



## Accuracy and stability of deep inspiration breath hold in gated breast radiotherapy – A comparison of two tracking and guidance systems



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### ABSTRACT

**Purpose:** To characterize reproducibility of patient breath-hold positioning and compare tracking system performance for Deep Inspiration Breath Hold (DIBH) gated left breast radiotherapy.

**Methods:** 29 consecutive left breast DIBH patients (655 fractions) were treated under the guidance of Calypso surface beacons with audio-feedback and 35 consecutive patients (631 fractions) were treated using C-RAD Catalyst HD surface imaging with audiovisual feedback. The Calypso system tracks a centroid determined by two radio-frequency transponders, with a manually enforced institutional tolerance, while the surface image based CatalystHD system utilizes real-time biometric feedback to track a pre-selected point with an institutional tolerance enforced by the Elekta Response gating interface. DIBH motion data from Calypso was extracted to obtain the displacement of breath hold marker in ant/post direction from a set-zero reference point. Ant/post point displacement data from CatalystHD was interpreted by computing the difference between raw tracking points and the center of individual gating windows. Mean overall errors were compared using Welch's unequal variance t-test. Wilcoxon rank sum test were used for statistical analysis with  $P < 0.05$  considered significant.

**Results:** Mean overall error for Calypso and CatalystHD were  $0.33 \pm 1.17$  mm and  $0.22 \pm 0.43$  mm, respectively, with t-test comparison P-value  $< 0.034$ . Absolute errors for Calypso and CatalystHD were  $0.95 \pm 0.75$  mm and  $0.38 \pm 0.30$  mm, respectively, with Wilcoxon rank sum test P-value  $< 2 \times 10^{-16}$ . Average standard deviation per fraction was found to be  $0.74 \pm 0.44$  mm for Calypso patients versus  $0.54 \pm 0.22$  mm for CatalystHD.

**Conclusion:** Reduced error distribution widths in overall positioning, deviation of position, and per fraction deviation suggest that the use of functionalities available in CatalystHD such as audiovisual biofeedback and patient surface matching improves accuracy and stability during DIBH gated left breast radiotherapy.

### 1. Introduction

Deep Inspiration Breath Hold (DIBH) techniques have become a standard method in tangential field beam photon treatment for left-sided breast cancer radiotherapy. The advantages of DIBH radiotherapy in this class of disease treatments have been established in recent years by several studies describing reduced complication risk via lower cardiac and pulmonary doses [1–7]. DIBH methods involves patient inhalation and breath-hold at the time of CT simulation to produce both geometric separation between the heart and chest wall, and increased lung volume during the scan. Planning proceeds on the breath-hold image set to generate acceptable dosimetric coverage to the tumor while minimizing exposure to surrounding normal tissues. Actualizing a

DIBH treatment plan is accomplished in part by coaching the patient to perform a breath-hold similar to that of the CT simulation scan during each treatment session. Accuracy and stability of the on-treatment breath-hold determines the extent to which dosimetric coverage matches with the theoretical planned coverage in the treatment planning system.

To optimize and manage DIBH respiratory motion, several direct real-time techniques and technologies have been investigated. Approaches range from mechanical surface tracking sensors [4], magnetic distance sensors [8] and IR and laser based surface motion tracking [9–14], to spirometer-based breathing control [15–17], radiofrequency (RF) transponder based surface tracking [18], and mixed-modality kV-IR fusion systems [19].

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Recent investigations of motion control methods which include some form of biofeedback have shown promise in further improving DIBH performance [20]. Park, et al. developed a quasi breath-hold method for respiratory motion management which utilized a custom (breathing based) audio visual feedback system (AVFB) and IR stereo-camera markers on the anterior chest/thorax [21]. A head mounted display with speakers sent feedback to volunteer subjects based on their own breathing trace along with a guided breathing trace used for beam-on/off triggering. Lee et al., for example, showed that AVFB improved correlation between an RPM (Varian, Palo Alto) surrogate and lung tumor motion, as measured by cine-MR, compared to free-breathing (FB) [22]. In another investigation, a commercially available laser displacement sensor was used to track a body surface marker and generate personalized respiration feedback signal to guide gated heavy ion therapy [23]. Higher effective dose rate and reduced treatment time were found when using the guided AVFB system. It was found by He et al. that the mean absolute deviation from the guidance feedback was significantly lower when compared to gated FB or un-gated therapy deviations. Moreover, they found lower mean absolute error when using a standard guidance FB curve than a patient-derived representative curve. Cervino et al. demonstrated statistically significant improvement in both breath-hold reproducibility and stability when using a camera-based visual feedback system containing positional guidance [24].

The Sentinal™(C-RAD, Uppsala, Sweden) laser-based system of surface matching for initial patient setup has been investigated with results indicating reproducible positional accuracy of < 0.5 mm at both the initial setup, after clinically relevant shifts in phantom studies [25] and with similar results in patient setup studies using tomotherapy delivery [26]. The Catalyst™(C-RAD, Uppsala, Sweden) system uses an optical camera in the treatment vault to align patient surfaces to a projected surface for treatment setup with mean setup errors comparable to cone-beam CT [27]. Together, the Sentinal/Catalyst system can be utilized for setup and triggered gating in DIBH left breast therapy, as described by Schonecker et al. in a DIBH vs. FB study [28]. Latency characteristics of the Catalyst gated beam in Elekta linacs have been published [29]. However, little has been reported thus far of any real-time effect on patient performance during clinical use of the Sentinal/Catalyst system for DIBH guidance in the treatment vault. Likewise, there is currently limited information regarding the accuracy or precision of the Calypso surface tracking and guidance system as used in DIBH RT.

In this manuscript, we characterize the breath-hold portion of motion via two commercial surface point tracking systems (Calypso and CatalystHD) as used in this institution for gated breath-hold treatment and compare system performance. The study captures the results of concurrent (but exclusive) use of both systems by multiple physicians during an approximately year long clinical transition to the Catalyst HD system from the Calypso system in DIBH gated left-sided breast radiotherapy.

## 2. Methods

This retrospective study consisted of 64 consecutive patients treated using DIBH external beam radiotherapy technique for left sided breast cancer treated between August, 2016 and February, 2018. 29 consecutive left breast DIBH patients (655 fractions) were treated under the guidance of Calypso (Varian Medical Systems, Palo Alto, CA) and after switching to the C-RAD system, 35 consecutive patients (631 fractions) were treated using Catalyst HD surface imaging system. Data was collected with IRB approval from the University hospital's humans subjects division.

### 2.1. Treatment planning

All patients underwent routine CT simulation on a breast board

using alpha cradle immobilization. Following a DIBH rehearsal, patients underwent CT simulations for both free-breathing and DIBH. BH guidance during CT simulation for Calypso patients was performed with the Varian Real-time Position Management (RPM) Respiratory Gating system (V 1.7.5). The RPM system involves optical tracking of a block containing 2 passive reflective markers, which is placed on the patient's chest or abdomen allowing breathing-synchronized CT acquisition [30]. Monaco (V 5.11.01) and Xio (V 5.1.0) (Elekta, Sweden) treatment planning systems (TPS) were used for both target volume delineation and treatment planning. Patients undergoing Calypso guided treatment were simulated using a surface RF transponder beacon placed 1 cm right and 2 cm inferior of the sternal fiducial marker. Calypso beacons and breath-hold marks were delineated in the TPS on the BH scan and coordinates transferred to the linac units for tracking in each treatment session. Patients simulated with C-RAD had a FB surface image generated with the Sentinal scanner prior to the FB CT scan. For the BH CT scan a  $\pm 2$  mm window was defined around the breath-hold position and patient was CT imaged during BH within the window. After treatment planning for CatalystHD patients, the Monaco created free-breathing external structure set was exported back to C-RAD system for comparison to the Sentinal acquired free-breathing surface image used for initial setup. For any system failures of either tracking system during treatment, a physical mark on the patient was used as a backup option with audio instruction to perform gated treatment.

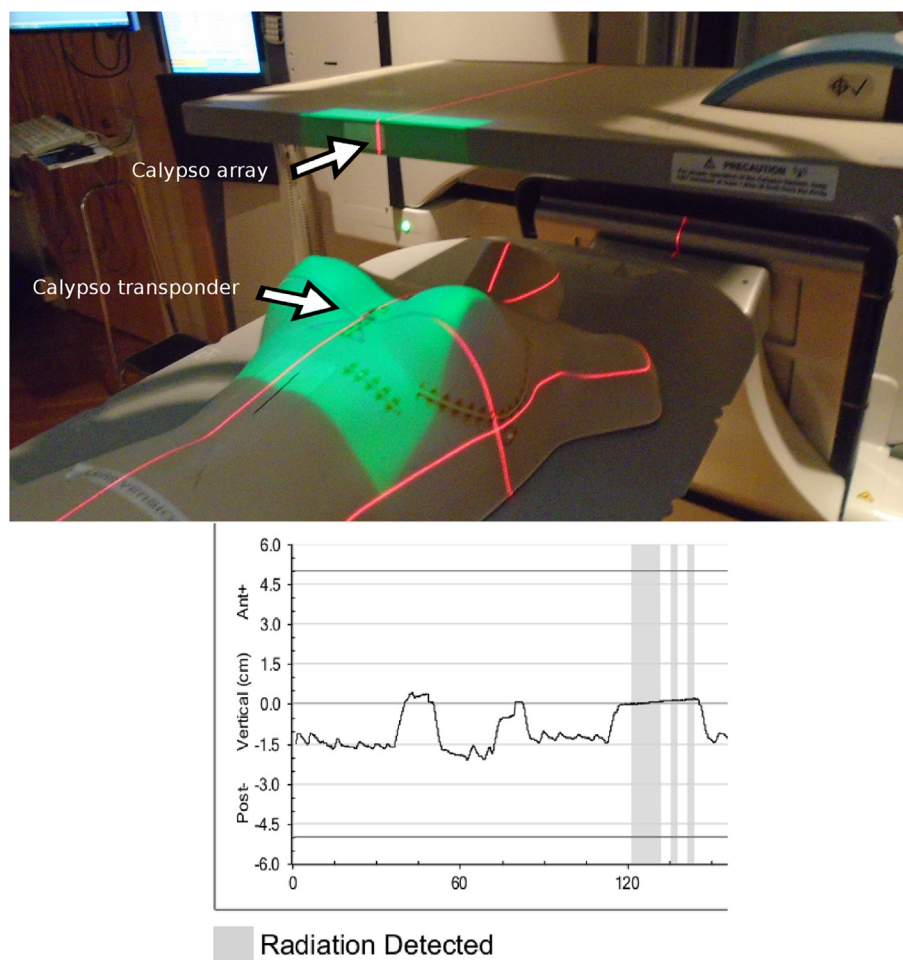
### 2.2. Calypso motion tracking

The Calypso surface beacon transponder system is a wireless external real-time motion tracking system based on radio-frequency markers under a tracking array [31,32]. By tracking a centroid determined by two rigidly connected radio-frequency transponders set on the patient surface, beacons act as both an intra-fraction motion tracker and indirect surrogate for internal anatomic positioning without significantly affecting photon skin sparing in opposed tangent beam configurations [18,33]. Patients in this study were setup on treatment day with a Calypso beacon placed on the anterior chest by therapy staff and aligned to the planned coordinates. Coordinates of the transponders were then zeroed out during a lateral skin marker verified practice breath-hold while on the treatment table. Motion of the 2-marker centroid was then tracked to show breath-hold performance and location of the centroid relative to the set-zero point and predefined tolerances. Zeroing out during breath-hold establishes the breath-hold position as the target position to be archived during gated treatment.

Fig. 1 shows the result of a typical breath-hold session as tracked in the Calypso system in the anteroposterior direction as printed from the system's session report. Shaded areas of Fig. 1 indicate beam-on during tracking as determined by a radiation sensor in the transponder detection array. While monitored outside the vault, treatment beams were run with breath-hold voice coaching via intercom and manually gated by therapists when breath-hold (visually indicated by the tracking module *outside* the vault) approached or exceeded predetermined tolerance limits of  $\pm 3$  mm. *Inside* the treatment room, the Calypso system provides no feedback to the patient regarding their own breath-hold position or the tolerance limits. Dynamic gating interface controller for enforcement of gating via tracking limits was not available at the institution, therefore making it possible for values to exceed the tolerance limits at the time beam-off was triggered.

### 2.3. C-RAD motion tracking

The CatalystHD is a Surface Guided Radiation Therapy (SGRT) system for the treatment vault that provides real-time information for patient setup, intra-fraction monitoring, both with regard to patient position and respiration, and gated treatments. It uses non-ionizing, near visible violet light (405 nm) from three ceiling mounted camera/projector units spaced approximately 120 degrees apart to project a



**Fig. 1.** Setup of the Calypso motion tracking in treatment (top). Partial printout of Calypso on-treatment motion tracking over time in the anteroposterior direction (bottom). The zero point is set to the breath-hold position, and tracking limits set to  $\pm 5$  cm though not enforced by dynamic gating interface controller. Manual gating was enforced at  $\pm 3$  mm. Calypso data for this study includes only tracking data taken during beam-on status, indicated by grey shaded portions of the report.

sequence of light patterns onto the patients' surface. The reflected light is captured by cameras in each unit to reconstruct a 3-dimensional surface of the patient at a manufacturer quoted frame rate of up to 200 f/s. An example is shown in Fig. 2. This surface is then compared with an external reference surface from either the treatment planning system or the Sentinel surface acquired during patient simulation. The dimensions of the reference surface can be adjusted by the user. The registration between the two surfaces is based on a non-rigid deformation algorithm that uses the reference geometry to discretize the interior body into tetrahedrons. Deformation of the source mesh is calculated by minimizing the total energy of the system. Using the Finite Element Method (FEM) and a non-rigid closest point algorithm, isocentric shifts are inferred through optimization with constraints for local rigidity and distance of the isocenter to the surface points [34].

The C-RAD system is seamlessly integrated into the MOSAIQ record and verify system and interfaces with the Elekta linear accelerators through the Elekta Response™ interface to trigger the radiation beam on/off. The workflow for DIBH is such that the patient is initially setup in the FB position using the cPositioning module that compares the live surface with the FB reference external surface from the planning system. The breath-hold position is based on the displacement of the same virtual surface tracking point that was placed during simulation. An example of this virtual tracking point is shown in Fig. 2. While this tracking point is transferred from simulation to the treatment room in 3D coordinates, similar to the Calypso system, only the anterior/posterior displacement of this point is used for breath-hold tracking and the gating window in the cRespiration mode. The BH is initiated through

semitransparent video goggles, which provide visual feedback to the patient (Cinemizer™ OLED, Carl Zeiss, Oberkochen, Germany). An additional constraint, which ensures that the patient is in the correct position during BH, is provided by the cMonitoring module. During the first BH a surface capture is obtained which constitutes the monitoring reference. The CatalystHD system continuously calculates the isocentric shift, which enables the detection of slower movements caused by patient relaxation or gradual position shifting. These deviations are typically not possible to detect using only the conventional (CCTV) room camera systems. Therefore, the beam can only be turned on if both criteria are satisfied. If during treatment the BH signal moves out of the predetermined gating window or the 3D vector of the monitoring surface displacement is larger than a certain amount the beam terminates automatically. Our in-house criteria for the automatically enforced gating windows is  $\pm 2$  mm and for the 3D displacement vector is 5 mm.

#### 2.4. Data processing and analysis

Raw three dimensional tracking data from the Calypso system was extracted manually by therapy staff using a licensed proprietary Varian research software (Calypso Patient Data Converter GA 1.9) during the final chart check after the completion of a patient's treatment course. Following extraction, the files (xml format) were converted to comma separated value files for further analysis. From the Calypso data we obtained the positional error data,  $z_C(t_i)$ , of the beacon's anteroposterior (AP) coordinate direction from its set-zero planned target position. For Calypso data, the set-zero position is the origin.

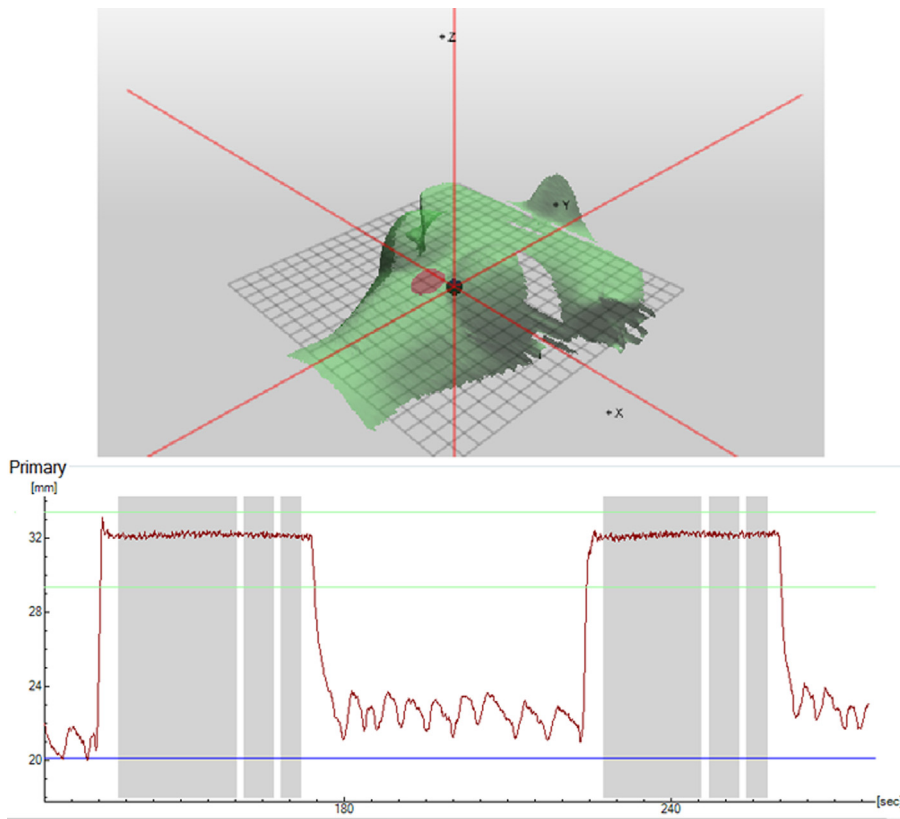


Fig. 2. CatalystHD setup and gating output. Surface image (top) is captured by the C-RAD Sentinel scanner during CT-simulation. A virtual point for tracking and breath-hold guidance is derived from averaging over a small user-defined region of surface (2 mm diameter red dot) in the scan. Scan origin is a dark green sphere with X-Y-Z coordinate system. Breath-hold gating result of on-treatment motion tracking over time in the anteroposterior direction is also shown (bottom). Enforced gating limits of  $\pm 2$  mm appear as green lines (above and below the intended breath-hold position here of 31.3 mm) while a baseline reference for free-breathing is shown in blue line (near 20 mm position).

In processing, raw Calypso data was reduced to data points indicating only that portion of the treatment delivery which occurs during a breath-hold by filtering out any points not possessing corresponding timestamp matched “beam-on” indicator tags in the output file. Similarly, CatalystHD data were restricted to those points which lie inside the predefined gating window used to enforce “beam-on” conditions during treatment. Missing fractions or sessions caused by system downtimes were considered ‘NA’ values in the analysis.

The mean raw positional errors per fraction,  $Z_C$ , for each Calypso fraction were computed using Eq. (1) where  $N_C$  was the number of extracted points (not including NA values) within the set of beam-on timeframes. Individual standard deviations,  $\sigma_C$ , for each Calypso fraction were computed with Eq. (2) and absolute positional errors  $|Z_C|$  per fraction computed by taking absolute value of  $Z_C$ .

$$Z_C = \frac{1}{N_C} \sum_{i=1}^{N_C} z_C(t_i) \quad (1)$$

$$\sigma_C = \sqrt{\frac{1}{N_C - 1} \sum_{i=1}^{N_C} (z_C(t_i) - \bar{z}_C)^2} \quad (2)$$

CatalystHD data was manually extracted per patient session from individual patient records in the C-RAD database. The CatalystHD system tracks and produces the AP coordinate by default in the file output. From these values we also computed the absolute value difference from the center of the planned gating window. All data were stored on locally encrypted machine and batch processed using R statistical programming language (version 3.3.3; R Foundation for Statistical Computing, Vienna, Austria) [35].

For CatalystHD, the mean raw positional error per fraction was computed using Eq. (3), where again  $N_{HD}$  was the number of extracted points (not including NA values) within the set of beam-on timeframes. Here, however, the target breath-hold position did not correspond to a zero-valued origin so the midpoint of the gating window  $z_{mid}$  was subtracted from each value in the averaging. Individual standard

deviations,  $\sigma_{HD}$ , for each CatalystHD fraction were computed with an equation identical in form to (2). Absolute positional errors  $|Z_{HD}|$  were computed as absolute value of  $Z_{HD}$ .

$$Z_{HD} = \frac{1}{N_{HD}} \sum_{i=1}^{N_{HD}} z_{HD}(t_i) - z_{mid} \quad (3)$$

Mean values over all fractions,  $N_f = 655$ ,  $N_f = 631$ , for Calypso ( $\bar{Z}_C$ ) and CatalystHD ( $\bar{Z}_{HD}$ ) respectively were computed similarly using Eq. (4). Averaging over all patient’s Z and  $|Z|$  within each corresponding fraction produces a set of longitudinal data for comparison over the course of treatment. We computed the set of mean positional errors per fraction number,  $Z_C^f$  and  $Z_{HD}^f$ , by Eq. (5) where  $Z_j$  represents the raw positional error for patient  $j$  within a particular fraction of the course, e.g. fraction 1, 2, 3...up to 28, and we sum over M patients where  $M = 29$  for Calypso and  $M = 35$  for CatalystHD.

$$\bar{Z} = \frac{1}{N_f} \sum_{i=1}^{N_f} Z_i \quad (4)$$

$$Z^f = \frac{1}{M} \sum_{j=1}^M Z_j \quad (5)$$

Comparisons between grouped raw positional errors and grouped absolute value errors were performed using Welch’s two sample t-test and Wilcoxon rank sum test, respectively, under the hypothesis that the means are the same, with significance level  $\alpha = 0.05$  [36]. Theoretical quantiles were generated and plotted against the data to validate normality assumptions of the statistical tests.

### 3. Results

Overall raw positional error distributions for both Calypso ( $Z_C$ ) and CatalystHD ( $Z_{HD}$ ) were found to be nearly symmetric and centered close to zero. Group size weighted averages (weighted by number of

**Table 1**

Total positional (Pos.) and absolute (Abs.) errors, averaged over all patients, all fractions with p-values computed from results of T-test (positional) and Wilcoxon test (absolute).

	Calypso	CatalystHD	$\Delta$	95% CI	p-value
Mean Pos. error	0.33 ± 1.17	0.22 ± 0.43	0.11	(0.008, 0.205)	0.034
Mean Abs. error	0.95 ± 0.75	0.38 ± 0.30	0.57	(0.502, 0.631)	<10 <sup>-16</sup>

fractions) are shown in Table 1, with mean positional error values  $\bar{Z}_C$  and  $\bar{Z}_{HD}$ , (averaged over all patients and fractions) of 0.33 mm and 0.22 mm, respectively. Though the raw means appear to be from statistically unique distributions (p = 0.03), they are not appreciably far apart ( $\Delta = 0.11$  mm).

Mean absolute error in the Calypso patient group  $\bar{|Z|}_C$  was 0.95 mm while the CatalystHD group mean absolute error value  $\bar{|Z|}_{HD}$  was 0.38 mm; a difference of 0.57 mm (Table 1, row 2). The difference in mean absolute errors of 0.57 demonstrates that the CatalystHD group exhibits significantly less displacement from the planned breath-hold mark (p < 2.2 × 10<sup>-16</sup>). Fig. 3a plots the overlaid un-normalized histograms of errors for the two groups exemplifying the difference in distribution width. The box and whiskers plot of the absolute error distributions in Fig. 3b demonstrates a significantly lower average displacement and narrower overall quantiles in CatalystHD patients than Calypso patients.

To investigate whether there was a learning curve associated with each system, we averaged over all patients within each similar fraction during the sequence of treatment. We found that the CatalystHD patient group  $Z_{HD}^f$  performed with lower mean absolute error and with smaller standard deviations among the set than that of Calypso patients  $Z_C^f$ . Individual fractions are shown in Fig. 4 with associated error bars of ± 1 standard deviation. Neither the CatalystHD group (blue square) nor Calypso (red circle) show difference in per-fraction averaged positional errors throughout the course of treatment. However, the absolute error comparison in Fig. 4b demonstrates a significant difference between the two groups, with a majority of the Calypso group having larger error than CatalystHD patients. The average width of each fraction’s distribution (standard deviation per fraction, shown as error bars in Fig. 4) was consistently less in the CatalystHD group. Correlation of

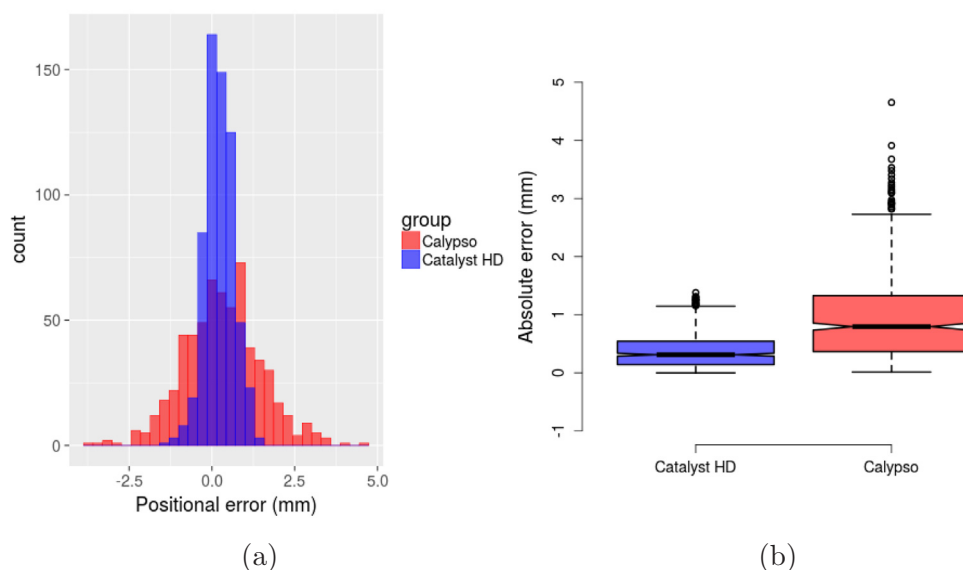
errors with fraction number was slightly positive for CatalystHD group (0.30) while slightly negative for Calypso (−0.39), though neither group’s performance appeared to show strong trend or indicate any sort of adaptive learning effect to a given system over time.

Averaging over each patient group’s individual standard deviations per fraction,  $\sigma_C$  and  $\sigma_{HD}$ , produces an overall metric for intrafractional variability. We computed an average over all standard deviations of  $\bar{\sigma}_C = 0.74 \pm 0.44$  mm for Calypso patients versus  $\bar{\sigma}_{HD} = 0.54 \pm 0.22$  mm for CatalystHD patients. Wilcoxon rank sum test with continuity correction between the groups produces W = 246560 with p-value < 2.2 × 10<sup>-16</sup>. The difference between the (non-normal) distribution of standard deviations among the two patient groups is shown in Fig. 5. The Calypso distribution of SD’s is wider than for CatalystHD patients, indicating an overall higher precision breath-hold in CatalystHD patients.

**4. Discussion**

This manuscript presents a comparison of two different commercial real-time tracking and guidance systems and shows significant improvement in patient DIBH performance using audiovisual feedback-based surface imaging over an audio-based RF system. The Calypso results found in this study agree with previous studies at this institution which showed overall breath-hold accuracy of 0.9 mm in the AP (Z coordinate) direction compared to laser/tattoo alignment [37,38]. In the previous studies high fidelity intrafractional motion data from the Calypso system was not available, whereas in this study we were able to quantify breath-hold motion to obtain a stability metric with increased confidence in accuracy of positional information and confirm that overall motion is within clinically acceptable limits. The Calypso results are also consistent with other investigations of audio-based voluntary DIBH such as that determined by EPID imaging during beam delivery [39].

Verification of the breath-hold throughout the entire fraction of treatment aids in determining the accuracy and stability of breath-holds with more refinement and helps to better derive methods to mitigate intra-fractional geometric miss. Consequences of geometric miss and previous efforts to mitigate intra-fraction motion have shown that dosimetric differences of up to 10% are possible with linear intrafractional shifts as low as 1 mm [40]. Though some dosimetric differences due to



**Fig. 3.** Unnormalized histograms of raw position errors  $Z_C$  for Calypso (red) and  $Z_{HD}$  CatalystHD (blue) patients (a), and notched boxplots of absolute positional error of Calypso  $|Z_C|$  and CatalystHD  $|Z_{HD}|$  patients (b). Both distributions in (a) are centered near zero (0.22 mm, 0.33 mm), however, distribution width for Calypso patients is noticeably wider than for CatalystHD. Significant difference in distributions is also seen in the absolute error comparison in (b). (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

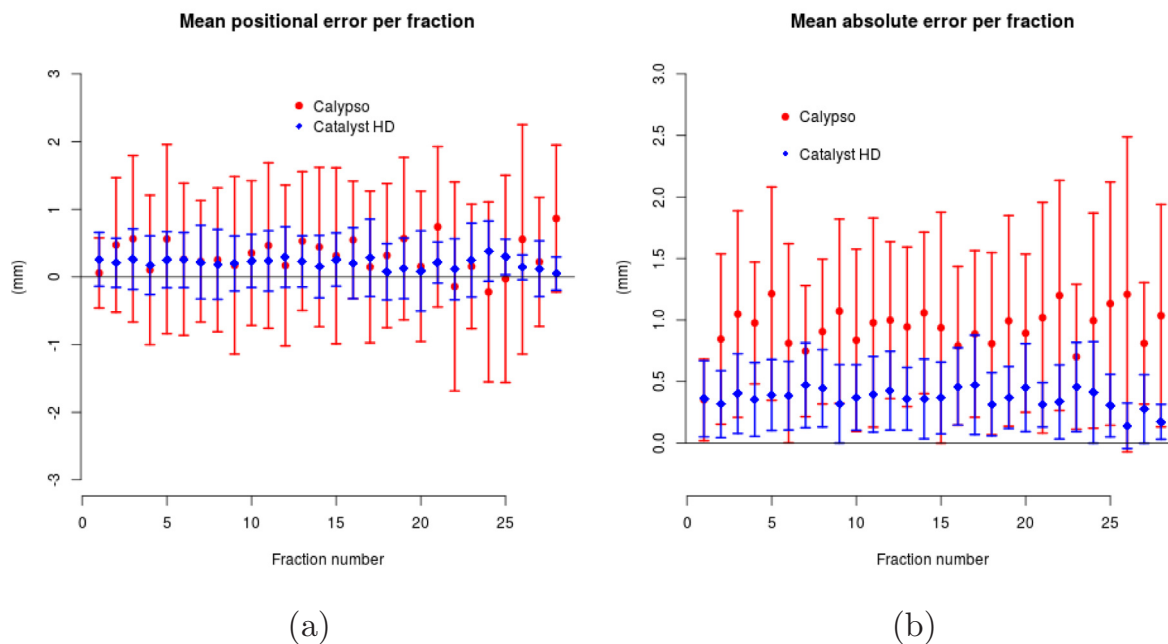


Fig. 4. Mean positional error (a) and absolute error (b) averaged over all patients in the  $N^{th}$  fraction (fraction number) of treatment. Due to differing fractionation schema (hypofractionation), there are fewer patients in the averages for  $N > 16$ . Error bars show the standard deviation of error among patients within  $N^{th}$  fraction.

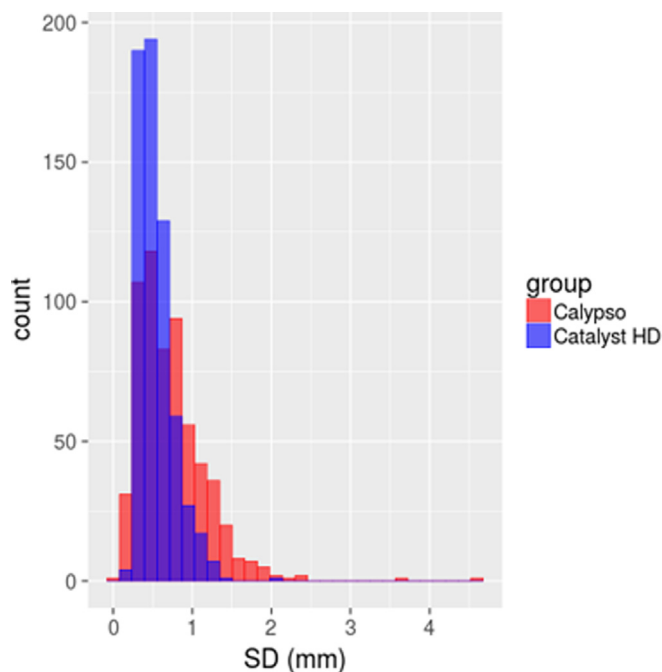


Fig. 5. Unnormalized histograms of standard deviations for Calypso (red) and CatalystHD (blue) patients. During beam-on, the CatalystHD patient group exhibits a narrower distribution of deviations than Calypso patients and an overall lower average per-fraction deviation. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

setup errors can be mitigated by using VMAT techniques [41], reducing the overall geometric miss by increasing DIBH accuracy provides a means to further reduce potential toxicity regardless of planning technique. The overall accuracy of DIBH positioning during beam-on is indicated by mean absolute value distributions of errors between planned/actual breath-hold position. Fig. 3b demonstrates a verifiable reduction in geometric miss when using CatalystHD imaging system

over Calypso verification, therefore lowering risk of under-dosing target and overdosing lung/heart during DIBH RT. The increased stability (precision) demonstrated by Figs. 4 and 5 in the surface-imaging group implies that improvements in accuracy can be maintained throughout the course of beam delivery and adds confidence that theoretic dosimetric benefits of breath-hold can be realized in practice.

The average intrafraction variability in both the CatalystHD (0.54 mm) and Calypso (0.74 mm) patient groups is comparable to previous published results of surface imaging system studies. Betgen et al. found an average intrabeam variability (standard deviation during a breath-hold) of 0.7 mm using an alignRT system (VisionRT, London, UK) [42]. Other recent studies of DIBH patients using the alignRT system have found intra-DIBH stability of intrafraction motion ranging from 0.66 mm in the anteroposterior direction [43] to intrafractional random errors of 1.13 mm and 1.06 mm for medial and tangent fields, respectively [44]. With respect to other studies of intrafractional motion using the CatalystHD system, the results of this study (0.38 mm absolute error) agree closely with the vertical maximum displacements found by Reitz et al. in their (non DIBH) investigation of right-sided breast cancer patients (0.39 mm) [45].

In the CatalystHD system, the gating window is computationally enforced by real-time visual feedback, limiting the overall possibility of deviations beyond initial settings. However, despite the gating window of  $\pm 2$  mm, the results show that patients using the CatalystHD system maintain their breath-hold within  $\pm 1$  mm of the planned target position more than 95% of the time (95.7%). The Calypso system, in comparison, had only 63.4% within  $\pm 1$  mm. The results suggest that the availability of visual biofeedback plays a more important role in influencing the accuracy and stability of breath-hold performance than gating window enforcement. They also suggest that with more focused real-time feedback from the Calypso system showing a tighter gating window, it may yield similar results to CatalystHD.

The quasi breath-hold study performed by Park et al. reported average absolute displacements  $< 0.8$  mm under audiovisual feedback breath-hold guidance (AVFB) and stability (mean absolute deviation) of  $< 0.5$  mm [21]. Here, the AVFB gating signal was computed from patient breathing pattern, rather than a threshold setting. The study by He et al. [23] also demonstrated mean absolute error between actual

and guidance breath-hold position ranging from 0.27 and 0.35 mm under various guidance methods which present full motion curves to the subject during simulated treatment. The CatalystHD system only shows the patient a solid 1-dimensional bar with a gating target box to breathe towards as guidance. Thus, as suggested by these previous studies, some additional improvement could be possible in CatalystHD DIBH performance by presenting more information-rich feedback to the patient during treatment.

Freisleder et al. reported an inherent latency in the CatalystHD system at  $851 \pm 100$  ms – a fixed length of time added to the overall beam delivery with respect to the patient breath-hold [29]. Latency does not appear to be a leading factor of result differences presented in this manuscript, as there is a similar if not longer human based beam-on latency when manually gating with Calypso. However, as non-invasive surface imaging grows in acceptance as a method for automated gating in complex RT techniques such as SBRT using high Monitor Unit beams, additional latency may strain patients' ability to achieve accurate breath-holds, making audiovisual biofeedback a more important technique to apply.

One of the main differences between the two systems examined in this study is that CatalystHD also monitors a time-averaged user-defined region of patient surface during treatment in addition to the breath-hold guidance. This secondary mechanism ensures that the beam-on status is also limited by rotations and translations of the surface, albeit at larger tolerances than the breath-hold window. It has been observed clinically in previous Calypso guided treatments that some patients arch their back during breath-hold to achieve the transponder position into breath-hold window, potentially introducing rotations and translations of the breast and chestwall relative to the planned position.

Some of the limitations of this study stem from a lack of rigid control over certain aspects of system use. Though protocols were used to position the CatalystHD surface tracking position on the sternal portion of the chestwall between the breasts, the consistency of that position as a surrogate for overall chestwall motion was not strictly confined in the study. With respect to achievement of toxicity reduction via geometric changes, the chest surface itself has limited utility as a surrogate for heart position [46]. Additionally, no systematic control over the area of the cropped surface used for initial surface image alignment was used. There is uncertainty in the initial setup which informs which baseline shifts (CatalystHD) and set-zero point (Calypso) are made whence DIBH is commenced, which could be as large as 6 mm [47]. The error in this study then can be considered additional to setup errors such as those established through portal imaging verification of chestwall excursion [28]. Initial alignment can also effect the orientation and magnitude of direction of BH and lead to misalignments of the tumor relative to the tracked surface position. Alignment of cine-MV imaging with the external motion tracking could potentially be employed to quantify overall deviations during intrafractional motion. In this study we also used a fixed gating window deemed appropriate for clinical use. Thus we have not been able to fully quantify the extent to which this window impacts accuracy, whether or not treatment becomes difficult for patients to achieve with a tighter window and/or begins to extend treatment time to clinically challenging levels.

## 5. Conclusion

This study describes the clinical effect of this institution's C-RAD CatalystHD implementation concurrent with Calypso treated patients in DIBH left breast RT. We found higher positional accuracy and improved precision for DIBH patients treated using CatalystHD. This was mainly attributed to visual biofeedback and additional surface monitoring. Despite the limitations of the study, the overall benefit to using focused audiovisual feedback systems appears to be positive. The results found in this investigation show that the use of CatalystHD is appropriate for clinical use and is comparable to existing surface imaging systems.

Future investigations should include further reductions of the gating window and evaluation of treatment efficiency.

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