Infrastructure for Building Population-Level Atlas of the Spatial Distribution of Lung Nodules Using the National Lung Screening Trial Dataset

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INTRODUCTION

- Lung nodule spatial distribution is non-homogenous across lung lobes
- Modern CT screening is highly sensitive, with most detected nodules being benign
- The influence of clinical variables on probabilistic nodule distribution lacks rigorous exploration

AIM

- Develop a pipeline to construct a population-level probabilistic lung nodule atlas
- Identify spatial trends to better guide clinical diagnosis, risk stratification, and personalized treatment strategies

FIGURE 2

Example of low-dose CT scan used for annual lung cancer screening on at-risk populations

Less than 5% of detected nodules turn out to be cancerous

DATA

- The National Lung Screening Trial is a large public dataset and seminal clinical trial that compared low-dose CT to standard chest X-Ray screening for reducing lung cancer deaths
- For this study, we used:
  - Low-dose CT scans (N=26,722), three annual screenings
  - Patient demographics and clinical history
  - Radiologic findings, treatments, and outcomes

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METHODS

- **Template[1]**: 3D standardized lung template generated from 30 subjects from the NLST dataset
- **Automatic segmentation[2]**: deployed TotalSegmentator on CT scans to delineate whole lung and individual lobes
- **Image registration[3]**: leveraged UniGradICON to warp diverse patient scans into the unified atlas space
- **Nodule detection[4]**: utilized MONAI's lung nodule detection model to locate centroid and bounding box of nodules

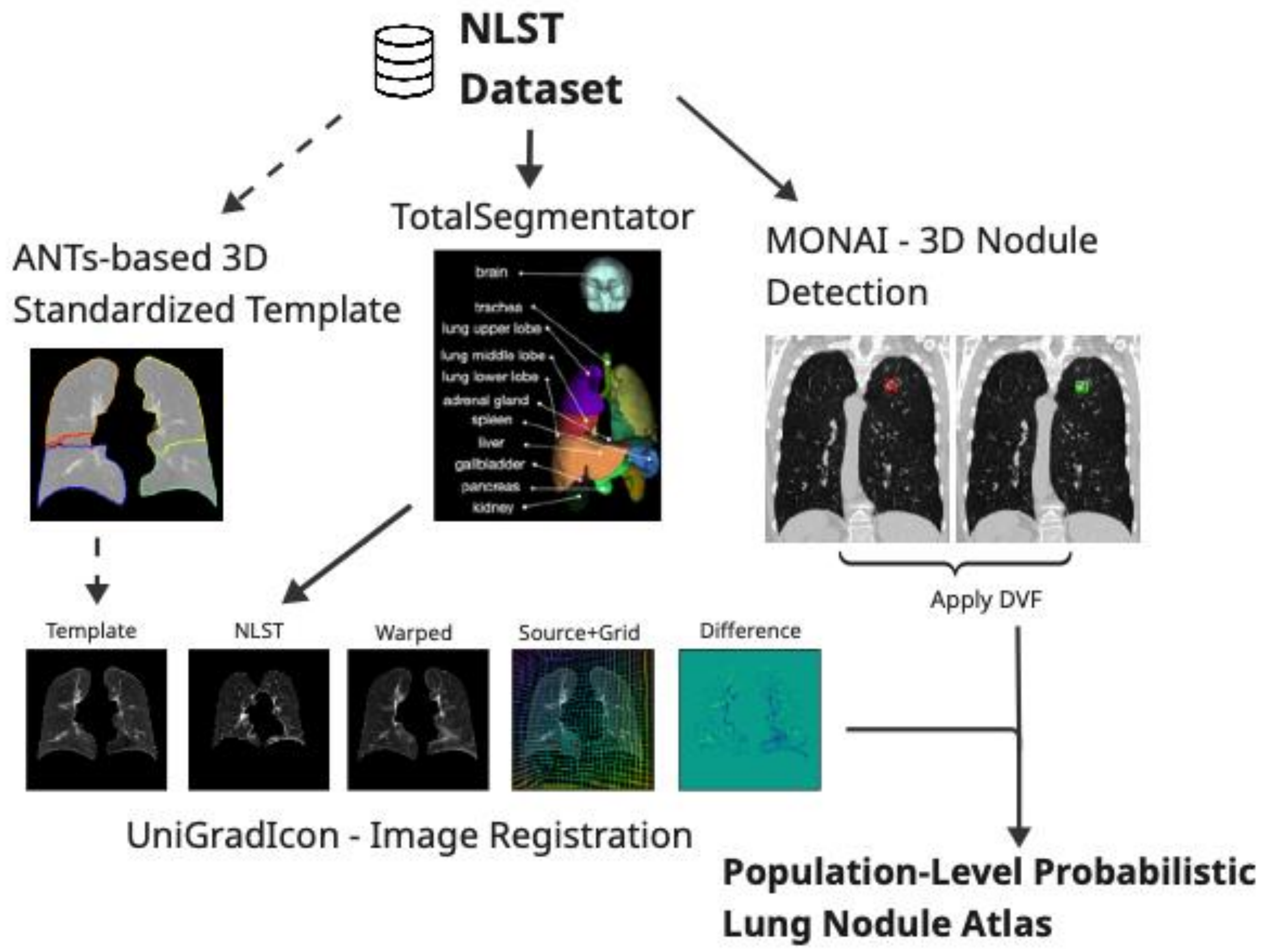

FIGURE 2

Proposed infrastructure for constructing a population-level lung nodule atlas

Ensembles various state-of-the-art tools into an automated pipeline

Maps discrete nodule coordinates into a standardized reference space to enable spatial analysis

RESULTS

- N=4,857 unique nodules > 10 mm in diameter
- **Image Registration**: Mean lobar Dice score improved from 0.38 to 0.91 following registration; Average relative volume difference was maintained at 4.4% for the whole lung and 7.9% across all lobes
- **Nodule Detection**: 87% of scans with recorded nodules had a detected centroid

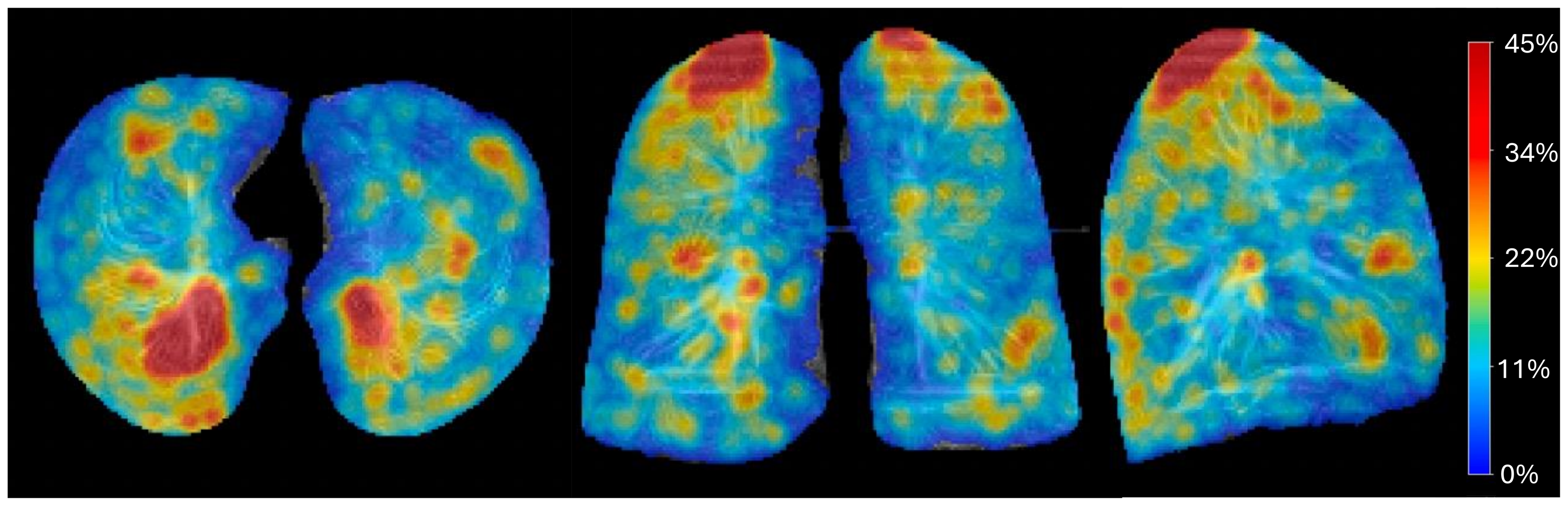

FIGURE 3

Green cross is detected centroid, red shaded area is ground truth lung nodule mask

On test set of 30 nodules with ground truth, mean distance between centroids = 2.04 mm

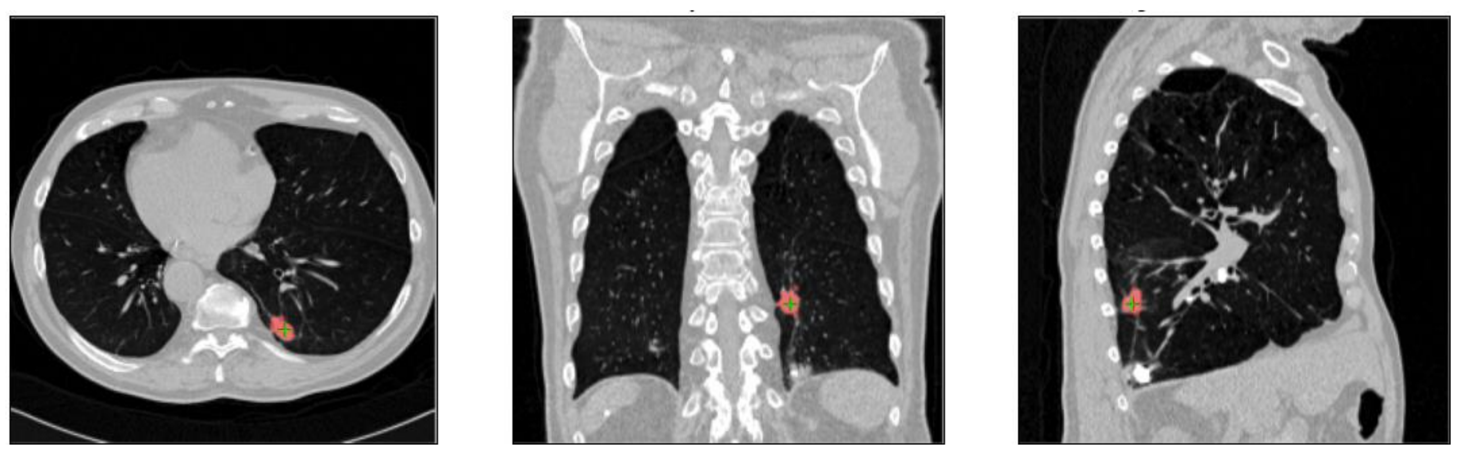

FIGURE 4

Heat map of nodule centroid location density in the atlas space, N=4,169, Sigma smoothing = 3 voxels

Color scale: % of peak density (max along projection)

- Nodules have the highest propensity to develop in the right upper lobe (30.5%)
- Agrees with literature[5], pattern driven by structure of right bronchus causing carcinogens to preferentially be directed into this area
- Preliminary heat maps also generated using survival, treatment modality, malignancy status, and histology data

CONCLUSIONS

Investigated distribution patterns of lung nodules on routine low-dose CT screening scans using publicly available data

Successfully ensembled modular AI workflow that can robustly handle large imaging datasets using off-the-shelf tools

Enabled population-level spatial analyses, unlocking the ability to map relationships between nodule distribution and clinical phenotypes

FUTURE DIRECTIONS

Finalize probabilistic heat maps for NLST cohort and other specific subcohorts (lung cancer, adenocarcinoma, etc.)

Curate in-house lung CT dataset to validate pipeline on separate data and compare resulting spatial analyses

Build interactive viewer to display trends and patterns of lung nodule distribution for clinicians to explore and interrogate