

# Four-dimensional diffusion-weighted magnetic resonance imaging for stereotactic body radiation therapy in patients with abdominal cancer: abridged secondary publication

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## KEY MESSAGES

1. Compared with T1- and T2-weighted four-dimensional magnetic resonance imaging, four-dimensional diffusion-weighted imaging (4D-DWI) enables higher tumour contrast-to-noise ratio and hence highly consistent gross tumour volume contours and low interobserver errors.
2. A deep learning-based 4D-DWI yields significant improvements in image quality including tumour contrast-to-noise ratio and image texture.
3. In patients with abdominal cancer, 4D-DWI demonstrates high detectability with accurate tumour motion and tumour delineation.
4. 4D-DWI has potential to improve the accuracy of

radiotherapy for mobile abdominal cancers and reduce radiation adverse effects.

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## Introduction

Abdominal tumours are major causes of cancer-related death in Hong Kong and worldwide. Liver cancer and pancreatic cancer are the third and fourth leading causes of cancer-related death, respectively, in Hong Kong.<sup>1</sup> The role of radiotherapy in abdominal tumour management is limited owing to radiation toxicity in non-target tissues. Stereotactic body radiation therapy (SBRT) has been used for management of early-stage abdominal tumours because it enables delivery of high-dose conformal radiotherapy with limited toxicity. Respiratory motion (can be up to 4 cm) is a major obstacle to achieving more effective SBRT for abdominal tumours.<sup>2</sup> Four-dimensional (4D) imaging plays an essential role in the management of tumour motion.<sup>2</sup> 4D computed tomography (CT) is ineffective for abdominal tumours owing to its low soft-tissue contrast, whereas 4D magnetic resonance imaging (MRI) exhibits superior soft-tissue contrast but suboptimal and inconsistent tumour contrast.<sup>3,4</sup> We therefore developed a novel 4D diffusion-weighted imaging (DWI) technique.<sup>5</sup> It has high tumour contrast-to-noise ratio (CNR) and does not require exogenous contrast medium. We aimed to evaluate

the efficacy of 4D-DWI for treatment planning in patients with abdominal tumours.

## Methods

We included 36 patients with abdominal tumour(s) in the liver or pancreas and four healthy volunteers. We developed and validated a robust sorting method based on anatomical features to improve image quality in 4D-MRI. We then developed the retrospective motion artefact suppression by synthetic radial k-space (R-MASSK), which can be integrated into the clinical 4D-MRI workflow to suppress motion artefacts and enhance image quality through simulated k-space resampling. We then developed a new (K-B-optimised) binning method to address the need for propeller reconstruction when sorting the blade data, thereby improving the k-space distribution. This method is intended to resolve an issue of 4D-DWI, in which amplitude data binning with continuous intervals to sort blade data could lead to non-uniform k-space sampling, leading to suboptimal results in subsequent reconstruction. We then developed a deep learning-based deformable image registration method—dual-supervised deformation estimation model—to improve 4D-MRI

image quality including 4D-DWI. We evaluated the efficacy of 4D-DWI in radiotherapy planning in terms of tumour CNR, gross tumour volume (GTV) dice similarity coefficient (DSC), and tumour motion error.

## Results

4D-MRI based on anatomic feature matching was able to improve image quality by reducing breathing-induced motion image artefacts. The R-MASSK method was capable of suppressing motion artefacts and enhancing the quality of clinically acquired 4D-MRI. The K-B-optimised binning method effectively improved the robustness of 4D-DW-propeller echo-planar imaging.

Our deep learning-based method of synthesising ultra-quality multiparametric 4D-MRI (including 4D-DWI) showed accurate tumour motion trajectory and significantly better image quality, compared with conventional 4D-MRI.

The tumour CNR increased from  $8.30 \pm 6.87$  in 4D-MRI to  $8.66 \pm 6.46$ ,  $22.49 \pm 21.54$ ,  $35.28 \pm 35.29$ , and  $29.81 \pm 24.36$  in T1-weighted 4D-MRI, T2-weighted 4D-MRI, 4D-DWI (b=50), and 4D-DWI (b=800), respectively. 4D-DWI enables higher tumour CNR. Reconstructed images in the sagittal view from a sample patient are shown in Fig 1.

Respectively in the superior-inferior, anterior-posterior, and medial-lateral directions, the relative motion errors were  $1.12 \pm 0.89$  mm,  $0.51 \pm 0.39$  mm,

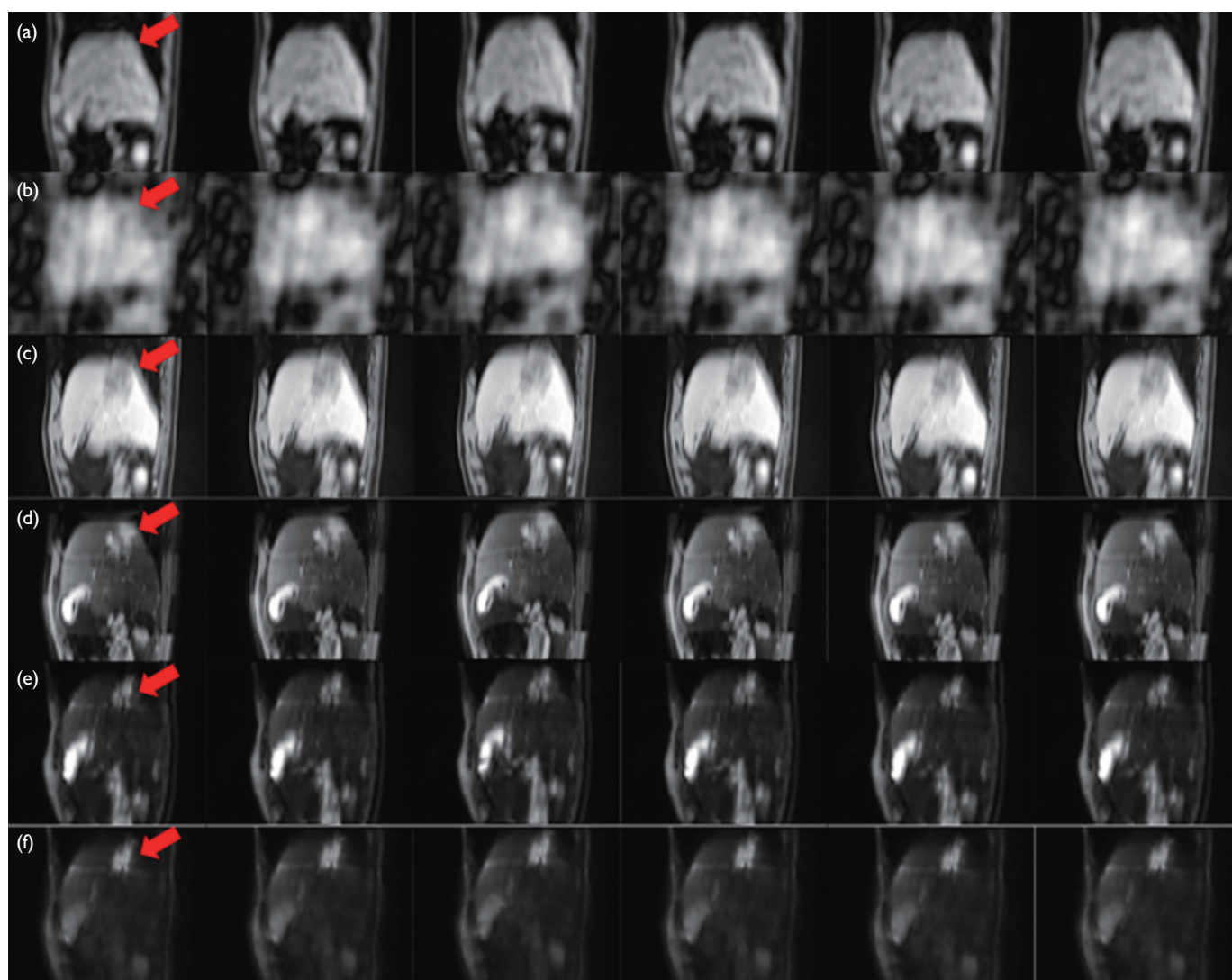


FIG 1. Reconstructed images in the sagittal view from a sample patient: (a) original four-dimensional (4D) magnetic resonance imaging (MRI), (b) downsampled 4D-MRI, (c) T1-weighted 4D-MRI, (d) T2-weighted 4D-MRI, (e) 4D-diffusion-weighted imaging (DWI) [b=50], and (f) 4D-DWI (b=800)

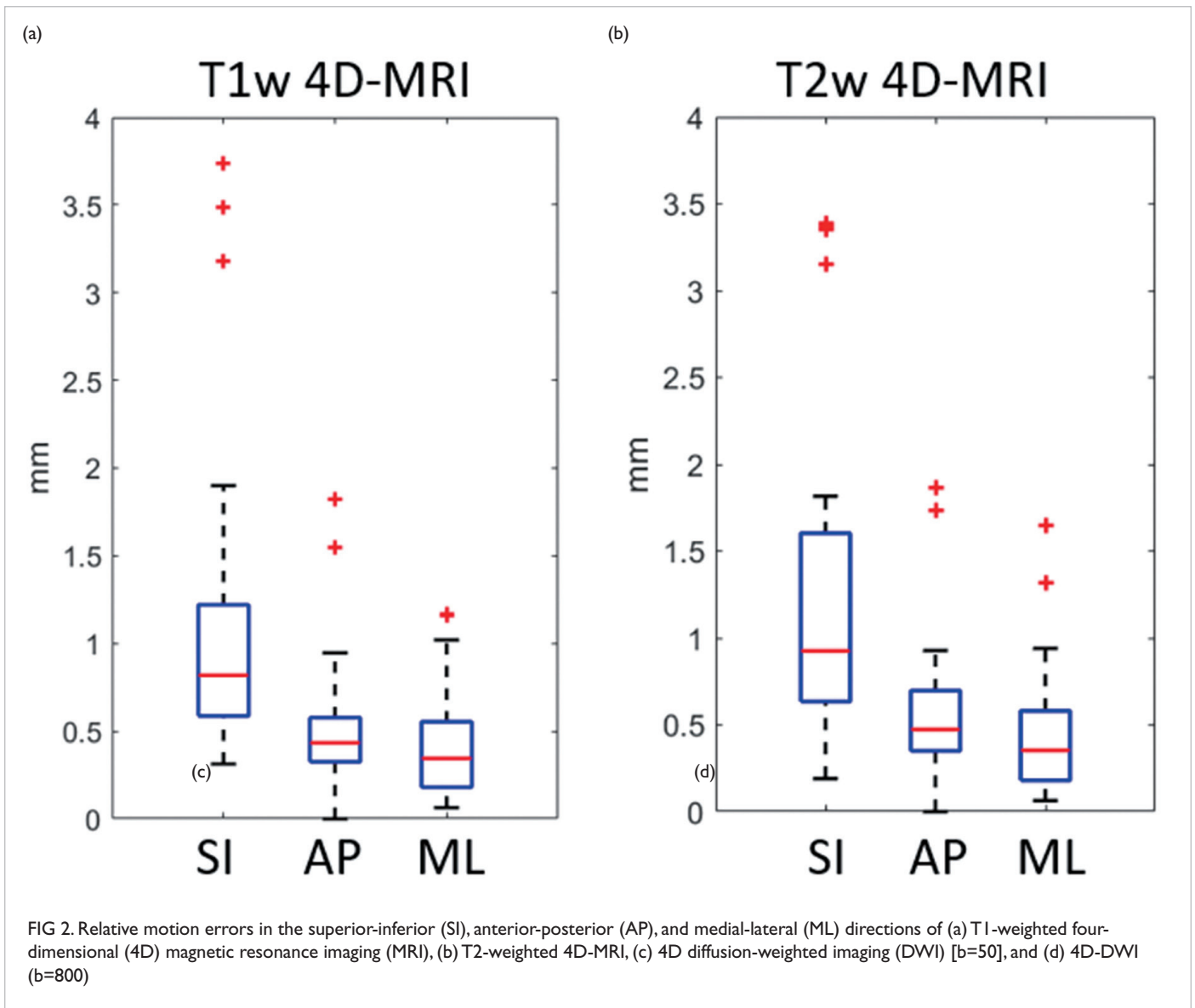


FIG 2. Relative motion errors in the superior-inferior (SI), anterior-posterior (AP), and medial-lateral (ML) directions of (a) T1-weighted four-dimensional (4D) magnetic resonance imaging (MRI), (b) T2-weighted 4D-MRI, (c) 4D diffusion-weighted imaging (DWI) [b=50], and (d) 4D-DWI (b=800)

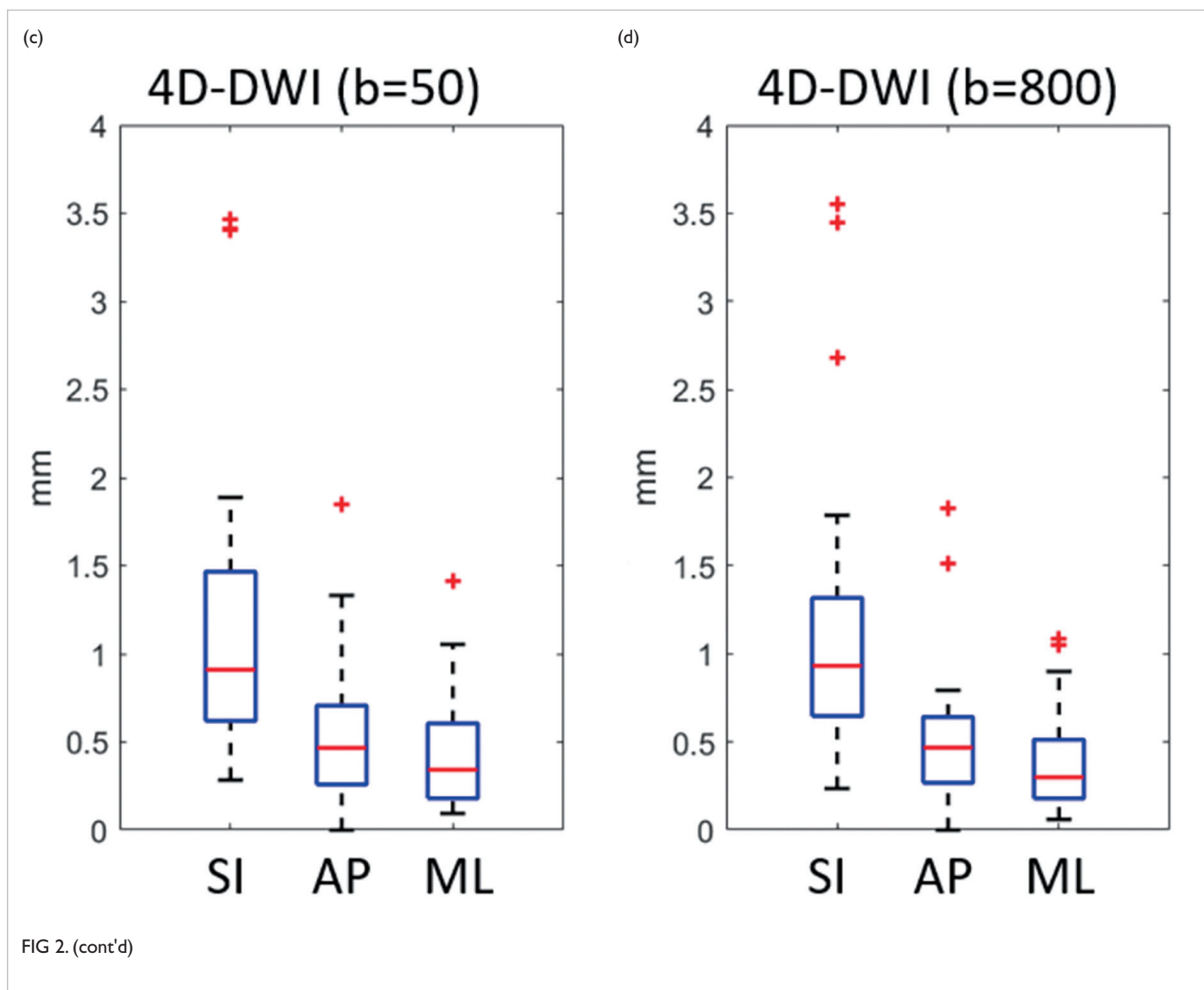
and  $0.41 \pm 0.31$  mm in T1-weighted 4D-MRI;  $1.24 \pm 0.93$  mm,  $0.55 \pm 0.39$  mm, and  $0.45 \pm 0.38$  mm in T2-weighted 4D-MRI;  $1.21 \pm 0.86$  mm,  $0.51 \pm 0.37$  mm, and  $0.42 \pm 0.32$  mm in 4D-DWI (b=50); and  $1.15 \pm 0.82$  mm,  $0.52 \pm 0.38$  mm, and  $0.38 \pm 0.28$  mm in 4D-DWI (b=800) [Fig 2].

Respectively in 4D-CT, T1-weighted 4D-MRI portal-venous phase, T2-weighted 4D-MRI, 4D-DWI, T1-weighted 4D-MRI delayed phase, and fused 4D-MRI, the interobserver means of the GTV DSC values were  $0.81 \pm 0.09$ ,  $0.85 \pm 0.08$ ,  $0.88 \pm 0.04$ ,  $0.89 \pm 0.08$ ,  $0.90 \pm 0.04$ , and  $0.95 \pm 0.02$ , whereas the inter-patient coefficients of variation of the DSC were 11.8%, 9.3%, 5.1%, 8.5%, 4.6%, and 2.4%. 4D-DWI resulted in highly consistent GTV contours

and low interobserver errors (Fig 3).

### Discussion

The visualisation of tumours and their motion is critical for tumour delineation, and 4D-DWI has high potential for precise management of tumour motion during radiotherapy. A robust sorting method based on anatomic feature matching largely reduces breathing-induced artefacts. It directly preserves organ/tissue structures by aligning or matching them in two groups of orthogonal images. The method uses external breathing signals to guide the sorting or reconstruction procedure, thereby requiring additional synchronisation and correlation



of the scans and breathing signals. Our new sorting method utilises changes in anatomic features across images to form bins and guide the sorting process, leading to better validity and accuracy.

The deep learning-based method led to significant improvements in image quality including tumour CNR and image texture. Deep learning-based 4D-DWI has advantages over conventional 4D-MRI, which relies on sorting algorithms and is thus vulnerable to irregular breathing and can cause stitching artefacts or missing slices. Furthermore, the spatial resolution of existing methods is often compromised owing to the time efficiency and data sufficiency requirements of 4D-MRI. Existing methods also have long acquisition times.

### Conclusions

The 4D-DWI technique is effective for accurately measuring tumour respiratory motion and delineating target volume in patients with abdominal cancer. It has high tumour CNR and minimal interobserver variability. This indicates that the detectability and accuracy of tumour motion and tumour delineation are better in 4D-DWI than in other types of 4D-MRI.

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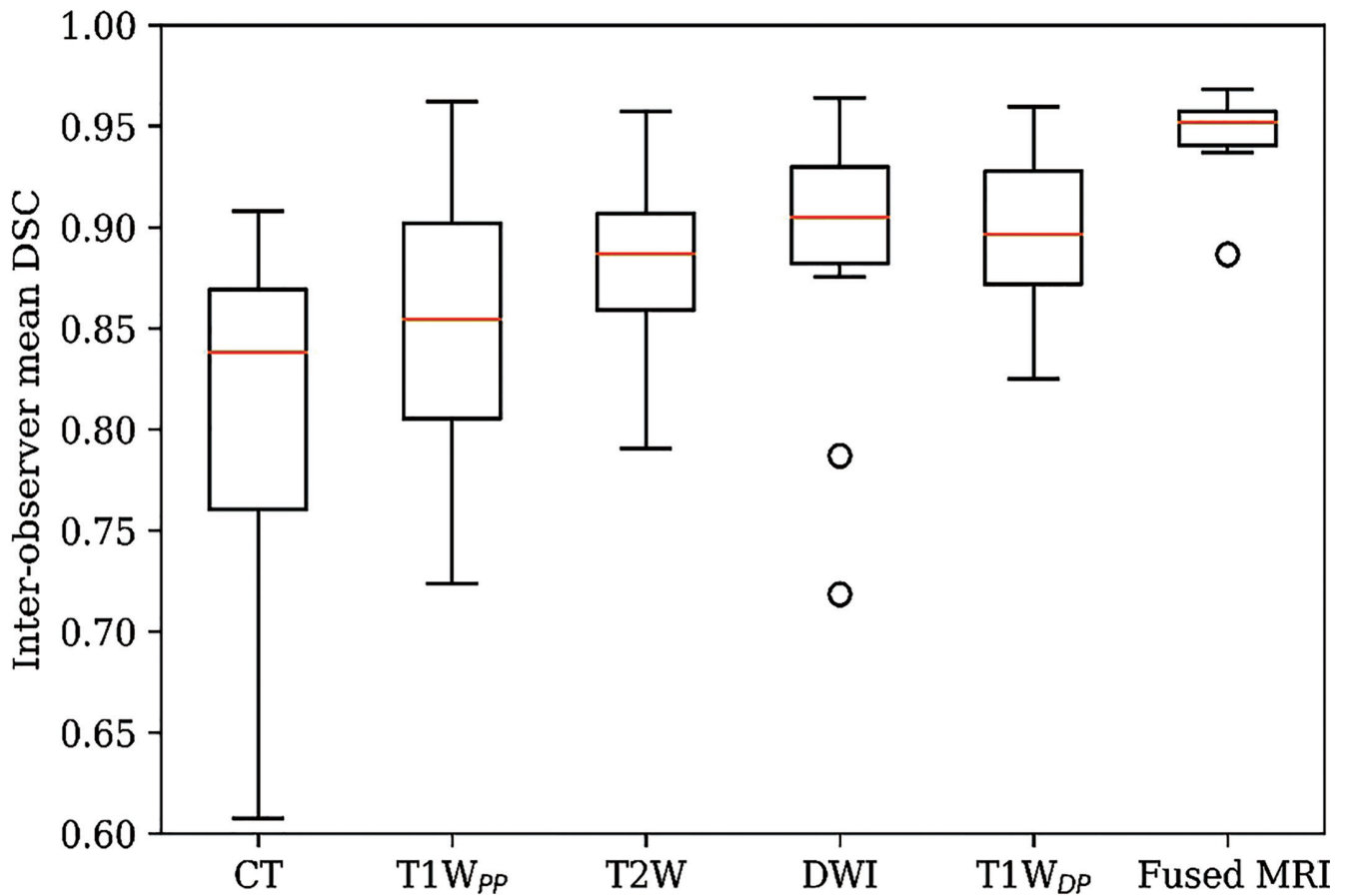


FIG 3. Interobserver means of gross tumour volume dice similarity coefficient (DSC) in computed tomography (CT) and various magnetic resonance imaging (MRI) sequences: T1-weighted portal-venous phase (T1W<sub>pp</sub>), T2-weighted (T2W), diffusion-weighted imaging (DWI), T1-weighted delayed phase (T1W<sub>DP</sub>), and fused MRI among patients with liver cancer.

from the Health and Medical Research Fund website (<https://rfs2.healthbureau.gov.hk>).

### Disclosure

The results of this research have been previously published in:

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