Supplementary

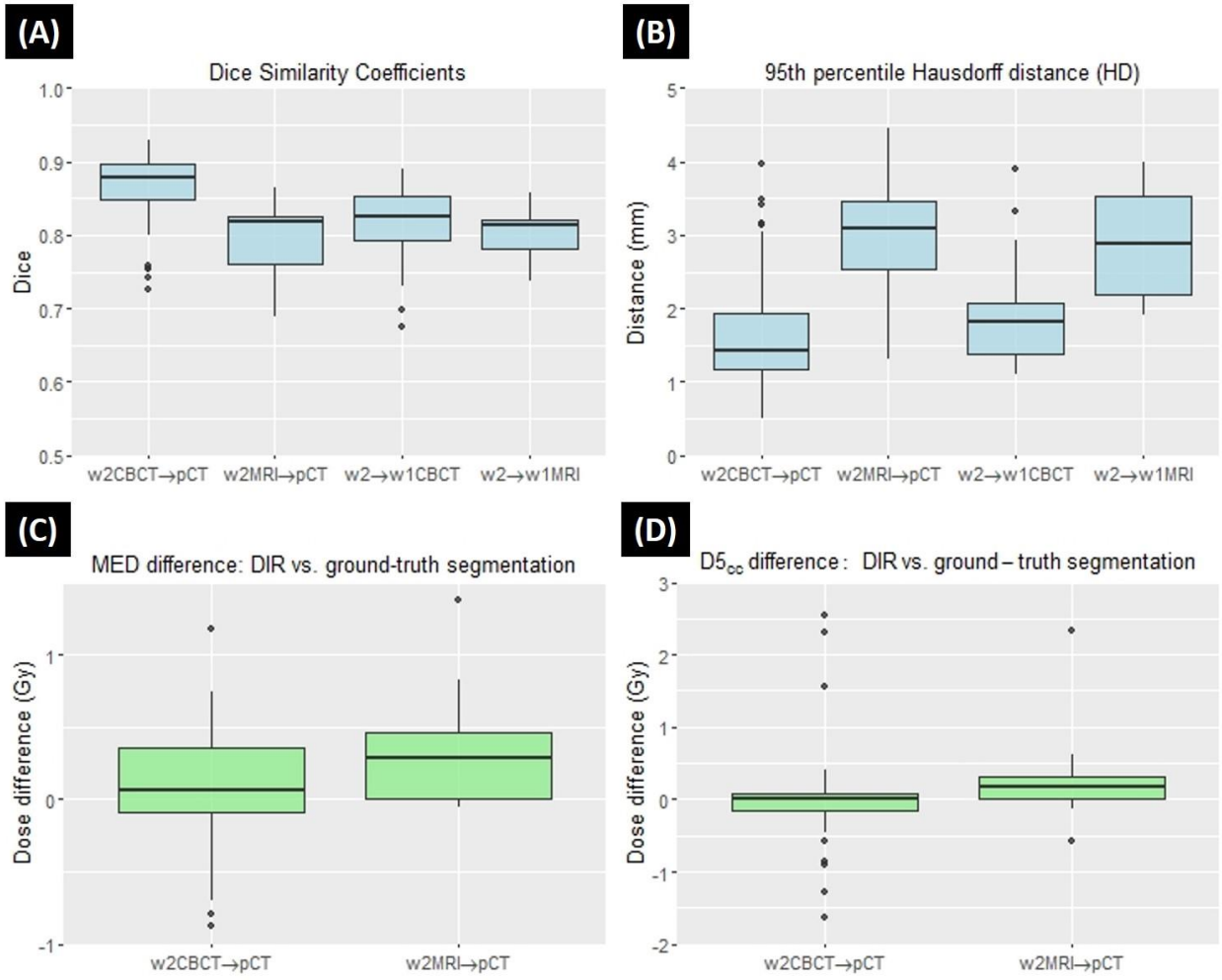
Early prediction of acute esophagitis for adaptive radiotherapy

S1-Registration evaluations

S1-1-External validation of DIR

An external publicly available longitudinal dataset (1) originally collected for investigating breathing patterns of locally advanced non-small cell lung cancer patients undergoing CRT was utilized for yet another independent testing. In this public dataset, planning 4DCT and 6 weekly 4D-CBCT were provided with planning esophagus contours for 13 patients. Image resolution for pCT and wCBCT were 0.98mm to 1.17mm in-plane spacing and 3mm slice thickness. For this dataset, contours of esophagus were first propagated from pCT to wCBCT via DIR (Section 2-3 and (2,3)), and a radiation oncologist reviewed and modified (when necessary) the contour on the wCBCT serving as the ground truth. Average DSC obtained for the wCBCT-pCT registrations of the external dataset (for all 6 weeks) was 0.80±0.09 (95% confidence-interval: 0.76-0.81) with average maximum (95th percentile) Hausdorff distances of 6.7mm (2.3mm). This dataset was also used to help find the optimal registration hyperparameters.

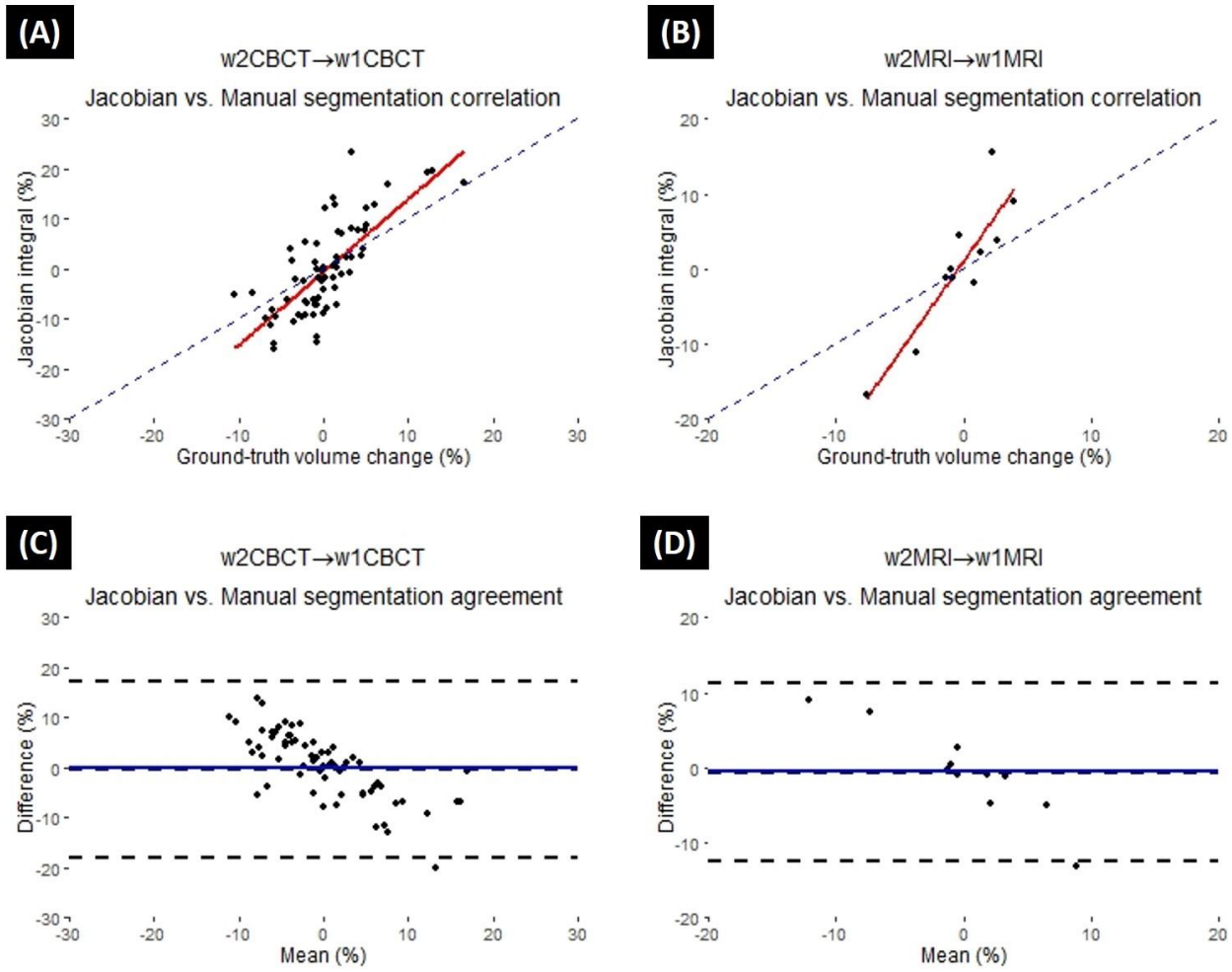
S1-2-Geometric and dosimetric evaluation of DIR



Supplemental Fig.1. Box plots showing geometric validations using (A) Dice similarity coefficient and (B) 95th percentile Hausdorff distance as well as dosimetric validations using the (C) MED and (D) $D5_{cc}$ (Gy) differences calculated between the DIR generated and ground-truth manual contours for all the registrations performed between pCT, w2CBCTs and w2MRIs.

S1-3-Evaluation of Jacobian map

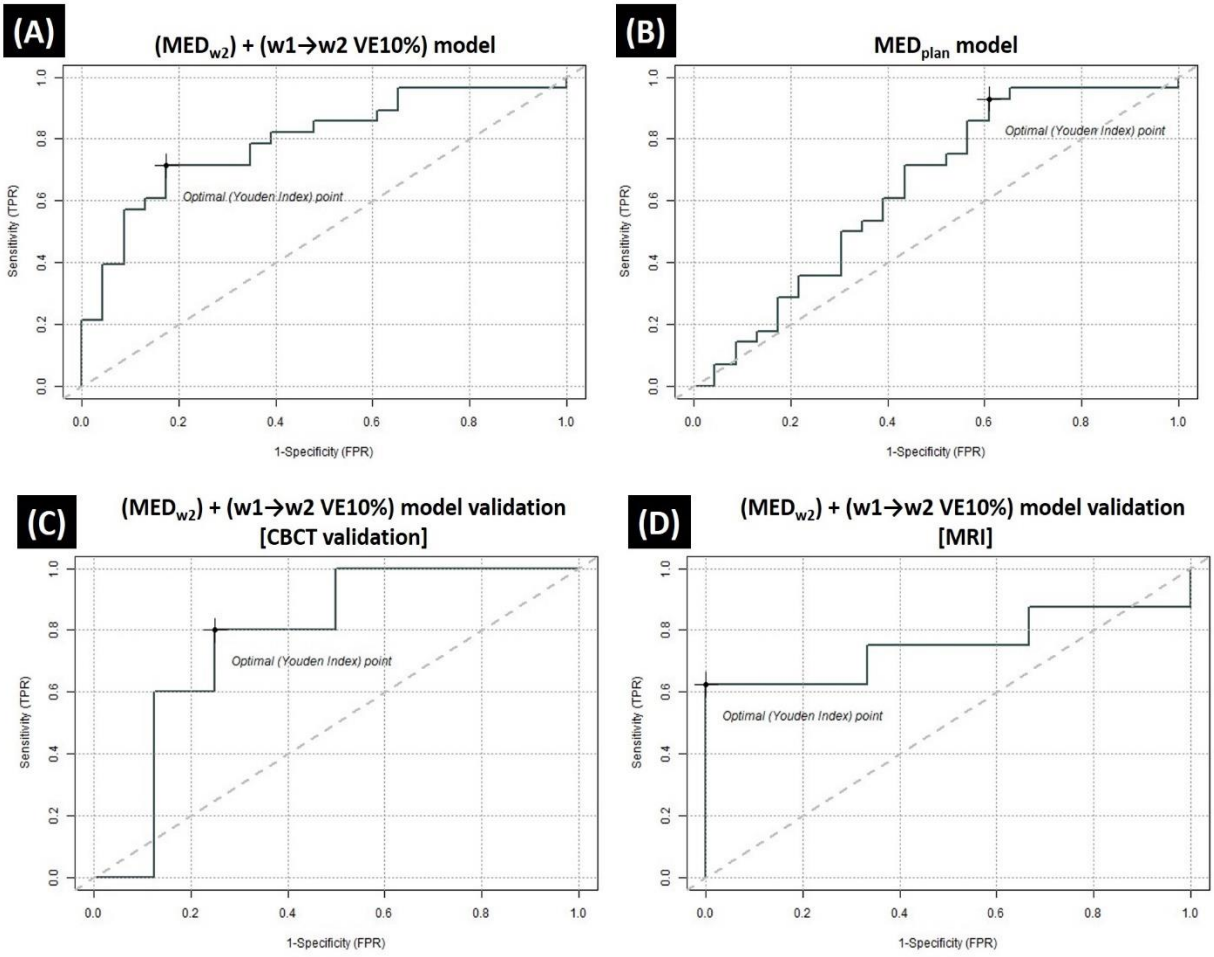
In our dataset, we assessed the accuracy of Jacobian maps where esophagus local volume change parameters were derived by comparing the weekly esophagus volume change calculated using Jacobian integral (i.e. voxel-wise local volume change) against the ground-truth manual segmentation for both CBCT and MRI cohorts (Supplemental Fig. 2).



Supplemental Fig.2. (Top) Scatter plot showing correlations between the weekly net esophagus volume change calculated using Jacobian integral versus the ground-truth manual segmentation for (A) wCBCT and (B) wMRI registrations. Red line is the linear regression line. (Bottom) Bland-Altman plot showing the agreements between the Jacobian integral method and ground-truth manual segmentation for (C)

wCBCT and (D) wMRI registrations. Solid blue lines show the mean difference between the two methods for (C) wCBCT and (D) wMRI registrations.

S2-ROC Curves



Supplemental Fig.3. ROC curves of (A) cross-validated proposed model using the combined MED_{w2} + w1→w2 VE10% CBCT training, (B) cross-validated MED_{plan} model using CBCT training and the proposed model externally validated using the (C) CBCT validation and (D) MRI data. For each sub-figure, optimal Youden index is given by black dot.

References

1. Hugo GD, Weiss E, Sleeman WC, et al. A longitudinal four-dimensional computed tomography and cone beam computed tomography dataset for image-guided radiation therapy research in lung cancer 2017;44:762-771.
2. XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX
3. Tustison NJ, Avants BB. Explicit b-spline regularization in diffeomorphic image registration. *Front Neuroinform* 2013;7:39.