Original Research Article

Adoption of respiratory motion management in radiation therapy

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ABSTRACT

Background and Purpose: A survey on the patterns of practice of respiratory motion management (MM) was distributed to 111 radiation therapy facilities to inform the development of an end-to-end dosimetry audit including respiratory motion.

Materials and methods: The survey (distributed via REDCap) asked facilities to provide information specific to the combinations of MM techniques (breath-hold gating – BHG, internal target volume – ITV, free-breathing gating – FBG, mid-ventilation – MidV, tumour tracking – TT), sites treated (thorax, upper abdomen, lower abdomen), and fractionation regimes (conventional, stereotactic ablative body radiation therapy – SABR) used in their clinic.

Results: The survey was completed by 78% of facilities, with 98% of respondents indicating that they used at least one form of MM. The ITV approach was common to all MM-users, used for thoracic treatments by 89% of respondents, and upper and lower abdominal treatments by 38%. BHG was the next most prevalent (41% of MM users), with applications in upper abdominal and thoracic treatment sites (28% vs 25% respectively), but minimal use in the lower abdomen (9%). FBG and TT were utilised sparingly (17%, 7% respectively), and MidV was not selected at all.

Conclusions: Two distinct treatment workflows (including use of motion limitation, imaging used for motion assessment, dose calculation, and image guidance procedures) were identified for the ITV and BHG MM techniques, to form the basis of the initial audit. Thoracic SABR with the ITV approach was common to nearly all respondents, while upper abdominal SABR using BHG stood out as more technically challenging. Other MM techniques were sparsely used, but may be considered for future audit development.

1. Introduction

Respiratory motion can degrade the quality and effectiveness of radiation therapy (RT) in treatments of the thorax and abdomen where tumour motion may be in the order of centimetres [1–6]. Challenges related to respiratory motion are present at all stages of the patient treatment pathway [6]. At simulation, respiratory-correlated or time-resolved imaging is required to capture the motion. If this imaging is not acquired correctly motion may not be accurately captured, leading to errors in target contouring and a potential geographic miss [7,8]. Changes in respiration between simulation and treatment may lead to target under- or over-doses depending on the nature of the change [8–10]. Such changes may not be obvious during the patient set-up and image guidance procedures, adding further scope for geographic miss [11–13]. During treatment planning, dose accumulation in the moving anatomy is commonly estimated using a single static image, leading to increased uncertainty in the 3D dose calculation [1,14–16]. This can vary in magnitude depending on the choice of image and the patient's

breathing characteristics [9,17]. While motion management (MM) can effectively mitigate these challenges, limitations remain which can contribute to sub-optimal treatment outcomes.

End-to-end dosimetry audits aim to capture potential mistakes made in the RT treatment pathway which may result in dosimetric errors [18]. Audit procedures are also frequently used for clinical trial credentialing, to ensure participating facilities are achieving a uniform minimum standard of treatment quality [19–23]. Dosimetry audits and clinical trial QA procedures involving simulated respiratory motion have shown worsened measurement outcomes with respect to their static equivalents [24–26]. While patterns of failure have been hypothesised to be related to the motion of the targets, rates of failure were not necessarily improved by the use of MM techniques, and no direct causes were established [24,25].

Recent data from Anastasi et al [27] suggested that some form of MM is used by 68 % of RT facilities globally [27], however, the patterns of use including means of implementing specific techniques were not captured. In this work, a survey was performed to capture the current extent of MM utilisation, as well as how MM was implemented practically at each stage in the treatment pathway. This data will inform the development of an end-to-end dosimetry audit explicitly for MM, ensuring that it is a true test of current practice, capable of rendering clinically meaningful outcomes.

2. Materials and methods

The survey was developed and distributed using Research Electronic Data Capture (REDCap) v10.8 [28]. It was distributed to 111 Australian Clinical Dosimetry Service (ACDS)-subscribed facilities in December 2020 (100 % of Australian, 40 % of NZ RT providers), and participants were given three months to respond. Facilities in the database were categorised by the type of healthcare provider (public or private), and geographic location (in a major capital city or not - metropolitan or regional). To ensure the collection of high quality data (eg – no duplications) and correct assignment to these demographics, responses were not anonymised during the collection phase, however, were anonymised for analysis.

The survey content (questions, format, and accompanying materials) was developed by the lead authors of this article, in consultation with experts within the Global Harmonisation Group (GHG) network [29], and the Quality Manager at the Australian Radiation Protection and Nuclear Safety Agency (ARPANSA). MM was defined as a treatment technique which aims to mitigate the effects of intra-fraction respiratory motion. This excluded instances where MM improves target-OAR geometry alone, hence, breast RT was not captured in this survey. Five types of MM were considered – motion encompassing techniques using an internal target volume (ITV) [30] or mid-ventilation (MidV) [31], gating techniques using breath-hold (BHG) and free-breathing (FBG) respiratory patterns, and tumour tracking (TT).

The survey was designed to capture highly granular data, such that each responding facility's pattern of practice for every combination of treatment site, MM technique and fractionation could be discerned. Responses were grouped into three main anatomical treatment sites rather than specific primary tumour groups – thorax, upper, and lower abdomen. For each MM technique, participants were asked for which treatment sites they applied, whether motion limitation strategies are used, what imaging is used for motion assessment and treatment planning, what image-guidance procedures are performed, and what types of treatment deliveries are used. Multiple responses were allowed for most questions, to capture all relevant pathways available to each facility, but respondents were not asked to provide estimates of caseloads or proportional use of each selection. In addition, facilities were asked to distinguish between voluntary- (eg – Varian Real-Time Position Management (RPM)) and spirometry-based (eg – Elekta Active Breathing Coordinator (ABC)) BHG, as well as a choice of breath-hold type (deep inspiration (DIBH), inspiration (IBH), or expiration (EBH)) where

relevant. The survey structure and selection options are outlined in Fig S1 in the Supplementary Material.

All statistical testing was conducted in Python (Python Software Foundation, Python Language Reference, v3.8 available at http s://www.python.org). To examine patterns of response between sub-groups, Z-tests of proportional difference were conducted using the statsmodels module (v0.12.2) [32]. This testing was used to examine differences in proportional selection of individual response options throughout the survey (treatment sites, MM techniques, use of motion limitation, use of imaging) between opposing groups identified in the response database (metropolitan/regional, public/private, motion limitation users/non-users).

Mann-Whitney U tests were conducted using the SciPy package (v1.7.1) [33] to test for differences in the number of selected responses for types of imaging (motion assessment, image guidance) used between opposing groups (same as above) in the response database. In all instances, two-sided exact p-values were reported, with significance defined at the 0.050 level.

3. Results

3.1. Response demographics

Eighty-seven out of 111 facilities completed the survey in full (78 %). Response rates from the major demographics were 84 % and 69 % for metropolitan and regional, and 75 % and 81 % for public and private facilities.

Eighty-five out of 87 respondents (98 %) used MM. 100 % of MM-users selected the ITV approach, 41 % BHG, 17 % FBG and 7 % TT. No respondents selected MidV. The use of each MM technique by treatment site and fractionation (relative to all MM-users) is shown in Fig. 1.a-b. The most common combination was thoracic SABR with the ITV approach (89 % of MM-users). While BHG was selected by 41 % of MM-users, only 8 % of respondents selected this technique for conventionally fractionated treatments. Selections for BHG SABR were divided between the upper abdominal and thoracic treatment sites (28 % and 25 % of MM-users respectively), while only 14 % of MM-users selected both.

BHG SABR showed a bias towards metropolitan, public facilities (Fig. 1.c-f), however, significant differences between opposing demographics were only observed for techniques with low utilisation overall (FBG SABR, BHG conventional). When examining total selections for each treatment site (in combination with any MM technique), there were no significant differences between metropolitan and regional facilities (p > 0.07 for all sites, Fig. 2.a-b), but there was a significant difference between public and private (p < 0.05, Fig. 2.c-d). Most notably, 60 % of public facilities but only 31 % of private facilities provided responses for upper abdominal SABR (p = 0.01).

Amongst BHG-users, 80 % of respondents indicated that they used a voluntary approach, with the remainder using a spirometry approach. The proportion of spirometry BHG-users was not significantly different to the proportion of respondents with Elekta linacs according to the ACDS database (34 %, p = 0.12). Gating on inhale was primarily selected for thoracic BHG (96 % SABR, 86 % conventional), while exhale was mostly selected for upper abdominal BHG (82 % SABR, 67 % conventional).

3.2. Pre-treatment clinical practice

Remaining results are focussed on the BHG and ITV MM techniques, due to them making up the majority of responses.

Motion limitation strategies were mostly selected for abdominal SABR treatments (Fig. 3). Abdominal compression accounted for 84 % of responses for motion limitation strategies, with other external immobilisation options (vacuum drape, thermoplastic cast) and continuous positive airway pressure (CPAP – one facility only) making up the
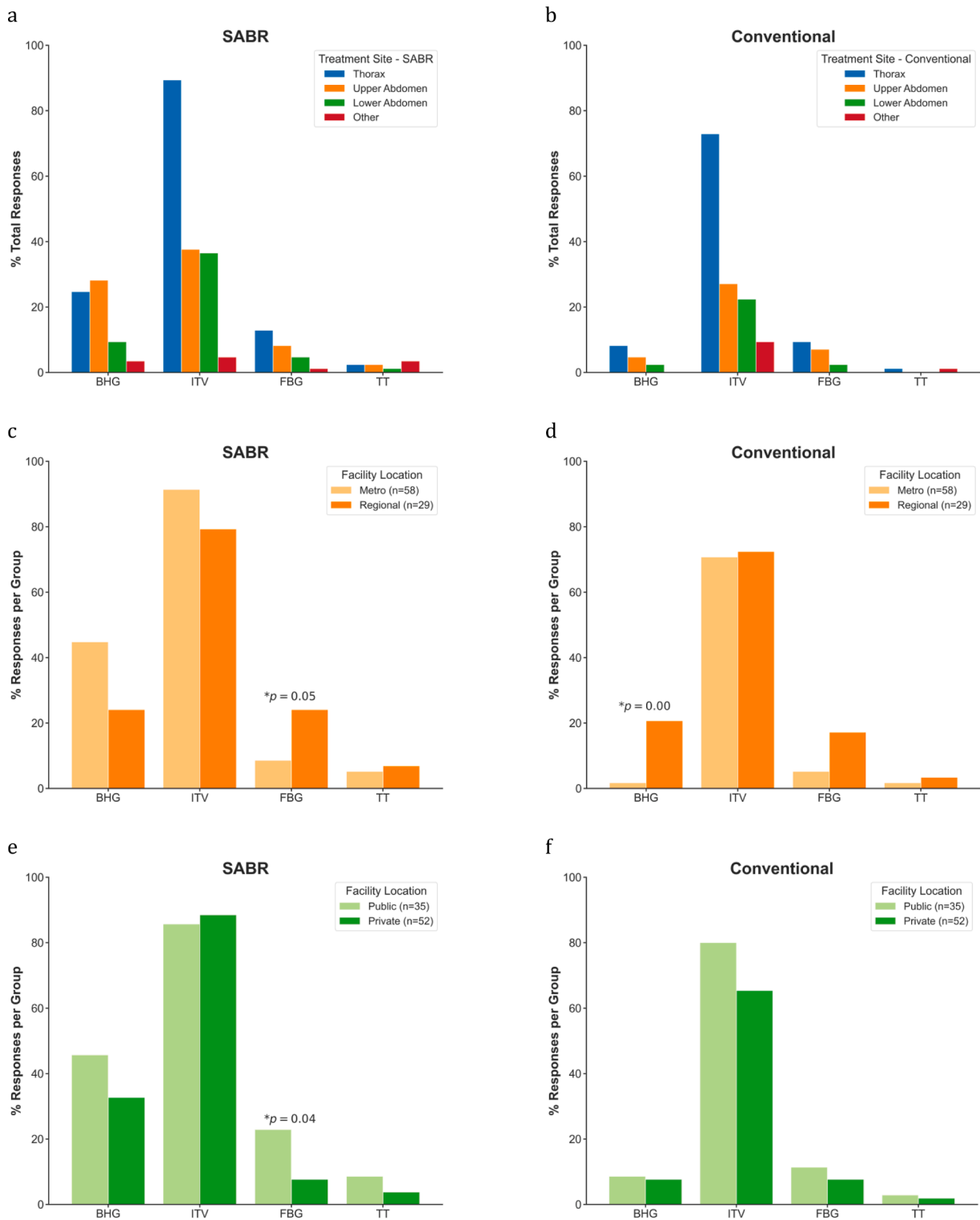
Fig. 1. Utilisation of each MM technique by treatment site for a) SABR and b) Conventional treatments as a percentage of total survey respondents. c) and d) show the total proportions within the metropolitan and regional demographics, and e) and f) for the public and private response groups.

remaining responses. There were no significant differences in utilisation of motion limitation between metropolitan and regional, or between public and private facilities for any treatment site (p > 0.07).

Many imaging modalities (3DCT, phase-binned 4DCT, PET-CT) were selected in similar proportions for motion assessment, regardless of choice of treatment site or fractionation (Fig. 4.a-d). The majority of respondents selected phase-binned 4DCT imaging for motion assessment

for both SABR (79 % respondents across all MM techniques) and conventional (83 %) fractionations. Selections of magnetic resonance imaging (MRI – including BH) and CT with contrast (CT +), however, were skewed towards upper abdominal SABR.

The choice of dataset used for dose calculation depended on the MM technique. For the BHG approach (Fig. 5.a) the most common choice for all treatment sites was BH CT (73 % SABR, 63 % conventional). In
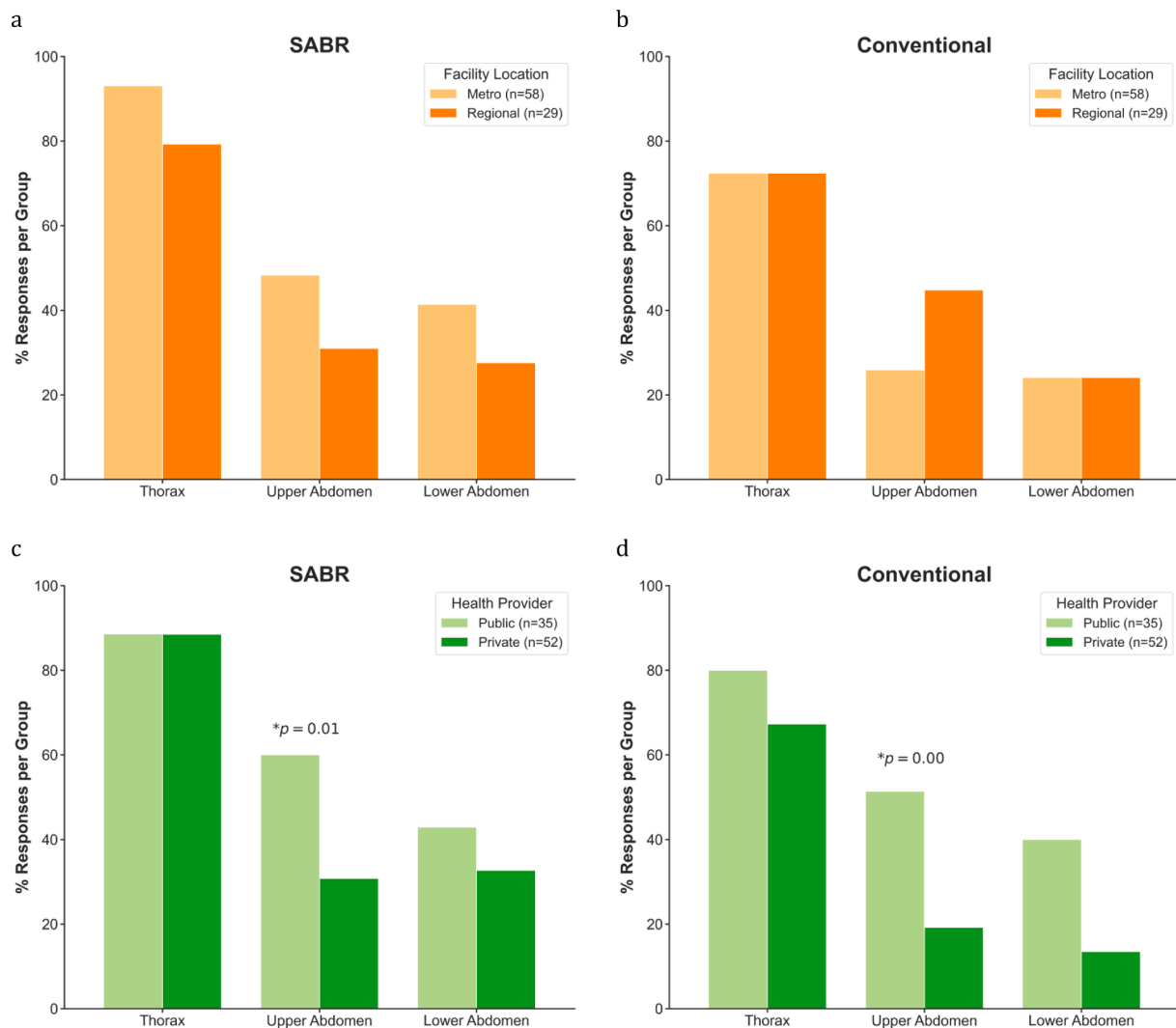
Fig. 2. Total use of motion management strategies for each treatment site within the metropolitan (a-b) and regional and public and private (c-d) demographic groups.

addition, all 'Other' responses were described as the 'average of multiple BH CTs' by these respondents (12 % SABR, 19 % conventional).

For the ITV approach (Fig. 5.b), the most common choice for all treatment sites was 4DCT AIP (74 % SABR, 58 % conventional). All 'Other' responses (8 % SABR, 11 % conventional) were described as 'a short 4DCT AIP spliced into a longer 3DCT' or similar.

3.3. Clinical practice at treatment

Selection of pre-treatment imaging modalities was different for each MM technique. For the ITV approach, the most commonly selected modality was 3D CBCT (66 %), while most respondents selected BHG CBCT (80 %) for BHG. Choice of BHG technique (voluntary or spirometry) did not significantly affect the number or type of imaging modalities selected (p > 0.30).

Selection of IGRT matching approach did not vary greatly between MM techniques, but patterns of response were different between treatment sites and fractionation. Responses for thoracic treatment sites were dominated by 'match to target' (96 % SABR, 81 % conventional). For the upper abdomen, rates of selection were similar between 'match to target' (75 % SABR, 58 % conventional) and 'soft tissue match to anatomical surrogate' (74 % SABR, 61 % conventional). A similar pattern was observed for lower abdominal sites. 'Match to fiducial markers in target' was also commonly selected for the upper abdomen,

predominantly for SABR treatments (68 %, 27 % conventional). All 'other' responses were selected for the upper abdomen (5 % SABR, 0 % conventional), and described as 'lipiodol'.

The most common treatment delivery type for all MM techniques was volumetric modulated arc therapy (VMAT), with 94 % of MM-users choosing this option for at least one form of MM. Intensity modulated RT (IMRT) was also selected for all MM techniques. No respondents utilised helical IMRT deliveries, and all respondents utilising robotic arm-based treatments selected TT as well as the ITV approach (2 % MM-users).

All respondents who utilised robotic arm deliveries (33 % TT-users) performed TT by linac tracking, and all others by couch tracking. Respondents with C-arm linacs provided comments describing the kV intrafraction monitoring (KIM) workflow used in trans-Tasman Radiation Oncology Group (TROG) trials [34,35], where the motion of the target is monitored in real-time via continuous kV imaging tracking the position of markers, but the treatment beam must be interrupted to manually reposition the patient via couch motions. No respondents utilised aperture adjustment methods for TT.

Overall, responses for each combination of MM technique (BHG or ITV) and treatment site (thorax or abdomen) showed clear patterns of selection, and the most common treatment pathways are depicted in Fig. 6.
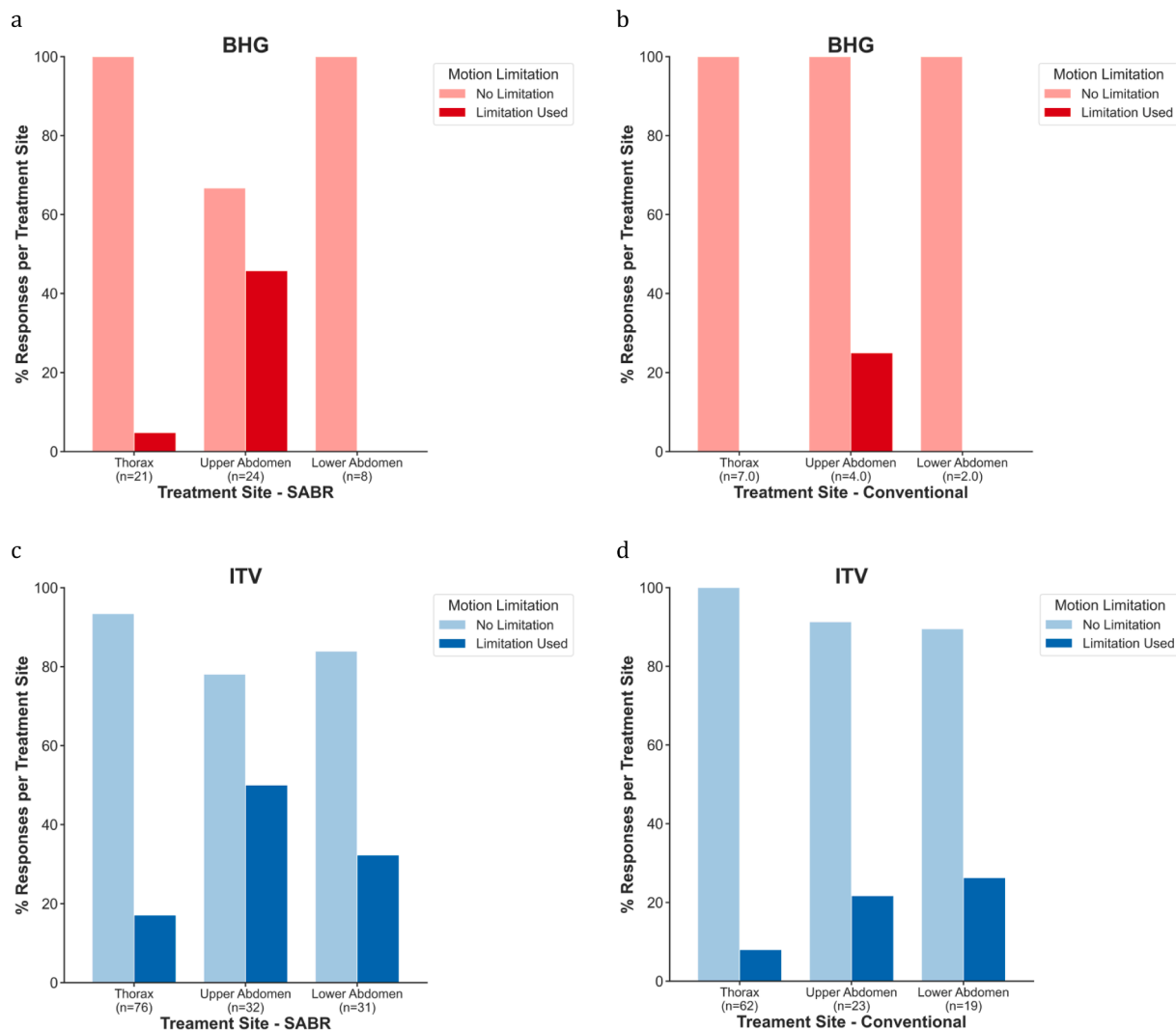
Fig. 3. Total use of motion limitation strategies in combination with the BHG (a-b) and ITV (c-d) techniques, for each treatment site.

4. Discussion

The survey responses provided a detailed picture of the workflows used by Australian and New Zealand RT facilities for each combination of MM technique, treatment site, and fractionation. The data collected in this survey showed that MM is widely used in the ANZ region, however, is generally limited to the ITV and BHG techniques. Hence, the workflows involved in implementing these techniques (Fig. 6) will form the basis of the initial audit design. Thoracic SABR with the ITV approach was common to nearly all respondents, establishing this as a high priority for the audit. Upper abdominal SABR, in particular using BHG, stood out as a more technically challenging treatment with a more complex treatment pathway, including motion limitation and additional imaging beyond 4DCT.

One interesting pattern in the response demographics was the skew towards regional facilities in the selection of some low response gating options, such as FBG. This was the least-represented demographic surveyed (69 %), so there was potentially some bias towards high MM-utility facilities in the responses. However, high utilisation of the less common MM techniques may also be a true result, influenced by the regional facility's lack of ability to refer cases to nearby hospitals.

Given that FBG and BHG have similar hardware requirements, the low interest in FBG may simply be related to its worse duty cycle, rather than a lack of access to technology [11]. Longer duty cycles and more gating events may exacerbate the internal-external correlation

uncertainty for facilities relying on external markers for monitoring/ gating on [36], however, too few responses for FBG were collected to determine whether this was a concern amongst survey respondents. Low utilisation of FBG (13 % respondents) was also captured by Anastasi et al [27]. Some studies of lung cancer patient cohorts have shown that the dosimetric benefits of FBG are modest compared to BHG [37,38], which may also contribute to its low utility.

We reported lower rates of response for TT than Anastasi et al [27] (7 % versus 17 %). This discrepancy was likely due to the lack of robotic-arm linacs in the ANZ data (2 % of respondents, versus 10 %), where TT is offered as a commercial solution. All TT-users with C-arm linacs indicated they had participated in TROG trials using the KIM software. The lack of commercial solutions for conventional linacs is clearly still a major barrier to implementing TT in the clinic outside of the research setting, despite mounting evidence showing its benefit and feasibility [39–41]. Currently in ANZ, facilities who participate in KIM trials for TT undergo a credentialing process for this software, but it does not involve dosimetric measurements [35]. Hence, an independent dosimetry audit administered by the ACDS would still address an unmet need for the few facilities that utilise TT, and as such is considered a long term goal for the audit.

The MidV approach was not utilised within the ANZ region, while the ITV approach was utilised by all MM-users. This result might reflect a preference for a standardised target volume definition based on established consensus guidelines, since MidV volume definitions are patient-
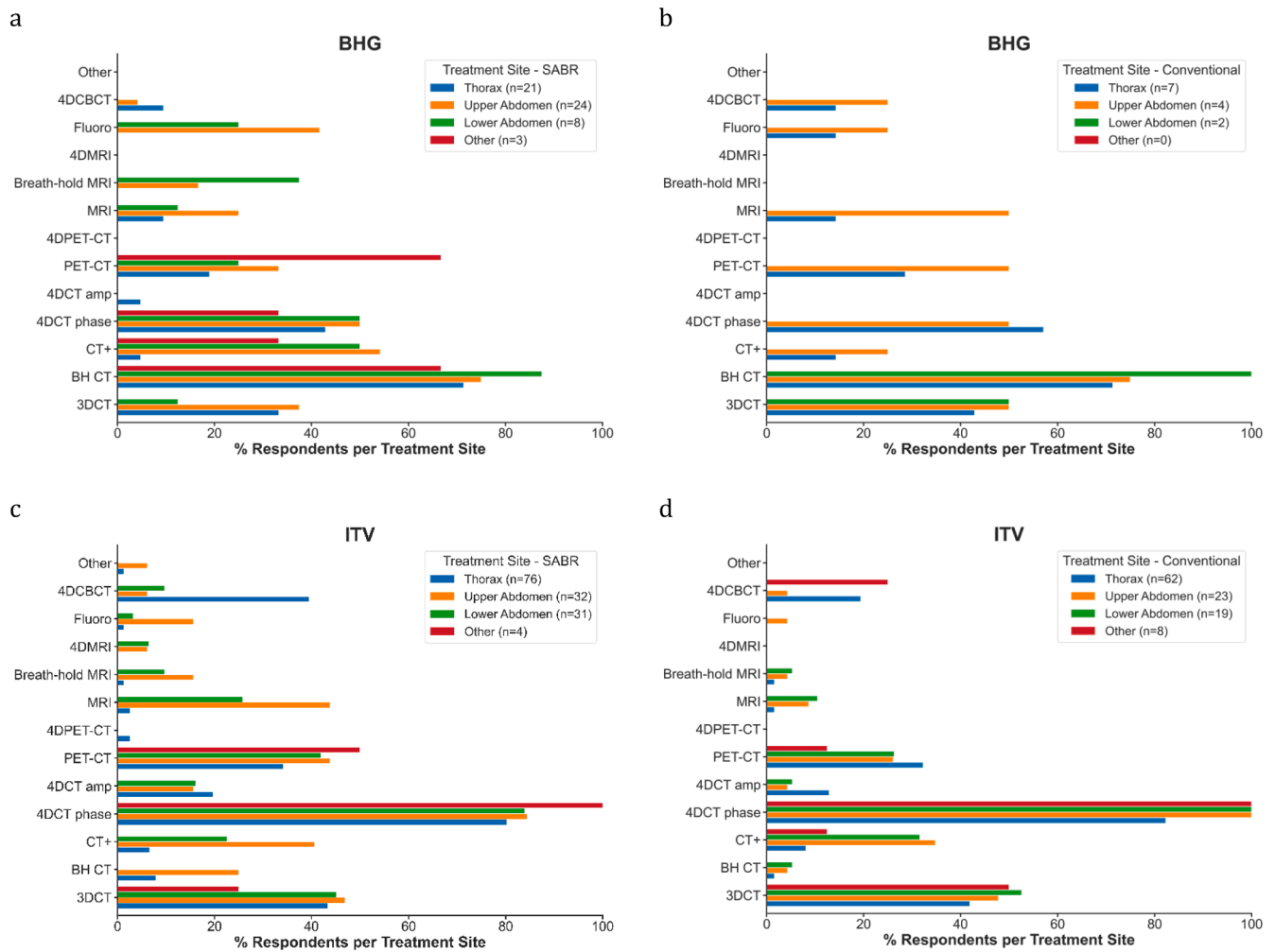
Fig. 4. Choice of imaging for motion assessment for each combination of fractionation, treatment site, and MM technique (a-b = BHG, c-d = ITV).
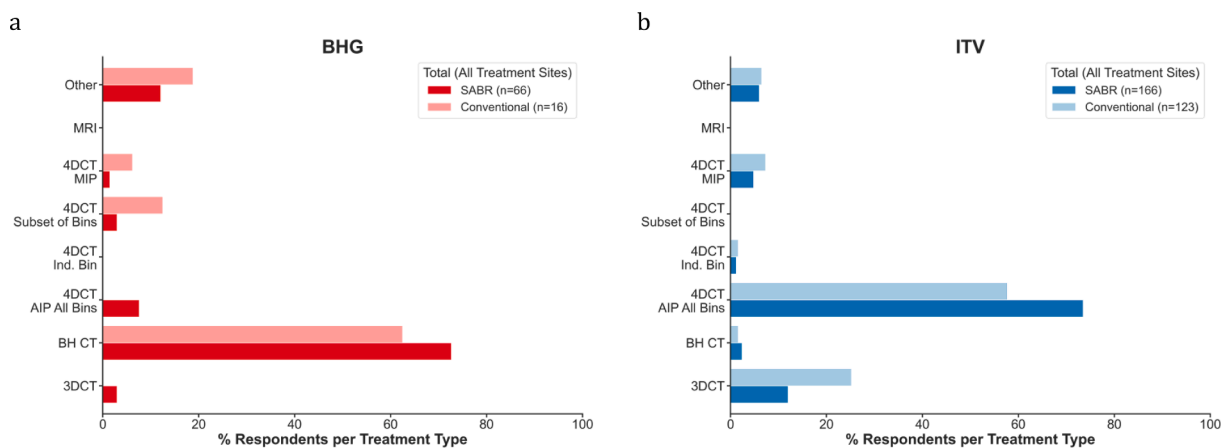

Fig. 5. Choice of imaging dose calculation for each combination of fractionation and MM technique (a = BHG, b = ITV).

specific and more labour intensive. It also may have been influenced by the regional phase III clinical trials conducted through TROG (09.02 CHISEL and 13.01 SAFRON II) which provided compelling clinical evidence for lung SABR [42,43]. The trial outcomes have formed the basis of regional consensus guidelines which specify an ITV be used [44,45], despite evidence from other regions which showed similar outcomes can be achieved using smaller treatment volumes with a MidV approach [46,47].

Selection of motion limitation strategies was mostly limited to abdominal SABR. Further, BHG SABR was the only MM technique for which the upper abdomen was the most common treatment site. Both results are consistent with current literature, which has shown that reducing target sizes with these techniques can improve tumour control probability in liver SABR at no cost to OARs by allowing higher prescription doses [47,48]. It would be ideal to incorporate abdominal compression in the audit due to its popularity of use, but this may not be
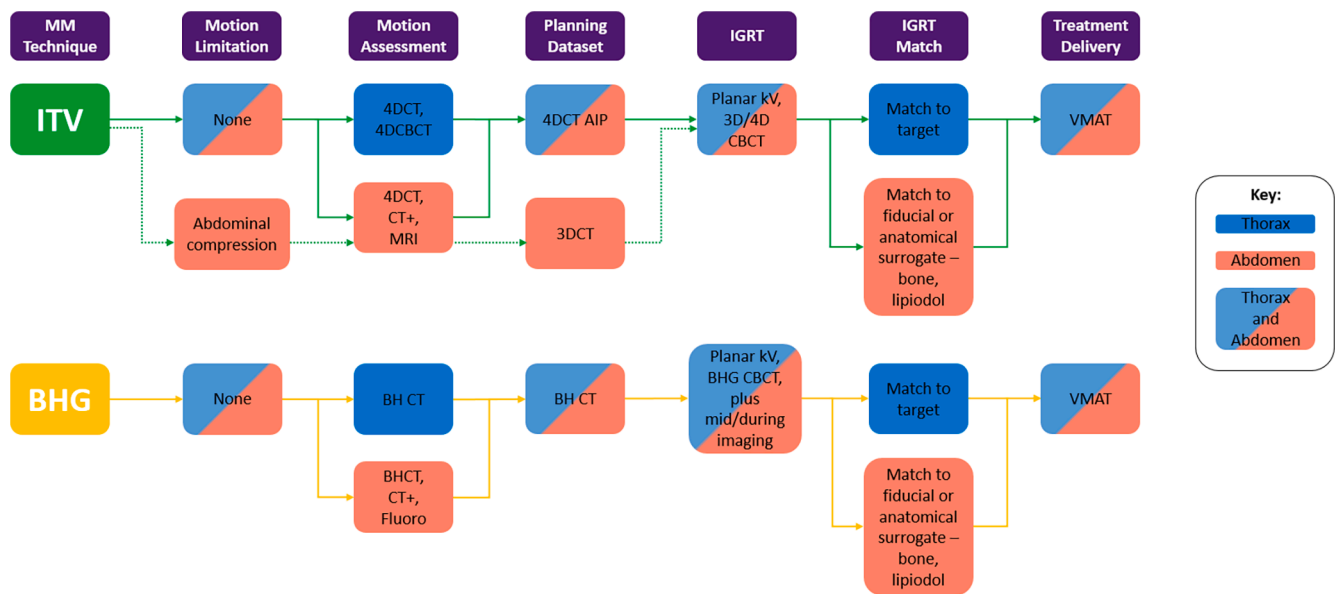
Fig. 6. Diagram summarising the key outcome of the survey – the most common treatment pathways for ITV and BHG treatments. Responses for upper and lower abdominal treatments have been combined, as well as for SABR and conventional treatments.

practical given the differences in mechanics between a human and a robotic phantom. Given the similarity in workflows between ITV with abdominal compression and the BHG approach (Fig. 6), however, it is not necessary to have an audit which addresses both techniques. The higher rate of selection of voluntary breath-hold over spirometry-based approaches (80 % vs 20 %) was most-likely attributed to the difference in vendor representation amongst the survey respondents. Despite one technology being more prevalent than the other, the audit must be compatible with both, but will potentially provide insight as to whether any differences in effectiveness exist between them, which was not captured in the survey.

Respiratory-correlated imaging (4DCT) was the mostly widely used imaging modality, common to all treatment sites. Including this imaging modality in the audit procedure will be essential to emulating a clinical motion assessment workflow. Upper abdominal SABR, however, also showed higher rates of response for non-planning CT imaging modalities (CT+, MRI, fluoroscopy), suggesting that a 4DCT alone is not always enough to completely visualise the target and assess its motion. For the audit to robustly test the motion assessment workflow treatments to the upper abdomen, the phantom should replicate this challenge. The target therefore should be low in contrast, but should also be implanted with fiducial markers or have other surrounding landmarks which allow the motion of the lesion to be estimated in a similar fashion to clinical treatments. This design will also enable clinically-representative image guidance procedures to be followed during the on-site dosimetry audit, which were found to be highly dependent on the treatment site.

The increased utilisation of non-CT imaging modalities for upper abdominal SABR was consistent across all demographics, suggesting that access to multi-modality imaging is an important consideration in treating this site. A lack of access to these imaging modalities may also explain why significantly fewer private facilities performed MM in upper abdominal SABR - many private facilities in ANZ are stand-alone clinics and may be less likely to have direct access to these imaging modalities compared to a hospital-based facility.

MM was used in combination with inverse-planned treatments by nearly every responding facility. Given that the ITV approach is the most-used technique, the interplay effect will need to be considered in the design of the audit measurements and scoring criteria. There is extensive literature on quantifying the interplay effect in various settings, with many publications suggesting that clinically significant dosimetric deviations can be introduced [2,49,50]. The degree of dose

deviation can vary depending on plan complexity, treatment time, or starting position in the respiratory cycle, hence, performing reproducible dosimetric measurements to compare with a national database will be challenging, and will be a crucial design consideration.

Overall, the use and implementation of MM was fairly homogenous amongst the major demographics. Selection of MM technique, use of motion limitation, types of imaging used for motion assessment, dose calculation and image guidance were comparable in every group. Hence, a streamlined and widely applicable audit design which can directly assess the accuracy of the common clinical workflows is achievable.

Declaration of Competing Interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: NH receives research funding from Varian Medical Systems for unrelated work, and Reflexion Medical for unrelated work. Other authors have no interests to declare.

Appendix A. Supplementary data

Anonymised response data are available at www.arpansa.gov.au/ mmoss. Supplementary data to this article can be found online at htt

ps://doi.org/10.1016/j.phro.2022.09.003.

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