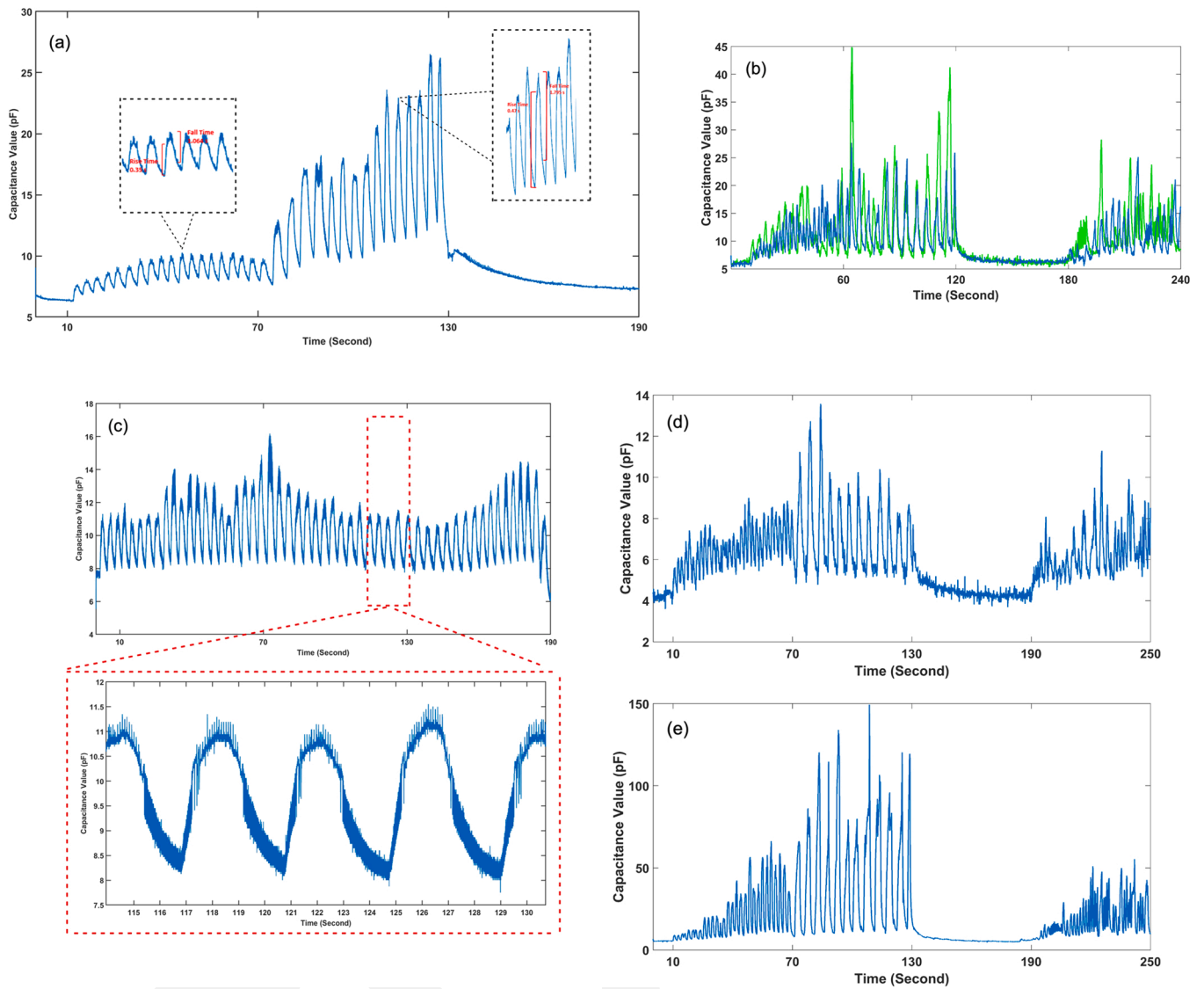


Fig. 3. Sensor characterization a) dynamic response of the sensor b) same sensor with two different subjects c) repeatability measurements d) respiration pattern recorded from nose e) respiration pattern recorded from mouth.

as

$$Parameter1 = \frac{DeepBreathingArea}{NormalBreathingArea} = \frac{A_3}{A_2} \quad (1)$$

where A_2 is the area under the curve of the normal breathing for 1 min and A_3 is the area under the curve of the deep breathing for 1 min. A_1 is

$$Parameter4 = \frac{\sum (DeepBreathingmax. - min.)}{DeepRespirationRate} \Bigg/ \frac{\sum (NormalBreathingmax. - min.)}{NormalRespirationRate} \quad (4)$$

the area of the base value which was not included.

The second parameter is the ratio of number of breaths (Fig. 5b), which was defined as

$$Parameter2 = \frac{DeepBreathingrespirationrate}{NormalBreathingrespirationrate} \quad (2)$$

The third parameter is the ratio of maximum capacitance values (over the base value) of deep breathing and normal breathing (Fig. 5c).

$$Parameter3 = \frac{DeepBreathingmaximumvalue}{NormalBreathingmaximumvalue} \quad (3)$$

The fourth parameter is the ratio of average maximum-minimum difference of deep breathing and normal breathing (Fig. 5d).

These parameters were calculated for all the subjects and statistical analyses were performed (Fig. 6).

Fig. 6 shows that area ratios and respiration rate ratios are not statistically different between any of the two groups. On the other hand, maximum amplitude ratios (parameter 3) and ratios of average maximum-minimum differences (parameter 4) are significantly different between the non-smoker group and the other two patient groups. The non-smoker group has higher averages for parameters 3 and

Table 2
Distribution of participants by group and gender.

Groups	Gender		Total	Age
	Female	Male		
Nonsmokers	9	21	30	18–27
Smokers	8	22	30	18–48
COPD	1	19	20	49–78
Pneumonia	6	15	21	35–82

4 than the other groups. The smoker group include two outliers who regularly exercise sports activities such as swimming and running. The smoker group and patient group were found to be statistically non-significant between them. In [2] researchers observed that regular smokers exhale lower-water-content breath when compared to non-smokers. Since deep breath contains more water molecules than normal breath, the water content difference between deep breath and normal breath can be used as a good indicator of the water content in exhaled breath. Observations with the parameters 3 and 4 agree with those by Ali et al. (2021).

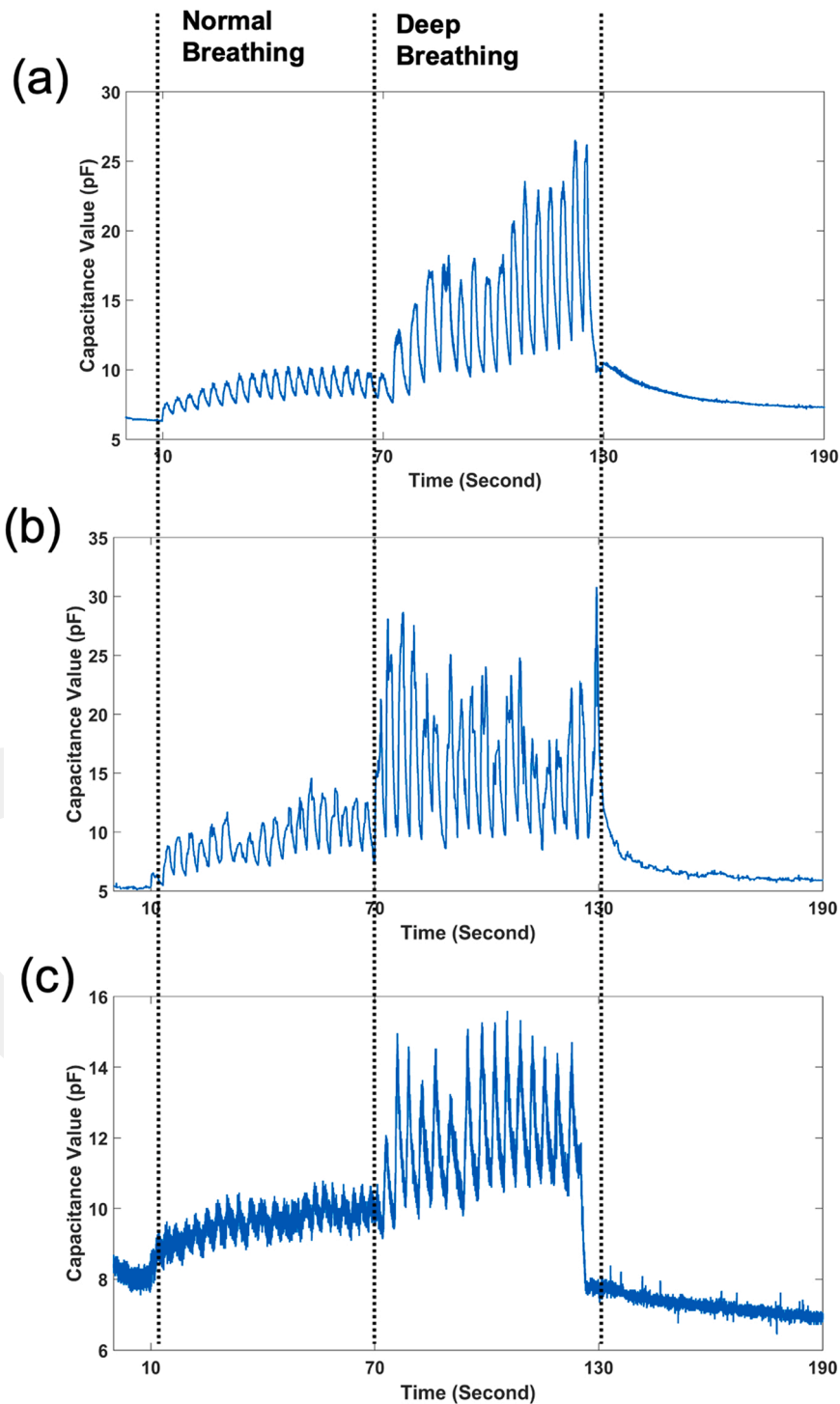


Fig. 4. A) Respiration pattern, variations in sensor capacitance with normal breathing and deep breathing, representative patterns of a) a nonsmoker subject b) a smoker subject c) a patient.

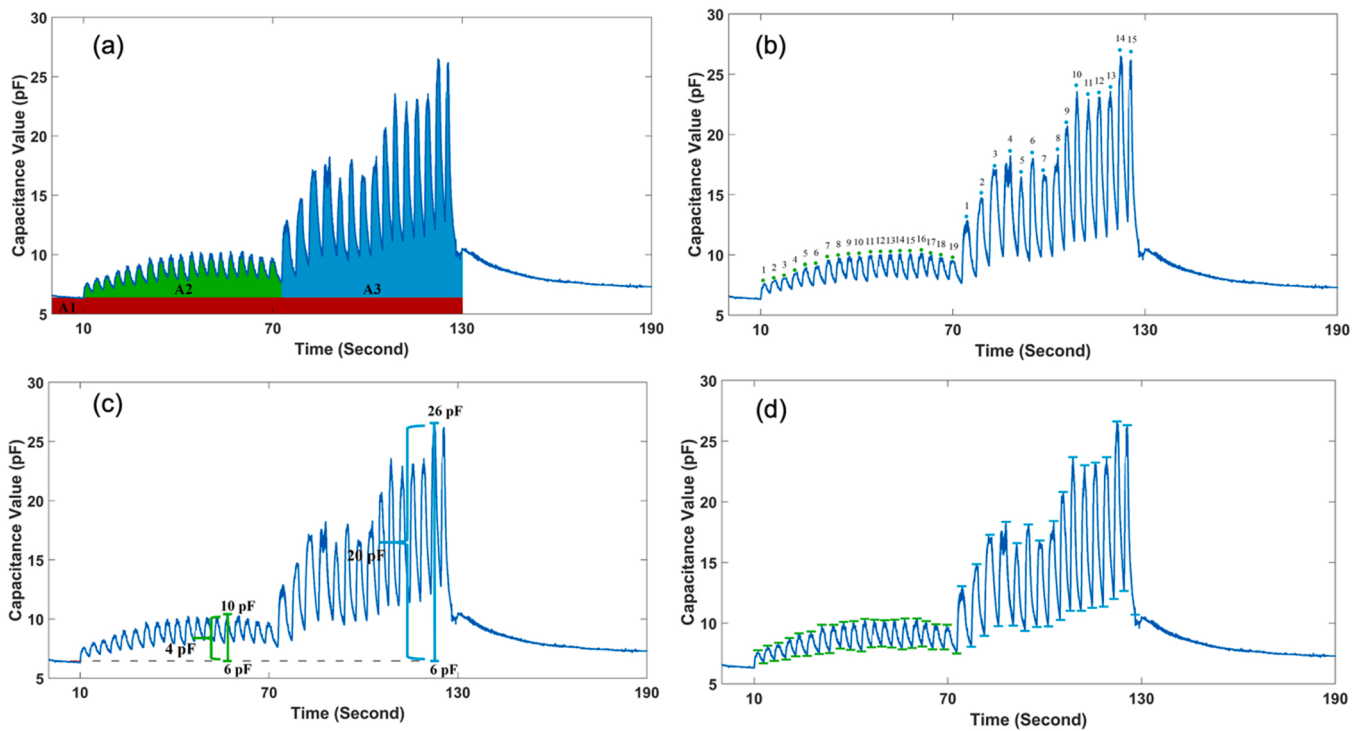


Fig. 5. Parameters defined to compare respiration patterns of subject groups. A) Area under the curve, B) Respiration rate, C) Maximum amplitude, D) Average of maximum to minimum difference.

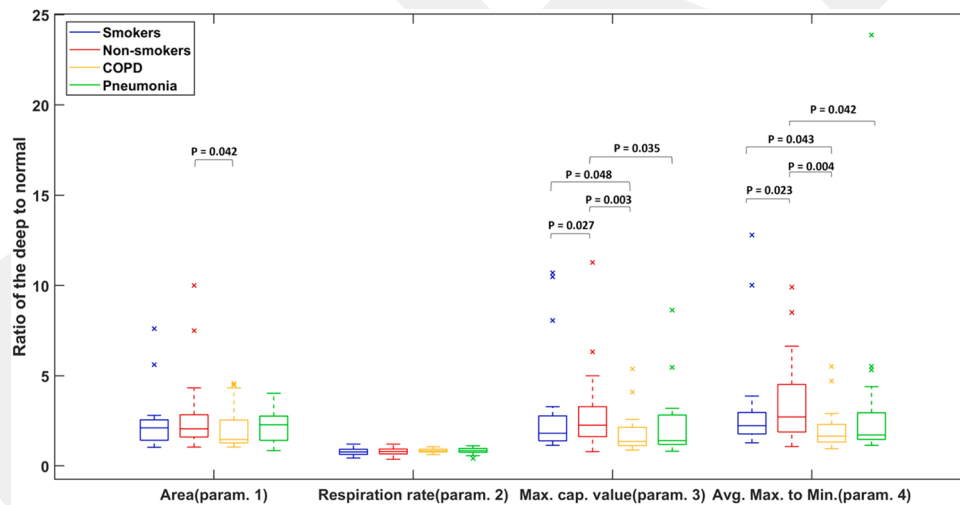


Fig. 6. Measurements of four ratio parameters for all subject groups, all other combinations are non-significant. The mean values from left to right in order [smoker (30 subjects), nonsmoker (30 subjects), COPD (20 subjects), Pneumonia (21 subjects)] parameter 1 = 2.1, 2.065, 1.47, 2.29, parameter 2 = 0.78, 0.805, 0.845, 0.85, parameter 3 = 1.82, 2.26, 1.36, 1.41, parameter 4 = 2.24, 2.62, 1.65, 1.72.

In addition, we also compared the differences instead of ratios (parameter 5) which was defined as the difference between the average changes deep breathing and normal breathing.

$$Parameter5 = \frac{\sum (DeepBreathing_{max.} - min.)}{DeepRespirationRate} - \frac{\sum (NormalBreathing_{max.} - min.)}{NormalRespirationRate} \quad (5)$$

Fig. 7 shows that parameter 5 obtained from respiration patterns of patients are statistically different between non-smokers and COPD, between non-smokers and Pneumonia, and between smokers and COPD. The smokers and Pneumonia groups are statically nonsignificant.

4. Discussion

The paper-based sensors have promising advantages such as being ultra-low cost, easily disposable, easily accessible and these systems can provide real-time, reliable data. The respiration monitoring systems based on paper sensors have been reported in the literature [6,8,11,15]. In those studies, the sensors were placed inside a facemask and paper’s hygroscopic response to the humidity of inhaled and exhaled air was converted to electrical signals. The measurements were only collected from healthy subjects and breathing index data were obtained from the respiration patterns. The results mostly depend on the experimental results, the theoretical equation to calculate the capacitance of the

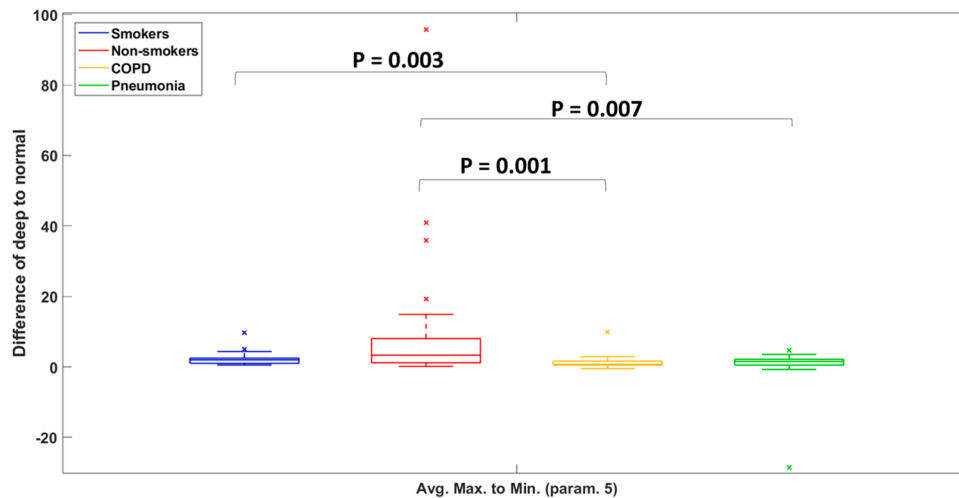


Fig. 7. Comparison of parameter 5 for all groups, all other combinations are non-significant. The mean values from left to right in order [smoker (30 subjects), nonsmoker (30 subjects), COPD (20 subjects), Pneumonia (21 subjects)] parameter 5 = 1.99, 3.3, 1.54, 0.75.

interdigitated electrode sensor was given in [8,13] and also considered in this study.

The humidity absorption characteristics were not reported by the manufacturer since the initial intent was to use it as a weighing paper. We tried several optimization studies for the paper-based sensor (not reported) to obtain the highest capacitance change for the same input of the humidity change. After optimizing the sensor geometry and material we collected data and we aimed to demonstrate the extension of the paper-based respiration monitoring towards biomedical applications. We collected normal and deep respiration data from three groups of 101 subjects composed of 30 smokers, 30 non-smokers and 41 patients. Then, we defined 5 parameters which can be calculated from the recorded respiration pattern and statistically analyzed these parameters. Our analysis reveals that paper-based respiration monitoring can be used to differentiate the humidity differences between smokers, non-smokers, and between patients and non-smokers. This result is quite promising, and further works may include data collection from patients who have other respiration disorders such as pulmonary edema.

The measurement system includes only an Arduino Nano board, a Bluetooth communication module, and a battery. The cost of the total system including all materials is less than 10 US dollars. The fabrication process is simple without requiring any microfabrication process unlike other interdigitated structures [4,7,9].

By using a low-cost set up, we were able to obtain respiration monitoring patterns from different groups. This study shows that more clinical tests can be conducted using paper-based humidity sensors. Previous study outcomes, such as humidity measurements for monitoring pulmonary edema [1] and water content measurements among smoker and non-smoker groups [2], support the potential applications of our study.

Research involving humans and animals statement

All patient samples in this study were obtained under the approval of the Clinical Research Ethics Committee of the Kayseri City Hospital (Approval date: 12.01.2022, Decision no:58, Kayseri, Turkey). All other human samples in this study were obtained under the approval of the Research Ethics Committee of the Abdullah Gül University (Approval date: 25.04.2022, Decision no:33079, Kayseri, Turkey). Written informed consent was obtained from all individuals/patients. The Declaration of Helsinki was followed throughout the study.

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CRediT authorship contribution statement

Kutay Icoz designed the study. Irfan Solak, Serife Gencer, Beyza Yıldırım, Emine Oznur collected the data, all authors analyzed the data. Dooyoung Hah, Emine Oznur and Kutay Icoz supervised the study. The manuscript was written through the contributions of all authors. All authors have read and agreed to the published version of the manuscript.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data Availability

Data will be made available on request.

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Author contributions

K.I. designed the study. I.S., S.G., B.Y. collected the data, all authors analyzed the data. D.H. and K.I. supervised the study. The manuscript was written through the contributions of all authors. All authors have read and agreed to the published version of the manuscript.

Informed consent

All authors authorize the publication of this manuscript.

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İrfan Solak received the B.S. degree in Electrical and Electronics Engineering from Aydın Adnan Menderes University in 2019 and M.S. degree in Electrical and Computer Engineering from Abdullah Gul University in 2022.

Şerife Genç is an undergraduate student pursuing B.S degree in Electrical and Electronics Engineering from Abdullah Gul University

Beyza Yıldırım is an undergraduate student pursuing B.S degree in Electrical and Electronics Engineering from Abdullah Gul University

Emine Öznur is a medical doctor at Kayseri City Hospital, Department of Chest Diseases, she received the M.D. degree from 19 Mayıs University in 2006 and she completed her residency in Chest Diseases at Erciyes University in 2012.

Dooyoung Hah received the Ph.D. degree in Electrical Engineering from the KAIST, Korea in 2000. He is currently an Assistant Professor of Electrical and Electronics Engineering at the Abdullah Gul University, Turkey. Before joining Abdullah Gul University, he has worked at the Louisiana State University, the University of California, Los Angeles and the Electronics and Telecommunications Research Institute (ETRI).

Kutay Icoz received the Ph.D. degree from Purdue University Biomedical Engr. Department in 2010. He worked at Harvard Medical School and Massachusetts General Hospital Department of Neurosurgery as a postdoctoral research fellow and at Intel Corporation Assembly & Test Technology Development Division Between as a senior engineer. He currently works as a faculty of Electrical-Electronics Engineering at Abdullah Gül University. His research focuses on novel applications of micro/nano technology on biology and medicine, biosensors, point of care devices and wearable biomedical devices.