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Review Article

A systematic review of the impact of abdominal compression and breath-hold techniques on motion, inter-fraction set-up errors, and intra-fraction errors in patients with hepatobiliary and pancreatic malignancies

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ABSTRACT

Background and purpose: Reducing motion is vital when radiotherapy is used to treat patients with 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 5 mm 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 > 5 mm motion, and 4 BH and 2 AC studies reported > 5 mm 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 between patients. 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]. However, 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 [21,29,30]. 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

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artefacts [19,31] and margins are required for many of these approaches [23], which hinders the delivery of high doses [32,33].

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 [34–36]. Different devices can be utilised for AC, including arches/plates, belts/bands, corsets, shells and immobilising the patient in the prone position [37–43]. The challenge with AC is whether it can effectively minimise motion for each patient, both at pre-treatment and during treatment [36,44,45], 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 [46]. 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 [46]. Alternatively, patients can enter BH with the help of machine-assisted systems using spirometers [46], or less commonly, mechanical ventilation [47]. 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 [48].

Recent surveys have highlighted that the adoption of motion mitigation approaches remains low, especially in abdominal radiotherapy [49–51]. 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 [52,53]. 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 CRD42021277784). The review question was developed using the PICOS framework, as shown in Table 1.

Table 1
PICOS framework of motion mitigation interventions in patients receiving HPB or pancreatic radiotherapy.

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 surrogateReports of patient experience, comfort, and tolerability
Study Design	Randomised controlled trials, non-randomised experimental studies, cohort studies and retrospective reviews

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 [16,17,54]. 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 [46]. This systematic review does not address these components separately. According to geometric uncertainty guidance [52,53], 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, Fig. 1.

Data extraction

Two reviewers (AW and YM) independently extracted information, including surname, year, baseline characteristics, motion mitigation

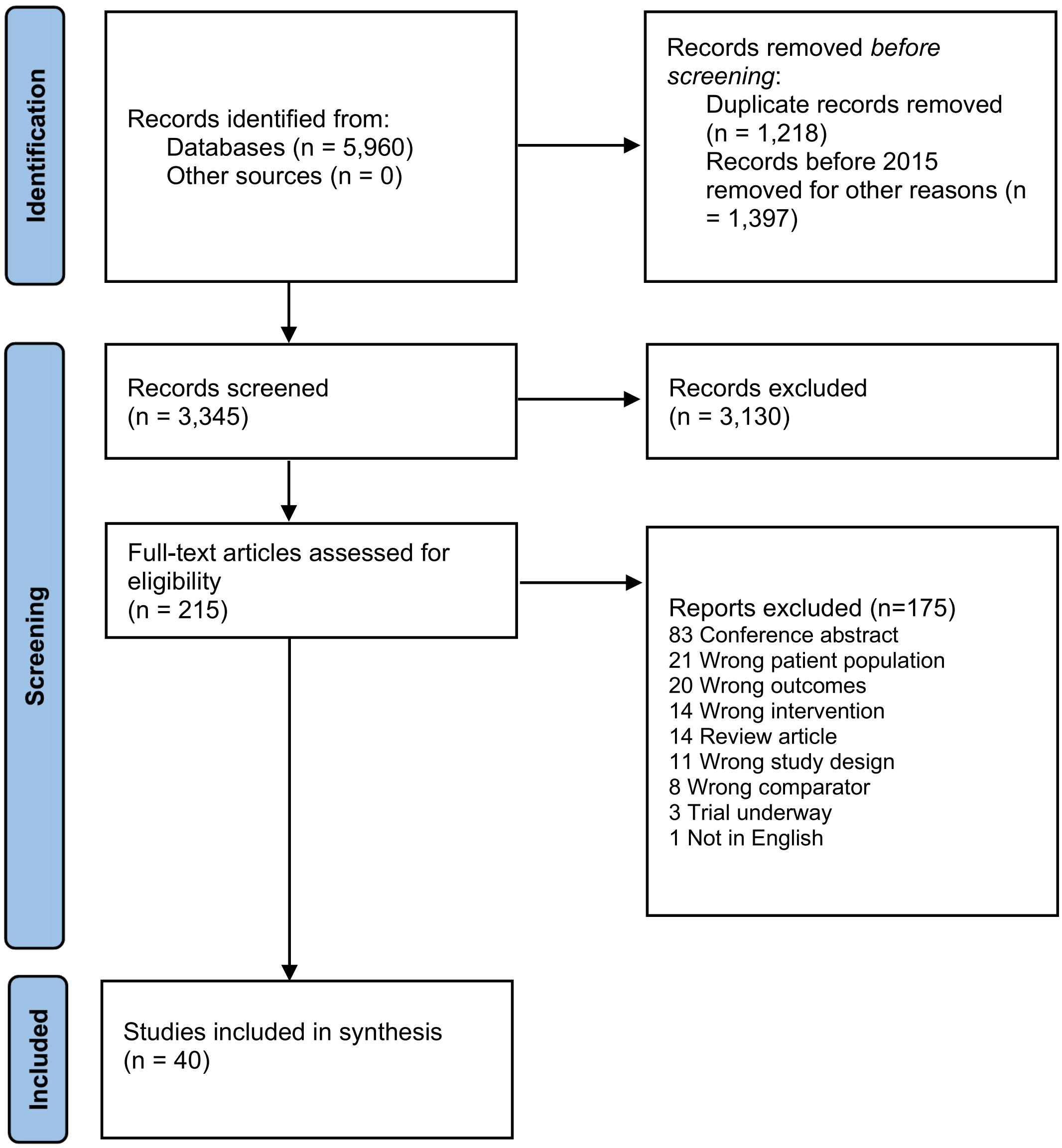

Fig. 1. PRISMA flow chart of the study selection procedure.

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 [55]. 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 [56]. 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 5 mm for metrics such as mean (M), standard deviation (SD), median, or similar measurements were specifically identified. 5 mm was chosen as patients are considered to have very mobile tumours if motion > 5 mm [46] 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 [37,39,43,57–67] and 26 focused on breath-hold techniques [68–93] (Table 2). No studies compared compression versus breath-hold. There were 20 studies focused on HPB patients [37,43,58–61,64,67,69,70,72,76,78–80,82,83,85,91,92], 13 studies focused on pancreatic patients [39,62,63,66,73,74,77,81,84,86,88,90,93] and 7 studies focused on patients with abdominal malignancies (mainly HPB and pancreas patients) [57,65,68,71,75,87,89]. Six studies measured motion at pre-treatment [37,39,60,64,71,79], 22 studies measured inter and/or intra-fraction errors on treatment

Table 2
Summary of all studies meeting inclusion criteria for systematic review.

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 [68]	16	Abdominal patients (majority liver and pancreas)	Breath-hold *DIBH*	Assisted	Fiducials or liver contour	On-treatment	CBCT and ultrasound
Brown et al. 2021 [69]	30	Liver	Breath-hold *DIBH* *endEBH*	Assisted	Diaphragm position	On-treatment	CBCT
Campbell et al. 2017 [62]	19	Pancreas	Compression *Belt* *Free breathing*		Fiducials in pancreas	On-treatment	CBCT
Choi et. al, 2019 [70]	69	Liver	Breath-hold *DIBH*	Unassisted	Liver contour	On-treatment	CT on rails
Chu et al. 2019 [57]	72	Abdominal patients (majority liver and pancreas)	Compression *Arch* *Free breathing*		Abdominal tumour	On-treatment	CBCT
Dreher et al. 2018 [58]	54	Liver	Compression *Arch* *Low pressure foil*		Bony anatomy and liver contour	Both	CT and CBCT
Farrugia et al. 2021 [71]	19	Abdominal patients (majority liver and pancreas)	Breath-hold *DIBH* *EBH* *IBH*	Assisted	Abdominal tumour if visualised, or fiducial or diaphragm	Pre-treatment	kV fluoroscopy
Fu et al. 2022 [72]	13	Liver	Breath-hold *EBH*	Unassisted	Bony anatomy and diaphragm	On-treatment	CBCT
Grimbergen et al.2022 [66]	13	Pancreas	Compression *Corset*		Pancreas GTV	On-treatment	MRI: coronal and sagittal cine MRI
Han-Oh et al.2021 [73]	20	Pancreas	Breath-hold *DIBH*	Assisted	Fiducials in pancreas	Both	CT and CBCT
Hashimoto et al.2019 [43]	324	Liver	Compression *Shell*		Fiducials in liver	Both	4DCT and fluoroscopy
Hill et al.2021 [74]	30	Pancreas	Breath-hold *DIBH*	Assisted	Fiducials in pancreas	On-treatment	CBCT
Hu et al.2016 [37]	72	Liver	Compression *Arch* *Free breathing*		Liver contour	Pre-treatment	4DCT
Hu et al.2017 [60]	99	Liver	Compression *Arch* *Free breathing*		Liver contour	Pre-treatment	4DCT
Hu et al.2017 [59]	42	Liver	Compression *Arch* *Free breathing*		Liver contour	Both	4DCT and MVCT
Huang et al.2020 [75]	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 [76]	59	Liver	Breath-hold *EBH*	Unassisted	Bony anatomy and diaphragm	On-treatment	CBCT and kV/kV
Lens et al. 2016 [77]	12	Pancreas	Breath-hold *DIBH*	Assisted	Fiducials in pancreas	On-treatment	CBCT and fluoroscopy
Lu et al. 2018 [78]	19	Liver	Breath-hold *DIBH*	Assisted	Bony anatomy and liver tumour	Both	CT and CBCT
Lu et al. 2020 [79]	44	Liver	Breath-hold *DIBH*	Assisted	Liver contour	Pre-treatment	CT
Mast et al. 2018 [80]	20	Liver	Breath-hold *DIBH*	Assisted	Bony anatomy and liver contour	Both	CT and CBCT
Miura et al. 2021 [91]	17	Liver	Breath-hold *EBH*	Unassisted	Liver contour	Both	CT and CBCT
Nakamura et al. 2015 [81]	11	Pancreas	Breath-hold *endEBH*	Unassisted	Bony anatomy and pancreas	On-treatment	CBCT and kV/kV
Naumann et al. 2020 [92]	7	Liver	Breath-hold *DIBH*	Unassisted	Liver contour	On-treatment	CBCT
Oliver et al. 2021 [82]	18	Liver	Breath-hold *deep* *EBH DIBH*	Unassisted	Diaphragm	On-treatment	CBCT
Placidi et al. 2020 [93]	8	Pancreas	Breath-hold *DIBH*	Unassisted	Pancreas GTV	On-treatment	MRI: 3DMRI
Qiu et al.2016 [83]	9	Liver	Breath-hold *deepEBH*	Unassisted	Liver contour	On-treatment	CBCT
Sasaki et al.2020 [84]	10	Pancreas	Breath-hold *endEBH*	Unassisted	Fiducials in pancreas	On-treatment	CBCT and kV/kV
Schneider et al.2023 [39]	12	Pancreas	Compression *Corset* *Free breathing*		Pancreas GTV	Pre-treatment	MRI: coronal and sagittal cine MRI and 4DMRI

(*continued on next page*)

Table 2 (*continued*)

Author & year	Total No. of patients	Treatment site	Motion mitigation	Assisted or unassisted BH	IGRT match structure	Pre or on-treatment measure	Imaging equipment
Sevillano et al.2020 [67]	13	Liver	Compression *Shell*		Fiducials in liver	Both	CT and fluoroscopy
Shimohigashi et al.2017 [61]	10	Liver	Compression *Arch with shell*		Fiducials in liver	Both	CT and 4DCBCT
Stick et al.2020 [85]	10	Liver	Breath-hold *DIBH*	Unassisted	Fiducials in liver	Both	CT and CBCT
Teboh et al.2020 [86]	19	Pancreas	Breath-hold *DIBH*	Assisted	Fiducials in pancreas	On-treatment	CBCT and kV/kV
Tyagi et al.2021 [63]	10	Pancreas	Compression *Belt* *Free breathing*		Pancreas GTV	Both	MRI: cine MRI and 3DMRI
VanGelder et al.2018 [64]	15	Liver	Compression *Belt* *Free breathing*		Liver contour	Pre-treatment	4DCT
Vogel et al.2018 [87]	13	Abdominal patients (majority liver and pancreas)	Breath-hold *DIBH*	Assisted	Diaphragm position	On-treatment	Ultrasound
Yorke et al.2016 [65]	19	Abdominal patients (majority liver and pancreas)	Compression *Belt* *Free breathing*		Fiducials in abdomen	Both	Fluoroscopy
Zeng et al.2019 [90]	8	Pancreas	Breath-hold *DIBH*	Unassisted	Fiducials in pancreas	On-treatment	CBCT and kV/kV
Zeng et al.2021 [88]	20	Pancreas	Breath-hold *DIBH*	Unassisted	Fiducials in pancreas	On-treatment	CBCT and kV/kV
Zeng et al.2022 [89]	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.

[57,62,66,68–70,72,74–77,81–84,86–90,92,93], and 12 studies assessed uncertainties at both pre-treatment and on-treatment [43,58,59,61,63,65,67,73,78,80,85,91]. There was variation in the IGRT structure(s) used to assess uncertainties, and 17 studies used fiducials [43,61,62,65,67,68,73–77,84–86,88–90] and 23 studies did not [37,57–60,63,64,66,67,69–72,78–83,87,91–93].

The studies had a high risk of bias (see supplementary material). Only 12 studies included ≥ 30 patients [37,43,57–60,69,70,74–76,79].

A total of fourteen studies employed abdominal compression as a motion mitigation technique [37,39,43,57–67]. Among these studies, 6 investigated the compression arch [37,57–61], 4 the compression belt [62–65], 2 the compression corset [39,66], and 2 the compression shell [43,67]. Twenty-six studies focused on breath-hold techniques for motion mitigation [68–93]. Among these studies, 20 investigated DIBH [68,70,73–75,77–80,85–90,92,93], 4 studies used EBH [71,72,76,91], 3 studies used endEBH [69,81,84], and 2 studies used deepEBH [82,83]. Within the BH category, 3 studies directly compared different breath-hold techniques [69,71,82]. Twelve studies employed spirometers, including ABC and SDX only, assisting the patient in breath-hold control [68,69,71,73–75,77–80,86,87]. Fourteen studies used an voluntary BH technique [70,72,76,81–85,88–93].

Motion uncertainty, defined as an IGRT structure deviation greater than 5 mm, was reported in 8/20 (40 %) of HPB studies [37,59–61,64,67,91,92], 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 > 5 mm [37,59–64,67,68,91–93]. This was in 4 compression arch studies [37,59–61], and 3 of these studies were from the same centre [37,59,60]. Two investigators measured using the liver contour [37,59,60,64] and two using liver fiducials [61,67]. There was one compression shell study [67] and one compression belt study [64] when the motion exceeded 5 mm. One study emphasised the significance of the position of the arch in achieving effective motion mitigation [37] None of the pre-treatment evaluations of BH studies reported motion exceeding 5 mm when BH was employed (Table 3 and supplementary material).

Considering on-treatment, 2 AC and 4 BH studies reported inter-fraction uncertainty exceeding 5 mm [62,63,68,91–93] (Table 4 and supplementary material). The AC studies were both using the compression belt [62,63]. Three of the 4 BH studies that had errors exceeding 5 mm for inter-fraction uncertainties were in DIBH, and 1 was in EBH [68,91–93]. Three of the studies used voluntary BH [91–93] and 1 study used assisted BH [68]. One study used fiducials and/or the liver contour to match [68], 1 matched to the liver contour [91] 1 matched to fiducials in the pancreas [62] and 3 matched to the pancreas [63,92,93].

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 > 5 mm [88]. The match structure used in this study was fiducials in the pancreas [88].

Guidance recommends that the mean, systematic and random error should be reported as a minimum [52]. Five studies did not report the mean [43,77,80,85,87], 5 studies did not report the systematic error [62,69,85,87,88], and 35 studies did not report the random error [37,39,57–69,71–77,79,81,82,84–93]. Nine studies reported the range [62,63,65,69,76,85,88,89], 2 that reported the median [63,85], 2 that reported the maximum [58,87] and 1 study that removed the error outliers (e.g., only reported errors within the mean 95 %) [39]. Additionally, different imaging modalities measured different values in the

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

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 et al. 2016 [37] *72 patients* *Compression arch* *Measurements of liver contour on 4DCT*	AC	(n = 26) No compression M = 10.94 mm SD = 2.28 mm (n = 19) Compression 1* **M = 5.81 mm** SD = 0.84 mm (n = 16) Compression 2* **M = 8.50 mm** SD = 1.22 mm (n = 11) Compression 3* **M = 10.99 mm** SD = 2.42 mm	(n = 26) No compression M = 3.35 mm SD = 1.55 mm (n = 19) Compression 1* M = 2.53 mm SD = 0.93 mm (n = 16) Compression 2* M = 2.18 mm SD = 0.72 mm (n = 11) Compression 3* M = 3.23 mm SD = 1.47 mm	(n = 26) No compression M = 9.53 mm SD = 2.62 mm (n = 19) Compression 1* M = 4.53 mm SD = 1.16 mm (n = 16) Compression 2* **M = 7.56 mm** SD = 1.30 mm (n = 11) Compression 3* **M = 9.95 mm** SD = 2.32 mm
Hu et al. 2017 [60] *99 patients* *Compression arch* *Measurements of liver contour on 4DCT*	AC	(n = 53) No compression M = 2.9 mm SD = 1.4 mm (n = 46) Compression M = 2.3 mm SD = 1.1 mm	(n = 53) No compression M = 3.1 mm SD = 1.3 mm (n = 46) Compression M = 2.9 mm SD = 1.2 mm	(n = 53) No compression M = 9.9 mm SD = 2.6 (n = 46) Compression **M = 5.3 mm** SD = 2.2 mm
Hu et al. 2017 [59] *42 patients* *Compression arch* *Measurements of liver contour on 4DCT and MVCT*	AC	(n = 15) No compression M = 3.38 mm SD = 1.59 mm (n = 27) Compression M = 2.13 mm SD = 1.05 mm	(n = 15) No compression M = 3.48 mm SD = 1.14 mm (n = 27) Compression M = 2.33 mm SD = 1.22 mm	(n = 15) No compression M = 9.83 mm SD = 3.00 mm (n = 27) Compression **M = 5.11 mm** SD = 2.05 mm
Sevillano et al. 2020 [67] *13 patients* *Compression shell* *Measurements of fiducials in liver on CT and fluoroscopy*	AC	Motion from inhale/exhale CT **M = 5.3 mm** SD = 4.1mm Fluoroscopy M = 4.1 mm SD = 2.1 mm	Motion from inhale/exhale CT M = 3.7 mm SD = 2.5mm Fluoroscopy M = 1.9 mm SD = 1.1 mm	Motion from inhale/exhale CT **M = 15.1 mm** **SD = 6.9 mm** Fluoroscopy **M = 9.5 mm** SD = 3.6 mm
Shimohigashi et al. 2017 [61] *10 patients* *Compression arch with shell* *Measurements of fiducials in liver on CT*	AC	CT M = 2.4 mm SD = 2.2mm CBCT M = 2.3 mm SD = 2.3 mm	CT M = 1.7 mm SD = 0.8mm CBCT M = 1.2 mm SD = 0.7 mm	CT **M = 5.3 mm** SD = 3.3mm CBCT M = 4.5 mm SD = 3.8 mm
VanGelder et al. 2018 [64] *15 patients* *Compression belt* *Measurements of liver contour on 4DCT*	AC	(n = 15) No compression M = 4.7 mm SD = 3.8 mm (n = 15) Compression **M = 5.4mm** SD = 4.2 mm	(n = 15) No compression M = 0.7 mm SD = 1.1 mm (n = 15) Compression M = 0.7mm SD = 1.0 mm	(n = 15) No compression M = 8.7 mm SD = 3.0 mm (n = 15) Compression **M = 8.0mm** SD = 3.8 mm

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 > 5 mm when motion mitigation applied.

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 [87], while a 2D cine MRI showed different values compared to a 4D MRI [66]. Finally, some studies may have underestimated errors by not considering initial bony match values in their final analysis [78,81], and some studies only analysed the final image before treatment delivery [74,82].

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 [37,76–79,81,85]. In one study, an information leaflet was given to patients [81]. 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 [62]. One AC belt study highlighted that several patients reported discomfort [64]. 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 [60]. In one study, a patient questionnaire found the compression corset to be well-tolerated, with no reported complaints or pain on average [39]. 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 [71]. Without personalised screening, EBH was the optimal technique, with superior reproducibility and stability compared with DIBH and IBH.

Table 4
Studies with on-treatment inter-fraction uncertainties > 5 mm.

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 [68] *16 patients* *Assisted DIBH* *Measurements of fiducials or liver contour on CBCT and ultrasound*	BH	M = -0.2 mm **SD = 7.2 mm**	M = 1.3 mm **SD = 5.7 mm**	M = 1.3 mm **SD = 7.5 mm**
Campbell et al. 2017 [62] *19 patients* *Compression belt* *Measurements of fiducials in pancreas on CBCT*	AC	(n = 19) No compression M = 7.3 mm R = 3.5–18.2 mm (n = 19) Compression **M = 5.3 mm** R = 1.9–**13.1 mm**	(n = 19) No compression M = 5.3 m R = 1.8–12.4 mm (n = 19) Compression **M = 5.3 mm** R = 1.3–**13.7 mm**	(n = 19) No compression M = 13.9 mm R = 4.7–35.5 mm (n = 19) Compression **M = 8.5 mm** R = 1.6–**17.1 mm**
Miura et al. 2021 [91] *17 patients* *Unassisted EBH* *Measurements of liver contour on CBCT*	BH	Non CECT M = 0.8 mm SD = 1.0 mm CECT M = 1.4 mm SD = 1.7 mm	Non CECT M = 0.6 mm SD = 1.0 mm CECT M = 1.2 mm SD = 1.3 mm	Non CECT M = 2.5 mm SD = 2.6 mm CECT **M = 6.4 mm** **SD = 6.4 mm**
Naumann et al. 2020 [92] *7 patients* *Unassisted DIBH* *Measurements of liver contour on CBCT*	BH	M = -0.5 mm **SD = 6.1 mm** R = **-13.0**–**12.0 mm**	M = 0.5 mm SD = 3.6 mm R = **-7.0**–**9.0 mm**	M = -1.5 mm SD = **7.6 mm** R = **-25.0**–**12.0 mm**
Placidi 2020 [93] *8 patients* *Unassisted DIBH* *Measurements of pancreas GTV on MRI*	BH	M = 0.0 mm SD = 3.5 mm	M = 1.5 mm **SD = 6.9 mm**	M = 2.3 mm **SD = 7.6 mm**
Tyagi 2021 [63] *10 patients* *Compression belt* *Measurements of pancreas GTV on MRI*	AC	M = 0.0 mm SD = 3.0 mm	M = -1.0 mm **SD = 9.0 mm**	M = -1.0 mm **SD = 11.0 mm**

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 > 5 mm when motion mitigation applied.

Table 5
Studies with intra-fraction uncertainties > 5 mm.

Lead author	MM	Reported intra-fraction uncertainties at treatment		
		Anterior-posterior direction	*Right-left direction*	*Superior-inferior direction*
Zeng 2021 [88] *20 patients Unassisted DIBH Measurements of fiducials in pancreas on CBCT and kV/kV*	BH			**M = 6 mm** R = 3–**8 mm**

BH = Breath-hold.
M = mean.
MM = Motion mitigation.
R = *range.*
Measurements in bold and underlined are where motion > 5 mm when motion mitigation applied.

However, implementing preplanning screening demonstrated in 56 % of participants, DIBH or IBH demonstrated superior reproducibility and BH time compared with EBH [71]. Patient factors were also considered, and one assisted BH study found under rigorous breath-hold respiratory control, DIBH correlated with body weight and height [75]. 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 [21,29,30]. 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 5 mm in at least one plane, including three AC arch studies from the same centre [37,59,60], one AC shell study [67], one AC arch with shell study [67], and one AC belt study [64] (Table 3). In 3 of these 6 studies, the average motion only exceeded 5 mm by less than 0.3 mm. Considering the inter-fraction set-up uncertainties, those that reported a systematic error greater than 5 mm included 1 assisted DIBH study [68], 2 voluntary DIBH studies [92,93], 1 voluntary EBH study [91] and 2 AC belt studies [62,63] (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 [61,62,67] 8 matched the tumour/organ [37,59,60,63,64,91–93] and 1 matched to both [68]. 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 [39,63,66,93]. 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 [49], DIBH remains most commonly used to reduce heart dose in left-sided cases, moving the treatment target away from critical structures [94]. 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 [48] underscore the importance of evaluating consistency from pre-treatment to treatment. With EBH, the patient is not forced out of their normal breathing pattern [46] and the consistency may be better, as, at rest, humans spend more of the breathing cycle in exhale [95,96]. 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 5 mm. 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 [97], 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 [46]. 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 [71]. 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 [71]. Three of the 4 BH studies reporting inter-fraction uncertainties > 5 mm 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 [46]. Only two studies used SGRT in BH [89,92], 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 [46]. 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 [68,69,87–90], 5 studies assessed motion between BHs [72,74,82,83,85], and 3 assessed both [76,77,84]. 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 [46] 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 > 5 mm 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 > 5 mm 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 6 mm in all planes

[37]. The inferior arch position was identified as the least effective in mitigating motion for HPB patients. 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 [62]. 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 5 mm [62,63]. 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 5 mm were in HPB patients. [37,59–61,64,67]. 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, the motion may be mitigated in pancreatic patients due to the closer location of the compression 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 [39].

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 [98]. 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 [62,64], and one study highlighted that gender and BMI affected the effectiveness of AC [60]; however, this finding is contradicted in a recent study, which showed that abdominal fat and BMI did not impact compression effectiveness [99]. In BH, personalised screening appeared to improve reproducibility [71], and one study highlighted that body weight and height impacted BH [75]. 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/intra-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 [52]. 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 [52], 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.

CRediT authorship contribution statement

Amanda Webster: Writing – original draft, Visualization, Validation, Software, Resources, Project administration, Methodology, Investigation, Funding acquisition, Formal analysis, Data curation, Conceptualization. **Yemurai Mundora:** Writing – review & editing, Validation, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Catharine H. Clark:** Writing – review & editing, Visualization, Validation, Supervision, Methodology, Formal analysis, Conceptualization. **Maria A. Hawkins:** Writing – review & editing, Supervision, Formal analysis, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Declaration of competing interest

None.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.radonc.2024.110581.

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