Prediction of Clinical Outcomes in Diffuse Large B-Cell Lymphoma (DLBCL) Utilizing Radiomic Features Derived from Pretreatment Positron Emission Tomography (PET) Scan

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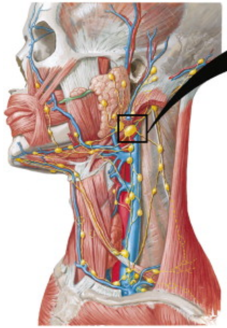
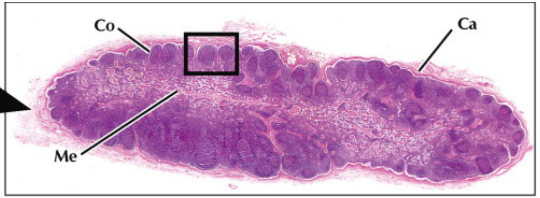
SCIT Seminar

January 6th , 2021

Diffuse Large B Cell Lymphoma

▼ **Lymph nodes and lymphatic drainage of mouth and pharynx.**

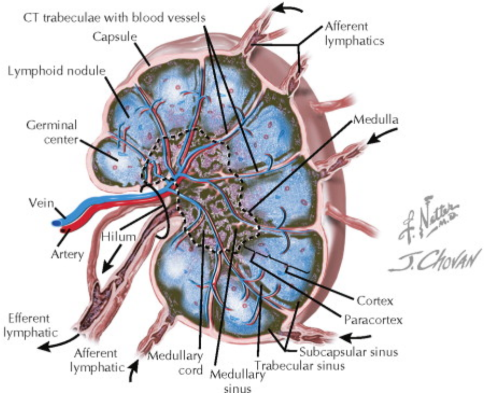




▲ **LM of a lymph node.** Surrounded by a capsule (**Ca**), it has an outer cortex (**Co**) and central medulla (**Me**). The hilum is not in the plane of section. The rectangle indicates the area seen at higher magnification in Fig. 9.5. 7×. *H&E.*

△ **Enlarged cervical lymph node in the neck.** (often first symptom in malignancies of tonsils fauces, and pharynx)

▼ **Three-dimensional schematic of a lymph node.**



Ovalle WK (2013) *Netter's Essential Histology* Philadelphia, Pennsylvania: Saunders

Pathology

Involved lymph nodes or tissues show partial or complete effacement of architecture by diffuse infiltration of medium- to large-sized lymphoid cells (Fig. 5.20).

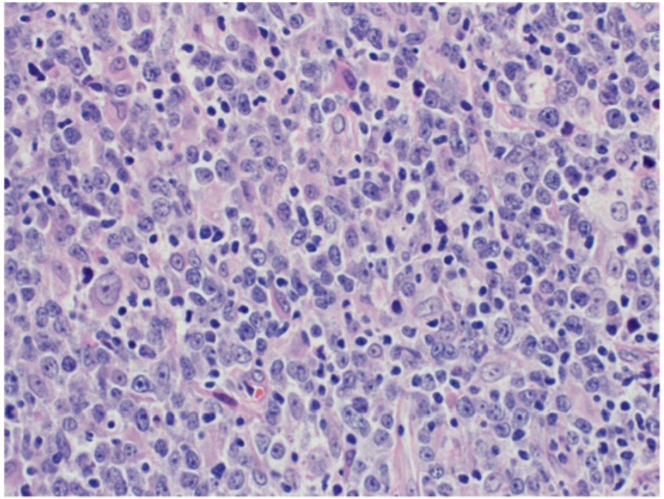
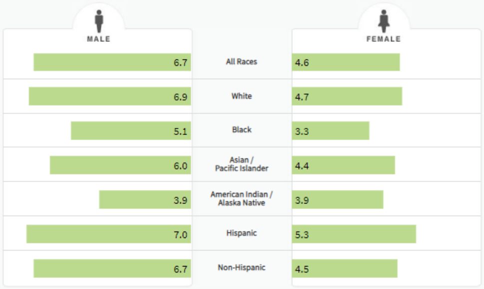


Fig. 5.20 Diffuse large B-cell lymphoma with sheets of large cells with irregular nuclei, open chromatin and one to several prominent nucleoli

Nasr M.R (2019) *Lymph Node Pathology For Clinicians* Cham, Switzerland: Springer Nature Switzerland AG

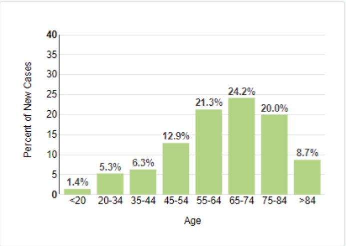
Demographics

Number of New Cases per 100,000 Persons by Race/Ethnicity & Sex: Diffuse Large B-Cell Lymphoma (DLBCL)



SEER 21 2012-2016, Age-Adjusted

Percent of New Cases by Age Group: Diffuse Large B-Cell Lymphoma

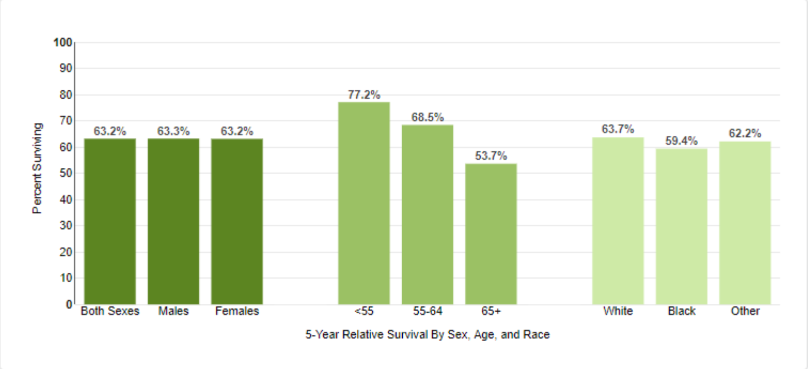


Diffuse large B-cell lymphoma is most frequently diagnosed among people aged 65-74.

Median Age At Diagnosis

66

5-Year Relative Survival by Sex, Age, and Race



SEER 18 2009-2015

NIH National Cancer Institute (2019) Cancer Stats Facts: NHL- Diffuse Large B Cell Lymphoma (DLBCL) Retrieved from https://seer.cancer.gov/statfacts/html/dlbcl.html

Survival Statistics

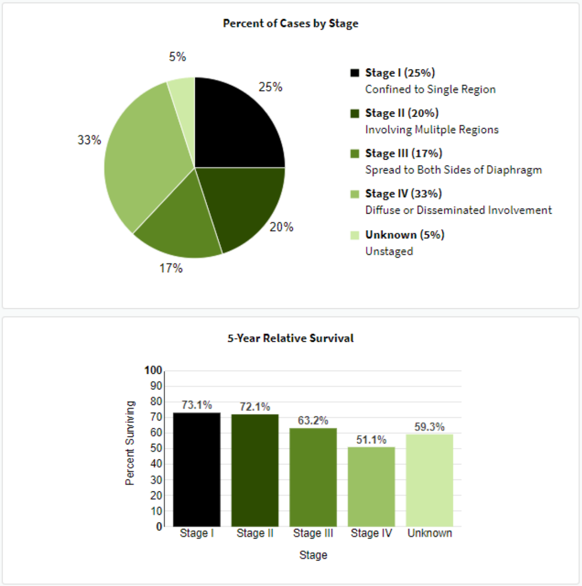
Number of New Cases and Deaths per 100,000: The number of new cases of diffuse large B-cell lymphoma was 5.6 per 100,000 men and women per year. The number of deaths was 1.8 per 100,000 men and women per year. These rates are age-adjusted and based on 2012-2016 cases and deaths.

How Many People Survive 5 Years Or More after Being Diagnosed with Diffuse Large B-Cell Lymphoma?

Relative survival statistics compare the survival of patients diagnosed with cancer with the survival of people in the general population who are the same age, race, and sex and who have not been diagnosed with cancer. Because survival statistics are based on large groups of people, they cannot be used to predict exactly what will happen to an individual patient. No two patients are entirely alike, and treatment and responses to treatment can vary greatly.

Based on data from SEER 18 2009-2015. Gray figures represent those who have died from diffuse large B-cell lymphoma. Green figures represent those who have survived 5 years or more.

Percent of Cases & 5-Year Relative Survival by Stage at Diagnosis: Diffuse Large B-Cell Lymphoma



SEER 18 2009-2015, All Races, Both Sexes by Ann Arbor Stage

NIH National Cancer Institute (2019) Cancer Stats Facts: NHL- Diffuse Large B Cell Lymphoma (DLBCL) Retrieved from https://seer.cancer.gov/statfacts/html/dlbcl.html

Positron Emission Tomography

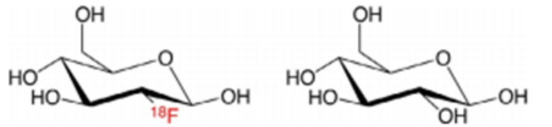


Fig. 11.3. The chemical structure of ^{18}F-fluorodeoxyglucose (FDG) (left) is very similar to glucose (right); in FDG the 2' hydroxyl group has been replaced by ^{18}F.

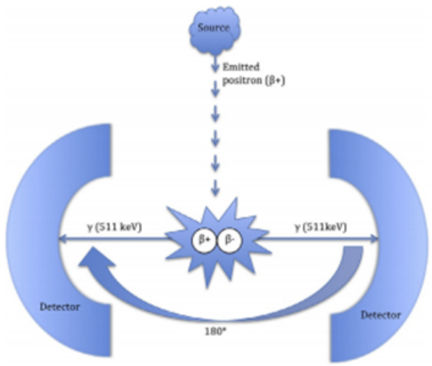
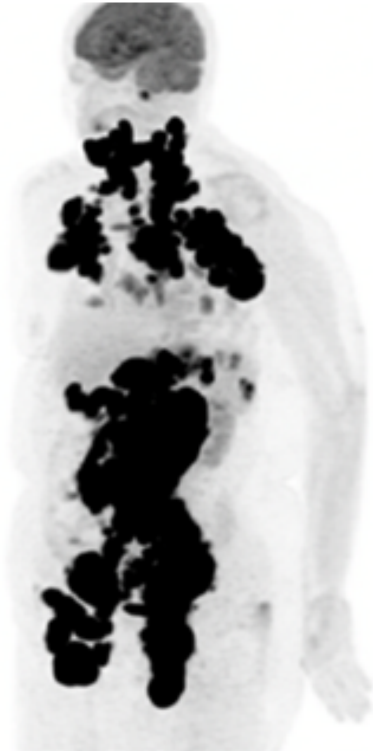


Fig. 11.1. After being emitted, positrons travel a distance before combining with an electron in an annihilation event. This results in the production of two antiparallel 511 keV photons which strike opposing detectors within a coincidence time window.



Masdeu J.C. (2016) *Handbook of Clinical Neurology , Neuroimaging, Part I* Amsterdam, Netherlands : Elsevier B.V.

Radiomics

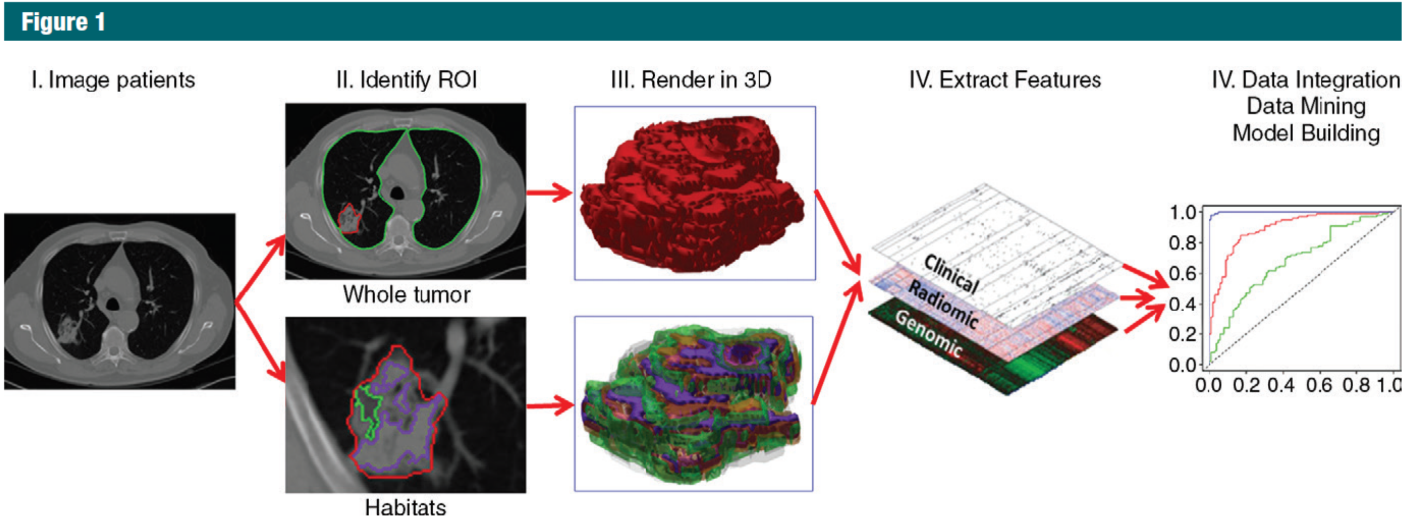


Figure 1: Flowchart shows the process of radiomics and the use of radiomics in decision support. Patient work-up requires information from disparate sources to be combined into a coherent model to describe where the lesion is, what it is, and what it is doing. Radiomics begins with acquisition of high-quality images. From these images, a region of interest *(ROI)* that contains either the whole tumor or subregions (ie, habitats) within the tumor can be identified. These are segmented with operator edits and are eventually rendered in three dimensions *(3D)*. Quantitative features are extracted from these rendered volumes to generate a report, which is placed in a database along with other data, such as clinical and genomic data. These data are then mined to develop diagnostic, predictive, or prognostic models for outcomes of interest.

1. Giles RJ et al (2016) *Radiomics: Images Are More Than Pictures, They Are Data* Radiology 278 (2): 563-577

Radiomics Workflow

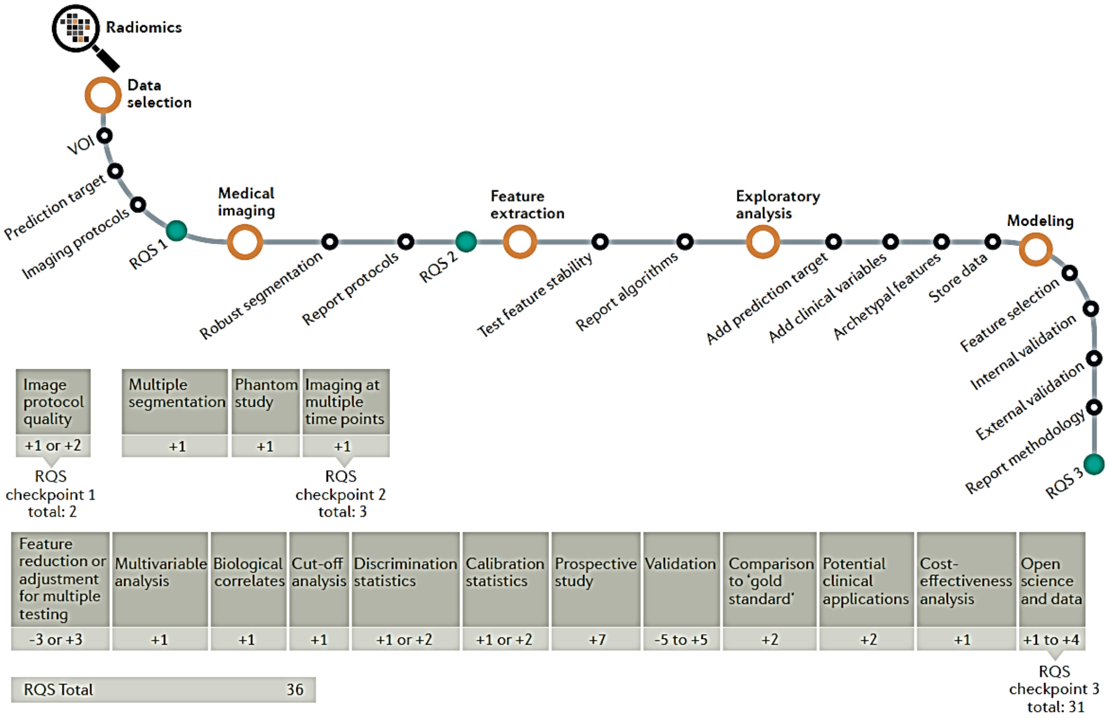


Figure 1 | **Flowchart depicting the workflow of radiomics and the application of the RQS.** The workflow includes the necessary steps in a radiomic analysis. The RQS both rewards and penalizes the methodology and analyses of a study, consequently encouraging the best scientific practice. RSQ, radiomics quality score; VOI, volume of interest.

2. Lambin P et al (2017) *Radiomics: the bridge between medical imaging and personalized medicine* Nature Reviews: Clinical Oncology 14: 750-762

Our Radiomic Workflow

Component of Workflow	Study Component	Justification
Prediction Target	2 yr Progression Free Survival OR Relapse	• Good predictor of 5 year overall survival[3]
Time Point	Pretreatment PET Scan	• Guidance of Treatment
Volume of Interest	Largest Lymphomatous Deposit (Qualitative Assessment)	• Most difficult lesions to resolve with treatment
Segmentation	Semi-Automatic PET Edge (MIM Software)[4]	• Minimizes effect of inter-reader variability
Feature Extraction	Pyradiomics[5] via Quantitative Imaging Feature Pipeline (QIFP)[6]	• Image Biomarker Standardization Initiative (IBIS) compliant

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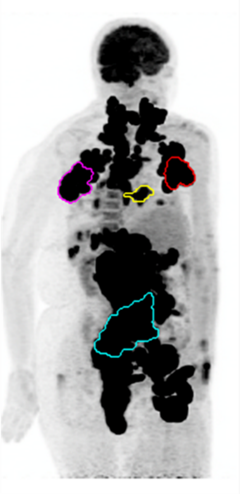
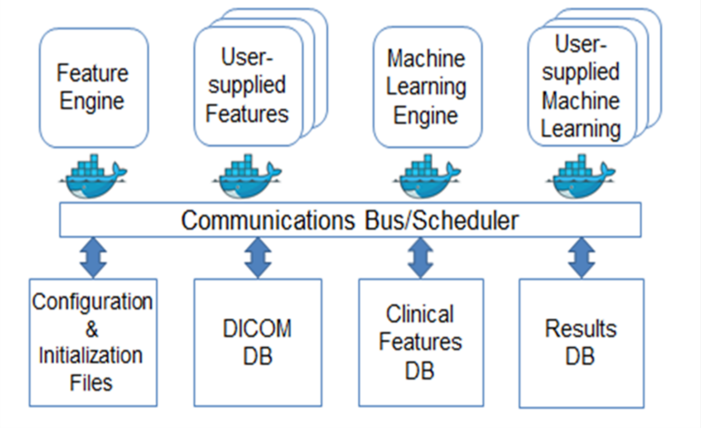
Implementation of Workflow

Imaging Dataset Characteristics	
Patient Population	-85 Patients Qualified (out of 1500+) -59/85: Achieved 2 year Progression Free Survival -26/85: Relapsed within 2 years after treatment
Scanners Used	-GE Discovery Series: 600, 690, 710, MI
Reconstruction Algorithms	-Ordered Subset Expectation Maximization (OSEM) -Q.Clear (Bayesian Based Reconstruction Method)





Quantitative Imaging Feature Pipeline

Types of Radiomic Features Extracted
Morphology
Texture
Size
Intensity

Feature Engine Results

6. Mattonen SA et al (2020) *Quantitative Imaging Feature Pipeline (QIFP): A web-based tool for utilizing, sharing, and building image processing pipelines* Journal of Medical Imaging 7(4):042803

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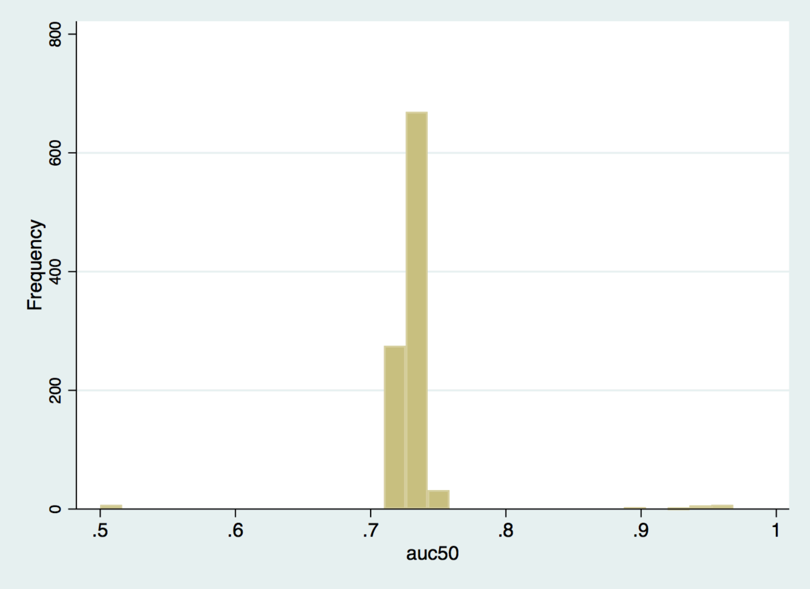
Results: Only Pyradiomics Features



Feature	Class	Frequency
Wavelet_LHH_Firstorder_Skewness	Intensity	993
log-sigma-1mm-3D_GLSZM_SizeZoneNonUniformityNormalized	Texture	993
Wavelet_HHH_GLSZM_GrayLevelNonUniformityNormalized	Texture	718

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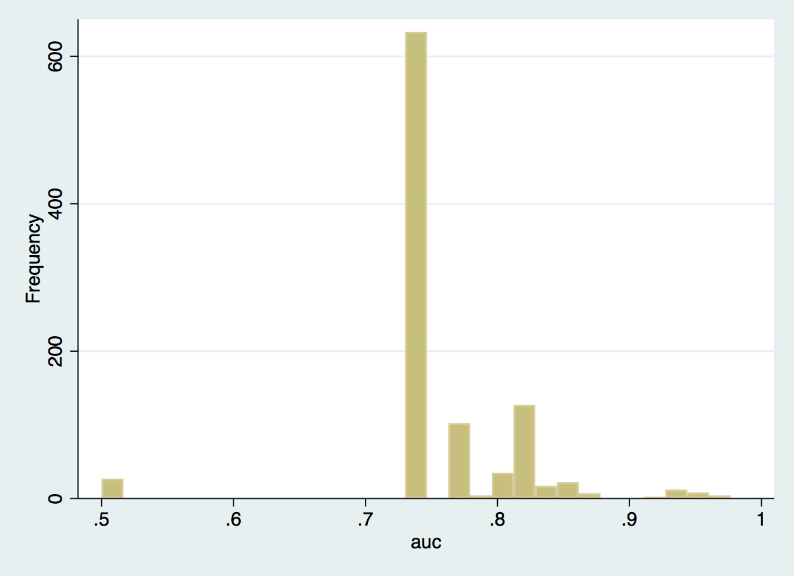
Pyradiomics + Clinical Features+ Conventional Quantitative PET Metrics

Demographics: Age, Sex, Ann Arbor Stage of Disease
Risk Factors: Presence of Autoimmune Condition, Previous Cancer Diagnosis, Transformed DLBCL
Treatment: Cycles Completed, Administered Dosage, Adjunct Therapy
Conventional PET Metrics: Standard Uptake Value (SUV) metrics, Volume, Tumor Lesion Glycolysis



Feature	Class	Frequency
Wavelet_LHH_Firstorder_Skewness	Intensity	973
log-sigma-1mm-3D_GLSZM_SizeZoneNonUniformityNormalized	Texture	973
Wavelet_LHH_GLSZM_ZoneEntropy	Texture	343
Wavelet_HHH_GLSZM_GrayLevelNonUniformityNormalized	Texture	243
Wavelet_LHL_GLSZM_GrayLevelNonUniformityNormalized	Texture	204
Wavelet_HHL_GLCM_IMC2	Texture	204

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Conclusion/Future Directions

- Intensity and Texture Features can potentially be used to predict clinical outcomes in DLBCL
- Introduced a clinical friendly approach to radiomics
- Findings have to be validated with other imaging datasets
- Incorporation of pathological features
- Compare Radiomics Approach Versus Deep Learning Approach

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References

1. Giles RJ et al (2016) *Radiomics: Images Are More Than Pictures, They Are Data* Radiology 278 (2): 563-577
2. Lambin P et al (2017) *Radiomics: the bridge between medical imaging and personalized medicine* Nature Reviews: Clinical Oncology 14: 750-762
3. Shi Q et al (2018) *Progression-Free Survival as a Surrogate End Point for Overall Survival in First-Line Diffuse Large B-Cell Lymphoma: An Individual Patient-Level Analysis of Multiple Randomized Trials (SEAL)* Journal of Clinical Oncology 36: 2593-2602
4. https://www.mimsoftware.com/radiationoncology/maestro
5. van Griethuysen, J. J. et al (2017) *Computational Radiomics System to Decode the Radiographic Phenotype.* Cancer Research, 77(21): e104–e107
6. Mattonen SA et al (2020) *Quantitative Imaging Feature Pipeline (QIFP): A web-based tool for utilizing, sharing, and building image processing pipelines* Journal of Medical Imaging 7(4):042803