Physics and Imaging in Radiation Oncology 34 (2025) 100751

Contents lists available at ScienceDirect

Physics and Imaging in Radiation Oncology

journal homepage: www.sciencedirect.com/journal/physics-and-imaging-in-radiation-oncology

Review Article

A systematic review of tumour position reproducibility and stability in breath-hold for radiation therapy of the upper abdomen

Briana Farrugia [a,b,*], Kerryn Brown [a], Kellie Knight [b], Caroline Wright [b]

[a] Austin Health, 145 Studley Rd, Heidelberg, Victoria 3084, Australia
[b] Monash University, Wellington Rd, Clayton, Victoria 3800, Australia

ARTICLE INFO

Keywords:
Radiation therapy
Breath-hold
Reproducibility
Stability

ABSTRACT

Background and purpose: Upper abdominal malignancies are relatively rare, and although surgery is considered the primary treatment option, radiation therapy has an emerging role in the management of liver, pancreas, kidney and adrenal gland tumours. Furthermore, stereotactic radiation therapy for the management of upper abdominal metastases is an expanding clinical indication. Breath-hold is one respiratory motion management strategy used in upper abdominal radiation therapy, and the reproducibility, and stability of breath-hold is critical for overall treatment accuracy.

Materials and methods: A systematic review of the literature was conducted in Medline, Embase and Cochrane databases with keyword and vocabulary terms related to radiation therapy, breath-hold and upper abdominal tumours.

Results: Following screening against the selection criteria, 41 studies were included. Breath-hold reproducibility was the most commonly reported outcome and exhale breath-hold was the most common type. Studies were either prospective or retrospective cohort studies, and the mean sample size was 19 participants. The risk of bias of each included study was assessed, and the mean quality assessment score for included studies was 90 % (77–100 %). Median exhale breath-hold cranio-caudal inter-fraction reproducibility was 0.6 mm, (IQR 0.3–1.6 mm), compared to inspiratory breath-hold 0.0 mm (IQR −0.6–2.97 mm). Stability measurements were ≤3 mm in 71 % of studies, irrespective of breath-hold type.

Discussion: Formulating institutional protocols for best clinical practice regarding breath-hold for upper abdominal tumours is challenging, given the significant variation in practices, interventions and definitions observed in the literature. Further investigation to individualise breath-hold strategies and safety margins is warranted.

1. Introduction

The incidence of primary upper abdominal malignancies is relatively low compared to other organ systems. Liver cancer, including hepatocellular carcinoma and cholangiocarcinoma, accounts for only 4.7 %, pancreas 2.6 % and kidney 2.2 % of all new cancer diagnoses annually worldwide [1]. Surgery is considered the primary treatment modality for liver, pancreatic, kidney and adrenal gland tumours; however, radiation therapy, particularly stereotactic body radiation therapy (SBRT), is an emerging treatment option for patients who may be unsuitable for surgical options [2–12]. Conversely, metastases to the upper abdomen, particularly the liver, are relatively common, with an estimated 14–27 % of colorectal cancer patients diagnosed with liver metastases [13,14]. Metastases from other primary tumour sites such as the breast, oesophagus, lung, stomach, and skin are also commonly reported [15,16]. Treatment of these secondary upper abdominal tumours using SBRT is increasing, especially for patients with oligometastatic disease, with local control rates of approximately 80 % and moderate toxicity observed [17]. Due to the complexity of dosimetry required in the SBRT setting, where high dose gradients, high peak tumour doses and tight conformity are necessary, whilst sparing critical organs at risk (OARs), the accuracy of planning and treatment delivery is crucial. Both gastrointestinal filling control and the management of respiratory motion must be considered [18]. Breath-hold (BH) strategies are one method of respiratory motion management in upper abdominal radiation therapy. Other potential strategies include encompassing motion

* Corresponding author at: PO Box 5555, Heidelberg, Victoria 3084, Australia.
E-mail addresses: Briana.farrugia@austin.org.au, briana.farrugia@monash.edu (B. Farrugia).

https://doi.org/10.1016/j.phro.2025.100751
Received 1 August 2024; Received in revised form 4 March 2025; Accepted 14 March 2025
Available online 25 March 2025

via an internal target volume (ITV), forced shallow respiration via an abdominal compression device, or respiratory gating or tracking methods [19]. BH is achieved either by requesting the patient to voluntarily hold their breath or assisting them to do so with a spirometry or surface monitoring system. Typically, several BHs are required to perform daily imaging and complete treatment delivery.

Particularly in the SBRT setting, it is crucial to ensure that acceptable reproducibility and stability are maintained to preserve the accuracy of radiation therapy delivery. BH time and patient tolerability are also important to ensure efficiency in the delivery of treatment. When considering the implementation of BH techniques clinically, there is substantial disparity in the available evidence across BH methodologies, leading to optimal strategy uncertainty. There is diversity in technique (exhale breath-hold (EBH), inhale breath-hold (IBH) or deep-inhale breath-hold (DIBH)); BH methods (voluntary or assisted); imaging methods (fluoroscopy, computed tomography (CT), magnetic resonance imaging (MRI) or ultrasound) and patient populations (patients or healthy volunteers with a variety of tumour sites) reported in the literature [20–24].

The aim of this is systematic review was to examine and summarise the current body of evidence describing the stability and reproducibility of tumour positions during BH techniques, as well as BH duration, for radiation therapy to upper abdominal tumours.

2. Materials and methods

2.1. Eligibility criteria

This systematic review follows the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) standards [25] and has registration through the Prospective Register of Systematic Reviews (PROSPERO). This systematic review protocol was developed using the Population, Intervention, Comparator/Control, Outcome, Study Design (PICOS) criteria to develop selection criteria according to the focus of this review and is summarized in Table 1 [26]. A database search was conducted on 8th February 2023. Studies were compared against the selection criteria, to include those that described in sufficient detail: the BH technique used, the pre-planning, planning and/or treatment imaging acquired, and the measurement procedure for BH reproducibility, stability and/or time. Conference abstracts and unpublished data were excluded. Only studies published with full text available in English were included. Studies were extracted by two authors using Covidence (Veritas Health Innovation Ltd, Melbourne, Australia, 2023).

Table 1
PICOS description of systematic review, in accordance with PRISMA statement.

P – Participants	Patients undergoing medical imaging in preparation for radiation therapy and/or radiation therapy treatment of kidney, liver, pancreas or adrenal gland tumours, using a breath hold technique. Healthy volunteers in lieu of the patient population described.
I – Interventions	Breath hold of at least one type (inhale, deep-inhale or exhale). Voluntary breath hold (i.e., no device used, participant voluntarily holds their breath) .Spirometry (e.g., Active Breathing Coordinator (ABC)).Infra-red tracking (e.g., Real-time Position Management) .Audio-feedback or visual-feedback coaching system (e.g., Abches) .
C – Comparison	No comparator used.
O – Outcome	Reproducibility of tumour (or surrogate) position in breath hold, measured on imaging.Stability of tumour (or surrogate) position in breath hold, measured on imaging. Breath hold time.
S – Study Design	Quantitative prospective or retrospective trials. Randomised, or non-randomised studies. Published in peer-reviewed journals, between the years 2003–2023.

2.2. Search strategy

The Cochrane Library, including Cochrane Central Register of Controlled Trials (CENTRAL), Medline, and Embase databases were searched for studies. The search strategy comprised keywords and controlled vocabulary terms including ‘radiotherapy’ and ‘tomography’ to include the radiation therapy and medical imaging fields; ‘liver’, ‘pancreas’, ‘adrenal gland’ and ‘kidney’ to include the upper abdominal tumour sites; and ‘breath-hold’ to include studies focused on BH strategies. All searches were limited to publications in English within the past 20 years. The reference lists of all included studies and relevant systematic reviews were also hand-searched for additional potentially eligible studies. Title, abstract and full-text citations of eligible studies were exported to the systematic review software Covidence.

The Cochrane Effective Practice and Organization of Care (EPOC) standard data collection form was adapted in Covidence for study characteristics and outcome data [27]. Two review authors (BF, KB) piloted the data collection form on one study, and then independently extracted relevant data from all included studies. Any disagreements in extracted data were resolved through discussion.

The two review authors independently assessed the risk of bias for each study using the criteria outlined in Quality Assessment Criteria for Evaluating Primary Research Papers from a Variety of Fields [28]. Each potential source of bias was judged against 14 questions, relating to study design, subject selection and characteristics, blinding, outcomes, analytical methods and results, and study conclusions. Answers scoring ‘yes’ were allocated 2 points, ‘partial’ were allocated 1 point and ‘no/not applicable’ were allocated 0 points. The overall score was then converted to a percentage, with a higher percentage indicating higher quality studies. Studies were not excluded on the grounds of their risk of bias. Any disagreements in the risk of bias assessment scores were resolved through discussion.

2.3. Definitions of BH techniques

There is no consensus in the published literature regarding the definitions of BH methods. In this systematic review, we defined BH types as ‘inhale’, ‘deep-inhale’ or ‘exhale’. We defined IBH as the participant taking a normal breath in and holding, with the air volume comparable to a typical, resting inhale breath. We defined DIBH as the participant taking a deep breath in and holding, with the air volume greater than a normal, resting inhale breath, typically $\geq$80 % of the maximum inhale volume. We defined EBH as the participant exhaling and holding, with the air volume comparable to a normal, resting exhale breath, typically $\leq$30 % of normal inhale volume.

We considered reproducibility to be the reliability with which the tumour, or appropriate surrogate, returned to the same geometric position from one BH to the next [29]. Reproducibility was required to have been measured under image guidance (e.g. kilovoltage (kV) or megavoltage (MV) radiograph, cone-beam computed tomography (CBCT)) by comparing the change in tumour/surrogate position to a baseline position (e.g. planning CT). Inter-fraction reproducibility was defined as the measured change in position from the reference planning CT dataset to the image of the day. Intra-fraction reproducibility was defined as the measured change in position from the first image to the subsequent image within an imaging/treatment session [29].

We defined stability (also referred to as intra-BH variation) as the reliability with which the tumour, or an appropriate surrogate, remained in the same geometric position during a BH [29]. Stability was also required to have been measured under image guidance (e.g. kV fluoroscopy, MRI, ultrasound) as the change in cranio-caudal (CC) tumour/surrogate position from the beginning to the end of a single BH [29].

We considered the length of time a participant was able to hold their breath to be the BH time.

3. Results

3.1. Quality assessment

Following screening against the selection criteria, 41 studies were included in this review, as shown in Fig. 1. The characteristics of the selected studies, including population, tumour site, BH intervention and type, number of participants, imaging methods and the results of the quality assessment are outlined in Table 2.

The included study designs were predominantly prospective or retrospective cohort studies. No studies included randomisation or blinding of investigators or participants, therefore three questions were precluded from the quality assessment. As a result, the final quality assessment scores were calculated as a score out of 22 from 11 questions, converted to a percentage. The mean quality assessment score for the included studies was 90 % (range 77–100 %). The mean number of participants in each study was 19 (range 2–59).

3.2. BH intervention and type

Of the 41 included studies, 36 reported on a single BH type. In 5 of the included studies, more than one BH type was compared (Table 2). EBH was the most frequently reported BH type (n = 25), followed by DIBH (n = 16), then IBH (n = 8). Most studies were conducted in populations of radiation therapy patients (n = 38), and using an assisted BH strategy, with only 2 studies using voluntary BHs with no interventional device.

There are several commercially available systems reported to support the clinical use of BH. Spirometry devices such as Active Breathing Coordinator (ABC)^{TM} (Elekta, Stockholm, Sweden) and SDX® (SAS DYN'R® Aix-en-Provence, France) were the most commonly reported (n = 22), with ABC being the most prevalent (n = 18). These systems support the patient to hold their breath by measuring airflow through a spirometer during respiration. A visual display indicates the preset BH air volume, with the operator able to control the patient's BH. Surface monitoring systems including Real-time Position Management (RPM) (Varian Medical Systems, Inc.) and Abches, a chest/abdomen monitoring system developed by Onishi, et al [30], were the next most frequently reported (n = 13), with RPM the most common (n = 8). Surface monitoring systems convert the motion of the chest or abdomen during respiration as measured by infrared tracking (RPM) or the rotational angle of a needle in a level meter (Abches), to a visual display. This visual display can be used by the operator to coach the patient's BH and may also be displayed to the patient for visual feedback.

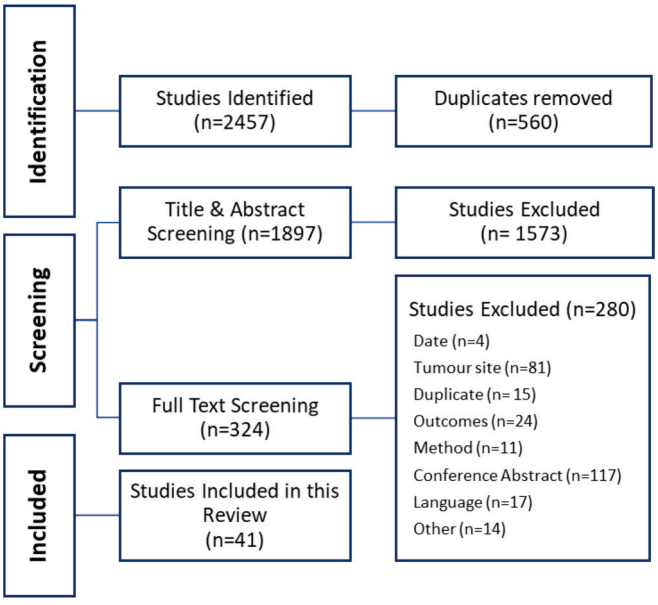

Fig. 1. PRISMA search results. Studies identified and screened against selection criteria, including reasons for study exclusion.

3.3. Reproducibility, stability and BH time

Of the 41 included studies, BH tumour position reproducibility was the most commonly included outcome, included in 40 papers. The majority of studies investigated reproducibility at the time of radiation therapy delivery (n = 28). Stability was reported in 7 studies. Fourteen studies reported BH time.

Table 3 summarises the reproducibility results, measured at pre-planning (prior to any radiation therapy planning or treatment commencing), planning (at the time of acquisition of radiation therapy planning imaging) or treatment (at the time of treatment delivery). Table 4 summarises the results of studies reporting on the stability of tumour/organ position.

Imaging by MV or kV coplanar radiographs, kV fluoroscopy or CBCT were the most commonly reported methods for measuring reproducibility and stability. Surrogates for tumour position were used in all but two studies, which instead measured the tumour GTV position directly. Surrogates included either a whole organ (liver or pancreas), the diaphragm/lung base position or implanted fiducial markers.

With respect to treatment reproducibility, studies reporting on EBH were most common (n = 17), with CC inter-fraction reproducibility median 0.6 mm, (IQR 0.3–1.6 mm), anterior-posterior (AP) median 0.8 mm, (IQR 0.42–1.28 mm) and left–right (LR) median 0.6 mm (IQR 0.15–1.4 mm) [31–47]. DIBH studies were the second most commonly reported (n = 12) with DIBH/IBH inter-fraction CC reproducibility median 0.0 mm (IQR −0.6–2.97 mm), AP median 1.1 mm (IQR −0.09–1.65 mm) and LR median 0.52 mm (IQR 0.11–1.35 mm) [23,24,31,48–54]. In 82 % of EBH studies, CC inter-fraction reproducibility was <2 mm compared to only 66 % of DIBH/IBH studies. CC inter-fraction and intra-fraction reproducibility for EBH and DIBH/IBH are presented in Fig. 2. Similar charts for AP and LR are available in the Supplementary Material (Fig. S1-2). Results were grouped by BH intervention.

Amongst the limited number of studies that reported on the stability of tumour position, mean stability measurements were in the range of 0–3 mm for 71 % of studies, irrespective of BH type. One study reported sub-millimetre stability in an EBH cohort [37]. Two studies reported stability for multiple BH types, with EBH being the most stable in both studies, compared to DIBH or IBH [55,56].

BH time was reported in one third of included studies. Significant variations in BH time were reported, ranging from 12 s(s) to 7.1 min. Van Kesteren et al. utilized mechanical ventilation of participants using a Hamilton MR1 ventilator (Hamilton Medical AG, Bonaduz, Switzerland), with hyperventilation to facilitate prolonged BH [57]. They reported inspiratory BH times of 2.0–11.1 min, and expiratory times of 1.8–10.2 min in their population of healthy volunteers. Excluding this outlying study, those reporting EBH times tended to be shorter (median 12.5 s (IQR 12–24.8 s)) than those reporting inspiratory times (median 31 s (IQR 25.7–54.5 s)). Farrugia et al. reported on the BH times across all three methods, with slightly reduced BH time for EBH, compared to IBH and DIBH, in keeping with other studies [55].

3.4. Other included studies

Seven studies reported results in a format that was unable to be included in the summary of results tables for reproducibility or stability. Mast et al. reported reproducibility of IBH compared to free-breathing, by investigating the margin reduction in clinical target volume (CTV) – planning target volume (PTV) in the cranio-caudal direction. In this study a 10 mm CC margin reduction was observed for IBH compared to FB [58]. Stam et al. reported box plots of stability and reproducibility of

Table 2
Characteristics of Included Studies and Quality Assessment Score.

Year	Author	Population	Tumour Site(s)	BH Intervention	BH Type	Participants	Imaging	Quality score (%)
2004	Kimura [20]	Healthy Volunteers	Liver	Spirometer	EBH, IBH	5	kV Fluoroscopy (PP)CT (P) *^	77
2005	Dawson [37]	RT Patients	Liver	ABC™	EBH	20	kV Fluoroscopy (PP)CT (P) *MV (T) ^	91
2006	Hawkins [34]	RT Patients	Liver	ABC™	EBH	13	kV Fluoroscopy (PP)CT (P) *kV, MV and CBCT (T) ^	95
2006	Eccles [35]	RT Patients	Liver	ABC™	EBH	21	kV Fluoroscopy (PP)CT (P) *MV (T) ^	100
2006	Dawson [38]	RT Patients	Liver	ABC™	EBH	21	kV Fluoroscopy (PP)CT * and MRI (P)MV^, kV^and CBCT^ (T)	77
2008	Zhao [24]	RT Patients	Liver	ABC™	DIBH	28	kV Fluoroscopy (PP) ^CT (P) *MV (T) ^	95
2010	Onishi [30]	RT Patients	Abdomen (Lung)	Spirometer	IBH	20	CT *^	100
2011	Nakamura [45]	RT Patients	Pancreas	RPM	EBH	10	CT *^	100
2012	Zhong [23]	RT Patients	Liver	ABC™	IBH	24	kV Fluoroscopy (PP)CT (P) *CBCT (T) *^	100
2012	Yue [32]	RT Patients	Liver	ABC™	EBH	28	CT (P) *CBCT (T) *^	91
2013	Takamatsu [39]	RT Patients	Liver, Gall Bladder, Pancreas	Abches, Voluntary, visual feedback	EBH	20	kV Fluoroscopy (PP)CT (P) *CBCT, kV and MV^ (T)	86
2013	Stam [59]	Patients Under Surveillance/ Awaiting Surgery	Kidney	Voluntary, video-guided	EBH	15	MRI *^	86
2013	Garibaldi [63]	RT Patients	Liver (Lung)	Voluntary with Exactrac	DIBH	8 (of 23 total)	CT (P) *^MV (T)	91
2013	Eccles [36]	RT Patients	Liver	ABC™	EBH	28	CT (P) *MV^and kV^ (T)	95
2015	Nakamura [69]	RT Patients	Pancreas	Voluntary with RPM visual feedback	EBH	11	CT (P) *kV and CBCT^ (T)	95
2016	Lens [70]	RT Patients	Pancreas	SDX®	IBH	12	kV Fluoroscopy (PP)CT (P)kV Fluoroscopy (T) *^	100
2016	Lens [56]	Healthy Volunteers	Pancreas	Voluntary	EBH, IBH, DIBH	16	MRI *^	86
2016	Kawahara [40]	RT Patients	Liver	Abches	EBH	59	kV Fluoroscopy (PP)CT (P) *kV and CBCT (T) ^	91
2017	Bae [44]	RT Patients	Liver, Pancreas	Not stated	EBH	20	kV Fluoroscopy (PP)CT (P) *kV (T) ^	95
2018	Vogel [60]	RT Patients	Adrenal, Liver, Spleen	ABC™	DIBH	13	CT and US (P)CBCT and US (T) *^	86
2018	Van Sornsen de Koste [61]	RT Patients	Adrenal, Pancreas (Lung)	Voluntary, video-guided	IBH	15	CT and MRI (P) *^	86
2018	Mast [58]	RT Patients	Liver	ABC™	IBH	20	CT (P) *^CBCT (T) ^	82
2018	Lu [50]	RT Patients	Liver (Lung)	ABC™	DIBH	19	CT (P) *^kV and CBCT^ (T)	86
2018	Kawahara [41]	RT Patients	Liver	Abches	EBH	59	kV Fluoroscopy (PP)CT (P) *kV and CBCT (T) ^	95
2019	Zeng [51]	RT Patients	Pancreas	RPM	DIBH	8	CT (P) *CBCT (T) ^	91
2019	Lee [71]	RT Patients	Liver, Pancreas (Breast, Lung)	ABC™	EBH	2 (of 12 total)	CT (P)CBCT (T)	91
2019	Boda-Heggemann [54]	RT Patients	Liver, Pancreas	ABC™	DIBH	14	CT and US * (P)CBCT and US^ (T)	91
2020	Teboh [48]	RT Patients	Pancreas	ABC™	DIBH	19	CT (P)CBCT and kV *^ (T)	86
2020	Sasaki [33]	RT Patients	Pancreas	RPM	EBH	13	CT (P) *kV^and CBCT (T)	100
2020	Lu [72]	RT Patients	Liver	ABC™	DIBH	44	CT (P) *^CBCT (T)	82
2020	Huang [53]	RT Patients	Liver, Bile Duct, Gall Bladder	SDX®	DIBH	42	CT (P) *kV and CBCT (T) ^	86
2020	Ashida [47]	RT Patients	Pancreas	RPM	EBH	10	CT (P) *kV and CBCT (T) ^	86
2021	Zeng [52]	RT Patients	Pancreas	RPM	DIBH	8	CT (P) *CBCT (T) ^	77
2021	Oliver [31]	RT Patients	Liver	RPM	EBH, DIBH	19	kV Fluoroscopy (PP)CT (P) *CBCT (T) ^	77
2021	Miura [43]	RT Patients	Liver	Abches	EBH	17	kV Fluoroscopy (PP)CT * and MRI (P)CBCT (T) ^	86
2021	Han-Oh [49]	RT Patients	Pancreas	ABC™	DIBH	20	CT (P) *^CBCT (T) ^	100
2021	Fracchiolla [62]	RT Patients	Liver	ABC™	EBH	17	CT (P) *kV (T) ^	86

(*continued on next page*)

Table 2 (*continued*)

Year	Author	Population	Tumour Site(s)	BH Intervention	BH Type	Participants	Imaging	Quality score (%)
2021	Farrugia [55]	RT Patients	Adrenal Gland, Liver, Pancreas	ABC™	EBH, IBH, DIBH	18	kV Fluoroscopy (PP) *^	100
2022	Zeng [73]	RT Patients	Ampulla, Liver, Pancreas	Bellows (planning) and Align RT (treatment)	DIBH	14	CT (P) *Align RT and CBCT^ (T)	82
2022	van Kesteren [57]	Healthy Volunteers	Liver	Hamilton MR1 mechanical ventilator	EBH, IBH, DIBH	15	MRI *^	86
2022	Fu [74]	RT Patients	Liver	Abches	EBH	13	CT (P) *CBCT (T) ^	91

Abbreviations: RT = Radiation therapy; ABC = Active Breathing Coordinator; RPM = Real-Time Position Management; IBH = Inhale/Inspiration Breath Hold; EBH = Exhale/Expiration Breath Hold; DIBH = Deep-Inhale/Inspiration Breath Hold; PP = Pre-Planning; P = Planning; T = Treatment; kV = Kilovoltage; CT = Computed Tomography; CBCT = Cone-Beam Computed Tomography; MV = Megavoltage; US = Ultrasound; MRI = Magnetic Resonance Imaging.
Annotations: * denotes imaging used as reference;^denotes imaging used to calculate reproducibility.

kidney position for each study participant [59]. Vogel et al. reported stability measurements of < 2 mm in 59 % of BH, 2–5 mm in 36 % of BH and > 5 mm in 5 % in the cranio-caudal direction [60]. A median interquartile range of diaphragm position reproducibility of 4.2 mm was reported by van Kesteren et al., when investigating prolonged DIBH, with 90 % of displacements < 12 mm [57]. van Sornsen de Koste et al. reported the percentage of GTV outside PTV area for each patient, ranging from 2.1-8.1 % (mean), and histogram plots of GTV centroid position relative to planning, with a mean of 1 mm [61]. An average residual 3D displacement vector of 2.2 mm was reported by Fracchiolla et al. in their cohort of liver SBRT patients [62]. Garibaldi et al. reported DIBH intra-fraction CC reproducibility and overall mean inter-fraction CC reproducibility of 2.3 mm in a combined cohort of lung and liver patients [63].

4. Discussion

A systematic review of the literature was performed, identifying 41 studies that reported on BH tumour position reproducibility, stability and time in upper abdominal radiation therapy. The most common BH type was EBH, with CC inter-fraction reproducibility measurements < 2 mm reported more commonly in EBH, compared to DIBH or IBH studies.

The upper abdomen is a challenging anatomical site for motion management. Radiation therapy of upper abdominal malignancies must account for motion resulting from respiration, along with daily variation in anatomy due to gastrointestinal organ filling and changes [64]. Particularly in the SBRT setting, where 0 mm action thresholds for target or patient positioning are common, understanding BH reproducibility and stability is essential to accurately determine appropriate PTV and PRV margins. Selecting the most favourable BH type and intervention may lead to improvements in both inter- and intra-fraction reproducibility and stability. In turn, this may avoid frequent re-imaging and the associated increase in radiation dose and negative impacts on patient experience.

During typical respiration, the direction and extent of motion are generally largest in the CC direction, followed by the AP direction [19]. In early studies, EBH was commonly selected as the technique of choice, as it was considered to be the most reproducible phase of the respiratory cycle [20,35,37]. When considering inter- and intra-fraction reproducibility at the time of radiation treatment delivery, poorer reproducibility was reported in the CC and AP, compared to LR directions, in keeping with the direction and extent of motion. When considering reproducibility in the CC direction, only one study reported results for both EBH and DIBH. Although the mean CC reproducibility of DIBH was 0 mm, compared to −0.3 mm for EBH, the authors noted increased standard deviation of errors of DIBH reproducibility and therefore suggested EBH was the more reproducible technique in their findings [31]. Though we found CC inter-fraction reproducibility of < 2 mm to be more frequently reported in EBH studies, the overlapping ranges of results do not indicate EBH to be a preferred BH type.

Potentially due to the comparatively abundant availability of treatment imaging data in standard radiation therapy workflows, studies infrequently investigated reproducibility from pre-planning (n = 2) or planning time points (n = 6). One study found that reproducibility was < 2 mm at all directions and time points, but planning measurements were smaller than those at treatment [50]. The authors proposed that individualised, intra-fractional-based margins are required to adequately account for reproducibility uncertainty.

The stability of tumour position during each BH is less frequently investigated but remains a crucial factor in accuracy of radiation therapy delivery. To observe and measure the stability of tumour position during BH, continuous imaging is required, however may not be feasible in many standard radiation therapy imaging protocols. Lens et al. and Farrugia et al. were the only two studies that reported results on all three BH types, with EBH being the most stable technique in both studies when compared to IBH and DIBH [55,56]. Inspiratory techniques resulted in > 2 mm stability in the study by Farrugia et al [55]. Notably, the results reported by Lens were considerably poorer than all other studies, with a range of 4.2–7.0 mm [56]. Using a strictly voluntary BH strategy with no interventional device or feedback to participants may have contributed to these results. The authors noted motion was most pronounced in the first 10 s of BH, suggesting a delay period prior to commencing imaging or treatment may result in improved stability [56].

Though BH time does not directly impact treatment accuracy, its influence on the patient's comfort and tolerability of treatment should not be discounted. Long treatment delivery times often seen in hypofractionated treatments, combined with repeated imaging can result in a substantial number of BHs required per fraction. When CBCT is used for image guidance with a stop-and-go approach, several BHs are required to obtain each CBCT image. The impact of even a small increase in BH time may facilitate fewer BHs required per image acquisition, reducing the burden on the patient. Similar BH times were reported across all BH types, with slightly longer times for inspiratory techniques. Van Kesteren et al. used a novel strategy of mechanical ventilation of participants to facilitate prolonged BH in their population of healthy volunteers [57]. They reported notably longer BH times than all other studies. However, the median age of 22 years, significant training time of 2 h, and required equipment may prohibit the applicability of this methodology in clinical practice.

Target and PRV margin calculations should ideally be personalised for each patient to encompass local procedures influencing setup position variation, imaging and quality assurance, and motion uncertainties. It is crucial to accurately account for the systematic and random uncertainties in BH reproducibility and stability in the generation of PTV and PRV margins. Particularly in the SBRT setting, where high dose

Table 3
Reproducibility of tumour position in breath-hold.

Pre-Planning Reproducibility

Author	BH Type	Reproducibility (mm, CC, mean)	Measurement structure
Farrugia [55]	EBH, IBH, DIBH	EBH 1.8 IBH 2.0 DIBH 2.7	Diaphragm or tumour/surrogate
Zhao [24]	DIBH	1.6	Diaphragm

Planning Reproducibility

Author	BH Type	Reproducibility (mm, mean)			Measurement structure
		CC	AP	LR	
Onishi [30]	IBH	^2.0			Lung base
Kimura [20]	EBH, IBH	^EBH 2.2 ^IBH 4.0 * EBH 2.1 * IBH 5.1	^EBH 2.0 ^IBH 2.3 * EBH 1.9 * IBH 3.0	^EBH 1.4 ^IBH 2.3 * EBH 1.1 * IBH 2.9	Diaphragm/thoracic wall
Eccles [35]	EBH	^−0.9	^−0.5	^0.2	Liver surface
Han-Oh [49]	DIBH	1.5	0.9	0.9	Fiducials in pancreas
Lu [50]	DIBH	−0.02	−0.18	0.03	Liver centroid
Lu [72]	DIBH	^2.2	^1.8	^0.7	Liver centroid

Treatment Reproducibility

Author	BH Type	Reproducibility (mm, mean)			Measurement structure	Fractionation	Number used to calculate reproducibility
		CC	AP	LR			
Lens [70]	IBH	^−0.2	^−0.5		Fiducials in pancreas	n/a	n/a
Zhong [23]	IBH	* −0.3	* −1.5	* 0.5	Liver contour	40–45 Gy/4–10#	All (4–10)
Oliver [31]	EBH, DIBH	* EBH −0.3 * DIBH 0.0	* EBH 0.1 * DIBH 0.3	* EBH 0.0 * DIBH −0.2	Diaphragm	27.5–60 Gy/5#	All (5)
Yue [32]	EBH	* −0.6 ^−0.4	* 1.3 ^−0.6	* −0.3 ^0.0	Lipiodol in liver	50–60 Gy/25–30#	All (25–30)
Takamatsu [39]	EBH	* 1.7		* 1.4	Diaphragm	50–62.5 Gy/20–30#	All (20–30)
Sasaki [33]	EBH	* −0.1	* 0.8	* 0.6	Fiducial in pancreas	48 Gy/15#	All (15)
Nakamura [45]	EBH	^0.1 * 0.3	^0.1 * 0.8	^0.0 * 0.3	POI within pancreas	n/a	n/a
Nakamura [69]	EBH	* 0.6	* −1.1	* 0.9	GTV and/or surrounding structures in pancreas	42–51 Gy/15#	All 15
Miura [43]	EBH	^1.0 * 2.5	^0.4 * 0.8	^0.4 * 0.6	Liver contour	40 Gy/4#	All (4)
Kawahara [41]	EBH	* 0.4 ^1.0	* 1.4	* −0.6	Diaphragm	48 Gy/4# or 60 Gy/8#	All (4 or 8)
Kawahara [40]	EBH	* Liver 1.4 * Diaphragm 1.3	* Liver 0.7 * Diaphragm 0.9	* Liver 1.4 * Diaphragm 0.7	Liver and diaphragm	Not stated	All
Hawkins [34]	EBH	* 1.6	* 3.1	* −1.5	Diaphragm	25.8–54 Gy/6#	All (6)
Fu [74]	EBH	* 0.6 ^1.2	* 0.1 ^0.1	* 0.3 ^−0.3	Diaphragm	36–50 Gy/5–6#	All (5–6)
Eccles [36]	EBH	* 1.2	* 1.2	* 1.8	Diaphragm	29–57 Gy/6#	All (6)
Eccles [35]	EBH	^1.5 * 3.4			Diaphragm		30.6–54 Gy/6#
Dawson [37]	EBH	* 1.1	* 1.3	* 1.6	Diaphragm	30.6–54 Gy/6#	All (6)
Dawson [38]	EBH	* 3.4 ^1.5			Diaphragm	24–57 Gy/6#	All (6)
Bae [44]	EBH	* 0.5	* 0.5	* 0.6	Fiducial – surgical clips in liver/pancreas	45–50.4 Gy/25–30#	2 per week (10–12)
Ashida [47]	EBH	* -0.2	* 0.4	* 1.4	Pancreas	54 Gy/30#	All
Teboh [48]	DIBH	* 3.0	* 2.0	* 1.5	Fiducials in pancreas	33 Gy/5#	All (5)
Han-Oh [49]	DIBH	* 1.9	* 1.1	* 1.2	Fiducial in pancreas	5# (dose not stated)	All (5)
Lu [50]	DIBH	* 3.0 ^1.3	* 2.6 ^1.2	* 1.8 ^0.6	Liver centroid	Not stated	All
Zhao [24]	DIBH	* 6.7			Diaphragm	40–58 Gy/20–29#	All (20–29)
Zeng [51]	DIBH	* −0.6			Fiducial in pancreas	75 Gy/25#	All (25)
Zeng [52]	DIBH	* Range 0.0–3.0			Fiducial in pancreas	67.5–75 Gy/15–25#	All (15–25)
Zeng [73]	DIBH	^1.0			Fiducial in liver/pancreas	40–75 Gy/10–25#	All (10–25)
Huang [53]	DIBH	* −0.9	* −0.5	* 0.4	Fiducial in liver, or proximal to target	Not stated	All
Boda-Heggemann [54]	DIBH	* −1.3	* 1.3	* −0.2	Fiducial in proximity to GTV or liver contour	60 Gy/5–12#	All (5–12)

Abbreviations: BH = Breath-Hold; IBH = Inhale/Inspiration Breath-Hold; EBH = Exhale/Expiration Breath-Hold; DIBH = Deep-Inhale/Inspiration Breath-Hold; CC = Cranio-Caudal; AP = Anterior-Posterior; LR = Left-Right; GTV = Gross Tumour Volume.
Annotations: * denotes inter-fraction reproducibility; ^denotes intra-fraction reproducibility.

Table 4
Stability of tumour position in breath-hold.

Author	BH Type	Stability (CC, mm, mean)	Measurement Structure
Hawkins [34]	EBH	2.0	Diaphragm
Eccles [35]	EBH	1.2	Diaphragm
Dawson [37]	EBH	0.6	Diaphragm
Lens [70]	IBH	4.2	Fiducials in pancreas
Lens [56]	EBH, IBH, DIBH	EBH 4.2 IBH 6.5 DIBH 7.0	Pancreas and diaphragm
Farrugia [55]	EBH, IBH, DIBH	EBH 1.9 IBH 2.5 DIBH 2.5	Diaphragm or tumour/ surrogate
Zhao [24]	DIBH	1.3	Diaphragm

Abbreviations: BH = Breath-Hold; IBH = Inhale/Inspiration Breath-Hold; EBH = Exhale/Expiration Breath-Hold; DIBH = Deep-Inhale/Inspiration Breath-Hold; CC = Cranio-Caudal.

gradients and shaping around critical OARs are essential, inadequately accounting for these uncertainties may result in potentially significant dosimetric consequences, including underdosing of the target volume or overdosing critical OARs.

Formulating institutional protocols for best clinical practice regarding BH for upper abdominal tumours is challenging, given the significant variation in practices, interventions and definitions observed in the literature. Further clinical studies investigating personalisation of BH interventions and individualised margins for PTVs and PRVs are warranted. In the paper by Farrugia, et al, an approach to personalise the selection of BH type on an individual patient basis was examined [55]. Participants attempted all BH types during pre-planning under kV fluoroscopy with the BH type with superior reproducibility and/or stability selected. Fewer participants screened into EBH (44 %), compared to inspiratory techniques (IBH (39 %) and DIBH (17 %)). Personalised selection of BH type resulted in superior reproducibility (0.92 mm), compared with their institutional standard EBH (1.79 mm).

Furthermore, in selecting the most appropriate BH type, there may be anatomical and dosimetric considerations to the selection of an inspiratory BH type compared to EBH. In the setting of breast radiation therapy, where DIBH is widely adopted, there are clear advantages in the use of DIBH to separate the left breast target area from underlying OARs, including the heart and lungs [29]. Similarly, DIBH can be advantageous in lung radiation therapy. With deep inspiration, the normal lung volume expands, potentially moving the target further from nearby OARs, and immobilising the tumour, facilitating a smaller volume of lung irradiated [29]. To our knowledge, no studies have yet evaluated the anatomic and dosimetric advantages of EBH compared to DIBH or IBH in the abdomen. The large, and less predictable anatomical variations, and spatial relationship between targets and OARs make research in this area challenging.

The overlapping ranges of reported reproducibility between spirometry, and surface monitoring interventions indicate no single system can be considered preferable. The influence of other factors, including patient training, patient coaching during treatment, the presence or absence of a visual feedback system, as well as individual patient capabilities must also be considered. In managing respiratory motion, the choice of interventional strategy must consider clinical effectiveness, patient suitability, resourcing implications, and physical limitations of hardware, software, and room capacity [19].

There are alternative strategies that do not include BH techniques. Free-breathing is often used as an alternative strategy for patients who are unable to comply with BH requirements. Free-breathing with a motion-encompassing ITV approach must account for potentially significant motion of tumour volumes, in the order of 5–50 mm [19,65,66]. This in turn can result in a large portion of otherwise healthy tissue being irradiated. Zeng, C. et al. compared respiratory gating and DIBH in a cohort of pancreatic cancer patients and found comparable accuracy and efficiency between techniques using RPM [52]. Stam, M. et al. investigated kidney motion using MRI during free-breathing gating and BH, finding variation in kidney position in the expiratory phase of free-breathing to be less than 2 mm in 80 % of patients [59]. Mast, M et al found significant reductions in PTV margins were possible with IBH, and 95 % of patients were able to comply with their BH procedure. This

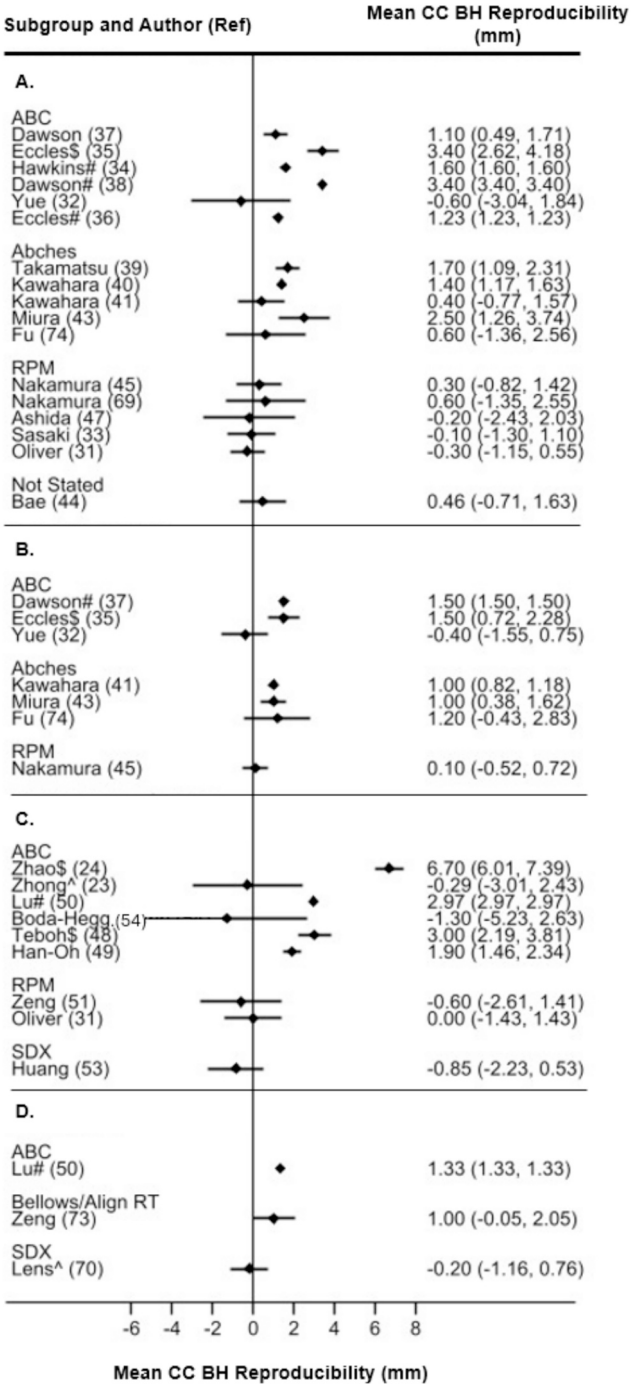

Fig. 2. Mean CC BH Reproducibility of Included Studies. Mean (mm) (and 95% confidence interval of mean) cranio-caudal BH position reproducibility of included studies for A. expiration inter-fraction; B. expiration intra-fraction; C. inspiration inter-fraction; and D. inspiration intra-fraction. # No error bars could be estimated as the standard deviation was not provided. $ Standard deviated estimated from range in values provided.^IBH used instead of DIBH.

compares to only 60–65 % of patients able to comply with BH requirements in a previous study [37]. Compared to free-breathing, a BH strategy in SBRT of liver lesions for instance, can significantly reduce the dose to normal liver tissue (V20 Gy, V30 Gy), and OARs such as the bowel [67].

One limitation in summarising the available literature was overcoming inconsistencies of both outcome measures and BH types among the included studies. Reproducibility, for instance, may be defined as inter-fraction or intra-fraction. Intra-fraction can also be further defined as the difference in position from one BH to the next, or one image to the next, where an image may be acquired during a single BH, or as a combination of multiple BHs, as is commonly required for CBCT acquisitions. Many of the included studies either did not define reproducibility clearly or gave very brief descriptions of how reproducibility measurements were conducted. In these cases, categorising reproducibility as inter- or intra-fraction required the author's best judgement, based on the descriptions available in each paper's methodology. Similarly, definitions of BH types varied amongst published studies, as there remains a lack of consensus in the literature. For instance, DIBH was defined by Zhao as 70–80 % of total lung capacity [24], but as 85 % by Huang [53], and as 100 % by Lens [56]. Categorisation into either IBH or DIBH required the author's discretion in many instances, based on the available descriptions provided in each study.

Another limitation in the evaluation of included studies was the frequent use of surrogates for tumour position in image guidance strategies, with fiducial markers used in lieu of direct visualisation of the tumour. Such markers included lipiodol, cavities following *trans*-arterial chemo-embolization and implanted surgical markers. In the absence of any markers, the diaphragm was often used as a surrogate for tumour motion. Yang et al, investigated the correlation between diaphragm and tumour position in a cohort of liver radiation therapy patients, finding high concordance with tumour position, particularly for tumours close to the diaphragm [68]. They concluded the diaphragm could be considered a reasonable surrogate for tumour motion.

A systematic review of the literature was conducted, and 41 studies were identified reporting on BH tumour position reproducibility, stability and time in upper abdominal radiation therapy. No single BH type or intervention could be considered preferable, as overlapping ranges of reproducibility and stability were reported among the studies. This systematic literature review comprehensively summarises the available evidence, therefore providing a starting point for departments, from which local practices can be further refined based on institutional-specific protocols.

CRediT authorship contribution statement

Briana Farrugia: Conceptualization, Methodology, Investigation, Formal analysis, Data curation, Writing – original draft, Writing – review & editing. **Kerryn Brown:** Investigation, Data curation, Writing – review & editing. **Kellie Knight:** Writing – review & editing, Supervision. **Caroline Wright:** Writing – review & editing, Supervision.

Funding

This review is supported by the Australian Government's Research Training Program.

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: Briana Farrugia reports financial support was provided by Australian Government's Research Training Program. If there are other authors, they declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgements

We acknowledge the help and support of Cochrane Effective Practice and Organization of Care (EPOC). We wish to thank Mark Tacey for assistance in the production of figures.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.phro.2025.100751.

References

[1] Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, et al. Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA: Cancer J Clin 2021;71:209. https://doi.org/10.3322/caac.21660.
[2] Forner A, Reig M, Bruix J. Hepatocellular carcinoma. Lancet 2018;391:1301–14. https://doi.org/10.1016/S0140-6736(18)30010-2.
[3] Llovet JM, Real MI, Montaña X, Planas R, Coll S, Aponte J, et al. Arterial embolisation or chemoembolisation versus symptomatic treatment in patients with unresectable hepatocellular carcinoma: a randomised controlled trial. Lancet 2002;359:1734–9. https://doi.org/10.1016/S0140-6736(02)08649-X.
[4] Hong TS. Radiotherapy for hepatocellular carcinoma with tumor vascular thrombus: ready for prime time? J Clin Oncol 2013;31:1619–20. https://doi.org/10.1200/JCO.2012.48.2703.
[5] Bujold A, Massey CA, Sykes J, Sherman M, Knox JJ, Dawson LA, et al. Sequential phase i and ii trials of stereotactic body radiotherapy for locally advanced hepatocellular carcinoma. J Clin Oncol 2013;31(13):1631–9. https://doi.org/10.1200/JCO.2012.44.1659.
[6] Klein JMD, Dawson LAMD. Hepatocellular carcinoma radiation therapy: review of evidence and future opportunities. Int J Radiat Oncol Biol Phys 2013;87:22–32. https://doi.org/10.1016/j.ijrobp.2012.08.043.
[7] Bibault J-E, Dewas S, Vautravers-Dewas C, Hollebecque A, Jarraya H, Lacornerie T, et al. Stereotactic body radiation therapy for hepatocellular carcinoma: prognostic factors of local control, overall survival, and toxicity. PLoS One 2013;8:e77472. https://doi.org/10.1371/journal.pone.0077472.
[8] Barry A, Knox JJ, Wei AC, Dawson LA. Can stereotactic body radiotherapy effectively treat hepatocellular carcinoma? J Clin Oncol 2016;34:404–8. https://doi.org/10.1200/JCO.2015.64.8097.
[9] Teague A, Lim K-H, Wang-Gillam A. Advanced pancreatic adenocarcinoma: a review of current treatment strategies and developing therapies. Ther Adv Med Oncol 2015;7:68–84. https://doi.org/10.1177/1758834014564775.
[10] Dobiasch S, Goerig NL, Fietkau R, Combs SE. Essential role of radiation therapy for the treatment of pancreatic cancer: Novel study concepts and established treatment recommendations. Strahlenther Onkol 2018;194:185–95. https://doi.org/10.1007/s00066-017-1227-5.
[11] Escudier B, Porta C, Schmidinger M, Rioux-Leclercq N, Bex A, Khoo V, et al. Renal cell carcinoma: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol 2016;27:v58–68. https://doi.org/10.1093/annonc/mdw328.
[12] Ippolito E, D'Angelillo RM, Fiore M, Molfese E, Trodella L, Ramella S. SBRT: A viable option for treating adrenal gland metastases. Rep Pract Oncol Radiother 2015;20:484–90. https://doi.org/10.1016/j.rpor.2015.05.009.
[13] Manfredi S, Lepage C, Hatem C, Coatmeur O, Faivre J, Bouvier A-M. Epidemiology and management of liver metastases from colorectal cancer. Ann Surg 2006;244:254–9. https://doi.org/10.1097/01.sla.0000217629.94941.cf.
[14] Engstrand J, Nilsson H, Strömberg C, Jonas E, Freedman J. Colorectal cancer liver metastases - a population-based study on incidence, management and survival. BMC Cancer 2018;18:78 -. https://doi.org/10.1186/s12885-017-3925-x.
[15] Zhao H-Y, Gong Y, Ye F-G, Ling H, Hu X. Incidence and prognostic factors of patients with synchronous liver metastases upon initial diagnosis of breast cancer: a population-based study. Cancer Manag Res 2018;10:5937–50. https://doi.org/10.2147/CMAR.S178395.
[16] Horn SR, Stoltzfus KC, Lehrer EJ, Dawson LA, Tchelebi L, Gusani NJ, et al. Epidemiology of liver metastases. Cancer Epidemiol 2020;67:101760. https://doi.org/10.1016/j.canep.2020.101760.
[17] Tree ACD, Khoo VSMD, Eeles RAP, Ahmed MMD, Dearnaley DPP, Hawkins MAMD, et al. Stereotactic body radiotherapy for oligometastases. Lancet Oncol 2013;14:e28–37. https://doi.org/10.1016/S1470-2045(12)70510-7.
[18] Benedict SH, Yenice KM, Followill D, Galvin JM, Hinson W, Kavanagh B, et al. Stereotactic body radiation therapy: the report of AAPM Task Group 101. Med Phys 2010;37:4078–101. https://doi.org/10.1118/1.3438081.
[19] Keall PJ, Mageras GS, Balter JM, Emery RS, Forster KM, Jiang SB, et al. The management of respiratory motion in radiation oncology report of AAPM Task Group 76. Med Phys 2006;33:3874–900. https://doi.org/10.1118/1.2349696.
[20] Kimura T, Hirokawa Y, Murakami Y, Tsujimura M, Nakashima T, Ohno Y, et al. Reproducibility of organ position using voluntary breath-hold method with spirometer for extracranial stereotactic radiotherapy. Int J Radiat Oncol Biol Phys 2004;60:1307–13. https://doi.org/10.1016/j.ijrobp.2004.07.718.
[21] Su L, Iordachita I, Zhang Y, Lee J, Ng SK, Jackson J, et al. Feasibility study of ultrasound imaging for stereotactic body radiation therapy with active breathing

coordinator in pancreatic cancer. J Appl Clin Med Phys 2017;18:84–96. https://doi.org/10.1002/acm2.12100.
[22] Yang W, Fraass BA, Reznik R, Nissen N, Lo S, Jamil LH, et al. Adequacy of inhale/exhale breathhold CT based ITV margins and image-guided registration for free-breathing pancreas and liver SBRT. Radiat Oncol 2014;9:11 -. https://doi.org/10.1186/1748-717X-9-11.
[23] Zhong R, Wang J, Jiang X, He Y, Zhang H, Chen N, et al. Hypofraction radiotherapy of liver tumor using cone beam computed tomography guidance combined with active breath control by long breath-holding. Radiother Oncol 2012;104:379–85. https://doi.org/10.1016/j.radonc.2011.11.007.
[24] Zhao J-D, Xu Z-Y, Zhu J, Qiu J-J, Hu W-G, Cheng L-F, et al. Application of active breathing control in 3-dimensional conformal radiation therapy for hepatocellular carcinoma: The feasibility and benefit. Radiother Oncol 2008;87:439–44. https://doi.org/10.1016/j.radonc.2007.12.006.
[25] Liberati A, Altman DG, Tetzlaff J, Mulrow C, Gøtzsche PC, Ioannidis JPA, et al. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: explanation and elaboration. PLoS Med 2009;6:e1000100. https://doi.org/10.1371/journal.pmed.1000100.
[26] O'Connor D, Green S, Higgins JP. Defining the review question and developing criteria for including studies. Cochrane Handbook for Systematic Reviews of Interventions; 2008. p. 81–94.
[27] (EPOC). CEPaOoC. Data collection form. EPOC resources for review authors. Available from epoc.cochrane.org/epoc-specific-resources-review-authors 2013. epoc.cochrane.org/epoc-specific-resources-review-authors; 2013.
[28] Kmet LM. Standard quality assessment criteria for evaluating primary research papers from a variety of fields. Cook RCLLS, editor.: Alberta Heritage Foundation for Medical Research (AHFMR) HTA Initiative #13. 2004.
[29] Aznar MC, Carrasco Fez P, Corradini S, Mast M, McNair H, Meattini I, et al. ESTRO-ACROP guideline: recommendations on implementation of breath-hold techniques in radiotherapy. Radiother Oncol 2023;185:109734. https://doi.org/10.1016/j.radonc.2023.109734.
[30] Onishi H, Kawakami H, Marino K, Komiyama T, Kuriyama K, Araya M, et al. A simple respiratory indicator for irradiation during voluntary breath holding: a one-touch device without electronic materials. Radiology 2010;255:917–23. https://doi.org/10.1148/radiol.10090890.
[31] Oliver PAK, Yewondwossen M, Summers C, Shaw C, Cwajna S, Syme A. Influence of intra- and interfraction motion on planning target volume margin in liver stereotactic body radiation therapy using breath hold. Adv Radiat Oncol 2021;6:100610. https://doi.org/10.1016/j.adro.2020.10.023.
[32] Yue J, Sun X, Cai J, Yin FF, Yin Y, Zhu J, et al. Lipiodol: a potential direct surrogate for cone-beam computed tomography image guidance in radiotherapy of liver tumors. Int J Radiat Oncol Biol Phys 2012;82(2):834–41. https://doi.org/10.1016/j.ijrobp.2010.12.050.
[33] Sasaki M, Nakamura M, Ono T, Ashida R, Yoshimura M, Nakata 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. J Radiat Res 2020;61:755–65. https://doi.org/10.1093/jrr/rraa054.
[34] Hawkins MA, Brock KK, Eccles C, Moseley D, Jaffray D, Dawson LA. Assessment of residual error in liver position using kV cone-beam computed tomography for liver cancer high-precision radiation therapy. Int J Radiat Oncol Biol Phys 2006;66:610–9. https://doi.org/10.1016/j.ijrobp.2006.03.026.
[35] Eccles C, Brock KK, Bissonnette JP, Hawkins M, Dawson LA. Reproducibility of liver position using active breathing coordinator for liver cancer radiotherapy. Int J Radiat Oncol Biol Phys 2006;64:751–9. https://doi.org/10.1016/j.ijrobp.2005.05.066.
[36] Eccles CLB, Lindsay PEP, Craig TDP, Kim JJMD, Dawson LAMD. Dosimetric impact of image-guided radiotherapy in liver stereotactic radiotherapy. J Med Imaging Radiat Sci 2013;44:5–13. https://doi.org/10.1016/j.jmir.2012.09.001.
[37] Dawson LA, Eccles C, Bissonnette JP, Brock KK. Accuracy of daily image guidance for hypofractionated liver radiotherapy with active breathing control. Int J Radiat Oncol Biol Phys 2005;62:1247–52. https://doi.org/10.1016/j.ijrobp.2005.03.072.
[38] Dawson LA, Eccles C, Craig T. Individualized image guided iso-NTCP based liver cancer SBRT. Acta Oncol 2006;45:856–64. https://doi.org/10.1080/02841860600936369.
[39] Takamatsu S, Takanaka T, Kumano T, Mizuno E, Shibata S, Ohashi S, et al. Reproducibility of diaphragm position assessed with a voluntary breath-holding device. Jpn J Radiol 2013;31(5):357–63. https://doi.org/10.1007/s11604-013-0199-3.
[40] Kawahara D, Ozawa S, Kimura T, Nakashima T, Aita M, Tsuda S, et al. Availability of applying diaphragm matching with the breath-holding technique in stereotactic body radiation therapy for liver tumors. Phys Med 2016;32:557–61. https://doi.org/10.1016/j.ejmp.2016.02.007.
[41] Kawahara D, Ozawa S, Nakashima T, Tsuda S, Ochi Y, Okumura T, et al. Interfractional diaphragm changes during breath-holding in stereotactic body radiotherapy for liver cancer. Rep Pract Oncol Radiother 2018;23(2):84–90. https://doi.org/10.1016/j.rpor.2018.01.007.
[42] Fu HJ, Chen PY, Yang HY, Tsang YW, Lee CY. Liver-directed stereotactic body radiotherapy can be reliably delivered to selected patients without internal fiducial markers – a case series. J Chin Med Assoc 2022;85:1028–32. https://doi.org/10.1097/JCMA.0000000000000798.
[43] Miura H, Ozawa S, Nakao M, Doi Y, Kubo K, Kenjo M, et al. Impact on liver position under breath-hold by computed tomography contrast agents in stereotactic body radiotherapy of liver cancer. Rep Pract Oncol Radiother 2021;26(6):1035–44. https://doi.org/10.5603/RPOR.a2021.0131.
[44] Bae JS, Kim DH, Kim WT, Kim YH, Park D, Ki YK. The role of surgical clips in the evaluation of interfractional uncertainty for treatment of hepatobiliary and pancreatic cancer with postoperative radiotherapy. Radiat Oncol J 2017;35:65–70. https://doi.org/10.3857/roj.2016.02019.
[45] Nakamura M, Shibuya K, Shiinoki T, Matsuo Y, Nakamura A, Nakata M, et al. Positional reproducibility of pancreatic tumors under end-exhalation breath-hold conditions using a visual feedback technique. Int J Radiat Oncol Biol Phys 2011;79(5):1565–71. https://doi.org/10.1016/j.ijrobp.2010.05.046.
[46] Nakamura M, Akimoto M, Ono T, Nakamura A, Yano S, Nakata M, et al. Interfraction positional variation in pancreatic tumors using daily breath-hold cone-beam computed tomography with visual feedback. J Appl Clin Med Phys 2015;16:5123. https://doi.org/10.1120/jacmp.v16i2.5123.
[47] Ashida R, Nakamura M, Yoshimura M, Mizowaki T. Impact of interfractional anatomical variation and setup correction methods on interfractional dose variation in IMPT and VMAT plans for pancreatic cancer patients: A planning study. J Appl Clin Med Phys 2020;21:49–59. https://doi.org/10.1002/acm2.12883.
[48] Teboh RF, Srinivasan S, Ng SP, Aliru ML, Herman JM. Setup management for stereotactic body radiation therapy of patients with pancreatic cancer treated via the breath-hold technique. Pract Radiat Oncol 2020;10(4):e280–9. https://doi.org/10.1016/j.prro.2019.10.012.
[49] Han-Oh S, Hill C, Kang-Hsin Wang K, Ding K, Wright JL, Alcorn 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. Adv Radiat Oncol 2021;6:100655. https://doi.org/10.1016/j.adro.2021.100655.
[50] Lu L, Diaconu C, Djemil T, Videtic GM, Abdel-Wahab M, Yu N, et al. Intra- and inter-fractional liver and lung tumor motions treated with sbrt under active breathing control. J Appl Clin Med Phys 2018;19(1):39–45. https://doi.org/10.1002/acm2.12220.
[51] Zeng C, Xiong W, Li X, Reyngold M, Gewanter RM, Cuaron JJ, et al. Intrafraction tumor motion during deep inspiration breath hold pancreatic cancer treatment. J Appl Clin Med Phys 2019;20(5):37–43. https://doi.org/10.1002/acm2.12577.
[52] Zeng C, Li X, Lu W, Reyngold M, Gewanter RM, Cuaron JJ, et al. Accuracy and efficiency of respiratory gating comparable to deep inspiration breath hold for pancreatic cancer treatment. J Appl Clin Med Phys 2021;22:218–25. https://doi.org/10.1002/acm2.13137.
[53] Huang T-J, Tien Y, Wu J-K, Huang W-T, Cheng J-C-H. Impact of breath-hold level on positional error aligned by stent/Lipiodol in Hepatobiliary radiotherapy with breath-hold respiratory control. BMC Cancer 2020;20:613–9. https://doi.org/10.1186/s12885-020-07082-y.
[54] Boda-Heggemann J, Sihono DSK, Streb L, Mertens L, Vogel L, Stieler F, et al. Ultrasound-based repositioning and real-time monitoring for abdominal SBRT in DIBH. Phys Med 2019;65:46–52. https://doi.org/10.1016/j.ejmp.2019.08.003.
[55] Farrugia B, Knight K, Wright C, Tacey M, Foroudi F, Chao M, 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. Int J Radiat Oncol Biol Phys 2021;111:1289–97. https://doi.org/10.1016/j.ijrobp.2021.08.001.
[56] Lens E, Gurney-Champion OJ, Tekelenburg DR, van Kesteren Z, Parkes MJ, van Tienhoven G, et al. Abdominal organ motion during inhalation and exhalation breath-holds: pancreatic motion at different lung volumes compared. Radiother Oncol 2016;121:268–75. https://doi.org/10.1016/j.radonc.2016.09.012.
[57] van Kesteren Z, Veldman JK, Parkes MJ, Stevens MF, Balasupramaniam P, van den Aardweg JG, et al. Quantifying the reduction of respiratory motion by mechanical ventilation with MRI for radiotherapy. Radiat Oncol 2022;17:99 -. https://doi.org/10.1186/s13014-022-02068-5.
[58] Mast M, Kouwenhoven E, Roos J, Geen S, Egmond J, Santvoort J, et al. Two years' experience with inspiration breath-hold in liver sbrt. Tech Innov Patient Support Radiat Oncol 2018;7:1–5. https://doi.org/10.1016/j.tipsro.2018.04.001.
[59] Stam MK, van Vulpen M, Barendrecht MM, Zonnenberg BA, Intven M, Crijns SPM, et al. Kidney motion during free breathing and breath hold for MR-guided radiotherapy. Phys Med Biol 2013;58:2235–45. https://doi.org/10.1088/0031-9155/58/7/2235.
[60] Vogel L, Sihono DSK, Weiss C, Lohr F, Stieler F, Wertz H, 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. Radiother Oncol 2018;129:441–8. https://doi.org/10.1016/j.radonc.2018.07.007.
[61] Sörnsen Koste JR, Palacios MA, Bruynzeel AME, Slotman BJ, Senan S, Lagerwaard FJ. MR-guided gated stereotactic radiation therapy delivery for lung, adrenal, and pancreatic tumors: a geometric analysis. Int J Radiat Oncol Biol Phys 2018;102:858–66. https://doi.org/10.1016/j.ijrobp.2018.05.048.
[62] Fracchiolla F, Dionisi F, Righetto R, Widesott L, Giacomelli I, Cartechini G, et al. Clinical implementation of pencil beam scanning proton therapy for liver cancer with forced deep expiration breath hold. Radiother Oncol 2021;154:137–44. https://doi.org/10.1016/j.radonc.2020.09.035.
[63] Garibaldi C, Catalano G, Baroni G, Tagaste B, Riboldi M, Spadea MF, et al. Deep inspiration breath-hold technique guided by an opto-electronic system for extracranial stereotactic treatments. J Appl Clin Med Phys 2013;14:14–25. https://doi.org/10.1120/jacmp.v14i4.4087.
[64] Abbas H, Chang B, Chen ZJ. Motion management in gastrointestinal cancers. J Gastrointest Oncol 2014;5:223–35. https://doi.org/10.3978/j.issn.2078-6891.2014.028.
[65] Case RBBS, Sonke J-J-P-D, Moseley DJPD, Kim JMD, Brock KKPD, Dawson LAMD. Inter- and intrafraction variability in liver position in non–breath-hold stereotactic

body radiotherapy. Int J Radiat Oncol Biol Phys 2009;75:302–8. https://doi.org/10.1016/j.ijrobp.2009.03.058.
[66] Suramo I, Päivänsalo M, Myllylä V. Cranio-caudal movements of the liver, pancreas and kidneys in respiration. Acta Radiol Diagn 1984;25:129–31. https://doi.org/10.1177/028418518402500208.
[67] Katano A, Noyama T, Morishima K, Nozawa Y, Yamashita H. Dosimetric comparison study between free breathing and breath hold techniques in patients treated by liver-directed stereotactic body radiation therapy. Curēus 2023;15:e40382. https://doi.org/10.7759/cureus.40382.
[68] Yang J, Cai J, Wang H, Chang Z, Czito BG, Bashir MR, et al. Is diaphragm motion a good surrogate for liver tumor motion? Int J Radiat Oncol Biol Phys 2014;90:952–8. https://doi.org/10.1016/j.ijrobp.2014.07.028.
[69] Nakamura M, Akimoto M, Ono T, Nakamura A, Kishi T, Yano S, et al. Interfraction positional variation in pancreatic tumors using daily breath-hold cone-beam computed tomography with visual feedback. J Appl Clin Med Phys 2015;16:108–16. https://doi.org/10.1120/jacmp.v16i2.5123.
[70] Lens E, Horst A, Bel Versteijne AE, Van Tienhoven G. Considerable pancreatic tumor motion during breath-holding. Acta Oncol 2016;55:1360–8. https://doi.org/10.1080/0284186X.2016.1221532.
[71] Lee S, Zheng Y, Podder T, Biswas T, Verma V, Goss M, et al. Tumor localization accuracy for high-precision radiotherapy during active breath-hold. Radiother Oncol 2019;137:145–52. https://doi.org/10.1016/j.radonc.2019.04.036.
[72] Lu L, Ouyang Z, Lin S, Mastroianni A, Stephans KL, Xia P. Dosimetric assessment of patient-specific breath-hold reproducibility on liver motion for SBRT planning. J Appl Clin Med Phys 2020;21:77–83. https://doi.org/10.1002/acm2.12887.
[73] Zeng C, Lu W, Reyngold M, Cuaron JJ, Li X, Cerviño L, et al. Intrafractional accuracy and efficiency of a surface imaging system for deep inspiration breath hold during ablative gastrointestinal cancer treatment. J Appl Clin Med Phys 2022;23:e13740. https://doi.org/10.1002/acm2.13740.
[74] Fu H-J, Chen P-Y, Yang H-Y, Tsang Y-W, Lee C-Y. Liver-directed stereotactic body radiotherapy can be reliably delivered to selected patients without internal fiducial markers—a case series. J Chin Med Assoc 2022;85:1028–32. https://doi.org/10.1097/JCMA.0000000000000798.