Impact of audiovisual biofeedback on interfraction respiratory motion reproducibility in liver cancer stereotactic body radiotherapy

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Abstract

Introduction

Irregular breathing motion exacerbates uncertainties throughout a course of radiation therapy. Breathing guidance has demonstrated to improve breathing motion consistency. This was the first clinical implementation of audiovisual biofeedback (AVB) breathing guidance over a course of liver stereotactic body radiotherapy (SBRT) investigating interfraction reproducibility.

Methods

Five liver cancer patients underwent a screening procedure prior to CT sim during which patients underwent breathing conditions (i) AVB, or (ii) free breathing (FB). Whichever breathing condition was more regular was utilised for the patient's subsequent course of SBRT. Respiratory motion was obtained from the Varian respiratory position monitoring (RPM) system (Varian Medical Systems). Breathing motion reproducibility was assessed by the variance of displacement across 10 phase-based respiratory bins over each patient's course of SBRT.

Results

The screening procedure yielded the decision to utilise AVB for three patients and FB for two patients. Over the course of SBRT, AVB significantly improved the relative interfraction motion by 32%, from 22% displacement difference for FB patients to 15% difference for AVB patients. Further to this, AVB facilitated sub-millimetre interfraction reproducibility for two AVB patients.

Conclusion

There was significantly less interfraction motion with AVB than FB. These findings demonstrate that AVB is potentially a valuable tool in ensuring reproducible interfraction motion.

Introduction

Stereotactic body radiotherapy (SBRT) is a high-precision, high-dose irradiation of a lesion in a small number of treatment fractions.[1] SBRT has been incorporated into the treatment of liver cancer due to its demonstrated effectiveness in clinical studies as well as improving survival rate[2, 3] with over 54% of American centres with SBRT capability treating liver cancer patients.[4] Liver tumours are highly mobile due to their proximity to the thoracic diaphragm. When this breathing motion is irregular, it exacerbates systematic and random errors,[5-7] compromising the quality of radiation therapy;[6, 8-11] which is a concern for hypofractionated treatments such as SBRT.

To counter this increase in systematic and random errors due to irregular breathing motion, a number of breathing guidance strategies have been investigated for patients to facilitate stable and reproducible breathing.[12-17] Such breathing guidance strategies have also been investigated with liver cancer patients with demonstrated benefits.[18, 19] A study by Linthout et al.[18] investigated the use of breathing guidance during lung and liver cancer radiotherapy and found that audio visual breathing guidance significantly reduced gated treatment times by 17%. The audiovisual biofeedback system, developed by Venkat et al.,[16] has demonstrated to facilitate regular respiratory motion of external surrogates, the thoracic diaphragm, and lung tumours.[15, 16, 20] However, based on a recently performed systematic review on breathing guidance interventions, only two of the 27 identified articles recruited liver cancer patients.[17] Despite being highly mobile tumours and treated with hypofractionated dose regimes, a gap in the literature exists in terms of investigating the use of breathing guidance with liver cancer patients during radiation treatment.

The objective of this study was to investigate the changes in the reproducibility of respiratory-related motion for liver cancer patients with an audiovisual biofeedback system. This study was also the first to implement a screening procedure prior to CT simulation to ensure that the most regular breathing condition (free breathing or audiovisual biofeedback) was utilised throughout the patient's subsequent course of SBRT.

Methods

The ethics, governance, legal, and regulatory processes were completed prior to the initiation of the clinical trial. The clinical trial was registered with the Australian New Zealand Clinical Trials Registry (ANZCTR), trial ID: ACTRN12613000110785. All five patients were male, had a median age of 59 (range: 53–75), all received 6 fractions of treatment with three patients receiving a prescribed dose of 36 Gy and two receiving 48 Gy. All treatments were based on the departmental SBRT protocol for liver cancers.

Audiovisual biofeedback

The audiovisual biofeedback system, developed by Venkat et al.,[16] utilises audio and visual prompts to facilitate regular and reproducible breathing. The real-time breathing signal is taken from the Real-time Position Management system (RPM, Varian Medical Systems, Palo Alto, USA). The setup of audiovisual biofeedback is shown in Figure 1.

The use of audiovisual biofeedback required the addition of a patient display with the controlling software operated by a radiation therapist. The patient display was held over the patient's head at a comfortable distance by a goose-neck clamp which was mounted to the patient couch.

Study workflow

A screening procedure was performed to ensure that the most regular breathing condition, either (i) free breathing or (ii) audiovisual biofeedback, was utilised throughout the patient's treatment. A training session was performed to familiarise the patient with the audiovisual biofeedback process. The training session involved a brief information video describing the audiovisual biofeedback system and how to follow it, followed by a brief practice session using the audiovisual biofeedback system. After the training session, breathing motion was monitored for

4 minutes for each breathing condition. Determining which breathing condition would be selected was based on the regularity of the 4 minutes of monitored breathing motion, quantified by the root mean square error (RMSE) in displacement;[16] the lower the RMSE value, the more regular the breathing motion. Decisions were made in situ using a RMSE analysis function of the audiovisual biofeedback software.

Computed tomography sim and treatment delivery proceeded as per the currently implemented clinical liver SBRT protocol with the addition of the audiovisual biofeedback setup, as shown in Figure 1, should that be the resultant decision from the screening procedure.

Data analysis

Breathing motion was extracted from the RPM text files. Breathing motion regularity, used in the screening procedure, was quantified as the root mean square error (RMSE) of displacement and period.[15-17, 21, 22] A lower RMSE value is indicative of a more regular respiratory signal. Equations for calculating RMSE are described by Venkat et al. and Pollock et al.[16, 23]

To assess interfraction reproducibility, respiratory displacement data was sorted into ten phase bins from 0% to 90% in 10% increments, as per standard for 4DCT imaging.[24-26] The mean difference of the displacement in each phase bin (m = 10) was compared for each fraction (n = 6) of treatment to the CT sim, normalised by CT sim amplitude (AmpCT), to determine the relative difference between what was planned to motion during treatment, as described by Equation 1.

$$\frac{\frac{1}{n}\sum_{i=1}^{n}\left|\frac{1}{m}\sum_{1}^{m} CT - Fx_{n}^{m}\right|}{Amp_{CT}}$$

Absolute interfraction reproducibility was also assessed by not normalising Equation 1 by AmpCT.

Results

Screening procedure

The screening procedure yielded the decision to utilise audiovisual biofeedback over a course of SBRT for three of the five recruited liver cancer patients while two patients underwent free breathing. Figure 2 shows the respiratory cycles across all patients for their FB and AVB breathing. Note Patient 3 and Patient 5, while the RMSE of these patients' AVB breathing was close to the average RMSE across all AVB patients, the free breathing of Patients 3 and Patient 5 was naturally very regular, more so than AVB. The average RMSE in displacement values across all patients in the screening procedure are given in Table 1.

CT sim and treatment delivery

Data presented here were organised into each individual patient's course of SBRT (CT sim → fraction 6), and mean ± standard deviation values for all audiovisual biofeedback and free breathing patients, respectively, in Figures 3 and 4. For the data presented as boxplots (Fig. 4), the horizontal edges of each box represent the 25th, 50th and 75th percentile values (bottom, middle and top lines of box, respectively). Whiskers represent other points extending out to 1.5 times the interquartile range. Any points beyond the whiskers ('+') are considered outliers.

Figure 3 shows the breathing displacements from the CT sim and each treatment fraction organised into 10 phase bins for patients 1–5. Interfraction motion consistency for the five patents is presented where the breathing signal was organised into 10 phase bins, from 0% to 90% in 10% increments. The displacement data from the phase bins from CT sim were compared to the phase bins from each treatment fraction.

The difference of each fraction of treatment to the CT sim are shown in Figure 4.

Audiovisual biofeedback significantly improved relative interfraction motion consistency by 32% ($P < 0.001$) from an average difference of 22% for free breathing to 15% for audiovisual biofeedback. Audiovisual biofeedback facilitated a non-significant improvement in absolute interfraction motion consistency compared to free breathing. However, as shown in Figure 4b, Patient 2 and Patient 3 produced sub-millimetre interfraction motion consistency through audiovisual biofeedback. While Patient 1 demonstrated good interfraction motion consistency in terms of relative difference, a poorer interfraction motion consistency was observed in terms of the absolute difference. This is because Patient 1 had the largest amplitude of the five patients (see Fig. 3), and therefore, by normalising the respiratory signal by its amplitude, the larger absolute differences corresponded to a lower relative difference.

Discussion

This was the first investigation into the use of breathing guidance during a course of liver SBRT to (i) use an initial screening procedure to ensure the most stable breathing condition is utilised for each patient, and (ii) assess the interfraction breathing motion reproducibility over the entire course of SBRT. For the five patients in this study, the screening procedure yielded the decision to utilise audiovisual biofeedback for three of the five patients. It should be noted that this was not a randomised trial, and by design, patients who did not have regular FB were assigned to AVB (and vice versa).

The mean RMSE in displacement during the screening procedure for audiovisual biofeedback patients in this study was 0.15 cm, comparable to the findings of a previous lung cancer patient audiovisual biofeedback study, which obtained average RMSE in displacement values of 0.14 cm for audiovisual biofeedback patients.[14, 27] Although the free breathing patients in this study yielded an average RMSE in displacement values of 0.17 cm, slightly lower than the RMSE values obtained in a previous cancer patient study (0.20 cm[28]) and either comparable to or less regular than RMSE values yielded in previous healthy volunteer studies (0.13 cm[15] and 0.16 cm[16]).

A significant improvement in interfraction motion reproducibility was observed from the use of audiovisual biofeedback, with 32% more agreement between respiratory motion during each treatment fraction and CT sim. It should be noted that the respiratory signal from the real-time position management (RPM) is an external surrogate and that good agreement of RPM as described in this study does not necessarily mean good agreement of anatomy although it may be a reasonable surrogate. This demonstrates that audiovisual biofeedback could be a useful tool in maintaining consistent interfraction breathing motion, minimising the deviation in respiratory motion from what was planned in CT sim to each treatment fraction, provided that respiratory amplitude does not exceed that of free breathing.

In conclusion, this was the first clinical implementation of audiovisual biofeedback utilising a screening procedure to ensure regular breathing is produced during the subsequent course of liver SBRT in addition to assessing interfraction breathing reproducibility. This screening procedure yielded the decision to utilise audiovisual biofeedback over a course of SBRT in 3/5 patients recruited into this study, with the other two patients receiving their SBRT under free breathing conditions. Audiovisual biofeedback improved the interfraction motion consistency over free breathing, demonstrating improved agreement between CT sim and treatment fraction respiratory motion. These findings demonstrate the effectiveness of audiovisual biofeedback as a potential tool in facilitating reproducible respiratory motion between CT sim and treatment delivery.

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Table 1. Screening procedure average ± STD RMSE values for audiovisual biofeedback and free breathing across all patients

RMSE in displacement		
Free breathing (cm)	**Audiovisual biofeedback (cm)**	**Improvement due to audiovisual biofeedback**
0.17 ± 0.09	0.15 ± 0.08	11% (*P* = 0.6)
RMSE in period		
Free breathing (s)	**Audiovisual biofeedback (s)**	**Improvement due to audiovisual biofeedback**
0.85 ± 0.46	0.56 ± 0.22	34% (*P* = 0.2)

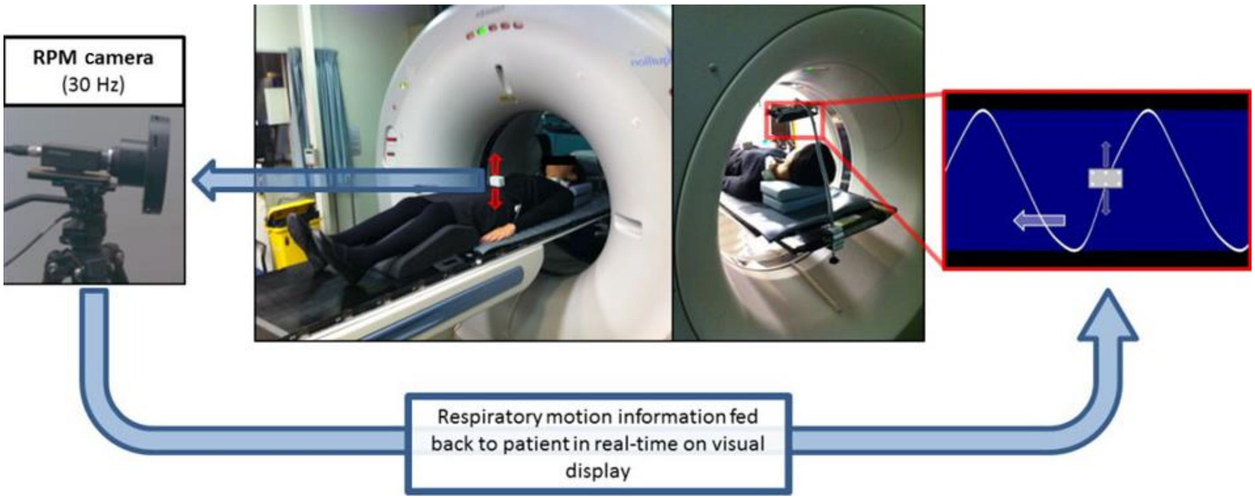

Figure 1. Study setup in CT sim room; biofeedback loop indicated with the RPM camera monitoring respiratory motion and displaying this respiratory motion to the patient in real time.

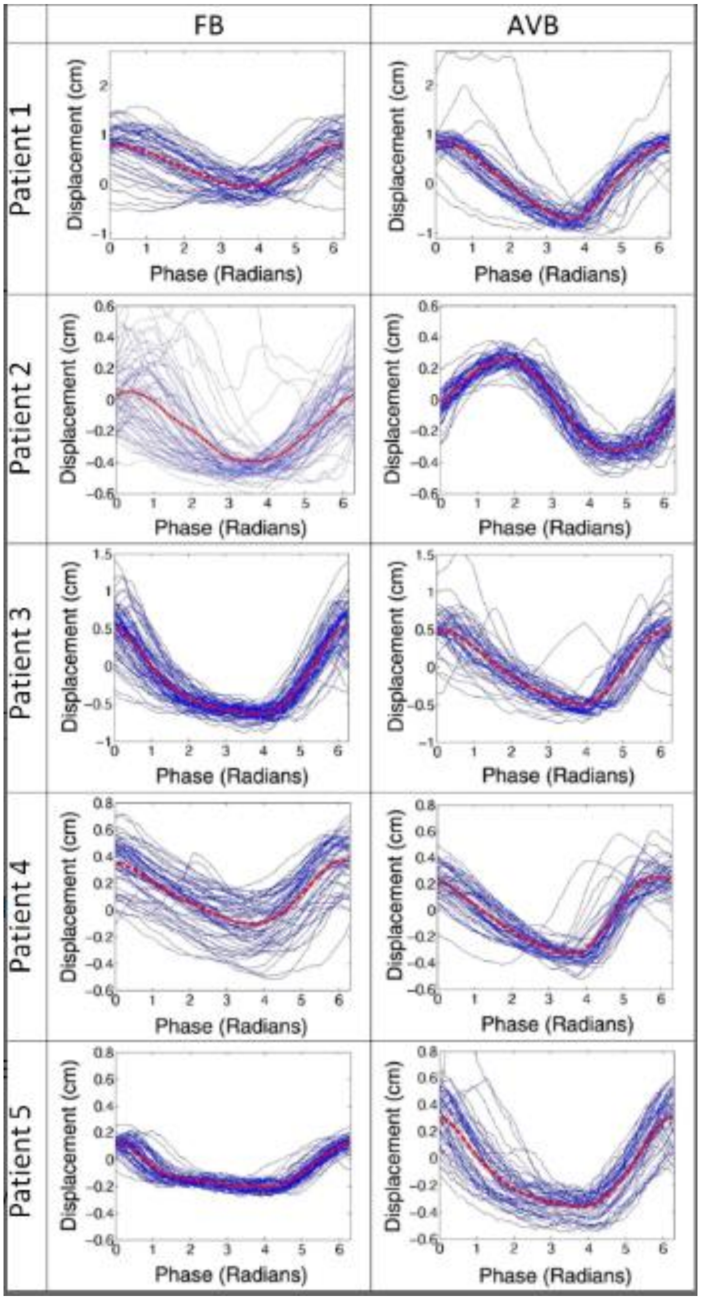

Figure 2. Plots of individual respiration cycles blue curves for each of the five patients' FB breathing left and AVB breathing right in the screening procedure. Average respiratory cycle indicated as the red dotted curve.

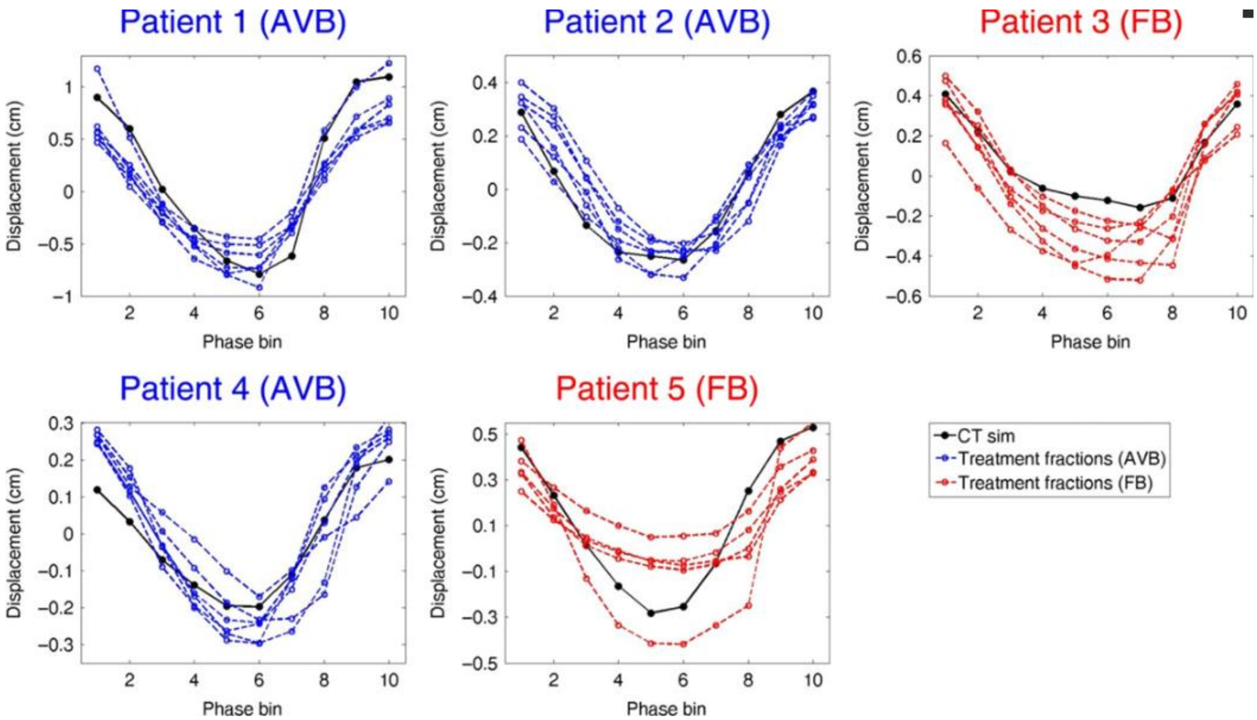

Figure 3. Breathing displacements organised into 10 phase bins for breathing motion during CT sim black line, filled markers and each fraction of treatment coloured line, hollow markers for free breathing red and audiovisual biofeedback blue patients.

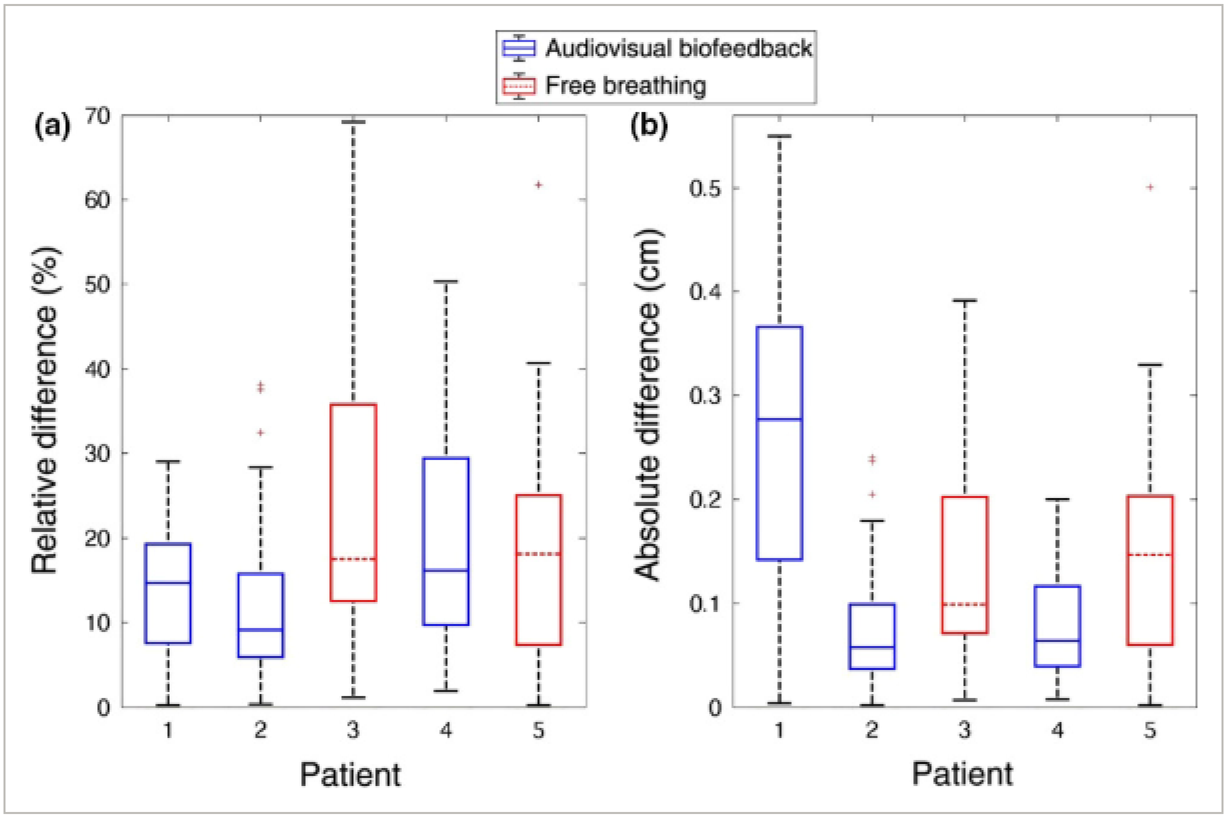

Figure 4. Average (a) relative difference, and (b) absolute difference between CT sim phase bins and the each fraction of treatment phase bins. Free breathing patients shown as red, audiovisual biofeedback patients shown as blue.