AI Deformable Dose Accumulation and Patient-Specific Uncertainty for MR-Guided Radiotherapy of Locally Advanced Pancreatic Cancer

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INTRODUCTION

MR-guided adaptive radiotherapy (MRgART) enables safe delivery of ablative doses to pancreatic tumors through improved soft-tissue visualization and daily anatomical adaptation, as demonstrated by the multi-institutional SMART trial.[1] However, complete tumor coverage is limited by uncertainty in the dose actually delivered to adjacent gastrointestinal organs at risk (OARs). Structures such as the duodenum, stomach, and bowel deform by more than 4 cm due to respiratory and digestive motion, forcing conservative dose constraints that can compromise target coverage.[2]

Deformable image registration (DIR) allows accumulated dose to be estimated across fractions. However, different DIR algorithms can produce different deformation vector fields (DVFs), and therefore different accumulated dose distributions. Even the same algorithm can yield different results depending on which fraction is chosen as the reference anatomy. This study evaluated dose variability when accumulating dose on different reference fractions for each DIR algorithm, as well as differences between originally planned and accumulated plans in pancreatic MRgART.

METHODS

Patients & Dose Accumulation. Eight patients treated with 5-fraction pancreatic SBRT (50 Gy in 5 fractions) on a 1.5T MR-Linac were retrospectively analyzed. Dose was accumulated using a direct dose mapping strategy, with each of the 5 fractions serving independently as the reference anatomy. This produced 20 deformations (5 accumulated doses) per registration mode and allowed us to assess how accumulated dose varies depending on which fraction is used as the reference.

Deformable Image Registration. Registration was performed with ProRSeg, a 3D convolutional LSTM network for joint registration and segmentation that progressively refines DVFs using contour guidance.[3] Three modes were compared: (1) standard intensity-based registration with no contour guidance, (2) AI-contour guided registration using the network's predicted segmentations, and (3) clinician-contour guided registration using ground truth contours.

Dose Evaluation. Dose-volume histograms (DVHs) and $D_{0.035cc}$ and D_{5cc} were extracted for the combined duodenum-stomach (duostomach), small bowel, and large bowel. Normal tissue complication probability (NTCP) was calculated for the duostomach using the Lyman-Kutcher-Burman model with EQD_{2Gy} conversion (n=0.10, m=0.21, TD50=56 Gy, α/β=3 Gy).[4] For each patient, the median NTCP difference between the accumulated and original reference plan across all 5 fractions was used to characterize bias from each registration method.

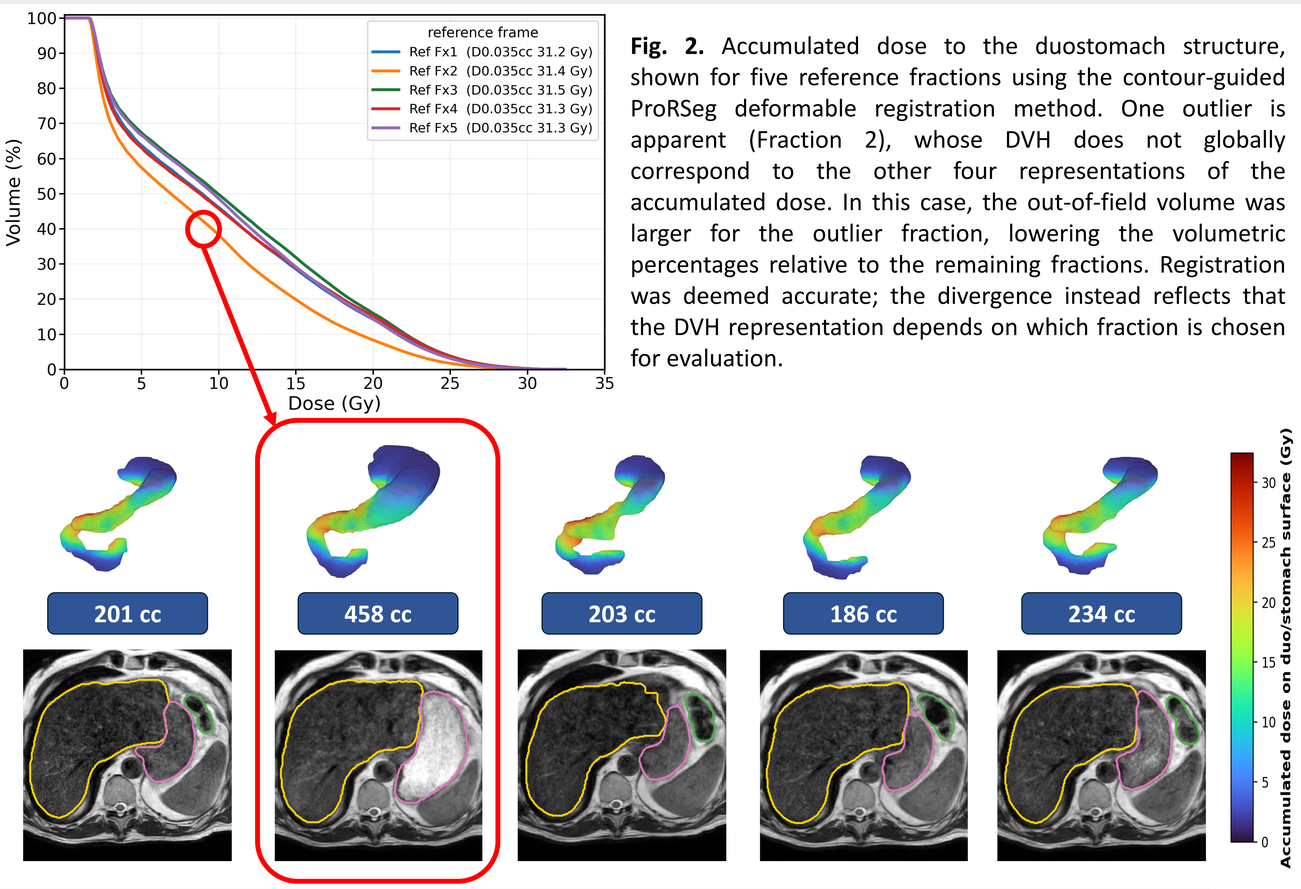

Fig. 2. Accumulated dose to the duostomach structure, shown for five reference fractions using the contour-guided ProRSeg deformable registration method. One outlier is apparent (Fraction 2), whose DVH does not globally correspond to the other four representations of the accumulated dose. In this case, the out-of-field volume was larger for the outlier fraction, lowering the volumetric percentages relative to the remaining fractions. Registration was deemed accurate; the divergence instead reflects that the DVH representation depends on which fraction is chosen for evaluation.

RESULTS

Dose variability across reference fractions. Accumulated dose depended on which fraction served as the reference anatomy. Contour-guided registration reduced this fraction-to-fraction variability across all GI OARs, with the tightest ranges under clinician-contour guidance (Table 1).

Change in NTCP. Contour-guided based NTCP values provided the lowest variation between DIR methods. It also showcased a low deviation between accumulated to initial reference plan, suggesting that adaptation is properly reflecting intended treatment plan (Table 1).

Table 1. Dose variation and NTCP change across accumulated reference fractions for each registration method. Median [Range].

OAR	Intensity guided	Predicted contour guided	Clinician-contour guided
	$D_{0.035cc}$ (Gy)		
Duostomach	6.2 [2.5–17.9]	6.8 [3.5–13.6]	4.5 [2.8–14.2]
Small Bowel	10.0 [3.1–26.4]	6.9 [2.7–27.7]	6.8 [4.6–9.9]
Large Bowel	3.6 [0.7–10.2]	2.1 [0.9–3.0]	2.6 [0.9–6.7]
	D_{5cc} (Gy)		
Duostomach	3.4 [0.7–8.9]	2.6 [0.9–9.4]	2.0 [0.6–4.4]
Small Bowel	5.4 [2.1–19.8]	3.1 [0.9–18.6]	2.2 [1.4–5.1]
Large Bowel	3.5 [1.3–7.3]	1.2 [0.9–3.2]	1.7 [0.9–3.3]
	ΔNTCP (%)		
Duostomach	+3.9 [−2.8, +58.7]	+1.4 [−2.1, +37.0]	+1.5 [−2.7, +4.0]

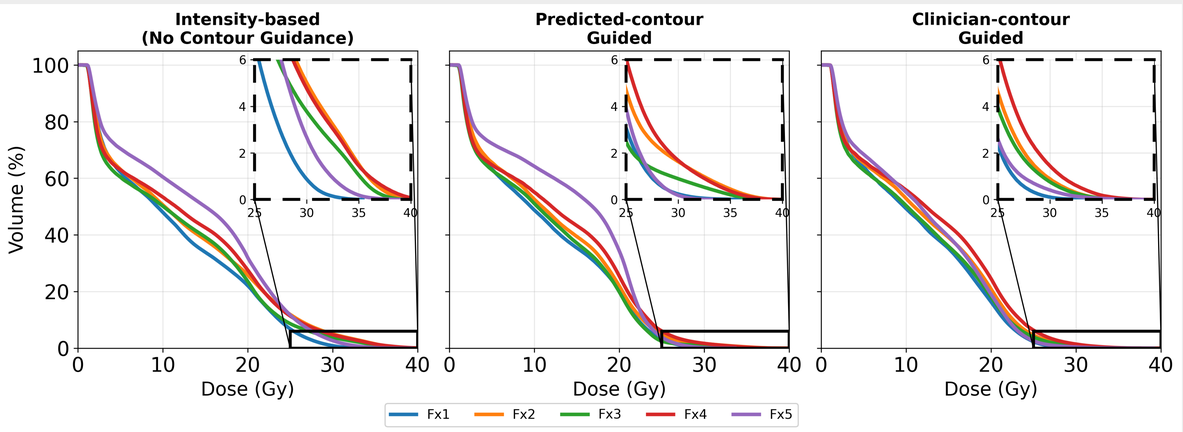

Fig. 1. Cumulative DVHs of the duostomach, showing the five-fraction accumulated dose recomputed with each fraction used as the reference frame for dose accumulation. Adding AI-predicted contour guidance to the registration brought four of the five reference accumulations (Fx1–Fx4) visually into closer global agreement, while the Fx5 dose representation continued to reflect a distinct interpretation. Once clinician contours were used to guide the registration, all five DVHs converged closer together, with clearly reduced inter-reference variability. The same ordering held at the high-dose end: the near-max dose (D2%) inter-reference IQR fell from 3.3 Gy for intensity-guided registration to 2.8 Gy with predicted-contour guidance and 2.0 Gy with clinician-contour guidance.

CONCLUSION

Contour-guided DIR methods reduced dose variation between accumulated reference fractions, indicating a more robust estimation of deformation in these more complex and mobile structures. Contour-guided NTCP values provided low deviation between the accumulated and initial reference plan, suggesting that adaptation properly reflects the intended treatment plan.

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