

Supplemental Methods

Radiomics Analysis

Radiomic features were extracted with the Standardized Environment for Radiomics Analysis software package based on guidelines from the Image Biomarker Standardization Initiative (IBSI). IBSI-compliant first-order statistical and higher-order 3D features were extracted from the PET and CT image volumes. PET/CT image volumes were co-registered and resampled with linear interpolation to have a 2 mm³ isotropic voxel size. Intensity discretization was implemented using fixed bin numbers with uniform quantization. Texture features were implemented with 3D matrices. A detailed list of the extracted radiomic features is available at the following repository: <https://github.com/ashrafinia/SERA/tree/master/Spreadsheets>.

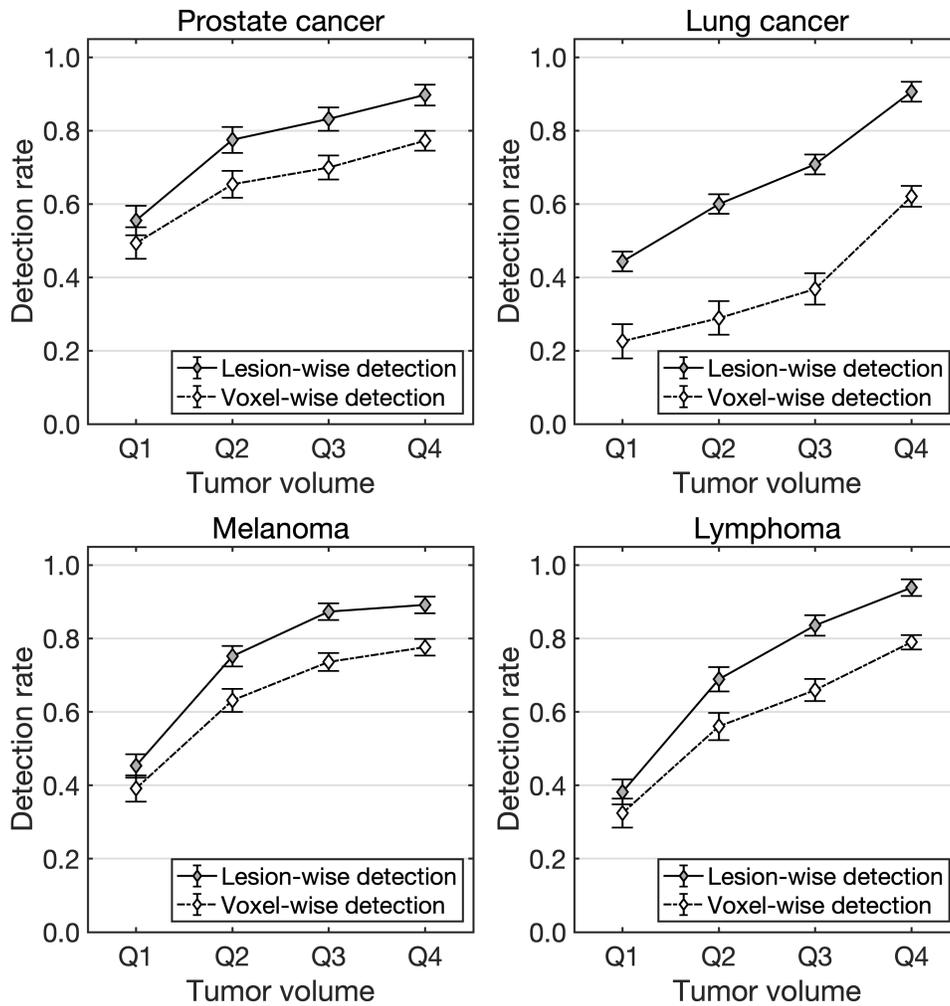
nnU-net Implementation

The nnU-net segmentation pipeline is based on convolutional neural networks and automatically configures itself, including preprocessing, network architecture, training, and post-processing procedures, based on domain knowledge from fixed, rule-based, and empirical parameters. A loss function combining cross-entropy loss and soft Dice loss was used during training. A 3D U-net network architecture using the hyperparameter optimization, training parameters, and post-processing procedures from the “3d_fullres” configuration was used.

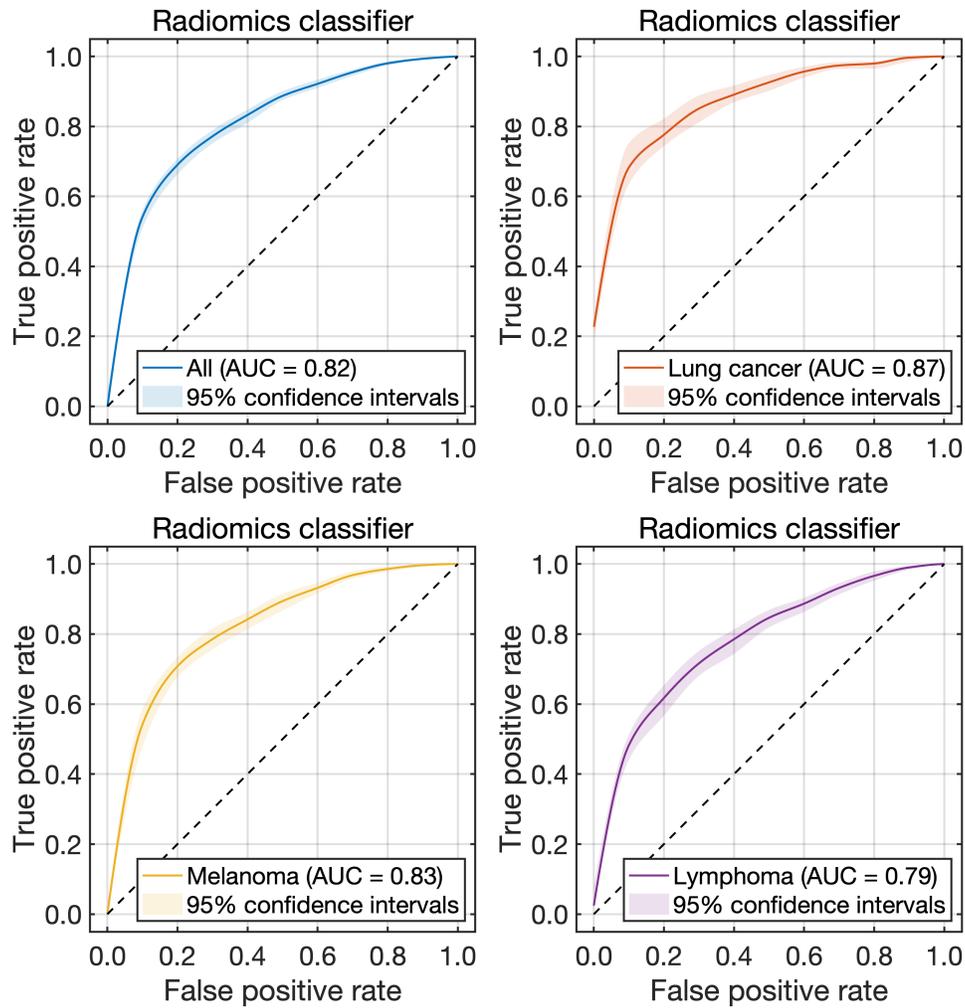
Code and Data Availability

The code used to compute IBSI-compliant radiomic features using the Standardized Environment for Radiomics Analysis software package can be found at: <https://github.com/ashrafinia/SERA>. The code used to train the nnU-net backbone can be found at: <https://github.com/MIC-DKFZ/nnUNet>.

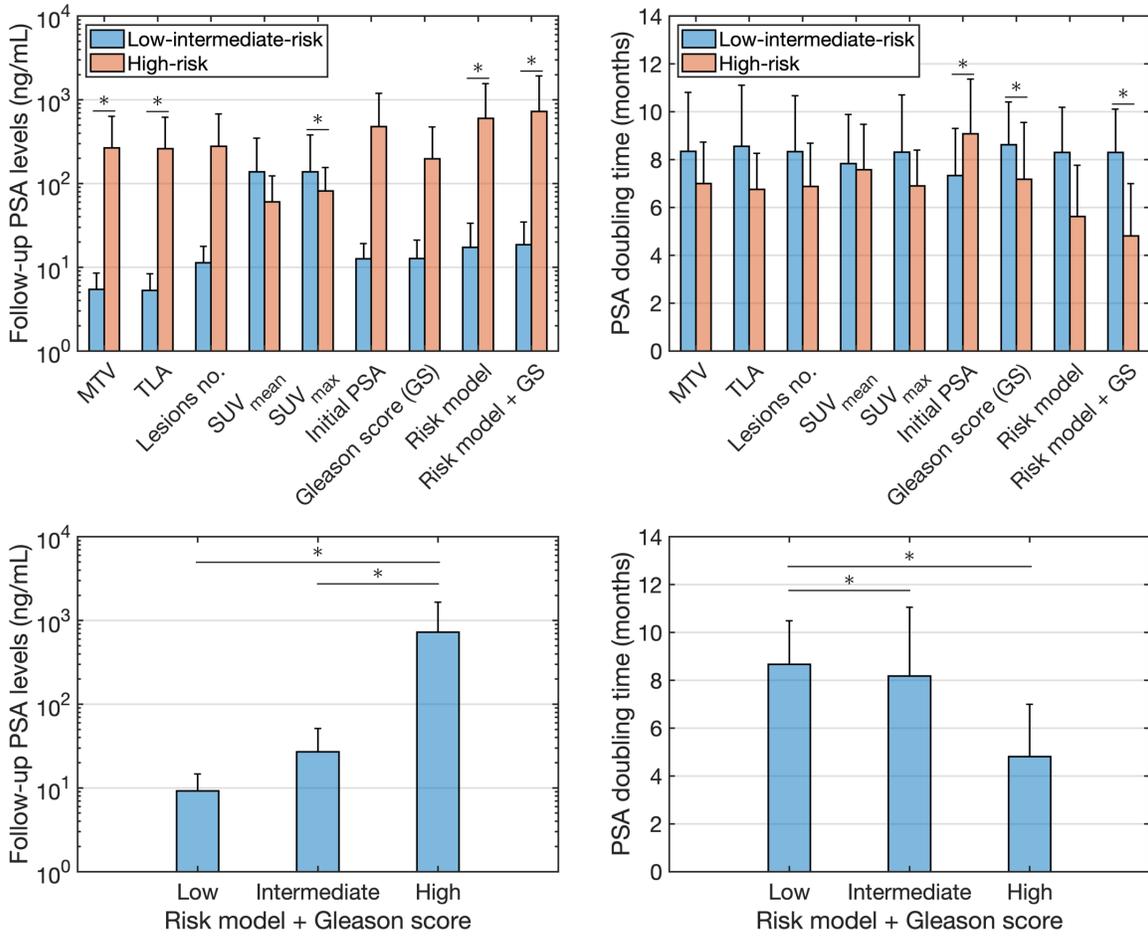
Publicly available data used in this study can be found at The Cancer Imaging Archive (<https://www.cancerimagingarchive.net/>) under the following digital object identifiers (DOIs): <https://doi.org/10.7937/gkr0-xv29>, <https://doi.org/10.7937/tcia.2019.8kap372n>, and <https://doi.org/10.7937/K9/TCIA.2016.21JUEBH0>.



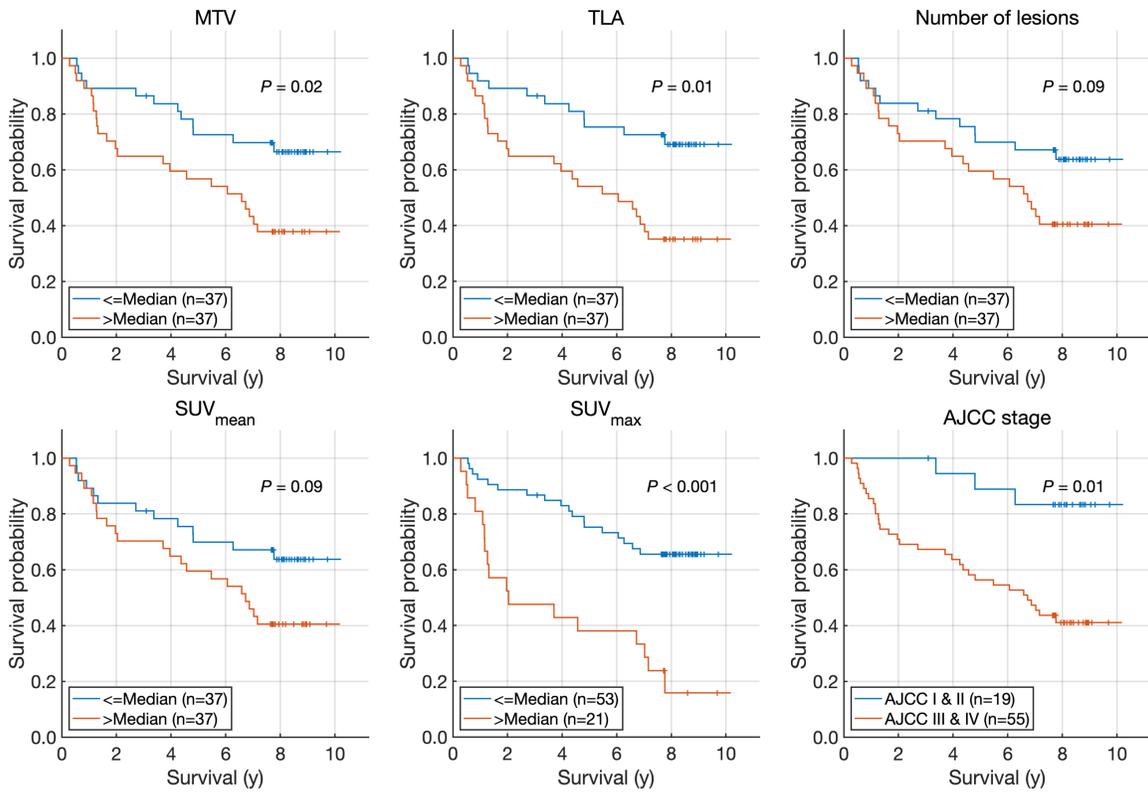
Supplemental Figure 1. Lesionwise and voxelwise detection rates by the DeepSSTL approach for each quartile of tumor volume. The lower quartile, median, and upper quartile of tumor volume were 0.52, 1.22, and 2.88 cm³ for prostate cancer, 1.53, 3.44, and 10.38 cm³ for lung cancer, 0.40, 1.01, and 2.79 cm³ for melanoma, and 0.40, 1.17, and 3.94 cm³ for lymphoma, respectively.



Supplemental Figure 2. Receiver-operating-characteristic curves of radiomics classifiers for detecting true-positive volumes of interest on ^{18}F -FDG PET/CT images from Dataset 3 of patients with lung cancer, melanoma, and lymphoma.



Supplemental Figure 3. Follow-up PSA levels and PSA doubling times for patients classified as low- to intermediate- vs. high-risk (top row). Follow-up PSA levels and PSA doubling times stratified by the risk model predictions combined with Gleason scores (bottom row).



Supplemental Figure 4. Kaplan-Meier survival curves for head and neck cancer patients stratified by MTV, TLA, number of lesions, SUV_{mean}, SUV_{max}, and AJCC staging.