# The internal–external respiratory motion correlation is unaffected by audiovisual biofeedback

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Abstract

This study evaluated if an audiovisual (AV) biofeedback causes variation in the level of external and internal correlation due to its interactive intervention in natural breathing. The internal (diaphragm) and external (abdominal wall) respiratory motion signals of 15 healthy human subjects under AV biofeedback and free breathing (FB) were analyzed and measures of correlation and regularity taken. Regularity metrics (root mean square error and spectral power dispersion metric) were obtained and the correlation between these metrics and the internal and external correlation was investigated. For FB and AV biofeedback assisted breathing the mean correlations found between internal and external respiratory motion were 0.96 ± 0.02 and 0.96 ± 0.03, respectively. This means there is no evidence to suggest ($p$-value = 0.88) any difference in the correlation between internal and external respiratory motion with the use of AV biofeedback. Our results confirmed the hypothesis that the internal–external correlation with AV biofeedback is the same as for free breathing. Should this correlation be maintained for patients, AV biofeedback can be implemented in the clinic with confidence as regularity improvements using AV biofeedback with an external signal will be reflected in increased internal motion regularity.

## Introduction

During lung cancer radiotherapy the planning target volume (PTV) must be made sufficiently large to encompass the clinical target volume (CTV) with enough margin such that tumor movement can be accommodated [1]. Due to respiratory motion there can be significant cyclic movement of a lung CTV, with its magnitude and consistency depending on: (a) tumor location within the lung; (b) subject-specific anatomy; and (c) subject behavior (e.g. ability to maintain a consistent breathing pattern) [2].

In order to reduce the required margins for the PTV, thereby minimizing the radiation dose to surrounding healthy tissue and making treatment more efficient, it would be desirable if some method could be developed for regulating and/or predicting this internal motion [3, 4]. Knowledge of how a tumor's location changes with time—both during one breathing cycle, and from one breathing cycle to the next over a protracted period of radiotherapy—would be invaluable in this regard. Measurements of respiratory-related internal motion of patient, however, are difficult to perform and also invasive in current clinical practice, so in many circumstances would be difficult to justify [5]. Various external techniques have therefore been pursued, the fundamental premise of which is that internal organ motion and external abdominal wall motion can be correlated with an acceptable level of accuracy.

One such technique to assist breathing regularity is audiovisual (AV) biofeedback [6, 7, 8], which relies on information regarding subject-specific external motion based on data acquired from a respiratory signal. This information is then used to create a breathing waveguide tailored to each subject, which can be followed in real time by the subject during radiotherapy. An infrared camera and external abdominal wall marker are used to show human subjects the current location of the abdominal wall, enabling self-regulation of breathing movements as they attempt to keep the marker position and waveguide aligned on a monitor screen. In addition to the external motion management, Kim et al. [9] have reported that AV biofeedback has been shown to reduce diaphragm motion irregularities in displacement and period by 46 and 81 %, respectively.

In clinical practice, techniques such as respiratory gating rely on good correlation between respiratory motion and external patient markers [10, 11], which has been shown to depend on individual patients. Some previous studies reported difficulties in achieving this due to a number of factors, including short term variability in phase relationships, despite average phase differences being removed and baseline shifts [2, 12]. Moreover, the respiratory guidance can cause further variation in the level of external and internal correlation because of its interactive intervention introduced to natural breathing. For instance, when using AV biofeedback subjects are encouraged only to follow a motion trace based on external behavior, which for some subjects may be intentionally achieved by movement of the abdominal wall independent of breathing cycle, resulting in a poor internal–external motion correlation. Examining this potential degradation of motion correlation with/without respiratory guidance is the focus for this work, which previously has not been fully investigated. If the level of external and internal correlation with AV biofeedback is maintained compared to that of free breathing, AV biofeedback can be implemented in the clinic with confidence as regularity improvements using AV biofeedback with an external signal will be reflected in increased internal motion regularity.

## Methods

### Data acquisition

The data for the current study was taken from fifteen healthy human subjects, recruited for two MRI sessions each as described in a previous study by Kim et al. [9]. Subjects were of ages 19–53, with a mean age of 31 years. Each subject performed two trials of (1) free breathing (FB), and (2) AV biofeedback assisted breathing. The order of the trials was alternated between FB and AV biofeedback. During an AV biofeedback session, the visual component involved a patient-specific visual guiding wave determined from patient's breathing pattern and a red ball moving up and down representing current abdominal position. Matching the red ball with the guiding wave on the screen, each patient can adjust their breathing in amplitude and period. Simultaneously, the audio component used a continuous classical music which had its tempo adjusted to encourage patients to adjust their breathing if the red ball deviated more than 15 % from the guiding wave.

One-dimensional internal displacement versus time data sets of the superior–inferior motion of the subject's diaphragm were measured from a series of 2D MRI images acquired using a 3 Tesla GE MRI scanner. The internal motion data were compared with external marker measurements taken by use of the Varian real-time position management (RPM) system. Internal diaphragm measurements were made using a fast-2D gradient recalled echo (fGRE) magnetic resonance pulse sequence at 196 ms per frame, whilst the RPM system measured external displacement at a frequency of 30 Hz. The internal and external signals were synchronized in situ with a respiratory bellows belt by direct signal matching [9].

### Analysis

Each of the fifteen human subjects were trialed on two different days, making a total of 30 studies from which 220 data sets were acquired, each corresponding to a session lasting approximately 100 s. The internal (diaphragm) and external (abdominal wall surface) measurements were then analyzed. The data sets had their overall mean phase shifts removed (over all data sets, in seconds, mean phase shift = −0.18, minimum = −0.38, maximum = 0.11, σ = 0.07), which were attributed primarily to experimental setup (specifically the timing of data acquisition commencement). The external measurements were then re-sampled to the lower frequency (196 ms sampling) to ensure both sets ran on the same time scale. The data sets were then compared with a linear fit, as well as Pearson's R-value (correlating each external cycle with its internal counterpart), the Spearman correlation coefficient, root mean square error (RMSE) in displacement and spectral power dispersion metric (SPDM) [9]. RMSE values arise by comparing the subject's diaphragm and abdominal wall movements to their average wave form found via Fourier analysis, and the SPDM metric is the second moment about the mean frequency in the frequency spectrum for a data set (scaled by fundamental frequency), a measurement of spectral complexity [13].

## Results

### Correlation between measurements of internal and external motions

For each data set the Pearson's R correlation between the external marker motion and the internal diaphragm motion over the 100 s trial length was computed. From the data two populations of correlations for FB and AV biofeedback-assisted breathing were obtained, which were compared using a Student's *t*-test and the Mann–Whitney U test [14]. Figure 1shows the distribution of these data sets. Mean Pearson's R correlations are 0.96 ± 0.02 and 0.96 ± 0.03 for FB and AV respectively. The two-sample *p*-value is 0.88, not significant at the 5 % level, and Mann–Whitney U value is 0.059. The alternative Spearman's correlation of breathing patterns gives mean 0.93 ± 0.04 and 0.95 ± 0.04 for FB and AV respectively with *p*and U values both <0.001. The Shapiro–Wilk test for normality returns values of <0.001 for both data sets, indicating the unlikelihood of normally distributed data, hence lending greater weight to the U test value.

Individual data sets demonstrate similarities in correlation between AV biofeedback and FB (Fig. 2). We see a <1 % difference in correlation strength at the 25 and 75 % (ranked by correlation) levels between AV and free breathing traces, a result of the similar distributions of correlations as in Fig. 1.

As demonstrated in Fig. 3 minimal correlation is found between the RMSE in displacement and the internal versus external correlation for both AV biofeedback (R = −0.33), whilst less is present for FB (R = 0.076). We also notice the significant separation between the two data sets, with the values for AV biofeedback presenting a decreased RMSE.

The correlations for the SPDM metric are weak, achieving R values of −0.0633 and −0.0471 for FB and AV biofeedback respectively.

## Discussion

The purpose of this study was to test the hypothesis that the internal–external correlation with AV biofeedback is the same as for free breathing which previously had not been investigated. Our results, acquired from an analysis of 15 human subjects, confirmed this hypothesis. We also found that breathing regularity measures do not correlate strongly with internal–external similarity.

Previous studies have indicated that AV biofeedback can result in significant reductions in the variability of both the period and the amplitude of a subject's breathing pattern [2, 6, 9, 15, 16]. An average improvement of 38 % has been seen in the RMSE in displacement, 82 % in the RMSE in Period, and 44 % in the baseline drift for individual breathing traces [9]. This, as the main goal of AV biofeedback, supports the case for it being a viable clinical technique, with its proper implementation likely to result in a marked decrease in residual organ motion. We have then gone on to show that this improvement in regularity does not come at the cost of poor internal–external motion correlation. This result means that image guidance methods that combine internal and external motion, such as the Cyberknife Synchrony (Accuray, Sunnyvale), ExacTrac (BrainLab, Feldkirchen) and other algorithms under development, e.g. Cho et al. [17] can be combined with the use of AV biofeedback. Furthermore, the implementation of AV biofeedback should not be detrimental to the operation of internal–external motion prediction algorithms.

This study's intent did not encompass any quantification by how much AV biofeedback could reduce organ motion and its variability, and hence the PTV, however previous studies [2] have demonstrated that even simplistic AV biofeedback mechanisms can reduce superior-inferior CTV–PTV margins from 1.1 to 0.8 [2], which could be further improved using the system.

With decreases in organ motion displacement variability, as measured by RMSE, our results demonstrate weak correlations between this value and the correlation of a subject's internal (diaphragm) and external (abdominal wall marker) motion. This supports the major result that there is no difference between free breathing and AV biofeedback in terms of internal–external correlation: should the internal–external correlation correlate strongly with RMSE, given that this metric has previously been shown to improve under AV biofeedback [9] there would therefore be an improved internal–external correlation associated with AV biofeedback.

In the case of the SPDM, this metric was found to display little evidence for correlation between internal and external motions on all data sets. The SPDM is derived via Fourier analysis, and renders a quantification of the spread of a signal's spectrum (e.g. the distribution of different periods or frequencies); large values correspond to a widely-spread spectrum, making it akin to a calculation of the spread of the breathing period distribution for a given subject in a given measurement session. Again, the lack of correlation supports our hypothesis that there is no change in internal–external correlation coupled with the use of AV biofeedback.

The possibility of weaker correlation under AV biofeedback use is brought about by the nature of the technique, as it solely requires the patient to bring their external motion into line with a set wave guide. Such a technique allows, and may even encourage, the patient to subconsciously move their abdominal wall out of synchronization with their breathing in order to stay on the waveguide. If this is done the benefits of AV biofeedback are reduced, as even though external motion is being regulated the internal motion can become less consistent.

With consistently good correlation, improvements in external motion regularity under AV biofeedback are translated to internal motion regularity, allowing confident use of this technique coupled only with measurements taken of a subject's abdominal motion. In future studies of the effectiveness of AV biofeedback and its derivatives only external measurements need be taken for study, as it is demonstrated herein that they correlate strongly with the internal motion the technique aims to regulate.

If internal–external correlation is reduced, predictions of given external readings also become less accurate, as one can no longer rely on these two motions proceeding coherently.

Since we have only studied the correlation between abdominal wall and diaphragm motion, in order to extend these predictions in such a way to cover lung tumor motion we require one major fundamental assumption, that the diaphragm is an accurate surrogate for lung tumor motion [18].

Previous studies have found the mean abdominal wall-diaphragm R correlation value observed for individual sessions to be 0.82–0.95 [2]. Our value of 0.96 compares favorably, with differences in our study likely being due to the use of healthy volunteers, whereas that done by Vedam et al. [2] was performed on lung cancer patients possessing a range of possible breathing difficulties.

With reliable correlation between internal and external motion comes the possibility of making real-time predictions of internal behavior using external measurements and a range of possible prediction algorithms [19, 20, 21] which although less accurate than image-guided radiotherapy do not increase radiation dose due to additional scanning being required [22]. As AV biofeedback has been shown to have no detrimental effect on correlation, whilst improving breathing regularity, should internal motion prediction be clinically desired it seems reasonable that AV biofeedback should be used in conjunction: consistent motion with minimal cycle-to-cycle variation allows accurate prediction, which can then be correlated to internal movements. In addition, if a breathing prediction method is going to be used external measurements of the subject using the respiratory monitoring system are necessary, and this represents most of the equipment required for AV biofeedback, the only additional requirement being a monitor to show the measurements being used by the prediction algorithm, so AV biofeedback use would be a logical next step.

A number of limitations already identified in the execution of this study could be rectified by future work. Use of patient volunteers rather than healthy subjects would provide more realistic circumstances for internal–external motion correlation, and would better test the usability of the AV biofeedback system. Should this be done, tumor rather than diaphragm motion could be tracked (as investigated in previous studies [23]), for this is the eventual area of interest, and is currently being assumed to correlate with diaphragm motion.

## Conclusion

In this study we have demonstrated that the improvements in breathing regularity obtained with AV biofeedback use, do not result in a decline in the correlation between a subject's internal (diaphragm) and external (abdominal wall) motions. This allows the application of AV biofeedback in clinical processes with confidence that regularity improvements appear in both internal and external motion, as well as allowing usage of only external motion observation in future studies of AV biofeedback.

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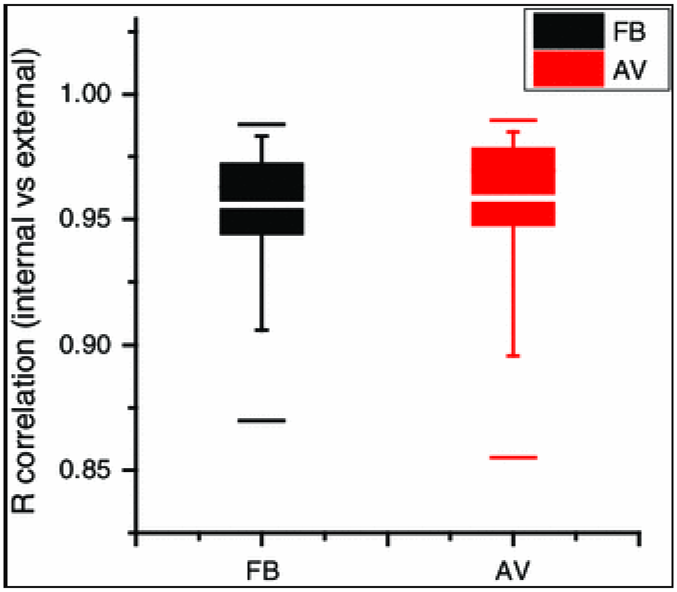


**Fig. 1**

*Box plot* comparing mean correlations for FB and AV. The *central white line* designates the mean, *boxes* cover 25/75 % of the data range, *whiskers* extend to 5/95 % and *markers* designate maximum and minimum values. *FB* free breathing, *AV* AV biofeedback

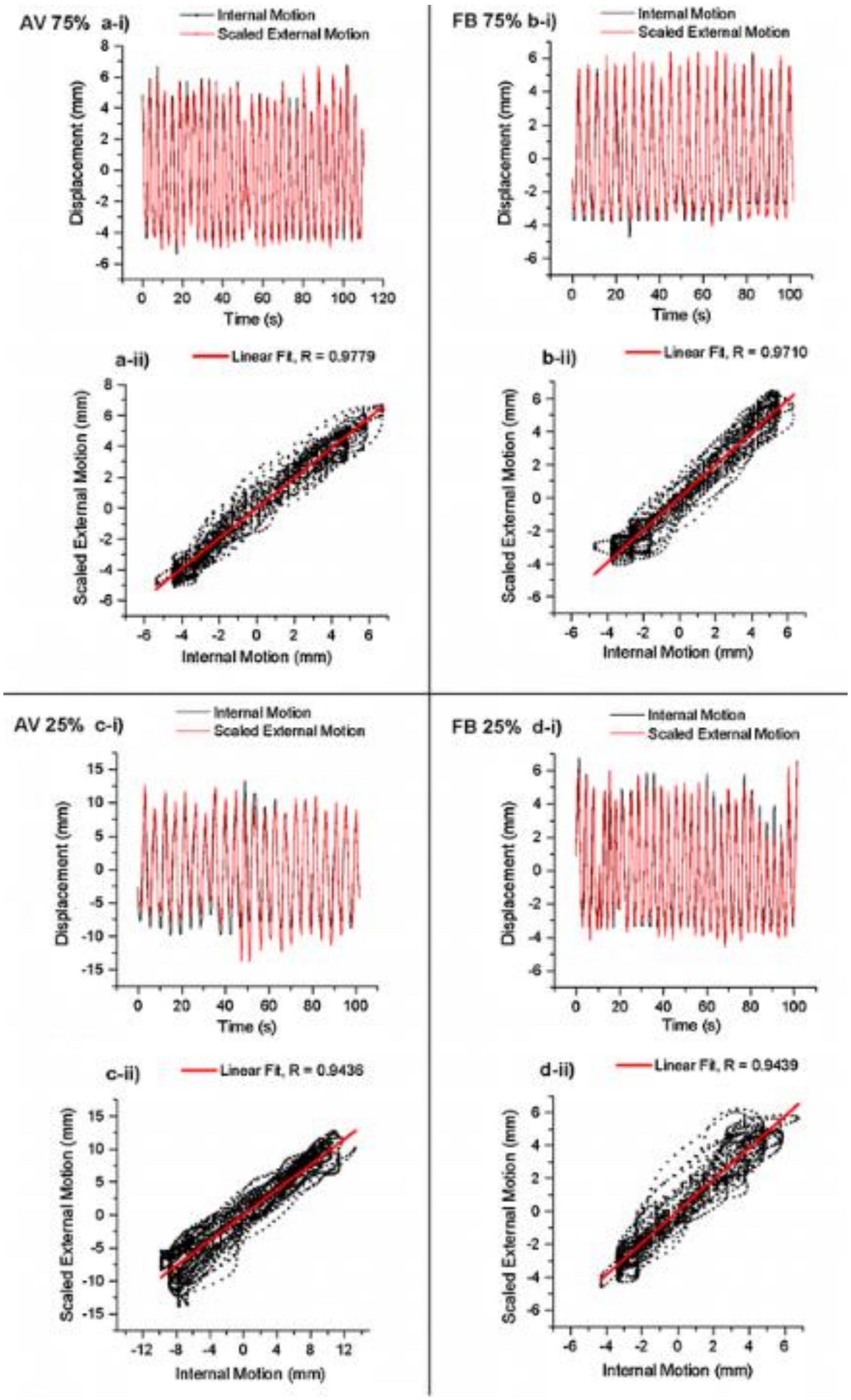


**Fig. 2**

Breathing traces (**i**) and comparison of internal and external motion over entire breathing session data sets (**ii**). Traces from subjects are ranked by correlation. **a**, **b** 75th % and **c**, **d** and 25th %. *FB*free breathing, *AV* AV biofeedback

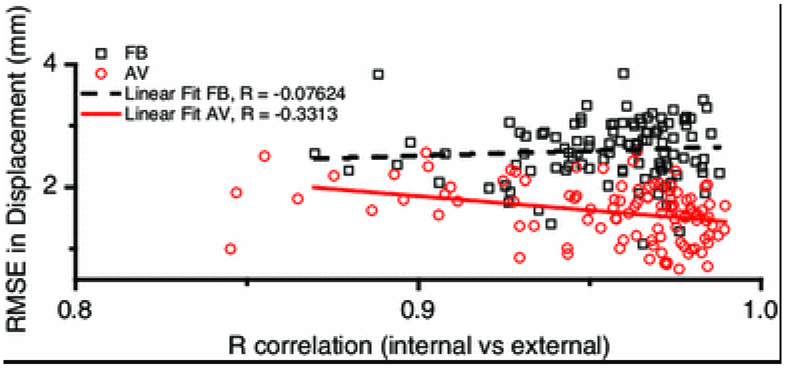


**Fig. 3**

Comparison of correlation with RMSE displacement for FB (*black*) and AV biofeedback (*red*). *FB*free breathing, *AV* AV biofeedback