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Original Research Article

Feasibility of simulation free abdominal stereotactic adaptive radiotherapy using an expedited pre-plan workflow

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ABSTRACT

Background and Purpose: Improved hounsfield-unit accuracy of on-board imaging may lead to direct-to-unit treatment approaches We aimed to demonstrate the feasibility of using only a diagnostic (dx) computed tomography (CT)-defined target pre-plan in an *in silico* study of simulation-free abdominal stereotactic adaptive radiotherapy (ART).

Materials and Methods: Eight patients with abdominal treatment sites (five pancreatic cancer, three oligometastases) were treated using an integrated adaptive O-Ring gantry system. Each patient's target was delineated on a dxCT. The target only pre-plan served primarily to seed the ART process. During the ART session, all structures were delineated. All simulated cases were treated to 50 Gy in 5 fractions to a planning target optimization structure (PTV_OPT) to allow for dose escalation within the planning target volume. Timing of steps during this workflow was recorded. Plan quality was compared between ART treatment plans and a plan created on a CT simulation scan using the traditional planning workflow.

Results: The workflow was feasible in all attempts, with organ-at-risk (OAR) constraints met in all fractions despite lack of initial OAR contours. Median absolute difference between the adapted plan and simulation CT plan for the PTV_Opt V95% was 2.0 %. Median absolute difference in the D0.5 cm^3 between the adapted plan and simulation CT plan was −0.9 Gy for stomach, 1.2 Gy for duodenum, −5.3 Gy for small bowel, and 0.3 Gy for large bowel. Median end-to-end workflow time was 63 min.

Conclusion: The workflow was feasible for a dxCT-defined target-only pre-plan approach to stereotactic abdominal ART.

1. Introduction

There is significant interest in streamlining the process of radiotherapy planning. One method for simplifying this process is to create treatment plans based on diagnostic imaging, eliminating the necessity of computed tomography (CT) simulation. This process is referred to as simulation-free radiotherapy or diagnostic CT-based treatment planning (dxCT-RT) and has been used in treatment of patients in palliative settings [1–4]. Two studies have recently demonstrated the feasibility of using diagnostic imaging in combination with online adaptive radiotherapy (ART) [5,6] to generate plans at first fraction without the need for simulation.

One such method where dxCT-ART may have an immediate impact is stereotactic body radiotherapy (SBRT) in abdominal malignancies [7–9]. In non-adaptive approaches to abdominal high-dose SBRT, there has been high-grade toxicity to the luminal gastrointestinal tract due to its proximity and sensitivity to radiotherapy as well as its inter-fraction and intra-fraction mobility [10–12]. These risks to bowel can be mitigated with use of ART, which, in combination with high-quality imaging, has been shown in prospective trials to reduce dose risks and clinical toxicities of upper abdominal SBRT [13–16]. Of note, in upper abdominal ART, pre-treatment plans developed from traditional CT or

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magnetic resonance imaging simulations are rarely delivered to the patient, as most fractions require daily adaptation [17,18]. This is due to the known, clinically significant variability in the daily anatomy of the upper abdomen [12,19]. The question then arises of whether there is any difference in using a dxCT-RT base plan instead of a simulation-based plan since neither is delivered to the patient. In this context, improved imaging technology and an integrated and efficient adaptive treatment planning system (TPS) could eliminate the need for simulation-based planning in abdominal SBRT.

We theorized that the initial treatment pre-plan could be constructed using only target contours created upon diagnostic scans, with the transfer of these targets to the adaptive system without initial organ-at-risk (OAR) contours in the preplan. We hypothesized we could then incorporate full OAR contours based on the patient's daily anatomy observed at the beginning of first treatment session, resulting in daily adaptive plans that maintain the quality of a standard simulation-based approach without the need for OAR contouring in the pre-plan. To test this hypothesis, we conducted a prospective, *in silico* study, as part of a prospective imaging clinical trial, to evaluate the feasibility of this method of a Streamlined Workflow In Simulation Free Treatments (SWIFT) for stereotactic abdominal ART.

2. Materials and methods

2.1. Patient selection and in silico treatment platform

Eight patients with abdominal malignancies (five with locally advanced pancreatic cancer and three with abdominal oligometastases) were imaged using a HyperSight CBCT (hCBCT) (Varian Medical Systems, Palo Alto, CA) on a prospective imaging study (NCT05427214) with the required ethics/data approvals and were included in this study. These patients were concurrently receiving adaptive radiotherapy separate from our study and followed all traditional radiotherapy workflow steps including CT simulation, full contouring sets, standard planning times, and pre-treatment checks. All patients were initially set up in an alpha cradle with one arm up. Following their standard radiotherapy treatments, patients were imaged on the hCBCT system at an end-exhale position. These images were later injected into a vendor-supplied emulator as the SWIFT primary dataset to simulate the SWIFT workflow. Description of the motion management, imaging, and TPS system is in the Supplementary Material A.

2.2. Pre-plan workflow

Each patient had a dxCT with IV contrast that was acquired during patient's diagnostic workup. This dxCT was used by the physician to define the gross tumor volume (GTV) for treatment planning. The GTV was then transferred onto the patient's registered hCBCT acquired during the imaging study with no modifications to the GTV. This hCBCT was used as the primary dataset for adaptive dose calculation. This was done for proof-of-concept purposes of calculating on an hCBCT for adaptive treatment planning in a hypothesized future version of the adaptive TPS. In Ethos Treatment Planning 1.1, the adaptive system deformed the underlying primary dataset to the CBCT acquired for on-table adaptive planning [20]. Establishing the hCBCT as the primary dataset in the adaptive system would create a minimally deformed hCBCT dose-calculation dataset for adaptive planning, thus matching our proposed workflow. This workflow is described in Supplementary Material B.

Once the GTV was transferred to the hCBCT, that dataset was imported into the TPS and a planning template based on a multi-institutional pancreas adaptive SBRT trial was applied (NCT05764720) [21]. In this current study, a clinical target volume (CTV) margin was used for patients with locally advanced pancreatic cancer to cover involved vasculature and lymph nodes as well as the celiac and superior mesenteric arteries. A CTV was not used for the patients with abdominal oligometastases. A uniform 5 mm expansion was used to generate a planning target volume (PTV) from either the GTV or CTV. All patients were treated to 50 Gy in 5 fractions to the PTV optimization structure (PTV_OPT). The PTV_OPT is a structure used in stereotactic adaptive radiotherapy that allows dose to be escalated to areas within the PTV while safely de-escalating dose at areas of PTV/OAR overlap. PTV_OPT generation can be reviewed in Supplementary Material C. All clinical constraints and goals as well as resources for the planning template used in this manuscript are presented in Supplementary Material C. Temporary dummy structures, such as small circles, were placed for all planning structures besides the GTV to ensure all adaptive-derived structures were applied within the planning template (Fig. 1). The planning template would not function properly during the adaptive process without all required planning structures present in the initial plan (i.e. needs filled structures to start the adaptive process), regardless of the correctness of that structure, therefore necessitating use of the dummy structures. The optimization objectives were not adjusted from the planning template except for the order of stomach, duodenum, small bowel, and large bowel within the template. These OARs were ranked within the highest priority section of the planning template based on proximity to the GTV on the dxCT (e.g. if the duodenum abutted the target whereas the large bowel was distant from the target, the duodenum was prioritized above the large bowel). Two three-quarter partial VMAT arcs were used, avoiding the arm by the patient's side. The plan was then optimized, dose calculated, and selected to be the initial plan for adaptive treatment. This "pre-plan" would not be delivered to the patient and was only used to import the GTV and planning template into the on-table adaptive workflow.

2.3. Adaptive workflow

To evaluate the SWIFT workflow, the same hCBCT that the GTV was transferred onto was injected into the ART emulator system. All temporary OAR structures were subsequently modified during the standard adaptive workflow by an advanced practice radiation therapist [17,18].

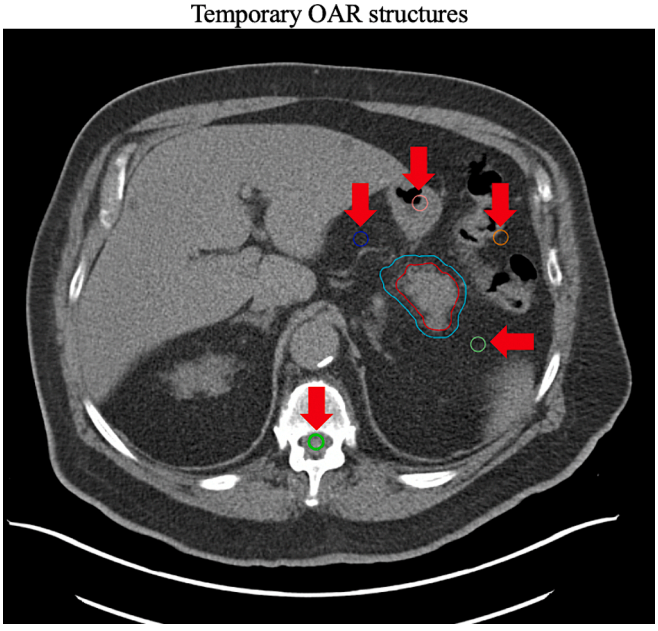


Fig. 1. The temporary OAR structures (denoted with red arrows) placed in the initial planning phase on the diagnostic CT. As the Ethos TPS will not accept a new structure within the online adaptive workflow, these temporary structures are placed which are then overridden and contoured based on the patient's anatomy-of-the-day on the hCBCT. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

Artificial intelligence auto-contouring defined the liver, duodenum, and stomach, and adjusted as needed. All other OAR structures were manually delineated by the adaptive user with no computer assistance (small bowel, large bowel, spinal cord, and kidneys).

The GTV (which was defined on the dxCT) was rigidly propagated and aligned on the hCBCT. Any GTV modifications needed were then applied by a physician. Once contour review was completed, all derived structures were created and the plan was optimized according to the planning template. Once optimization was complete, the adaptive plan was chosen for treatment. The SWIFT workflow would be considered successful if the adapted plans created met all clinical goals and constraints, most importantly meeting our luminal gastrointestinal OAR hard constraint of D0.5 cm^3 < 33 Gy. The time for dxCT target contouring, pre-plan setup, pre-plan optimization, adaptive contouring, and adaptive optimization was captured and reported, and further details of the tasks done in each step are described in Supplementary Material B.

2.4. Plan quality verification

The SWIFT workflow had a pre-plan not suitable for comparison with the traditional approach. Therefore, an alternative plan quality verification was needed in this study. Initial adaptive treatment plans with full OAR and planning structure contouring were also developed using the same planning template and objectives as described above on the patient's simulation CT (simCT). Target and OAR objective metrics (Table 1) and PTV, CTV, GTV, and PTV_Opt V95%Rx were compared between the SWIFT-derived plan (hCBCT plan) and the traditional simCT-derived plan (Fig. 2).

All plans had ion chamber point dose and portal dosimetry measurements performed. In addition, each plan had a secondary dose calculation using Mobius3D. Absolute ion chamber measurement < 3 % from calculated and portal dosimetry gamma pass rate > 95 % (3 %/3mm, 5 % threshold) were considered to be passing measurement-based QA. Secondary dose calculation 3D gamma pass rate > 90 % (3 %/2mm, 10 % threshold) was considered passing.

3. Results

The SWIFT workflow was completed successfully in all eight patients, and despite lack of initial OAR contouring on the dxCT plan, OAR hard constraint metrics for the luminal gastrointestinal structures were met in all fractions in the adapted plan.

Comparative planning data are presented in terms of absolute differences between the hCBCT plan and the simCT plan in Table 1. The median (minimum, maximum) absolute difference of the PTV V95% in the hCBCT plan compared to the simCT plan was −3.2 % (−14.6 %, 2.3 %). The median absolute difference between the CTV V95% in the hCBCT plan compared to the simCT plan was −2.7 % (−5.6 %, 0.6 %). The median absolute difference between the GTV V95% in the hCBCT plan compared to the simCT plan was –2.0 % (−15.2 %, 9.7 %). The median absolute difference reported between the PTV_OPT V95%Rx in the hCBCT plan compared to the simCT plan was 2.0 % (0.0 %, 6.4 %). PTV_OPT represents the treatment optimization volume that prescription dose is expected to fully cover. The percent differences in target coverages are depicted graphically in Fig. 3.

Table 1
Differences in target and OAR metrics. Presented are the absolute differences between the relevant target and OAR metrics between the hCBCT adapted plans used for *in silico* treatment delivery and the simCT plans.

Objective	Median absolute difference (minimum, maximum) in hCBCT compared to simCT plans
PTV V100% (% volume)	0.9 (−15.1, 12.5)
CTV V100% (% volume)	−3.0 (−4.8, 1.1)
GTV V100% (% volume)	−1.8 (−14.7, 11.1)
Body V25 Gy (cm^3)	−66.2 (−299.1, 171.7)
Monitor units	1378 (−1245, 2713)
Stomach D0.5 cm^3 (Gy)	0.9 (−8.5, 1.6)
Duodenum D0.5 cm^3 (Gy)	1.2 (−3.5, 6.3)
Small bowel D0.5 cm^3 (Gy)	−5.3 (−16.8, −0.4)
Large bowel D0.5 cm^3 (Gy)	−3.2 (−16.0, 5.3)

There were minimal differences in dose delivered to the critical gastrointestinal luminal structures across all plans (Table 1), with the widest variations demonstrated for differences in small bowel dosing in the hCBCT plan compared to the simCT plan (median absolute difference of −5.3 Gy). In addition, the absolute values of dose to critical gastrointestinal structures are included in Supplementary Material D. The largest variations were demonstrated in the patient with the omental metastasis. In this patient, the difference between the D0.5 cm^3 in the hCBCT plan and the simCT plan was 1.6 Gy for stomach, 3.9 Gy for duodenum, −14.3 Gy for small bowel, and 0.5 Gy for large bowel. These differences were attributed to the mobility of the target between scans, resulting in larger differences in the OAR dosing.

Timing data are presented in Table 2 for each of the eight patients. Mean end-to-end workflow time was 63 min. Four of the eight cases were completed in under 60 min while all eight cases were completed in under 90 min.

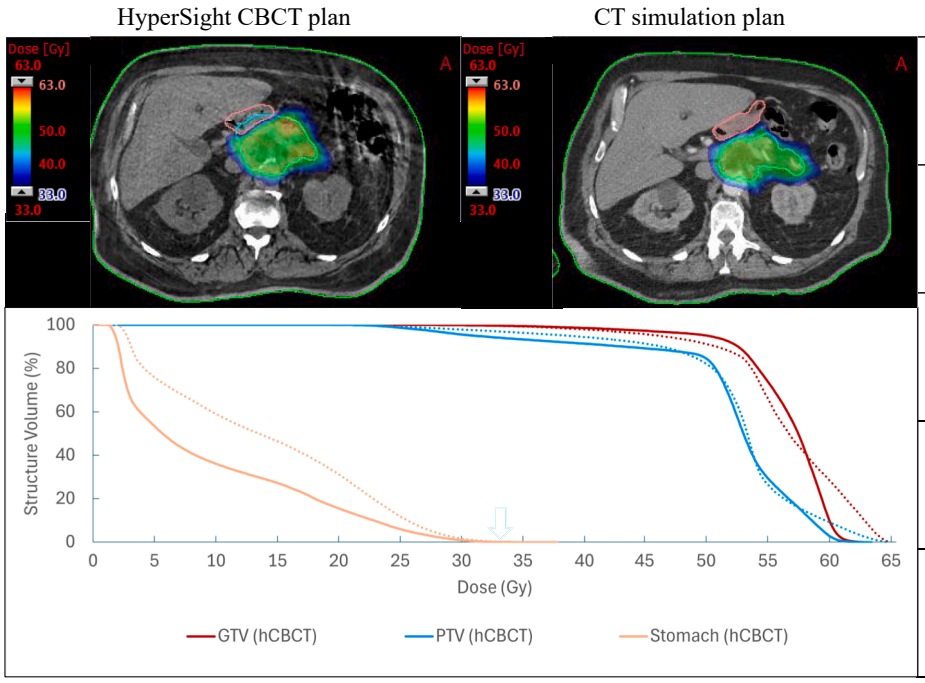
All plans passed portal dosimetry QA and secondary dose calculation check. One hCBCT plan failed ion chamber measurement at 6.3 %.

4. Discussion

We demonstrated the feasibility of a rapid, simulation-free adaptive stereotactic radiotherapy for abdominal lesions, utilizing a target-only diagnostic imaging pre-plan method with a projected time-from-image-import-to-beam-on of under 90 min. In this *in silico* study, an end-to-end simulation-free adaptive SBRT workflow (diagnostic imaging import through final plan approval) was successfully completed in all patients, with no clinical difference in plan quality compared to a traditional simulation-based workflow. Therefore, rapid simulation-free adaptive treatment approaches may be a viable option for patients in the future, including for complex abdominal SBRT.

CT-ART has been clinically implemented in a variety of disease sites, and *in silico* data suggests that simulation-free CT-ART workflows may be feasible [22–25]. These feasibility studies have importantly led to several *in vivo* studies evaluating simulation-free CT-ART workflows, including for bone metastases and hippocampal avoidance whole brain radiotherapy [5,6]. This *in silico* study represents the next evolution in simulation-free CT-ART planning, as it is a first of its kind workflow to incorporate modifications such as dummy OAR structures to condense the paradigm even further.

The demand for novel approaches to expedite our traditional workflows has increased in the past several years as technology has improved. With adequate tools and computational power, the need for multiple days for contouring and planning is increasingly becoming unnecessary in certain patient populations. This is evident by the broader acceptance of adaptive radiotherapy, where traditional treatment planning workflows have been compressed into an on-table session with excellent clinical outcomes [5,15]. One such effort which has notable similarity to our SWIFT workflow is the FAST-METS study [5]. In this study, Nielson et al. used CT-guided adaptive technology to enable same-day IMRT for bone metastases. Remarkably, consultation and treatment were conducted in under two hours in this study across 47 patients in palliative indications. In addition, rapid simulation-free workflows can compete with other specialties that offer similar types of approaches such as same day mapping and treatment of liver lesions with Y90 [26]. It also compresses the work required of the radiotherapy team before initiating



OAR constraint	Met in hCBCT plan?	Met in CT sim plan?
Stomach V33Gy<0.5 cc	✓	✓
Duodenum V33Gy<0.5 cc	✓	✓
Small bowel V33Gy<0.5 cc	✓	✓
Large bowel V33Gy<0.5 cc	✓	✓

Fig. 2. A plan comparison between the plan created based on the patient's anatomy-of-the-day on the hCBCT (top left) and a plan based on the patient's CT simulation imaging (top right). The Dose Volume Histogram (bottom) demonstrates fidelity of GTV (red) and PTV (cyan) coverage between the hCBCT (squares) and simulation CT (triangles) plans, and both plans meet the V33 constraint (blue arrow) for the stomach (pink). (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

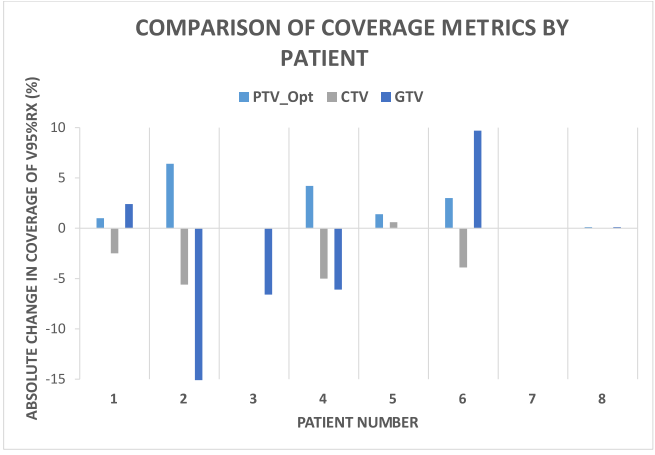


Fig. 3. Absolute change in target coverage for the GTV (dark blue), CTV (silver), and PTV_Opt V95% (light blue). Positive changes in coverage represent higher coverage in the hCBCT plan compared to the simCT plan, whereas negative changes represent lower coverage in the hCBCT plan compared to the simCT plan. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

treatment. This, in turn, increases the return on investment of hospitals when developing radiation therapy treatment plans. Thus, a simulation-free workflow is a mutually beneficial approach to radiation therapy for both patients and the treatment facility in terms of return on time invested.

Confidence in both target and OAR delineation using high-quality imaging is paramount in the safety of the SWIFT approach. On-board imaging units are fast approaching the quality level of CT simulation images in terms of structure visualization and contour construction [27,28]. In this *in silico* study, hCBCT contours may vary from the dxCT due to expected anatomical changes from day-to-day motion, changes in positioning, and time-lapse from diagnostic imaging. Fig. 4 demonstrates this scenario through several cases in which, there were significant anatomic changes from dxCT to hCBCT. Given the degree of changes that can occur, the prescribing physician should take care to account for potentially significant target changes and may consider not utilizing SWIFT in particularly complex patient targets and anatomy. This technique is highly procedural, akin to brachytherapy, and therefore consistency in the treatment planning team is a necessity for each case to limit risk from intra-observer variability. Additional risk assessment and mitigation strategies can be drawn from brachytherapy. We would only recommend implementation of a SWIFT workflow in clinics that are regimented in their approach to a specific disease site with a large volume of clinical experience and rely on template-based approaches to generate adaptive radiotherapy plans. We suggest adequate review of dxCT imaging, communicating unique anatomical scenarios for collective treatment team understanding.

Importantly, there were changes in OAR anatomy between simCT and hCBCT, which are reflected in the larger changes in PTV/CTV/GTV coverage but not in the PTV_OPT coverage. For reference, a previous study analyzing the daily change in PTV and PTV_Opt coverage during adaptive pancreas SBRT for over 150 pancreatic patients saw a 95 % confidence interval (~2 standard deviations) change of 13 % for PTV V95% and 5 % for PTV_Opt V95% [29]. In our study the mean PTV_OPT V95% change was 2.0 %, which is in line with this prior adaptive studies [16]. This highlights how the SWIFT workflow and adaptive plans at large must be robust to substantial OAR changes within a plan. Because of this, our approach could generate acceptable treatment plans (high/consistent PTV_Opt coverage while respecting OAR doses), even though OARs are not included in the target-only diagnostic pre-plan optimization.

All Ethos adaptive plans use the imaging isocenter as the plan isocenter. Because the CBCTs were acquired in an imaging study, the imaging isocenter was not always optimally positioned relative to the target. The only plan to fail ion chamber measurement was an hCBCT plan with an isocenter to IC distance of 7.7 cm, the largest of all measured plans. The hCBCT plans in general had lower secondary dose

Table 2
Timing data is presented in minutes for each of the major steps of the workflow for all eight *in silico* attempts. The "target contour" step was the time it took the physician to draw initial target contours on the diagnostic CT. The "plan setup" step was the time it took the physicist to add dummy structures and create any necessary planning structures needed for initial optimization. The "optimization" step was the time it took for the initial plan based on the diagnostic image to be optimized. The "adaptive contour" step was the time it took for the physician to verify target contours as well as correct/create OAR contours within the contour ring. "Adaptive optimization" was the time it took the TPS to optimize the new adaptive plan as well as project the initial plan on the anatomy-of-the-day, and the time it took for the physician and physicist to evaluate the plans and select the adaptive plan for treatment.

Patient	Target contouring (min)	Initial plan set-up (min)	Initial plan optimization (min)	Adaptive contouring (min)	Adaptive optimization (min)	Total end-to-end workflow time (min)
1	7	6	5	28	9	57
2	11	7	6	42	7	73
3	2	6	4	15	5	33
4	13	8	16	23	9	69
5	10	5	15	31	8	70
6	6	6	15	50	9	86
7	6	5	5	15	4	35
8	5	4	5	13	7	35
Median	7	6	6	26	8	63

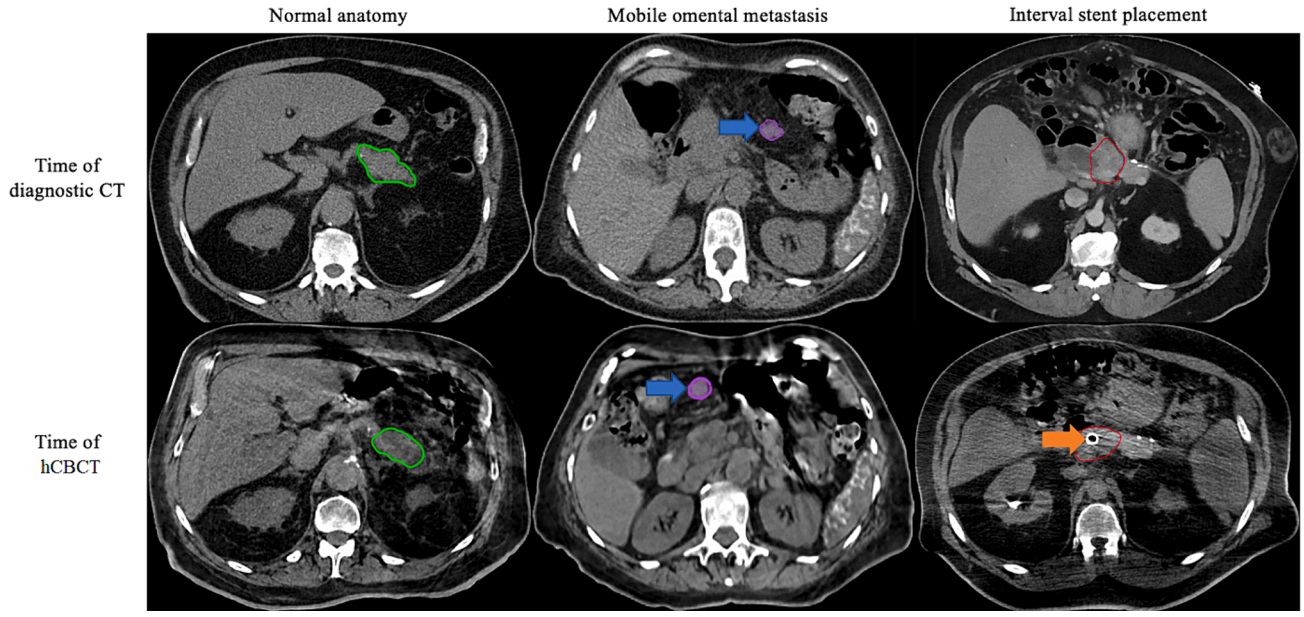


Fig. 4. Examples of patient anatomy at time of diagnostic CT (top row) and time of hCBCT (bottom row). The left demonstrates a target (green) with minimal anatomic change from initial to treatment time point. In the middle, the blue arrow indicates an omental metastasis (purple) which moved substantially from the time of diagnostic CT to hCBCT, a not uncommon occurrence with omental metastases. On the right, the orange arrow indicates a biliary stent which was included in the target (red) at time of hCBCT, but had not yet been placed at time of diagnostic CT. The middle and right cases indicate patient situations that may not be ideal for the described workflow. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

calculation gamma passing rates compared to the simCT plans that had plan isocenter within the target. Further investigation on the deliverability of off central axis treatment plans in Ethos is warranted but should be avoided in SWIFT. Dosimetric data of the Ethos/Halcyon beam-matched model across several machines has been demonstrated previously [30,31]. This underscores the importance of implementing workflows to aid in patient setup so the isocenter is optimally positioned for simulation-free workflows. We will investigate this further in future versions of the Ethos system, which is better suited for this process.

Templated approaches to radiation therapy planning are increasing within the field as evidenced by multiple platforms and diseases utilizing this approach [25,32,33]. This ensures consistency during the SWIFT approach and limits ill-advised on-table planning choices that may create situations of unsuccessful on-table adaptive planning. However, compressed and templated workflows might also not be the highest quality plan compared to plans generated over many hours. Further research is needed to quickly and effectively identify the best possible dose distribution and plan parameters for a given patient [34].

Additional limitations of the current workflow are that Ethos TPS version 1.1 does not directly calculate dose on the hCBCT. This was resolved in version 2.0 of the TPS as preliminary data suggests that direct hCBCT calculation is safe [35,36]. The second limitation of this study is the small number of cases evaluated in this manuscript, although we hope that this data serves as proof of feasibility to drive and invigorate future SWIFT research. Despite these potential limitations, our SWIFT approach used a planning template designed for a multi-institutional trial for adaptive pancreatic cancer with limited modifications, thus ensuring credence of our templated approach. Lastly, it should be noted that the presence of bowel gas may induce intra-fractional bowel motion and CBCT artifacts which may introduce uncertainty into this workflow and should be accounted for in any CT-guided abdominal ART workflow, including this one.

To conclude, we found that SWIFT is feasible, *in silico*, for use in generating treatment plans from a diagnostic image to delivery in abdominal SBRT in under 90 min. Simulation-free and target-only optimization may reduce time-to-treatment for many disease sites, even for complex, definitive treatment, thus furthering the efficiency of radiation therapy.

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CRediT authorship contribution statement

Alex T. Price: Conceptualization, Methodology, Visualization. **Joshua P. Schiff:** Formal analysis, Investigation, Visualization. **Alice Silberstein:** Writing, Data curation. **Robbie Beckert:** Investigation, Data curation. **Tianyu Zhao:** Data curation, Resources. **Geoffrey D. Hugo:** Funding acquisition, Supervision. **Pamela P. Samson:** Supervision, Funding acquisition. **Eric Laugeman:** Methodology, Investigation, Data curation, Project administration. **Lauren E. Henke:** Conceptualization, Funding acquisition, Supervision.

Declaration of Competing Interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: Tianyu Zhao and Pamela Samson report support for attending meetings and/or travel from Varian Medical Systems. Pamela Samson and Lauren Henke report payment or honoraria from Varian Medical Systems. Lauren Henke reports consulting fees from Varian Medical Systems and Radiologica. Lauren Henke reports payment or honoraria from Luso-Palex. Alex Price reports support attending meetings and/or travel from Sun Nuclear Corporation. The research performed in this work was funded by Varian Medical Systems with payment made to the institution.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.phro.2024.100611.

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