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Short Communication

Intrapulmonary percussive ventilation leading to 20-minutes breath-hold potentially useful for radiation treatments

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ABSTRACT

We developed a training protocol based on Intrapulmonary Percussive Ventilation in order to prolong breath-hold while nearly suppressing the thorax motion. This protocol allowed ten subjects to achieve a 20-minutes-breath-hold, while reducing the residual surface motion to 1 mm around its mean position for more than 95% of the breath-hold duration.

Gating techniques have been developed to overcome breathing-related tumour motion uncertainties during irradiation. In this technique, the treatment is divided in multiple short beams solely delivered during selected phases of the breathing cycle. Deep-inspiration breath-hold (DIBH) is a technique in which the treatment is delivered during the end-inspiratory plateau and which advantageously combines motion suppression with better heart spearing (for left breast irradiation) or better lung sparing thanks to pulmonary inflation [1–3]. However, DIBH is limited by the 20–60 s duration of voluntary apnea [4,5]. This is especially an issue while considering complex treatments that last for more than 10 min due to image-guidance, intensity-modulated radiation therapy or proton therapy. Complex treatments thus require several repeated breath-holds and faced reproducibility issues. Several non-invasive approaches have already been explored to prolong breath-hold duration (Jet ventilation, prolonged breath-hold with mechanical ventilation, high frequency percussive ventilation) [6–13]. In this study, we investigated another technique to prolong breath-hold in unsedated subjects, based on a common and non-invasive Intrapulmonary Percussive Ventilation (IPV) device (Pegaso A-Cough Perc). Our aim was to develop a standardised and simple training protocol to achieve easy and prolonged breath-holds (>10 min) all the while nearly suppressing thorax motion. This is indeed an essential step before considering the clinical implementation of such technique for radiation treatments of mobile tumours.

Materials and methods

This study was approved by the Institutional Medical Ethics Committee (B403201732715) and registered in Clinical Trials (NCT03226925).

Participants

Healthy volunteers, aged from 18 to 50 years, were recruited. They signed a written informed consent form in accordance with the Declaration of Helsinki and the current guidelines for Clinical Good Practice. Exclusion criteria included any apnea diving experience, previous use of an IPV device, recent respiratory infection

Abbreviations: IPV, intrapulmonary percussive ventilation; BHPV, breath-hold-percussive-ventilation; FiO_2, Fraction of Inspired Oxygen; I/E, inspiratory-expiratory ratio; ppm, percussions per minute; 10min-BHPV, breath-hold-percussive-ventilation during 10 min; 1min-BHPV, breath-hold combined to IPV of 1 min; S1, first training session; SC, Subjects' comfort; Sci, Subjects' comfort after the first 1min-BHPV; SCf, Subjects' comfort after the final BHPV.

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(<1 month) and any chronic cardiac or respiratory disease. Additional exclusion criteria were linked to the limitations of IPV [14–16].

Materials and settings

IPV was performed through the use of a Pegaso device (Pegaso A-Cough Perc, DIMA Italia, Italy) in percussion mode with a mouth interface connexion (Oracle 452, Fisher & Paykel Healthcare, New Zealand). During the breath-hold combined to IPV (breath-hold-percussive-ventilation, BHPV), the volunteers were conscious, non-sedated, non-intubated and breathing ambient air (FiO_2 21%). To avoid dry throat sensation, the IPV device was connected to a heated humidifier (MR850, Fisher & Paykel Healthcare, New Zealand). Following the recommendations of Dellamonica et al., the humidifier was placed on the circuit, downstream of the IPV device (Fig. 1) [17].

Design and outcomes

The training protocol was divided into different sessions repeated over different days (Supplement 1).

Training sessions

Volunteers underwent at least 3 training sessions of 30 min in order to get used to the IPV, to personalize the BHPV settings to maximize comfort, and to achieve a BHPV of 10 min (10 min-BHPV). If necessary, additional sessions could be proposed until achievement of a 10 min-BHPV. Medical parameters (pulse oximetry (SpO_2) and heart rate (HR)) were continuously monitored using a finger pulse oximeter (Onyx, Nonin, USA).

Assessment session

After these training sessions, volunteers were installed in a pseudo-treatment position (supine position with arms above the head) and were asked to perform a final BHPV. This final BHPV had to last at least 10 min but could be prolonged up to 20 min if spontaneous resumption of breathing had not occurred in the meantime. During this final BHPV, the residual thoracic motion was tracked and measured using an optical tracking system (GateCT, VisionRT, London, UK) with an infra-red surface camera focusing on a point close to the xiphoid process [18,19]. The respiratory trace obtained with VisionRT expressed the average displacement of the tracked point over time. Stabilisation time (time to obtain a stabilized tracked position) and stable phase duration (period for which tracked posistion is stable) were recorded (Fig. 2). Motion deviations were expressed in millimetre around the mean position during the stable phase (average of all maximal and minimal positions) and expressed in percentage (%) of the total duration of the stable phase.

Comfort assessment

Subjects' comfort (SC) was evaluated after a first BHPV of 1 min (1 min-BHPV) performed during the first training session (SCi) and compared to the comfort level obtained after the final BHPV (SCf). Comfort was evaluated based on a self-assessment numeric scale graduated from 0 (“maximum comfort”) to 10 (“total discomfort”) [20].

Statistical analysis

Statistical tests were performed using SPSS 25.0 for Windows (IBM corp., USA). Parametric or non-parametric tests were used to compare the data generated according to normality. A p-value lower than 0.05 was considered statistically significant.

Results

Ten subjects (5 women and 5 men, 21.6 ± 2.1 years) were recruited. Four subjects achieved the 10 min-BHPV goal after 3 training sessions, and 6 subjects required an additional training session. After BHPV settings adjustment, the average IPV settings were: mean percussion frequency of 99 ± 12 ppm; median I/E of 1.5/1.0; mean airway pressure of 37 ± 5 cmH_2O.

During all sessions, neither SpO_2 nor HR changed. At breakpoint, none of the subjects was distressed, nor experienced disturbed breathing. The mean comfort score significantly changed after settings adjustment with SCi and SCf scores of 5.7 ± 1.6 and 1.6 ± 0.9, respectively (71.9% improvement of mean SC).

All the subjects were able to perform a final BHPV of 20 min. Of these 20 min-BHPV, the mean time necessary to get a stable phase was 2.1 ± 3.3 min but seven out of 10 volunteers had a stabilization time shorter than 0.6 min. The mean stable phase lasted for 16.6 ± 5.5 min. In seven out of 10 volunteers, the motion deviations were small with only 1 mm around the mean position (Supplement 2).

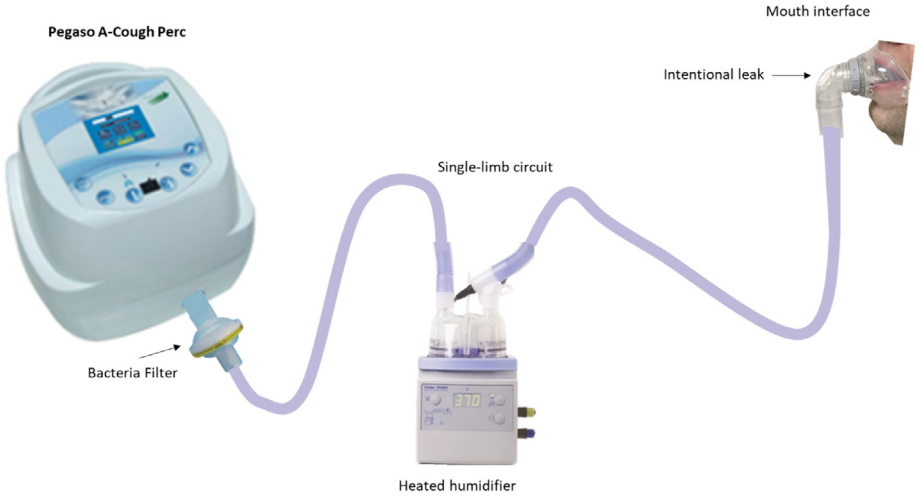

Fig. 1. Illustration of circuit and humification coupled with intrapulmonary percissive ventilation.

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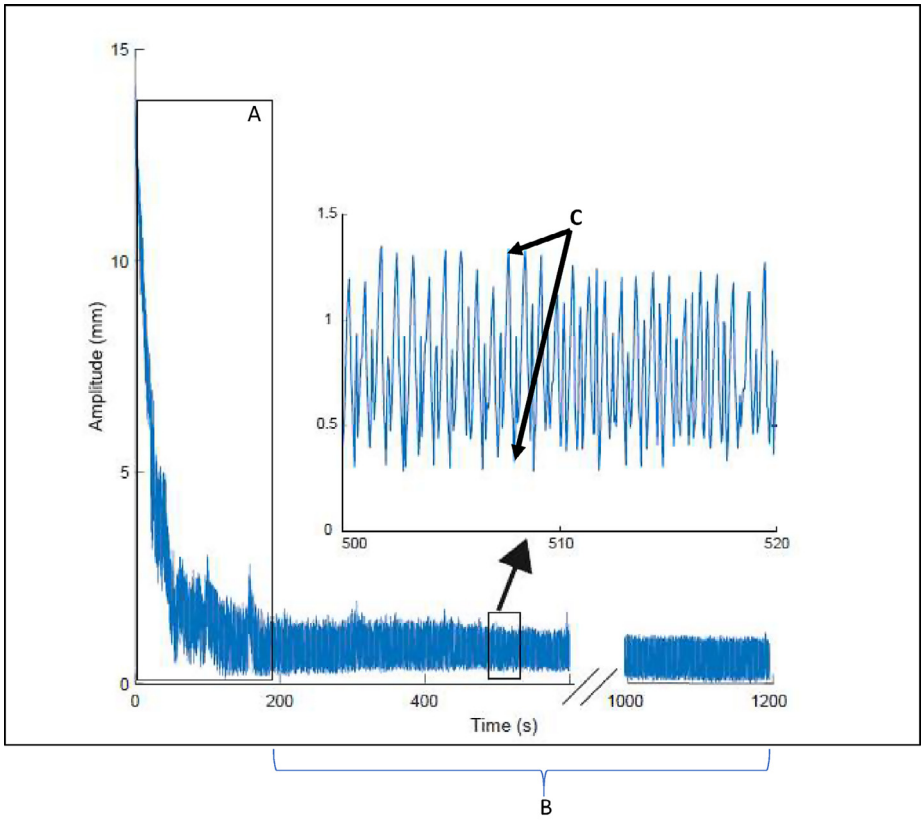

Fig. 2. Displacement of the tracked point obtained with VisionRT.

Discussion

This study demonstrates that healthy subjects could easily and safely achieve a prolonged breath-hold thanks to a common IPV device. All the subjects reached the maximal duration of 20 min. These good results reflect a good combination of settings adjustments, therapeutic education and training sessions. The significant changes in the SC assessment scores (71.9% improvement of mean SC) confirm indeed that the BHPV settings adjustments played a key role in subject's comfort.

Our protocol is characterized by a minimum of 3 training sessions before the final assessment session. This allowed a good familiarization with the technique and a reduction of the stress induced by this kind of procedure. Considering that only one additional session was required for six volunteers, we believe that this training protocol was appropriate.

Compared to most of the previous published data, our 20 min-BHPV duration is longer than the breath-hold technique proposed by Parkes et al. (5.3 ± 0.2 min), although our results are not completely comparable as the used methodology differs [10,11]. Our BHPV durations were also longer than the results obtained by Peguret et al. who used a non-invasive approach based on modified Jet Ventilation (7.6 min) and Prior et al. who used a non-invasive high frequency percussive ventilation approach (11.6 min) [8,9]. Our results are similar to those of Ogna et al., where apnea-like breath hold lasted from 11.3 to 20.0 min [7].

Percussions settings were also different in our protocol. Our mean percussion frequency was 99 ± 12 ppm, whereas Peguret et al. used a 250 up to 600 ppm percussion frequency [7–9]. Our settings were indeed lower in order to favour ventilation through increased pressure and decreased frequency keeping in mind that smaller diaphragmatic motion is observed when the frequency is increased [16]. In a preliminary trial testing BHPV during 10 and 20 min, we assessed $PtcCO_2$ in two subjects and we observed similar changes in $PtcCO_2$ than previous studies [7,8]. As such, we did not monitor this parameter in this trial since the measurement of $PtcCO_2$ was an additional constraint for subjects.

It is important to highlight that no additional O2 or preparatory phases were required during this trial. The non-invasive technique developed by Parkes et al. relies on hypocapnia consecutive to a preparatory phase with non-invasive mechanical hyperventilation and hyperoxygenation with FiO_2 at 60%. This enabled spontaneous prolonged breath-holds lasting for more than 5 minutes after training sessions [10,11]. Peguret et al. obtained prolonged breath-holds in healthy volunteers and patients treated for thoracic tumours with a modified HFPV technique and also the use of hyperoxygenation (FiO_2 100%) [6–9]. However, these techniques might not be appropriate for patients with severe respiratory comorbidities where induced hypocapnia or hyperoxygenation can be difficult to control. Therefore, our protocol, which does not rely on hyperoxygenation and/or hyperventilation may be easier to implement in clinical practice in radiotherapy, especially for patients with potentially severe pulmonary comorbidities. But obviously this should be addressed in the future with other trials focusing on patients receiving radiotherapy.

Some limitations are however important to address. First, for safety purposes, only healthy subjects took part in this trial. Therefore, it is not possible to extrapolate the results of this study to patients. The home-made algorithm to adapt the IPV settings was also configured for healthy subjects and might need to be further adapted in further studies with patients. Second, results are only based on external motion analyses. The respiratory motion was

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measured by an infrared camera acquiring surface images. These results cannot be compared to the previous studies assessing internal tumour motion during breath-hold/apnea. So far, no good internal-external correlation model allows us to extrapolate our results. Internal motion under BHPV would clearly be of high interest and will be assessed after some MRI-directed device adaptations (tubes adaptation). However, this trial is an important first step that allows us to consider further trials with patients for internal tumour motion assessment.

Finally, as the external motion was quantified only during one final BHPV assessment, the inter-session motion reproducibility could not be assessed.

In conclusion, this training protocol combined breath-hold with IPV using a commercially available device, without additional oxygen or preliminary hyperventilation. As a result, a 20 min-BHPV could easily and safely be achieved while maintaining a good comfort level. These results are encouraging in the field of radiotherapy for respiratory-related mobile tumours and can be added to the results focusing on apnea prolongation and breath-hold techniques. Further trials are obviously required to assess the 20-min-BHPV feasibility in patients and to analyse internal residual tumour motion.

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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.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.radonc.2019.09.024.

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