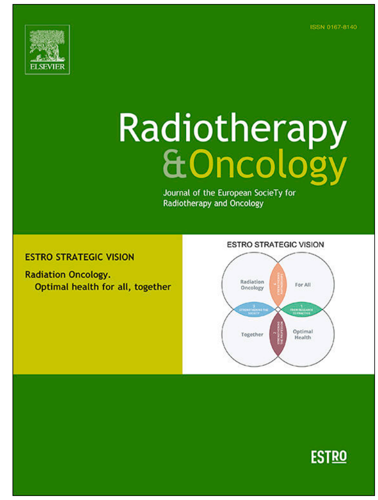
Journal Pre-proofs



Review Article

To compress or to breath-hold? A systematic review of the impact of motion mitigation techniques on motion, interfraction set-up errors, and intrafraction errors in patients with hepatobiliary and pancreatic malignancies

Amanda Webster, Yemurai Mundora, Catharine H. Clark, Maria A. Hawkins

PII: S0167-8140(24)03559-X
DOI: https://doi.org/10.1016/j.radonc.2024.110581
Reference: RADION 110581

To appear in: *Radiotherapy and Oncology*

Received Date: 24 January 2024
Revised Date: 12 September 2024
Accepted Date: 5 October 2024

Please cite this article as: Webster, A., Mundora, Y., Clark, C.H., Hawkins, M.A., To compress or to breath-hold? A systematic review of the impact of motion mitigation techniques on motion, interfraction set-up errors, and intrafraction errors in patients with hepatobiliary and pancreatic malignancies, *Radiotherapy and Oncology* (2024), doi: https://doi.org/10.1016/j.radonc.2024.110581

on motion, interfraction set-up errors, and intrafraction errors in patients with hepatobiliary and pancreatic malignancies

1. Author(s) full name(s) written as First Name then Last Name, and highest academic degree(s):

Amanda Webster, MSc [1,2]

Yemurai Mundora, BSc [1]

Catharine H. Clark, PhD[2,3,4]

Maria A. Hawkins, FRCR[1,2]

2. The name(s) of the institution(s), section(s), division(s), and department(s) where the study was performed and the institutional affiliation(s) of the author(s) at the time of the study:

1. Cancer Division, University College London Hospitals NHS Foundation Trust, London, UK
2. Department of Medical Physics and Biomedical Engineering, University College London, London, UK
3. Radiotherapy Physics, University College London Hospitals NHS Foundation Trust, London, UK
4. National Physical Laboratory, Teddington, UK

3. Acknowledgment of any presentation of this material, to whom, when, and where: Not applicable

4. Acknowledgment of financial support, including grant numbers:

This work was supported by the Radiation Research Unit at the Cancer Research UK City of London Centre Award [C7893/A28990].

MAH is supported by the National Institute for Health and Care Research (NIHR) Biomedical Research Centre (BRC) at University College London Hospitals NHS Foundation Trust (UCLH).

5. Explanation of any conflicts of interest:

None

6. Name, address, business telephone number, and e-mail address of corresponding author:

Amanda Webster

Radiotherapy Department

University College London Hospital

235 Euston Road

Journal Pre-proofs

London

NW1 2BU

Telephone: 0203447314

Email: Amanda.webster2@nhs.net

Highlights:

Forty studies reported motion and on-treatment errors when using abdominal compression or breath-hold.

No studies compared abdominal compression and breath-hold.

AC may effectively diminish motion; however, its efficacy is not uniform. BH may immobilise motion; however, it can be inconsistent between fractions.

Patient experience and tolerability of motion mitigation are underreported.

Keywords:

hepatobiliary malignancies, pancreatic malignancies, systematic review, motion management, motion mitigation

Structured abstract:

Background and purpose: Reducing motion is vital in treating hepatobiliary (HPB) and pancreatic malignancies. Abdominal compression (AC) and breath-hold (BH) techniques aim to minimise respiratory motion, yet their adoption remains limited, and practices vary. This review examines the impact of AC and BH on motion, set-up errors, and patient tolerability in HPB and pancreatic patients.

Materials and methods: This systematic review, conducted using PRISMA and PICOS criteria, includes publications from January 2015 to February 2023. Eligible studies focused on AC and BH interventions in adults with HPB and pancreatic malignancies. Endpoints examined motion, set-up errors, intra-fraction errors, and patient tolerability. Due to study heterogeneity, Synthesis Without Meta-Analysis was used, and a 5mm threshold assessed the impact of motion mitigation.

Results: In forty studies, 14 explored AC and 26 BH, with 20 on HPB, 13 on pancreatic, and 7 on mixed cohorts. Six studied pre-treatment, 22 inter/intra-fraction errors, and 12 both. Six AC pre-treatment studies showed >5mm motion, and 4 BH and 2 AC studies reported >5mm inter-fraction errors. Compression studies commonly investigated the arch and belt, and DIBH was the predominant BH technique. No studies compared AC and BH. There was variation in the techniques, and several studies did not follow standardised error reporting. Patient experience and tolerability were under-reported.

Conclusion: The results indicate that AC effectively reduces motion, but its effectiveness may vary. BH can immobilise motion; however, it can be inconsistent between fractions. The review underscores the need for larger, standardised studies and emphasizes the importance of considering the patient's perspective for tailored treatments.

Introduction

Patients with abdominal malignancies, including hepatobiliary (HPB) and pancreatic malignancies, exhibit some of the lowest rates of 5-year survival compared to other tumour sites [1, 2]. Advances in radiotherapy technology permit the delivery of stereotactic body radiotherapy (SBRT) and proton beam radiotherapy (PBT) to HPB and pancreatic patients [3-12]. There are challenges in tumour visualisation, the proximity of the radiosensitive gastrointestinal (GI) tract and the need to deliver a high dose to cure these malignancies [8-18]. Addressing motion is key to tackling these challenges [8-12, 18-22]. Motion can include respiration, peristalsis, and gastric filling [20, 22-28]. Respiration motion is generally the largest source of motion and may be in the order of centimetres, with the craniocaudal direction often being the most affected [21, 29-31]. Motion can be accounted for by using techniques such as gating, an internal target volume (ITV), mid-ventilation and tracking [23]. However, the challenges remain as the visualisation is often difficult due to imaging artefacts [19, 32] and margins are required for many of these approaches [23], which hinders the delivery of high doses [33, 34].

Motion can be minimised by utilising two respiratory motion mitigation approaches Abdominal Compression (AC) and Breath Hold (BH). Abdominal compression involves the application of external pressure to the abdominal region during pre-treatment and treatment sessions. This pressure aims to minimise organ motion, specifically by reducing respiratory motion [35-37]. Different devices can be utilised for AC, including arches/plates, belts/bands, corsets, shells and immobilising the patient in the prone position [38-44]. The challenge with AC is whether it can effectively minimise motion for each patient, both at pre-treatment and during treatment [37, 45, 46], and whether they can tolerate the equipment. Breath-hold requires patients to hold their breath at a specific point in the respiratory cycle. The patient can be instructed to hold their breath within a phase of inhaling or exhaling. Both approaches can be deep or extended [47]. Equipment, such as audiovisual feedback systems and external surrogates, can be employed to guide patients into a voluntary BH, thus relying on the patient achieving the BH [47]. Alternatively, patients can enter BH with the help of machine-assisted systems using spirometers [47], or less commonly, mechanical ventilation [48]. The challenge with BH lies in its ability to hold the patient at the same level of BH (phase and amplitude of the breathing cycle) on each occasion [49].

Recent surveys have highlighted that the adoption of motion mitigation approaches remains low, especially in abdominal radiotherapy [50-52]. From the patient's perspective, both approaches require them to tolerate additional equipment and procedures compared to standard radiotherapy immobilisation. BH techniques require active participation from the patient to hold their breath and maintain this, whereas the patient must tolerate the compression equipment for AC techniques.

Overall, the literature lacks systematic reviews addressing AC and BH's effectiveness on radiotherapy pre-treatment and treatment errors in patients with abdominal malignancies. The patient perspective of motion mitigation has also not been addressed. Thus, this systematic review aims to assess AC and BH techniques' impact on motion and set-up consistency in patients with HPB and pancreatic malignancies. Specifically, motion and set-up consistency errors primarily encompass motion, online inter-fraction set-up errors and intra-fraction motion [53, 54]. The secondary aim is to assess the patient experience.

Materials and Methods

Overview

This systematic review was conducted according to the preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA). The protocol was registered at https://www.crd.york.ac.uk/PROSPERO/ (Review registry CRDXXXXXX). The review question was developed using the PICOS framework, as shown in Table 1.

Literature search

The literature search was performed using CINAHL, Embase, EMCare and MEDLINE. The search strategy for Ovid MEDLINE is included in the supplementary material. The search terms were modified as appropriate for each database. The reference lists of relevant studies were also searched. Studies published in English from January 2015 until February 2023 were included. All studies assessing motion and the associated errors during radiotherapy were eligible, regardless of study design (retrospective or prospective). Grey literature, such as unpublished studies, abstracts, and conference posters without adequate detail, were excluded. The search terms included all abdominal tumour sites, but only HPB and pancreatic studies were included.

Eligibility criteria

The inclusion criteria were adults (over 18 years of age) with hepatobiliary and pancreatic malignancies receiving radiotherapy using a motion mitigation intervention. SBRT/SABR treatments were included. Motion mitigation was considered to require a patient to tolerate additional equipment and procedures compared to standard radiotherapy immobilisation, namely abdominal compression and breath-hold. The exclusion criteria were volunteers, simulated studies, studies when the measurements were not taken on the liver, pancreas or an appropriate surrogate, studies in the prone position and phantom studies.

Defined endpoints

The primary study endpoints encompassed motion and the consistency of an Image-Guided Radiation Therapy (IGRT) match structure, which was defined as the treatment target and/or relevant surrogates (e.g., dome of the diaphragm, fiducials, or radio-opaque markers). Treatment target surrogates were accepted due to challenges visualising abdominal malignancies on X-ray imaging. This is due to tumour size, location, density, contrast, overlapping anatomy and motion artefacts [16, 17, 55]. Parameters including pre-treatment motion, online inter-fraction setup errors, and intra-fraction motion were evaluated to assess inconsistencies. BH can have two intra-fraction motion components, including 1) Intra-BH variation within a single breath-hold and 2) BH-to-BH variation from one breath-hold to the next within one treatment fraction [47]. This systematic review does not address these components separately. According to geometric uncertainty guidance [53, 54], studies should report the mean, systematic, and random components of these errors in the anterior/posterior, left/right and superior/inferior directions. However, studies using different approaches, such as the median and range, were also included. The secondary endpoint of patient experience, comfort and tolerability of the motion mitigation equipment was also included. The information was manually extracted from the selected studies' text with no standardised measure to assess this.

Screening

The articles were screened for duplication. Two reviewers (AW and YM) performed the initial study selections. Next, the two reviewers independently examined the full text of all articles identified using the PICOS framework (Table 1). Results were then compared, and disagreements were discussed and resolved by consensus. Five studies were discussed with a third reviewer (CC) to check if they should be included in the review. A PRISMA flow chart of the study selection procedure was produced, Figure 1.

Data extraction

Two reviewers (AW and YM) independently extracted information, including surname, year, baseline characteristics, motion mitigation approach, whether breath-hold was assisted, IGRT match structure, pre-treatment or on-treatment measurement, and imaging equipment. For the primary endpoint, the motion at pre-treatment, inter-fraction set-up errors, and intra-fraction motion were extracted. Additionally, reports of patient experiences were extracted from the studies that met the primary endpoint. Disagreements were discussed and resolved by consensus.

Quality Assessment

Two authors (AW and YM) completed the quality assessment. The Cochrane Handbook for Systematic Reviews of Interventions and the Risk of Bias Guidance was adapted [56]. The adapted tool used six domains to rank bias as low, medium, or high risk. These domains include selection bias, performance bias, detection bias, attrition bias, reporting bias, and others.

Data synthesis

Heterogeneity in study outcomes precluded meta-analyses and statistical synthesis. Therefore, a synthesis without meta-analysis (SWiM) was utilised [57]. Textual summaries of the included studies were used to aid the synthesis process. The SWiM checklist can be found in the supplementary material. Studies reporting motion or errors exceeding 5mm for metrics such as mean (m), standard deviation (SD), median, or similar measurements were specifically identified. 5mm was chosen as patients are considered to have very mobile tumours if motion >5mm [47] and it is a tolerance commonly utilised when assessing motion [28]. This threshold is clinically relevant but also pragmatic, considering the inherent heterogeneity in study outcomes and the elevated risk of bias in studies.

Results

Between January 2015 and February 2023, forty relevant studies were retrieved. Out of these, 14 studies explored compression techniques [38, 40, 44, 58-68] and 26 focused on breath-hold techniques [69-94] (Table 2). No studies compared compression versus breath-hold. There were 20 studies focused on HPB patients [38, 44, 59-62, 65, 68, 70, 71, 73, 77, 79-81, 83, 84, 86, 92, 93], 13 studies focused on pancreatic patients [40, 63, 64, 67, 74, 75, 78, 82, 85, 87, 89, 91, 94] and 7 studies focused on patients with abdominal malignancies (mainly HPB and pancreas patients) [58, 66, 69, 72, 76, 88, 90]. Six studies measured motion at pre-treatment [38, 40, 61, 65, 72, 80], 22 studies measured inter and/or intra-fraction errors on treatment [58, 63, 67, 69-71, 73, 75-78, 82-85, 87-91, 93, 94], and 12 studies assessed uncertainties at both pre-treatment and on-treatment [44, 59, 60, 62, 64, 66, 68, 74, 79, 81, 86, 92]. There was variation in the IGRT structure(s) used to assess uncertainties, and 17 studies used fiducials [44, 62, 63, 66, 68, 69, 74-78, 85-87, 89-91] and 23 studies did not [38, 58-61, 64, 65, 67, 68, 70-73, 79-84, 88, 92-94].

The studies had a high risk of bias (see supplementary material). Only 12 studies included ≥ 30 patients [38, 44, 58-61, 70, 71, 75-77, 80].

A total of fourteen studies employed abdominal compression as a motion mitigation technique [38, 40, 44, 58-68]. Among these studies, 6 investigated the compression arch [38, 58-62], 4 the compression belt [63-66], 2 the compression corset [40, 67], and 2 the compression shell [44, 68]. Twenty-six studies focused on breath-hold techniques for motion mitigation [69-94]. Among these studies, 20 investigated DIBH [69, 71, 74-76, 78-81, 86-91, 93, 94], 4 studies used EBH [72, 73, 77, 92], 3 studies used endEBH [70, 82, 85], and 2 studies used deepEBH [83, 84]. Within the BH category, 3 studies directly compared different breath-hold techniques [70, 72, 83]. Twelve studies employed spirometers, including ABC and SDX only, assisting the patient in breath-hold control [69, 70, 72, 74-76, 78-81, 87, 88]. Fourteen studies used an voluntary BH technique [71, 73, 77, 82-86, 89-94].

Motion uncertainty, defined as an IGRT structure deviation greater than 5mm, was reported in 8/20 (40%) of HPB studies [38, 60-62, 65, 68, 92, 93], 4/13 (31%) of the pancreatic studies, and 1/7 (14%) of the abdominal studies. Tables 3-5 and the supplementary material highlight these studies.

Specifically, within the pre-treatment compression studies, there were 6 AC studies where motion was >5mm [38, 60-65, 68, 69, 92-94]. This was in 4 compression arch studies [38, 60-62], and 3 of these studies were from the same centre [38, 60, 61]. Two investigators measured using the liver contour [38, 60, 61, 65] and two using liver fiducials [62, 68]. There was one compression shell study [68] and one compression belt study [65] when the motion exceeded 5mm. One study emphasised the significance of the position of the arch in achieving effective motion mitigation [38] None of the pre-treatment evaluations of BH studies reported motion exceeding 5mm when BH was employed (Table 3 and supplementary material).

Considering on-treatment, 2 AC and 4 BH studies reported inter-fraction uncertainty exceeding 5mm [63, 64, 69, 92-94] (Table 4 and supplementary material). The AC studies were both using the compression belt [63, 64]. Three of the 4 BH studies that had errors exceeding 5mm for inter-fraction uncertainties were in DIBH, and 1 was in EBH [69, 92-94]. Three of the studies used voluntary BH [92-94] and 1 study used assisted BH [69]. One study used fiducials and/or the liver contour to match [69], 1 matched to the liver contour [92] 1 matched to fiducials in the pancreas [63] and 3 matched to the pancreas [64, 93, 94].

Intra-fraction motion was low (<5mm) in all abdominal compression studies that reported it (Table 5 and supplementary material). There was one voluntary DIBH study that reported an intra-fraction uncertainty >5mm [89]. The match structure used in this study was fiducials in the pancreas [89].

Guidance recommends that the mean, systematic and random error should be reported as a minimum [53]. Five studies did not report the mean [44, 78, 81, 86, 88], 5 studies did not report the systematic error [63, 70, 86, 88, 89], and 35 studies did not report the random error [38, 40, 58-70, 72-78, 80, 82, 83, 85-94]. Nine studies reported the range [63, 64, 66, 70, 77, 86, 89, 90], 2 that reported the median [64, 86], 2 that reported the maximum [59, 88] and 1 study that removed the error outliers (e.g., [illegible]) reported errors within the mean [illegible] [illegible]. Additionally, different imaging modalities measured different values in the same plane. For example, a BH study recorded a maximum superior-to-inferior measurement of 10.39 mm with kV imaging and 8.79 mm with ultrasound imaging [88], while a 2D cine MRI showed different values compared to a 4D MRI [67]. Finally, some studies may have underestimated errors by not considering initial bony match values in their final analysis [79, 82], and some studies only analysed the final image before treatment delivery [75, 83].

Limited patient experience was reported in the studies, and given the paucity of reports on patient input, all aspects, including comfort, experience, patient information, tolerability, and training, were collated. Overall, the information and training given to patients was the most reported aspect of patient experience. Seven studies mentioned a training session [38, 77-80, 82, 86]. In one study, an information leaflet was given to patients [82]. In AC studies, one investigation emphasized the individual determination of belt pressure settings for each patient. The settings were established before the patient experienced pain or discomfort and, as a result, were guided by the patient's subjective assessment rather than the physiological impact on the patient [63]. One AC belt study highlighted that several patients reported discomfort [65]. One AC belt study evaluated factors such as gender, age, body mass index (BMI), history of transarterial chemoembolization, history of liver resection, tumour area, number of tumours, and tumour size (diameter). The univariate analysis highlighted the significant impacts of gender and BMI on abdominal compression effectiveness [61]. In one study, a patient questionnaire found the compression corset to be well-tolerated, with no reported complaints or pain on average [40]. In BH, one assisted ABC study mentioned a personalised screening approach when deciding which type of BH to proceed with, e.g., EBH, DIBH, and IBH [72]. Without personalised screening, EBH was the optimal technique, with superior reproducibility and stability compared with DIBH and IBH. However, implementing preplanning screening demonstrated in 56% of participants, DIBH or IBH demonstrated superior reproducibility and BH time compared with EBH [72]. Patient factors were also considered, and one assisted BH study found under rigorous breath-hold respiratory control, DIBH correlated with body weight and height [76]. The breath-hold durations required in all BH studies varied from 15 to 30 seconds, depending on the specific study requirements and techniques employed.

Discussion

Between January 2015 and February 2023, 40 studies assessed the effects of AC and BH in mitigating respiratory motion for patients with HPB and/or pancreatic malignancies. Without motion mitigation, it has been shown that respiratory motion can be in the order of centimetres [21, 29, 31]. The approaches varied widely, and no meta-analysis was performed due to study heterogeneity. Consequently, the results are presented narratively. No studies compared AC and BH. Six pre-treatment studies had motion greater than 5mm in at least one plane, including three AC arch studies from the same centre [38, 60, 61], one AC shell study [68], one AC arch with shell study [68], and one AC belt study [65] (Table 3). In 3 of these 6 studies, the average motion only exceeded 5mm by less than 0.3mm. Considering the inter-fraction set-up uncertainties, those that reported a systematic error greater than 5mm included 1 assisted DIBH study [69], 2 voluntary DIBH studies [93, 94], 1 voluntary EBH study [92] and 2 AC belt studies [63, 64] (Table 4). Inter-fraction set-up errors remain relevant when using motion mitigation approaches because couch shifts cannot always correct for variations in the breath-hold level or deformation caused by inconsistent compression. These findings highlight that AC can reduce motion but does not consistently do so for each patient, as seen in the pre-treatment session. BH can hold the patient in a phase of the breathing cycle; however, it is important to consider the inconsistency in inter-fraction errors, as shown in Tables 3 and 4.

There was variability in the IGRT structure selected to estimate uncertainties. In the 12 studies exhibiting motion, 3 matched fiducials [62, 63, 68] 8 matched the tumour/organ [38, 60, 61, 64, 65, 92-94] and 1 matched to both [69]. The suitability of using match structures is a major clinical challenge when treating patients with HPB and pancreatic malignancies. These tumours are often not visible on X-ray imaging, necessitating a surrogate, such as the diaphragm. However, the distance between the tumour and the surrogate and the relative motion should be considered. Alternatively, fiducials may be used; however, they may migrate over time and require an interventional procedure. Centres may have MRI imaging for treating these patients, and four studies met the inclusion criteria for this review [40, 64, 67, 94]. Although not captured in this review's endpoints, these studies offer valuable insights into treatment target movement, volume changes, and adaptive radiotherapy needs. However, small sample sizes and limited imaging techniques like cine imaging highlight the need for larger, more comprehensive studies. Centres should consider equipment availability and potential limitations when introducing or using motion management.

Efforts should prioritize identifying and addressing the most significant sources of uncertainty first with a minimum of 30 patients, followed by fine-tuning the approach.

The most reported motion mitigation technique was DIBH (n=20). Initially developed for breast cancer patients [50], DIBH remains most commonly used to reduce heart dose in left-sided cases, moving the treatment target away from critical structures [95]. In abdominal SBRT, BH aims to reduce respiratory-related tumour motion. Clinically, adapting DIBH for non-superficial lesions requires careful consideration, as this review and recent research on lung and lymphoma patients [49] underscore the importance of evaluating consistency from pre-treatment to treatment. With EBH, the patient is not forced out of their normal breathing pattern [47] and the consistency may be better, as, at rest, humans spend more of the breathing cycle in exhale [96, 97]. EBH may also be used in conjunction with abdominal compression. In this review, 9 studies reported EBH, and the results look promising as only 1/9 studies reported uncertainties greater than 5mm. However, the differentiation between deep inspiration/expiration and inspiration/expiration has not been explored enough. Caution should be taken, and a systematic review from 2021 categorizes these two techniques together [98], when in fact, the aim of both techniques is different. In a deep BH, the patient is being instructed out of their normal breathing cycle, whereas with EBH or IBH, the patient remains within their normal breathing cycle [47]. Moving forward, the term breath-hold should not be used interchangeably, and further research should investigate the nuances in the different approaches.

The duration of a BH is important, with variations spanning 15 to 30 seconds. One study shed light on the consistency of the BH over time when comparing different BH techniques [72]. It found that EBH was the optimal technique for a cohort of patients without personalised screening when assessing the tumour position and stability over time. However, upon introducing personalised screening, DIBH or IBH demonstrated superior reproducibility and BH durations [72]. Three of the 4 BH studies reporting inter-fraction uncertainties >5mm used a voluntary technique. Assessing whether using a machine to assist the patient into a BH improves reliability is an important future consideration in abdominal radiotherapy. Additionally, poor implementation of the technique may introduce bias in the results [47]. Only two studies used SGRT in BH [90, 93], and the correlation between external and internal surfaces is still to be determined. It has not been explored when using AC. Intra-fraction motion can be dichotomised into two main components for BH: BH-to-BH variation and intra-BH variation [47]. However, the ESTRO-ACROP guideline was unavailable during the review's conceptualization, so many included BH studies did not use this particular terminology, complicating interpretation. It appeared that 6 studies measured motion during a single and/or multiple BHs [69, 70, 88-91], 5 studies assessed motion between BHs [73, 75, 83, 84, 86], and 3 assessed both [77, 78, 85]. From this review, regardless of the component of intra-fraction BH motion assessed, only one study noted a motion of 6 mm, indicating low intra-fraction BH motion. Future studies should reference the recent guideline [47] to better facilitate comparisons.

Specifically reviewing the AC data, the type of equipment used appeared to yield slightly different results. Three arch studies, 1 shell study, 1 arch with shell study and 1 belt study illustrated motion > 5mm at pre-treatment. The data suggested that the arch/shell technique may not minimise the motion as much as the AC belt. The 3 arch studies reporting motion > 5mm were from the same centre, which may bias the findings. Nonetheless, this centre was able to give information on the impact of the position of the arch in reducing errors, and if positioned correctly, the arch can reduce motion to less than 6mm in all planes [38]. The inferior arch position was identified as the least effective in mitigating motion. However, centres must exercise caution when positioning the AC equipment too superiorly, as this may potentially interfere with the patient's ribs. Only one study addressed the level of compression applied [63]. There is no consensus on whether the maximum pressure tolerable for the patient should be used or if the compression should be adjusted for patient comfort. On-treatment only AC belt studies reported inter-fraction uncertainties greater than 5mm [63, 64]. Centres must plan consistent belt positioning for each fraction and adjust it if the patient's anatomy changes, such as weight loss or gain.

Tumour location is important, and the prevalence of errors in HPB patients is higher than in pancreatic patients (40% versus 31%). Specifically, within studies assessing pre-treatment motion, all 6 studies reporting motion greater than 5mm were in HPB patients. [38, 60-62, 65, 68]. Within the HPB patients, no studies assessed if the specific location of the HPB tumour impacted motion. This warrants further investigation as malignancies closer to the diaphragm dome may exhibit larger motion. Compared to HPB malignancies, pancreatic malignancies are further away from the dome of the diaphragm and may not be as impacted by respiratory motion. Alternatively, in the case of compression, motion may be mitigated in pancreatic patients due to the closer location of the device. AC equipment must be positioned below the ribs, which may impact pancreatic patients more. One study compared pancreatic motion with and without compression, and compression significantly reduced motion [illegible].

Many authors emphasize that motion mitigation should be tailored to the patient, but current research does not yet determine the best approach. The patient perspective is currently underemphasized when determining the optimal approach. In contrast, studies on breast cancer patients delve into various aspects such as thoracic and abdominal breathing techniques, home-based preparation for deep inspiration breath-hold (DIBH), and patient experiences [99]. For patients with abdominal malignancies undergoing motion mitigation, such explorations in comfort, experience, patient information, tolerability, and training remain lacking. The patient impact of undergoing an interventional procedure when using fiducials has not been explored. In AC, the discomfort was highlighted in two studies [63, 65], and one study highlighted that gender and BMI affected the effectiveness of AC [61]; however, this finding is contradicted in a recent study, which showed that abdominal fat and BMI did not impact compression effectiveness [100]. In BH, personalised screening appeared to improve reproducibility [72], and one study highlighted that body weight and height impacted BH [76]. It has not been explored whether the patient is more comfortable taking a deep inspiration BH instead of holding their breath at exhale. Overall, AC and BH appear to be tolerated; however, further investigations, including a thorough exploration of the patient's perspective, are needed.

The systematic review did not include patient experience in its search terms, limiting information on these secondary endpoints to studies meeting the primary criteria. Therefore, it may not capture all available data on patient experiences with motion mitigation. While this systematic review has covered geometric uncertainties, notably motion and inter-fraction errors, it has not addressed all sources of geometric errors, e.g., delineation, interobserver matching error, etc. Additionally, the review focused only on translational errors. The findings are limited by the variability in the approaches taken and the small patient cohorts, which impacts the generalizability of the results and precludes meta-analysis. To assess geometric uncertainties, it is recommended that more than 30 patients be analysed for meaningful statistical results [53]. The results underscored a notable variability in the calculating and reporting uncertainties, with a particularly significant underreporting of random errors. Given that random errors in SBRT treatments often manifest behaviour similar to systematic errors [53], and with the increasing utilisation of SBRT, it is imperative to address these errors in future analyses. The findings also suggested that discrepancies in error measurements arise when employing different imaging modalities or when estimating errors in distinct imaging planes on identical images.

Conclusion

This systematic review of 40 studies from January 2015 to February 2023 assessed AC and BH effectiveness in mitigating respiratory motion and errors in HPB and/or pancreatic radiotherapy patients. Among the 40 studies, there was significant heterogeneity and generally poor quality. The results indicate AC's motion-reducing capabilities and BH's ability to hold the patient in a phase of the breathing cycle. The aim of each technique slightly differs, as do the issues that arise when utilising them. AC appears inconsistent between patients and BH varies from pre-treatment and between fractions. No comparison has been made between the two techniques. The importance of patient perspectives has been understated, and there is a noticeable gap in understanding which motion mitigation technique suits individual patients best. This review serves as a starting point for future research considerations, with studies needing to include more than 30 patients, adhere to standard reporting guidance, and incorporate the patient perspective.. Future efforts should focus on personalizing motion management to deliver precise treatment and tailoring approaches to both technical requirements and patient-specific needs.

References:

1. EUROCARE. https://www.eurocare.it/Publications/tabid/61/Default.aspx#eu5. 2007 [cited 2023.

2. England, P.H. *National statistics Cancer survival in England for patients diagnosed between 2014 and 2018, and followed up to 2019*. 2021; Available from: https://www.gov.uk/government/statistics/cancer-survival-in-england-for-patients-diagnosed-between-2014-and-2018-and-followed-up-until-2019/cancer-survival-in-england-for-patients-diagnosed-between-2014-and-2018-and-followed-up-to-2019.

3. Alrabiah, K., et al., *The evolving role of radiation therapy as treatment for liver metastases.* Journal of the National Cancer Center, 2022. **2**(3): p. 183-187.

4. Chen, C.P., *Role of Radiotherapy in the Treatment of Hepatocellular Carcinoma.* J Clin Transl Hepatol, 2019. **7**(2): p. 183-190.

5. Hall, W.A. and K.A. Goodman, *Radiation therapy for pancreatic adenocarcinoma, a treatment option that must be considered in the management of a devastating malignancy.* Radiat Oncol, 2019. **14**(1): p. 114.

6. Rutenberg, M.S. and R.C. Nichols, *Proton beam radiotherapy for pancreas cancer.* J Gastrointest Oncol, 2020. **11**(1): p. 166-175.

7. Wang, N., et al., *Progress in Radiotherapy for Cholangiocarcinoma.* Front Oncol, 2022. **12**: p. 868034.

8. Shanker, M.D., et al., *Stereotactic ablative radiotherapy for hepatocellular carcinoma: A systematic review and meta-analysis of local control, survival and toxicity outcomes.* J Med Imaging Radiat Oncol, 2021. **65**(7): p. 956-968.

9. Petrelli, F., et al., *Stereotactic body radiotherapy for colorectal cancer liver metastases: A systematic review.* Radiother Oncol, 2018. **129**(3): p. 427-434.

10. Mahadevan, A., et al., *Stereotactic Body Radiotherapy (SBRT) for liver metastasis – clinical outcomes from the international multi-institutional RSSearch® Patient Registry.* Radiation Oncology, 2018. **13**(1): p. 26.

11. Petrelli, F., et al., *Stereotactic Body Radiation Therapy for Locally Advanced Pancreatic Cancer: A Systematic Review and Pooled Analysis of 19 Trials.* Int J Radiat Oncol Biol Phys, 2017. **97**(2): p. 313-322.

12. Vornhulz, M., et al., *Role of stereotactic body radiation in the enhancement of the quality of life in locally advanced pancreatic adenocarcinoma: a systematic review.* Radiat Oncol, 2022. **17**(1): p. 108.

13. Brock, K.K., *Imaging and image-guided radiation therapy in liver cancer.* Semin Radiat Oncol, 2011. **21**(4): p. 247-55.

14. Chaudhary, V. and S. Bano, *Imaging of the pancreas: Recent advances.* Indian J Endocrinol Metab, 2011. **15**(Suppl 1): p. S25-32.

15. Nadarevic, T., et al., *Magnetic resonance imaging for the diagnosis of hepatocellular carcinoma in adults with chronic liver disease.* Cochrane Database Syst Rev, 2022. **5**(5): p. CD014798.

16. Nadarevic, T., et al., *Computed tomography for the diagnosis of hepatocellular carcinoma in adults with chronic liver disease.* Cochrane Database Syst Rev, 2021. **10**(10): p. CD013362.

17. Tummala, P., O. Junaidi, and B. Agarwal, *Imaging of pancreatic cancer: An overview.* J Gastrointest Oncol, 2011. **2**(3): p. 168-74.

18. Shadad, A.K., et al., *Gastrointestinal radiation injury: symptoms, risk factors and mechanisms.* World J Gastroenterol, 2013. **19**(2): p. 185-98.

19. Dhont, J., et al., *Image-guided Radiotherapy to Manage Respiratory Motion: Lung and Liver.* Clinical Oncology, 2020. **32**(12): p. 792-804.

20. Keall, P.J., et al., *The management of respiratory motion in radiation oncology report of AAPM Task Group 76.* Medical Physics, 2006. **33**(10): p. 3874-3900.

21. Yoganathan, S.A., et al., *Magnitude, Impact, and Management of Respiration-induced Target Motion in Radiotherapy Treatment: A Comprehensive Review.* Journal of medical physics, 2017. **42**(3): p. 101-115.

22. Li, H., et al., *AAPM Task Group Report 290: Respiratory motion management for particle therapy.* Med Phys, 2022. **49**(4): p. e50-e81.

23. Bertholet, J., et al., *Real-time intrafraction motion monitoring in external beam radiotherapy.* Phys Med Biol, 2019. **64**(15): p. 15TR01.

24. Case, R.B., et al., *Inter- and intrafraction variability in liver position in non-breath-hold stereotactic body radiotherapy.* International journal of radiation oncology, biology, physics, 2009. **75**(1): p. 302-8.

25. Dhont, J., et al., *The long- and short-term variability of breathing induced tumor motion in lung and liver over the course of a radiotherapy treatment.* Radiotherapy and Oncology, 2018. **126**(2): p. 339-346.

26. Doi, Y., et al., *Quantifying esophageal motion during free-breathing and breath-hold using fiducial markers in patients with early-stage esophageal cancer.* PLoS ONE, 2018. **13**(6): p. e0198844.

27. Hoffmann, L., et al., *Setup strategies and uncertainties in esophageal radiotherapy based on detailed intra- and interfractional tumor motion mapping.* Radiotherapy and Oncology, 2019. **136**: p. 161-168.

28. Brandner, E.D., et al., *Motion management strategies and technical issues associated with stereotactic body radiotherapy of thoracic and upper abdominal tumors: A review from NRG oncology.* Med Phys, 2017. **44**(6): p. 2595-2612.

29. Burton, A., et al., *Adoption of respiratory motion management in radiation therapy.* Phys Imaging Radiat Oncol, 2022. **24**: p. 21-29.

30. Yoganathan, S.A., et al., *Magnitude, Impact, and Management of Respiration-induced Target Motion in Radiotherapy Treatment: A Comprehensive Review.* J Med Phys, 2017. **42**(3): p. 101-115.

31. Mostafaei, F., et al., *Variations of MRI-assessed peristaltic motions during radiation therapy.* PLoS One, 2018. **13**(10): p. e0205917.

32. Rodríguez-Romero, R. and P. Castro-Tejero, *The influence of respiratory motion on CT image volume definition.* Med Phys, 2014. **41**(4): p. 041701.

33. Gargett, M., et al., *Clinical impact of removing respiratory motion during liver SABR.* Radiation Oncology, 2019. **14**(1): p. N.PAG-N.PAG.

34. Velec, M., et al., *Effect of breathing motion on radiotherapy dose accumulation in the abdomen using deformable registration.* International Journal of Radiation Oncology Biology Physics, 2011. **80**(1): p. 265-272.

35. Eccles, C.L., et al., *Comparison of liver tumor motion with and without abdominal compression using cine-magnetic resonance imaging.* International Journal of Radiation Oncology, Biology, Physics, 2011. **79**(2): p. 602-608.

36. Heinzerling, J.H., et al., *Four-Dimensional Computed Tomography Scan Analysis of Tumor and Organ Motion at Varying Levels of Abdominal Compression During Stereotactic Treatment of Lung and Liver.* International Journal of Radiation Oncology Biology Physics, 2008. **70**(5): p. 1571-1578.

37. Wunderink, W., et al., *Reduction of Respiratory Liver Tumor Motion by Abdominal Compression in Stereotactic Body Frame, Analyzed by Tracking Fiducial Markers Implanted in Liver.* International Journal of Radiation Oncology Biology Physics, 2008. **71**(3): p. 907-915.

38. Hu, Y., et al., *4D-CT scans reveal reduced magnitude of respiratory liver motion achieved by different abdominal compression plate positions in patients with intrahepatic tumors undergoing helical tomotherapy.* Med Phys, 2016. **43**(7): p. 4335.

39. Lovelock, D.M., et al., *The effectiveness of a pneumatic compression belt in reducing respiratory motion of abdominal tumors in patients undergoing stereotactic body radiotherapy.* Technol Cancer Res Treat, 2014. **13**(3): p. 259-67.

40. Schneider, S., et al., *Reduction of intrafraction pancreas motion using an abdominal corset compatible with proton therapy and MRI.* Clinical and Translational Radiation Oncology, 2023. **38**: p. 111-116.

41. Ami, K., et al., *Proton radiotherapy as a treatment strategy to increase survival in locally advanced pancreatic cancer in the body and tail: a retrospective study.* Radiat Oncol, 2023. **18**(1): p. 131.

42. Ostyn, M., E. Weiss, and M. Rosu-Bubulac, *Respiratory cycle characterization and optimization of amplitude-based gating parameters for prone and supine lung cancer patients.* Biomedical Physics & Engineering Express, 2020. **6**(3): p. 035002.

43. Kim, Y.S., et al., *Differences in abdominal organ movement between supine and prone positions measured using four-dimensional computed tomography.* Radiotherapy and Oncology, 2007. **85**(3): p. 424-428.

44. Hashimoto, S., et al., *Effect of a Device-Free Compressed Shell Fixation Method on Hepatic Respiratory Movement: Analysis for Respiratory Amplitude of the Liver and Internal Motions of a Fiducial Marker.* Practical Radiation Oncology, 2019. **9**(2): p. E149-E155.

45. Eccles, C.L., et al., *Interfraction liver shape variability and impact on GTV position during liver stereotactic radiotherapy using abdominal compression.* International Journal of Radiation Oncology Biology Physics, 2011. **80**(3): p. 938-946.

46. Daly, M., et al., *Radiotherapy respiratory motion management in hepatobiliary and pancreatic malignancies: a systematic review of patient factors influencing effectiveness of motion reduction with abdominal compression.* Acta Oncologica, 2022. **61**(7): p. 833-841.

47. Aznar, M.C., et al., *ESTRO-ACROP guideline: Recommendations on implementation of breath-hold techniques in radiotherapy.* Radiother Oncol, 2023. **185**: p. 109734.

48. Vakaet, V., et al., *Prolonging deep inspiration breath-hold time to 3 min during radiotherapy, a simple solution.* Clin Transl Radiat Oncol, 2021. **28**: p. 10-16.

49. Hoffmann, L., et al., *Repeated deep-inspiration breath-hold CT scans at planning underestimate the actual motion between breath-holds at treatment for lung cancer and lymphoma patients.* Radiotherapy and Oncology, 2023. **188**.

50. Anastasi, G., et al., *Patterns of practice for adaptive and real-time radiation therapy (POP-ART RT) part I: Intra-fraction breathing motion management.* Radiotherapy and oncology : journal of the European Society for Therapeutic Radiology and Oncology, 2020. **153**: p. 79-87.

51. Zhang, Y., et al., *A survey of practice patterns for real-time intrafractional motion-management in particle therapy.* Phys Imaging Radiat Oncol, 2023. **26**: p. 100439.

52. Ball, H.J., et al., *Results from the AAPM Task Group 324 respiratory motion management in radiation oncology survey.* J Appl Clin Med Phys, 2022. **23**(11): p. e13810.

53. Tudor, G.S.J., et al., *Geometric Uncertainties in Daily Online IGRT: Refining the CTV-PTV Margin for Contemporary Photon Radiotherapy*. British Institute of Radiology, 201[illegible].

54. Radiologists, T.R.C.o., *On target 2: updated guidance for image-guided radiotherapy*. 2021.

55. Jayaprakasam, V.S., et al., *Role of Imaging in Esophageal Cancer Management in 2020: Update for Radiologists.* AJR Am J Roentgenol, 2020. **215**(5): p. 1072-1084.

56. Higgins JPT, T.J., Chandler J, Cumpston M, Li T, Page MJ, Welch VA (editors), *Cochrane Handbook for Systematic Reviews of Interventions version 6.4 (updated August 2023)*, ed. Cochrane. 2023.

57. Campbell, M., et al., *Synthesis without meta-analysis (SWiM) in systematic reviews: reporting guideline.* BMJ, 2020. **368**: p. l6890.

58. Chu, K.Y., et al., *Impact of abdominal compression on setup error and image matching during radical abdominal radiotherapy.* Technical Innovations and Patient Support in Radiation Oncology, 2019. **12**: p. 28-33.

59. Dreher, C., et al., *Evaluation of the tumor movement and the reproducibility of two different immobilization setups for image-guided stereotactic body radiotherapy of liver tumors.* Radiation Oncology, 2018. **13**(1): p. 15-15.

60. Hu, Y., et al., *Clinical benefits of new immobilization system for hypofractionated radiotherapy of intrahepatic hepatocellular carcinoma by helical tomotherapy.* Medical Dosimetry, 2017. **42**(1): p. 37-41.

61. Hu, Y., et al., *Magnitude and influencing factors of respiration-induced liver motion during abdominal compression in patients with intrahepatic tumors.* Radiation Oncology, 2017. **12**(1): p. 9-9.

62. Shimohigashi, Y., et al., *Tumor motion changes in stereotactic body radiotherapy for liver tumors: an evaluation based on four-dimensional cone-beam computed tomography and fiducial markers.* Radiation Oncology, 2017. **12**(1): p. 61-61.

63. Campbell, W.G., et al., *An evaluation of motion mitigation techniques for pancreatic SBRT.* Radiotherapy and Oncology, 2017. **124**(1): p. 168-173.

64. Tyagi, N., et al., *Feasibility of ablative stereotactic body radiation therapy of pancreas cancer patients on a 1.5 Tesla magnetic resonance-linac system using abdominal compression.* Physics & Imaging in Radiation Oncology, 2021. **19**: p. 53-59.

65. Van Gelder, R., et al., *Experience with an abdominal compression band for radiotherapy of upper abdominal tumours.* Journal of Medical Radiation Sciences, 2018. **65**(1): p. 48-54.

66. Yorke, E., et al., *Kilovoltage Imaging of Implanted Fiducials to Monitor Intrafraction Motion With Abdominal Compression During Stereotactic Body Radiation Therapy for Gastrointestinal Tumors.* International Journal of Radiation Oncology, Biology, Physics, 2016. **95**(3): p. 1042-1049.

67. Grimbergen, G., et al., *Intrafraction pancreatic tumor motion patterns during ungated magnetic resonance guided radiotherapy with an abdominal corset.* Physics and Imaging in Radiation Oncology, 2022. **21**: p. 1-5.

68. Sevillano, D., et al., *Definition of internal target volumes based on planar X-ray fluoroscopic images for lung and hepatic stereotactic body radiation therapy. Comparison to inhale/exhale CT technique.* Journal of applied clinical medical physics, 2020. **21**(8): p. 56-64.

69. Boda-Heggemann, J., et al., *Ultrasound-based repositioning and real-time monitoring for abdominal SBRT in DIBH.* Physica Medica, 2019. **65**: p. 46-52.

70. Brown, E., et al., *Intrafraction cone beam computed tomography verification of breath hold during liver stereotactic radiation therapy.* Journal of Medical Radiation Sciences, 2021. **68**(1): p. 52-59.

71. Choi, G.W., et al., *Assessment of setup uncertainty in hypofractionated liver radiation therapy with a breath-hold technique using automatic image registration-based image guidance.* Radiation Oncology, 2019. **14**(1): p. 9-9.

72. Farrugia, B., et al., *A Prospective Trial Demonstrating the Benefit of Personalized Selection Of Breath-Hold Technique for Upper-Abdominal Radiation Therapy Using the Active Breathing Coordinator.* International Journal of Radiation Oncology Biology Physics, 2021. **111**(5): p. 1289-1297.

73. Fu, H.-J., et al., *Liver-directed stereotactic body radiotherapy can be reliably delivered to selected patients without internal fiducial markers-A case series.* Journal of the Chinese Medical Association : JCMA, 2022. **85**(10): p. 1028-1032.

74. Han-Oh, S., et al., *Geometric Reproducibility of Fiducial Markers and Efficacy of a Patient-Specific Margin Design Using Deep Inspiration Breath Hold for Stereotactic Body Radiation Therapy for Pancreatic Cancer.* Advances in Radiation Oncology, 2021. **6**(2).

75. Hill, C.S., et al., *Fiducial-based image-guided SBRT for pancreatic adenocarcinoma: Does inter-and intra-fraction treatment variation warrant adaptive therapy?* Radiation Oncology, 2021. **16**(1).

76. Huang, T.J., et al., *Impact of breath-hold level on positional error aligned by stent/Lipiodol in Hepatobiliary radiotherapy with breath-hold respiratory control.* Bmc Cancer, 2020. **20**(1): p. 9-9.

77. Kawahara, D., et al., *Interfractional diaphragm changes during breath-holding in stereotactic body radiotherapy for liver cancer.* Reports of Practical Oncology and Radiotherapy, 2018. **23**(2): p. 84-90.

78. Lens, E., et al., *Considerable pancreatic tumor motion during breath-holding.* Acta Oncologica, 2016. **55**(11): p. 1360-1368.

79. Lu, L., et al., *Intra- and inter-fractional liver and lung tumor motions treated with SBRT under active breathing control.* Journal of Applied Clinical Medical Physics, 2018. **19**(1): p. 39-45.

80. Lu, L., et al., *Dosimetric assessment of patient-specific breath-hold reproducibility on liver motion for SBRT planning.* Journal of Applied Clinical Medical Physics, 2020. **21**(7): p. 77-83.

81. Mast, M., et al., *Two years' experience with inspiration breath-hold in liver SBRT.* Technical Innovations and Patient Support in Radiation Oncology, 2018. **7**: p. 1-5.

82. Nakamura, M., et al., *Interfraction positional variation in pancreatic tumors using daily breath-hold cone-beam computed tomography with visual feedback.* Journal of applied clinical medical physics / American College of Medical Physics, 2015. **16**(2): p. 5123.

83. Oliver, P.A.K., et al., *Influence of intra- and interfraction motion on planning target volume margin in liver stereotactic body radiation therapy using breath hold.* Advances in radiation oncology, 2021. **6**(1): p. 100610-100610.

84. Qiu, J.J., et al., *The Feasibility and Efficiency of Volumetric Modulated Arc Therapy-Based Breath Control Stereotactic Body Radiotherapy for Liver Tumors.* Technology in Cancer Research and Treatment, 2016. **15**(5): p. 674-682.

85. Sasaki, M., et al., *Positional repeatability and variation in internal and external markers during volumetric-modulated arc therapy under end-exhalation breath-hold conditions for pancreatic cancer patients.* Journal of Radiation Research, 2020. **61**(5): p. 755-765.

86. Stick, L.B., et al., *Intrafractional fiducial marker position variations in stereotactic liver radiotherapy during voluntary deep inspiration breath-hold.* British Journal of Radiology, 2020. **93**(1116): p. 20200859-20200859.

87. Teboh, R.F., et al., *Setup Management for Stereotactic Body Radiation Therapy of Patients With Pancreatic Cancer Treated via the Breath-Hold Technique.* Practical Radiation Oncology, 2020. **10**(4): p. e280-e289.

88. Vogel, L., et al., *Intra-breath-hold residual motion of image-guided DIBH liver-SBRT: An estimation by ultrasound-based monitoring correlated with diaphragm position in CBCT.* Radiotherapy and Oncology, 2018. **129**(3): p. 441-448.

89. Zeng, C., et al., *Accuracy and efficiency of respiratory gating comparable to deep inspiration breath hold for pancreatic cancer treatment.* Journal of Applied Clinical Medical Physics, 2021. **22**(1): p. 218-225.

90. Zeng, C., et al., *Intrafractional accuracy and efficiency of a surface imaging system for deep inspiration breath hold during ablative gastrointestinal cancer treatment.* Journal of Applied Clinical Medical Physics, 2022. **23**(11): p. e13740.

91. Zeng, C., et al., *Intrafraction tumor motion during deep inspiration breath hold pancreatic cancer treatment.* Journal of Applied Clinical Medical Physics, 2019. **20**(5): p. 37-43.

92. Miura, H., et al., *Impact on liver position under breath-hold by computed tomography contrast agents in stereotactic body radiotherapy of liver cancer.* Reports of Practical Oncology and Radiotherapy, 2021. **26**(6): p. 1035-1044.

93. Naumann, P., et al., *Feasibility of Optical Surface-Guidance for Position Verification and Monitoring of Stereotactic Body Radiotherapy in Deep-Inspiration Breath-Hold.* Frontiers in Oncology, 2020. **10**: p. 573279.

94. Placidi, L., et al., *On-line adaptive MR guided radiotherapy for locally advanced pancreatic cancer: Clinical and dosimetric considerations.* Technical Innovations and Patient Support in Radiation Oncology, 2020. **15**: p. 15-21.

95. Lu, Y., et al., *Comparison of Deep Inspiration Breath Hold Versus Free Breathing in Radiotherapy for Left Sided Breast Cancer.* Front Oncol, 2022. **12**: p. 845037.

96. Shakhih, M.F.M., A.A. Wahab, and M.I.M. Salim, *Assessment of inspiration and expiration time using infrared thermal imaging modality.* Infrared Physics & Technology, 2019. **99**: p. 129-139.

97. Hult, P., B. Wranne, and P. Ask, *A bioacoustic method for timing of the different phases of the breathing cycle and monitoring of breathing frequency.* Medical Engineering & Physics, 2000. **22**(6): p. 425-433.

98. Sharma, M., et al., *A systematic review and meta-analysis of liver tumor position variability during SBRT using various motion management and IGRT strategies.* Radiotherapy and oncology : journal of the European Society for Therapeutic Radiology and Oncology, 2022. **166**: p. 195-202.

99. Professor Heidi Probst, J.U., Keeley Rosbottom ,Dr Maria Burton, Mel Lindley ,Helen Clough, Jane Barry, Russ Mather, Jon Willis. *RESPIRE*. [cited 2023 19/07/23]; Available from: https://respire.org.uk/.

100. Daly, M., et al., *Feasibility of abdominal fat quantification on MRI and impact on effectiveness of abdominal compression for radiotherapy motion management.* Technical Innovations & Patient Support in Radiation Oncology, 2024. **29**.

1. **Searches in OVID:**

***

Database: Ovid MEDLINE(R) ALL <1946 to February 13, 2023>

Search Strategy:

----

1 ((abdominal or compression*) adj3 (corset* or belt* or arch* or plate*)).mp. [mp=title, book title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] (3347)

2 abdominal compression*.mp. [mp=title, book title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] (693)

3 (breath* adj2 (control or coordinat* or monitor* or management or hold*)).mp. [mp=title, book title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] (11976)

4 respiratory motion*.mp. [mp=title, book title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] (3103)

5 motion mitigation.mp. [mp=title, book title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] (120)

6 motion management.mp. [mp=title, book title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] (636)

7 position management.mp. [mp=title, book title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] (161)

8 SDX.mp. [mp=title, book title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] (161)

9 spirom*.mp. [mp=title, book title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary

concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] (38241)

10 Breath Holding/ (1426)

11 spirometry/ or bronchospirometry/ (23366)

12 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 10 (19271)

13 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 (57855)

14 radiotherap*.mp. [mp=title, book title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] (369593)

15 proton beam therap*.mp. [mp=title, book title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] (1537)

16 proton therap*.mp. [mp=title, book title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] (6798)

17 magnetic resonance.mp. [mp=title, book title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] (854852)

18 intensity modulated radiation therapy.mp. [mp=title, book title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] (6388)

19 stereotactic body radiation therapy.mp. [mp=title, book title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] (3787)

20 volumetric modulated arc therapy.mp. [mp=title, book title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] (3008)

21 Stereotactic body radiation therapy.mp. [mp=title, book title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word,

organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] (3787)

22 Volumetric modulated arc therapy.mp. [mp=title, book title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] (3008)

23 Rapid Arc.mp. [mp=title, book title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] (52)

24 radiotherapy/ or exp chemoradiotherapy/ or exp heavy ion radiotherapy/ or radiosurgery/ or radiotherapy setup errors/ or radiotherapy, adjuvant/ or exp radiotherapy, high-energy/ or radiotherapy, image-guided/ or re-irradiation/ or x-ray therapy/ (130182)

25 Magnetic Resonance Imaging/ (466688)

26 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 (1223494)

27 12 and 26 (7013)

28 Abdom*.mp. [mp=title, book title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] (465293)

29 ?esophag*.mp. [mp=title, book title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] (210396)

30 stomach.mp. [mp=title, book title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] (261744)

31 liver.mp. [mp=title, book title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary

concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] (1227414)

32 pancrea*.mp. [mp=title, book title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] (373082)

33 adrenal gland*.mp. [mp=title, book title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] (82318)

34 kidney*.mp. [mp=title, book title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] (957377)

35 abdominal node*.mp. [mp=title, book title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] (145)

36 hepatobiliary.mp. [mp=title, book title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] (15562)

37 28 or 29 or 30 or 31 or 32 or 33 or 34 or 35 or 36 (3161499)

38 27 and 37 (2544)

39 14 or 15 or 16 or 18 or 19 or 20 or 21 or 22 or 23 or 24 (392009)

40 12 and 37 and 39 (871)

41 limit 40 to english language (849)

****

2 SWiM checklist

3. Risk of bias quality assessment

4 All studies addressing pre-treatment motion, inter-fraction uncertainties and intrafraction uncertainties

Ta[illegible]

Population	Hepatobiliary patients, pancreatic patients, radiotherapy (including photons and protons), stereotactic radiotherapy (SABR/SBRT)
Intervention	Motion mitigation approaches, including abdominal compression and breath-hold
Comparators	No motion mitigation, free breathing
Outcomes	Measurements of motion at pre-treatment, online inter-fraction set-up errors, and intra-fraction motion on the liver, pancreas, or an appropriate surrogate Reports of patient experience, comfort, and tolerability
Study Design	Randomised controlled trials, non-randomised experimental studies, cohort studies and retrospective reviews

Author & year	Total No. of patients	Treatment site	Motion mitigation	Assisted or unassisted BH	IGRT match structure	Pre or on-treatment measure	Imaging equipment
Boda-Heggemann et al. *2019 [69]*	16	Abdominal patients (majority liver and pancreas)	Breath-hold *DIBH*	Assisted	Fiducials or liver contour	On-treatment	CBCT and ultrasound
Brown et al. *2021 [70]*	30	Liver	Breath-hold *DIBH* *endEBH*	Assisted	Diaphragm position	On-treatment	CBCT
Campbell et al. *2017 [63]*	19	Pancreas	Compression *Belt* *Free breathing*		Fiducials in pancreas	On-treatment	CBCT
Choi et. al *2019 [71]*	69	Liver	Breath-hold *DIBH*	Unassisted	Liver contour	On-treatment	CT on rails
Chu et al. *2019 [58]*	72	Abdominal patients (majority liver and pancreas)	Compression *Arch* *Free breathing*		Abdominal tumour	On-treatment	CBCT
Dreher et al. *2018 [59]*	54	Liver	Compression *Arch* *Low pressure foil*		Bony anatomy and liver contour	Both	CT and CBCT

Fa *2021 [72]*		l patients (majority liver and pancreas)	*DIBH* *EBH* *IBH*		l tumour if visualised, or fiducial or diaphragm	treatment	fluoroscopy
Fu et al. *2022 [73]*	13	Liver	Breath-hold *EBH*	Unassisted	Bony anatomy and diaphragm	On-treatment	CBCT
Grimbergen et al. *2022 [67]*	13	Pancreas	Compression *Corset*		Pancreas GTV	On-treatment	MRI: coronal and sagittal cine MRI
Han-Oh et al. *2021 [74]*	20	Pancreas	Breath-hold *DIBH*	Assisted	Fiducials in pancreas	Both	CT and CBCT
Hashimoto et al. *2019 [44]*	324	Liver	Compression *Shell*		Fiducials in liver	Both	4DCT and fluoroscopy
Hill et al. *2021 [75]*	30	Pancreas	Breath-hold *DIBH*	Assisted	Fiducials in pancreas	On-treatment	CBCT
Hu et al. *2016 [38]*	72	Liver	Compression *Arch* *Free breathing*		Liver contour	Pre-treatment	4DCT
Hu et al. *2017 [61]*	99	Liver	Compression		Liver contour	Pre-treatment	4DCT

			Arch *Free breathing*				
Hu et al. *2017 [60]*	42	Liver	Compression *Arch* *Free breathing*		Liver contour	Both	4DCT and MVCT
Huang et al. *2020 [76]*	42	Abdominal patients (majority liver and pancreas)	Breath-hold *DIBH*	Assisted	Fiducials in abdomen or liver contour	On-treatment	CBCT and kV/kV
Kawahara et al. *2018 [77]*	59	Liver	Breath-hold *EBH*	Unassisted	Bony anatomy and diaphragm	On-treatment	CBCT and kV/kV
Lens et al. *2016 [78]*	12	Pancreas	Breath-hold *DIBH*	Assisted	Fiducials in pancreas	On-treatment	CBCT and fluoroscopy
Lu et al. *2018 [79]*	19	Liver	Breath-hold *DIBH*	Assisted	Bony anatomy and liver tumour	Both	CT and CBCT
Lu et al. *2020 [80]*	44	Liver	Breath-hold *DIBH*	Assisted	Liver contour	Pre-treatment	CT
Mast et al. *2018 [81]*	20	Liver	Breath-hold *DIBH*	Assisted	Bony anatomy and liver contour	Both	CT and CBCT

Mi *2021 [92]*			*EBH*	d	contour		CBCT
Nakamura et al. *2015 [82]*	11	Pancreas	Breath-hold *endEBH*	Unassisted	Bony anatomy and pancreas	On-treatment	CBCT and kV/kV
Naumann et al. *2020 [93]*	7	Liver	Breath-hold *DIBH*	Unassisted	Liver contour	On-treatment	CBCT
Oliver et al. *2021 [83]*	18	Liver	Breath-hold *deepEBH* *DIBH*	Unassisted	Diaphragm	On-treatment	CBCT
Placidi et al. *2020 [94]*	8	Pancreas	Breath-hold *DIBH*	Unassisted	Pancreas GTV	On-treatment	MRI: 3DMRI
Qiu et al. *2016 [84]*	9	Liver	Breath-hold *deepEBH*	Unassisted	Liver contour	On-treatment	CBCT
Sasaki et al. *2020 [85]*	10	Pancreas	Breath-hold *endEBH*	Unassisted	Fiducials in pancreas	On-treatment	CBCT and kV/kV
Schneider et al. *2023 [40]*	12	Pancreas	Compression *Corset* *Free breathing*		Pancreas GTV	Pre-treatment	MRI: coronal and sagittal cine MRI and 4DMRI

Se *2020 [68]*			n *Shell*		in liver		fluoroscopy
Shimohigashi et al. *2017 [62]*	10	Liver	Compression *Arch with shell*		Fiducials in liver	Both	CT and 4DCBCT
Stick et al. *2020 [86]*	10	Liver	Breath-hold *DIBH*	Unassisted	Fiducials in liver	Both	CT and CBCT
Teboh et al. *2020 [87]*	19	Pancreas	Breath-hold *DIBH*	Assisted	Fiducials in pancreas	On-treatment	CBCT and kV/kV
Tyagi et al. *2021 [64]*	10	Pancreas	Compression *Belt* *Free breathing*		Pancreas GTV	Both	MRI: cine MRI and 3DMRI
VanGelder et al. *2018 [65]*	15	Liver	Compression *Belt* *Free breathing*		Liver contour	Pre-treatment	4DCT
Vogel et al. *2018 [88]*	13	Abdominal patients (majority liver and pancreas)	Breath-hold *DIBH*	Assisted	Diaphragm position	On-treatment	Ultrasound
Yorke et al. *2016 [66]*	19	Abdominal patients (majority	Compression *Belt*		Fiducials in abdomen	Both	Fluoroscopy

		liver and pancreas)	*Free breathing*				
Zeng et al. *2019 [91]*	8	Pancreas	Breath-hold *DIBH*	Unassisted	Fiducials in pancreas	On-treatment	CBCT and kV/kV
Zeng et al. *2021 [89]*	20	Pancreas	Breath-hold *DIBH*	Unassisted	Fiducials in pancreas	On-treatment	CBCT and kV/kV
Zeng et al. *2022 [90]*	14	Abdominal patients (majority liver and pancreas)	Breath-hold *DIBH*	Unassisted	Fiducials in abdomen	On-treatment	kV/kV

4DCT = 4-dimensional computed tomography

Assisted = utilizing spirometry-based equipment, e.g., ABC or SDX

CBCT = cone beam computed tomography

DIBH = deep inspiration breath-hold

EBH = expiration breath-hold

kV = kilovoltage image. kV/kV = 2D orthogonal imaging pair

Unassisted = breath-hold reliant on the patient

Table 3: Studies with pre-treatment motion >5mm

Author, year, *study details*	**MM**	**Reported measurement of motion at pre-treatment on IGRT structure(s)**		
		Anterior-posterior direction	*Right-left direction*	*Superior-inferior direction*

Hu *72 patients* *Compression arch* *Measurements of liver contour on 4DCT*		compression M=10.94mm SD=2.28mm (n=19) Compression 1* **M=5.81mm** SD=0.84mm (n=16) Compression 2* **M=8.50mm** SD=1.22mm (n=11) Compression 3* **M=10.99mm** SD=2.42mm	compression M=3.35mm SD=1.55mm (n=19) Compression 1* M=2.53mm SD=0.93mm (n=16) Compression 2* M=2.18mm SD=0.72mm (n=11) Compression 3* M=3.23mm SD=1.47mm	compression M=9.53mm SD=2.62mm (n=19) Compression 1* M=4.53mm SD=1.16mm (n=16) Compression 2* **M=7.56mm** SD=1.30mm (n=11) Compression 3* **M=9.95mm** SD=2.32mm
Hu et al. 2017 [61] *99 patients* *Compression arch* *Measurements of liver contour on 4DCT*	AC	(n=53) No compression M=2.9mm SD=1.4mm (n=46) Compression M=2.3mm SD=1.1mm	(n=53) No compression M=3.1mm SD=1.3mm (n=46) Compression M=2.9mm SD=1.2mm	(n=53) No compression M=9.9mm SD=2.6 (n=46) Compression **M=5.3mm** SD=2.2mm
Hu et al. 2017 [60] *42 patients* *Compression arch* *Measurements of liver contour on 4DCT and MVCT*	AC	(n=15) No compression M=3.38mm SD=1.59mm (n=27) Compression M=2.13mm SD=1.05mm	(n=15) No compression M=3.48mm SD=1.14mm (n=27) Compression M=2.33mm SD=1.22mm	(n=15) No compression M=9.83mm SD=3.00mm (n=27) Compression **M=5.11mm** SD=2.05mm
Sevillano et al. 2020 [68] ***13 patients*** ***Compression shell*** *Measurements of fiducials in liver on CT and fluoroscopy*	AC	Motion from inhale/exhale CT **M=5.3mm** SD=4.1mm Fluoroscopy M=4.1mm SD=2.1mm	Motion from inhale/exhale CT M=3.7mm SD=2.5mm Fluoroscopy M=1.9mm SD=1.1mm	Motion from inhale/exhale CT **M=15.1mm** **SD=6.9mm** Fluoroscopy **M=9.5mm** SD=3.6mm
Shimohigashi et al. 2017 [62] *10 patients* *Compression arch with shell* *Measurements of fiducials in liver on CT*	AC	CT M=2.4mm SD=2.2mm CBCT M=2.3mm SD=2.3mm	CT M=1.7mm SD=0.8mm CBCT M=1.2mm SD=0.7mm	CT **M=5.3mm** SD=3.3mm CBCT M=4.5mm SD=3.8mm

Va ***15 patients*** ***Compression belt*** *Measurements of liver contour on 4DCT*		compression M=4.7mm SD=3.8mm (n=15) Compression **<u>M=5.4mm</u>** SD=4.2mm	compression M=0.7mm SD=1.1mm (n=15) Compression M=0.7mm SD=1.0mm	compression M=8.7mm SD=3.0mm (n=15) Compression **<u>M=8.0mm</u>** SD=3.8mm

AC=Abdominal compression,

BH=Breath-hold

M= Mean

MM=Motion mitigation

n=Number of patients

SD = standard deviation

**Compression 1=Positioned on the cephalic area between the subxiphoid and umbilicus*

Compression 2=Positioned on the caudal area between the subxiphoid and the umbilicus

Compression 3=Positioned on the caudal umbilicus

Measurements in bold and underlined are where motion > 5mm when motion mitigation applied

Author, year, *study details*	**MM**	**Reported inter-fraction uncertainties at treatment**		
		Anterior-posterior direction	*Right-left direction*	*Superior-inferior direction*
Boda-Heggemann et al. 2019 [69] *16 patients* *Assisted DIBH* *Measurements of fiducials or liver contour on CBCT and ultrasound*	BH	M=-0.2mm **SD=7.2mm**	M=1.3mm **SD=5.7mm**	M=1.3mm **SD=7.5mm**
Campbell et al. 2017 [63] *19 patients* *Compression belt* *Measurements of fiducials in pancreas on CBCT*	AC	(n=19) No compression M=7.3mm R=3.5-18.2mm (n=19) Compression **M=5.3mm** R=1.9-**13.1mm**	(n=19) No compression M=5.3m R=1.8-12.4mm (n=19) Compression **M=5.3mm** R=1.3-**13.7mm**	(n=19) No compression M=13.9mm R=4.7-35.5mm (n=19) Compression **M=8.5mm** R=1.6-**17.1mm**
Miura et al. 2021 [92] *17 patients* *Unassisted EBH* *Measurements of liver contour on CBCT*	BH	Non CECT M=0.8mm SD=1.0mm CECT M=1.4mm SD=1.7mm	Non CECT M=0.6mm SD=1.0mm CECT M=1.2mm SD=1.3mm	Non CECT M=2.5mm SD=2.6mm CECT **M=6.4mm SD=6.4mm**
Naumann et al. 2020 [93] *7 patients* *Unassisted DIBH* *Measurements of liver contour on CBCT*	BH	M=-0.5mm **SD=6.1mm** R=**-13.0-12.0mm**	M=0.5mm SD=3.6mm R=**-7.0-9.0mm**	M=-1.5mm SD=**7.6mm** R=**-25.0-12.0mm**
Placidi 2020 [94] *8 patients* *Unassisted DIBH*	BH	M=0.0mm SD=3.5mm	M=1.5mm **SD=6.9mm**	M=2.3mm **SD=7.6mm**

Measurements of pancreas GTV on MRI				
Tyagi 2021 [64] *10 patients* *Compression belt* *Measurements of pancreas GTV on MRI*	AC	M=0.0mm SD=3.0mm	M=-1.0mm **SD=9.0mm**	M=-1.0mm **SD=11.0mm**

AC=Abdominal compression

BH=Breath-hold

CECT=Contrast enhanced computed tomography

M=Mean

MM=Motion mitigation

R =Range

SD = Standard deviation

Measurements in bold and underlined are where motion > 5mm when motion mitigation applied

Author, year, *study details*	**MM**	**Reported inter-fraction uncertainties at treatment**		
		Anterior-posterior direction	*Right-left direction*	*Superior-inferior direction*
Boda-Heggemann et al. 2019 [69] *16 patients* *Assisted DIBH* *Measurements of fiducials or liver contour on CBCT and ultrasound*	BH	M=-0.2mm **SD=7.2mm**	M=1.3mm **SD=5.7mm**	M=1.3mm **SD=7.5mm**
Campbell et al. 2017 [63] *19 patients* *Compression belt* *Measurements of fiducials in pancreas on CBCT*	AC	(n=19) No compression M=7.3mm R=3.5-18.2mm (n=19) Compression **M=5.3mm** R=1.9-**13.1mm**	(n=19) No compression M=5.3m R=1.8-12.4mm (n=19) Compression **M=5.3mm** R=1.3-**13.7mm**	(n=19) No compression M=13.9mm R=4.7-35.5mm (n=19) Compression **M=8.5mm** R=1.6-**17.1mm**
Miura et al. 2021 [92] *17 patients* *Unassisted EBH* *Measurements of liver contour on CBCT*	BH	Non CECT M=0.8mm SD=1.0mm CECT M=1.4mm SD=1.7mm	Non CECT M=0.6mm SD=1.0mm CECT M=1.2mm SD=1.3mm	Non CECT M=2.5mm SD=2.6mm CECT **M=6.4mm SD=6.4mm**
Naumann et al. 2020 [93] *7 patients* *Unassisted DIBH* *Measurements of liver contour on CBCT*	BH	M=-0.5mm **SD=6.1mm** R=**-13.0-12.0mm**	M=0.5mm SD=3.6mm R=**-7.0-9.0mm**	M=-1.5mm SD=**7.6mm** R=**-25.0-12.0mm**
Placidi 2020 [94] *8 patients* *Unassisted DIBH*	BH	M=0.0mm SD=3.5mm	M=1.5mm **SD=6.9mm**	M=2.3mm **SD=7.6mm**

Measurements of pancreas GTV on MRI				
Tyagi 2021 [64] *10 patients* *Compression belt* *Measurements of pancreas GTV on MRI*	AC	M=0.0mm SD=3.0mm	M=-1.0mm **SD=9.0mm**	M=-1.0mm **SD=11.0mm**

AC=Abdominal compression

BH=Breath-hold

CECT=Contrast enhanced computed tomography

M=Mean

MM=Motion mitigation

R =Range

SD = Standard deviation

Measurements in bold and underlined are where motion > 5mm when motion mitigation applied

Lead author	MM	Reported intra-fraction uncertainties at treatment		
		Anterior-posterior direction	*Right-left direction*	*Superior-inferior direction*
Zeng 2021 [89] *20 patients* *Unassisted DIBH Measurements of fiducials in pancreas on CBCT and kV/kV*	BH			**<u>M=6mm</u>** R=3-**<u>8mm</u>**

BH=Breath-hold

M= mean

MM=Motion mitigation

R = range

Measurements in bold and underlined are where motion > 5mm when motion mitigation applied

Table 6: SWiM is intended to complement and be used as an extension to PRISMA

SWiM reporting item	Item description	Page in manuscript where item is reported	Other*
Methods			
1 Grouping studies for synthesis	1a) Provide a description of, and rationale for, the groups used in the synthesis (e.g., groupings of populations, interventions, outcomes, study design)	Protocol page 4 Defined endpoints page 5 Data extraction page 6	
	1b) Detail and provide rationale for any changes made subsequent to the protocol in the groups used in the synthesis	NA	
2 Describe the standardised metric and transformation methods used	Describe the standardised metric for each outcome. Explain why the metric(s) was chosen, and describe any methods used to transform the intervention effects, as reported in the study, to the standardised metric, citing any methodological guidance consulted	Defined endpoints page 5	
3 Describe the synthesis methods	Describe and justify the methods used to synthesise the effects for each outcome when it was not possible to undertake a meta-analysis of effect estimates	Data synthesis page 6	
4 Criteria used to prioritise results for summary and synthesis	Where applicable, provide the criteria used, with supporting justification, to select the particular studies, or a particular study, for the main synthesis or to draw conclusions from the synthesis (e.g., based on study design, risk of bias assessments, directness in relation to the review question)	Protocol page 4 Defined endpoints page 5 Data extraction page 6 Quality assessment page 6 and supplementary material Data synthesis page 6	
SWiM reporting item	**Item description**	**Page in manuscript where item is reported**	**Other***
5 Investigation of heterogeneity in reported effects	State the method(s) used to examine heterogeneity in reported effects when it was not possible to undertake a meta-analysis of effect estimates and its extensions to investigate heterogeneity	Protocol page 4 Defined endpoints page 5 Data extraction page 6 Quality assessment page 6 and supplementary material Data synthesis page 6	
6 Certainty of evidence	Describe the methods used to assess certainty of the synthesis findings	Define endpoints page 5	

7 Data presentation methods	Describe the graphical and tabular methods used to present the effects (e.g., tables, forest plots, harvest plots). Specify key study characteristics (e.g., study design, risk of bias) used to order the studies, in the text and any tables or graphs, clearly referencing the studies included	TABLES and figures page 5, 6, 7, 8, 9, 10, 11, 12, 13, and supplementary materials	
Results			
8 Reporting results	For each comparison and outcome, provide a description of the synthesised findings, and the certainty of the findings. Describe the result in language that is consistent with the question the synthesis addresses, and indicate which studies contribute to the synthesis	Results page 6, 7, 8, 9, 10, 11, 12, 13, 14	
Discussion			
9 Limitations of the synthesis	Report the limitations of the synthesis methods used and/or the groupings used in the synthesis, and how these affect the conclusions that can be drawn in relation to the original review question	Limitations page 16	

Study ID	Selection bias	Allocation bias	Performance bias	Attrition bias	Detection bias	Reporting bias	Funding bias
Boda-Heggemann 2019	High	High	High	Low	Some concerns	Low	Some concerns
Brown 2021	High	Some concerns	High	Low	High	Low	Low
Campbell 2017	Some concerns	Low	High	Low	Some concerns	Low	Low
Choi 2019	High	Some concerns	High	Low	Some concerns	Low	Low
Chu 2019	High	High	High	Low	Some concerns	Low	Low
Dreher 2018	High	Some concerns	High	Low	Some concerns	Low	Low
Farrugia 2021	High	Some concerns	Some concerns	Low	High	Some concerns	Low
Fu 2022	High	Some concerns	Some concerns	Low	Some concerns	Low	Low
Grimbergen 2022	High	Some concerns	High	Low	Some concerns	Some concerns	Low
Han-Oh 2021	High	High	High	Low	High	High	Some concerns
Hashimoto 2019	High	Some concerns	High	Low	Some concerns	Low	Low
Hill 2021	High	High	High	Low	Some concerns	Low	Low

Hu	concerns	concerns			concerns		
Hu 2017	High	Low	High	Low	Some concerns	Low	Low
Hu 2017	Some concerns	Some concerns	High	Low	Some concerns	Low	Low
Huang 2020	High	High	High	Low	Some concerns	Low	Low
Kawahara 2018	High	High	High	Low	Some concerns	Low	Low
Lens 2016	High	High	High	Some concerns	Some concerns	Low	Some concerns
Lu 2018	High	High	High	Some concerns	Some concerns	Low	Some concerns
Lu 2020	Some concerns	Some concerns	High	Low	Some concerns	Low	Low
Mast 2018	High	Some concerns	Some concerns	Some concerns	Some concerns	Some concerns	Low
Miura 2021	High	Some concerns	Some concerns	Low	Some concerns	Some concerns	Low
Nakamura 2015	High	Some concerns	Some concerns	Some concerns	High	Some concerns	Low
Naumann 2020	High	High	High	Low	High	Some concerns	Low
Oliver 2021	High	High	High	Low	Some concerns	Low	Low
Placidi 2020	High	Some concerns	Some concerns	Some concerns	High	Some concerns	Low

Qi[illegible]	[illegible]	[illegible] concerns	[illegible] concerns	[illegible] concerns	[illegible]	[illegible] concerns	
Sasaki 2020	High	Some concerns	Some concerns	Low	Some concerns	Some concerns	Low
Schneider 2023	Some concerns	Some concerns	Some concerns	High	Some concerns	Some concerns	Low
Sevillano 2020	High	High	High	Low	Some concerns	Low	Low
Shimohigashi 2017	High	High	High	Low	Some concerns	Low	Low
Stick 2020	High	High	High	Low	Some concerns	Low	High
Teboh 2020	High	High	High	Low	Some concerns	Low	Low
Tyagi 2021	High	High	High	Low	Some concerns	Low	Some concerns
VanGelder 2018	High	High	High	Low	Some concerns	Low	Low
Vogel 2018	High	High	High	Low	Some concerns	Low	Some concerns
Yorke 2016	High	High	High	Low	Some concerns	Low	Some concerns
Zeng 2019	High	High	High	Low	Some concerns	Low	Some concerns
Zeng 2021	High	High	High	Low	Some concerns	Low	Some concerns
Zeng 2022	High	Some concerns	Some concerns	Some concerns	High	High	Low

Author & year	MM	Motion measurement		
		Anterior-posterior direction	*Right-left direction*	*Superior-inferior direction*
Dreher 2018	AC	Vacuum motion Max=4.8mm Compression motion Max=4.4mm	Vacuum motion Max=5.4mm Compression motion Max=4.8mm	Vacuum motion Max=6.3mm Compression motion Max=3.9mm
Farrugia 2021	BH			EBH Reproducibility M=1.79mm SD=1.49mm Stability M=1.94mm SD=2.74mm DIBH Reproducibility M=2.69mm SD=2.54mm Stability M=2.48mm SD=1.92mm IBH Reproducibility M=1.97mm SD=1.86mm Stability M=2.50mm SD=2.28mm
Han-Oh 2021	BH	Inter-breath variation M=0.9mm SD=0.4mm	Inter--breath variation M=0.9mm SD=0.5mm	Interbreath variation M=1.5mm SD=0.9mm
Hashimoto 2019	AC	SD=0.2mm σ=1.1mm	SD=0.3mm σ=1.3mm	SD=0.8mm σ=2.4mm
Hu 2016	AC	No compression M=10.94mm SD=2.28mm Compression 1 **M=5.81mm** SD=0.84mm Compression 2 **M=8.50mm** SD=1.22mm Compression 3 **M=10.99mm** SD=2.42mm	No compression M=3.35mm SD=1.55mm Compression 1 M=2.53mm SD=0.93mm Compression 2 M=2.18mm SD=0.72mm Compression 3 M=3.23mm SD=1.47mm	No compression M=9.53mm SD=2.62mm Compression 1 M=4.53mm SD=1.16mm Compression 2 **M=7.56mm** SD=1.30mm Compression 3 **M=9.95mm** SD=2.32mm

Hu		M=2.9mm SD=1.4mm Compression M=2.3mm SD=1.1mm	SD=1.3mm Compression M=2.9mm SD=1.2mm	m SD=2.6 Compression **M=5.3mm** SD=2.2mm
Hu 2017	AC	No compression M=3.38mm SD=1.59mm Compression M=2.13mm SD=1.05mm	No compression M=3.48mm SD=1.14mm Compression M=2.33mm SD=1.22mm	No compression M=9.83mm SD=3.00mm Compression **M=5.11mm** SD=2.05mm
Lu 2018	BH	M=-0.18mm SD=1.36mm σ=0.97mm	M=0.03mm SD=0.75mm σ=0.39mm	M=0.02mm SD=1.55mm σ=1.41mm
Lu 2020	BH	M=1.80mm SD=2.51mm	M=0.4mm SD=0.6mm	M=1.0mm SD=1.3mm
Mast 2018	BH	Stability σ=1.0mm	Stability σ=1.0mm	Stability σ=1.2mm
Miura 2021	BH	M=0.4mm SD=0.9mm	M=0.4mm SD=0.6mm	M=1.0mm SD=1.3mm
Schneider 2023	AC	2DCine no compression M95%= 1.5mm (SD = 0.5mm) 4DMRI no compression M95%= 2.1mm (SD = 2.4mm) 2DCine compression M95%= 1.0mm (SD = 0.6mm) 4DMRI compression M95%= 1.6mm (SD = 0.9mm)	2DCine no compression M95%= 1.7mm (SD = 1.1mm) 4DMRI no compression M95%= 3.1mm (SD = 2.2mm) 2DCine compression M95%= 1.3mm (SD = 0.9mm) 4DMRI compression M95%= 2.7mm (SD = 1.5mm)	2DCine no compression M95%= 6.9mm (SD = 3.1mm) 4DMRI no compression M95%= 9.3mm (SD = 4.5mm) 2DCine compression M95%= 3.7mm (SD = 1.5mm) 4DMRI compression M95%= 4.6mm (SD = 2.1mm)
Sevillano 2020	AC	Motion from inhale/exhale CT **M=5.3mm** SD=4.1mm Fluoroscopy M=4.1mm SD=2.1mm	Motion from inhale/exhale CT M=3.7mm SD=2.5mm Fluoroscopy M=1.9mm SD=1.1mm	Motion from inhale/exhale CT **M=15.1mm SD=6.9mm** Fluoroscopy **M=9.5mm** SD=3.6mm
Shimohigashi 2017	AC	CT M=2.4mm SD=2.2mm CBCT M=2.3mm SD=2.3mm	CT M=1.7mm SD=0.8mm CBCT M=1.2mm SD=0.7mm	CT **M=5.3mm** SD=3.3mm CBCT M=4.5mm SD=3.8mm
Stick 2020	BH			Median=0.9mm R=0.4-2.4mm

Ty		Median=1.7mm R=0.7-7.0mm Free-breathing Median=2.6mm R=1.2-6.9mm	Median=2.1mm R=0.6-6.3mm Free-breathing Median=5.2mm R=2.2-10.1mm	Median=4.1mm R=1.4-10.0mm Free-breathing Median=7.4mm R=4.8-9.5mm
VanGelder 2018	AC	No compression M=4.7mm SD=3.8mm Compression <u>**M=5.4mm**</u> SD=4.2mm	No compression M=0.7mm SD=1.1mm Compression M=0.7mm SD=1.0mm	No compression M=8.7mm SD=3.0mm Compression <u>**M=8.0mm**</u> SD=3.8mm
Yorke 2016	AC	Compressed R=5-7mm Free-breathing R=5-15mm		

AC=Abdominal compression, BH=Breath-hold, MM=Motion mitigation

Lead author	MM	Inter-fraction uncertainties		
		Anterior-posterior direction	*Right-left direction*	*Superior-inferior direction*
Boda-Heggemann 2019	BH	M=-0.2mm **SD=7.2mm**	M=1.3mm **SD=5.7mm**	M=1.3mm **SD=7.5mm**
Campbell 2017	AC	No compression M=7.3mm R=3.5-18.2mm Compression **M=5.3mm** R=1.9-**13.1mm**	No compression M=5.3m R=1.8-12.4mm Compression **M=5.2mm** R=1.3-**13.7mm**	No compression M=13.9mm R=4.7-35.5mm Compression **M=8.5mm** R=1.6-**17.1mm**
Choi 2019	BH	M=-0.3mm SD=1.5mm σ=2.2mm	M=-0.1mm SD=1.1mm σ=1.9mm	M=-0.4mm SD=2.4mm σ=2.2mm
Chu 2019	AC	No compression pancreas M=3.2mm SD=1.33mm Compression pancreas M=4.0mm SD=2.2mm No compression liver M=1.4mm SD=1.4mm Compression liver M=0.4mm SD=0.6mm	No compression pancreas M=3.6mm SD=2.4mm Compression pancreas M=3.5mm SD=2.1mm No compression liver M=0.9mm SD=0.7mm Compression liver M=0.6mm SD=0.8mm	No compression pancreas M=5.4mm SD=3.3mm Compression pancreas M=3.3mm SD=2.2mm No compression liver M=1.7mm SD=1.6mm Compression liver M=0.8mm SD=1.2mm
Dreher 2018	AC	Vacuum M=-1.1mm SD=4mm Compression M=0.9mm SD=4.3mm	Vacuum M=1.6mm SD=9.5mm Compression M=1.6mm SD=2.9mm	Vacuum M=-2.8mm SD=8.7mm Compression M=0.8mm SD=4.4mm
Fu 2022	BH	M=0.1mm SD=0.7mm	M=0.6mm SD=3.6mm	M=0.3mm SD=0.5mm
Han-Oh 2021	BH	M=1.1mm SD=0.4mm	M=1.2mm SD=0.4mm	M=1.9mm SD=1.0mm
Hashimoto 2019	AC	SD=1.8mm σ=1.5mm	SD=2.0mm σ=1.6mm	SD=3.7mm σ=3.0mm
Hill 2021	BH	M=2.9mm SD=1.7mm	M=3.1mm SD=1.8mm	M=3.5mm SD=2.2mm

Hu		M=3.77mm SD=3.21mm Compression M=1.67mm SD=1.91mm	M=2.97mm SD=2.47mm Compression M=2.23mm SD=1.79mm	M=4.85mm SD=4.04mm Compression M=4.10mm SD=3.36mm
Huang 2020	BH	M=-0.05mm SD=0.25mm	M=0.04mm SD=0.24mm	M=-0.09mm SD=0.37mm
Kawahara 2018	BH	M=1.4mm SD=2.2mm R=0.4-8.0mm	M=-0.6mm SD=1.8mm R=-7.0-6.0mm	M=0.4mm SD=4.6mm R=-14.0-15.0mm
Lu 2018	BH	M=-0.93mm SD=3.20mm σ=1.77mm	M=0.67mm SD=1.77mm σ=1.62mm	M=-1.33mm SD=3.87mm σ=1.86mm
Mast 2018	BH	SD=0.4mm σ=0.3mm	SD=0.2mm σ=0.3mm	SD=0.2mm σ=0.3mm
Miura 2021	BH	Non CECT M=0.8mm SD=1.0mm CECT M=1.4mm SD=1.7mm	Non CECT M=0.6mm SD=1.0mm CECT M=1.2mm SD=1.3mm	Non CECT M=2.5mm SD=2.6mm CECT **M=6.4mm** **SD=6.4mm**
Nakamura 2015	BH	M=-1.1mm SD=2.1mm	M=0.9mm SD=2.1mm	M=0.6mm SD=3.3mm
Naumann 2020	BH	M=-0.5mm **SD=6.1mm** R=**-13.0-12.0mm**	M=0.5mm SD=3.6mm R=**-7.0-9.0mm**	M=-1.5mm SD=**7.6mm** R=**-25.0-12.0mm**
Oliver 2021	BH	DIBH M=0.3mm SD=1.3mm deepEBH M=0.1mm SD=0.8mm	DIBH M=-0.2mm SD=0.8mm deepEBH M=0.0mm SD=1.0mm	DIBH M=0.0mm SD=1.5mm deepEBH M=-0.3mm SD=0.8mm

Pla				
Qiu 2016	BH	M=3.4mm SD=2.6mm σ=3.1mm	M=2.2mm SD=1.9mm σ=1.5mm	M=7.0mm SD=5.6mm σ=4.8mm
Sasaki 2020	BH	M=0.8mm SD=2.2mm	M=0.6mm SD=1.5mm	M=-0.1mm SD=2.2mm
Shimohigashi 2017	AC	M=0.8mm SD=0.7mm	M=0.6mm SD=0.5mm	M=1.3mm SD=1.0mm
Teboh 2020	BH	M=2.0mm SD=1.4mm	M=1.7mm SD=0.8mm	M=3.2mm SD=2.5mm
Tyagi 2021	AC	M=0.0mm SD=3.0mm	M=-1.0mm **SD=9.0mm**	M=-1.0mm **SD=11.0mm**
***AC=Abdominal compression, BH=Breath-hold, MM=Motion mitigation**				

Lead author	MM	Intra-fraction uncertainties		
		Anterior-posterior direction	*Right-left direction*	*Superior-inferior direction*
Boda-Heggemann 2019	BH	M=1.6mm SD=0.6mm	M=0.7mm SD=0.3mm	M=1.3mm SD=0.5mm
Brown 2021	BH	endEBH M=1.8mm R=0-0.2mm DIBH M=1.6mm R=0-0.4mm	endEBH M=1.5mm R=0-0.2mm DIBH M=1.6mm R=0-0.2mm	endEBH M=2.0mm R=0-3mm DIBH M=2.2mm R=0-6mm
Fu 2022	BH	M=0.1mm SD=1.1mm	M=-0.3mm SD=0.6mm	M=1.2mm SD=3.0mm
Grimbergen 2022	AC	M=2.3mm SD=1.1mm	M=1.4mm SD=0.6mm	Cranial M=4.2mm SD=1.9mm Sagittal M=3.9mm SD=1.7mm
Hill 2021	BH	M=2.0mm SD=1.3mm	M=2.0mm SD=0.9mm	M=2.3mm SD=1.4mm
Hu 2017	AC	M=0.33mm SD=0.44mm	M=0.41mm SD=0.46mm	M=0.86mm SD=0.80mm
Kawahara 2018	BH			M=1.0mm SD=0.7mm
Lens 2016	BH	Between BHs M=-0.5mm SD=0.8mm		Between BHs M=-0.2mm SD=1.7mm
Oliver 2021	BH	DIBH M=0.2mm SD=2.5mm deepEBH M=0.0mm SD=1.2mm	DIBH M=0.3mm SD=1.1mm deepEBH M=-0.2mm SD=0.7mm	DIBH M=-0.1mm SD=2.7mm deepEBH M=-0.7mm SD=1.2mm
Qiu 2016	BH	M=1.0mm SD=1.3mm σ=1.1mm	M=0.7mm SD=0.9mm σ=1.0mm	M=0.7mm SD=1.4mm σ=1.2mm

Sa				SD=0.7mm External marker M=0.5mm SD=0.5mm
Shimohigashi 2017	AC	M=1.3mm SD=1.0mm	M=0.6mm SD=0.5mm	M=0.4mm SD=0.3mm
Stick 2020	BH			Median=3mm R=0.1-1.4mm
Vogel 2018	BH			kV Max=10.39mm Ultrasound Max=8.79mm
Yorke 2016	AC			M=0.1mm SD=2.1mm
Zeng 2019	BH			M=-0.6mm SD=2.9mm
Zeng 2021	BH			**M=6mm** R=3-**8mm**
Zeng 2022	BH			Displacement motion during treatment M=1mm SD=2mm
***AC=Abdominal compression, BH=Breath-hold, MM=Motion mitigation*				

Figure 1: PRISMA flow chart of the study selection procedure