Prediction of Progression of Liver Metastases with Random Survival Forests

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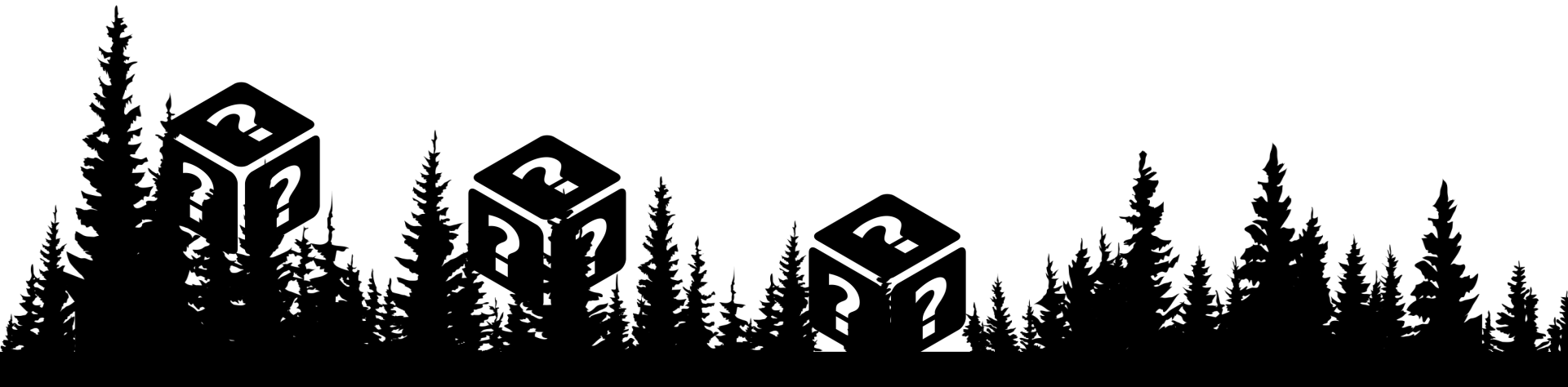


Objective

To develop a model to predict number of **months of freedom from local progression** for patients with colorectal liver metastases

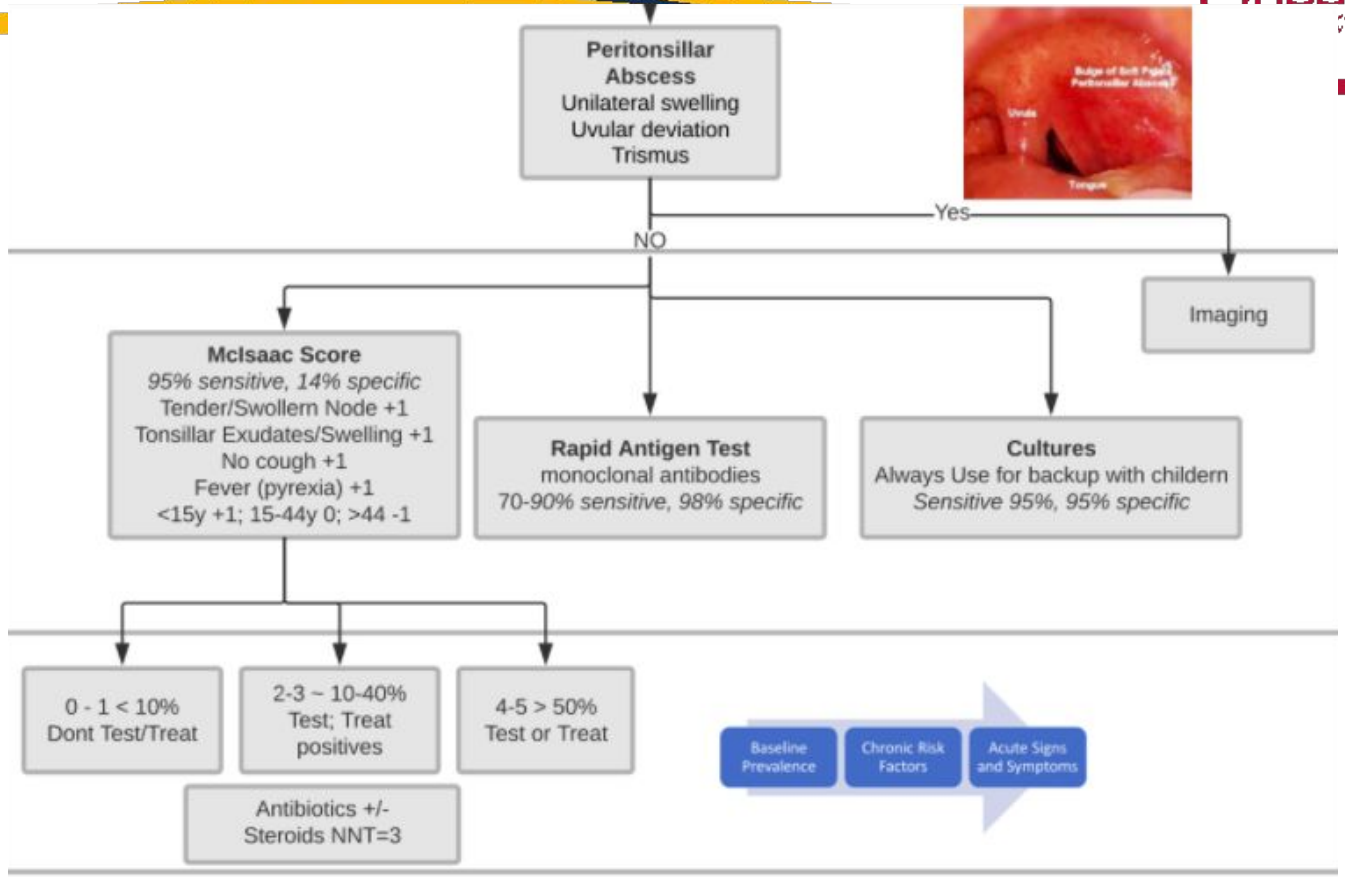
Motivating Idea

- Radiomics = characterize texture quantitatively

- Survival prediction:
  - Survival forest to create decision trees [1]
  - Evaluate predictive power of features

[1] Ishwaran, H., Kogalur, U. B., Blackstone, E. H., & Lauer, M. S. (2008). Random survival forests. *The annals of applied statistics*, *2*(3), 841-860.

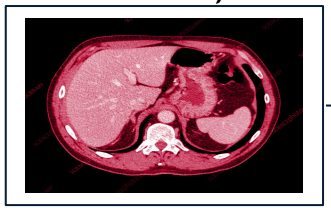
Motivating Idea



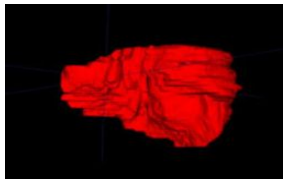
Method

Input:
Liver CT Scan

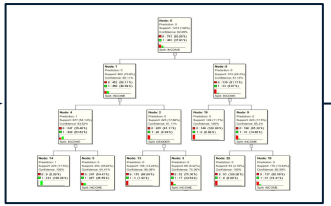
Preprocessing:
Segmentation,
Normalization, Scaling



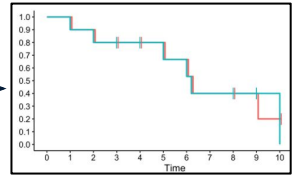
Radiomic Feature
Extraction



Survival Forest
Model



Output:
Predicted Survival



Data Processing

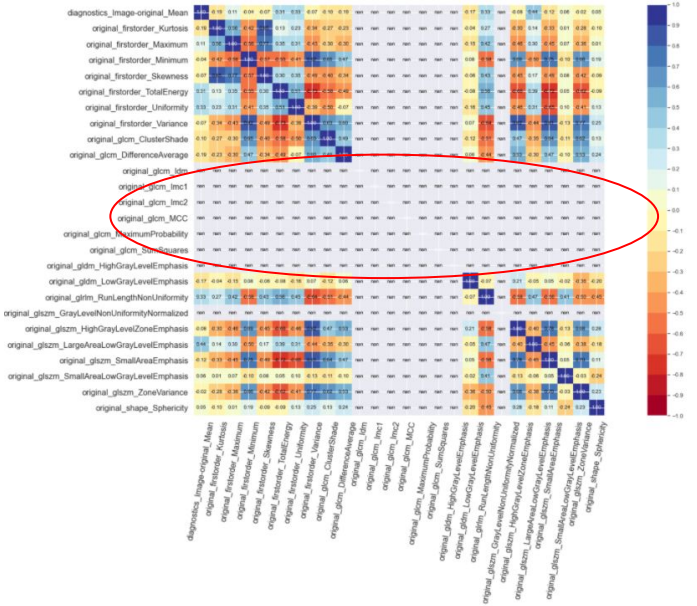
- 103 radiomic features extracted

```
Index(['filename', 'FFLP', 'FFLP_in_months', 'diagnostics_Image-original_Mean',
       'original_shape_MajorAxisLength',
       'original_shape_Maximum2DDiameterColumn',
       'original_shape_Maximum3DDiameter', 'original_shape_MeshVolume',
       'original_shape_MinorAxisLength', 'original_shape_Sphericity',
       ...
       'original_glszm_SmallAreaHighGrayLevelEmphasis',
       'original_glszm_SmallAreaLowGrayLevelEmphasis',
       'original_glszm_ZoneEntropy', 'original_glszm_ZonePercentage',
       'original_glszm_ZoneVariance', 'original_ngtdm_Busyness',
       'original_ngtdm_Coarseness', 'original_ngtdm_Complexity',
       'original_ngtdm_Contrast', 'original_ngtdm_Strength'],
      dtype='object', length=106)
```

- Too many features/variables, have to remove irrelevant ones!

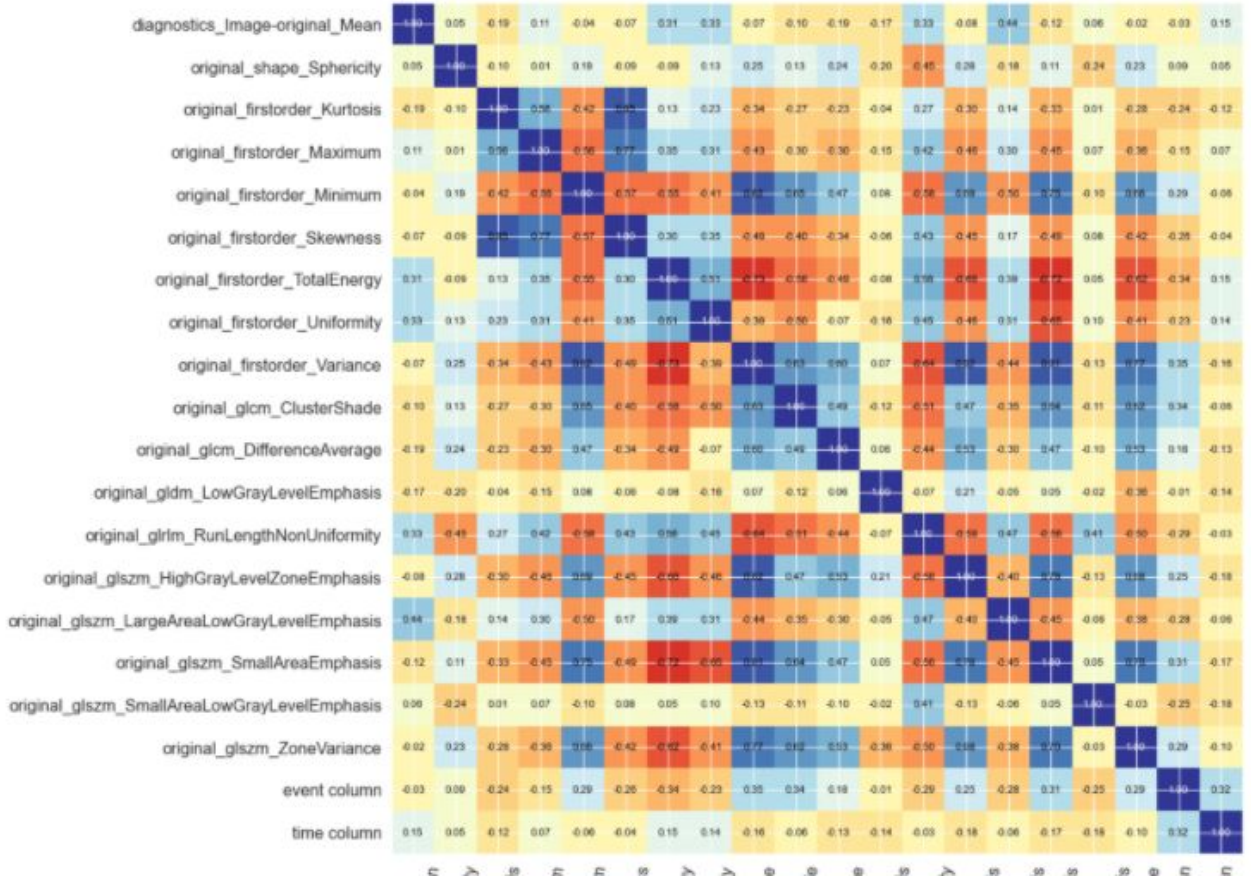
Data Processing

- Features removed if variance is 0 or if variance inflation factor is >10 (colinear)
- (Classic biostats) visualizing linear correlation



Data Processing

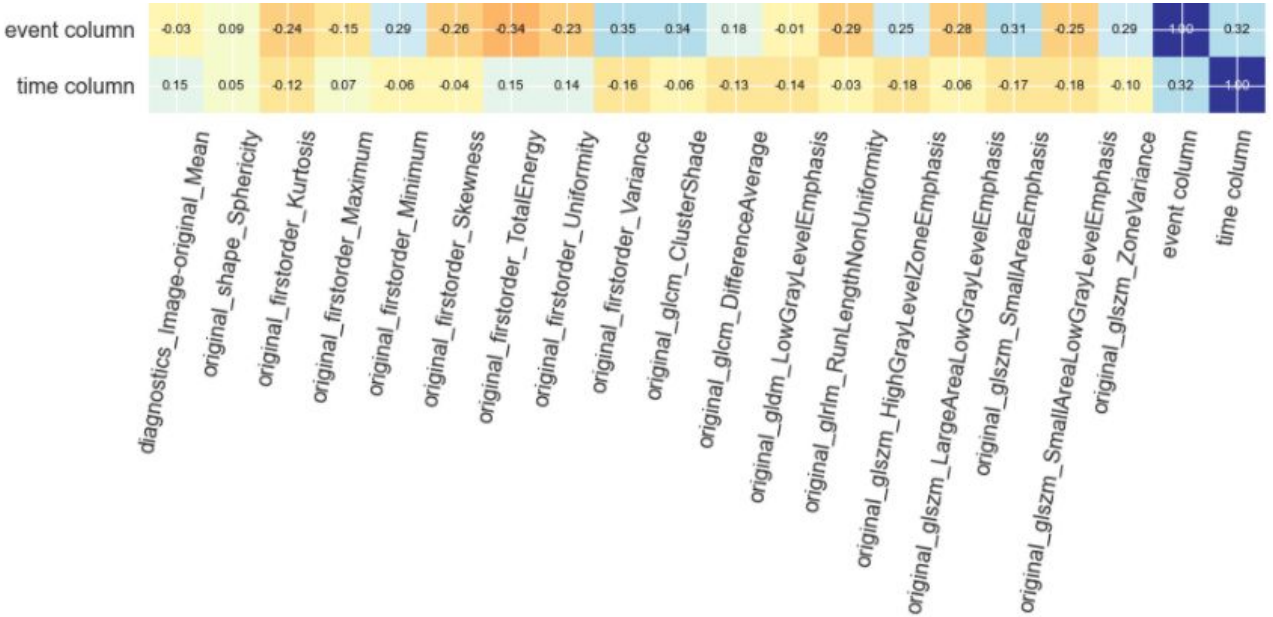
- 17 feature remain



Data Processing

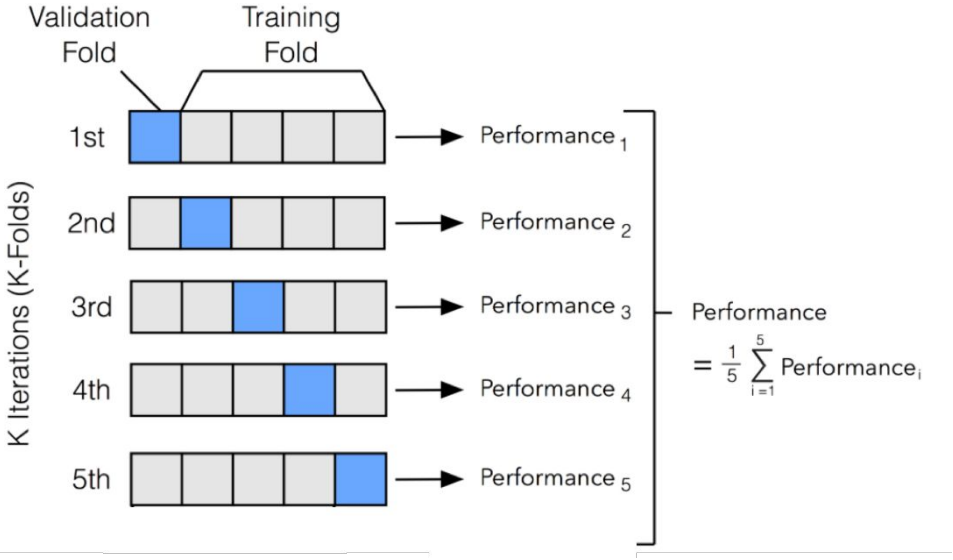
- Corrs of interest

- Linear analysis insufficient!



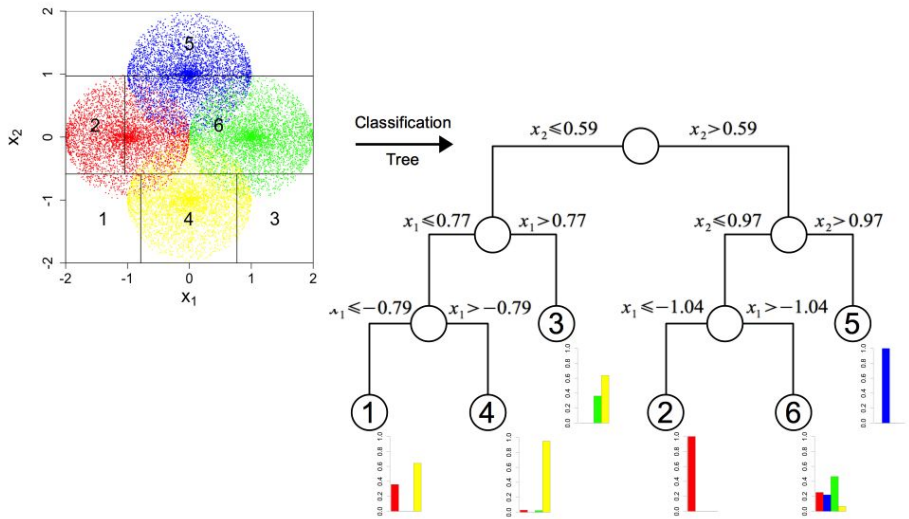
Data Processing

- Data split to training set and testing set



Data Processing

- Decision tree built by random survival forest, method by Ishwaran et al. [3]



[3] Ishwaran, H., Kogalur, U. B., Blackstone, E. H., & Lauer, M. S. (2008). Random survival forests. *The annals of applied statistics*, *2*(3), 841-860.

Data Processing

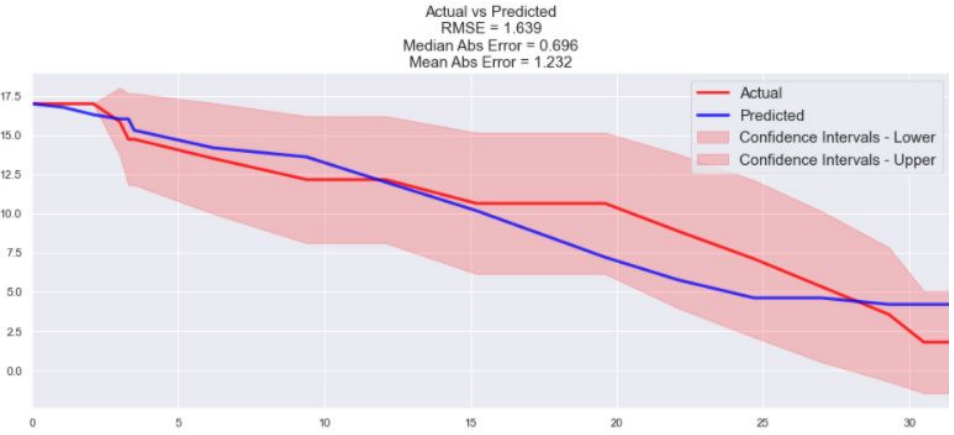
- Acc measured by concordance index & integrated brier score

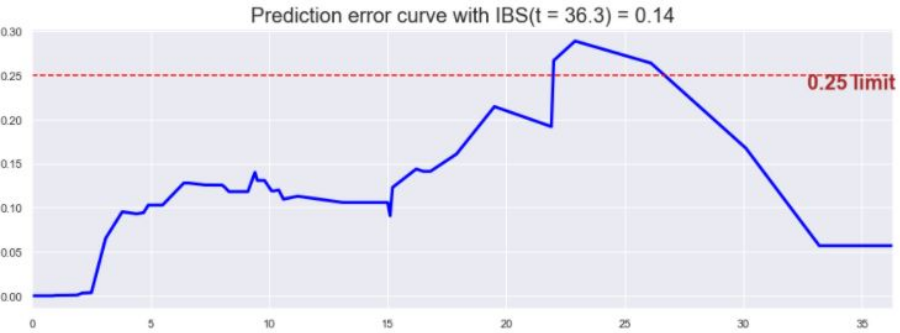
- Parameters optimized by testing range of combinations

(#trees, max depth, min node, CI)

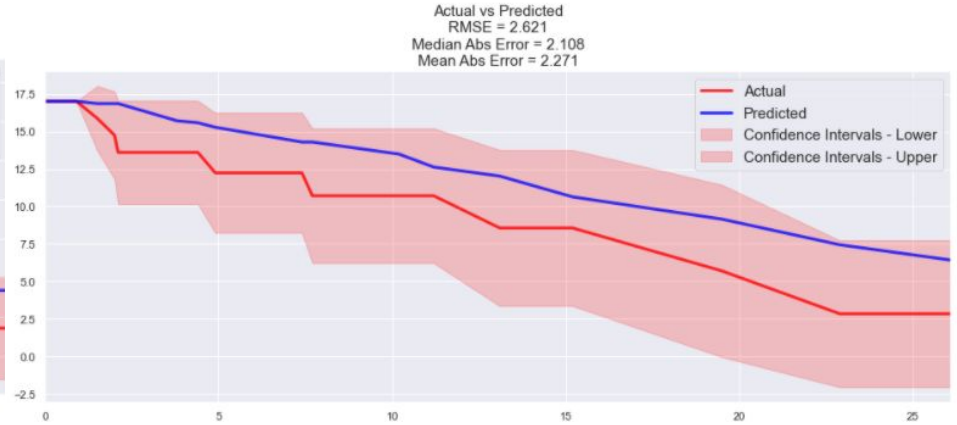
```
200 5 12 0.7073334582546055
200 10 1 0.7749166567864365
200 10 2 0.7907249154186112
200 10 3 0.7878906598836855
200 10 5 0.7523719676346994
200 10 10 0.7071159123628991
200 10 12 0.7247035410778362
200 12 1 0.8000265074452932
200 12 2 0.7903188757019562
200 12 3 0.8037903897825578
200 12 5 0.767438445401023
200 12 10 0.7134517770795967
200 12 12 0.6877935076233995
200 15 1 0.7625906865682286
200 15 2 0.7384229038180379
200 15 3 0.8271195290405593
200 15 5 0.7525655589725745
200 15 10 0.7376218144881928
200 15 12 0.6801483236742727
```

Results





CI: 0.82
IBS: 0.18



CI: 0.62
IBS: 0.11

Results

- C-Index: 0.73 ± 0.09
- IBS: 0.14 ± 0.03

- Wang et al. (2017): 5 clin. variables, Cox hazard to determine which are “predictive”
  - N = 300, Predictive power score **~0.52** (0.46-0.64) !!!

Results - Feature Importances

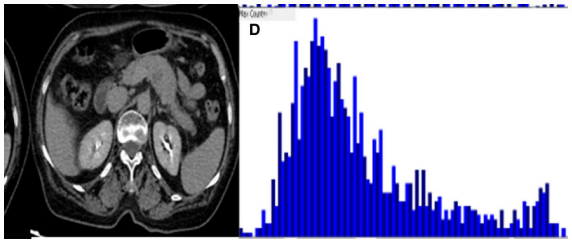
	feature	importance	pct_importance
0	original_firstorder_Skewness	4.644735	0.113659
1	original_firstorder_TotalEnergy	4.497643	0.110060
2	original_glszm_HighGrayLevelZoneEmphasis	4.485823	0.109770
3	original_glszm_SmallAreaLowGrayLevelEmphasis	4.410820	0.107935
4	original_firstorder_Minimum	4.052323	0.099162
5	original_firstorder_Variance	3.498336	0.085606
6	original_glszm_LargeAreaLowGrayLevelEmphasis	3.388589	0.082921
7	original_glszm_SmallAreaEmphasis	2.965303	0.072562
8	original_glrlm_RunLengthNonUniformity	2.799906	0.068515
9	original_glszm_ZoneVariance	2.614715	0.063983
10	original_glcm_ClusterShade	1.294747	0.031683
11	original_gldm_LowGrayLevelEmphasis	0.776879	0.019011
12	original_firstorder_Maximum	0.525391	0.012857
13	original_glcm_DifferenceAverage	0.485674	0.011885
14	original_shape_Sphericity	0.424621	0.010391
15	original_firstorder_Kurtosis	-0.376139	0.000000
16	original_firstorder_Uniformity	-1.458684	0.000000
17	diagnostics_Image-original_Mean	-1.758048	0.000000

What does this mean?

Results - Feature Importances

$$\text{total energy} = V_{voxel} \sum_{i=1}^{N_p} (\mathbf{X}(i) + c)^2$$

$$\text{skewness} = \frac{\mu_3}{\sigma^3} = \frac{\frac{1}{N_p} \sum_{i=1}^{N_p} (\mathbf{X}(i) - \bar{X})^3}{\left(\sqrt{\frac{1}{N_p} \sum_{i=1}^{N_p} (\mathbf{X}(i) - \bar{X})^2} \right)^3}$$



What does this mean?

Next Steps?

Improve accuracy

- Algorithmic improvements to modelling?
- Addition of clin. variables? Only used Radiomics
- More data is better, can have more k-folds (stdev high right now)
  - Especially for nonlinear related variables

Thank you!

Appendix 1: Related Work (all from surgical resections)

- Beppu et al. (2012): 6 clin. variables, Cox hazard to stratify risk
  - N = 727, thresholded to 3 bins
  - HR = 1.79 but 95% CI = 1.36-2.37
- Wang et al. (2017): 5 clin. variables, Cox hazard to determine which are “predictive”
  - N = 300, Predictive power score ~0.52 (0.46-0.64)
- 5+ more studies: regression only, only linear method

[3] T. Beppu et al., “A nomogram predicting disease-free survival in patients with colorectal liver metastases treated with hepatic resection: Multicenter data collection as a project study for hepatic surgery of the Japanese Society of Hepato-Biliary-Pancreatic Surgery,” J. Hepatobiliary. Pancreat. Sci., 2012.
[4] K. Wang, W. Liu, X. L. Yan, J. Li, and B. C. Xing, “Long-term postoperative survival prediction in patients with colorectal liver metastasis,” Oncotarget, vol. 8, no. 45, pp. 79927–79934, 2017.

Appendix 1: Related Work (all from surgical resections)

- Rahmim et al. (2019): 51 PET radiomic features + Cox hazard
  - N = 52, HR= 4.02 for progression free survival
  - Shows correlation, but doesn't predict time-to-event

[5] A. Rahmim et al., "Prognostic modeling for patients with colorectal liver metastases incorporating FDG PET radiomic features," Eur. J. Radiol., vol. 113, no. December 2018, pp. 101–109, 2019.