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Assessment of Intrafractional Displacements in Surface-Guided Inspiration Breath-Hold Stereotactic Body Radiation Therapy

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Abstract

Background: Stereotactic Body Radiation Therapy (SBRT) delivers high radiation doses to tumours with steep dose gradients, minimising exposure to surrounding healthy tissues. Surface-guided Inspiration Breath-Hold (IBH) is particularly useful for thoracic and upper abdominal tumours, where respiratory motion can affect target position.

Aim: This retrospective cohort study aimed to assess whether GTV or anatomical surrogate intrafractional displacement during surface-guided IBH remains ≤0.5 cm when surface guidance confirms reproducible breath-hold throughout treatment. The study also evaluated the accuracy and precision of an SBRT protocol using IBH monitored by Surface Guided Radiation Therapy (SGRT). Intrafractional displacement was compared between lung and liver cohorts.

Materials and Methods: Offline reviews were performed for 86 lung SBRT patients (182 fractions) and 124 liver SBRT patients (159 fractions).

Results: In the liver cohort, the greatest mean intrafractional displacement was observed in the vertical (VRT) direction (0.087 cm), while mean shifts in lateral (LAT) and longitudinal (LNG) directions were -0.031 cm and -0.042 cm, respectively. The highest SD was observed in LNG (±0.275 cm). Mean 3D displacement was 0.351 ± 0.181 cm.

In the lung cohort, the greatest mean displacement was observed in the LNG direction (-0.092 cm), followed by LAT (-0.025 cm) and VRT (0.036 cm). The highest SD was also observed in LNG (±0.251 cm). Mean 3D displacement was 0.298 ± 0.186 cm. Significant differences between liver and lung cohorts were observed for VRT, LNG, and 3D displacement (p=0.0140, p=0.0331, and p=0.0032, respectively).

Conclusion: The hypothesis that intrafractional displacement during surface-guided IBH is consistently ≤0.5 cm was not confirmed. Nevertheless, the protocol provided adequate geometric accuracy for most treatments, demonstrating high positional stability during SBRT. Significant differences between lung and liver cohorts suggest that region-specific considerations may be warranted when applying surface-guided IBH SBRT

Keywords: SBRT, inspiration breath-hold (IBH), surface-guided radiotherapy (SGRT), intrafraction motion, lung tumors, liver tumors, geometric accuracy

Background

According to the World Health Organisation (WHO) estimates in 2019, cancer ranks as the first or second leading cause of death before the age of 70 in most countries worldwide, with incidence and mortality rates rapidly increasing. The most commonly diagnosed cancer is female breast cancer, followed by lung, colorectal, prostate, and stomach cancers. However, lung cancer remains the leading cause of cancer death, followed by colorectal, liver, stomach, and female breast cancers [1]. Thanks to improvements in early detection and various treatment modalities such as radiation therapy, surgery, chemotherapy, immunotherapy, and hormonal therapy, many cancers have become curable. Here, radiation therapy plays a vital role since approximately half of all cancer patients will undergo radiation therapy during their illness, contributing to around 40% of curative treatment for cancer [2]. As a primary treatment option, patients at Specialty Hospital Radiochirurgia Zagreb receive SBRT, often in combination with other previously mentioned modalities.

Stereotactic Body Radiation Therapy

Stereotactic Radiosurgery (SRS) is a radiation therapy technique that safely delivers a high dose of radiation to the target volume for the treatment of malignant and benign tumours, blood vessel defects, or functional

disorders in the brain, using fewer fractions [3, 4]. The high dose per fraction and hypo-fractionated scheme have demonstrated satisfactory therapeutic effects with low toxicity in treating small-sized tumours, resulting in ablative effects and tumour control rates previously associated only with surgical resection [5, 6]. The successful outcomes and curative potential of SBRT in treating many primary tumours, along with long-term survival without disease symptoms related to the irradiation of oligometastatic disease, make SBRT a reasonable treatment option if surgery is unavailable or if the patient declines it [7].

Lung SBRT

Lung cancer is the leading cause of cancer deaths in most countries worldwide. The optimal treatment option for stage I non-small cell lung cancer (NSCLC) is surgery; however, a significant number of these patients are deemed inoperable. For inoperable cases, published evidence suggests that SBRT is a safe and feasible approach with results comparable to surgery [8]. Although there is a lack of randomised trials comparing SBRT and surgery in operable cases of early-stage NSCLC, existing evidence from case-control studies indicates equivalence between sublobar resection and SBRT [9]. An important aspect that needs to be considered when we talk about lung SBRT is that it is estimated that 20-54% of cancer patients have lung metastases during the course of their disease, and that lung metastases are the second most common malignant neoplasm of the lung. With that mentioned, it is essential to note that evidence exists supporting the clinical benefit and limited toxicity of SBRT in treating lung oligometastases [10]. In some studies, comparing surface-guided DIBH with the conventional free-breathing four-dimensional (FB-4D) technique in lung stereotactic body radiation therapy (SBRT), DIBH showed a significant reduction in planning target volume (PTV) and a dose reduction to organs at risk (OAR), as well as a higher dose gradient index (DGI) [11].

Liver SBRT

It is estimated that each year, 696,000 deaths occur from primary liver cancer, making it the third most common cancer death worldwide [12]. Similar to lung cancer, surgical resection is the standard treatment approach for solitary or metastatic liver tumours, but with a lot of cases being unresectable, the use of SBRT as a curative modality has increased [13]. The most common primary liver tumour is hepatocellular carcinoma (HCC), and according to Japanese data, only 38% of patients are suitable for surgery [14]. In cases when HCC is challenging to treat with other modalities, SBRT has shown potential to improve the prognosis with high LC and OS rates with acceptable toxicities [15, 16]. In the case of cholangiocarcinoma (CCC), the second most common liver tumour, there is a lack of robust evidence supporting the role of SBRT. Still, preliminary results have shown effectiveness in LC with acceptable treatment-related toxicities [14, 17].

SBRT is most commonly used in the treatment of liver metastases because only 20-30% of patients with liver-only metastases are potentially resectable [14]. Results from an extensive, multi-institutional study have shown that SBRT has reasonable local control (LC) and overall survival (OS) in patients with liver metastases [18]. Similar to the lung, liver SBRT in DIBH, utilising SGRT and IGRT, showed feasibility and a significant reduction in irradiated volume [19].

From indication to treatment at Radiochirurgia Zagreb

Every patient treated at the Specialty Hospital Radiochirurgia Zagreb is first presented to the institutional multidisciplinary tumour board (MTD), where imaging studies, pathology reports, and all available clinical data are presented and reviewed in detail to ensure an accurate diagnosis and identify the most suitable treatment options. If SBRT is indicated, the patient undergoes simulation Computed Tomography (CT) imaging for treatment planning. Usually, MTD does not indicate whether the patient should be treated in IBH or not; that decision is made by radiation oncologists (RO), medical physicists (MP), and radiation therapy technologists (RTT) during CT simulation, depending on the patient's overall condition. In some particular cases, when critical OARs are close to the treated target and dose escalation is necessary, SBRT in IBH is indicated by institutional MTD. The patient then undergoes IBH testing and breathing coaching, if needed, before CT simulation.

Inspiration Breath-Hold training

When institutional MTD indicates SBRT in IBH as a treatment option, the patient is scheduled for IBH testing on the LINAC, where the treatment will be delivered, ensuring consistency between the testing and the actual treatment environment. Before testing, patients receive counselling and detailed instructions regarding the breath-hold technique. They are advised to take a moderate, comfortable breath-hold rather than a deep one, because, in our experience, moderate and comfortable breath-holds are more sustainable and easier to reproduce. Before testing, patients are positioned on the treatment couch as they will be during treatment. An image of the patient's skin surface is captured using the surface-guided radiotherapy system, Optical Surface Management System (OSMS-AlignRT®).

This system generates a three-dimensional map of the patient's external surface geometry by projecting structured light with a speckle pattern.

The region of interest (ROI) for monitoring breath-hold reproducibility is placed on the upper abdomen, over the rib cage.

During IBH testing, patients are instructed to inhale and hold their breath multiple times moderately. The OSMS-AlignRT® system continuously monitors the ROI in real-time, providing feedback on patient motion in all six degrees of freedom.

The threshold for breath-hold reproducibility evaluation is set to ±0.3 cm for vertical (VRT), longitudinal (LNG), lateral (LAT), and rotational directions.

If patients demonstrate consistent and reproducible breath-holds within the defined tolerances during the initial training and testing, they proceed to the CT simulation. If they fail the testing, they are referred to a hospital's respiration therapist for further IBH coaching.

Treatment simulation

Before planning calculations and treatment, patients undergo CT simulation imaging. While CT images are used for treatment planning, magnetic resonance imaging (MRI) provides better soft-tissue evaluation, and positron emission tomography (PET) identifies the disease on the metabolic level. This additional imaging is helpful for image registration and transferring the information about the disease from MRI and PET to the CT scans [20]. At our institution, in addition to simulation CT imaging, patients undergoing liver SBRT also undergo further MRI imaging, which includes T1-weighted in- and opposed-phase and T2-weighted TSE images acquired in IBH, along with additional DWI. In some cases, both lung and liver SBRT patients also undergo PET-CT imaging.

As mentioned before, for some of the patients, institutional MTD indicates SBRT in IBH. Still, for others, RTTs play the major role in that decision during the CT simulation, depending on the patient's overall physical condition, and they are tested for breath-hold reproducibility on the CT machine immediately before the simulation.

Once the patient positioning and immobilisation are determined, patients are tested for breath-hold reproducibility and duration. When they show the ability for IBH, a CT scan is performed.

Patient positioning, immobilisation devices, and other relevant information for treatment are saved in the patient notes to ensure reproducibility and prevent setup errors and inaccuracies during treatment.

Treatment planning

Following CT and MRI simulation, the RO delineates the CTV and OARs. Once this contouring process is complete, the MP begins calculating the treatment plan. The RO prescribes the dose required for the CTV and, in collaboration with the MP, determines an appropriate fractionation scheme. To account for potential patient and setup variability, an isotropic margin of ±0.5 cm is added to the CTV to create the PTV.

All treatment plans for patients included in this study were created in the Varian Eclipse™ treatment planning system (TPS).

Once the plan is finalised, the patient's skin reference surface for setup is created from CT simulation data and sent to the OSMS-AlignRT® system.

Treatment

After the treatment plan is calculated, the patient undergoes the SBRT treatment itself. All patients included in this study were treated on the Varian Edge® LINAC, a radiosurgery system dedicated to intracranial and extracranial radiosurgery treatments [21].

During the treatment, the patient is immobilised and positioned on the treatment couch, according to the prewritten setup notes from the CT simulation. Patient positioning is determined according to the reference surface generated from CT simulation data with the OSMS-AlignRT®. Before the start of treatment, the patient is instructed to perform an IBH, and an image of the patient's skin surface is captured. The ROI for monitoring breath-hold reproducibility is then placed on the upper abdomen, over the rib cage.

A CBCT scan is then performed to correct setup inaccuracies and validate the GTV position against the reference simulation CT. Typically, a CBCT is performed with 2-4 breath-holds, monitored with a ±0.3 cm threshold on the OSMS-AlignRT®. When the GTV is not clearly visible on the CBCT and simulation CT, which often occurs in liver SBRT, the appropriate anatomical surrogates, such as the diaphragm and liver vessel position, can be assessed and used to correct for the setup inaccuracies [22]. When we are certain that our GTV or anatomical surrogate position is correct, the patient is instructed to take another breath-hold. If the breath-hold is the same as before, the treatment couch is shifted during that breath-hold, another image of the patient's skin surface is captured, and treatment can start. If the patient can maintain a reproducible breath-hold according to our surface-guided system, another CBCT is performed in the middle of the fraction to correct for intrafractional displacements. In the case of lung SBRT, the GTV is usually clearly visible on the CBCT and simulation CT, so the intrafractional displacement of that visible GTV is corrected, as shown in Figure 1.

In contrast, for liver SBRT, if the GTV is not visible, the diaphragm, liver vessels, or surgical clips in close prox-

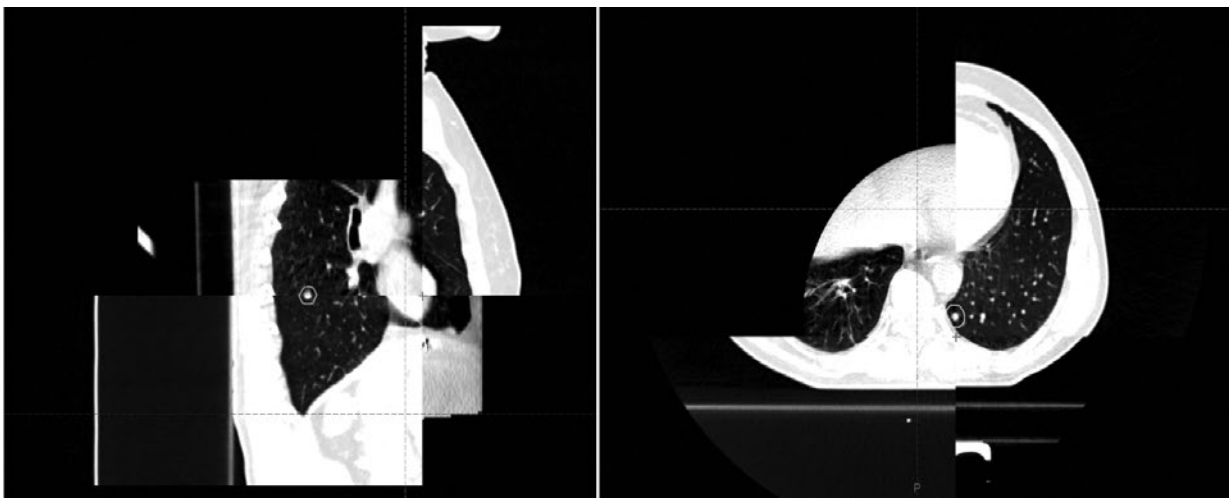


Figure 1: GTV position correction in lung SBRT done in IBH. (Source: Author)

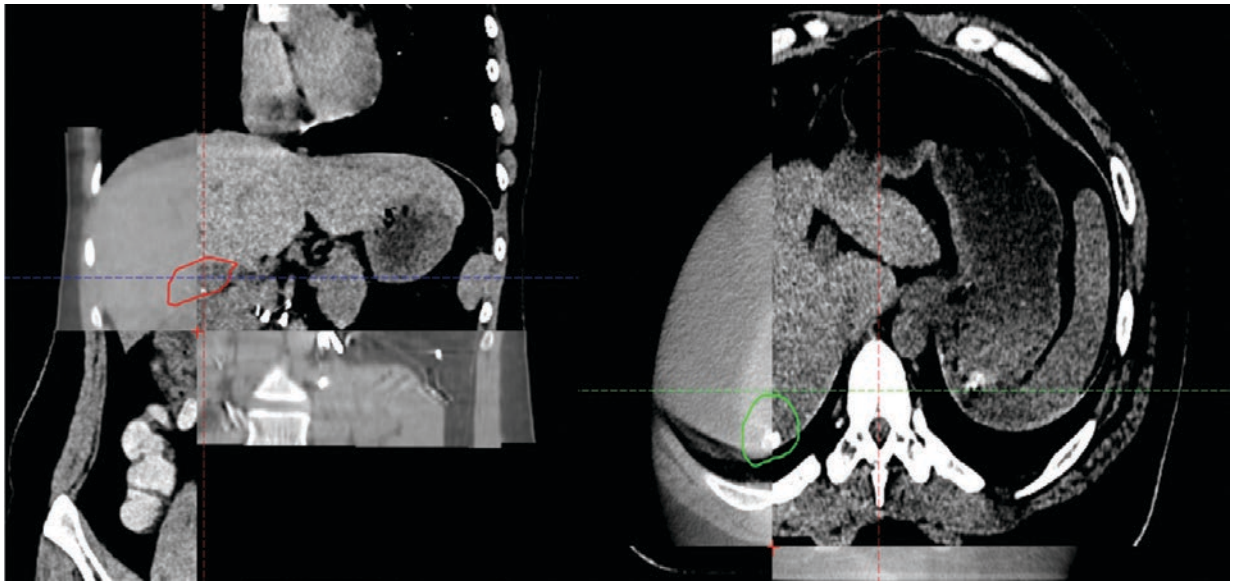


Figure 2: Diaphragm position correction in liver SBRT done in IBH. (Source: Author)

imity to the tumour position are corrected, as shown in Figure 2.

After the intrafractional displacement correction is completed, the couch shift is reapplied during the patient's breath-hold, an image of the patient's skin surface is captured, and the treatment continues.

If the patient moves or changes the amplitude of their breath-hold according to the surface-guidance system, CBCT is performed more frequently for additional correction.

After the treatment is conducted, the patient can go home with a referral for the first follow-up, typically scheduled 3 months post-treatment.

Preparatory work

As preparation for conducting this study, several studies have been reviewed that have evaluated intrafractional displacement in lung and liver SBRT during surface-guided DIBH in combination with IGRT.

As shown in Table 1, the number of studies analysing intrafractional displacement in surface-guided DIBH is limited. The number of patients included is usually lower, with differences in quantification metrics and displacement-direction information stated.

Considering the above, this study was designed to include more patients and fractions, with uniform metric quantification and displacement-direction information, for both lung and liver SBRT patients treated with IBH.

Objectives and Aims

The aim of this study was to confirm the hypothesis that, when OSMS-AlignRT® shows that patients maintain reproducible IBH during the whole treatment, GTV or anatomical surrogate intrafractional displacement during surface-guided IBH is ≤ 0.5 cm, which is used as the isotropic CTV-PTV margin in our institution.

The primary objective of this study was to assess the intrafractional accuracy and precision of our SBRT protocol using the IBH technique monitored by OSMS-AlignRT®. Specifically, we aimed to evaluate differences in couch position in the three main translational directions (VRT, LNG, LAT) from the start of treatment to the middle

Table 1: Publication review on intrafractional displacement for lung and liver SBRT in surface-guided DIBH

Study	Year	Tumour site	Sample size	Metric	Direction	Displacement (cm)
P. Naumann et al.	2020	Liver Lung	10 patients 41 fraction	Mean	3D	Lung: 0.16 (-0.39-0.05) Liver: 0.12 (-0.27-0.28)
E. Brown, E. Muscat, P. O'Connor, H. Liu, Y. Y. Lee, and D. Pryor	2020	Liver	8	Mean	LNG LAT VRT	0.2 (0-0.3) 0.15 (0-0.2) 0.18 (0-0.2)
D. Nguyen et al.	2023	Lung	13 patients 73 fractions 175 CBCTs	Median	LNG LAT VRT	0.12 (0.01-0.17) 0.1 (0.07-0.11) 0.08 (0.07-0.13)
L. B. Stick, I. R. Vogelius, S. Risum, and M. Josipovic	2020	Liver	10 patients	Median	LNG	0.3 (0.01-1.4)
C. Zeng et al.	2022	Liver	1 patient 2 metastases	Mean	3D	0.8 (0.6-1) 1.1 (1.1-1.2)

of the fraction, when a CBCT check is performed to verify and adjust positioning. Positional differences between the initial and middle fraction CBCT, which were analysed and quantified, are shown in Figure 3.

As an additional objective, a comparison of lung and liver cases for each of the translational directions was conducted to determine whether there is a significant difference in intrafractional displacement between lung and liver surface-guided SBRT in IBH.

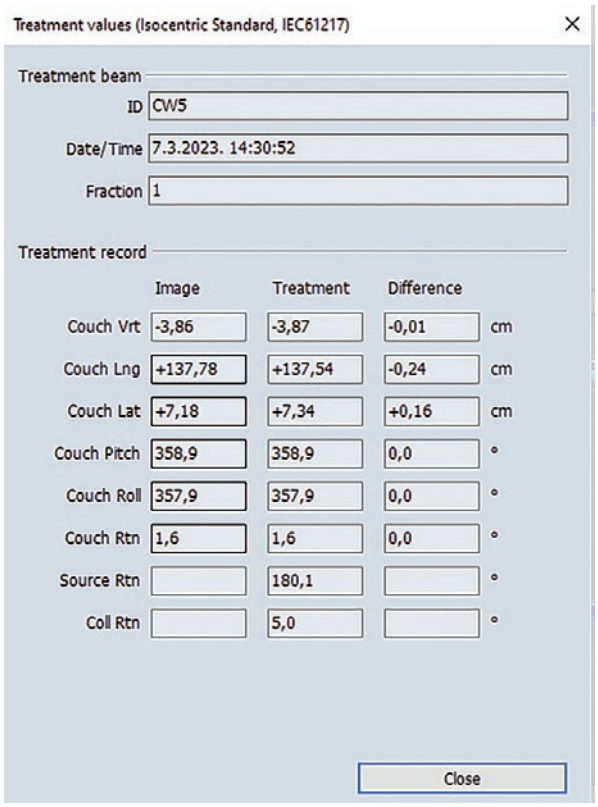


Figure 3: Positional differences between the initial and middle fraction CBCT. (Source: Author)

Materials and Methods

Data for this study were collected retrospectively by reviewing all offline review records found in the Aria® oncology information system of patients with lung and liver SBRT treated with surface-guided IBH from 2021 to 2024 at our institution. The analysis included only those patients who could maintain consistent and reproducible IBH, as per our institutional protocol. Examples of the offline reviews included in this study are shown in Figure 4, where it can be seen that after one or two initial CBCTs, done for patient setup, the next one is performed in the middle of the fraction for correction of intrafractional displacement, indicating that the patient could maintain stable and reproducible IBH through the entire treatment.

In Figure 5, examples of offline reviews excluded from this study are shown. More than one CBCT during the treatment, and a CBCT done in the middle of the same arch, are indicators that the patient moved or could not maintain reproducible IBH during the entire treatment.

Data collection

The initial data collection step was to identify all patients treated for lung and liver SBRT with surface-guided IBH from 2021 to 2024. The offline reviews of all those patients were checked, and based on the offline review, patients were included or excluded from this study.

If the patient met the inclusion criteria, the patient's age, sex, name of the PTV, treatment time, fraction, and positional difference between two CBCTs in VRT, LNG, and LAT directions in centimetres were manually extracted and stored in two separate Microsoft Excel files, one for lung SBRT and one for liver SBRT. In those files, the 3D Euclidean distance was calculated in a separate column.

As a second step, code for the software R [23] was created that utilises those Microsoft Excel files for statistical analysis and the creation of visual representations in the form of boxplot graphs, histograms for each translational direction, and 3D scatter plots.

Between 2021 and 2024, a total of 681 patients with liver and lung SBRT received surface-guided IBH treatment at our institution. Of those, the 210 patients' offline reviews met the criteria for indicating stable and reproducible IBH and were included in this study. The analysis included 86 lung SBRT and 124 liver SBRT patients, with 182 and 159 fractions, respectively. According to the offline review, the remaining 471 patients had multiple CBCTs done during the treatment, which indicated patient movement or changes in breath-hold, so they were excluded from this study.

Table 2 shows patients' demographics and treatment characteristics.



Figure 4: Example of offline reviews used in this study. (Source: Author)

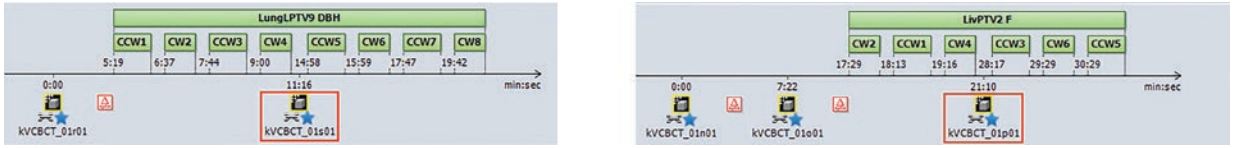


Figure 5: Example of offline review excluded from this study. (Source: Author)

Table 2: Patient demographics and treatment characteristics

Parameter	Lung SBRT	Liver SBRT
Number of patients	86	124
Sex (M/F)	38/48	74/50
Mean age (years)	60.2 ± 13.6	59.1 ± 10.8
Number of fractions	182	159
Average treatment time	24 min 23 sec	24 min 18 sec

Statistical Analysis

For statistical analysis, the software R was used. Microsoft Excel files were imported into R, and the mean, standard deviation (SD), median, and 95% confidence interval (95% CI) of positional differences for each of the three main translational directions (VRT, LNG, LAT) were calculated. 3D Euclidean distance for providing spatial displacement information was automatically calculated in a Microsoft Excel file, with visual representation done in R.

If, in some cases, intrafractional displacement exceeded a 0.5 cm margin, the number and percentage of those fractions were also determined.

Before comparing results between lung SBRT and liver SBRT data, the Shapiro-Wilk test was performed to check the data distribution.

Since the data were not normally distributed across all directions, as shown in Table 3, the non-parametric Mann-Whitney U test was used to compare the differences between the liver and lung SBRT data for each of the translational directions, including 3D displacement.

Table 3: Shapiro-Wilk test results for Region and Direction

Region	Direction	Shapiro-Wilk p-value	Distribution
Liver	VRT	0.00565	Not normal
Liver	LNG	0.0102	Not normal
Liver	LAT	0.0903	Normal
Liver	3D	0.0629	Normal
Lung	VRT	0.000522	Not normal
Lung	LNG	0.0743	Normal
Lung	LAT	0.0106	Not normal
Lung	3D	3.88×10^{-5}	Not normal

Additionally, boxplot graphs and histograms of intrafractional displacements in all directions, along with a 3D scatter plot of spatial distribution, were created to facilitate visual inspection and interpretation of the data.

Results

In liver SBRT patients, the most considerable intrafractional directional displacement has been observed in the mean VRT direction (0.087 cm), with lower mean values of -0.031 cm and -0.042 cm for the LAT and LNG directions, respectively, indicating intrafractional drift of the liver in the posterior–cranial–left lateral direction. The highest SD value has been observed in the LNG direction (±0.275 cm), indicating greater interpatient variability in the caudo-cranial direction. Low median values have indicated minimal displacement for 50% of the fractions in all directions. When looking into the 95% CI, all directions have excluded zero, indicating that the intrafractional displacements in all directions are not random, but rather systematic. The observed 3D mean displacement has been 0.351 ± 0.181 cm, suggesting that for some patients, spatial intrafractional displacement has exceeded a ±0.5 cm isotropic margin.

In lung SBRT patients, the highest mean intrafractional displacement has been observed in the LNG direction (-0.092 cm), with lower mean values of -0.025 cm and 0.036 cm for LAT and VRT directions, respectively, indicating intrafractional drift of the lung similar to the liver, in the posterior–cranial–left lateral direction, with predominantly cranial displacement. Also, identical to the liver, the highest SD value has been observed in the LNG direction. In lung cases, low median values have also been observed, and the 95% CI has excluded zero, indicating a minimal shift for 50% of the fractions, with a systematic trend in all directions. The 3D spatial displacement has been 0.298 ± 0.186 cm, indicating that there has been a possibility of exceeding the used margin in some cases.

Table 4 shows descriptive statistics for liver and lung SBRT patients treated with surface-guided IBH.

Table 4: Descriptive statistics of Intrafractional displacement by Region and Direction

Region	Direction	Mean ± SD (cm)	Median (cm)	95% CI low	95% CI high
Liver	VRT	0.087 ± 0.180	0.050	0.061	0.113
Liver	LNG	– 0.042 ± 0.275	– 0.030	– 0.082	– 0.002
Liver	LAT	– 0.031 ± 0.196	0.000	– 0.060	– 0.003
Liver	3D	0.351 ± 0.181	0.350	0.325	0.377
Lung	VRT	0.036 ± 0.161	0.030	0.014	0.059
Lung	LNG	– 0.092 ± 0.251	– 0.080	– 0.128	– 0.057
Lung	LAT	– 0.025 ± 0.157	0.000	– 0.047	– 0.003
Lung	3D	0.298 ± 0.186	0.281	0.272	0.325

Figure 6 shows a boxplot of intrafractional displacement across all translational directions, and we observed that most displacements in both liver and lung patients remained within ±0.5 cm in all directions. However, each direction has shown at least one outlier exceeding this margin, which indicates that, while intrafractional motion has been well controlled when using surface-guided IBH,

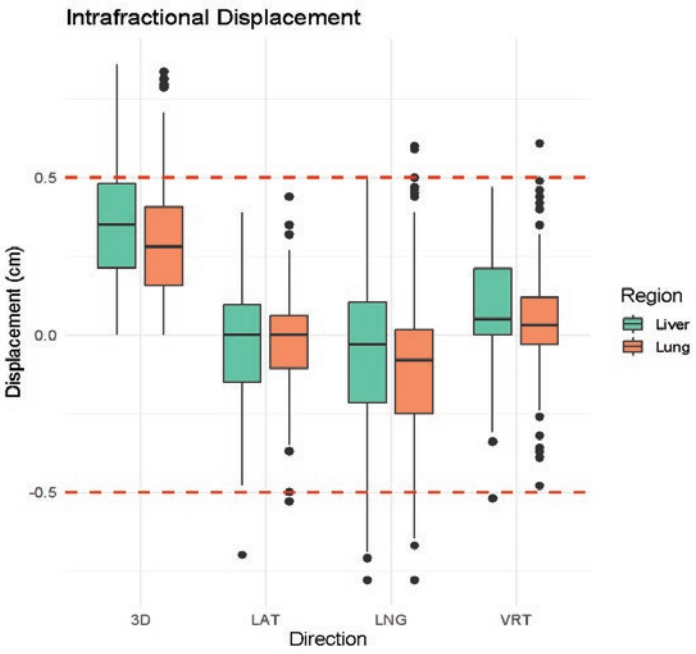


Figure 6: Boxplot graph of Intrafractional displacements in all directions. (Source: Author)

rare but significant excursions have occurred. In particular, both liver and lung patients have exhibited the most frequent margin exceedances in the longitudinal direction, consistent with the high SD values for both groups.

To further visualise the distribution of intrafractional displacements, histograms have been created for each translational direction (LAT, LNG, VRT) and the 3D vector magnitude separately for liver (Figure 7) and lung patients (Figure 8). In both the liver and lung groups, the LAT and LNG directions have been approximately centred around zero but have displayed some asymmetry, particularly in the LNG axis, with a skew toward negative values consistent with cranial displacement. The VRT direction also has shown a skew toward positive values in liver patients, indicating posterior drift. The 3D displacement has exhibited a distribution toward higher values in liver patients compared to lung patients, indicating greater spatial motion in the liver group.

The 3D scatter plot shown in Figure 9 has provided a comprehensive spatial overview of the intrafractional displacements, illustrating the simultaneous relationship between VRT, LNG, and LAT displacements, with each point representing a single treatment fraction. It is evident that although both groups are centred around the origin, the liver data have appeared more dispersed, indicating greater spatial motion in the liver group.

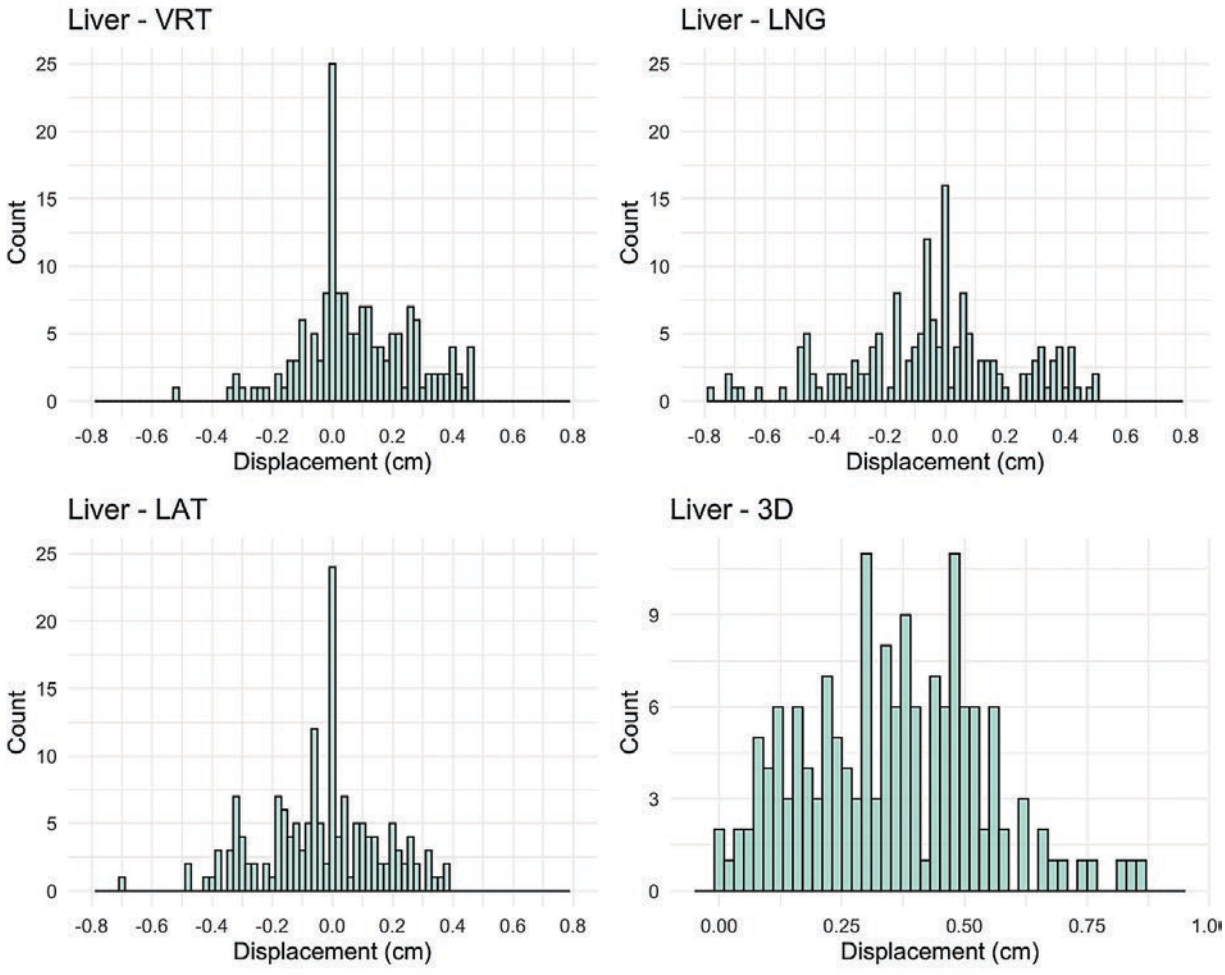


Figure 7: Histograms of liver Intrafractional displacements. (Source: Author)

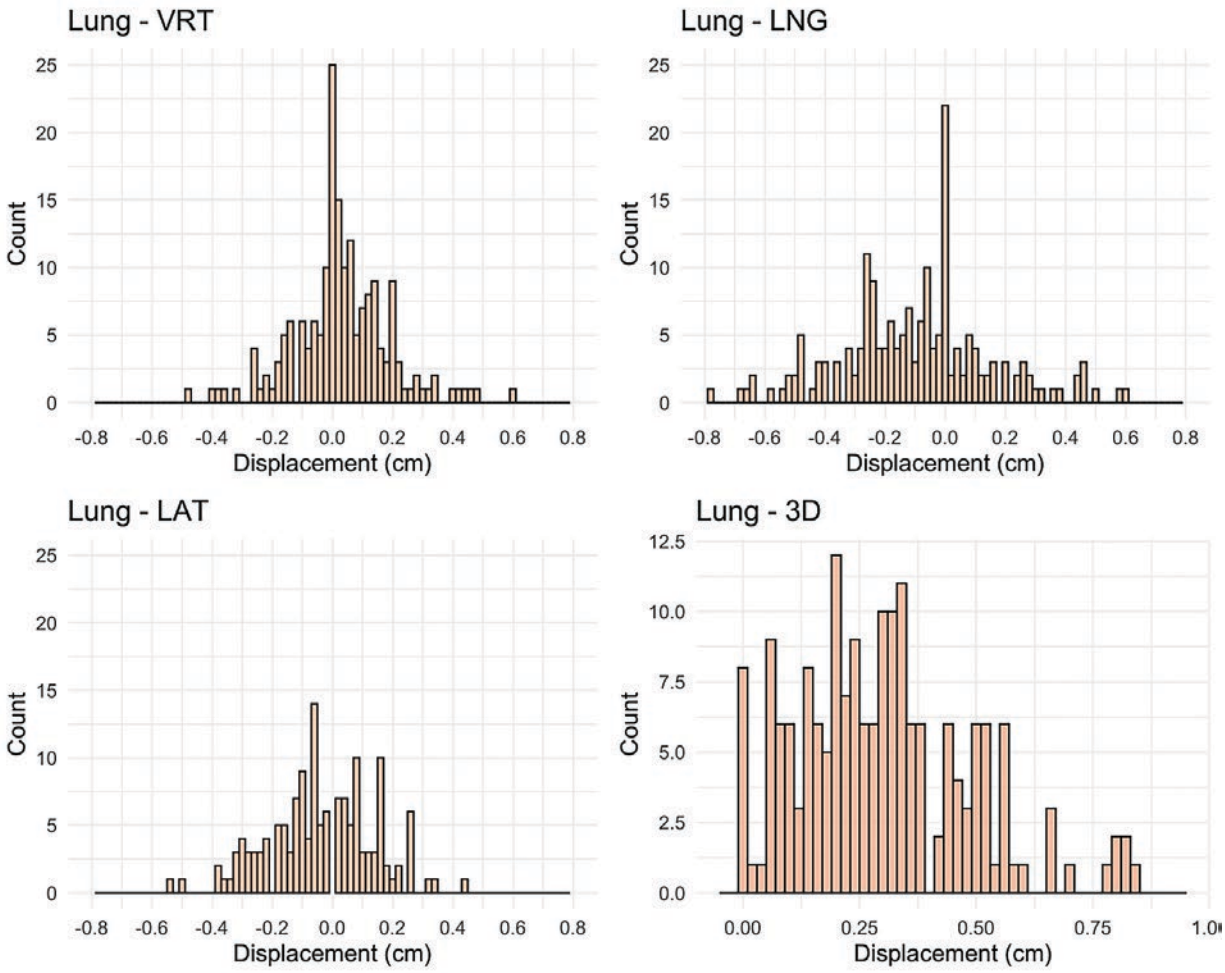


Figure 8: Histograms of lung Intrafractional displacements. (Source: Author)

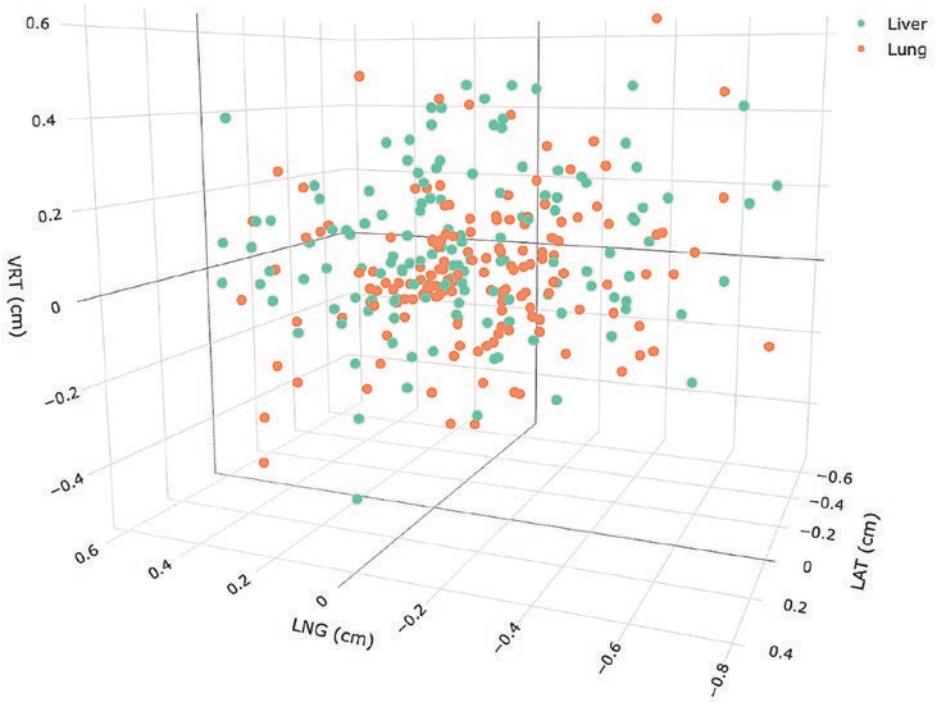


Figure 9: 3D scatter plot of Intrafractional displacements for liver and lung patients. (Source: Author)

Since the intrafractional displacement in all directions has exceeded the ±0.5 cm margin at least once, the number and percentage of those fractions have been determined. The highest number of exceedances has been observed in the 3D spatial direction, with 31 fractions (19.5%) for liver patients and 27 fractions (14.8%) for lung patients, respectively. When examining each translational direction separately, the highest number of exceedances has been, as mentioned above, in the LNG direction for both groups: 7 fractions (4.4%) for liver patients and 11 fractions (6.04%) for lung patients.

The summary of fractions with displacements exceeding ±0.5 cm can be seen in Table 5.

Table 5: Fractions with displacements exceeding ± 0.5 cm by direction and region

Region	Direction	Exceeding	Total	Percentage
Liver	3D	31	159	19.5%
Liver	LAT	1	159	0.63%
Liver	LNG	7	159	4.4%
Liver	VRT	1	159	0.63%
Lung	3D	27	182	14.8%
Lung	LAT	1	182	0.55%
Lung	LNG	11	182	6.04%
Lung	VRT	1	182	0.55%

As previously mentioned, the comparison of liver and lung data has been conducted using the Mann-Whitney U test. The results shown in Table 6 have revealed significant differences in VRT, LNG, and overall 3D spatial intrafractional displacement between liver and lung SBRT patients treated with surface-guided IBH (p-values = 0.0140, 0.0331, and 0.0032, respectively). These findings have aligned with prior results from descriptive analysis between these two groups, indicating that liver patients have experienced greater posterior intrafractional motion, while lung patients have exhibited more pronounced cranial intrafractional motion. In contrast, no significant difference has been found in LAT direction ($p = 0.786$), suggesting that lateral motion patterns have been similar for both anatomical regions when treated with surface-guided IBH. The results for 3D displacement have shown a significant difference between liver and lung patients ($p = 0.0032$), supporting the indication that the liver group has experienced higher spatial intrafractional motion during surface-guided IBH SBRT.

Table 6: Statistical comparison between lung and liver data

Direction	Mann-Whitney p-value
VRT	0.0140
LNG	0.0331
LAT	0.786
3D	0.0032

Discussion

In this large retrospective single-centre study, intrafractional displacement during surface-guided IBH SBRT was evaluated in liver and lung SBRT patients across a total of 341 treatment fractions. The cohort included 159 liver and 182 lung fractions.

The results demonstrated excellent positional stability, with mean directional displacements remaining well below the institutional isotropic CTV-PTV margin of ±0.5 cm.

The largest mean displacement was noted in the VRT direction for liver patients (0.087 cm) and in the LNG direction for lung patients (-0.092 cm). Both groups exhibited high variability in the LNG direction, with an SD of 0.275 cm for the liver and 0.251 cm for the lung, respectively.

Despite favourable average results, boxplot analysis showed that at least one outlier was identified in each direction that surpassed this margin.

The highest number of fractions surpassing a ±0.5 cm margin was observed in the 3D spatial direction, accounting for 19.5% of liver fractions and 14.8% of lung fractions. Additionally, in LNG directions, 4.4% of liver fractions and 6.04% of lung fractions exceeded this margin.

The histogram analysis conducted on both the liver and lung groups demonstrated a skew toward positive values in the VRT direction and negative values in the LNG direction, respectively, thereby visually confirming the findings derived from descriptive statistics. A 3D histogram revealed a broader distribution toward higher values in liver patients compared to lung patients, indicating that spatial displacement is not only greater in magnitude but also more variable in the liver group, which is further confirmed by the 3D scatter plot.

Shapiro-Wilk test p-values below 0.5 in five of eight region-direction combinations justified the use of the Mann-Whitney U test, which revealed significant differences in VRT, LNG, and 3D displacement between liver and lung patients ($p = 0.0140$, 0.0331, and 0.0032, respectively), while lateral shifts did not differ ($p = 0.786$).

These results support indications that during surface-guided IBH, intrafractional displacement of the liver is predominantly posterior, with higher spatial displacement, while in lung cases, intrafractional displacement is predominantly cranial.

When compared with previous publications, the mean 3D spatial displacements of 0.351 cm for liver patients and 0.298 cm for lung patients are somewhat higher than those previously reported, where mean 3D displacements were 0.12 cm and 0.16 cm for liver and lung patients, respectively [19].

Reported directional means of 0.2 cm (LNG), 0.15 cm (LAT), and 0.18 cm (VRT) for liver patients [24] are higher than those in this study, but have similar SD values.

Median displacements in the lung group were comparable to previously published values [25].

This study's results indicated the greatest variability in the LNG direction for both lung and liver patients, which is consistent with prior reports [26].

Some cases reported in the literature observed higher displacements with 3D values exceeding 0.8 cm in an individual patient [27], which supports this study's finding that rare but high excursions do occur.

Overall, when compared with the published literature, this study confirms the general magnitude and directionality of intrafractional displacements in patients treated with surface-guided IBH SBRT, with some differences in results that can potentially be attributed to variations in sample size.

One of the strengths of this study is its large sample size, uniform imaging with SGRT workflow, and standardised analysis methodology; however, its retrospective design and reliance on couch shift data for target displacement present a limitation, as this approach may not fully capture real-time target motion.

Despite these limitations, this study's findings provide valuable insight into intrafractional displacements in surface-guided IBH liver and lung SBRT, highlighting areas for future optimisation.

Conclusion

The results of this study demonstrated that the mean displacement along each axis was well below the ±0.5 cm margin; however, some fractions exceeded this threshold, most frequently in the 3D spatial direction and in the LNG direction. Consequently, the hypothesis cannot be accepted, as the current protocol provides adequate geometric accuracy for most treatments, but it is not universally applicable.

Differences in anatomical displacement were also noted. Liver targets showed larger posterior (VRT) and overall 3D shifts, while lung targets demonstrated greater superior/cranial (LNG) intrafractional motion. These findings suggest that a uniform isotropic margin may not adequately address axis-specific drift patterns, and that site-specific anisotropic margins tailored to individual anatomical sites could be more effective.

Despite its retrospective design and reliance on couch-shift data, this study derives significant advantages from a large cohort, a uniform SGRT workflow, and a standardised analytical framework.

Although intrafractional displacement excursions occurred and the main hypothesis wasn't confirmed, these results provided valuable insights and essential information for refining our protocol and approach to treating liver and lung targets with surface-guided IBH SBRT.

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Procjena intrafrakcijskog pomaka u stereotaktičkoj radioterapiji uz navođenje površinom i zadržavanje daha u inspiriju

Sažetak

Uvod: Stereotaktička radioterapija tijela (SBRT) omogućuje primjenu visokih doza zračenja na tumor uz strme gradijente doze i minimalno ozračenje okolnog zdravog tkiva. Površinski vođeni inspiracijski breath-hold (IBH) osobito je koristan kod tumora prsnog koša i gornjeg abdomena, gdje respiratorno gibanje može značajno utjecati na položaj cilja.

Cilj: Cilj ove retrospektivne kohortne studije bio je procijeniti intrafrakcijski pomak GTV-a ili anatomskog surogata tijekom površinski vođenog IBH-a u slučajevima u kojima je površinskim praćenjem potvrđeno održavanje reproducibilnog IBH-a tijekom cijelog tretmana. Također je procijenjena intrafrakcijska točnost i preciznost SBRT protokola primjenom IBH-a praćenog površinski vođenom radioterapijom (SGRT). Uspoređeni su intrafrakcijski pomaci između kohorti pacijenata s tumorima pluća i jetre.

Materijali i metode: Analizirane su frakcije 86 pacijenata liječenih SBRT-om zbog tumora pluća (182 frakcije) i 124 pacijenta s tumorima jetre (159 frakcija).

Rezultati: U kohorti tumora jetre najveći srednji intrafrakcijski pomak zabilježen je u vertikalnom (VRT) smjeru (0,087 cm), dok su srednji pomaci u lateralnom (LAT) i longitudinalnom (LNG) smjeru iznosili -0,031 cm i -0,042 cm. Najveća standardna devijacija zabilježena je u LNG smjeru (±0,275 cm). Srednji 3D pomak iznosio je 0,351 ± 0,181 cm.

U kohorti tumora pluća najveći srednji pomak zabilježen je u LNG smjeru (-0,092 cm), dok su pomaci u LAT i VRT smjeru iznosili -0,025 cm i 0,036 cm. Najveća standardna devijacija također je zabilježena u LNG smjeru (±0,251 cm). Srednji 3D pomak iznosio je 0,298 ± 0,186 cm.

Statistički značajne razlike između kohorti utvrđene su za VRT, LNG i 3D pomak ($p = 0,0140$, 0,0331 i 0,0032).

Zaključak: Studija nije potvrdila da je intrafrakcijski pomak tijekom površinski vođenog IBH-a uvijek ≤ 0,5 cm. Protokol osigurava odgovarajuću geometrijsku točnost u većini tretmana, uz značajne razlike između plućne i jetrene kohorte koje ukazuju na potrebu za regionalno prilagođenim pristupom.

Ključne riječi: SBRT, inspiracijski breath-hold (IBH), površinski vođena radioterapija (SGRT), intrafrakcijski pomak, tumori pluća, tumori jetre, geometrijska točnost