



JOHNS HOPKINS
M E D I C I N E

Challenges in the Omics Landscape

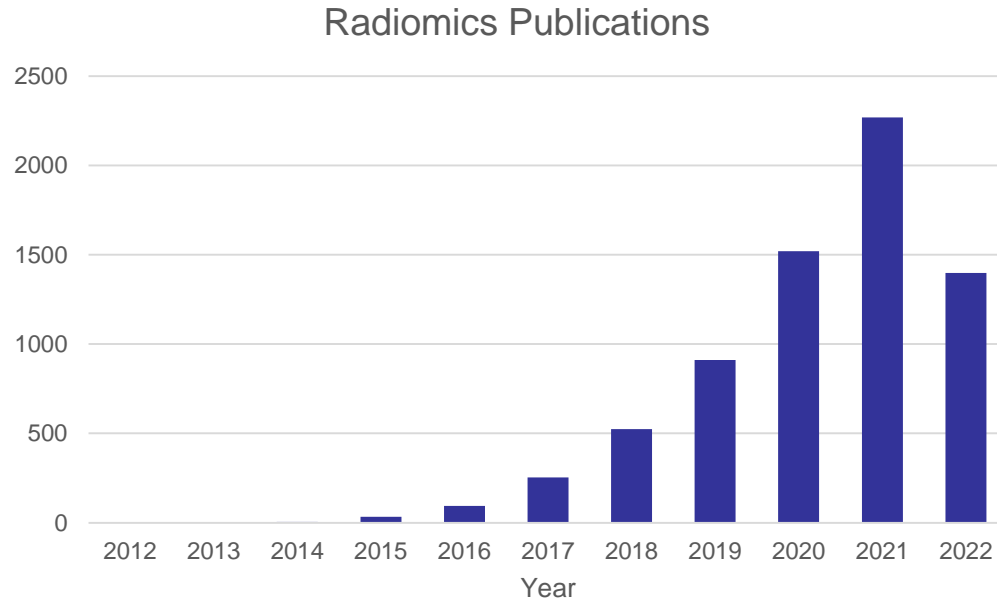
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July 12, 2022

Disclosures

- Nothing to disclose

Radiomics Publications



Limitations to Radiomics Expansion

- Image acquisition settings
- Radiomics software
- Patient artifacts
- Validity of statistical analysis
- Multi-institutional data

Garbage in Garbage **OUT**



Limitations to Radiomics Expansion

- Image acquisition settings
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Image Acquisition Settings: Tube Current

- Images acquired on GE and Toshiba at 10-12 different mAs settings
- Variability compared to inter-patient variability of 106 NSCLC patients
- **Tube current unlikely to significantly affect radiomics features for patients**

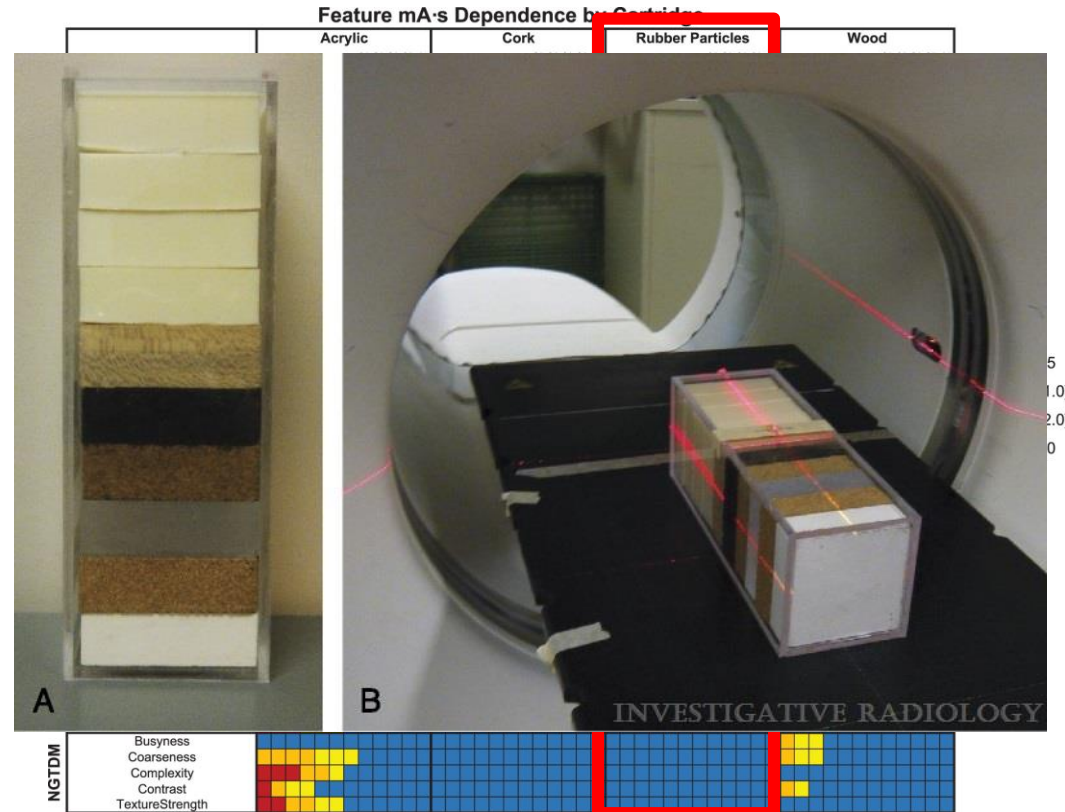
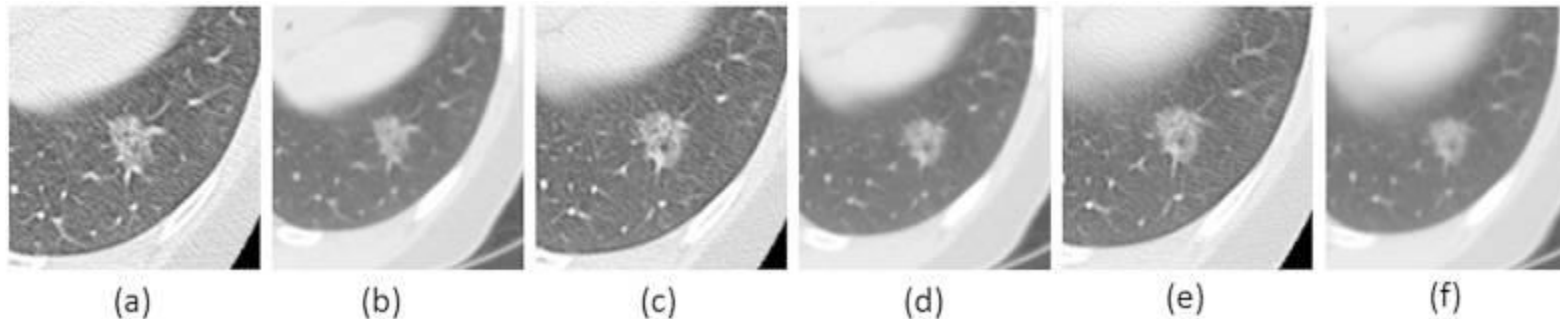


Image Acquisition Settings: Reconstruction Kernel

- Lung phantoms¹ and patients^{2,3} analyzed using different kernels
- **Significant difference between sharp and smooth or standard and lung reconstructions**



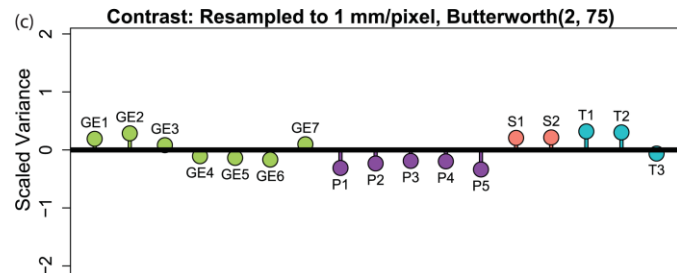
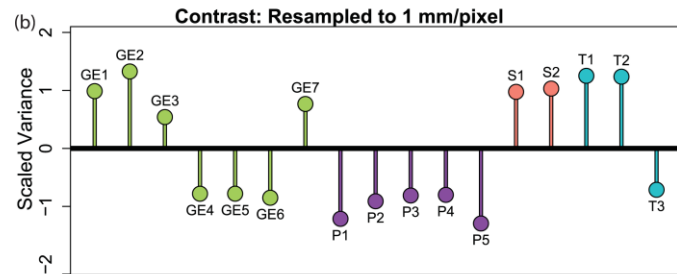
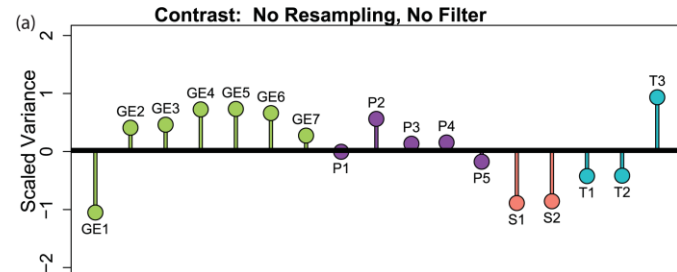
¹Zhao, Binsheng, et al. "Exploring variability in CT characterization of tumors: a preliminary phantom study." *Translational oncology* 7.1 (2014): 88-93.

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³Lu, Lin, et al. "Assessing agreement between radiomic features computed for multiple CT imaging settings." *PloS one* 11.12 (2016): e0166550.

Image Acquisition Settings: Voxel Size

- Phantom studies^{1,2} with CCR phantom rubber cartridge
- Patient study³ with 8 lung cancer patients reconstructed with 5 FOVs
- **Resampling reduces impact of voxel size**
 - **Butterworth smoothing needed in patient study**



¹Shafiq-ul-Hassan, Muhammad, et al. "Intrinsic dependencies of CT radiomic features on voxel size and number of gray levels." Medical physics 44.3 (2017): 1050-1062.

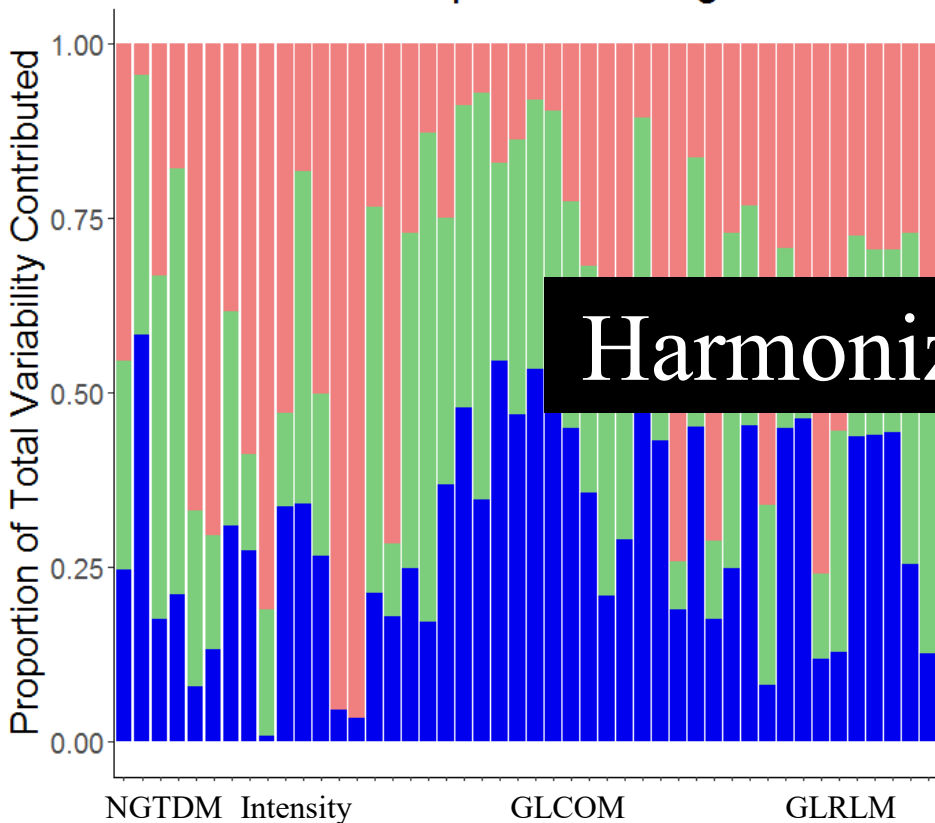
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³Mackin, Dennis, et al. "Harmonizing the pixel size in retrospective computed tomography radiomics studies." PloS one 12.9 (2017): e0178524.

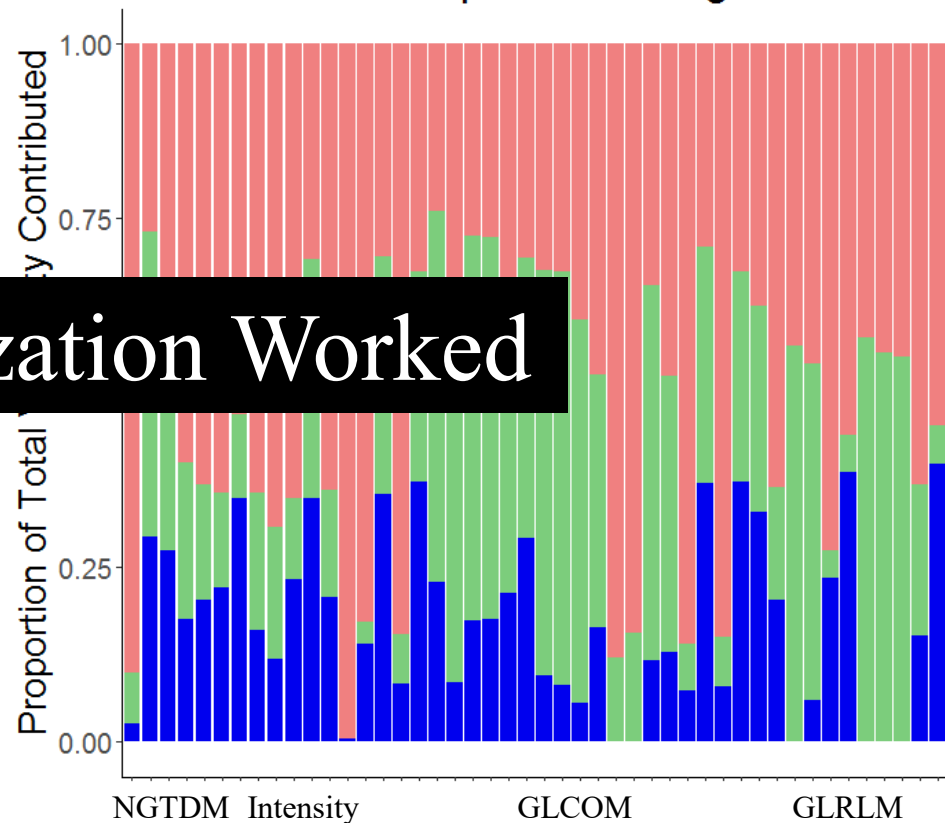
Image Acquisition Settings: Inter-scanner Variability

- Scanned updated CCR phantom on 100 CT scanners using local head protocol, local chest protocol, and control protocol (specific acquisition and reconstruction settings to minimize vendor differences)
- $Total\ Variability = \sqrt{\sigma_{manufacturer}^2 + \sigma_{scanner}^2 + \sigma_{residual}^2}$
- Total variability in control 57% less than total in chest
- Total variability in control 52% less than total in head
- **Control protocol reduce variability >50%**

Local Head Protocol:
Bit Depth Rescaling



Control Protocol:
Bit Depth Rescaling



Harmonization Worked

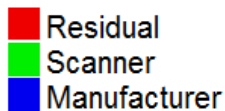


Image Acquisition Settings: Summary

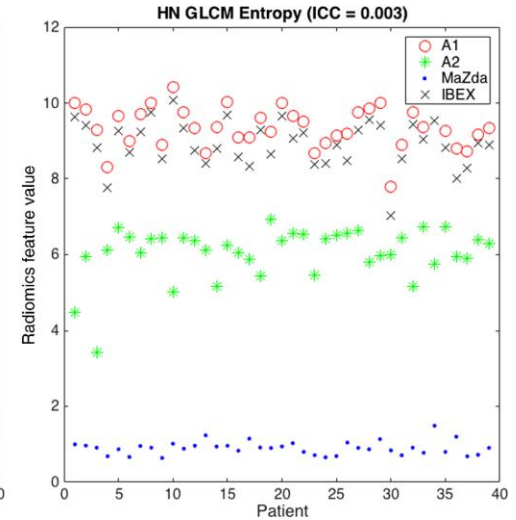
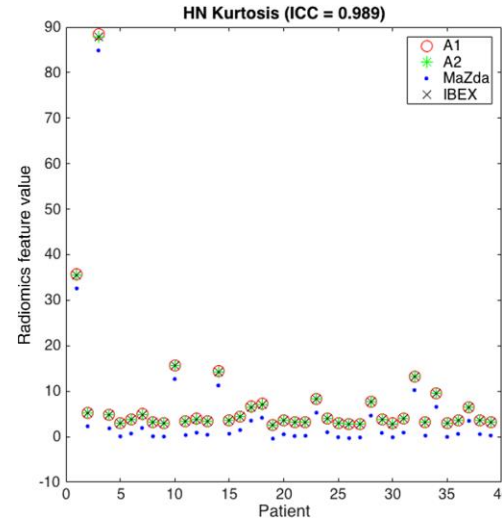
- Tube Current: not likely to significantly impact features
- Reconstruction Kernel: do not use dissimilar kernels together
- Voxel Size: resampling and smoothing reduce impact
- Control Protocol: reduces variability >50% compared to local head and chest protocols

Limitations to Radiomics Expansion

- Image acquisition settings
- **Radiomics software**
- Patient artifacts
- Validity of statistical analysis
- Multi-institutional data

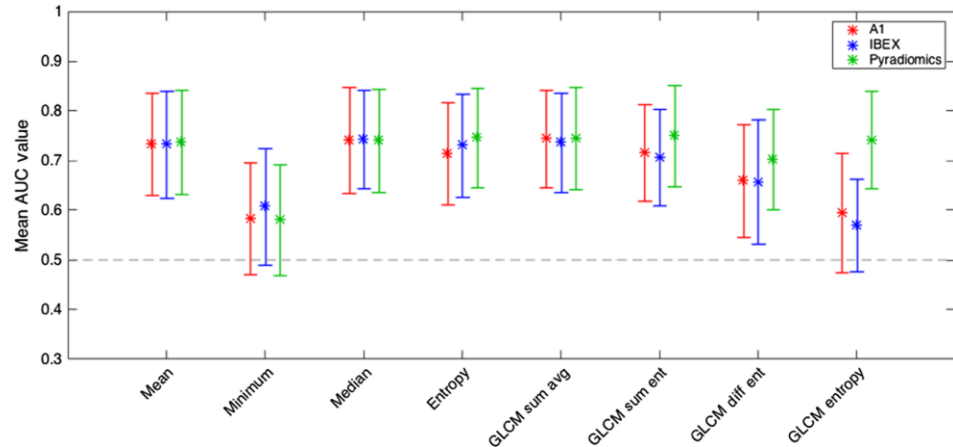
Radiomics Software: Inter-software Variability

- Comparison of 2 in house algorithms, IBEX, and MaZda for 39 HN patients
- Significant differences but high ICC values on first order features
- Package defaults for GLCM parameters very different



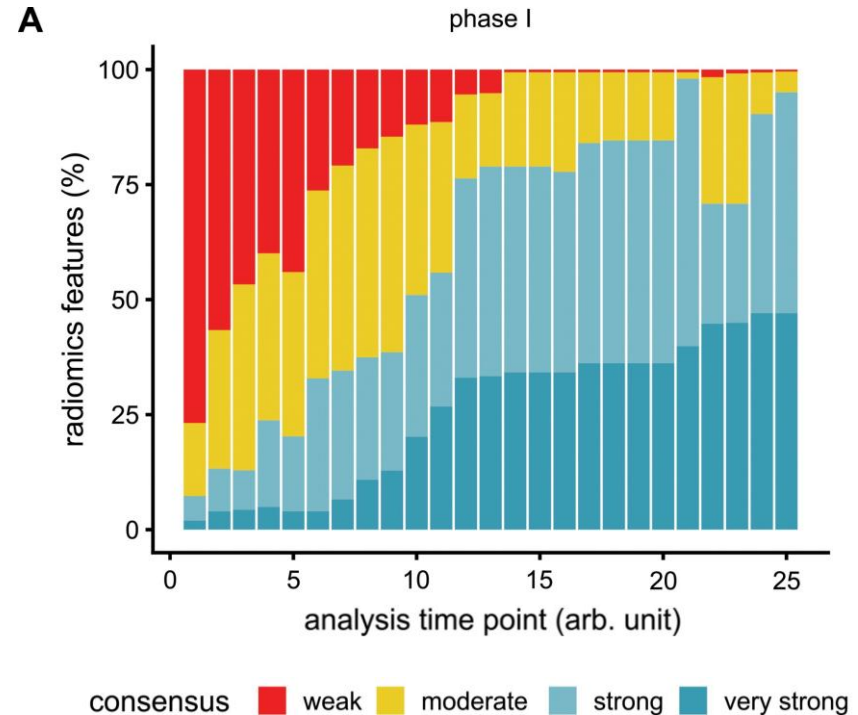
Radiomics Software: Inter-software Variability

- Analyzed 105 esophageal cancer patients with in house, IBEX, PyRadiomics with 8 features
- Logistic regression to classify radiation pneumonitis
- Differences in classification ability



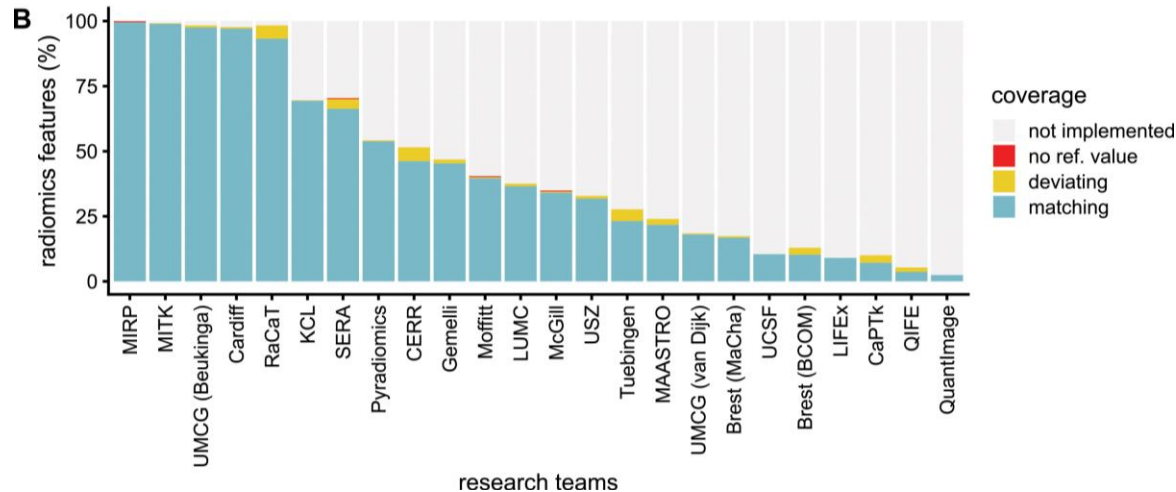
Radiomics Software: Initiatives

- Image Biomarker Standardization Initiative
- 25 research teams with different radiomics software
- Iteratively analyzed features from a digital phantom and CT scan of lung cancer patient
- Final data set: TCIA data set of multi-modality imaging of 51 sarcoma patients
 - 167 features good reproducibility



Radiomics Software: Initiatives

- Feature definitions published
- Compliance with IBSI can be checked against reference values

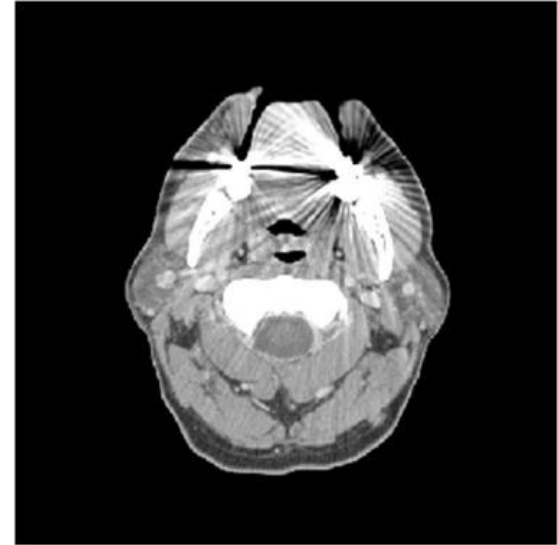


Limitations to Radiomics Expansion

- Image acquisition settings
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Patient Artifacts

- Streak artifacts
 - Features values robust to removing up to 50% of volume
- Presence of bone
 - Affects HU but difference minimal compared to variability among patients

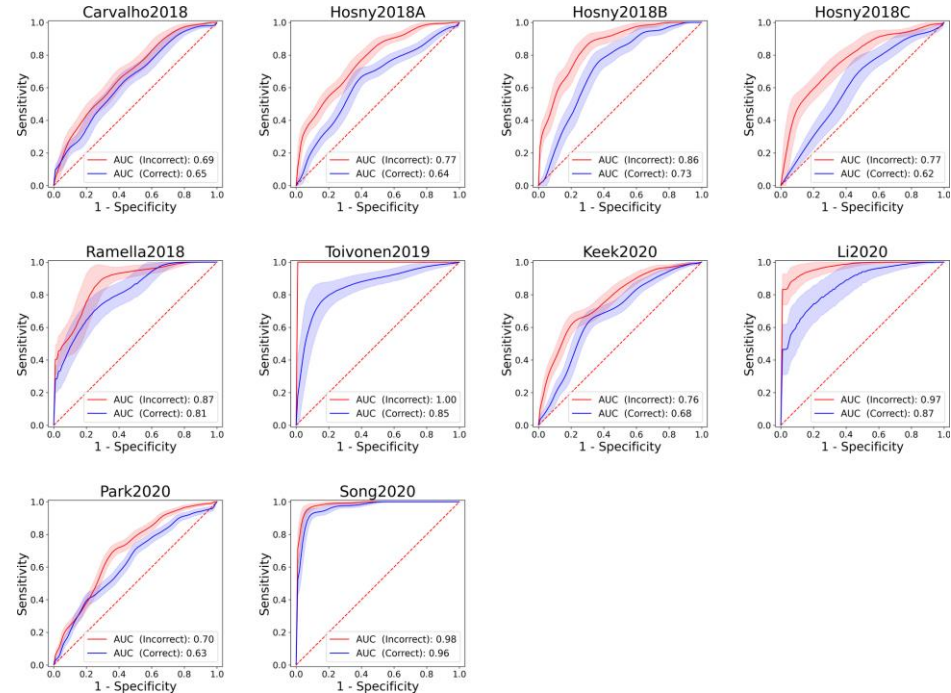


Limitations to Radiomics Expansion

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- **Validity of statistical analysis**
- Multi-institutional data

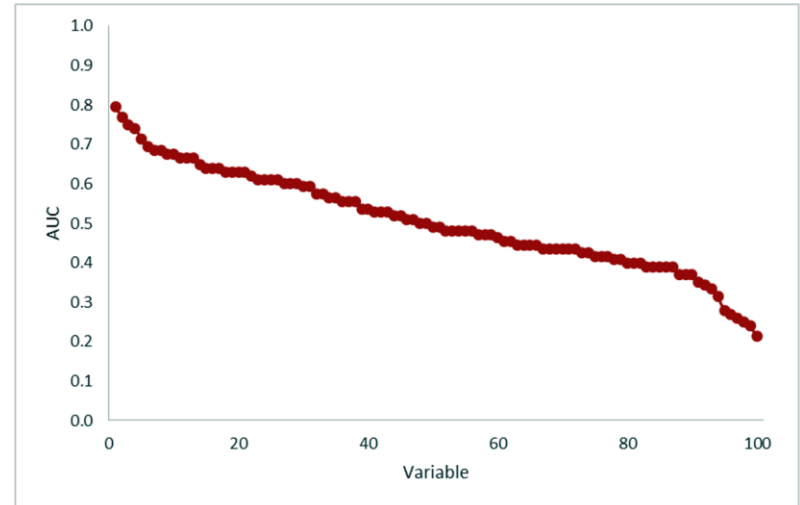
Validity of Statistical Analysis

- Feature selection before cross validation can cause large positive bias
- 10 datasets
 - 8 high dimensional-fewer samples than features
- Datasets with higher dimensionality more prone to positive bias



Validity of Statistical Analysis: Things To Look For

- Multiple hypothesis testing correction¹
- Independent validation dataset¹
- 22 checklist items from Transparent Reporting of multivariable prediction model for Individual Prognosis or Diagnosis²

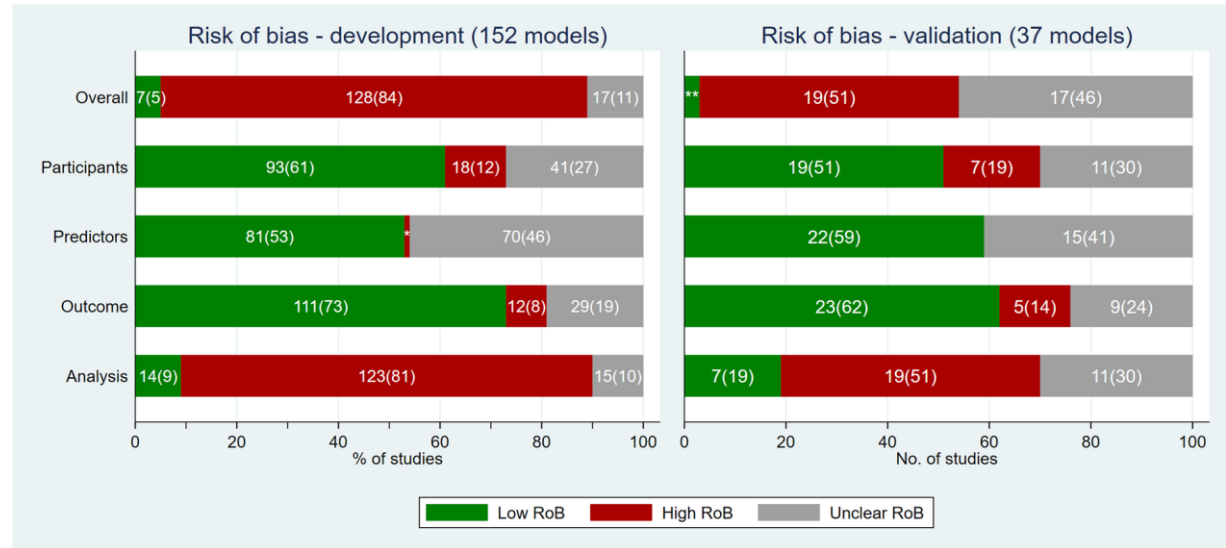


¹Chalkidou, Anastasia, Michael J. O'Doherty, and Paul K. Marsden. "False discovery rates in PET and CT studies with texture features: a systematic review." PloS one 10.5 (2015): e0124165.

²Collins, Gary S., et al. "Transparent reporting of a multivariable prediction model for individual prognosis or diagnosis (TRIPOD): the TRIPOD statement." Journal of British Surgery 102.3 (2015): 148-158.

Validity of Statistical Analysis: Risk of Bias

- Used Prediction model Risk Of Bias Assessment Tool (PROBAST) for prognostic models using machine learning in oncology



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Multi-institutional Data

- Most studies are single institution data
- Multi-institutional data incorporate many of the differences in acquisition covered and differences in patient demographics
- TCIA
 - 151 human collections, 10 phantom collections

Questions Remaining

- What about other modalities?

Robustness

Reproducibility

Classification performance

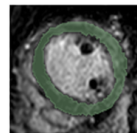
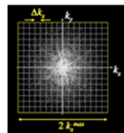
Image acquisition

Reconstruction

Segmentation

Post-processing

Feature extraction



MRI

- Field strength
- Sequence design
- Matrix size (acquired)
- Field of view
- Slice thickness
- Acceleration techniques
- Vendor
- Contrast timing
- Movement

- Matrix size (reconstructed)
- Reconstruction technique

- Manual 2D
- Manual 3D
- Semi-automated 2D
- Semi-automated 3D
- Automated 2D
- Automated 3D
- Size of the ROI

- Image interpolation ('resampling' / 'rescaling')
 - Grid alignment
 - Pixel sizing
- Intensity discretisation ('rebinning')
- Normalisation

- Mathematical formula
- Post-processing platform

CT

- Tube voltage
- Milliampere
- Pitch
- Field of view / pixel spacing
- Slice thickness
- Acquisition mode
- Vendor
- Contrast timing
- Movement

- Reconstruction matrix
- Slice thickness
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PET

- Field of view / pixel spacing
- Slice thickness
- Injected activity
- Acquisition time
- Scan timing
- Duty cycle
- Vendor
- Movement

- Reconstruction matrix
- Slice thickness
- Reconstruction technique (algorithm, PSF, FOV, subsets, iterations, FWHM)
- Attenuation correction

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- What about segmentation variability?

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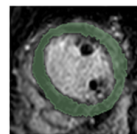
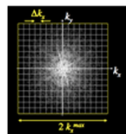
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Questions Remaining

- What about other modalities?
- What about segmentation variability?
- What about deep learning radiomics?



Garbage in Garbage **OUT**



Summary

- Resample images, use only similar reconstruction kernels, consider radiomics control protocol
- Different software may not be compatible, consider following IBSI
- Be careful in statistical analysis or false positive results may occur

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Thank You!