Investigating a Novel CT Density-Based Approach to Regional Lung Ventilation Mapping

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ABSTRACT

Functional-avoidance radiotherapy steers dose away from well-ventilated lung, which requires an accurate, patient-specific ventilation map. The standard approach derives ventilation from the Jacobian of a deformable image registration (DIR) of 4DCT, but the Jacobian is a derivative of the displacement field and amplifies registration error.

We exploit 5DCT's 25 free-breathing scans: for each voxel, ventilation is the negative slope of log-density vs breathing amplitude. 25 independent density measurements per voxel, with no displacement-field derivative.

Across 204 patients, HU-based and Jacobian ventilation agreed at whole-lung and regional scales; both reproduced their fine detail well above their mutual agreement; and HU uniquely yields a per-voxel confidence map.

KEY FINDINGS

0.99
Whole-lung agreement slope ($R^2 = 0.93$)

0.74
Regional-scale agreement (0.51 per voxel)

0.73
HU reproducibility (vs 0.67 for Jacobian)

25×
Density measurements per voxel

204
Patients analyzed

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INTRODUCTION

Functional-avoidance radiotherapy reduces pulmonary toxicity by directing dose away from well-ventilated lung, which requires an accurate, patient-specific map of regional ventilation. The established method computes ventilation from the Jacobian of a deformable image registration (DIR) between breathing states of a 4DCT.

Because the Jacobian is a spatial derivative of the estimated displacement field, it is sensitive to registration errors that are hard to detect and can corrupt the ventilation estimate. 5DCT instead acquires 25 fast free-breathing scans, densely sampling each voxel's density across the breathing cycle, enabling ventilation estimation directly from CT density.

METHODS & MATERIALS

Patients & imaging
204 patients imaged with 5DCT (25 sequential fast-helical free-breathing CT scans each).

Registration
Two-stage deformable registration (deedsBCV, then pTV) aligned the 24 scans to a reference image.

HU-based ventilation
Per lung voxel, log-density is regressed against the breathing amplitude at which that voxel was imaged, across all 25 scans; specific ventilation is the negative slope, the fractional lung expansion per unit amplitude. The 25 samples also yield a per-voxel goodness-of-fit.

Jacobian ventilation
Computed conventionally from the DIR displacement fields (Jacobian determinant), for the same voxels.

Analysis
Whole-lung agreement (patient-mean regression); voxel-wise agreement (Spearman; Dice of top-20% regions); agreement vs spatial scale; and split-half reproducibility (25 scans split into two amplitude-balanced halves).

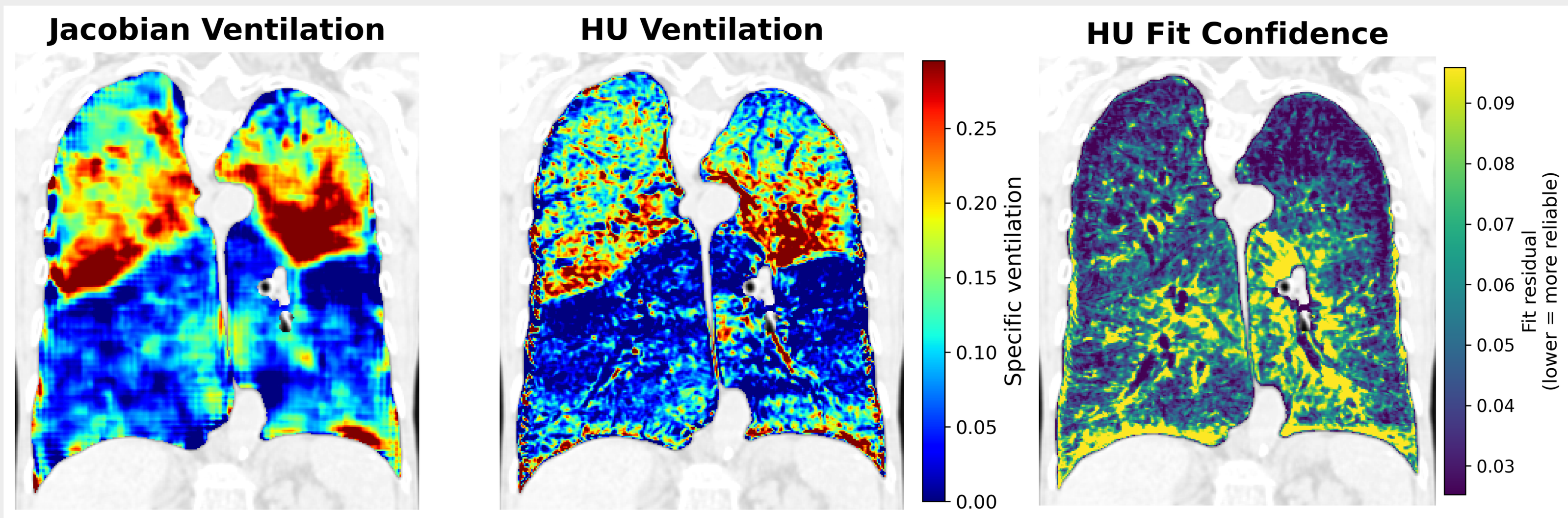

Fig. 1. Coronal maps of specific ventilation (the fractional lung expansion per normalized breath) for one patient: Jacobian-based (left), HU-based (middle), and the HU per-voxel fit residual (right; lower = more reliable). The two methods show concordant patterns; HU recovers finer heterogeneity and uniquely provides a per-voxel confidence map. Color scale is per-patient.

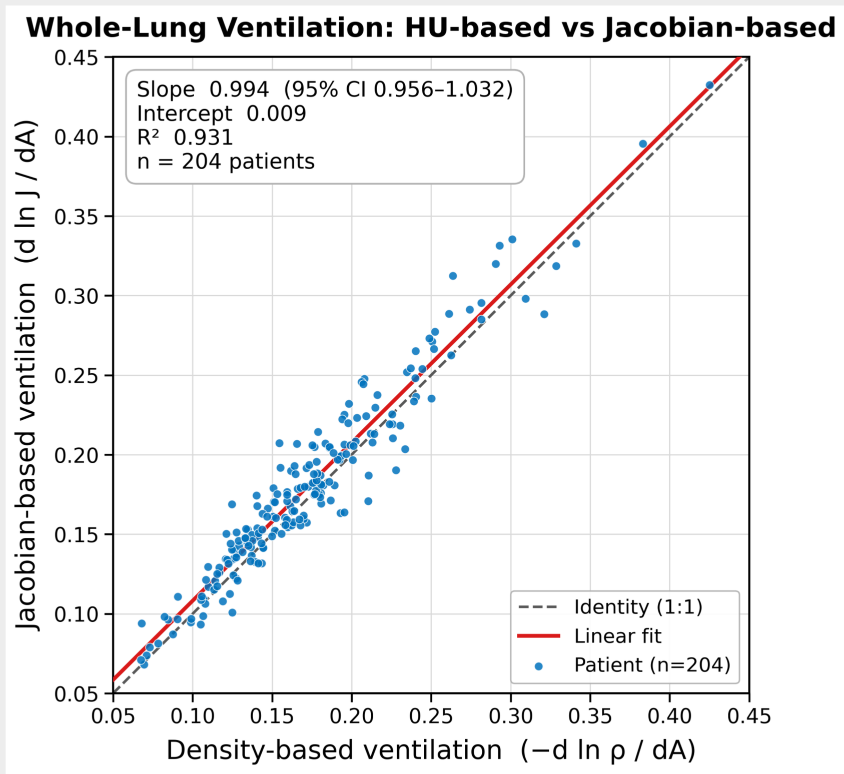

Fig. 2. Whole-lung agreement: Patient-mean HU vs Jacobian specific ventilation (n = 204). Slope 0.99 (95% CI 0.96–1.03), $R^2 = 0.93$; the fit overlies the identity line.

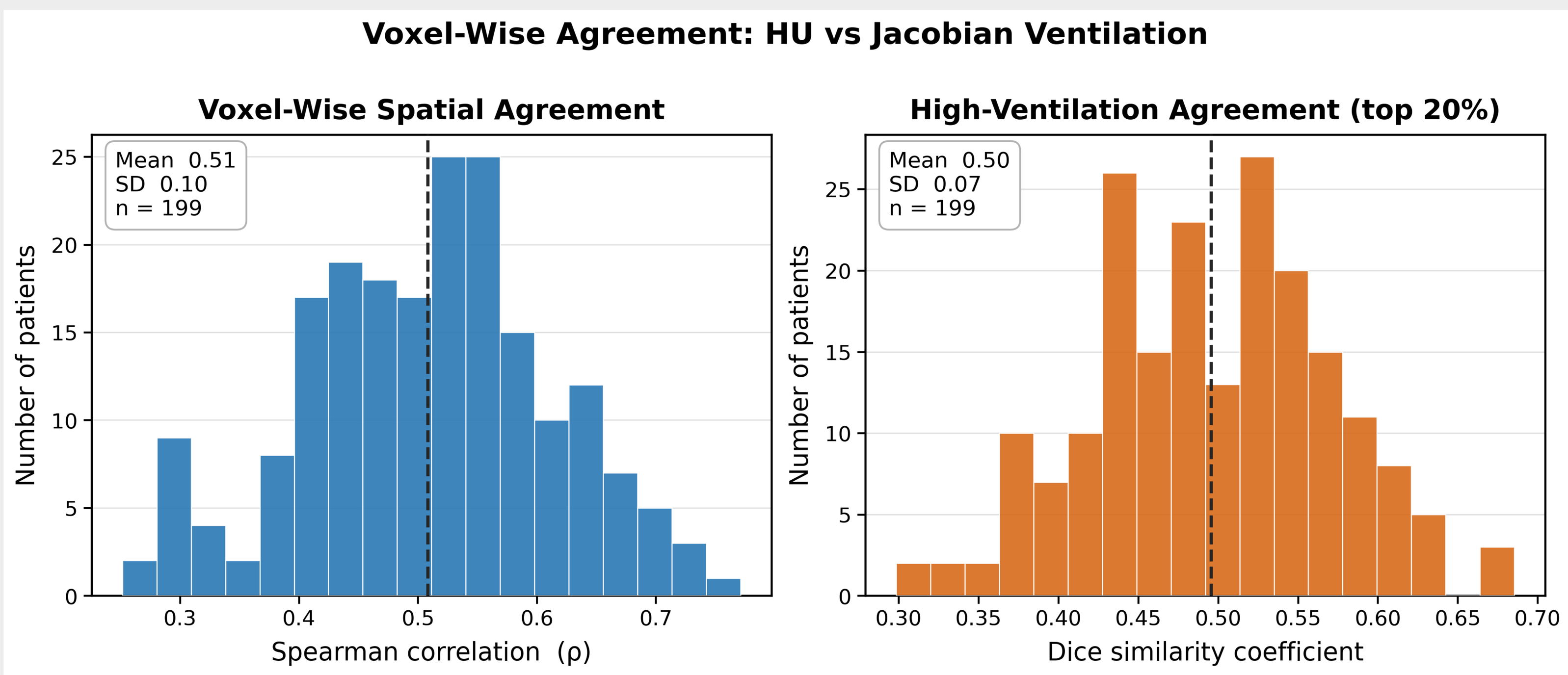

Fig. 3. Voxel-wise spatial agreement across patients: Spearman correlation (left; mean 0.51) and Dice overlap of the top-20% ventilation regions (right; mean 0.50). Moderate at the voxel level.

RESULTS

HU-based and Jacobian specific ventilation showed concordant spatial patterns, with HU recovering finer heterogeneity and adding a per-voxel confidence map (Fig. 1). The two agreed excellently at the whole-lung level (Fig. 2; slope 0.99, $R^2 = 0.93$) and moderately per-voxel (Fig. 3; Spearman 0.51, Dice 0.50). Agreement rose to ~0.74 at the ~1.5 cm regional scale relevant to planning (Fig. 4). Both methods reproduced their own maps (HU 0.73, Jacobian 0.67 mean) well above their mutual agreement (0.51), with HU modestly the more reproducible (Fig. 5).

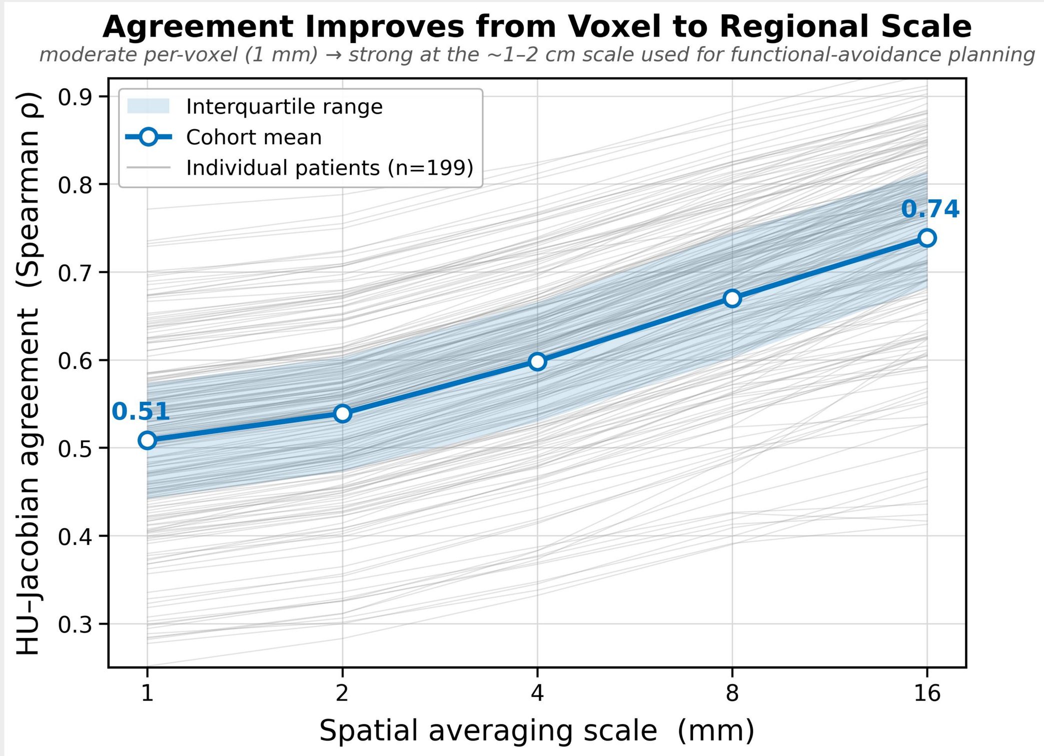

Fig. 4. Agreement vs spatial scale (n = 199). HU–Jacobian Spearman rises from 0.51 per voxel (1 mm) to 0.74 at ~1.5 cm, the regional scale relevant to functional-avoidance planning. Part of the rise is the expected effect of spatial averaging.

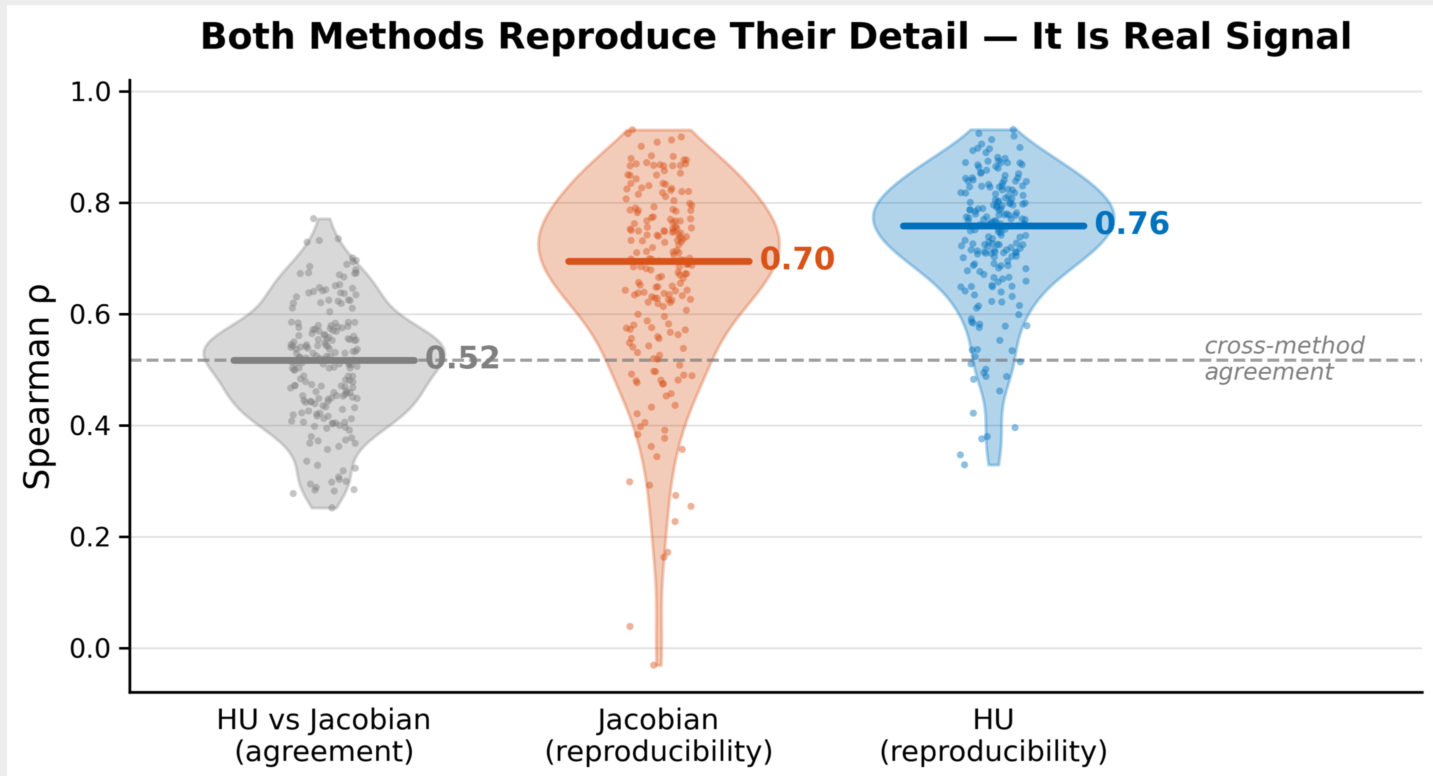

Fig. 5. Split-half reproducibility. Both methods reproduce their own maps (HU 0.76, Jacobian 0.70 median) well above the two methods' mutual agreement (0.52) — the fine detail is reproducible signal, not noise. HU is modestly but significantly more reproducible (higher in 62% of patients; $p < 10^{-13}$).

DISCUSSION

Two ventilation estimates from fundamentally different signals, CT density and DIR-derived deformation, agree at the whole-lung and regional scales relevant to functional-avoidance planning.

The moderate voxel-level agreement is not noise: each method reproduces its own fine detail (0.73, 0.67) well above the two methods' mutual agreement (0.51), so both reproducibly capture real structure, and the voxel-scale differences reflect a genuine distinction between density- and deformation-based ventilation.

Advantages: The HU method uses 25 independent density measurements per voxel rather than a displacement-field derivative, recovers finer detail, and provides a per-voxel confidence map the Jacobian cannot supply.

Caveats: The Jacobian is not a ground truth, so this is a cross-comparison, not validation; the rise in agreement with scale is partly the expected effect of averaging; and external validation is still needed.

CONCLUSIONS

HU-based ventilation mapping from 5DCT is a viable alternative to Jacobian-based ventilation: it agrees at whole-lung and regional scales while offering finer spatial detail, a per-voxel confidence metric, and modestly higher reproducibility.

Future work: Validation against external reference standards (pulmonary function; nuclear-medicine or dual-energy CT ventilation) and evaluation for functional-avoidance treatment planning.

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