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Breathing adapted radiotherapy using optical real-time thoractic localization

Rebecca Ljungqvist

Supervision

Sven Bäck, Fredrik Nordström, Sofie Ceberg och Charlotte
Thornberg, Malmö

This work has been performed at
Medical Radiation Physics, Skane University Hospital, Malmö

Department of Medical Radiation Physics,
Clinical Sciences, Lund
Lund University

Abstract

Purpose: The aim of this work is to investigate the ability of a laser positioning system for breathing-adapted radiotherapy (BART), also known as respiratory gating. C-RAD installed the Sentinel system at the Skåne University Hospital (SUS) in Malmö during an appointed time for the purpose of evaluation on the pre-clinical gating prototype. It is also to develop a visual coaching method for the Sentinel system and to investigate the feasibility of this coaching method, by evaluating both reproducibility and stability for the deep-inspiration breath hold (DIBH) technique. Furthermore, to compare two real-time positioning systems for BART; Sentinel vs. Varian Real-time Position Management (RPM) system. **Methods and material:** Latency measurements were carried out on the Sentinel and the RPM system. The latter system is at present in clinical use at SUS in Malmö. A latency measuring device was developed and constructed, using an object of detection attached to a pneumatic piston, an AVR microprocessor, a crystal oscillator, and eight light-emitting diodes. To evaluate the developed visual coaching method, 19 female healthy volunteers were recruited to perform DIBHs using both audio coaching and the developed visual coaching method. The Sentinel system was used to monitor the thoracic AP-PA motion for all volunteers. MATLAB was used to read and plot data from the gating system output files. All reproducibility and stability calculations were also done in MATLAB. **Results:** All volunteers improved the reproducibility of DIBHs with the developed visual coaching method compared to audio coaching. 38% of the volunteers had improvements less than 1 mm, 46% had an improvement between 1 – 2 mm, and 15% had an improvement larger than 2 mm. In terms of stability, 23% showed no improvement with the developed visual coaching method. 46% had improvements less than 1 mm, 23% had an improvement between 1 – 2 mm, and 8% had an improvement larger than 2 mm. For the latency measurements, the arithmetic mean and the standard deviation was calculated to be $192.1 \pm 16.5 \mu\text{s}$ for the RPM system and $94.3 \pm 16.0 \mu\text{s}$ for the Sentinel system. **Conclusions:** The Sentinel system had a latency comparable with the RPM system. Both stability and reproducibility of DIBHs was improved using the developed visual coaching method. The results indicate that the Sentinel system is a promising system for BART.

Keywords: Breathing-adapted radiotherapy, respiratory gating, left-sided breast cancer, latency, deep-inspiration breath hold, audio coaching, visual coaching

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1 Introduction

The objective of a radiotherapeutic treatment is to kill all malignant cells while avoiding, to greatest reasonable extent, irradiation of healthy surroundings. An utmost limiting aspect is thus prescribed dose deliverance to the target volume, due to target positional uncertainties and inaccuracies in patient and beam set-up. To account for this, and achieve full coverage of the target, a standardized method is to treat a volume larger than the target [1]. The size of this planning target volume (PTV) depends on the size of the clinical target volume (CTV), an anatomical-clinical concept including the visible or palpable tumor and/or malignant subclinical diseases. It also depends on the set-up margin through all the treatment sessions as well as internal organ movements. The latter margin encompass physiological variations that affect the size and shape of the CTV. The site of the CTV, which may vary with e.g. bladder filling, also states a decisive condition for the PTV. Irradiation of adjacent normal tissue is clearly inevitable to a certain extent, contingent on the treatment technique used and the localisation of the tumor.

In order to account for tumor movement due to respiration, rather than applying additional margins, a treatment plan can potentially be based on breathing-adapted radiotherapy (BART), sc. respiratory gating. For left-sided breast cancer patients, the effect of margin modification is in general smaller relative the effect of different breathing phases [2]. The rate of locoregional relapse as well as the risk of death from breast cancer is reduced for premenopausal patients with lymph node positive breast cancer if chemotherapy is combined with postoperative radiation therapy [3]. Adjuvant radiotherapy is accordingly given after breast-conserving surgery to improve survival. The clinical term adjuvant refers to an additional or supplementary treatment. If locoregional lymph nodes are included in the target definition, i.e. the two standard tangential photon fields covering the remaining breast are arranged deep, the probability of heart complications is higher [4]. Positive correlation has been observed between cardiac dose-volume and the level of excess risk of cardiac mortality from ischemic heart disease [5] as well as the relevance between the irradiated lung volume and radiation pneumonitis [6]. This pneumonitis is an early phase of an injury with symptoms manifesting 1-6 months after radiation therapy [7], leading to fibrosis, an irreversible stage, and subsequently functional lung impairment [8]. Late radiogenic heart and lung sequelae are therefore reducing the survival benefit from the adjuvant radiotherapy.

There are several breathing manouvers for BART, e.g. deep-inspiration breath hold (DIBH) which denotes intervals of breath hold, at almost 100% vital capacity, with free breathing (FB) between the holds [9]. The hold can limit the tumor from moving during treatment delivery. A feature of the deep inspiration is an increased distance between the heart and the treated breast volume [18]. Another constituent, referable to the expansion of the lung, is a relatively reduced lung density [10]. If the treatment margins must not be increased, on behalf of tumor immobilization, healthy tissue can be spared and the prescribed dose to the CTV can conceivably be escalated [10]. The DIBH technique can provide shorter treatment times compared to end-expiration (EG) gating or end-inspiration (IG) gating. This is due to the duration of the breath hold when several more monitor units can be delivered than during a short inhale or exhale. IG, due to the inspiration features, provides dosimetric benefits for left-sided breast cancer patients [2]. This gating technique have been in clinical use at the Skåne University Hospital (SUS) in Malmö since 2007.

Different breathing manoeuvres have been investigated in a CT-study with 17 patients (eight with right-sided and nine with left-sided breast cancer) [2]. The manoeuvres included FB, IG, EG, DIBH, and end-expiration breath-hold (EBH). For the patients with left-sided breast cancer, it was concluded that EBH and EG increased the irradiated heart volume, the median left anterior descending coronary artery (LADCA) volume and the lung volumes, compared to FB. However, the dosimetric benefits were favourable with DIBH compared to FB. The median ipsilateral relative lung volume receiving more than 50% of the prescription dose (V_{50}), for both right- and left-sided cancers, was 29.5% for IG and 27.7% for DIBH. The LADCA V_{50} was 22.4% for IG and 3.6% for DIBH. The median heart V_{50} was 2.8% for IG and 1.9% for DIBH. Compared to FB, the dose was reduced for both IG and DIBH. With FB, the V_{50} was 19.2% for the heart, 45.6% for the ipsilateral lung and 88.9% for the LADCA.

Coaching, or feedback, to the patients during the gating procedure can be employed through visual and/or audio promptings. It has been shown that audio coaching improves FB reproducibility in terms of respiration frequency [11]. Without simultaneous visual prompting, the breathing amplitude was characterized by variety. Amplitude stability is of decisive importance for DIBH reproducibility. For this breathing manouever, baseline drift has been observed after breath holds [12]. A considered explanation for this is muscle tension due to the hold and that it takes several breathing cycles for the muscles to subsequently be relaxed. Therefore altogether, considering DIBH,

a coaching method of visual character is to be preferred for this breathing technique. In previous literature [9], a graphic representation of the chest-wall excursion, i.e. the respiratory signal as a function of time, has been investigated for DIBH. Horizontal lines indicated the gating window. The reproducibility and stability of the DIBHs was improved with the visual coaching as the average value changed from 2.1 mm and 1.5 mm, respectively for the non-coached series of DIBHs, to 0.5 mm and 0.7 mm. Changes larger than 2 mm, considered significant changes, was observed in 35% of the subjects regarding reproducibility and 15% in terms of stability. Presumably, a curve can be unnecessarily difficult to interpret for patients who are not acquainted with this type of graphic representation. Based on this assumption, the feedback to the volunteers in this study was therefore opted to be represented with a plain bar.

During all gating procedures, it is of fundamental importance that no delay (latency) exists between the point in time when the patient enters the gating window until the trigger signal is derived for beam on. C-RAD installed the Sentinel system at the Skåne University Hospital (SUS) in Malmö during an appointed time for the purpose of evaluation. Latency measurements were carried out on this system and the Varian Real-Time Position Management (RPM) system, implemented and in clinical use at SUS Malmö, for a comparison. The Sentinel system is today commercially available for patient positioning and motion detection during treatment delivery, but the respiratory gating module is still under development. Both gating systems are described below (see *Material and methods*) with emphasis on treatment sessions, in that the Sentinel unit was installed in the linear accelerator room only.

The aim of the present work is to investigate the feasibility of the bar and to evaluate both reproducibility and stability of DIBH with this visual coaching method, compared to audio coaching. Possible autocorrelation will be investigated by repeating and alternating the coaching session (audio and visual sessions). The aim is also to evaluate the Sentinel gating prototype. An important aspect here is the system latency time, for which the measurements can, potentially, verify the time axis reproducibility. If the latency time is comparable with the RPM system latency, the amplitude axis reproducibility can be investigated by simultaneous measurements, using both systems at the same time, with an amplitude comparison for the breathing curves.

2 Theory

2.1 Principles of breathing-adapted radiotherapy

Breathing-adapted radiotherapy (BART) implies that the treatment beam is enabled only during a part of the respiratory cycle. Metaphorically speaking, like a gate closing (beam hold) at all time outside an upper and a lower threshold, encompassing a window (beam enable). OARs' position and motion during breathing are of decisive importance for the placement of the gating window. It can be dosimetrically favourable if the window is placed where the tumor motion, as a result of respiration, is most limited.

Phase-based gating implies that the beam is enabled during a specified phase of the respiratory cycle, whereas amplitude-based gating is based on respiration amplitude. The latter one can account for non-cyclic respiratory motion techniques, e.g. DIBH.

There are several techniques proposed for BART. An example is the breath-hold technique, in terms of different breathing manouvers. This technique can be either controlled, using a spirometer, or voluntary; free breathing. A spirometer, also known as 'active breathing coordinator' (ABC) device, measure the air volume inspired and expired and is used to force a breath-hold at a pre-defined lung volume [13, 14]. The advantage of the controlled form is a potentially good intra-session reproducibility of respiration volume [15]. Patient discomfort, a higher set-up complexity and, due to pressure variations, subtle associations between target motion and respiration measurement are however considerable disadvantages.

2.1.1 Left-sided breast cancer techniques

The rate of locoregional and systemic relapse is decreased for premenopausal women and overall survival is improved, if chemotherapy is combined with post-operative¹ adjuvant radiotherapy [3, 16]. High cardiopulmonary dose-volumes can however outweigh the survival benefit [17]. Intensity-modulated radiation therapy (IMRT) is inferior to BART in terms of over-all reduction of doses to all OARs for breast cancer patients [15]. BART can decrease the dose to OARs, comparable with amount possible with IMRT, thus without compromising dose to other organs [18]. The dose to contralateral OARs, in particular the contralateral breast, is increased with IMRT (multiple field, inverse planning) photons [19]. Only two-field energy-modulated proton plans

¹Modified radical mastectomy with dissection of level I and II axillary lymph nodes.

using IMRT can potentially minimise the dose to the heart, both lungs and the contralateral breast while simultaneously preserving breast-cancer target dose homogeneity. Electronic compensation (two-field 'IMRT') in combination with BART can achieve a higher target dose homogeneity and sparing of dose to OARs simultaneously [2].

The heart and the LADCA is pulled inferiorly when the chest wall is expanded during inspiration [18], i.e. the spatial distance between the left-sided breast volume and both the heart and the LADCA is increased. The ipsilateral lung density in the treatment field is modified with BART [2]. During the inspiration phase, the absolute lung volume irradiated is larger than during other respiratory phases. The relative lung volume irradiated is, however, the smallest with inflation. The relative lung dose is most relevant and thus the optimal respiratory phase for treatment in terms of lung sparing is during inspiration.

EBH has been investigated for breast cancer, since this technique potentially minimises target motion due to respiration [15]. It was shown that although it presents a higher reproducibility than inspiration techniques, it does not enable internal margin (IM) reduction. The cardio-pulmonary doses are unacceptably high using EBH [15] and it increases the doses to the OARs more than FB [2].

2.2 Breathing exercise

The aim of the breathing exercise, prior to the reference/simulation session on the CT, is to find the optimal individual settings for the patient. Another aspect of the exercise is that it acquaintances the patient with both the equipment used for the respiratory gating and the procedure itself. The patient can also receive feedback from the nursing personnel in how to breathe in a more reproducible and stable manner. Moreover, the exercise functions as a means to find the optimal individual breathing phase to provide comfort during the treatments. The phase differs between individuals and it is meaningful to verify it for each patient, since the speed of the automatic audio instruction is to be synchronized with it. The instructions from the workstation speakers guides the patient when to "*breathe in*" and "*breathe out*".

The audio prompting rate is accordingly, from the breathing exercise, settled prior to the CT acquisition and the treatment sessions. The gating window (beam-on window) is also determined for each patient during the exercise.

It constitutes of two threshold lines, separated by a margin that is adequate for the breathing technique that is appointed for the treatment. For deep-inspiration breath hold (DIBH), for instance, the gating window distinguish a tolerance for minor movement during the breath hold.

When using free-breathing (FB) gating technique, the size of the gating window must not exceed the normal breathing amplitude, otherwise dose blurring may occur. The breathing amplitude when gated should then be at least twice as large as when breathing ordinarily in a relaxed manner, to increase the spatial separation between the treated left-sided breast volume and the LADCA as well as the cardiac volume. It should, however, typically not be greater than three times the normal amplitude since it may exhaust the patient and can be difficult to maintain under the duration of the CT scan or a treatment session.

2.3 CT acquisition

Prospective CT implies image acquisition during a specified phase of the respiratory cycle, a step-and-shoot procedure. There is no table movement during the acquisition, aside from after each obtained image whereas the table moves to the sequential position, preceding the next scan.

Retrospective CT (4DCT) implies spiral scanning and image acquisition during the whole respiratory cycle. Designated software is used to order the images with the corresponding phase, on the grounds that the treatment plan generally is constructed from a certain position of the cycle. A disadvantage of retrospective CT is that this technique substantially increases the radiation dose compared to prospective CT. The retrospective images provides, however, the possibility of visualizing the movement of the tumor during respiration.

2.4 Latency

The term latency denotes the time delay in the gating system. That is, the time from when the object of detection, located on the on the treatment couch, enters the gating window - until the gating system triggers the signal for beam hold.

To be able to detect any possible fluctuations, the latency measurements will be executed several times for each gating system at different occasions. A

latency measuring device will be developed and constructed, using a pneumatic piston to bring a detectable object into a gating window that is set just above the object, according to the plan drawing below (figure 1):

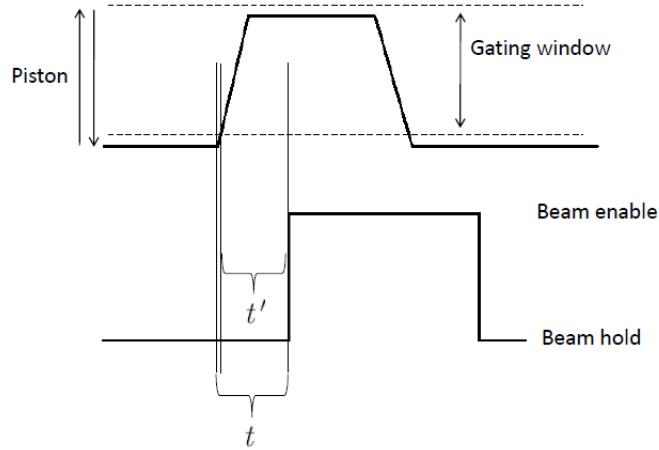


Figure 1: The latency time is denoted with t . Since there is a small amplitude margin between the piston and the gating window, it is the time denoted by t' that is measured in practise. The time difference between t and t' , however, is small and of no significance in this context.

2.5 Respiratory coaching

Reproducibility and stability of coached and non-coached series of DIBHs have been studied and defined in quantitatively manners, by Cerviño et al. [9]. Reproducibility R , expressed in mm, was defined as:

$$R = \underbrace{\max(d_i)}_{i=[1,n]} - \underbrace{\min(d_i)}_{i=[1,n]} \quad (1)$$

where d_i is the average level of each DIBH in the series (figure 2a) and n is the number of DIBHs in the series. A small R represents a small amplitude variation and therefore a good reproducibility. Stability S , expressed in mm, was defined as the maximum amplitude change during a DIBH, among all DIBHs in the series:

$$S = \underbrace{\max}_{i=[1,n]} \{ |m_i| \Delta t \} \quad (2)$$

where m_i is the slope of the linear fit to each DIBH (figure 2b) and Δt is the duration of the DIBH.

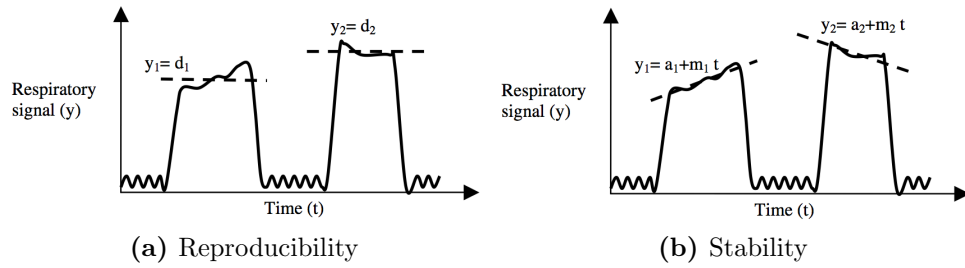


Figure 2: Graphical representations of the parameters for the reproducibility and stability definitions [9]. Figure courtesy of Cerviño et al.

3 Methods and material

3.1 Varian's RPM

The Varian Real-time Position Management (RPM) system 1.7 (Varian Oncology Systems, Palo Alto, CA 94304) utilizes a lightweight hollow plastic box, illustrated in figure 3. It is positioned approximately between the umbilicus and the xyphoid process (at the base of the sternum), although patient anatomy and treatment prescription have a decisive role of the placement point.

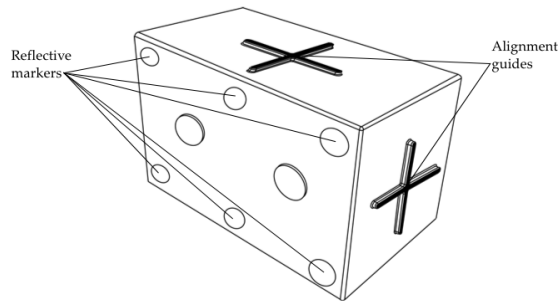


Figure 3: A six-dot marker box. Each reflective marker dot is approximately 5 mm in diameter. Figure courtesy of Varian.

Infrared light is emitted towards the box from a wall-mounted illuminator ring surrounding a charge-coupled device (CCD) camera (figure 4) in the linear accelerator treatment room.

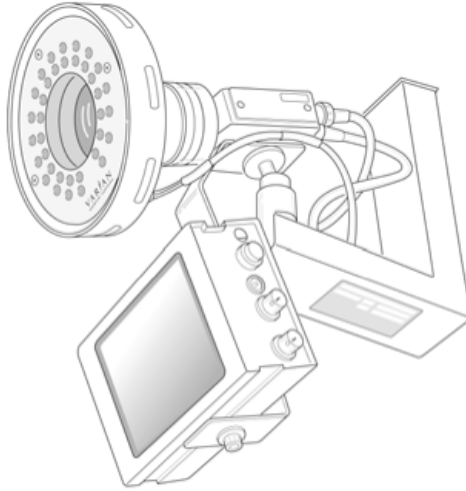


Figure 4: A wall-mounted unit, incorporating an illuminator ring, a CCD camera and a LCD (Liquid Crystal Display) monitor. Figure courtesy of Varian.

The camera registers the reflection from six passive retroreflective marker dots located on one side of the box, facing the camera. In turn, the software in a Windows-based personal computer (PC), located in the control room and connected to the camera via an ethernet cable, interprets the images sent by the camera.

The six-dot marker box is used for finer tracking in three dimensions (vertical, lateral and longitudinal), while the original two-marker block was used to track vertical motion only. A six-dot marker can also be used to display pitch (rotation around the lateral axis), roll (rotation around the longitudinal axis) and yaw (rotation around the vertical axis) position data in coordinates based on the camera or couch.

Beam hold is triggered by the RPM system within the gating threshold that is established during the reference/simulation session on the CT (figure 5).

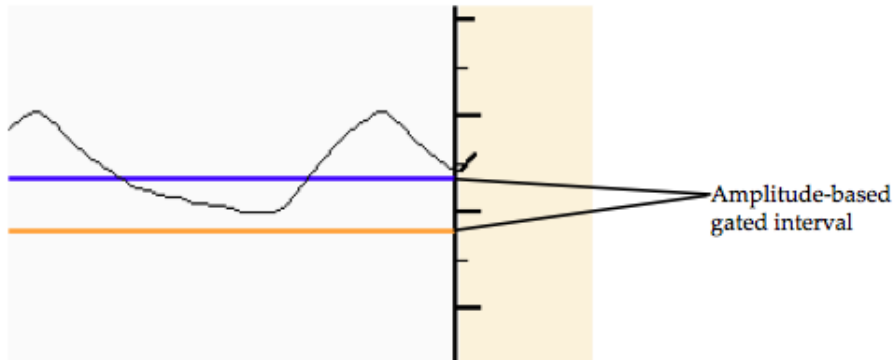


Figure 5: An example of amplitude-based gating, using the lower part of the expiration and a part of the inspiration phase. The horizontal lines defines the gating window, i.e. the amplitude for which, in terms of position, the tumor is the most stable during the respiratory cycle. Figure courtesy of Varian.

3.2 C-RAD's Sentinel

Sentinel is a patient positioning and monitoring system, consisting of a laser scanner and a camera mounted in a single unit entitled 'LS200' (figure 6).



Figure 6: The LS200 unit. Figure courtesy of C-rad.

The unit is fixedly attached to the ceiling about 1.5 – 2 m from the gantry

(figure 7) and connected to a KVM (Keyboard, Video and Mouse) switch² in the linear accelerator treatment room. The switch is in turn connected to a Windows-based PC in the control room via an ethernet cable.

The designated software is using the *Sentinel c4D* application as a platform, containing all the basic functions such as data import/export and data-analysis tools, etc. In addition there are other modules of applications, of which *cPosition* is used for patient positioning. A scan is performed at the setup of the patient before every treatment fraction, and all deviations from the reference position are presented as suggested movements for all six degrees of freedom. Longitudinal, lateral and vertical translation as well as isocenter rotation can be adjusted by moving the couch. Pitch and roll can be corrected by moving the body of the patient. The reference position data can either be created by using the Sentinel laser scanner, or by importing patient outline from the DICOM-RT Plan (RT-structure).

The *cMotion* module detects motion and is thus used as a monitor of patient movement outside pre-defined tolerance levels during treatment delivery, whereas *cRespiration* functions as the gating module.

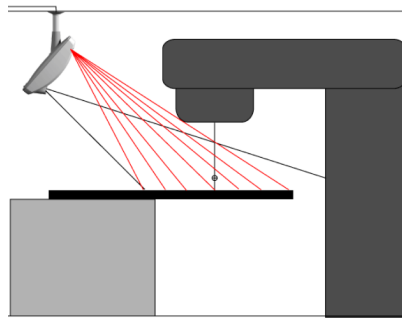


Figure 7: The LS200 is projecting laser lines which are registered by the camera. The unit is ceiling mounted about 1,5-2 meters from the gantry in the treatment room. Figure courtesy of C-rad.

The laser is classified 2M since the maximum output is 1 mW at 10 cm distance from the source. A cylinder lens is used to diverge the beam and thus the power is reduced with distance from the laser scanner device. According to the swedish radiation safety authority *Strålsäkerhetsmyndigheten* (*SSM*), the blink reflex normally constitutes a sufficient protection if an eye is exposed to a 2M laser. The Sentinel system sweeps red visible laser lines

²A KVM switch supports control of multiple computers connected to the switch from one keyboard, video display unit or mouse.

of 690 nm on the topical body region of the patient while the camera records images. The positioning laser wavelength is commonly visible green and does not interfere with the camera recording.

The Sentinel software uses a laser line triangulation algorithm to reconstruct the 3D surface of the patient. During motion detecting, a higher frame rate can be accomplished by lowering the several contours used for the high resolution image for patient positioning. While executing the set-up positioning of the patient, by matching with a reference image, it is possible to exclude surface regions in it that decreases the positioning accuracy (figure 8). Impairments as such are typically due to heavy motion from breathing.

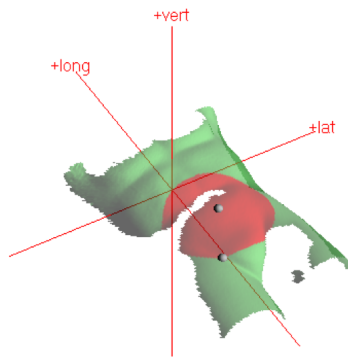


Figure 8: A region in the reference image, marked by red, with significant movement from breathing. This area is therefore excluded from matching, to improve the accuracy, when positioning the patient. Figure courtesy of C-rad.

3.3 Latency measurement

A latency measuring device was built, consisting of a piston and a circuit board. The circuits were used for measuring the time and included an AVR microcontroller and a crystal oscillator, operating at 4 MHz (figure 9). This type of mechanical resonance oscillator provides high accuracy in output frequency over supply voltage and temperature, compared to microcontroller clocks that are based on electrical phase-shift circuits [20].

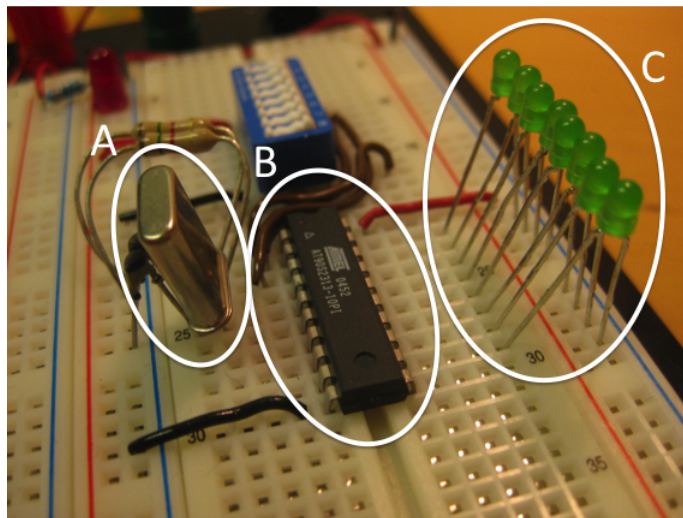


Figure 9: The crystal oscillator (A), the AVR microprocessor (B), and eight light-emitting diodes (C).

The object of detection was an RPM box assembled on a pneumatic piston (figure 10), which uses pressurized gas to move binarily (either up or down).

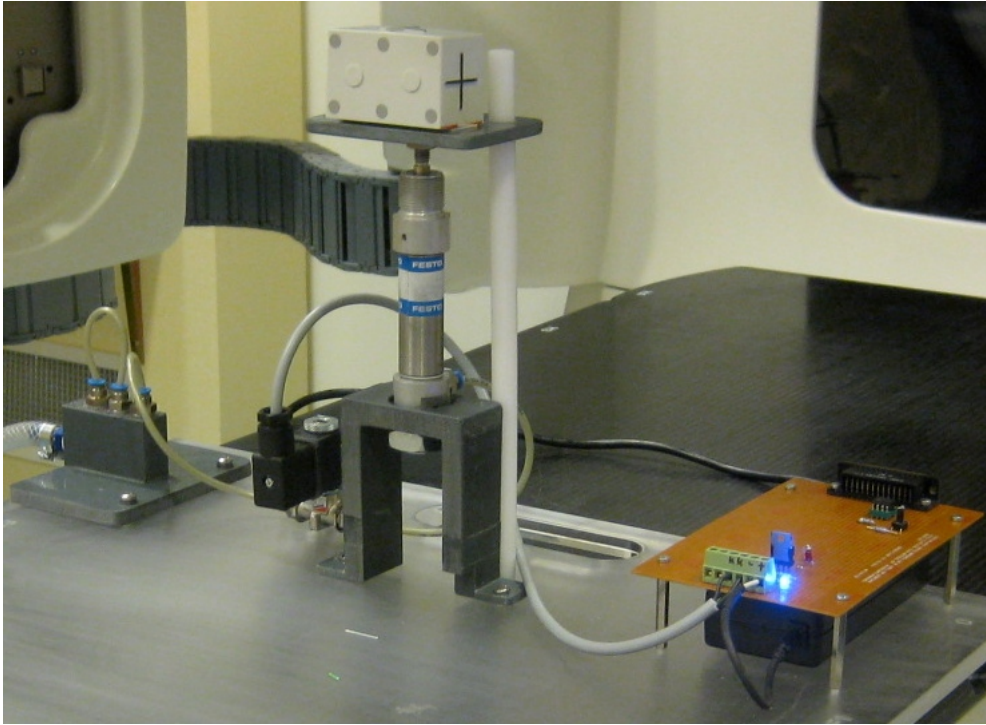


Figure 10: The RMP box assembled on the pneumatic piston.

The RMP box is required for the RMP system to work, by virtue of the infrared reflective markers, but it works also for motion detection when assigning the Sentinel system if covered with paper or other material to constitute a non-glossy surface for the reference image.



Figure 11: The cardboard assembled on the pneumatic piston.

A cardboard, attached to the piston (figure 11), constituted the scanned surface for the reference image (figure 12).

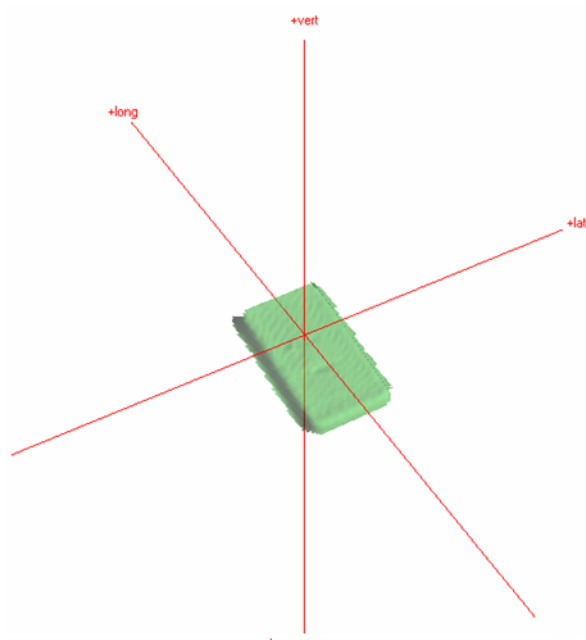


Figure 12: A reconstructed 3D surface of the cardboard.

ATMEL AT90S2313-10PI is an 8-bit AVR microcontroller with programmable flash memory. It has 32 x 8 general purpose working registers, i.e. 32 storage sites with 8 bits capacity. Three of these registers were used to store the result for a measurement, starting with the least significant bit 0 ($2^0 = 1$) at the right part of the string, to 255 at the end of the left part (figure 13).

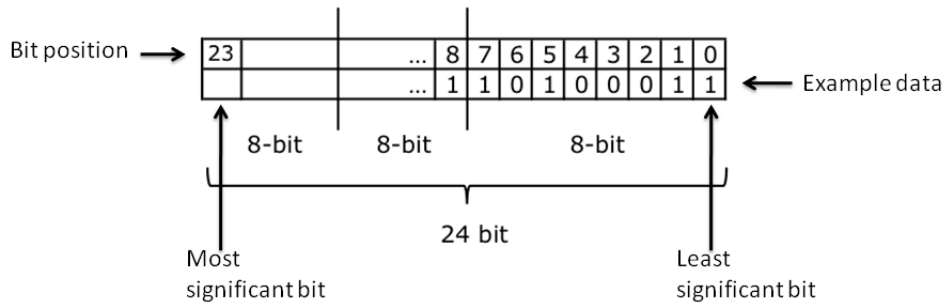


Figure 13: Illustration of the bit positions. Three registers were used to store the result from a measurement, each of 8 bits capacity. The storage order is Big Endian, starting with the least significant bit (lowest value).

Since the operating voltages for the microcontroller is between 4.0 – 6.0 V, a 5 V signal to pin D0 (figure 14) was derived from a switch used for driving the piston. The trigger pulse for beam on from the RPM and the Sentinel system, respectively, was also 5 V, to pin D1. Port B (B0-B7) are bi-directional I/O ports and drives eight light-emitting diodes (LED's).

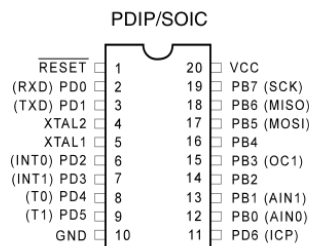


Figure 14: Pin configuration. VCC is the supply voltage pin and GND is the ground pin. PD0 is Port D, Bit 0 and PD1 is Port D, Bit 1. Port B (B0-B7) serves to drive the eight LED's. Figure courtesy of ATMEL.

Assembly language was used for the programming of the microcontroller. The program written included two loops, where the first one instructed the microcontroller to wait for a signal to D0. The second loop instructed the

microcontroller to count the number of clock cycles until the beam-on pulse was derived to D1 from the gating system.

Eight LED's were used to alternately display the result for each bit in the three registers. The result (0 or 1) was then multiplied with the corresponding bit value, whereafter all the values were added, to give the number of clock cycles that the microprocessor required. Since the counting is only every tenth cycle, the sum was multiplied by ten to give the actual number of clock cycles between the initiating signal to D0 and the trigger pulse (beam on) to D1.

3.4 Respiratory coaching

3.4.1 Subject characteristics

Cerviño et al. recruited 15 volunteers and 5 patients in their coaching study. Power calculation to determine the appropriate sample size for this study was not executed since the study by Cerviño et al. provided a guideline on the number of subjects needed. Statistical considerations must thus be applied on the results of this study, for hypothesis testing. A number of 20 – 22 female healthy volunteers was requested for this study, 19 of them participated. The age range was 20 – 58 and the median age was 24 years old. All volunteers were given the same instructions, as follows;

- They were to receive several sets of alternated instructions, both audio and visual.
- At "breathe in" they were supposed to breathe in, when ready, and hold at approximately 100% vital capacity until told to "breathe out".
- After an elapsed hold and until the following instruction (next "breathe in"), they were to breathe freely in a relaxed manner.
- The importance of laying down relaxed without any tension, and not to arch the back. If the back is arched, the chest would come up and erroneously indicate that the volunteer is breathing in.
- When performing a breath hold, to breath in and hold with the chest (thoracic breathing).
- Abdominal breathing was allowed between given instructions.
- The concept of the visual feedback, how it correlates with their breathing and the task for them to execute.

The volunteers were positioned supinely on the linear accelerator treatment couch, in the dedicated fixation for breast cancer patients at SUS in Malmö. A LCD screen, beside the coach, displayed the visual feedback to the volunteers. The breath hold duration was 15 s. Breathing impedance is generally not a concern for breast cancer patients and therefore the hold for DIBH can easily be endured for that amount of time if the patient is otherwise healthy.

Half the group (eight volunteers) received the video instructions first, thereafter the audio instructions. The other group of volunteers received the opposite order of instructions. All sets of instructions were repeated three times, making allowance for observing, or rejecting, autocorrelation.

The tolerance level, i.e. gating window, was set individually for each volunteer after observing two-three short DIBH (with no visual feedback) at the set up.

3.4.2 Respiration monitoring

The Sentinel system was used for respiration monitoring of all volunteers, due to evaluation purposes on the gating prototype.

3.4.3 Audio coaching

The volunteers were told verbally when to "breathe in" and "breathe out".

3.4.4 Visual coaching

A bar visualized the anterior-posterior movement of the chest, at a tracking region located 2 cm medially from the mammary papilla at the left breast. The region location was selected on the grounds of left-sided breast cancer patients constituting a possible clinical target group for the gating module of the Sentinel system.

Two upper lines indicated a gating window of 2 mm and a third lower line was set just above normal breathing (above baseline). When the bar overstepped the uppermost line, the bar turned red to alert the volunteer. In other cases, i.e. during free breathing and DIBH within the gating window, the bar maintained a green colour (figure 15).

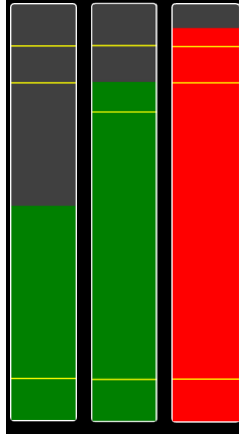


Figure 15: The bar indicates the anterior-posterior movement of the chest, hence representing the thoracic breathing pattern. If the volunteer exceeds the gating window, presented as the two upper lines, the bar turns from the color of green to red.

3.4.5 MATLAB

MATLAB was used to read and plot data from the .xml files produced by the Sentinel system. All reproducibility and stability calculations, using the definitions proposed by Cerviño et al. (2009), were also done in MATLAB.

The figure below (figure 16), depicted from MATLAB for one of the volunteers, serves to illustrate how the calculations were executed for a DIBH. The data between the initial and end time point of a hold is fit by two lines in MATLAB for this example. The first line (a) corresponds to the average amplitude (see reproducibility, eq. 1), while the other line (b) is fit with the method of least squares (see stability, eq. 2).

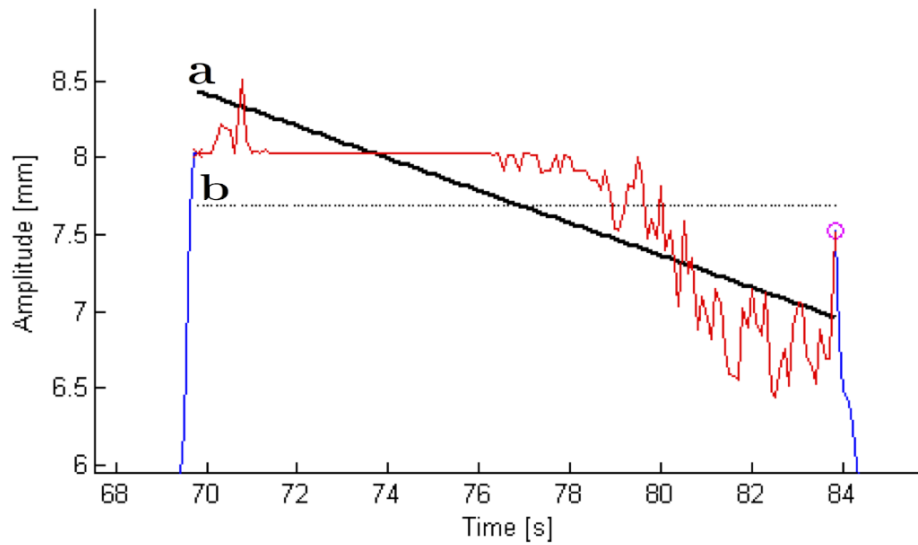


Figure 16: The line denoted with (a) shows a fit with least squares and line (b) shows the average amplitude level for a DIBH.

MATLAB was also used to read, extract, and plot data from the .vxp files produced by the RPM system.

The export files (.xml and .vxp) are structured with headers, patient ID, date of the session, scale factors, as well as respiration data (amplitude, phase, timestamp).

4 Results and discussion

4.1 Latency measurements

The latency measurements were executed five times at three different occasions, a total of fifteen measurements on each system. The results from the measurements are listed in table 1.

Table 1: Latency measurement results for the RPM and the Sentinel system.

Latency [μs]	
<i>RPM</i>	<i>Sentinel</i>
204.97	96.08
200.65	81.65
170.28	119.54
188.52	71.24
212,54	94,19
194.72	107.34
212.75	250.41
188.63	81.36
213.74	243.79
194.84	153.14
195.42	88.56
155.33	120.21
178.78	78.44
192.23	96.73
177.62	96.70

The arithmetic mean and the standard deviation was calculated to be $192.1 \pm 16.5 \mu s$ for the RPM system and $118.6 \pm 56.0 \mu s$ for the Sentinel system.

During the second occasion of measurements for the Sentinel system, three values ($250.41 \mu s$, $243.79 \mu s$, and $153.14 \mu s$) clearly diverged from the other observations for this system (figure 17). If these values were to be excluded

from the arithmetic mean and standard deviation calculations, the result would be $94.3 \pm 16.0 \mu\text{s}$ for the Sentinel system.

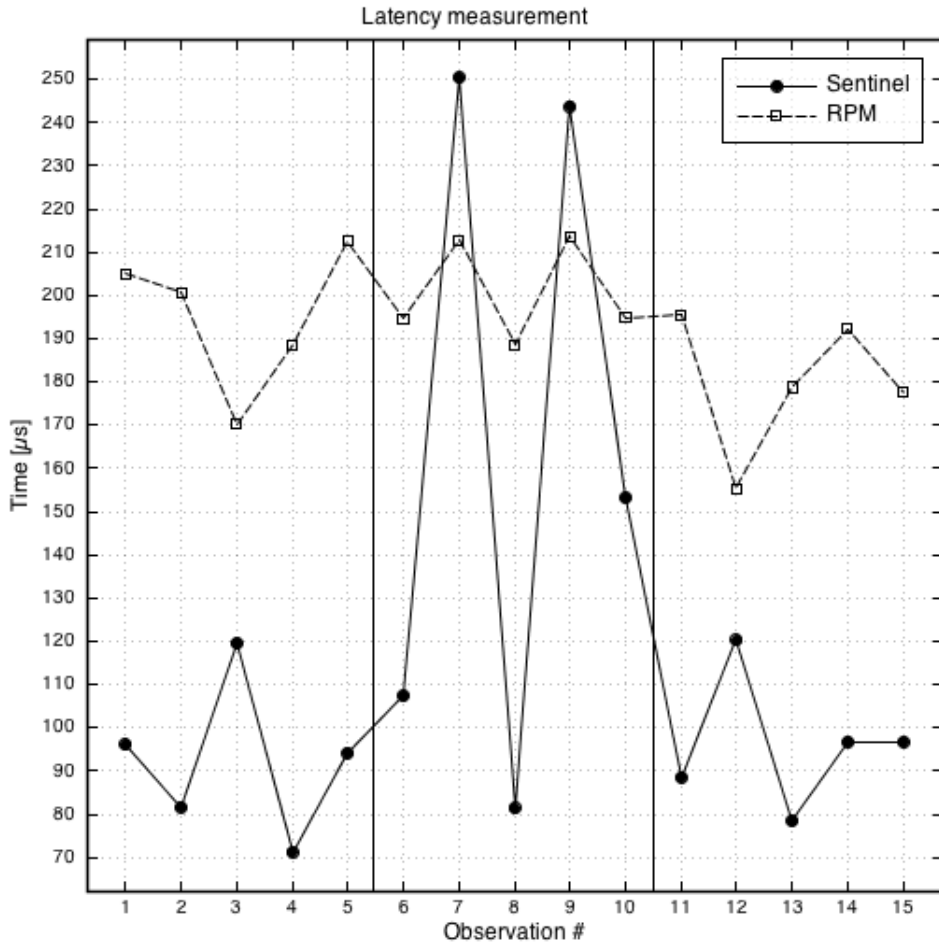


Figure 17: The result from the latency measurements. The latency time observed during the 7th, 9th and 10th observation for the Sentinel system clearly differs from the other observations for this system.

There is no explanation for the divergence at present and to conclude on whether the divergence is reproducible or not, more measurements at different occasions must to be executed for the Sentinel system.

4.2 Respiratory coaching

The volunteers were, as for audio coaching, instructed verbally when to breathe in and breathe out. The denominated 'visual' coaching method here is therefore to some extent to be regarded as audio visual, although the audio promptings were not given at a concluded nor a fixed rate. It is therefore beyond the bounds of possibility to reason around the reproducibility of the breathing frequency in this study. The constancy of frequency is, compared to the constancy of amplitude and as mentioned earlier in the introduction, not of importance for the DIBH technique [11]. That is apart from, within realm of possibility, long treatment times if the patient is very rarely performing the DIBHs. The main prospect of verbal promptings is the potential to study the time it takes for the volunteers to get back to baseline after an executed DIBH.

Table 2 and 3 shows the results for the volunteers in terms of reproducibility and stability improvements respectively. The number of volunteers included in the study was decreased to only 13. This was partly due to loss of data in the .xml files that were recorded and partly because a number volunteers had to perform a different number of sessions than the others, due to difficulties in the set-up procedure and software bugs in the gating prototype.

Table 2: Reproducibility average.

Reproducibility improvement	Number of volunteers	Percentage of volunteers [%]
No improvement	0 (0/13)	0
< 1 mm	5 (5/13)	38
1-2 mm	6 (6/13)	46
> 2 mm	2 (2/13)	15

Table 3: Stability average.

Stability improvement	Number of volunteers	Percentage of volunteers [%]
No improvement	3 (3/13)	23
< 1 mm	6 (6/13)	46
1-2 mm	3 (3/13)	23
> 2 mm	1 (1/13)	8

Figure 18 shows two, typical, examples of audio coaching vs. visual coaching.

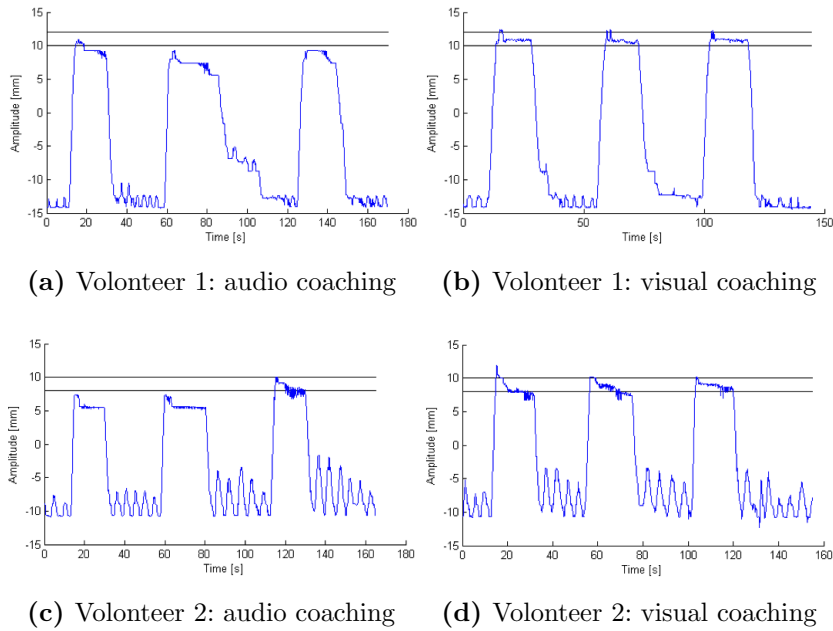


Figure 18: Two representative examples of audio coaching vs. visual coaching. Volunteer 1 improved the stability of DIBHs with visual coaching, compared to audio coaching. Volunteer 2, on the other hand, had a better stability with audio coaching, since she did not compensate for the fluctuation of the bar while remaining within the gating window. However, the reproducibility of DIBHs were improved with visual coaching for this volunteer.

No statistical analysis is to be performed for the 13 volunteers since they were too few in terms of statistical significance for this type of study. The stability improvement can potentially be increased if the bar is introduced

with greater inertia, since the volunteers tried to compensate for the constant movement of the bar during the visual coaching sessions.

A gating window of 2 mm, used during the sessions, is to be considered small in this context, and could potentially be increased by approximately 1 mm. Future work is to include more volunteers, using a bar that is less sensitive while it displays the AP-PA movement of the chest to the volunteer, and to perform statistical analyses on the result.

Since the Sentinel system had a latency time comparable with the RPM system, both systems could be used simultaneously (figure 19) for a comparison on the amplitude reproducibility of the Sentinel system. RPM is a validated and controlled system and could therefore constitute a principle guideline. The amplitude reproducibility is of interest to investigate since a short latency time is of no importance for the conclusions on whether the Sentinel system is a promising system for gating, if, the tracking ability is poor.

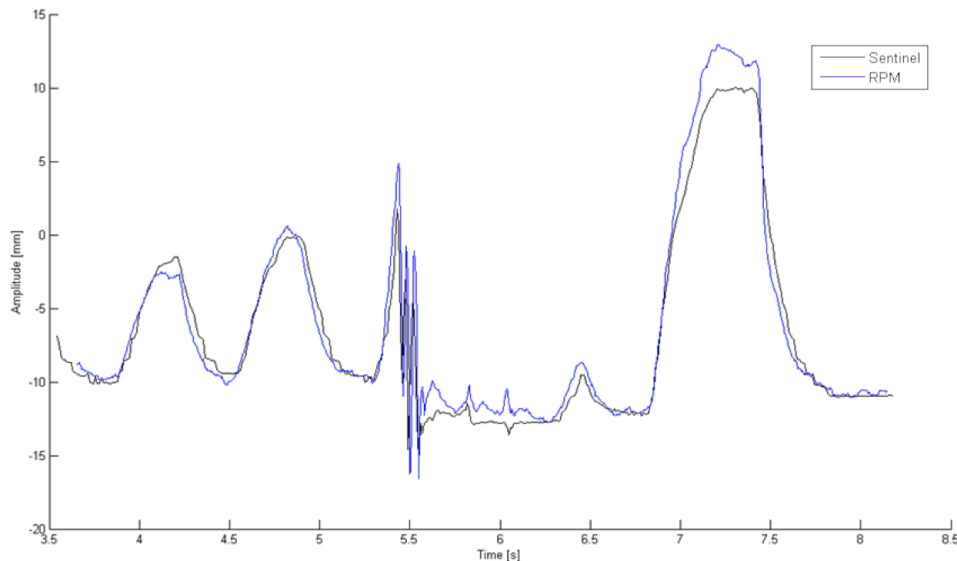


Figure 19: The result for both gating systems in use simultaneously. The movement of the curves is similar and the amplitude of the Sentinel system is comparable to the RPM system. Both curves were manually overlaid using MATLAB.

At present, the Sentinel system can be used for breathing tracking in 2D. In the future it would be beneficial to use the surface potential for this system and employ 3D tracking, with different tolerance levels on a surface.

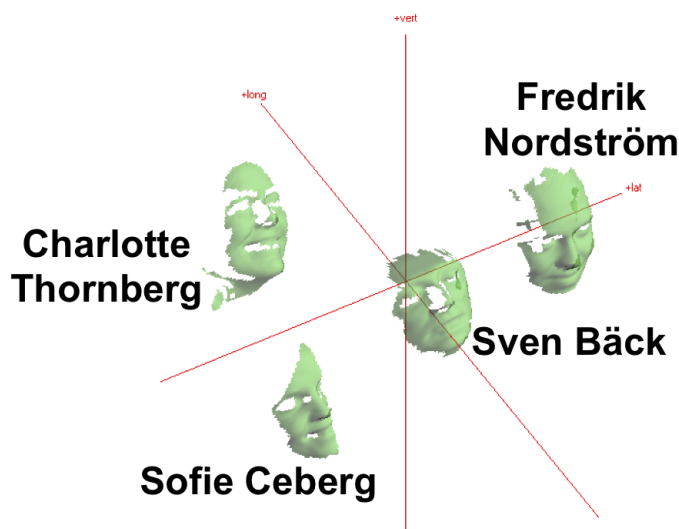
For instance, both abdominal and thoractic breathing can then be tracked simultaneously, to ensure that the patient is breathing in a correct manner. It would also be beneficial in the future to implement image guidance as a complement to respiratory monitoring, in order to account for internal organ movements. Image guidance can indicate also if the back of the patient is arched and the chest level is erroneously indicating that the patient is breathing in.

5 Conclusions

The Sentinel system had a latency comparable with the RPM system. Both stability and reproducibility of DIBHs was improved using the developed visual coaching method. The Sentinel system is a promising system for BART.

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