Article Title: "A Near-Field Radio-Frequency System for Continuous Left and Right Lung Volume Sensing"

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Dear Editors and Reviewers,

We appreciate the opportunity to respond to the reviewers' detailed and helpful feedback and have revised the manuscript accordingly. This document contains our point-by-point reply to the reviewer's comments and questions along with the respective changes in the manuscript. We have also slightly modified the layout of the manuscript, by moving Fig. 1 to Page 2 instead of 3, and changing the position of Fig. 2, to improve the readability of the manuscript. We further upload a copy of the manuscript with each of the changes highlighted, as well as a clean copy without highlighting.

Thank you. Sincerely,

Aakash Kapoor

Reviewer 1: Comments and Responses

Overall Comments

This paper proposes a novel wearable sensor for continuous monitoring of individual lung volumes. It is interesting. I would like to make the following comments.

Reviewer 1 Comment 1

In section II, part A, the description of the sensing principle is too simple and unclear. It is best for the author to combine figure to illustrate the sensing principle.

Author Response: We appreciate the reviewer's comment and agree that the figure does not highlight the electromagnetic basis for the near-field RF sensing principle clearly. We have modified the manuscript by updating Fig. 1 to better highlight the EM signal model and we hope that it helps illustrate the sensing principle more clearly.

Reviewer 1 Comment 2

RF signals are usually sensitive to humidity information. Has the author studied the effect of inhaled air humidity on experiments?

Author Response: We thank the reviewer for this comment as it is important to consider environmental factors such as humidity for general applicability. While we did not study the effect of relative humidity on the received signal strength experimentally, prior studies[1] indicate that measurable changes in the received signal strength for UHF RF signals require a large variation in humidity over a significant propagation distance. In the case of the proposed near-field RF systems, the distances between transceivers and sensing objects are not long enough for measurable effects of inhaled air humidity.

Reviewer 1 Comment 3

Are there any special fixtures or probe layout requirements? Does the position and bond status of the probe affect the experimental results?

Author Response: We thank the reviewer for highlighting this very important point of discussion. Due to the near-field coupling of EM energy to underlying tissues, our system does not require special fixtures or a specific probe layout. Furthermore, the bond status of the probe does not affect the results, unlike the body electrodes used in systems such as ECG and electrical impedance. However, the position of the probe is of note, since variations in position may cause significant changes to the signal quality while leaving timing features intact [30]. In order to minimize variance in signal quality, we employed two key precautions. Firstly, we ensured that the probes were secured laterally across the chest to maximize distance between lateral sensor pairs to enhance sensing localization and reduce impacts from chest surface motion. Secondly, we employed key signal quality metrics such as SNR and linearity for computing lung tidal volumes which ensures an adaptive selection of the best channel(s), as detailed in Sec III.D.

Reviewer 1 Comment 4

Is the signal measured by the sensor a relative change or an absolute value? What is the repeatability for different individuals?

Author Response: The NFRF sensing system measures relative changes of the internal tissue motion. In order to obtain absolute values in cm^3, a one-point or two-point calibration of the system using a suitable ground truth, such as spirometer, is required. The measured signal magnitude depends on the relative placement of the NFRF sensors with the underlying tissue in motion, necessitating the need for a separate calibration stage for every individual. After the sensors are fitted onto an individual, we perform an automatic direct-path interference cancellation (DPIC) step which minimizes direct-path interference and modifies gains for each Tx and Rx to ensure that the SDR ADC is operating within proper limits. The NFRF tidal volume measurements were acquired after DPIC tuning and gain adjustment to be calibrated by the reference spirometer. This individual calibration precludes the sensor from being repeatable across subjects for absolute tidal volume measurements. However, since the sensors can measure relative changes, they may be used for monitoring changes in relative lung capacities, i.e. left lung vs right lung, over a period of time.

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[1] N. C. Yi Lim et al., "Review of Temperature and Humidity Impacts on RF Signals," 2020 13th International UNIMAS Engineering Conference (EnCon), Kota Samarahan, Malaysia, 2020, pp. 1-8, doi: 10.1109/EnCon51501.2020.9299327.

Reviewer 2: Comments and Responses

Overall Comments

N/A

Reviewer 2 Comment 1

The introduction is well-written. The author provides a good comparison between wearable strain sensors, including respiratory inductance plethysmography (RIP) and electrical impedance tomography (EIT). However, please briefly explain why NRFR was chosen over other techniques for continuous monitoring.

Author Response: We would like to thank the reviewer for their kind words. NFRF sensors provide a promising alternative to other sensing techniques such as RIP and strain sensors without requiring the use of tension belts across the abdomen, which is cumbersome and may interfere with medical procedures. The belt needs to be fitted to capture the full breathing cycle, maintaining sufficient tension under the minimal perimeter, and thus can be uncomfortable at maximum inhalation. Unlike EIT, NFRF does not require skin-touch electrodes, which can be uncomfortable for long-term wear, especially under heavy perspiration. Thus, although the other modalities have their respective advantages, the proposed study evaluates the feasibility of the NFRF approach in the porcine model to investigate their clinical applicability. We have revised the manuscript in Sec. I and have reproduced our changes below –

"Near-field radio-frequency (NFRF) sensing provides a promising alternative to the above methods, without requiring the use of tension belts across the abdomen or skin-touch electrodes, which are uncomfortable and not suitable for long-term wear, especially under heavy perspiration."

Reviewer 2 Comment 2

In the experimental section, it is mentioned that separate computers were used for measurements with the spirometer and NRFR sensors, resulting in different time stamps. Please provide a detailed explanation of how data synchronization was performed for subsequent analysis.

Author Response: Thank you for highlighting this concern. The NFRF sensor data were acquired using a custom LabView program, which stores base timestamp for each recorded data file. Spirometer data was recorded using ICULab software which recorded initial time stamps for each file. For each set of measurements, data files contained relative time stamp values along with measured data. The two data streams were synchronized by aligning time stamps with respect to each other. While this suffices as an initial synchronization step, it may leave ambiguity owing to small offsets in between the system clocks themselves. Empirically, we observed a difference up to 10 seconds between the two systems, providing an initial estimate for correction. A secondary verification of synchronization was performed by comparing clinical annotations and ventilation pause epochs recorded parallelly in ICULab and LabView, resulting in minor adjustments for the time offset between the two data streams. In response to this comment, we have augmented the description of data synchronization in Sec. II.C to better clarify our methodology, reproduced below –

"Spirometer (NM3 monitor; Respironics Inc.) and NFRF sensors were controlled using two different computers running ICULab (KleisTEK Advanced Electronic Systems) and a custom LabView (National Instruments Corp.) program, respectively. The two data streams were synchronized by aligning recorded time stamps. A subsequent synchronization validation step was performed by aligning clinical annotations and epochs of ventilatory pauses within a 10 second window, yielding precise data stream alignment to under 0.1s."

Reviewer 2 Comment 3

For Figure 2, please include an illustration of the actual experimental setup along with the schematic.

Author Response: The manuscript has been modified with a perspective schematic in Fig. 2, which better illustrates the experimental setup, along with the arrangement of various instruments in the procedure room. We would like to apologize for being unable to show a picture of the actual experimental setup in the procedure room. Displaying pictures of the animal under invasive experimental study violates the IACUC requirements. This regulation means to avoid hints of animal cruelty and respect animal rights.

Reviewer 2 Comment 4

In Figure 6, include the standard deviation for the average of the five overlaying breaths to provide additional context.

Author Response: We thank the reviewer for this comment. In order to quantify the deviation of the five overlaying breaths with their mean waveform, each of which are vectors of length 1000, we compute the average MAPE among the individual breaths and the average waveform. We have modified Fig. 6 with the mean RMSE values and have modified the figure caption to better provide context, reproduced below –

"**Fig. 6. Time-domain signal visualization:** Synchronized NFRF and Spirometry signals were segmented, and an average signal template was generated by overlaying 5 consecutive breaths, showing an average RMSE of 1.86% and 4.89% among the individual breaths and the average signal template respectively."

Reviewer 2 Comment 5

In the Results section, please quantify the agreement between the baseline performance of the NRFR and the ground truth.

Author Response: Among the various methods of quantifying sensor performance, Bland-Altman plots have a long history of use, especially in biomedical applications, wherein differences of the proposed and reference sensors are plotted with respect to the mean. In Fig. 7(a), we highlight the performance of the NFRF sensors which show a mean difference of 17.63±53.65 mL with the spirometer measurements across all stages of the tidal volume intervention. During the study, lung tidal volumes are varied from 150 mL to 640 mL using mechanical ventilation, highlighting the low bias of NFRF sensors across a wide range of tidal

volumes. We further quantify the performance of the NFRF sensing system using a correlation plot in Fig. 7(b) where NFRF tidal volume estimates show an average correlation coefficient of 0.92 with reference spirometer and a mean average percentage error (MAPE) of 9.18%, which is within the limits of acceptable error for human clinical applications, typically at 15% MAPE [41][42]. We hope our modifications to the manuscript in Sec. IV.A will be satisfactory.

Reviewer 2 Comment 6

In the Results section B, clarify how the calibration scheme in Equation 10 was modified to use only the left and right channels for estimating tidal volumes for the left and right lungs, respectively.

Author Response: The reviewer is correct to note that the left and right channels were used for estimating tidal volumes for the left and right lungs, respectively. The NFRF sensors are placed laterally across the chest, with one antenna pair on the left side of the chest and the other antenna pair on the right side of the chest of the porcine model. Each channel is individually calibrated with respect to the reference spirometer, as highlighted in Eqs. 8 and 9, and combined using a suitable quality weighting factor to obtain an overall tidal volume estimate using Eq. 10. For detecting lung obstruction, we modify Eq. 10 to combine only channels associated with the left antenna pair to estimate for the left lung tidal volume, and vice versa for the right lung tidal volume. We have added this clarification in Results section B, reproduced below:

"NFRF sensors were placed laterally across the chest, as shown in Fig. 2, with one antenna pair on the left side of the chest and the other antenna pair on the right side, which ensured localized coupling for each antenna pair to the motion of the nearest lung. Every NFRF channel was individually calibrated to the reference spirometer before the start of the procedure, using Eq. 8. However, instead of using all channels to evaluate the overall tidal volume, we modified Eq. 10 to combine channels corresponding to the left antenna pair for left lung tidal volume, and vice versa for the right lung tidal volume."

Reviewer 2 Comment 7

How accurately does the proposed dual-band NRFR sensor capture unbiased lung tidal volumes? Please quantify the agreement with the gold-standard spirometer to provide a clear comparison.

Author Response: Please also see the Reviewer 2 Comment 5. The bias of the proposed NFRF sensor is quantified by the Bland-Altman plot shown in Fig. 7(a). After calibration with the spirometer, NFRF estimates for tidal volumes show an average mean offset of 17.63±53.65 mL with respect to the spirometer measurement, which is within acceptable limits for human clinical applications.