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Breathing adapted radiotherapy of breast cancer: Investigation of two different gating techniques and visual guidance, using optical surface scanning and pressure monitoring

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ANDAS FÖR HJÄRTATS SKULL

Bröstcancer är den vanligaste cancerformen hos kvinnor i Sverige och står ensam för 30 % av cancerdiagnoserna. Detta innebär att varje dag får 20 kvinnor beskedet att de har drabbats av bröstcancer. Idag får ungefär 50 % av alla cancerpatienter strålbehandling och på strålbehandlingsavdelningen vid Skånes universitetssjukhus (SUS) behandlas flertalet bröstcancerpatienter dagligen.

Vanligast är att patienterna kommer till strålbehandlingsavdelningen efter att ha genomgått kirurgi där antingen hela eller delar av bröstet har tagits bort. Vid strålbehandling bestrålar man det sjuka området med högenergetisk strålning. Strålningen tar sig in i vävnaden och förstör cellerna. Genom att bestråla det område där tumören var placerad hoppas man kunna förstöra tumörceller som kirurgin inte lyckats ta bort, vilket minskar risken för att sjukdomen ska komma tillbaka.

Problem kan uppstå när en patient har cancer i vänster bröst eftersom man vid bestrålning av detta område även levererar en viss strålning till hjärtat. Hur noggrant man än riktar strålningen ligger hjärtat och bröstet ofrånkomligt nära varandra. Studier har visat att personer som överlevt sin vänstersidiga bröstcancer har en förhöjd risk att insjukna i hjärtsjukdomar.

För att minska strålningen till hjärtat kan man använda sig av en behandlingsteknik som kallas gating. Med gating utnyttjar man att avståndet mellan hjärta och bröst rent anatomiskt blir större då man andas in. Genom att låta patienten djupandas på ett visst förbestämt sätt kan man se till att endast bestråla då hjärtat är så långt ifrån bröstet som möjligt och därmed undvika att bestråla hjärtat.

Dessa gatingbehandlingar tar ofta lång tid och det kan vara ansträngande för patienten att andas i önskad takt och amplitud. I detta examensarbete har en alternativ gatingmetod jämförts med den befintliga i hopp om att kunna förbättra behandlingen och göra det lättare för patienterna. Man har även tittat på om det skulle hjälpa patienterna att få se och följa sin andning på en skärm under själva behandlingen genom så kallad visuell guidning.

Den befintliga metoden innebär att patienten djupandas kontinuerligt enligt ett visst tempo. Vid varje andetag levereras en viss mängd strålning. Den nya metoden innebär att patienten, istället för att djupandas kontinuerligt, tar färre djupa andetag och istället håller andan under en längre tid. På detta sätt kan mer strålning levereras per andetag.

Resultaten av examensarbetet visar att i dagsläget, när man ej har tillgång till visuell guidning, är den befintliga tekniken bättre än den nya. Dock visade det sig att visuell guidning var till stor hjälp och att det hade varit till stor fördel om detta infördes. Om visuell guidning införs bör man dock byta ut den nuvarande tekniken till den nya. Detta hade resulterat i bättre och snabbare behandlingar vilket hade varit bra för patienterna och även hälsoekonomiskt gynnsamt.

ABSTRACT

Background and purpose: Post-operative adjuvant radiotherapy of left-sided breast cancer patients is associated with cardiac and pulmonary complications. By utilizing different respiratory gating techniques, the absorbed dose to the heart and lung can decrease. The purpose of this study was to evaluate and compare enhanced inspiration gating (EIG) and deep inspiration breath hold (DIBH). The use of visual guidance for both the techniques was also evaluated.

Material and methods: Twenty healthy female volunteers were included in the study. The volunteers performed both EIG and DIBH, with and without visual guidance. Based on a practice session a 3 mm gating window was introduced at an individual amplitude for both EIG and DIBH. To monitor the breathing and to have access to visual guidance the Catalyst (C-RAD positioning AB, Uppsala, Sweden) was used. Parameters such as reproducibility, stability and attendance in the gating window (P_{GW}) were evaluated. Possible advantages of a pre-set delay of the irradiation when the patient's chest entered the gating window were also investigated. The study also included pressure measurements with the I-scan system and sensor model 9801 (Tekscan Inc., South Boston, USA) which was placed under the patients scapulas. These novel pressure measurements were used to evaluate if there was any risk of patient lifting to enter the gating window, and thus not increasing the spatial distance between the heart and the target volume. The last step in the study was to see how long the volunteers were able to hold their breath in the gating window.

Results: Spontaneously, without visual guidance, the volunteers breathed significantly deeper using DIBH compared to EIG, and thus increased the distance between the heart and the target volume. The average chest amplitude for EIG was 10.8 ± 4.7 mm (1 SD) and for DIBH 12.9 ± 5.8 mm. The reproducibility and P_{GW} improved for both techniques when visual guidance was used. The stability did not indicate any particular trend. The pressure measurements showed that there was a possible risk that the volunteers lifted from the couch, which was more prominent for high amplitudes (~2.5 cm) and when visual guidance was used. On average the volunteers where able to hold their breath for 57.2 ± 22.5 s.

Conclusion: According to this study there are major advantages using DIBH and visual guidance. DIBH resulted in higher amplitudes which could result in sparing of cardiac and pulmonary dose. To prevent patient lifting, patients should not be pushed to perform too high amplitudes. There are no benefits regarding reproducibility, stability and P_{GW} of changing gating method from EIG to DIBH if no visual guidance can be provided.

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ABBREVIATIONS

BART: Breathing Adapted Radiotherapy

EIG: Enhanced Inspiration Gating

FB: Free Breathing

MU: Monitor Units

LAD: Left Anterior Descending coronary artery

DIBH: Deep Inspiration Breath Hold

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1. INTRODUCTION

In Sweden 55 000 people are diagnosed with cancer each year. According to the Swedish Cancer Society this means that one third of all now living swedes will at some point of their life receive the information that they have cancer. Thanks to research, cancer treatment has developed and today the 10 year survival is 60 % [1].

Approximately half of all cancer patients undergo radiotherapy, either as an independent treatment or in a combination with other treatment forms such as surgery and chemotherapy. The idea of treating cancer with ionizing radiation is not a new phenomenon as it was first used in the end of the 19th century. Since then there has been a major development and today's technology can offer increasingly complex treatment methods [1].

To avoid unwanted side effects or radiation induced cancer it is important to spare as much normal tissue as possible. In order to achieve this goal but in the same time cover the entire target volume, different kind of treatment techniques are continuously developing.

One of these techniques is breathing adapted radiotherapy (BART), where the radiation is delivered only at a certain phase during the respiratory cycle. One patient group who benefits from BART is breast cancer patients. Breast cancer is the most common cancer form among women in Sweden and stands alone for 30 % of the cancer diagnoses. This means that nearly 20 women will be diagnosed with breast cancer in Sweden every day [1]. By using different respiratory techniques, so called gating techniques, absorbed dose to heart and lungs can be decreased, although maintaining the dose coverage of the target volume[2–4] .

It is shown that these kind of gating treatments are especially beneficial for left-sided breast cancer patients since the heart sometimes ends up inside the radiation field [2–6]. Studies show that radiation of the heart and lungs may lead to cardiac and pulmonary complications which in the end can result in a shortened life [6, 7]. By utilizing the natural movement of the chest wall and heart during deep breathing, where the heart moves in a caudal direction, the separation between the breast and the heart is maximized at the end-in inspiration phase. In this position the relative lung volume and heart inside the radiation field decreases [3–5]. This ultimately means a reduction of cardiac morbidity and mortality along with pulmonary complications for these patients [3].

Since 2007, left-sided breast cancer patients at SUS have been offered treatment using a gating technique called Enhanced Inspirations Gating (EIG). The patient then continuously breathes deeply to increase the spatial distance between the heart and the target volume. EIG is the used method because it enables continuous verification of the initial position, i.e. the baseline before and after the deep breath take. By continuously verifying the breathing baseline any unwanted patient lifting or baseline drift can be

detected and corrected during a field. This is not possible for DIBH because one field often is delivered during one breath hold. Another common gating technique is the Deep Inspiration Breath Hold (DIBH) method [2, 4, 5, 8–10]. Instead of continuously breathing deeply, the patient takes fewer but longer deep breaths, in between the deep breaths they perform normal breathing until they reach baseline. Before any possible shift of gating technique is considered at the radiotherapy department at SUS, a thorough evaluation regarding the stability and reproducibility is needed. Furthermore, a study investigating possible lifting effects due to the DIBH technique is highly desired.

2. AIM

The aim of this study was to evaluate if the clinic should shift respiratory gating technique from EIG to DIBH for radiotherapy of left-sided breast cancer patients.

A breathing study with 20 volunteers was carried out to compare the two methods using different parameters such as reproducibility, stability, attendance in the gating window (P_{GW}) and amplitude. Visual guidance, i.e. the patients can see their breathing curve during treatment, was also evaluated for both gating techniques.

Damkjær *et al.* [11] have previously shown that the DIBH method leads to higher breathing amplitudes compared to EIG. Because of this increase in amplitude there have been concerns if the patients actually are capable to enter the gating window with proper technique for all breaths. The proper technique is to enter the gating window by filling the lungs with air, since this will create the desired distance between the breast and the target volume. If the patient is forced to perform too high amplitudes the fear is that the patient will enlist the help of her own body and enter the gating window by lifting from the couch. This lift would depend on posture changes of the patient such as spinal arching or the utilization of the armrests to push up the thorax. This phenomenon will further on be referred as patient/volunteer lifting.

Because there have been no verification of the occurrence of patient lifting during DIBH the method has not been used at SUS. When adding visual guidance the suspicion of patient lifting grows even bigger due to the fact that the patients will see how far off, in accordance to the gating window, they are. If a patient for example is tired after all the breathing, and thus cannot enter the gating window, the risk is that she will compensate the missing amplitude by lifting her body. To investigate this dilemma a pressure sensor was placed between the volunteer's shoulders and the set-up fixation to investigate any indications or contraindications of lifting.

The DIBH method also requires the patients to hold their breath and at the same time keep the chest at a certain breathing amplitude. To get an indication of a reasonable time for the breath hold a final step in the study was to test the volunteer's ability to hold their breath.

Furthermore, monitoring respiratory gating using surface scanning was also investigated using the Catalyst system (C-RAD positioning AB, Uppsala, Sweden).

Questions to be answered were:

- Will the amplitude between the two methods differ naturally or is it unchanged?
- Will the visual guidance help or hinder the volunteers?
- Can any possible patient lifting be detected?
- Can patient lifting vary between the same amplitude with or without visual guidance?
- How high breathing amplitudes are the volunteers capable to perform?
- How long DIBHs are possible before the volunteers feel uncomfortable or fatigue?

3. THEORY

3.1 ENHANCED INSPIRATION GATING

The EIG method uses the above-mentioned anatomical characteristics, i.e. that the distance between the heart and the breast increases during inhalation. The patient continuously perform deep breathing and by limiting the irradiation to the end-in inspiration phase, both cardiac and pulmonary doses can be reduced compared to a conventional, non-gated treatment (Figure 1) [3, 12].

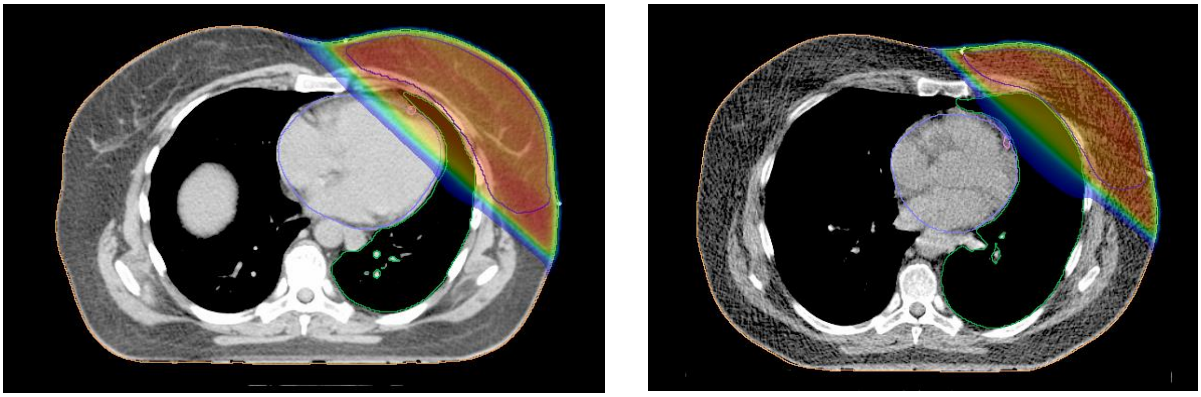


Figure 1: Transverse CT-images showing the proportion of the heart ending up inside the radiation field for FB (left) and EIG (right). The images are obtained at the same position, according to the vertebras, for the same patient.

The EIG treatment at SUS follows a clinical protocol that was established in 2007. According to this protocol the patient should first undergo respiratory training before the treatment starts. During this session the patient starts to breathe normally (Figure 2) while the breathing is monitored by the Varian Real-time Position Management system (Varian Medical Systems, Palo Alto, CA). The amplitude during this so called free breathing (FB) is noted and the patient's baseline is found. The baseline marks the lowest amplitude of the respiration curve during FB.

Subsequently, the patient is asked to perform deeper breaths and at the same time follow the trainers voice when to breathe in and out. According to protocol the amplitude should now triple compared to the amplitude during FB and preferably this amplitude should lie around 1 cm. Instead of the trainers voice the patient is now asked to follow an audio coach and between breaths the patient should return to the baseline. The trainer should now manually adapt the time between the audio coach's "breath-in" and "breath-out" so that the breathing curve starts to resemble a square wave. At the same time it is important that the patient is able to breathe stable and reproducible.

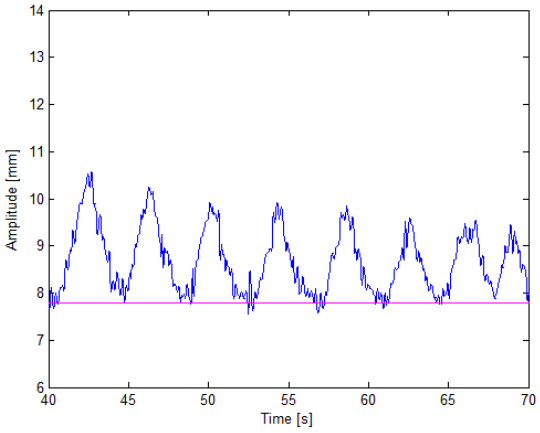


Figure 2: Typical FB curve, the pink line represents the baseline.

The next step in the protocol is to verify the so called gating window. To not introduce any larger residual motion during beam-on compared to FB, the size of the gating window should not exceed the FB amplitude. The window will be positioned so that it covers the highest amplitude of the coached breathing curve (Figure 3). It is thus only within this gating window, when the distance between the heart and the target volume is maximized, irradiation will occur. Consequently when the amplitude of the patient's breathing is outside the gating window, no radiation will be delivered. According to Damkjær *et al.* usually 10-30 monitor units (MU) can be delivered in a single EIG-breath, depending on the width of the gating window and the breathing pattern of the patient [11].

The dosimetric benefits of EIG compared to FB was demonstrated by Korreman *et al.* [2], Nemoto *et al.* [12] and Edvardsson *et al.* [3]. Korreman showed that the median heart volume receiving 50 % or more of the prescribed dose ($V_{50\%}$) was reduced from 19.2 % to 2.8 % for FB and EIG, respectively. The left anterior descending (LAD) coronary artery $V_{50\%}$ was reduced from 88.9 % with FB to 22.4 % with EIG. Nemoto *et al.* [12] showed the same cardiac dose sparing results where the mean left ventricular $V_{50\%}$ was 2.9 % and 0.2 %

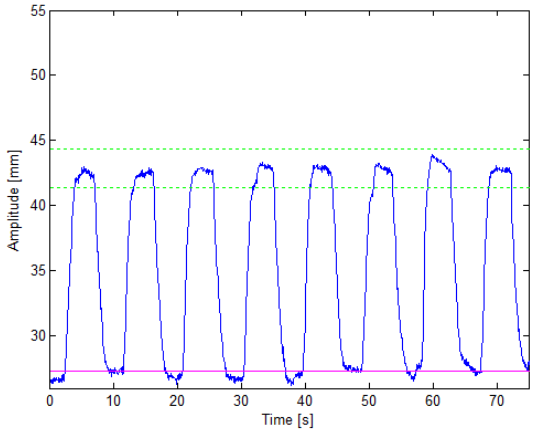


Figure 3: EIG breathing curve, the pink line represents the baseline and the green lines represent the gating window.

for FB and EIG, respectively. Edvardsson *et al.* [3]showed that the average V_{25Gy} between FB and EIG was reduced from 50.3% to 18.4% for LAD and from 4.2% to 1.2 % for the heart.

The pulmonary dose is also reduced using EIG compared to FB. According to Korreman *et al.* [2] the median ipsilateral relative lung $V_{50\%}$ was reduced from 45.6 % to 29.5 % for FB and EIG, respectively. Nemoto *et al.* [12] showed that the median lung volume receiving 20 Gy (V_{20Gy}) or more was 5.0 % for FB and 4.7 % for EIG and Edvardsson *et al.* [3] showed that the average V_{20Gy} for the ipsilateral lung was reduced from 26.3 to 22.7 for FB and EIG, respectively.

3.2 Deep Inspiration Breath Hold

Contrary to EIG, were the patient continuously breathes deeply, the DIBH method instead implies fewer but longer breaths (Figure 4). The separation becomes even more evident with DIBH, compared to EIG, because the technique also implies that the patient takes deeper breaths and therefore obtains a larger lung volume than with the EIG approach [11, 12].

According to Damkjær *et al*. [11] the median pulmonary volume increased significantly from a mean value of 1982 cm^3 with EIG to 2286 cm^3 with DIBH. This increase in volume also leads to an increase in mean inspiration level. For visual guided DIBH and audio coached EIG the mean inspiration level were 20.5 mm and 16.6 mm, respectively. According to Nemoto *et al*. [12] the mean anteroposterior chest wall excursion during audio coached EIG and non-coached DIBH was 10.9 mm and 21.3 mm, respectively. This is one of the reasons that speaks for DIBH, because this difference in amplitude and pulmonary volume can possibly result in a greater saving of cardiac and pulmonary dose [2, 11, 12].

As with the EIG method, patients treated with DIBH should also undergo respiratory training, with either audio or visual coaching before treatment. During this training, the patient's baseline will be identified as well as the gating window. The position of the gating window should be individualized for each patient, based on the size of the anteroposterior chest wall excursion when the patient is requested to take a deep breath [4]. The DIBH method requires that the patient is able to hold her breath at a stable level. The length of the breath hold can advantageously be long since this means that more MU can be delivered, yet not too long to bring any discomfort to the patient.

The time of the breath hold varies between different studies but is approximately around 20 s [4, 5, 8, 10]. This means that more MU can be delivered to the patient during a single breath compared to EIG. According to Damkjær *et al*. [11] as much as 200 MU can be delivered, without beam interruption, in just one 20 s long breath hold.

The number of deep inspirations a patient has to accomplish during a treatment varies depending on number of fields and MU which in turn depends on diagnosis and treatment area. It would be desirable that an entire field could be delivered to the patient during only one breath hold. This would mean that the number of deep inspirations will coincide with the number of fields.

It has been shown that after a DIBH some patients have problems returning to the baseline. However, this baseline drift can be remedied by allowing the patient to breathe normal , i.e. performing FB, after the DIBH and in this way get back to the baseline (Figure 5) [8, 13].

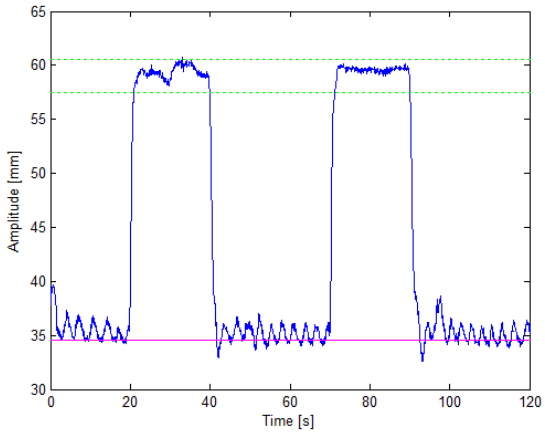


Figure 4: Two DIBHs, each 20 seconds long, with related baseline and gating window.

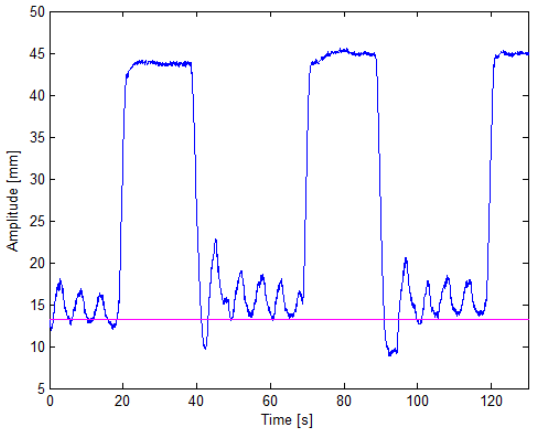


Figure 5: Two DIBH curves where the volunteer first end up below the baseline and then find its way back.

There are several studies which show that there are advantages in terms of dose reduction with DIBH. Most of these studies compares DIBH with FB and results show a dose reduction in both pulmonary and cardiac doses [2, 4, 5, 9, 10]. Both Vikström *et al*. [4] and Hjelstuen *et al*. [10] showed a significantly reduction in the average ipsilateral lung V_{20Gy} when comparing FB and DIBH, from 12.2 % to 10.0 % and 44.5 % to 32.7 %, respectively. The difference between the results in the two studies is due to different definitions of the target. Vikström *et al*. only defined the left breast as the target while Hjelstuen *et al*. additionally included lymph nodes in the supraclavicular region, axilla and the internal mammary chain.

According to Korreman *et al.* [2] the median heart $V_{50\%}$ was reduced from 19.2 % to 1.9 % for FB and DIBH, respectively. Pedersen *et al.* [5] showed similar results where the median heart $V_{50\%}$ was reduced from 8 % for FB to1 % with DIBH.

Reduction of absorbed dose to LAD has been shown using DIBH [2, 4, 5, 9, 10]. According to Pedersen e*t al.* [5] the median LAD $V_{50\%}$ was reduced from 54 % to 5 % for FB and DIBH, respectively. A significant reduction in mean dose for the LAD was shown by Vikström *et al*. [4] where the mean dose was 18.1 Gy with FB and 6.4 Gy with DIBH.

But naturally, it is not of interest only to compare FB and DIBH but also to compare EIG and DIBH. Studies have shown that there also are significant dose savings between these two different gating methods [11]. Damkjær *et al*. [11] showed that the relative lung $V_{20\%}$ was reduced from 29.6 % for EIG to 27.1 % with DIBH.

When it comes to the cardiac doses, Nemoto *et al.* showed that the median left ventricle $V_{50\%}$ was reduced from 0.2 % to 0 % for EIG and DIBH, respectively [12]. Korreman *et al.* showed similar dose-saving results for the heart where $V_{50\%}$ was reduced from 2. 8% to 1.9 % and the LAD $V_{50\%}$ was reduced from 22.4% to 3.6% with EIG and DIBH, respectively [2]. But on the other hand none of these results were statistically significant.

For certain patients the DIBH method has managed to get the heart completely outside the radiation field [4, 10]. In two different studies, containing 17 patients, the percentage of patients where the heart managed to get entirely outside the radiation field was 58.8 % [4] and 41.2 % [10]. This was compared to radiation during FB where the heart never got completely outside the field.

3.3 Reproducibility and Stability

For this study the reproducibility and stability is defined according to Cerviño *et al*. [8]. The reproducibility for both EIG and DIBH is expressed in millimetres and a lower value corresponds to a better reproducibility. The reproducibility is defined as the maximum difference between different peaks according to equation 1:

$$R = \max_{i=[1,n]}\{d_i\} - \min_{i=[1,n]}\{d_i\} \qquad (1)$$

where R is the reproducibility, d_i is the average level of each peak in the series and n is the number of peaks in the series (Figure 6).

The stability for both EIG and DIBH is expressed in millimetres and a lower value corresponds with better stability. The stability is defined as the maximum of the amplitude change between the initial and end time points of a peak when it is fit by a line with least squares, according to equation 2:

$$S = \max_{i=[1,n]}\{|m_i|\Delta t\} \qquad (2)$$

where S is the stability, m_i is the slope of the linear fit to each peak and Δt is the duration of the peak (Figure 7). In this study Δt was approximately 20 s for DIBH and 4.5 s for EIG.

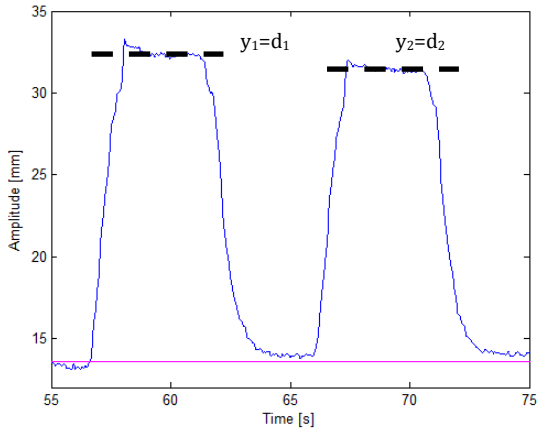


Figure 6: A graphical illustration of the reproducibility parameters

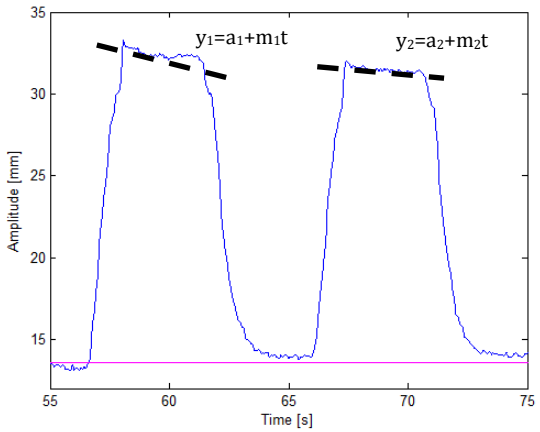


Figure 7: A graphical illustration of the stability parameters

3.4 The Catalyst System

The Catalyst (C-RAD positioning AB, Uppsala, Sweden) is an optical surface scanning system used for patient set-up, patient monitoring and gating within radiotherapy. The system consists of a projector (ViALUX DLP three high-power LED) which projects light on the desired surface [18]. The projected light is 405 nm which results in visible blue light. On the same unit (Figure 8) there also is a camera (CCD Pike F032B GOF ASG16) that captures the projected light on the surface; the camera resolution is 640 x 480 pixels and the system can perform three scans per second. To determine the distance to the object, the Catalyst system uses the phenomena of optical triangulation to construct a 3D surface of the object [14]. It also uses a non-rigid algorithm to calculate the displacement of the isocenter [15].

The Catalyst should be placed on a stable position inside the treatment room, tentatively in the ceiling. The dimensions of the unit is 620 mm x 280 mm x 400 mm (L*W*H) and the positional scanning volume is 800 mm x 1300 mm x 700 mm (X*Y*Z) [14]. For best results there should be no object between the Catalyst unit and the surface intended to be scanned, it is also of importance that the surface is dry and clear of unwanted reflections which may give false data to the camera [16].

Figure 8: The Catalyst unit (www.c-rad.se).

It is important that the patient is positioned correctly throughout the whole treatment chain and that the patient lies still during a treatment session. The radiation is delivered in accordance with a treatment plan that has been developed based on a reference image from the previous CT-scan. To achieve the best possible treatment the patient must be

positioned within the margins defined in the reference image. Using the Catalyst during patient set-up has been shown by Thornberg *et al*. [17] to decrease the set-up deviations compared to conventional set-up using tattoos and lasers. Another useful feature is the ability to monitor the patient's surface during treatment and ensure that the patient lies still. The Catalyst also can provide monitoring of the breathing motion and in this way implement gating treatments where the radiation is only delivered at a specific part of the breathing cycle [14, 16]. All aforementioned features are included in the Catalyst system's three applications: cPosition, cMotion and cRespiration [14].

cPosition

By importing reference data from the CT-scan the personnel can, when positioning the patient before treatment, see both a live surface image and the reference surface image of the patient (Figure 9) [14]. The Catalyst then makes suggestions on which adjustments that needs to be done to get the live image and the reference image in agreement [14].

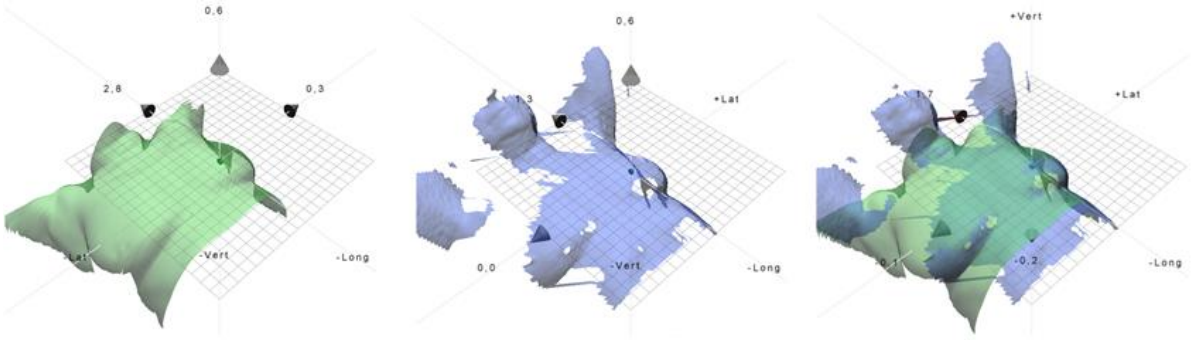


Figure 9: The reference image (green), the live image (blue) and both images matched together.

There are two different tolerance levels that can be set manually; 1) The target tolerance is defined as the maximum allowable deviation between the isocenter of the reference image and the calculated isocenter from the live image [16]. If the deviation does not coincide within the pre-set tolerance, the numbers on the monitor will be red and show the suggested adjustments needed (Figure 10). When the isocenter is within the tolerance level the numbers will be white [16].

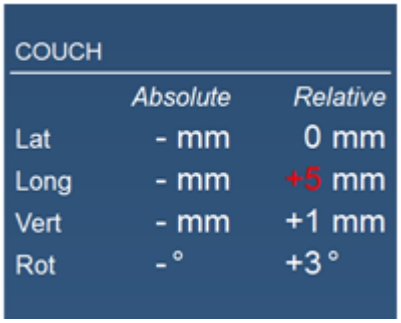


Figure 10: The red number warns that the patient is outside the pre-set target tolerance in longitudinal direction.

2) The surface tolerance is defined as the maximum allowable local difference between the surfaces in the reference and the live image [16]. As in 1) the Catalyst system suggests movements to be within a pre-set tolerance level when the reference surface image and the live surface image differs [16]. This will be shown as a colour map projected directly onto the patient's skin. The colour map shows the part of the surface that is positioned too low by projecting green light (~528 nm), or too

high by projecting red light (~624 nm), compared to the reference image [14]. In this way set-up rotations can be discovered and since there is no ionizing radiation in the room when the Catalyst is on the setup adjustments can be done on site [14].

The colour map is also useful for positioning of extremities, such as arms during breast treatment, since these usually do not have any markings that the personnel can use. The system can contribute to the positioning in 6 degrees of freedom: Longitudinal, Vertical, Lateral, Pitch, Roll and Rotation [14]. The accuracy of the positioning is within 1mm for a rigid body [14].

cMotion

When the patient is in the correct position the personnel will leave the room and start the treatment. By using the application cMotion, a continuous monitoring of the patient movement can be observed and help to verify that the patient is lying still during the entire treatment [14]. But if the patient, for any reason, change their position and gets outside the set tolerance levels the system will alert the personnel and break the beam. The accuracy of the motion detection is within 1mm for a rigid body [14].

cRespiration

Monitoring of the breathing motion is possible with the cRespiration application. By projecting a gating point anywhere on the desired surface the varying breathing amplitude can be presented for this particular point. The radius of the point is adjustable and it is also possible to use a secondary gating point (Figure 11). This function can be used to perform gating treatments [14].

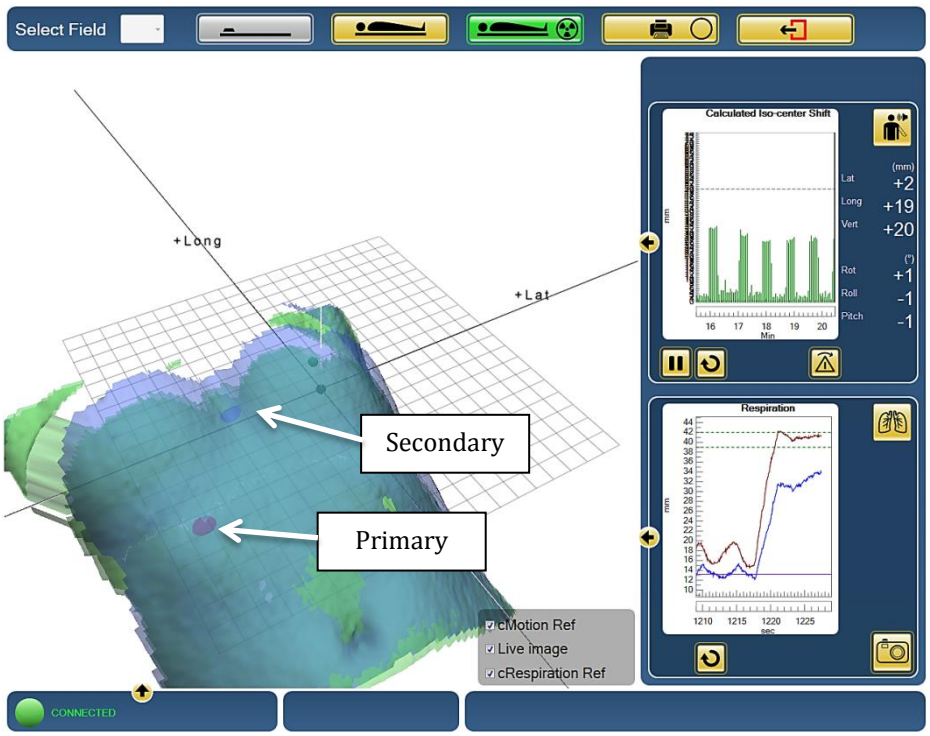


Figure 11: The Catalyst interface showing a volunteer performing DIBH with two gating points placed on her chest.

The system is also able to provide the patient with visual guidance during the gating treatments. During the visual, coaching the patient will see the breathing motion presented as an orange bar that moves up and down in accordance with her breathing. The patient also sees a blue line which is the baseline and a green window which symbolizes the gating window. When the patient breathes the orange bar will move and when it is inside the green window the breathing amplitude is correct (Figure 12).

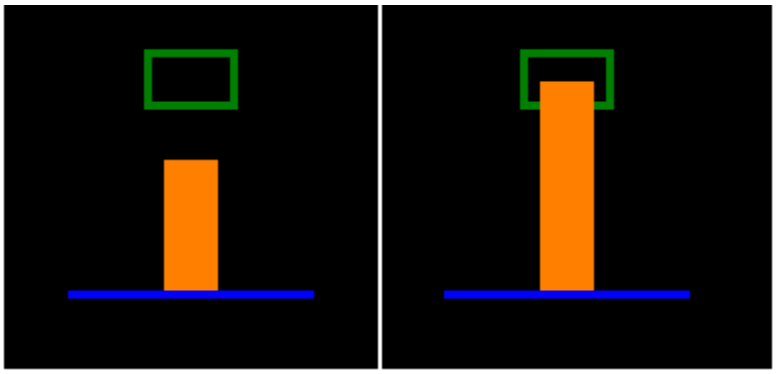


Figure 12: A visualization of the visual guidance. The blue line represents the baseline, the green window represents the gating window and the orange bar represents the breathing.

3.5 Pressure Measurements

For pressure measurements the I-scan system and sensor model 9801 (Tekscan Inc., South Boston, USA) was used (Figure 13). The sensor has 96 sensing elements, also called sensels, positioned in 16 rows and 6 columns where each element measures the pressure individually (Figure 14) [18]. The sensor is flexible and 0.15 mm thick [18, 19]

The pressure sensor consists of two layers of very thin polyester sheets Between the sheets there is a pressure sensitive material patented by Tekscan Inc. [18]. On the inside the two sheets are coated with opposite electric conductors with the pressure sensitive material acting as an insulator, preventing the flow of electricity through the circuit. When pressure is applied to the sensor the electrical conductivity of the pressure sensitive material increases. The increase is linear with regards to the amount of pressure applied [18].

Figure 13: The sensor (Model 9801).

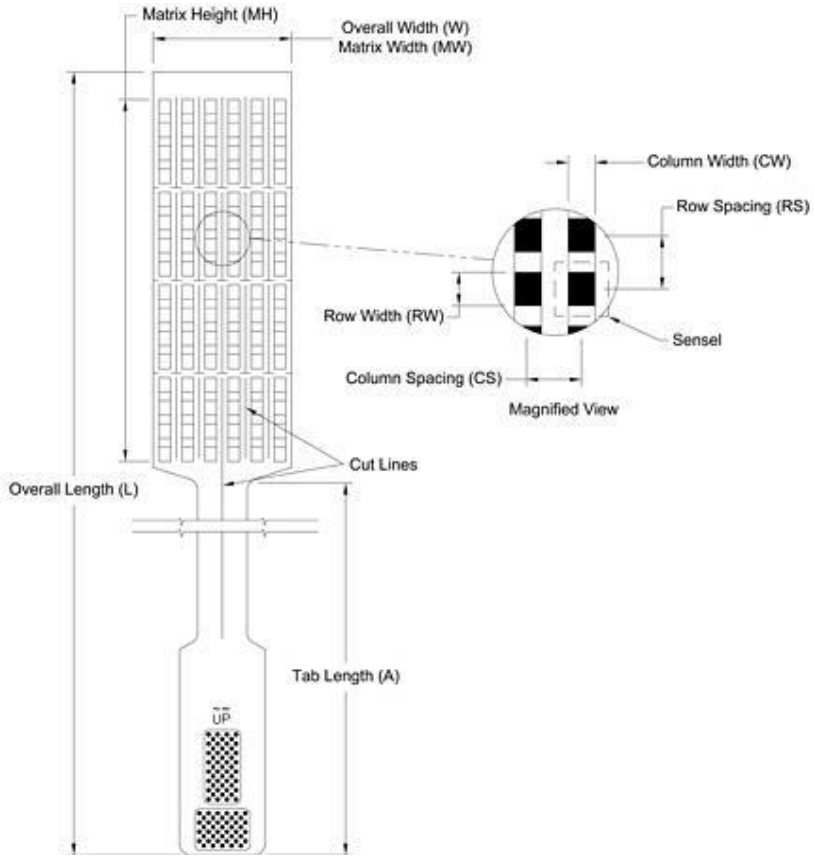


Figure 14: A schematic representation of the sensor with sensels (www.tekscan.se).

Equilibration and calibration of the sensor is needed prior to measurements. The equilibration ensures that two different sensels, exposed to the same pressure, provides the same signal. The calibration creates a conversion constant which relates the signal to a certain amount of pressure expressed in units of kilopascal (kPa) [18].

During measurements the sensor is connected to a computer via a transducer (Tekscan. Model EH-2) (Figure 15). It is possible to collect data both dynamically and statically and it can be presented either as numerical text files or as visual pictures. It is also possible to see dynamical changes of pressure as a movie loop [18, 19].

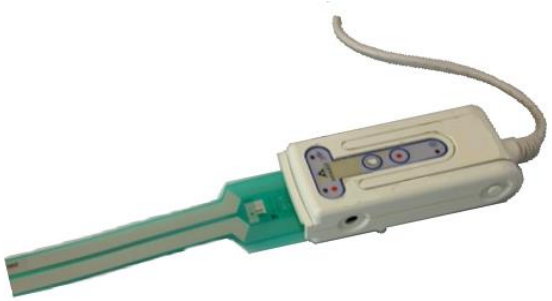


Figure 15: Sensor connected to the transducer.

The pressure was visualized and every square represents a sensel and different colours represent different amount of pressure (Figure 16). The pressure is highest on the sensels with red colour and, according to the scale at the side of the picture, lowest on the sensels with blue colour.

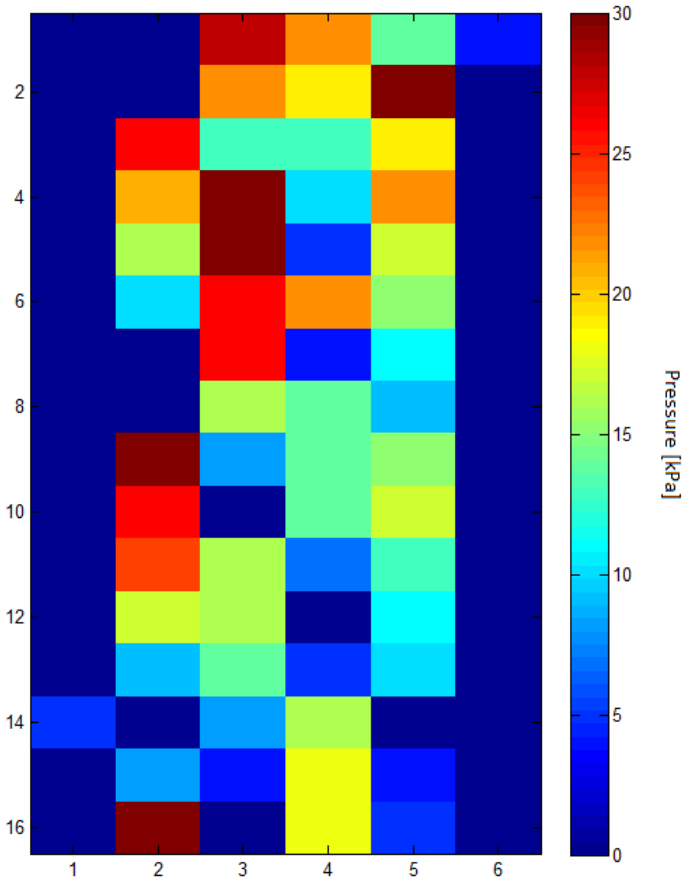


Figure 16: Example of a pressure distribution collected in static mode. Every square represents a sensel of the sensor and the color of the square is related to the pressure.

4. Material and Methods

The study included 20 healthy female volunteers. Besides the information given to them, none of the volunteers had any prior knowledge of the methods or techniques used in the study. The median age of the volunteers was 27 (range 23-61) years. The study was divided into four parts: An amplitude study, comparison of different parameters (reproducibility, stability and P_{GW}) between EIG and DIBH with and without visual guidance, pressure measurements and a breath hold study. The study structure is illustrated as a flowchart (Figure 17).

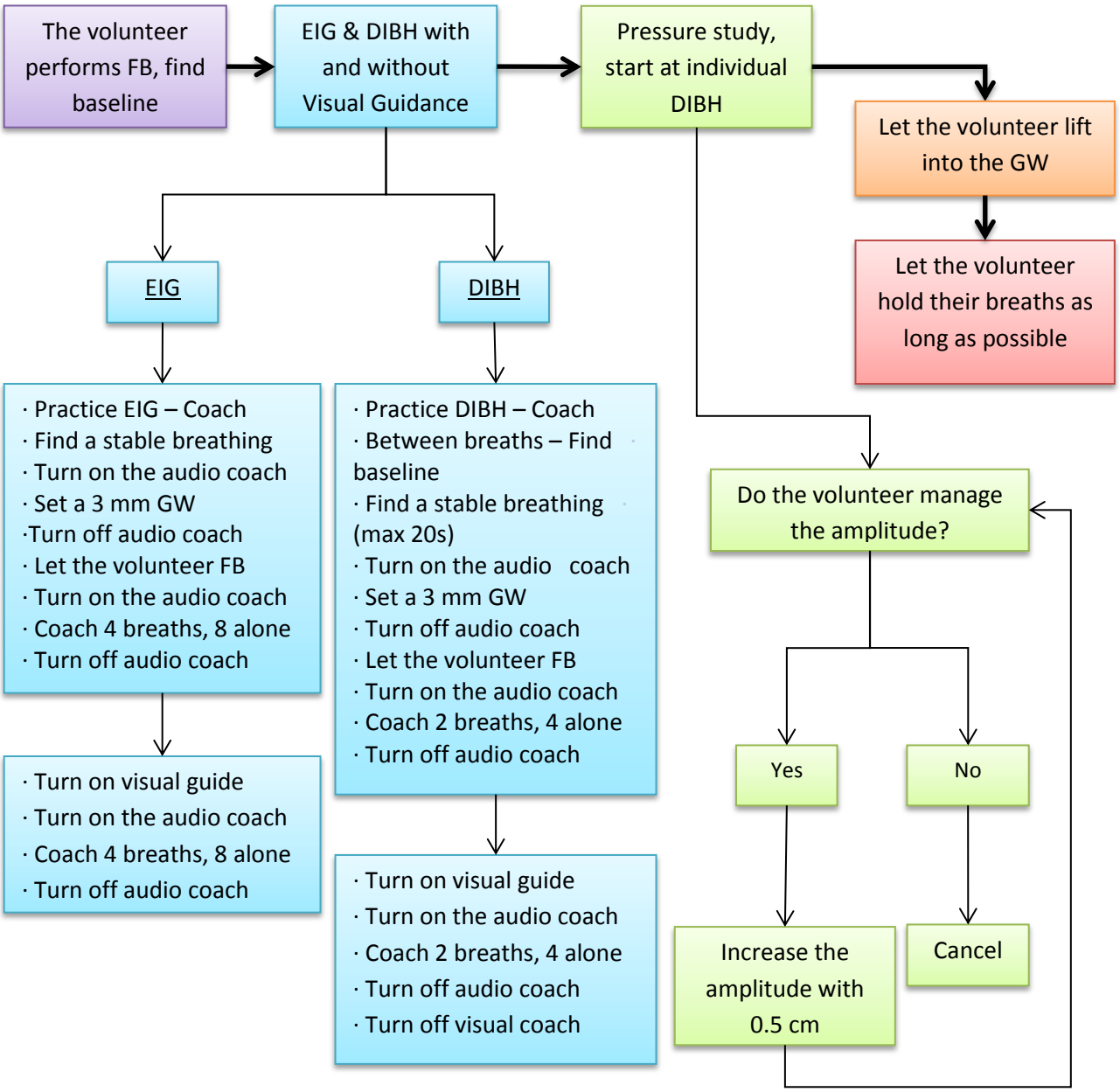


Figure 17: The study structure represented as a flowchart (GW is short for gating window).

When the volunteers arrived they began with a separate review of the study's different parts and how they ought to be performed. If the volunteer had any questions or concerns about the study they were discussed at this occasion. All volunteers were given the same information and by the same person. The study took place in a treatment room at the radiotherapy department at SUS in Lund.

Figure 18: Posiboard™ (www.civco.com).

Figure 19: Periscope spectacles.

The volunteers got to see the treatment room and major items such as the linear accelerator, the Catalyst and the laser system used for positioning were pointed out. During the study the volunteers had no clothing on their upper body and they were fixated in a Posiboard™ – 2 Breastboard (CIVCO Medical Solutions) (Figure 18).

For visual guidance, a screen was placed at the foot end of the couch (Figure 20) and in order to see the screen the volunteers used a pair of periscope spectacles (Figure 19) which angled their vision 90 degrees. Due to the spectacles the volunteers could see the screen where the Catalyst system's visual guidance program was shown.

Figure 20: Picture of the treatment room and the screen used for visual guidance

At SUS the respiration is normally monitored by the Varian Real-time Position Management (RPM) system 1.7 or Varian TrueBeam integrated gatingsystem. When using this system, a marker block i.e. a small box with reflecting markers, is placed just below the right breast to detect the

respiratory motion. In this study the respiration was instead monitored with the Catalyst system and the amplitude was measured both at the usual position of the RPM marker block (primary gating point) and at the middle of sternum (secondary gating point) (Figure 21). For this study, only data from the primary gating point was used, which enables comparison with data from the RPM-system which is clinically used today. The radius of the point was set to 10 mm. The standard deviation of the signal, in the relevant treatment room, was measured to be 0.15 mm for a static rigid body. The volunteers were placed according to the lasers, with the isocenter approximately in the middle of the left breast, to clinically resemble a breast cancer patient setup.

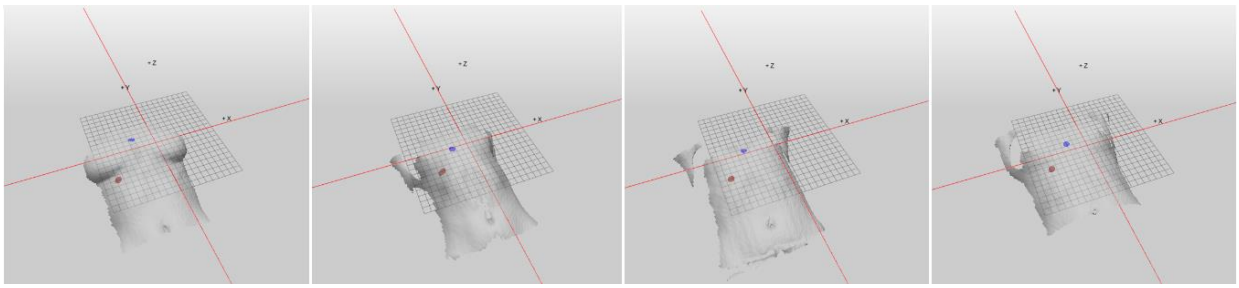


Figure 21: Position of the primary (red) and secondary (blue) gating point for four different volunteers. The red axes represent the isocenter.

4.1 AMPLITUDE STUDY

The volunteers got a short briefing about the two gating methods, EIG and DIBH, and how they differed. The volunteers was told to find an individual breathing amplitude that they felt comfortable with for the two different methods and was therefore not influenced to breath deeper with either one of the techniques. This information was neglected to investigate if the volunteers, without being influenced, had different breathing amplitudes for the two different methods. This is clinically relevant since higher amplitudes can have a dose sparing effect for the organs at risk. The volunteers also got a tutorial on how the audio and visual coach should be followed.

The volunteers started to practice one of the two methods, half of the volunteers started with EIG and the other half started with DIBH. The study was constructed in this way to avoid potential biases such as fatigue of the volunteer while performing the second technique or that the volunteer had been accustomed after the first gating method and therefore performing better during the second. Every volunteer needed a different amount of time to find the breathing amplitude which they felt comfortable with, this amplitude will later be called the volunteer´s individual amplitude. A 3 mm gating window was set, manually, based on the amplitude of the breaths during this practice session. When the gating window was set, the amplitude was defined as the distance between the baseline and the lower limit of the gating window.

4.2 Reproducibility, Stability & P_{GW}

One of the main tasks of this study was to investigate the stability and reproducibility, when comparing EIG and DIBH, with and without visual guidance. Further, the time in percentage that the central part of the peaks was inside the gating window was also evaluated. The latter will further be referred to as P_{GW}. These parameters are relevant from a clinical point of view; the reproducibility represents how easy it is to repeat a predetermined breathing pattern, the stability represents the anteriorposterior chest wall excursion during a breath and can therefore say something about a potential width of the gating window and P_{GW} represents the time inside the gating window that ultimately decides the amount of MU delivered during each breath.

For each method all volunteers started without visual guidance at the individual amplitude. To give them a reasonable chance to find the gating window they were verbally instructed, during the first breaths, what amplitude they had relative to the window. This was done to create as equal conditions as possible compared to the EIG treatments in the clinic where the patients receive help from the personnel to find the gating window. This coaching was performed by the same person who had held in the informative conversation in the beginning and will further be referred to as verbal assistance. When calculating reproducibility, stability and P_{GW} the coached breaths in the beginning were excluded.

For EIG the audio coach was set to say “breath-in” and “breath-out” with an interval of 4.5 s, totally the volunteers took 12 EIG breaths. The verbal assistance was performed for the first 4 breaths and subsequently the volunteers took 8 breaths on their own with only the audio coach (Figure 22). Then the visual guidance was turn on and the same procedure was carried out (Figure 23).

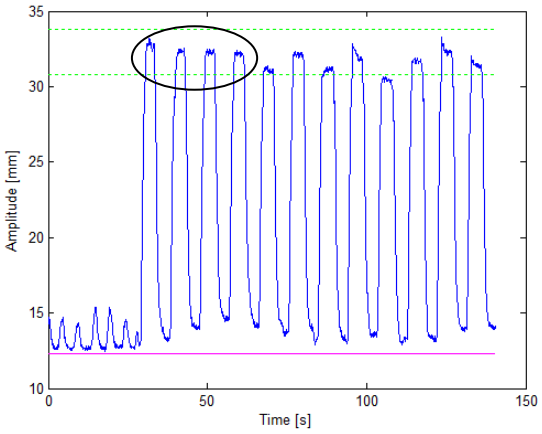


Figure 22: EIG breathing curve without visual guidance for volunteer 7. The black circle marks the peaks during verbal assistance.

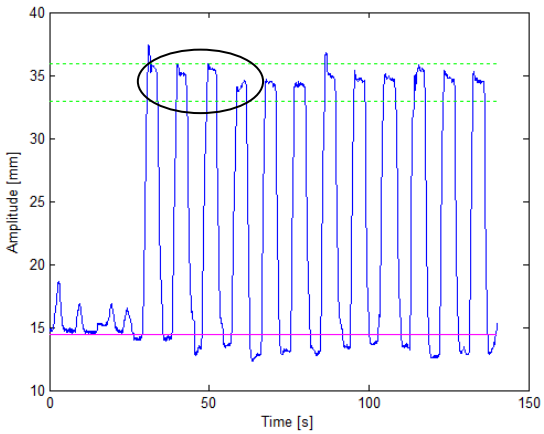


Figure 23: EIG breathing curve with visual guidance for volunteer 7. The black circle marks the peaks during verbal assistance.

For DIBH the audio coach was set to 20 s long breath holds, between each breath hold an interval of 30 s was set for the patient to recover. Totally the volunteers took 6 DIBHs. The verbal assistance was performed for 2 breaths and subsequently the volunteers took 4 breaths on their own with only the audio coach (Figure 24). Then the visual guidance was turn on and the same procedure was carried out (Figure 25).

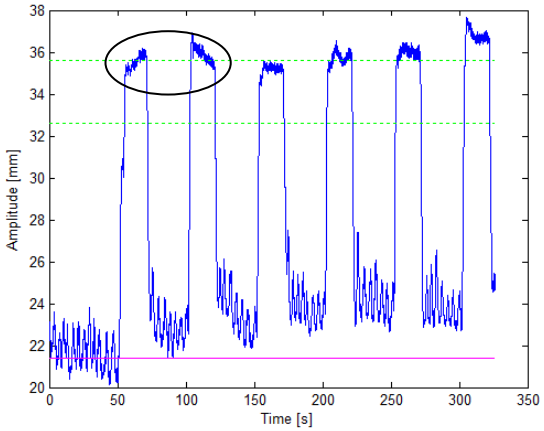


Figure 24: DIBH breathing curve without visual guidance for volunteer 9. The black circle marks the peaks during verbal assistance.

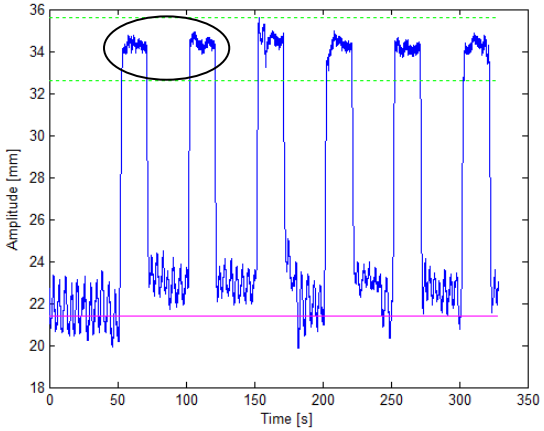


Figure 25: DIBH breathing curve with visual guidance for volunteer 9. The black circle marks the peaks during verbal assistance.

To define the average level of each breath, d_i from theory part 3.3 (equation 1), a MATLAB program was created which first roughly sorted out the respiratory peaks depending on their amplitude and width. Only peaks with higher amplitudes than 90 % of the lower limit of the gating window and a width of 10 s (50% of 20 s) for DIBH and 2.25 s (50% of 4.5 s) for EIG were included. In some special cases these values had to be adjusted in order to find all the peaks.

When a peak was identified 15 s (75% of 20 s) in the middle of the peak was selected (Figure 26) for DIBH and 3.375 s (75% of 4.5 s) for EIG. From this middle section an average value was calculated.

For an individual amplitude cut-off, independent of the peak amplitude according to the gating window, the assumption was made that the peaks were in the middle of a virtual gating window. Together with this assumption, and a 3 mm width of the gating window, the amplitude cut-off was 1.5 mm below the calculated average value (Figure 27).

To this final peak a linear fit was made, used in the stability calculations (Figure 28). A new average value was calculated for the remaining peak and represents d_i in the reproducibility calculations. The time, in percentage, that the defined peaks were inside the gating window was calculated (P_{GW}).

For the DIBH method there frequently was a small peak in the beginning of the breath hold. This overshot probably depended on the sensitivity of the orange bar in the visual guidance program. When the volunteers took a deep breath to enter the gating window the bar moved too fast and they could not stop in time and needed to compensate. Therefor an investigation was made to see if the different parameters improved by adding a delay. This means that the radiation will not be connected to when the patient enters the gating window, but will instead be induced after a predetermined delay time after the entering. In this study a delay of one second was introduced, this means that the first second of the breathing curve was excluded. To not distort the curve, and in this way affect the stability, one second in end was also omitted. Another argument to exclude the last second was that a whole field is supposed to be delivered before the gating curve exits the gating window, and hence the last second is not of interest. The reproducibility, stability and P_{GW} were calculated on this shortened curve (Figure 29). Reproducibility and stability were calculated according to theory part 3.3.

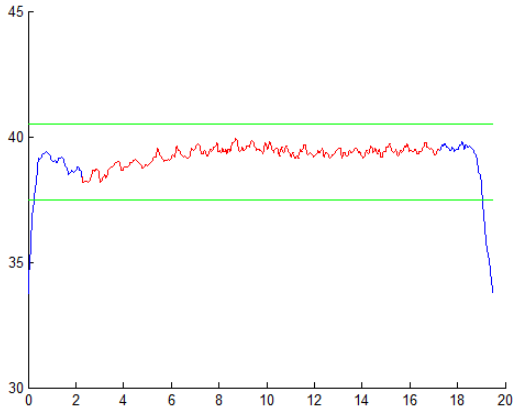


Figure 26: A DIBH peak cut at 90% of the lower gating window limit for volunteer 13. The red part represents the 15 s in the middle of the peak wherefrom an average value was calculated.

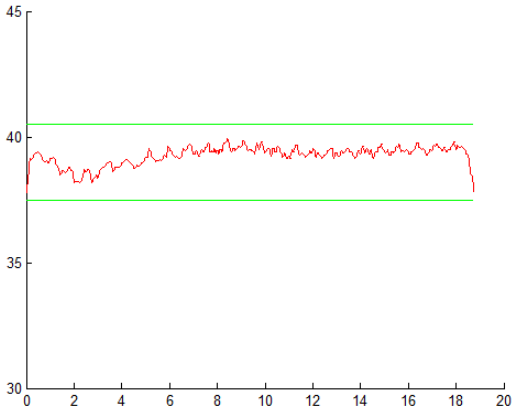


Figure 27: A DIBH peak, for volunteer 13, cut 1.5 mm below the average value from Figure 26.

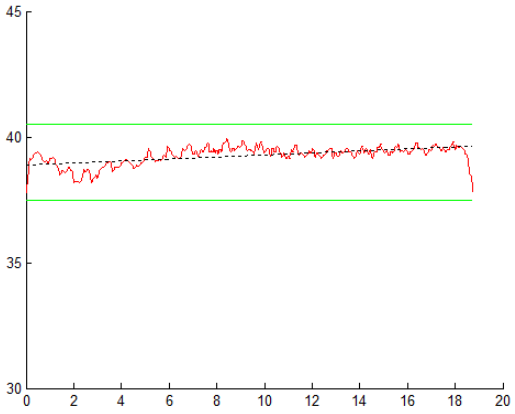


Figure 28: A DIBH peak, for volunteer 13, with a linear fit.

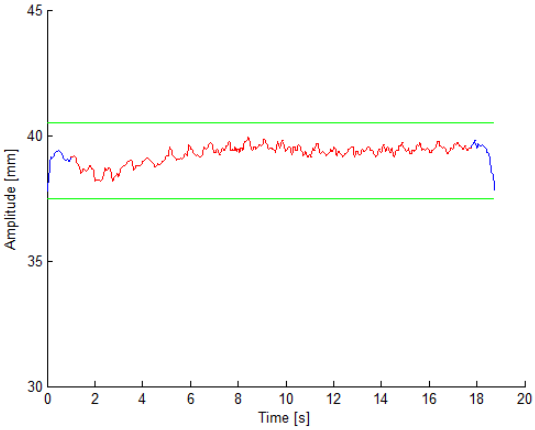


Figure 29: A DIBH peak, for volunteer 13, with 1 s omitted (blue parts) at the beginning and end.

4.3 PRESSURE MEASUREMENTS

In this part of the study a pressure sensor, placed under the volunteer's scapular region (Figure 30), was used. The sensor was positioned at a specific position, according to the fixation, for each volunteer and was thus not individualized depending on the anatomy.. In order to not affect the pressure distribution the sensor advantageously should be placed upon a flat surface; therefore a rectangular PMMA plate was manufactured and placed between the fixation and the volunteer. The pressure sensor was then placed directly on the PMMA plate. The sensor was calibrated and equilibrated regularly during the study. The resulting pressure was presented as the average pressure of the entire sensor.

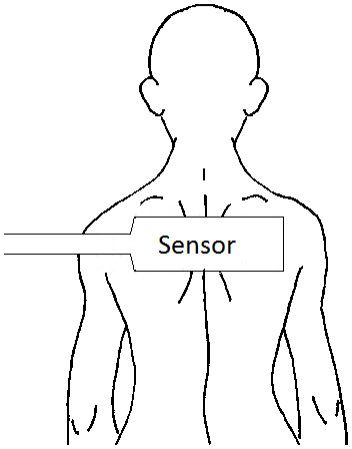


Figure 30: Schematic sketch over the position of the sensor.

The measurements were only made during DIBH and every measurement started with a few seconds of FB. The pressure during FB was of interest since it was used as a reference of how the pressure was during normal respiration compared to when the volunteer implemented DIBH. The volunteers started without visual guidance and found the gating window only with verbal assistance. The audio coached breath hold was pre-set to 20 s. The gating window was then raised by 5 mm and did the volunteer manage this raise the amplitude was increased further with additional 5 mm. The study was terminated when the volunteers were unable to perform the breath hold; however, no volunteer was allowed to increase the amplitude more than three times. The same measurements were then performed again, but this time the volunteer had access to visual guidance.

For the last part of the pressure measurements the volunteers were asked to enter the gating window without inhaling air but instead by lifting or arching their back. During this part the gating window was set to the individual DIBH amplitude.

4.4 BREATH HOLD

Finally the volunteer's ability to hold their breath was tested. The visual guidance was turned on and the gating window was set to the individual DIBH amplitude. They only got one attempt and the volunteers were instructed to hold their breath as long as possible without feeling any discomfort or falling outside the gating window.

The start time of the breath hold began when the volunteer had found a stable level of the amplitude and ended when the level stopped being steady or when the volunteer let out the air. This definition of the breath hold is relevant from a clinical point of view, since the time a volunteer can stay at a stable amplitude represents the time a patient can be positioned inside the gating window. A longer breath hold implies more delivered MU per breath.

4.5 STATISTICAL TESTS

To investigate if the difference between two datasets were statistically significant statistical tests were performed. To know which test to perform one first had to investigate whether the calculated data was normally distributed or not, which was done using a Shapiro-Wilks test ($\alpha = 0.05$). If the test indicated normally distributed data a paired t-test was carried out and if not a Wilcoxon signed-rank test for matched pairs was used.

5. RESULTS

5.1 AMPLITUDE STUDY

The Shapiro-Wilks test indicated normally distributed data and a paired t-test was carried out. The null hypothesis for the statistical test was:

H_0: There is no difference between the average amplitude for the two methods at the 0.05 level of significance.

The average amplitude was significantly increased for DIBH compared to EIG (Table 1).

Table 1: Comparison of the EIG and DIBH amplitudes. Data shown as average value ± one standard deviation (SD) and p-value for a paired t-test.

Method	Average amplitude ± 1 SD [mm]	p
EIG	10.8 ± 4.7	0.01
DIBH	12.9 ± 5.8	

5.2 REPRODUCIBILITY, STABILITY & P_{GW}

The Shapiro-Wilks test indicated that not all data was normally distributed and therefore a Wilcoxon signed-rank test for matched pairs was performed. The null hypothesis for the statistical test was:

H_0: There is no median difference between the reproducibility/stability/P_{GW} for the same method with or without visual guidance at the 0.05 level of significance.

Reproducibility

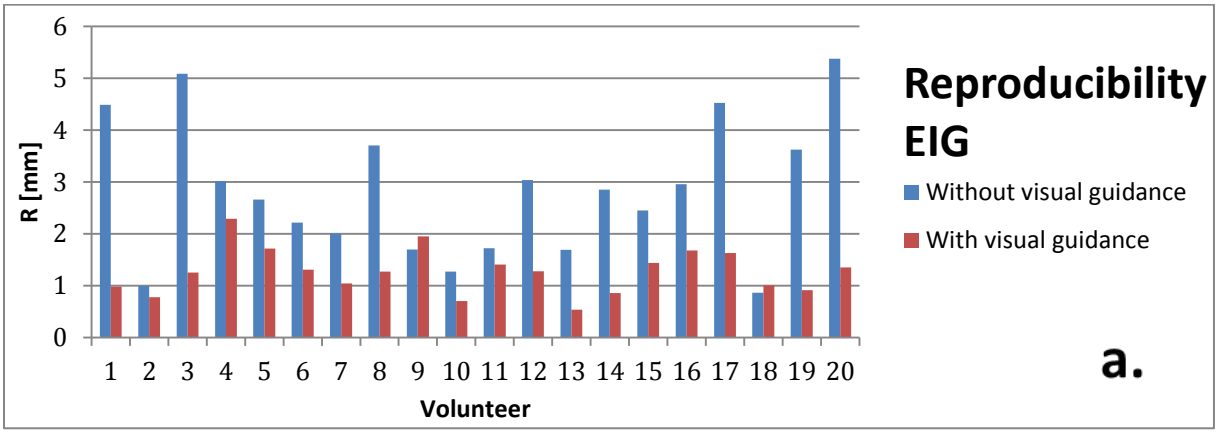
The reproducibility was significantly improved for EIG with visual guidance compared to EIG without visual guidance (Table 2). The individual reproducibility values are presented in tabular format (Appendix I) and as a bar chart (Figure 31 a). The reproducibility with visual guidance was improved for all except two volunteers.

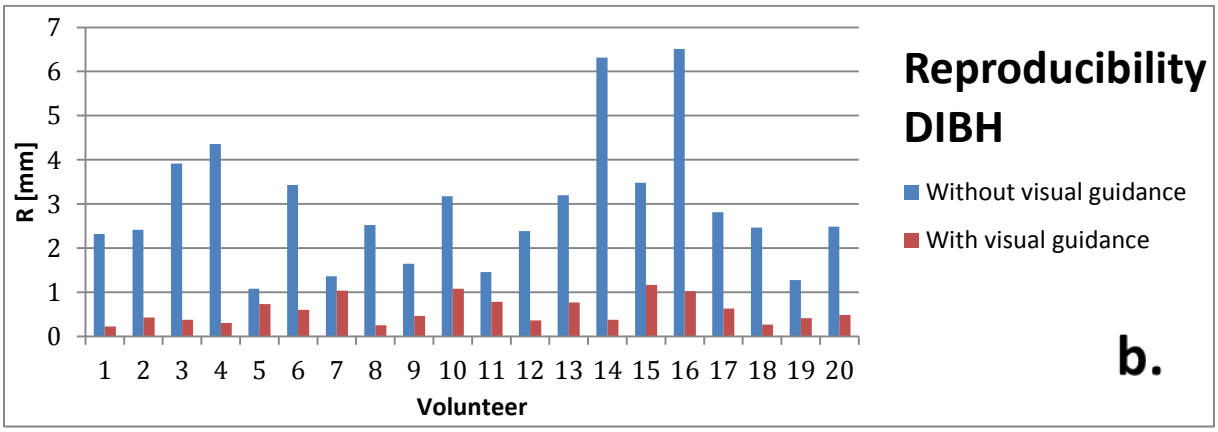
The reproducibility was significantly improved for DIBH with visual guidance compared to DIBH without visual guidance (Table 2). The individual reproducibility values are presented in tabular format (Appendix II) and as a bar chart (Figure 31 b). The reproducibility with visual guidance was improved for all volunteers.

The reproducibility was significantly improved for $DIBH_{delay}$ with visual guidance compared to $DIBH_{delay}$ without visual guidance (Table 2). The individual reproducibility values are presented in tabular format (Appendix III) and as a bar chart (Figure 31 c). The reproducibility with visual guidance was improved for all volunteers.

Table 2: Comparison of the reproducibility between the different methods, both with and without visual guidance. Data shown as median values (range) and p values for a Wilcoxon signed rank test.

	Method	Median R (range) [mm]	p
EIG	Without visual guidance	2.8 (0.9-5.4)	< 0.001
	With visual guidance	1.3 (0.5-2.3)	
DIBH	Without visual guidance	2.5 (1.1-6.5)	< 0.001
	With visual guidance	0.5 (0.2-1.2)	
$DIBH_{delay}$	Without visual guidance	2.7 (1.1-6.5)	< 0.001
	With visual guidance	0.5 (0.2-1.4)	





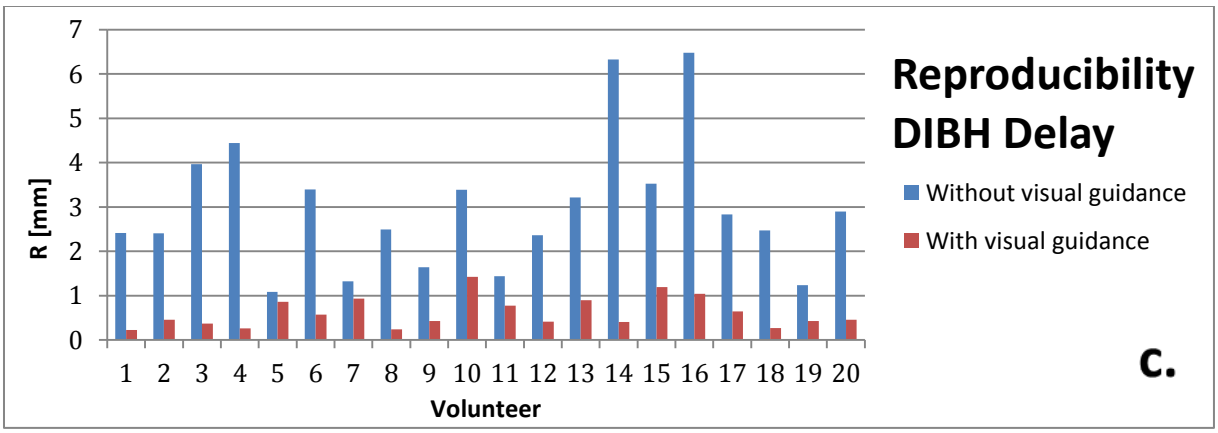


Figure 31: The reproducibility for all the volunteers with visual guidance (red) and without visual guidance (blue) for EIG (a), DIBH (b) and $DIBH_{delay}$ (c).

Stability

The stability was significantly poorer for EIG with visual guidance compared to EIG without visual guidance (Table 3). The individual stability values are presented in tabular format (Appendix I) and as a bar chart (Figure 32 a). For 7 volunteers the stability was better with visual guidance.

The stability was significantly improved for DIBH with visual guidance compared to DIBH without visual guidance (Table 3). The individual stability values are presented in tabular format (Appendix II) and as a bar chart (Figure 32 b). For 14 volunteers the stability was better with visual guidance.

The stability with $DIBH_{delay}$ showed no significantly difference between with or without visual guidance (Table 3). The individual stability values are presented in tabular format (Appendix III) and as a bar chart (Figure 32 c). For 14 volunteers the stability was better with visual guidance.

Table 3: Comparison of the stability between the different methods, both with and without visual guidance. Data shown as median values (range) and p values for a Wilcoxon signed rank test.

	Method	Median S (range) [mm]	p
EIG	Without visual guidance	0.6 (0.0-1.5)	0.02
	With visual guidance	0.7 (0.2-3.1)	
DIBH	Without visual guidance	0.7 (0.1-3.7)	0.02
	With visual guidance	0.4 (0.0-1.7)	
$DIBH_{delay}$	Without visual guidance	0.7 (0.1-4.0)	0.05
	With visual guidance	0.3 (0.0-1.9)	

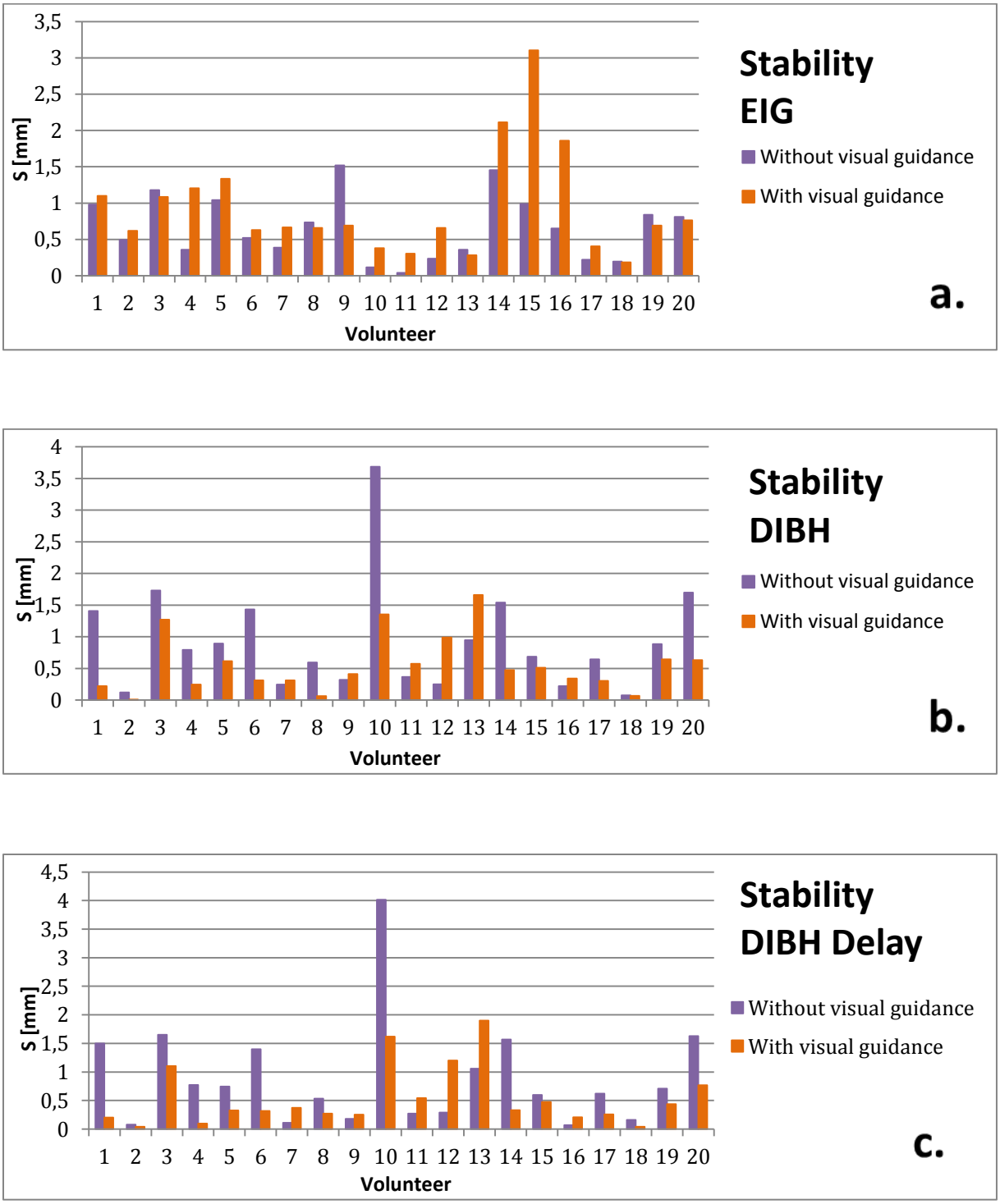


Figure 32: The stability for all the volunteers with visual guidance (orange) and without visual guidance (purple) for EIG (a), DIBH (b) and $DIBH_{delay}$ (c).

P_{GW}

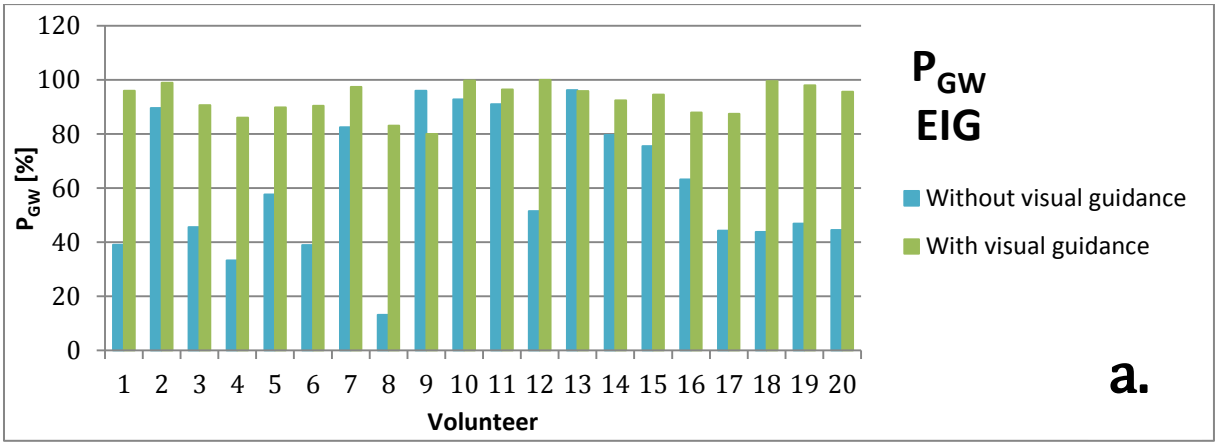
P_{GW} was significantly improved for EIG with visual guidance compared to EIG without visual guidance (Table 4). The individual P_{GW} values are presented in tabular format (Appendix I) and as a bar chart (Figure 33 a). The P_{GW} with visual guidance is improved for 18 of the 20 volunteer.

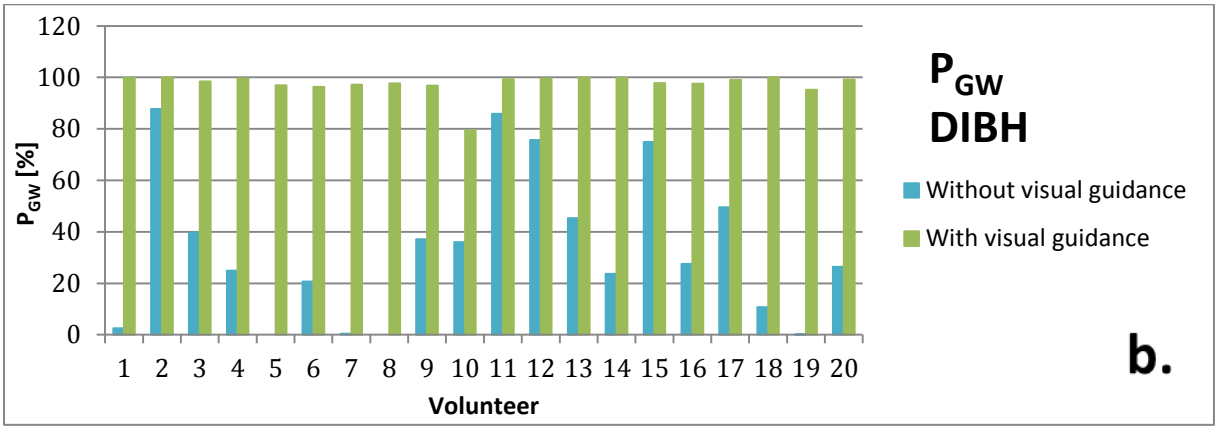
P_{GW} was significantly improved for DIBH with visual guidance compared to DIBH without visual guidance (Table 4). The individual P_{GW} values are presented in tabular format (Appendix II) and as a bar chart (Figure 33 b). The P_{GW} with visual guidance is improved for all volunteers.

P_{GW} was significantly improved for $DIBH_{delay}$ with visual guidance compared to $DIBH_{delay}$ without visual guidance (Table 4). The individual P_{GW} values are presented in tabular format (Appendix III) and as a bar chart (Figure 33 c). The P_{GW} with visual guidance is improved for all volunteers.

Table 4: Comparison of P_{GW} between the different methods, both with and without visual guidance. Data shown as median values (range) and p values for a Wilcoxon signed rank test.

	Method	Median P_{GW} (range) [%]	p
EIG	Without visual guidance	54.6 (13.1-96.2)	**<0.001**
	With visual guidance	95.1 (80.0-100)	
DIBH	Without visual guidance	26.9 (0.0-87.8)	**<0.001**
	With visual guidance	98.7 (79.4-100)	
$DIBH_{delay}$	Without visual guidance	27.8 (0.0-89.5)	**<0.001**
	With visual guidance	98.9 (75.3-100)	





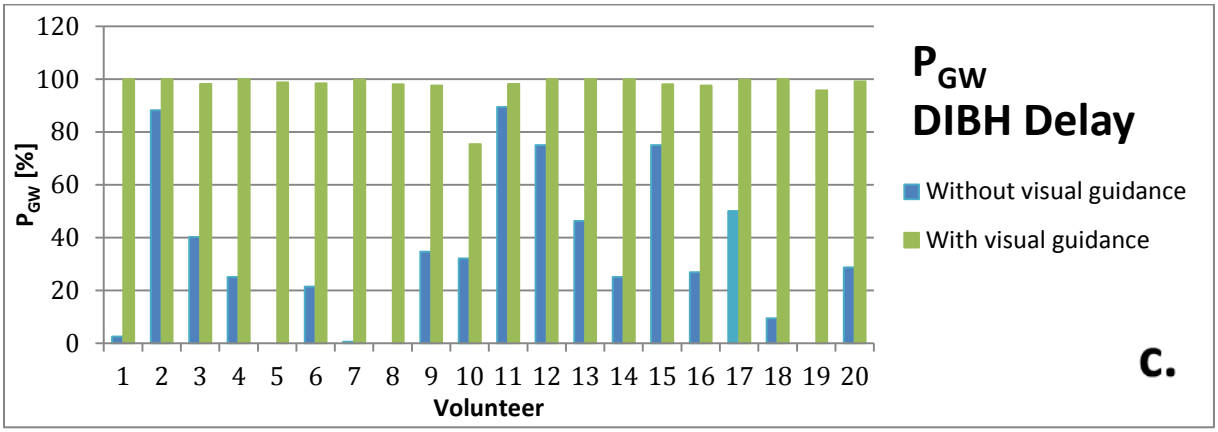


Figure 33: P_{GW} for all the volunteers with visual guidance (green) and without visual guidance (turquoise) for EIG (a), DIBH (b) and $DIBH_{delay}$ (c).

Comparison between DIBH and $DIBH_{delay}$

To investigate the use of a delay the result from DIBH and $DIBH_{delay}$ was compared. The Shapiro-Wilks test indicated that not all data was normally distributed and therefore a Wilcoxon signed-rank test for matched pairs was performed. The null hypothesis for the statistical test was:

H_0: There is no median difference between the reproducibility/stability/P_{GW} for two different methods with visual guidance at the 0.05 level of significance.

The results indicate that there is no significant difference for the reproducibility, stability and P_{GW} between DIBH and $DIBH_{delay}$ with visual guidance (Table 5).

Table 5: Comparison of the reproducibility, stability and P_{GW} between two different methods (DIBH and $DIBH_{delay}$) with visual guidance. Data showing p values for the different variables for a Wilcoxon signed rank test.

Method 1	Method 2	Variable	p
DIBH with visual guidance	$DIBH_{delay}$ with visual guidance	R	0.33
		S	0.68
		P_{GW}	0.07

5.3 Pressure measurements

The results from the pressure measurements were difficult to interpret; however one could always see pressure differences when a volunteer performed a breath (EIG/DIBH). One could even see a pressure difference during FB (Figure 34).

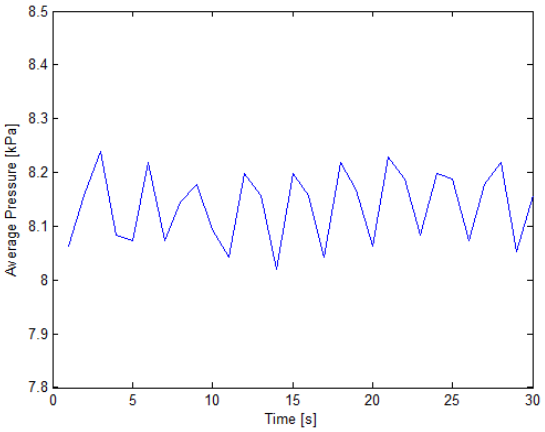


Figure 34: FB pressure curve for volunteer 10.

By visually assessing and comparing the different measurements the volunteers was divided into three groups; 1) No volunteer lifting, 2) Possible volunteer lifting 3) Difficult to interpret (Table 6). Beneath is a short description of the criteria needed to end up in a certain group and some explaining figures.

Table 6: The number of volunteers ending up in the different groups.

Group	Number of volunteers
1. No volunteers lifting	9
2. Possible volunteer lifting	7
3. Difficult to interpret	4

1) Nine volunteers ended up in group number 1, i.e. no volunteer lifting. For these patients, a rise in pressure for all amplitudes was present. Before and after a breath the pressure was approximately the same, and it could be compared to the pressure during FB. For some of the volunteers these peaks differed from how their amplitude looked while performing the lift. All the volunteers ending up in this group followed the above mentioned criteria.

An example of a volunteer belonging to this group is shown below (Figure 35-38). The average pressure during FB was approximately between 16-19 kPa and every curve started around this level. At every DIBH, represented by a black arrow, the pressure increased and lay approximately around 20-27 kPa depending on the amplitude. However, the pressure dropped to almost 10 kPa when the volunteer was asked to lift into the gating window (Figure 39).

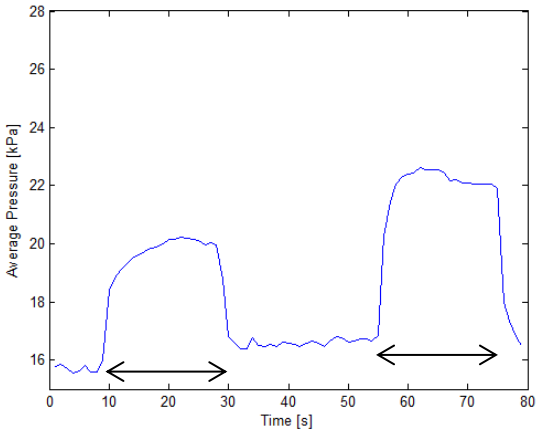


Figure 35: Pressure curves for volunteer 18, amplitude 1 & 2 without visual guidance.

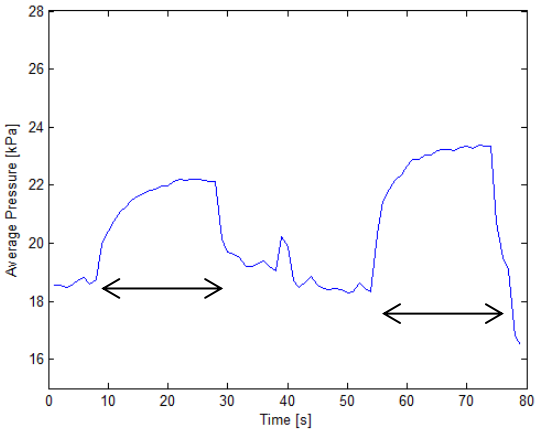


Figure 36: Pressure curves for volunteer 18, amplitude 1 & 2 with visual guidance.

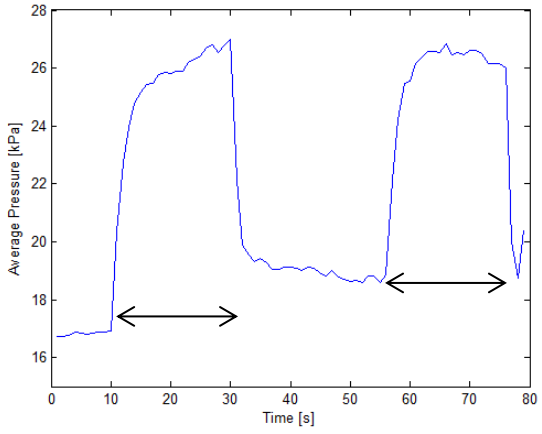


Figure 37: Pressure curve volunteer 18, amplitude 3 & 4 without visual guidance.

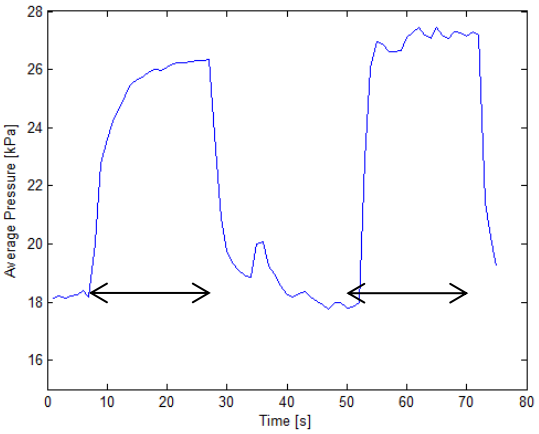


Figure 38: Pressure curve volunteer 18, amplitude 3 & 4 with visual guidance.

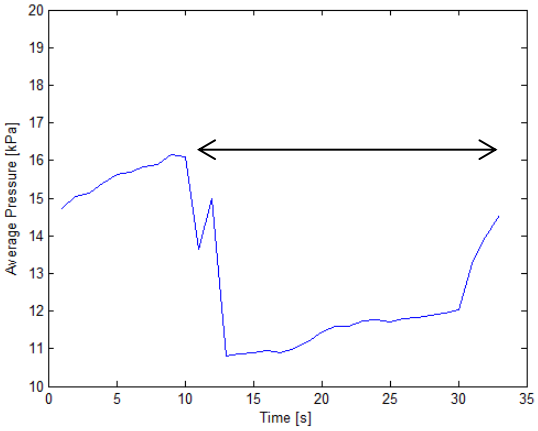


Figure 39: Lifting into the gating window for amplitude 1, volunteer 18.

2) Seven volunteers ended up in group number 2, i.e. possible volunteer lifting. Contrary to group 1, these volunteers did not always have an increase in pressure during a DIBH. Suspicions of lifting arise if the pressure fell below the pressure during FB. For some of the volunteers these drop-like peaks coincide with the shape of the lifting curve.

An example of a volunteer belonging to this group is shown below (Figure 40-43). The average pressure during FB was approximately 11 kPa and every curve started around this level. Every DIBH is represented by a black arrow. For amplitude 1 and 2, both with and without visual guidance, the pressure increased to approximately 13-14.5 kPa. However, for peak 3 and 4 the pressure instead decreased to around 8 kPa for peak 3 and around 3-4 kPa for peak 4. This reduction may be explained by a possible lift and even more convincing is that the lifting curve has the same drop-like appearance (). It should be clarified that this connection was not true for all volunteers. All volunteers ending up in this group had similar curves dropping below the pressure during FB.

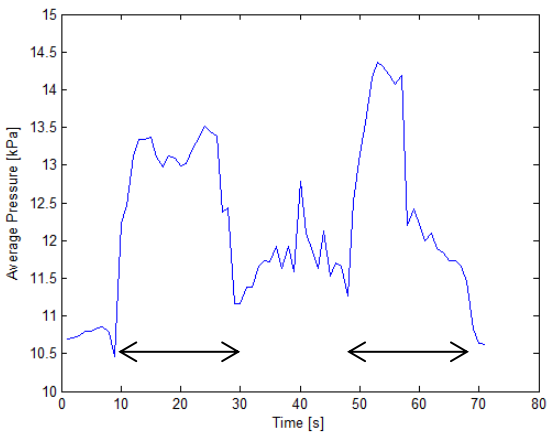


Figure 40: Pressure curve volunteer 6, amplitude 1 & 2 without visual guidance.

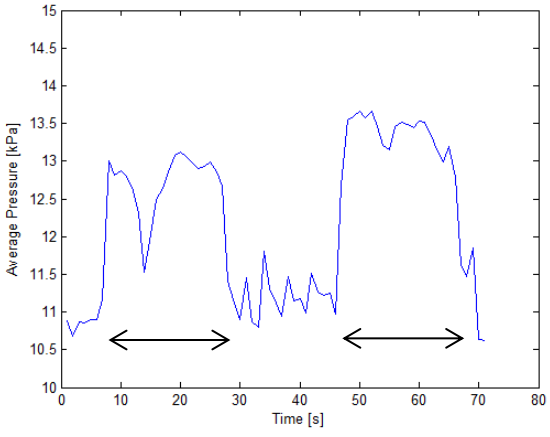


Figure 41: Pressure curve volunteer 6, amplitude 1 & 2 with visual guidance.

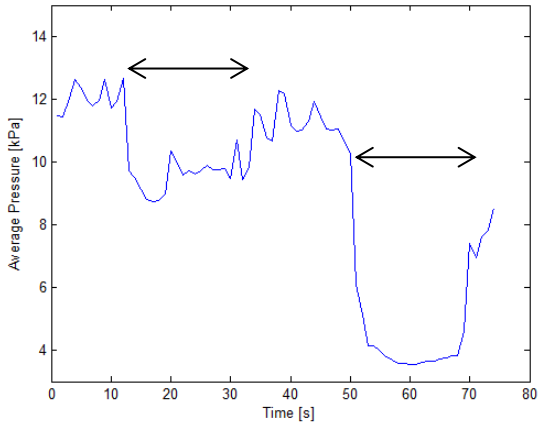


Figure 42: Pressure curve volunteer 6, amplitude 3 & 4 with visual guidance.

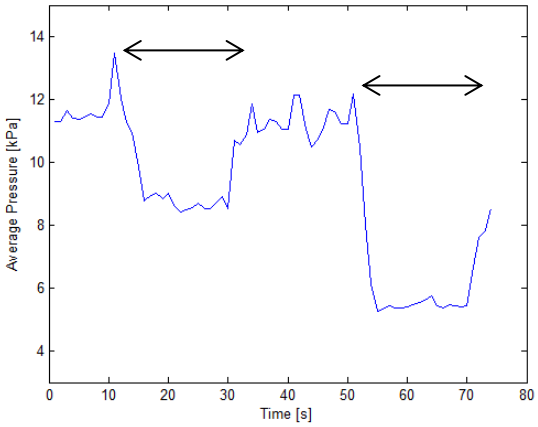


Figure 43: Pressure curve volunteer 6, amplitude 3 & 4 without visual guidance.

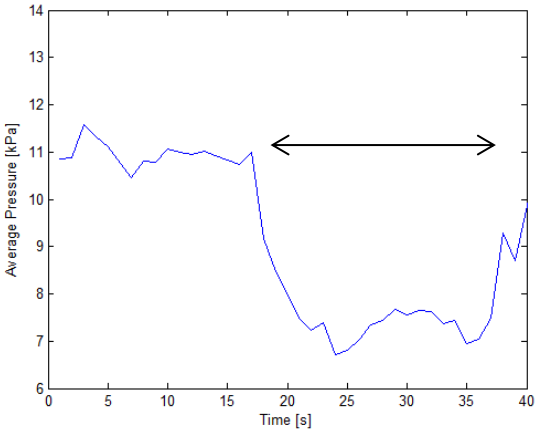


Figure 44: Lifting into the gating window for amplitude 1, volunteer 6.

3) Four volunteers ended up in group number 3, i.e. results difficult to interpret. For two of these volunteers the difficulty was to interpret peak 3 and 4 with visual guidance and for the other two it was difficult to see when the DIBHs had occurred.

5.4 BREATH HOLD

The average breath hold for the 20 volunteers was 57.2 ± 22.5 s (Appendix IV) ranging from 20.39 to 93.56 s. For some volunteers there were some difficulties deciding when the volunteer had found a stable level, which according to Material & Methods (part 4.4) were when the timekeeping started. A recurring phenomenon was a peak in the beginning of the respiratory curve (Figure 45). This peak occurred because the volunteers wanted to fill their lungs with as much air as possible before this test, however, it was often too much and they came above the gating window. The peak is the adjustment the volunteers had to do to enter the gating window. The timekeeping for this kind of breath holds started after the peak.

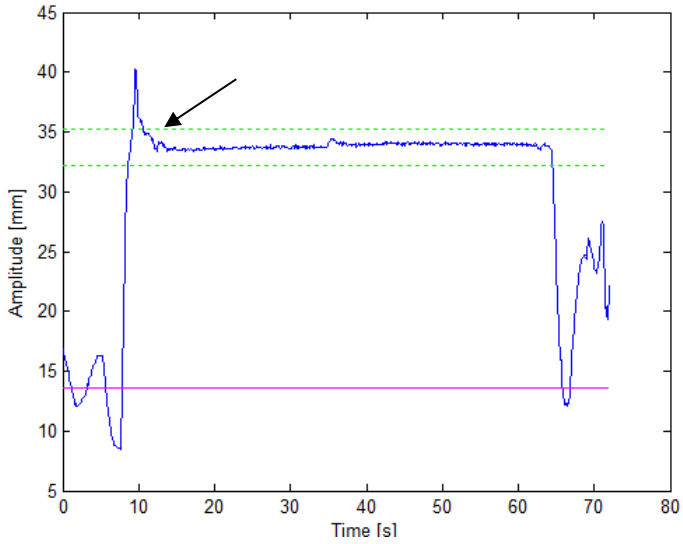


Figure 45: Breath hold curve for volunteer 7. The black arrow indicates the start of the timekeeping.

Another problem of definition was when the amplitude started to be unstable. One example of this was a volunteer that first had the distinctive peak in the beginning and could then hold a stable amplitude level for about 20 s (Figure 46). Around 47 s, on the x-axis, it looks like the volunteer starts to perform FB up at the set amplitude level. This amplitude cannot be considered as stable and led to a stop in the timekeeping indicated by the black arrow in the figure. The volunteer actually released her breath around 90 s.

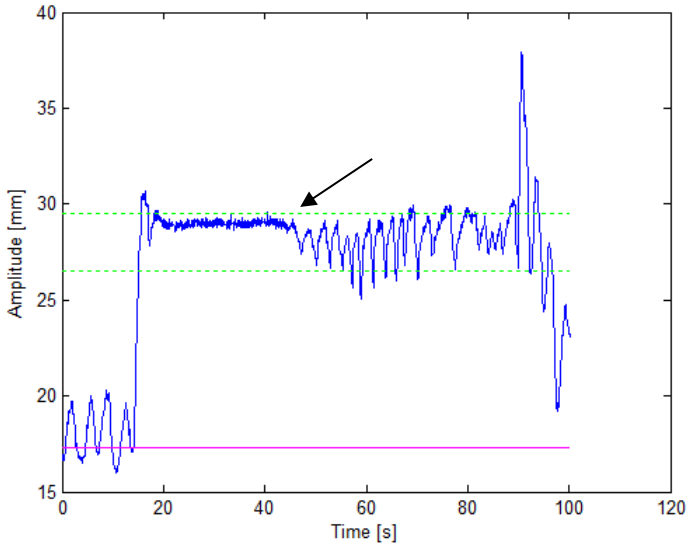


Figure 46: Breath hold curve for volunteer 17.

6. DISCUSSION

6.1 AMPLITUDE STUDY

The result from the amplitude study showed, in accordance with Damkjær *et al.* [11], that there is a significant difference in the amplitude between EIG and DIBH. This means that the volunteers unaffected had higher amplitudes when performing DIBH compared to EIG.

This result is in favor for the DIBH technique since higher amplitudes increases the separation between the breast and the target volume and can have a dose sparing effect for the organs at risk. If DIBH was to be introduced at SUS the amplitude could possibly be increased, compared to the current amplitude for EIG, without creating any discomfort for the patient during treatment.

6.2 REPRODUCIBILITY, STABILITY & P_{GW}

The result showed that there was a significant difference in reproducibility for all three techniques comparing with and without visual guidance. The results indicated that the reproducibility was better with visual guidance for both EIG ($p<0.001$), DIBH ($p<0.001$) and $DIBH_{delay}$ ($p<0.001$). These results are consistent with those of Cerviño *et al.* [8].

A better reproducibility is always desirable because this also indicates the robustness of the method. The reproducibility is a measurement of how well a patient can breathe according to a required breathing pattern. A method which has poor reproducibility indicates that it is difficult for the patient to repeat the amplitudes. Furthermore it is important to point out that the reproducibility has nothing to do with whether the peak is inside the gating window or not.

For EIG there was a significant difference between the stability with and without visual guidance ($p=0.02$). According to the results the stability was worse if the volunteer had access to visual guidance. This seems contradictory because one would think that the stability actually would be better with visual guidance.

An explanation to this could be that the visual guide was set to 4.5 s during EIG and the volunteers was instructed to breath in and find the gating window as fast as possible. The poorer stability value with visual guidance may have to do with difficulty for the volunteer to quickly find the gating window due to the sensitivity of the orange bar used in the visual guidance program. In this way the stability value for EIG may be misleading.

The stability for DIBH showed, in accordance with Cerviño *et al.* [8], a significant ($p=0.02$) improvement with visual guidance. This result differs from the EIG stability, which is probably due to that the time for the breath hold was 20 s and that the volunteers could find the gating window without stressing.

A better stability is interesting from a clinical point of view since it could lead to a reduction of the gating window and in this way decrease intrafractional movements during treatment.

A good reproducibility and stability would mean nothing clinically if the peaks did not end up inside the gating window. That was why it was of great interest to examine P_{GW}. For all three methods P_{GW} improved significantly ($p<0.001$) and for some volunteers the improvement was tremendous, especially for DIBH and $DIBH_{delay}$, when changing from without to visual guidance. In the clinic this could lead to shorter treatment times which are desirable for both the patient and the personnel.

Comparing EIG and DIBH without visual guidance the reproducibility, stability and P_{GW} was better for EIG compared to DIBH. Changing to DIBH without having access to visual guidance will not lead to improved treatments, instead poorer. These results are reassuring because in the current situation, without access to visual guidance, the method used at SUS is EIG.

Comparing EIG and DIBH with visual guidance shows that both the reproducibility, stability and P_{GW} is better for DIBH. This means that if SUS in the future introduce visual guidance equipment the preferable method to use is DIBH. A new question that will arise is if a delay should be used? According to the results of this study no significant difference could be detected for a 1 second delay. This means that this sort of delay would not affect the reproducibility, stability or P_{GW}.

6.3 PRESSURE MEASUREMENTS

The results of the pressure measurements showed that it is possible to discover volunteer lifting with this technique. Important to note is that this was an entirely new approach and has to our knowledge not been used previously. However, the measurements actually showed that there were differences in pressure during breathing. Nevertheless the results were hard to interpret.

A limitation of the method was that there was no correlation between the breathing and the pressure curve. The decision of when a DIBH had occurred, during the pressure curve, was visually decided based on knowledge of the length and the approximately starting time for the DIBH.

Another limitation of the method was the positioning of the sensor. The first difficulty was to place it on the exact same position for every volunteer. Perhaps it would have been better to follow an anatomical landmark and in this way place the sensor individually for each volunteer. It was also difficult to know if the sensor remained at the same position throughout the study.

In this study the presented parameter was the average pressure for the entire sensor. In the future it would have been interesting to look at other parameters, for example the pressure distribution over the entire sensor. It would also be interesting to obtain a

quantitative value over the average pressure which could be comparable between the volunteers. Attempts were made in the study but without success since a gradual loss of sensitivity of the sensor was found as the measurements progressed. The sensor was exposed for high pressures, higher than it is accustomed to, and therefore it had to be calibrated and equilibrated periodically. This means that comparison of pressure could not be made between the volunteers, but only for each individual.

All the pressure curves was visually evaluated and if there was any doubt about the results the volunteer ended up in group number 3. The method was not optimal and the results need to be looked at with a critical view. For this study the assumption that a drop in pressure below the FB pressure indicated a possible volunteer lifting was made. However, a drop in pressure is not for certain equal to a lift. The measurements while the volunteer tried to lift into the gating window showed different results. For some volunteers the pressure decreased and for some it instead increased. However, one can never know if the volunteer really understood the instructions and actually lifted into the gating window without filling their lungs with air.

For the nine volunteers in group 1, no volunteer lifting could be seen for any of the amplitudes. This is reassuring results, because lifting at a treatment would mean that the wanted separation between the breast and the target volume is not fulfilled.

For the seven volunteers in group 2, a potential volunteer lifting was seen. One can never be 100 % sure that the decrease in pressure is caused by a lift, which is why the group is named possible volunteer lifting. Normally at SUS the patients getting treated with gating are informed that they should not lift and that they are supposed to breath with the chest, i.e. not abdominal breathing. This information was left out for the volunteers. If this was included maybe fewer volunteers would end up in group 2.

A interesting thing for the volunteers in group 2 is that the suspected volunteer lifting always occurs for the highest amplitudes, 3 and 4 if the volunteer managed 4 amplitudes and 2 and 3 if the volunteer managed 3 amplitudes. Volunteer lifting could never be seen for amplitude 1 which was the volunteer's individual amplitude. Another observation was that the lifting more often occurred while the volunteer had access to visual guidance. The reason for this may be that when the volunteers saw that they had problem to reach the gating window, at the higher amplitudes, they unknowingly helped to enter the gating window by lifting there body.

To summarize the results there is a risk of patient lifting for DIBH, which seems to be more frequent with visual guidance. Because the lift often happens during the higher amplitudes one should be careful, when using visual guidance, to not push the volunteers to too high amplitudes above the amplitude which they felt comfortable with.

6.4 BREATH HOLD

The results of the breath hold study show that the volunteers without any problems could perform a 20 s DIBH. It also indicated that an even longer time could be implemented since the mean time was 57.2 s. Irradiation for 57.2 s would mean that 572 MU could be delivered for a linear accelerator with the doserate 600 MU per minute, which is the case for the True Beams (© 1999-2014 Varian Medical Systems, Inc., California, USA) installed at SUS.

However, it is important to keep in mind that the study was performed for healthy, relatively young, volunteers. To say that the results can be directly transferred to patients would be incorrect. But considering only women with breast cancer, which usually is a patient group in relatively good condition, a long DIBH could be feasible.

From a clinical point of view, for breast cancer patients, a 57.2 s long breath hold is not relevant. The fields delivered to a breast cancer patient never exceed approximately 150 MU which can, according to the information provided above, be delivered in 15 s. To have some margins and avoid running out of time a reasonable duration of the breath hold is 20 s. It is very rare to deliver two consecutive fields since the linear accelerator must change the multileaf collimator (MLC) and sometimes the gantry angle between each field. During this time there is no use of a breath hold.

There is however other patient groups where long DIBHs would be of interest. This would, for example, be lung cancer patients receiving gating treatment. These patients can have fields up to several hundred MU and a longer DIBH time could be of interest. However, lung cancer patients usually are in a worse condition than breast cancer patients and they will most likely not be able to perform such long breath holds.

7. CONCLUSION

With today's circumstances, when the clinic does not have access to visual guidance, a change of method to DIBH would not result in any benefits in reproducibility, stability or P_{GW}. Without visual guidance all three parameters were better with EIG.

An interesting result was that the majority of the volunteers, unaffected, had higher breathing amplitudes with DIBH compared to EIG. Perhaps the parameters were better for EIG but the prospect to have higher amplitudes with DIBH is alluring. The higher amplitudes can have potential dose sparing effects, due to larger spatial separation between the target volume and organs at risk.

For both EIG and DIBH, almost every volunteer performed better with visual guidance. The volunteer's had no problems with the Catalyst system's visual guide and thought it was easily understood. Overall, the greatest advantage with the visual guidance was improved P_{GW}. Clinically this would lead to a shortened treatment time which is positive in many perspectives. If the clinic was to introduce visual guidance in the future a change of method should be taken into account. With access to visual guidance, the superior method is DIBH. There were no advantages with adding a 1 second delay since it did not significantly affect the parameters investigated.

Possible volunteer lifting was seen and was more prominent for visual guidance and for high amplitudes. To prevent patient lifting, too high amplitudes should be avoided.

The average breath hold for the volunteers was 57.2 s. This meant that a 20 second long DIBH, which is a clinically relevant duration for breast cancer patients, should be feasible.

Finally, according to this study the superior technique without access to visual guidance is EIG and with access to visual guidance the superior technique is DIBH.

8. FUTURE PROSPECTS

It has been both motivating and rewarding to design and implement this study. Everything from inviting the volunteers to the finished result has been instructive. Off course, retrospectively, there is more interesting point of views to investigate.

Based on already collected data one could for example look at and evaluate the baseline drift which often occurred when the volunteers did not have access to visual guidance (Figure 22, Figure 24). Instead of looking at the reproducibility and stability in accordance to the gating window one could look at the reducibility and stability in accordance to the baseline. Evaluation of the baseline drift would tell if the volunteers empty their lungs properly between each breath. This is important since it indicates that the volunteer relaxes between each breath, this to avoid tension which could result in possible patient lifting.

It would also be interesting to investigate the data collected from the secondary gating point positioned at sternum. If the Catalyst in the future will be used for gating treatments, where is the optimal location for the gating point?

An addition to the study could have been the use of a spirometer. In this way it would be possible to look at the baseline drift using the lung volume; do the volunteers fill their lungs with equal amount of air for each breath and do they empty their lungs properly. It would be interesting to correlate the spirometer with the catalyst and see if the amplitude changes in accordance to the lung volume. A final thing would be to correlate the spirometer and the pressure measurements, and in this way verify detection of a possible lift. The spirometer can detect when the patient does not inhale enough air and together with a possible lift from the pressure measurements this could verify a lift.

In order to proceed, in accordance to the study results, it would be interesting to implement DIBH with visual guidance on selected patients and at the same time perform a treatment planning study. The study would investigate the dosimetric gain of the increased amplitude comparing EIG and DIBH. If there is a significant gain the next step would be to establishing DIBH with visual guidance as standard in the clinic.

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APPENDIX I

Result from EIG measurements. Data shown as individual reproducibility, stability and P_{GW} values for each volunteer and median value (range).

	EIG			EIG (visual guidance)		
Volunteer	R [mm]	S [mm]	P_{GW} [%]	R [mm]	S [mm]	P_{GW} [%]
1	4.5	1.0	39.1	1.0	1.1	95.9
2	1.0	0.5	89.6	0.8	0.6	98.9
3	5.1	1.2	45.6	1.3	1.1	90.7
4	3.0	0.4	33.2	2.3	1.2	86.1
5	2.7	1.0	57.7	1.7	1.3	89.8
6	2.2	0.5	38.9	1.3	0.6	90.4
7	2.0	0.4	82.5	1.0	0.7	97.4
8	3.7	0.7	13.1	1.3	0.7	83.1
9	1.7	1.5	95.9	2.0	0.8	80.0
10	1.3	0.1	92.7	0.7	0.4	99.8
11	1.7	0.0	90.9	1.4	0.3	96.4
12	3.0	0.2	51.5	1.3	0.7	100
13	1.7	0.4	96.2	0.5	0.3	95.8
14	2.9	1.5	79.6	0.9	2.1	92.5
15	2.5	1.0	75.5	1.4	3.1	94.5
16	3.0	0.7	63.2	1.7	1.9	88.0
17	4.5	0.2	44.3	1.6	0.4	87.4
18	0.9	0.2	43.8	1.0	0.2	99.6
19	3.6	0.8	46.9	0.9	0.7	98.0
20	5.4	0.8	44.5	1.4	0.8	95.6
Median (range)	2.8 (0.9-5.4)	0.6 (0.0-1.5)	54.6 (13.1-96.2)	1.3 (0.5-2.3)	0.7 (0.2-3.1)	95.1 (80.0-100)

APPENDIX II

Result from DIBH measurements. Data shown as individual reproducibility, stability and P_{GW} values for each volunteer and median value (range).

	DIBH			DIBH (visual guidance)		
Volunteer	R [mm]	S [mm]	P_{GW} [%]	R [mm]	S [mm]	P_{GW} [%]
1	2.3	1.4	2.6	0.2	0.2	99.9
2	2.4	0.1	87.8	0.4	0.0	100
3	3.9	1.7	39.7	0.4	1.3	98.4
4	4.4	0.8	24.9	0.3	0.2	99.5
5	1.1	0.9	0	0.7	0.6	97.0
6	3.4	1.4	20.8	0.6	0.3	96.3
7	1.4	0.3	0.5	1.0	0.3	97.2
8	2.5	0.6	0	0.3	0.1	97.7
9	1.6	0.3	37.1	0.5	0.4	96.9
10	3.2	3.7	36.0	1.1	1.4	79.4
11	1.5	0.4	85.8	0.8	0.6	99.3
12	2.4	0.3	75.7	0.4	1.0	99.5
13	3.2	1.0	45.3	0.8	1.7	100
14	6.3	1.5	23.7	0.4	0.5	99.8
15	3.5	0.7	74.9	1.2	0.5	97.8
16	6.5	0.2	27.5	1.0	0.3	97.6
17	2.8	0.6	49.6	0.6	0.3	99.1
18	2.5	0.1	10.7	0.3	0.1	100
19	1.3	0.9	0	0.4	0.6	95.2
20	2.5	1.7	26.4	0.5	0.6	99.1
Median (range)	2.5 (1.1-6.5)	0.7 (0.1-3.7)	26.9 (0.0-87.8)	0.5 (0.2-1.2)	0.4 (0.0-1.7)	98.7 (79.4-100)

APPENDIX III

Result from $DIBH_{delay}$ measurements. Data shown as individual reproducibility, stability and P_{GW} values for each volunteer and median value (range).

		$DIBH_{delay}$		**$DIBH_{delay}$ (visual guidance)**		
Volunteer	R [mm]	S [mm]	P_{GW} [%]	R [mm]	S [mm]	P_{GW} [%]
1	2.4	1.5	2.5	0.2	0.2	100
2	2.4	0.1	88.3	0.5	0	100
3	4.0	1.7	40.2	0.4	1.1	98.1
4	4.4	0.8	25	0.3	0.1	100
5	1.1	0.7	0	0.9	0.3	98.7
6	3.4	1.4	21.4	0.6	0.3	98.4
7	1.3	0.1	0.5	0.9	0.4	99.7
8	2.5	0.5	0	0.2	0.3	98.0
9	1.6	0.2	34.7	0.4	0.3	97.6
10	3.4	4.0	32.1	1.4	1.6	75.3
11	1.4	0.3	89.5	0.8	0.5	98.2
12	2.4	0.3	75	0.4	1.2	100
13	3.2	1.1	46.3	0.9	1.9	100
14	6.3	1.6	25	0.4	0.3	100
15	3.5	0.6	75	1.2	0.5	98.0
16	6.5	0.1	26.9	1.0	0.2	97.5
17	2.8	0.6	50.0	0.6	0.3	99.7
18	2.5	0.2	9.4	0.3	0	100
19	1.2	0.7	0	0.4	0.4	95.7
20	2.9	1.6	28.7	0.5	0.8	99.1
Median (range)	2.7 (1.1-6.5)	0.7 (0.1-4.0)	27.8 (0.0-89.5)	0.5 (0.2-1.4)	0.3 (0.0-1.9)	98.9 (75.3-100)

APPENDIX IV

Individual breath hold time for each volunteer and average value ± 1 standard deviation (SD).

VOLUNTEER	BREATH HOLD TIME [S]
1	84.0
2	55.5
3	76.7
4	58.7
5	90.6
6	46.1
7	51.9
8	60.9
9	75.7
10	20.4
11	26.2
12	28.7
13	76.1
14	53.5
15	93.6
16	72.4
17	28.9
18	49.9
19	67.0
20	26.9
AVERAGE ± 1 SD	57.2 ± 22.5