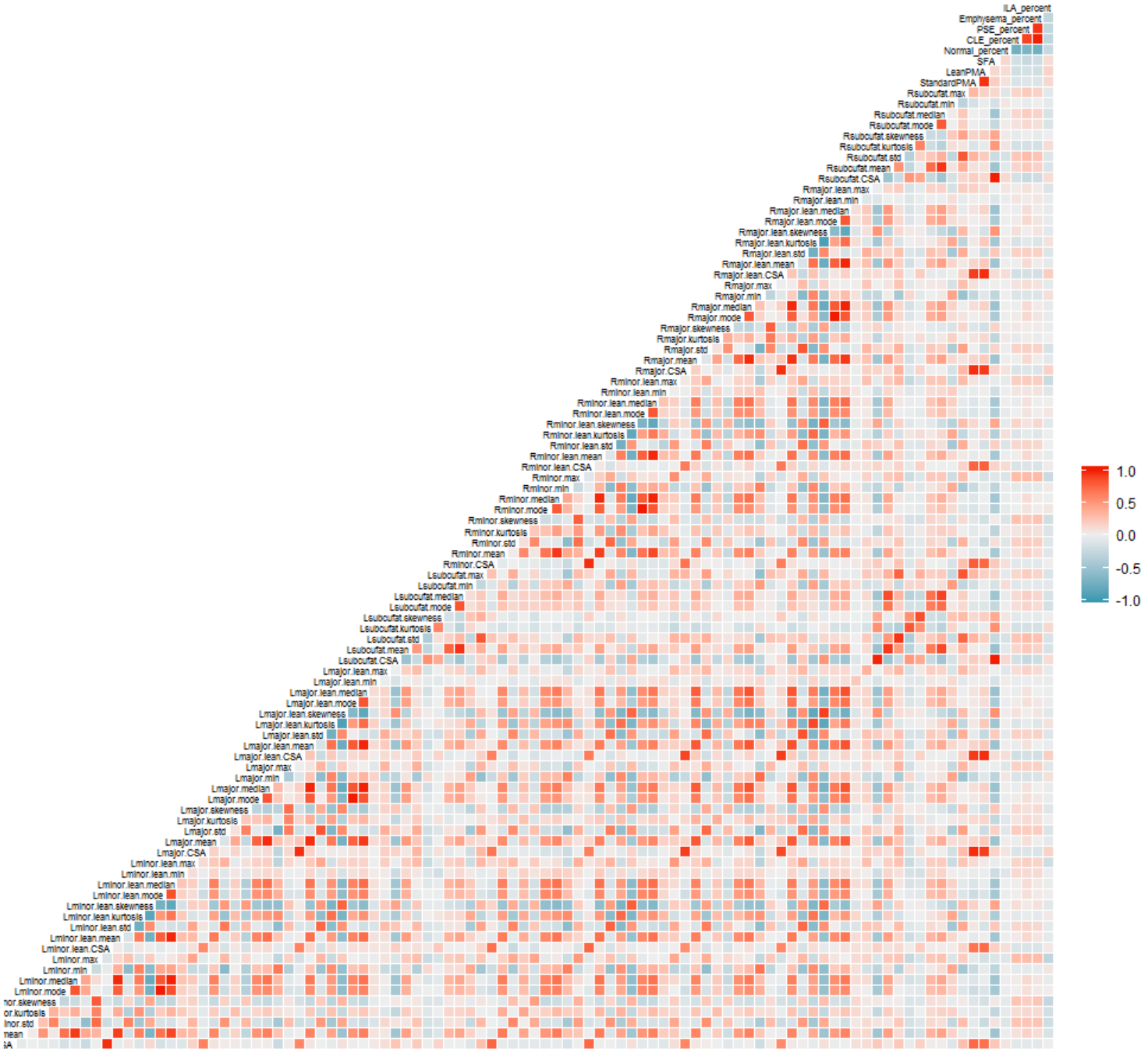
COPD Clustering Analysis
Combined DECAMP cohorts

Report date: September 25, 2017

Figure 1: Matrix for Spearman's rank correlation (98 variables)



Variables that were removed for being highly (≥ 0.80) correlated with other variables:

- Removed variables that were in 10 pairs of highly correlated variables:
    1. Lmajor.median

- Removed variables that were in 8 pairs of highly correlated variables:

    1. Lmajor.lean.mean
    2. Lmajor.lean.median
    3. Rmajor.lean.median
    4. Rmajor.median

- Removed variables that were in 6 pairs of highly correlated variables:
    1. Lminor.lean.median
    2. Lminor.median
    3. Rminor.lean.median
    4. Rminor.median
    5. StandardPMA

- Removed variables that were in 4 pairs of highly correlated variables:

    1. LeanPMA
    2. Lmajor.CSA
    3. Lmajor.lean.CSA
    4. Lsubcufat.median
    5. Rmajor.CSA
    6. Rmajor.lean.CSA
    7. Rsubcufat.median

- Removed variables that were in 3 pairs of highly correlated variables:

    1. Lmajor.lean.kurtosis
    2. Lmajor.lean.skewness
    3. Rmajor.lean.kurtosis
    4. Rmajor.lean.skewness

- Removed variables that were in 2 pairs of highly correlated variables:

    1. CLE_percent
    2. Emphysema_percent
    3. Lmajor.lean.std
    4. Lmajor.mean
    5. Lsubcufat.CSA
    6. Lsubcufat.max
    7. Lsubcufat.std
    8. PSE_percent
    9. Rmajor.lean.mean
    10. Rmajor.lean.std
    11. Rmajor.mean

12. Rsubcufat.CSA
13. Rsubcufat.max
14. Rsubcufat.std
15. SFA

- Removed variables that were in 1 pair of highly correlated variables:
    1. Lminor.lean.mode
    2. Lminor.lean.CSA
    3. Lminor.lean.mean
    4. Lminor.skewness
    5. Lminor.lean.mode
    6. Lminor.lean.skewness
    7. Lmajor.lean.mode
    8. Lsubcufat.mean
    9. Lsubcufat.kurtosis
    10. Lsubcufat.skewness
    11. Rminor.lean.CSA
    12. Rminor.lean.mean
    13. Rminor.lean.mode
    14. Rminor.lean.skewness
    15. Rmajor.lean.mode

50 variables were removed for having high correlation.

At this point, 2 baseline scans were removed for not having complete data on the remaining 48 variables, leaving 414 baseline scans.

Table 1: Number of variables removed and remaining after removing pairs of highly correlated variables for different correlation thresholds

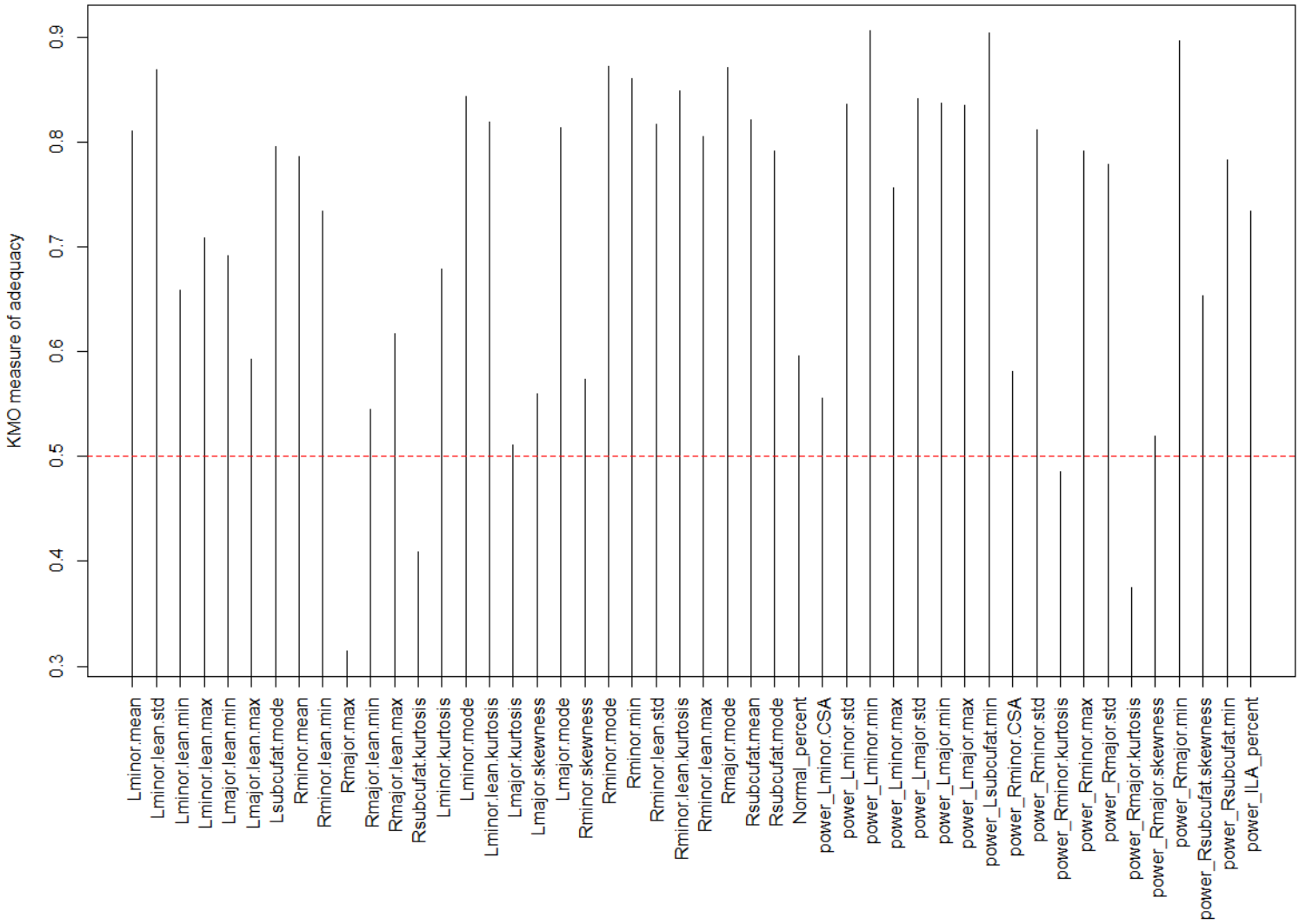
Correlation threshold	*Number of variables removed*	*Number of variables remaining*
0.80	50	48
0.85	43	55
0.90	35	63
0.95	24	74

Table 2: Skewness for raw analysis variables and transformed analysis variables (35 variables were considered for transformation; 19 variables with skewed distributions were transformed using log/inverse transformations)

	Raw variable's skewness	*Log/Inverse transformed variable's skewness*
Lminor.CSA[1]	0.90	-0.06
Lminor.std[1]	1.82	0.47
Lminor.kurtosis	4.06	13.02
Lminor.mode	-1.06	-1.50
Lminor.min[2]	-4.33	-0.90
Lminor.max[2]	1.95	0.26
Lminor.lean.kurtosis	4.17	7.67
Lmajor.std[1]	2.52	0.82
Lmajor.kurtosis	4.61	-5.68
Lmajor.skewness	2.50	-5.07
Lmajor.mode	-1.52	4.16
Lmajor.min[2]	-6.64	-0.72
Lmajor.max[2]	2.08	0.19
Lsubcufat.min[2]	-7.02	3.03
Rminor.CSA[1]	0.95	-0.07
Rminor.std[1]	1.38	0.29
Rminor.kurtosis[2]	5.74	-3.51
Rminor.skewness	2.04	-16.23
Rminor.mode	-0.96	5.11
Rminor.min	-1.24	-1.66
Rminor.max[1]	1.92	0.76
Rminor.lean.std	-0.46	-1.11
Rminor.lean.kurtosis	2.33	-7.78
Rminor.lean.max	-3.22	-3.69
Rmajor.std[1]	10.19	1.43
Rmajor.kurtosis[2]	9.85	1.67
Rmajor.skewness[2]	3.68	-3.08
Rmajor.mode	-1.46	11.44
Rmajor.min[2]	-4.58	-0.57
Rsubcufat.mean	1.23	-4.36
Rsubcufat.skewness[2]	6.70	-4.03
Rsubcufat.mode	1.89	-18.21
Rsubcufat.min[2]	-7.19	2.84
Normal_percent	-1.32	-2.52
ILA_percent[1]	2.77	0.22

[1] Log-transformed variable
[2] Inverse-transformed variable

Figure 2: Kaiser-Meyer-Olkin measure of adequacy plot (48 variables)



Variables with low (< 0.5) KMO measures:

1. Rmajor.max
2. Rsubcufat.kurtosis
3. power_Rminor.kurtosis
4. power_Rmajor.kurtosis

4 variables with low KMO measures were removed.

Table 3: Proportion of variance explained for each factor (34 factors)

	Sum.of squared.loadings	*Proportion.of variance.explained*	*Cumulative.proportion of.variance.explained*
Factor1	6.24	0.14	0.14
Factor2	2.66	0.06	0.20
Factor3	2.43	0.06	0.26
Factor4	2.31	0.05	0.31
Factor5	1.84	0.04	0.35
Factor6	1.80	0.04	0.39
Factor7	1.72	0.04	0.43
Factor8	1.72	0.04	0.47
Factor9	1.65	0.04	0.51
Factor10	1.63	0.04	0.54
Factor11	1.12	0.03	0.57
Factor12	0.99	0.02	0.59
Factor13	0.98	0.02	0.62
Factor14	0.94	0.02	0.64
Factor15	0.93	0.02	0.66
Factor16	0.93	0.02	0.68
Factor17	0.93	0.02	0.70
Factor18	0.91	0.02	0.72
Factor19	0.90	0.02	0.74
Factor20	0.79	0.02	0.76
Factor21	0.64	0.01	0.77
Factor22	0.56	0.01	0.79
Factor23	0.52	0.01	0.80
Factor24	0.50	0.01	0.81
Factor25	0.50	0.01	0.82
Factor26	0.44	0.01	0.83
Factor27	0.38	0.01	0.84
Factor28	0.32	0.01	0.85
Factor29	0.21	0.00	0.85
Factor30	0.18	0.00	0.86
Factor31	0.15	0.00	0.86
Factor32	0.13	0.00	0.86
Factor33	0.13	0.00	0.87
Factor34	0.11	0.00	0.87

Table 4: Number of factors removed and number remaining after factor analysis for different cumulative proportion of variance explained thresholds

Cumulative proportion of variance explained threshold	*Number of factors needed*	*Number of variables removed*	*Number of variables remaining*
0.70	20	25	19
0.75	25	20	24
0.80	31	15	29
0.85	34	11	33

Figure 4: Spearman rank correlations for the standardized analysis variables

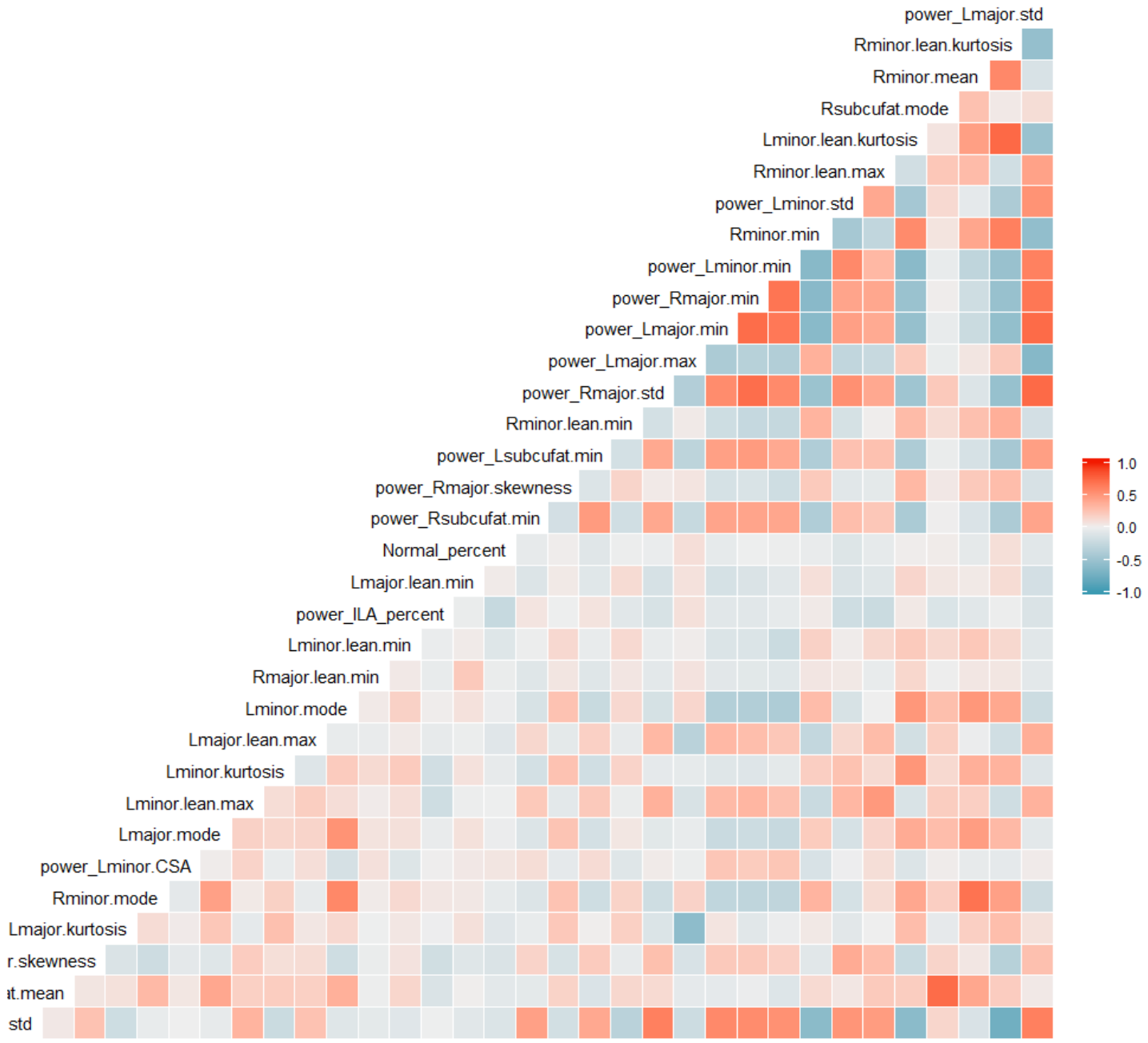
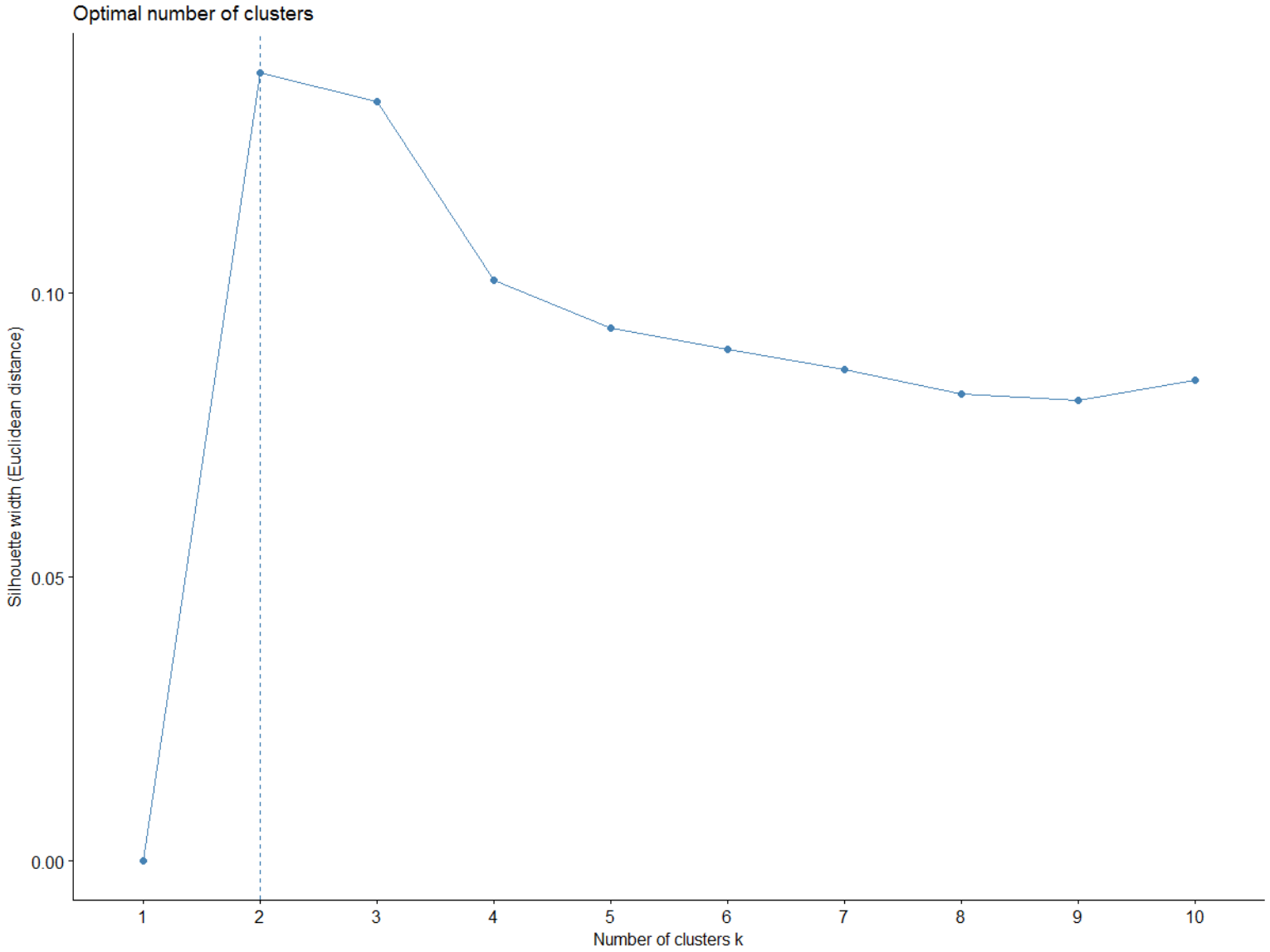


Figure 5: Average silhouette width plot to determine the optimal number of clusters to use



2-MEANS CLUSTER ANALYSIS

Figure 6: Plot of the first two principal components of the analysis variables for the 2-means clusters

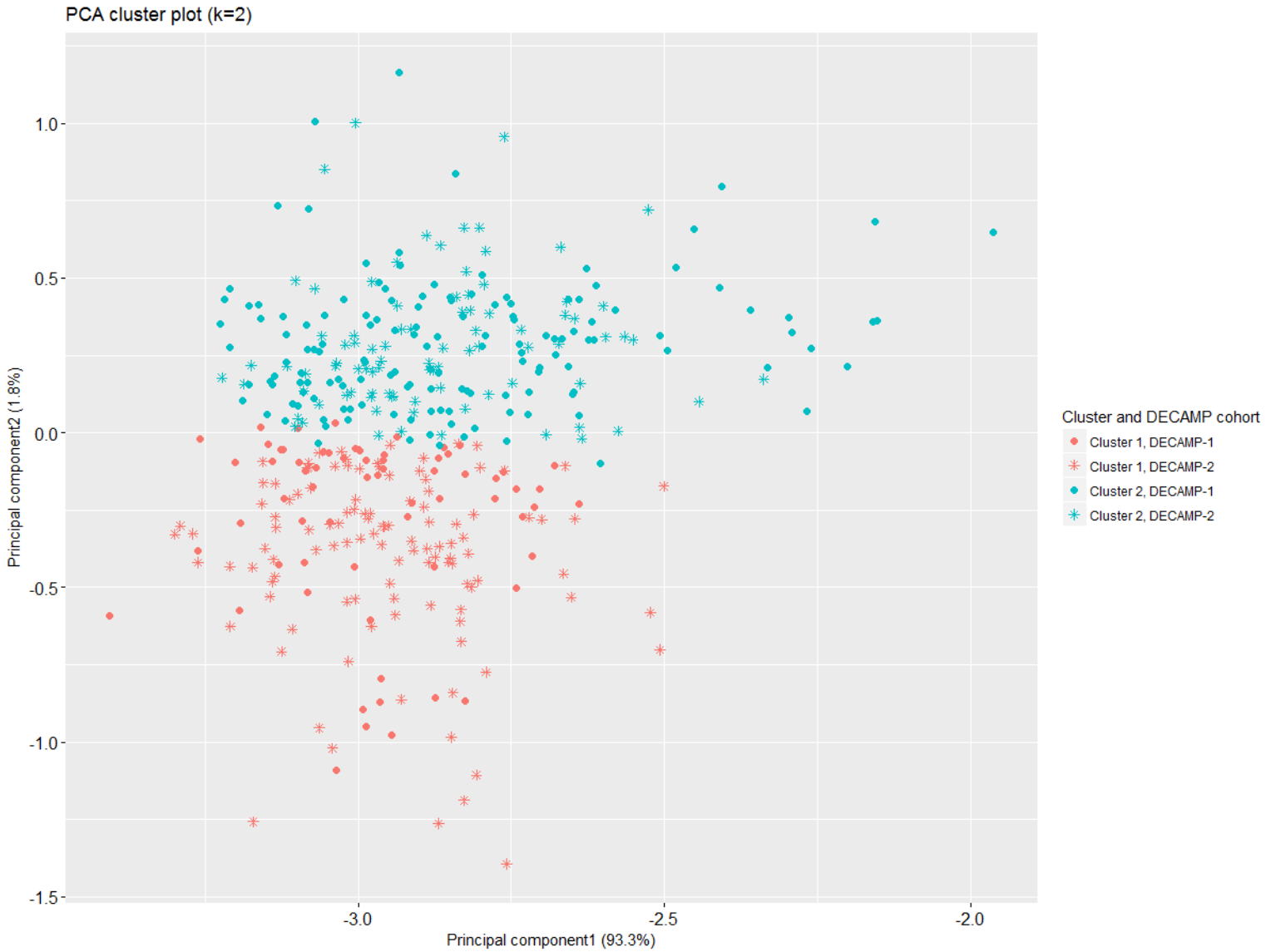


Figure 7: Silhouette plot for the 2-means clusters

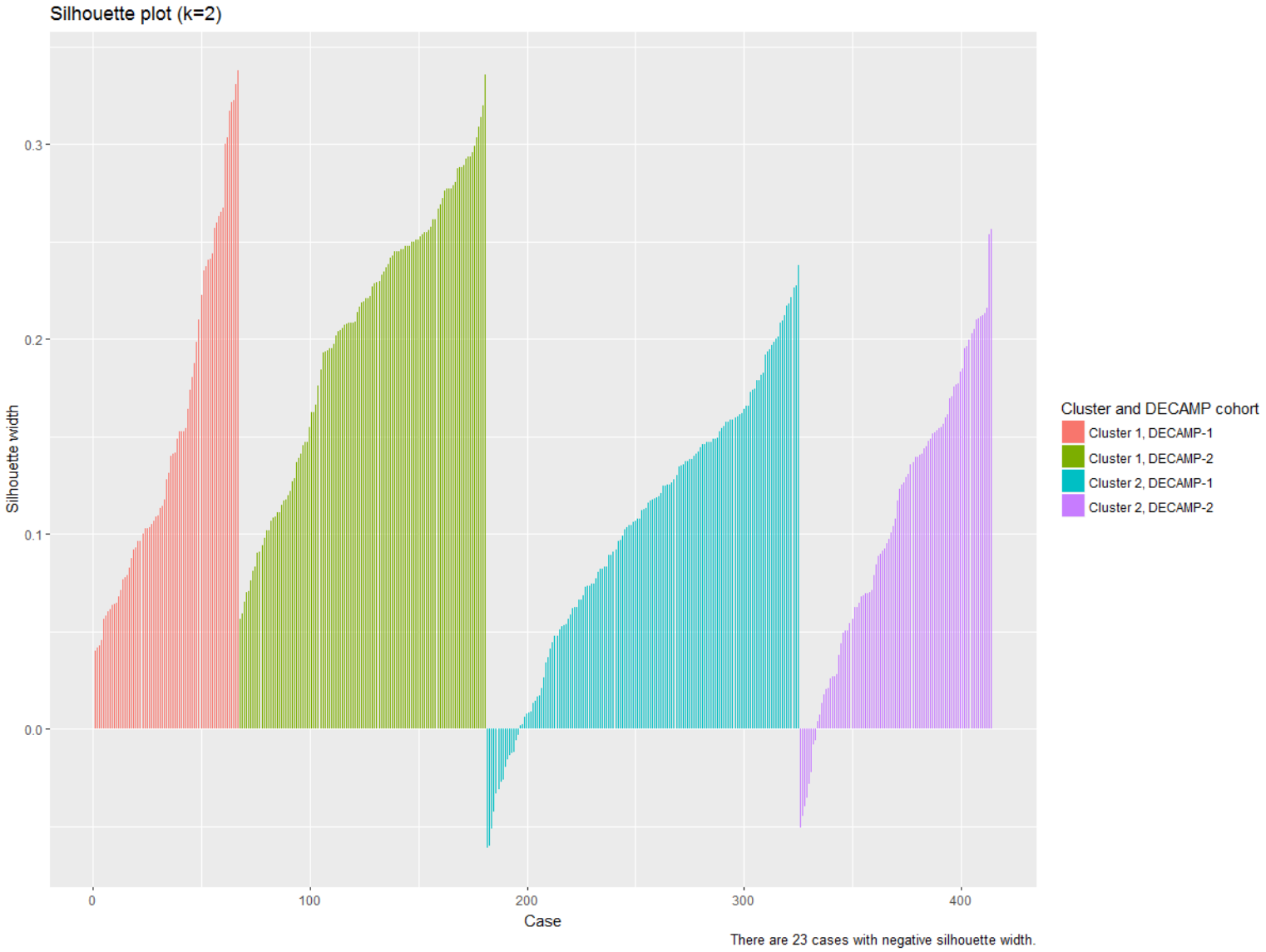


Table 5: 2-means clustering analysis variables summary

	Cluster 1	*Cluster 2*	
	Mean ± SD	*Mean ± SD*	*ANOVA P-value*
Rminor.lean.std	0.75 ± 0.12	0.57 ± 0.15	<0.001
Rsubcufat.mean	0.28 ± 0.13	0.33 ± 0.17	0.004
Rminor.skewness	0.24 ± 0.12	0.22 ± 0.15	0.268
Lmajor.kurtosis	0.08 ± 0.13	0.04 ± 0.08	0.003
Rminor.mode	0.58 ± 0.17	0.70 ± 0.12	<0.001
power_Lminor.CSA	0.48 ± 0.17	0.42 ± 0.17	<0.001
Lmajor.mode	0.69 ± 0.17	0.77 ± 0.10	<0.001
Lminor.lean.max	0.98 ± 0.05	0.90 ± 0.19	<0.001
Lminor.kurtosis	0.05 ± 0.07	0.08 ± 0.13	0.004
Lmajor.lean.max	1.00 ± 0.01	0.97 ± 0.10	<0.001
Lminor.mode	0.60 ± 0.18	0.74 ± 0.12	<0.001
Rmajor.lean.min	0.00 ± 0.00	0.02 ± 0.13	0.077
Lminor.lean.min	0.02 ± 0.08	0.07 ± 0.17	0.002
power_ILA_percent	0.47 ± 0.17	0.50 ± 0.17	0.082
Lmajor.lean.min	0.00 ± 0.00	0.01 ± 0.08	0.086
Normal_percent	0.74 ± 0.22	0.75 ± 0.22	0.685
power_Rsubcufat.min	0.20 ± 0.19	0.08 ± 0.09	<0.001
power_Rmajor.skewness	0.56 ± 0.06	0.57 ± 0.05	0.113
power_Lsubcufat.min	0.25 ± 0.18	0.14 ± 0.06	<0.001
Rminor.lean.min	0.00 ± 0.01	0.02 ± 0.08	0.002
power_Rmajor.std	0.27 ± 0.08	0.17 ± 0.09	<0.001
power_Lmajor.max	0.23 ± 0.15	0.42 ± 0.18	<0.001
power_Lmajor.min	0.69 ± 0.09	0.48 ± 0.14	<0.001
power_Rmajor.min	0.71 ± 0.09	0.51 ± 0.13	<0.001
power_Lminor.min	0.71 ± 0.10	0.49 ± 0.17	<0.001
Rminor.min	0.59 ± 0.15	0.78 ± 0.09	<0.001
power_Lminor.std	0.47 ± 0.12	0.34 ± 0.14	<0.001
Rminor.lean.max	0.98 ± 0.05	0.89 ± 0.19	<0.001
Lminor.lean.kurtosis	0.05 ± 0.03	0.13 ± 0.10	<0.001
Rsubcufat.mode	0.29 ± 0.08	0.32 ± 0.12	0.039
Rminor.mean	0.46 ± 0.14	0.56 ± 0.14	<0.001
Rminor.lean.kurtosis	0.09 ± 0.05	0.21 ± 0.14	<0.001
power_Lmajor.std	0.44 ± 0.12	0.26 ± 0.09	<0.001

Table 6: 2-means clustering raw analysis variables summary

	Cluster 1	*Cluster 2*	
	Mean ± SD	*Mean ± SD*	*ANOVA P-value*
Rminor.lean.std	32.86 ± 3.13	28.12 ± 4.02	<0.001
Rsubcufat.mean	-97.08 ± 12.37	-92.74 ± 16.91	0.004
Rminor.skewness	-0.09 ± 1.13	-0.23 ± 1.50	0.268
Lmajor.kurtosis	6.56 ± 13.59	3.28 ± 8.20	0.003
Rminor.mode	27.93 ± 20.53	42.35 ± 14.08	<0.001
Lminor.CSA	636.75 ±188.54	573.04 ±157.94	<0.001
Lmajor.mode	35.81 ± 21.19	46.38 ± 12.40	<0.001
Lminor.lean.max	89.36 ± 1.82	86.38 ± 7.09	<0.001
Lminor.kurtosis	2.37 ± 4.28	4.33 ± 8.14	0.004
Lmajor.lean.max	89.96 ± 0.22	89.14 ± 3.07	<0.001
Lminor.mode	27.31 ± 20.75	43.33 ± 13.59	<0.001
Rmajor.lean.min	-50.00 ± 0.00	-49.98 ± 0.13	0.077
Lminor.lean.min	-49.88 ± 0.40	-49.67 ± 0.85	0.002
ILA_percent	9.37 ± 7.79	10.94 ± 10.14	0.086
Lmajor.lean.min	-50.00 ± 0.00	-49.97 ± 0.23	0.086
Normal_percent	73.68 ± 19.57	74.47 ± 19.61	0.685
Rsubcufat.min	-251.72 ±127.72	-206.67 ± 33.69	<0.001
Rmajor.skewness	-0.07 ± 1.13	-0.24 ± 1.79	0.268
Lsubcufat.min	-240.54 ± 94.02	-203.63 ± 14.97	<0.001
Rminor.lean.min	-49.97 ± 0.18	-49.55 ± 1.83	0.002
Rmajor.std	48.81 ± 11.86	37.71 ± 21.65	<0.001
Lmajor.max	319.13 ±211.23	166.79 ±109.45	<0.001
Lmajor.min	-168.03 ± 74.27	-103.90 ± 23.10	<0.001
Rmajor.min	-169.27 ± 69.16	-105.02 ± 23.20	<0.001
Lminor.min	-148.74 ± 60.76	-90.47 ± 24.20	<0.001
Rminor.min	-150.74 ± 43.57	-94.98 ± 25.46	<0.001
Lminor.std	48.56 ± 14.34	38.10 ± 12.65	<0.001
Rminor.lean.max	89.21 ± 2.06	85.48 ± 8.01	<0.001
Lminor.lean.kurtosis	-0.55 ± 0.40	0.39 ± 1.19	<0.001
Rsubcufat.mode	-108.77 ± 12.49	-105.67 ± 16.92	0.039
Rminor.mean	19.37 ± 14.20	29.27 ± 13.69	<0.001
Rminor.lean.kurtosis	-0.57 ± 0.37	0.40 ± 1.04	<0.001
Lmajor.std	50.22 ± 14.03	34.41 ± 6.68	<0.001

Table 7: 2-means non-clustering imaging variables summary

	Cluster 1	*Cluster 2*	
	Mean ± SD	*Mean ± SD*	*ANOVA P-value*
Lminor.mean	20.72 ± 13.92	30.92 ± 13.87	<0.001
Lminor.skewness	-0.08 ± 1.06	-0.07 ± 1.58	0.942
Lminor.median	24.58 ± 14.19	36.10 ± 12.63	<0.001
Lminor.max	205.55 ± 137.23	182.78 ± 136.89	0.094
Lminor.lean.CSA	556.78 ± 169.94	545.45 ± 153.97	0.478
Lminor.lean.mean	23.36 ± 9.10	30.31 ± 10.95	<0.001
Lminor.lean.std	32.78 ± 2.79	28.24 ± 3.70	<0.001
Lminor.lean.skewness	-0.28 ± 0.32	-0.81 ± 0.37	<0.001
Lminor.lean.mode	27.31 ± 20.75	43.33 ± 13.59	<0.001
Lminor.lean.median	26.03 ± 11.26	36.31 ± 11.83	<0.001
Lmajor.CSA	1749.27 ± 566.50	1535.90 ± 526.26	<0.001
Lmajor.mean	23.99 ± 16.91	31.83 ± 11.00	<0.001
Lmajor.skewness	0.23 ± 1.42	-0.72 ± 1.02	<0.001
Lmajor.median	28.82 ± 16.88	39.34 ± 11.53	<0.001
Lmajor.lean.CSA	1500.88 ± 501.12	1475.01 ± 519.93	0.610
Lmajor.lean.mean	27.01 ± 10.10	32.94 ± 9.83	<0.001
Lmajor.lean.std	33.17 ± 2.75	29.09 ± 3.32	<0.001
Lmajor.lean.kurtosis	-0.45 ± 0.49	0.54 ± 0.99	<0.001
Lmajor.lean.skewness	-0.38 ± 0.34	-0.93 ± 0.36	<0.001
Lmajor.lean.mode	35.81 ± 21.19	46.38 ± 12.40	<0.001
Lmajor.lean.median	30.38 ± 12.23	39.52 ± 10.83	<0.001
Lsubcufat.CSA	2921.62 ±1588.38	2118.62 ±1390.15	<0.001
Lsubcufat.mean	-98.17 ± 12.57	-94.14 ± 16.28	0.006
Lsubcufat.std	41.31 ± 11.00	33.23 ± 10.44	<0.001
Lsubcufat.kurtosis	2.84 ± 6.21	2.50 ± 1.95	0.419
Lsubcufat.skewness	0.94 ± 0.71	0.92 ± 0.75	0.764
Lsubcufat.mode	-109.41 ± 14.08	-105.76 ± 19.70	0.036
Lsubcufat.median	-103.96 ± 11.80	-100.25 ± 16.54	0.011
Lsubcufat.max	99.71 ± 91.61	42.23 ± 40.66	<0.001
Rminor.CSA	630.38 ± 187.07	567.33 ± 178.45	0.001
Rminor.std	48.81 ± 14.33	36.52 ± 11.23	<0.001
Rminor.kurtosis	2.49 ± 5.32	4.04 ± 8.82	0.037
Rminor.median	23.17 ± 13.88	35.27 ± 13.14	<0.001
Rminor.max	204.64 ± 142.07	167.15 ± 128.08	0.005
Rminor.lean.CSA	548.66 ± 165.65	541.26 ± 175.63	0.663
Rminor.lean.mean	22.45 ± 8.91	29.59 ± 11.35	<0.001
Rminor.lean.skewness	-0.25 ± 0.31	-0.82 ± 0.39	<0.001
Rminor.lean.mode	27.93 ± 20.53	42.35 ± 14.08	<0.001
Rminor.lean.median	24.93 ± 11.12	35.56 ± 12.53	<0.001
Rmajor.CSA	1749.54 ± 526.58	1579.22 ± 526.25	0.001
Rmajor.mean	25.21 ± 14.95	33.53 ± 11.52	<0.001

Rmajor.kurtosis	4.53 ± 9.46	7.02 ± 19.74	0.118
Rmajor.mode	37.87 ± 19.92	47.88 ± 13.00	<0.001
Rmajor.median	30.77 ± 15.40	40.74 ± 12.11	<0.001
Rmajor.max	290.93 ± 177.01	251.86 ± 487.86	0.306
Rmajor.lean.CSA	1507.22 ± 472.13	1502.27 ± 516.29	0.920
Rmajor.lean.mean	28.23 ± 9.37	33.98 ± 9.94	<0.001
Rmajor.lean.std	33.13 ± 2.94	29.23 ± 3.40	<0.001
Rmajor.lean.kurtosis	-0.43 ± 0.54	0.63 ± 1.18	<0.001
Rmajor.lean.skewness	-0.42 ± 0.32	-0.96 ± 0.40	<0.001
Rmajor.lean.mode	37.94 ± 19.61	47.88 ± 13.00	<0.001
Rmajor.lean.median	32.02 ± 11.15	40.70 ± 11.17	<0.001
Rmajor.lean.max	89.80 ± 1.09	89.47 ± 2.45	0.093
Rsubcufat.CSA	2838.22 ±1663.34	2054.47 ±1320.53	<0.001
Rsubcufat.std	44.91 ± 22.95	34.03 ± 10.62	<0.001
Rsubcufat.kurtosis	13.04 ± 58.89	2.66 ± 3.61	0.008
Rsubcufat.skewness	1.44 ± 2.78	0.88 ± 0.78	0.004
Rsubcufat.median	-103.22 ± 11.32	-99.11 ± 16.82	0.005
Rsubcufat.max	197.07 ± 547.13	46.08 ± 52.33	<0.001
StandardPMA	4765.94 ±1352.43	4255.49 ±1253.54	<0.001
LeanPMA	4113.54 ±1202.06	4063.98 ±1239.63	0.683
SFA	5759.84 ±3224.45	4173.09 ±2697.01	<0.001
CLE_percent	12.42 ± 14.43	11.08 ± 15.25	0.365
PSE_percent	4.53 ± 5.90	3.51 ± 4.90	0.056
Emphysema_percent	16.95 ± 19.57	14.59 ± 19.56	0.225

Table 8: 2-means clustering clinical variables summary (full cohort, N=414)

	Cluster 1		*Cluster 2*		
	N	*Median (Range)*	*N*	*Median (Range)*	*Kruskal-Wallis* P-*value*
Age (years)	181	65.0 (50.0, 88.0)	233	65.0 (49.0, 89.0)	0.741
BMI	167	28.8 (18.1, 49.4)	215	25.4 (14.0, 66.3)	<0.001
Pack year history	174	41.0 (15.5, 155.0)	228	45.0 (2.5, 150.0)	0.386
FEV1 (% predicted)	167	71.0 (28.0, 118.0)	218	77.0 (20.0, 129.0)	0.078
FEV1 decline (mL/yr)	110	53.4 (-6152.9, 2920.0)	111	18.3 (-1085.1, 713.8)	0.005

	N (%)	*N (%)*	P-*value for independence (including Not reported/ Unknown data)*	P-*value for independence (excluding Not reported/ Unknown data)*
Gender			0.776	0.776
Female	36 (0.2)	49 (0.2)		
Male	145 (0.8)	184 (0.8)		
Race			0.563	0.563
White	138 (0.8)	167 (0.7)		
Black	27 (0.1)	40 (0.2)		
Other	16 (0.1)	26 (0.1)		
Ethnicity			0.017	0.026
Hispanic	1 (0.0)	9 (0.0)		
Non-Hispanic	169 (0.9)	198 (0.8)		
Not reported/Unknown	11 (0.1)	26 (0.1)		
BMI			<0.001	<0.001
Underweight	1 (0.0)	15 (0.1)		
Normal	40 (0.2)	86 (0.4)		
Pre-obese	54 (0.3)	63 (0.3)		
Obese class I	43 (0.2)	34 (0.1)		
Obese class II/III	29 (0.2)	17 (0.1)		
Not reported/Unknown	14 (0.1)	18 (0.1)		

Smoking status			0.478	0.243
Current smoker	67 (0.4)	100 (0.4)		
Former smoker	100 (0.6)	117 (0.5)		
Not reported/Unknown	14 (0.1)	16 (0.1)		
Number of exacerbations per year			0.727	0.697
0	41 (0.2)	47 (0.2)		
> 0	86 (0.5)	109 (0.5)		
Not reported/Unknown	54 (0.3)	77 (0.3)		
Inhaled corticosteroids[1]			0.009	0.034
Yes	72 (0.4)	66 (0.3)		
No	105 (0.6)	151 (0.6)		
Not reported/Unknown	4 (0.0)	16 (0.1)		
FEV1 decline (mL/yr)			<0.001	<0.001
≥ 40	66 (0.4)	37 (0.2)		
< 40	44 (0.2)	74 (0.3)		
Not reported/Unknown	71 (0.4)	122 (0.5)		
COPD status[2]			0.868	0.889
Yes	87 (0.5)	112 (0.5)		
No	80 (0.4)	106 (0.5)		
Not reported/Unknown	14 (0.1)	15 (0.1)		
GOLD COPD[2] stage			0.548	0.443
I	15 (0.1)	23 (0.1)		
II	48 (0.3)	61 (0.3)		
III	22 (0.1)	20 (0.1)		
IV	2 (0.0)	8 (0.0)		
No COPD[2]	80 (0.4)	106 (0.5)		
Not reported/Unknown	14 (0.1)	15 (0.1)		

[1] Inhaled corticosteroids within 2 weeks prior to study registration
[2] Calculated COPD status using lower limit of normal

Table 9: 2-means clustering clinical variables summary (subset with RNA sequencing data, N=164)

	Cluster 1		*Cluster 2*		
	N	*Median (Range)*	*N*	*Median (Range)*	*Kruskal-Wallis* P-*value*
Age (years)	69	65.0 (50.0, 80.0)	95	65.0 (49.0, 82.0)	0.830
BMI	66	28.5 (20.4, 49.4)	85	25.4 (15.8, 43.9)	0.001
Pack year history	69	40.0 (19.5, 155.0)	95	42.0 (20.0, 150.0)	0.355
FEV1 (% predicted)	69	73.0 (28.0, 118.0)	95	77.0 (26.0, 115.0)	0.489
FEV1 decline (mL/yr)	45	54.2 (-2212.1, 2920.0)	48	20.3 (-1085.1, 561.1)	0.070

	N (%)	*N (%)*	P-*value for independence (including Not reported/ Unknown data)*	P-*value for independence (excluding Not reported/ Unknown data)*
Gender			0.361	0.361
Female	10 (0.1)	19 (0.2)		
Male	59 (0.9)	76 (0.8)		
Race			0.632	0.632
White	53 (0.8)	67 (0.7)		
Black	10 (0.1)	16 (0.2)		
Other	6 (0.1)	12 (0.1)		
Ethnicity			0.687	0.509
Hispanic	0 (0.0)	2 (0.0)		
Non-Hispanic	64 (0.9)	86 (0.9)		
Not reported/Unknown	5 (0.1)	7 (0.1)		
BMI			0.003	0.003
Underweight	0 (0.0)	7 (0.1)		
Normal	15 (0.2)	31 (0.3)		
Pre-obese	25 (0.4)	33 (0.3)		
Obese class I	19 (0.3)	10 (0.1)		
Obese class II/III	7 (0.1)	4 (0.0)		
Not reported/Unknown	3 (0.0)	10 (0.1)		

Smoking status			0.744	0.606
Current smoker	28 (0.4)	43 (0.5)		
Former smoker	37 (0.5)	48 (0.5)		
Not reported/Unknown	4 (0.1)	4 (0.0)		
Number of exacerbations per year			0.458	0.639
0	14 (0.2)	24 (0.3)		
> 0	40 (0.6)	57 (0.6)		
Not reported/Unknown	15 (0.2)	14 (0.1)		
Inhaled corticosteroids[1]			0.008	0.023
Yes	31 (0.4)	24 (0.3)		
No	37 (0.5)	62 (0.7)		
Not reported/Unknown	1 (0.0)	9 (0.1)		
FEV1 decline (mL/yr)			0.003	0.005
≥ 40	27 (0.4)	15 (0.2)		
< 40	18 (0.3)	33 (0.3)		
Not reported/Unknown	24 (0.3)	47 (0.5)		
COPD status[2]			0.531	0.531
Yes	39 (0.6)	49 (0.5)		
No	30 (0.4)	46 (0.5)		
Not reported/Unknown	0 (0.0)	0 (0.0)		
GOLD COPD[2] stage			0.888	0.888
I	7 (0.1)	9 (0.1)		
II	23 (0.3)	29 (0.3)		
III	8 (0.1)	8 (0.1)		
IV	1 (0.0)	3 (0.0)		
No COPD[2]	30 (0.4)	46 (0.5)		
Not reported/Unknown	0 (0.0)	0 (0.0)		

[1] Inhaled corticosteroids within 2 weeks prior to study registration
[2] Calculated COPD status using lower limit of normal

3-MEANS CLUSTER ANALYSIS

Figure 8: Plot of the first two principal components of the analysis variables for the 3-means clusters

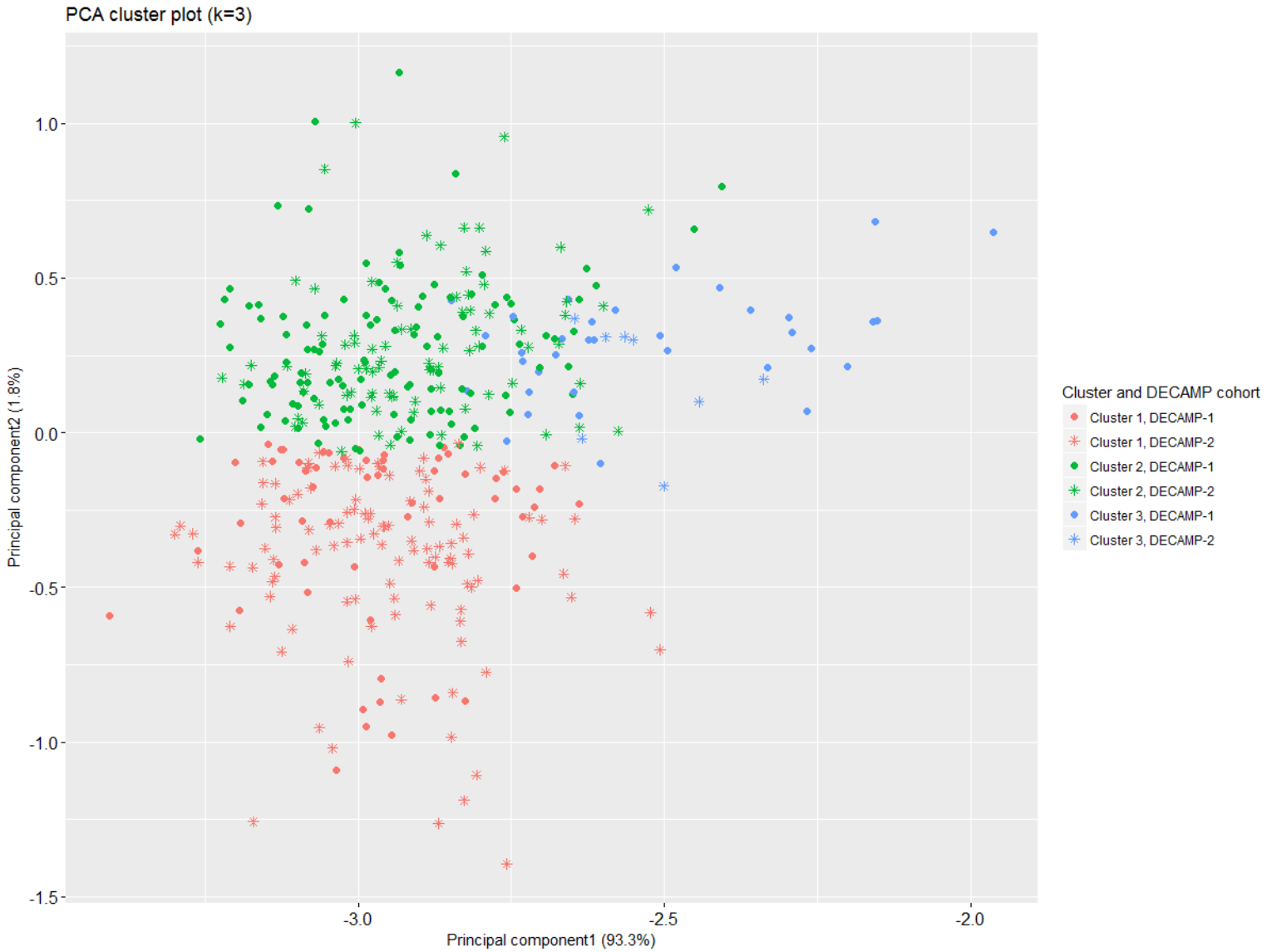


Figure 9: Silhouette plot for the 3-means clusters

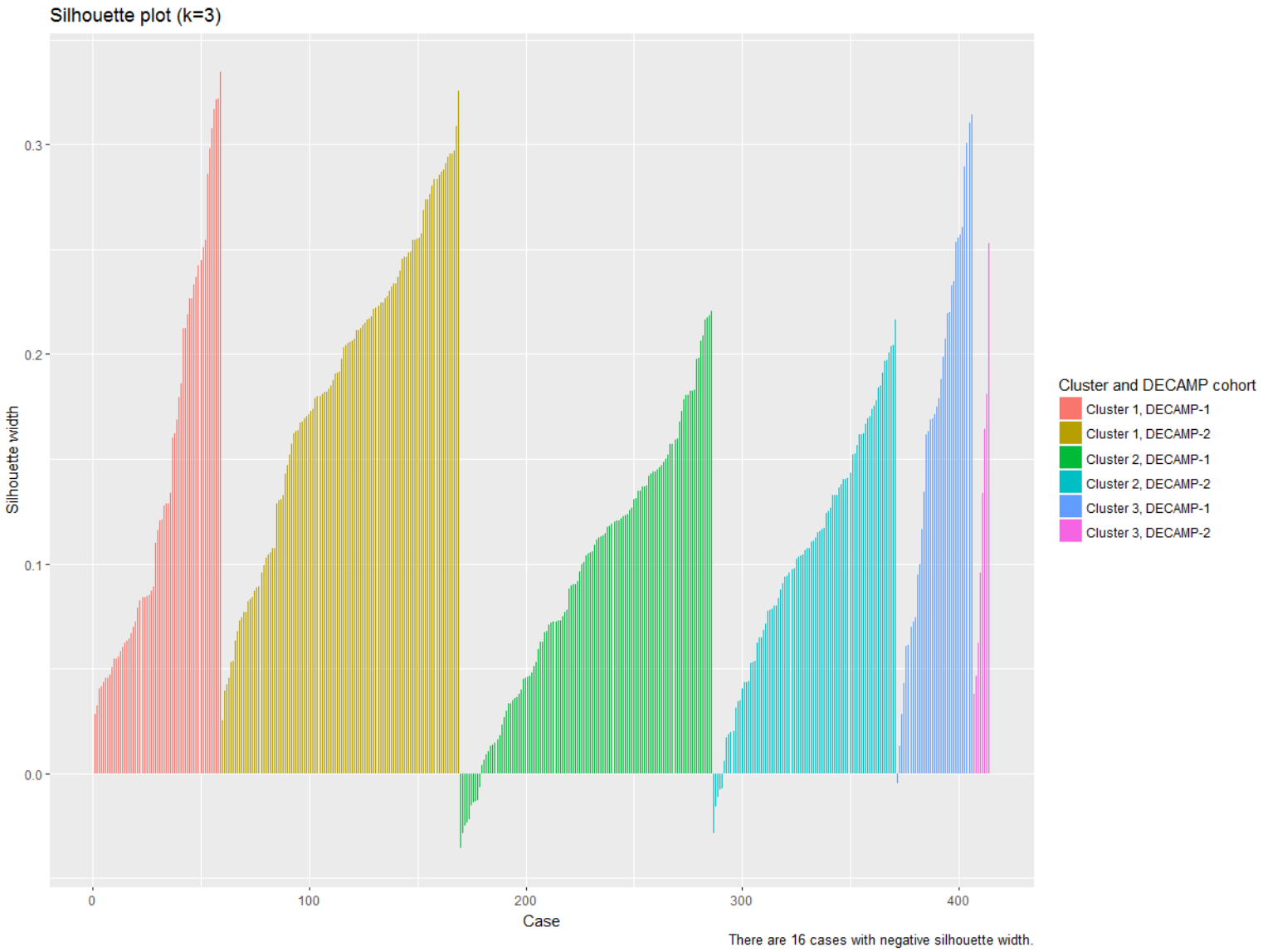


Table 10: 3-means clustering analysis variables summary

	Cluster 1	*Cluster 2*	*Cluster 3*	
	Mean ± SD	*Mean ± SD*	*Mean ± SD*	*ANOVA* P-*value*
Rminor.lean.std	0.75 ± 0.12	0.59 ± 0.15	0.51 ± 0.12	<0.001
Rsubcufat.mean	0.27 ± 0.12	0.36 ± 0.17	0.20 ± 0.10	0.647
Rminor.skewness	0.24 ± 0.11	0.24 ± 0.16	0.15 ± 0.05	0.007
Lmajor.kurtosis	0.07 ± 0.14	0.05 ± 0.08	0.05 ± 0.08	0.024
Rminor.mode	0.58 ± 0.17	0.72 ± 0.11	0.61 ± 0.14	<0.001
power_Lminor.CSA	0.49 ± 0.17	0.42 ± 0.17	0.43 ± 0.17	<0.001
Lmajor.mode	0.68 ± 0.17	0.79 ± 0.09	0.69 ± 0.11	<0.001
Lminor.lean.max	0.98 ± 0.04	0.97 ± 0.05	0.59 ± 0.25	<0.001
Lminor.kurtosis	0.05 ± 0.07	0.10 ± 0.14	0.02 ± 0.02	0.455
Lmajor.lean.max	1.00 ± 0.01	0.98 ± 0.08	0.94 ± 0.16	<0.001
Lminor.mode	0.59 ± 0.18	0.76 ± 0.11	0.63 ± 0.12	<0.001
Rmajor.lean.min	0.00 ± 0.00	0.02 ± 0.14	0.00 ± 0.00	0.346
Lminor.lean.min	0.02 ± 0.07	0.08 ± 0.18	0.01 ± 0.05	0.092
power_ILA_percent	0.47 ± 0.17	0.46 ± 0.17	0.61 ± 0.15	0.001
Lmajor.lean.min	0.00 ± 0.00	0.01 ± 0.08	0.00 ± 0.00	0.361
Normal_percent	0.74 ± 0.22	0.73 ± 0.23	0.81 ± 0.15	0.178
power_Rsubcufat.min	0.20 ± 0.19	0.08 ± 0.09	0.10 ± 0.14	<0.001
power_Rmajor.skewness	0.56 ± 0.07	0.57 ± 0.05	0.58 ± 0.05	0.056
power_Lsubcufat.min	0.26 ± 0.18	0.14 ± 0.06	0.15 ± 0.09	<0.001
Rminor.lean.min	0.00 ± 0.01	0.02 ± 0.09	0.00 ± 0.02	0.071
power_Rmajor.std	0.27 ± 0.08	0.18 ± 0.10	0.13 ± 0.06	<0.001
power_Lmajor.max	0.23 ± 0.15	0.40 ± 0.17	0.44 ± 0.21	<0.001
power_Lmajor.min	0.69 ± 0.09	0.50 ± 0.14	0.45 ± 0.16	<0.001
power_Rmajor.min	0.72 ± 0.09	0.53 ± 0.13	0.48 ± 0.11	<0.001
power_Lminor.min	0.72 ± 0.09	0.50 ± 0.17	0.50 ± 0.15	<0.001
Rminor.min	0.58 ± 0.15	0.77 ± 0.09	0.78 ± 0.09	<0.001
power_Lminor.std	0.47 ± 0.12	0.37 ± 0.15	0.25 ± 0.09	<0.001
Rminor.lean.max	0.98 ± 0.05	0.96 ± 0.07	0.60 ± 0.25	<0.001
Lminor.lean.kurtosis	0.05 ± 0.03	0.13 ± 0.10	0.09 ± 0.06	<0.001
Rsubcufat.mode	0.29 ± 0.09	0.33 ± 0.12	0.25 ± 0.05	0.847
Rminor.mean	0.46 ± 0.15	0.59 ± 0.12	0.42 ± 0.13	0.002
Rminor.lean.kurtosis	0.08 ± 0.05	0.22 ± 0.14	0.18 ± 0.12	<0.001
power_Lmajor.std	0.44 ± 0.12	0.28 ± 0.10	0.22 ± 0.07	<0.001

Table 11: 3-means clustering raw analysis variables summary

	Cluster 1	*Cluster 2*	*Cluster 3*	
	Mean ± SD	*Mean ± SD*	*Mean ± SD*	*ANOVA* P-*value*
Rminor.lean.std	32.98 ± 3.13	28.63 ± 4.08	26.52 ± 3.20	<0.001
Rsubcufat.mean	-97.91 ± 11.57	-89.63 ± 16.95	-105.34 ± 9.43	0.647
Rminor.skewness	-0.08 ± 1.12	-0.08 ± 1.59	-0.94 ± 0.47	0.007
Lmajor.kurtosis	6.37 ± 13.78	3.57 ± 8.52	3.63 ± 8.00	0.024
Rminor.mode	27.34 ± 20.57	44.23 ± 12.74	31.79 ± 17.09	<0.001
Lminor.CSA	643.32 ±189.31	569.85 ±155.48	579.97 ±169.17	<0.001
Lmajor.mode	35.01 ± 21.01	48.56 ± 11.84	36.35 ± 13.15	<0.001
Lminor.lean.max	89.41 ± 1.56	89.03 ± 1.88	74.56 ± 9.48	<0.001
Lminor.kurtosis	2.34 ± 4.31	5.03 ± 8.59	0.60 ± 1.16	0.455
Lmajor.lean.max	89.97 ± 0.17	89.40 ± 2.37	88.14 ± 4.92	<0.001
Lminor.mode	25.98 ± 20.34	46.03 ± 12.43	31.42 ± 13.59	<0.001
Rmajor.lean.min	-50.00 ± 0.00	-49.98 ± 0.14	-50.00 ± 0.00	0.346
Lminor.lean.min	-49.90 ± 0.36	-49.62 ± 0.92	-49.93 ± 0.26	0.092
ILA_percent	9.59 ± 7.86	9.51 ± 9.37	16.37 ± 11.17	0.002
Lmajor.lean.min	-50.00 ± 0.00	-49.97 ± 0.25	-50.00 ± 0.00	0.361
Normal_percent	73.55 ± 19.60	73.37 ± 20.51	79.95 ± 13.29	0.178
Rsubcufat.min	-251.97 ±130.33	-207.00 ± 31.79	-216.70 ± 61.52	<0.001
Rmajor.skewness	-0.04 ± 1.15	-0.28 ± 1.82	-0.18 ± 1.46	0.276
Lsubcufat.min	-242.67 ± 96.81	-203.45 ± 12.27	-206.37 ± 25.25	<0.001
Rminor.lean.min	-49.97 ± 0.17	-49.49 ± 1.95	-49.91 ± 0.37	0.071
Rmajor.std	49.30 ± 11.95	38.95 ± 23.06	33.03 ± 5.87	<0.001
Lmajor.max	315.95 ±212.18	179.27 ±126.59	163.14 ±101.73	<0.001
Lmajor.min	-170.04 ± 76.34	-106.93 ± 23.85	-99.63 ± 24.78	<0.001
Rmajor.min	-172.29 ± 70.14	-107.84 ± 24.96	-97.84 ± 17.34	<0.001
Lminor.min	-152.51 ± 61.07	-90.94 ± 24.22	-89.72 ± 21.83	<0.001
Rminor.min	-153.15 ± 43.60	-96.72 ± 25.90	-92.91 ± 25.79	<0.001
Lminor.std	49.06 ± 14.51	39.90 ± 13.01	30.59 ± 5.35	<0.001
Rminor.lean.max	89.24 ± 1.97	88.35 ± 3.14	72.95 ± 10.65	<0.001
Lminor.lean.kurtosis	-0.59 ± 0.34	0.46 ± 1.23	-0.05 ± 0.75	<0.001
Rsubcufat.mode	-109.17 ± 12.54	-103.64 ± 17.40	-114.53 ± 8.08	0.847
Rminor.mean	18.85 ± 14.32	32.11 ± 11.68	15.20 ± 13.03	0.002
Rminor.lean.kurtosis	-0.60 ± 0.35	0.42 ± 1.04	0.14 ± 0.94	<0.001
Lmajor.std	50.46 ± 14.35	35.75 ± 7.53	31.59 ± 4.26	<0.001

Table 12: 3-means non-clustering imaging variables summary

	Cluster 1	*Cluster 2*	*Cluster 3*	
	Mean ± SD	*Mean ± SD*	*Mean ± SD*	*ANOVA P-value*
Lminor.mean	19.89 ± 13.52	34.46 ± 11.97	14.74 ± 10.32	0.002
Lminor.skewness	-0.09 ± 1.05	0.11 ± 1.66	-0.86 ± 0.47	0.082
Lminor.median	23.72 ± 13.80	39.06 ± 10.81	22.36 ± 11.96	<0.001
Lminor.max	206.04 ± 139.10	204.75 ± 139.52	84.02 ± 37.74	<0.001
Lminor.lean.CSA	560.40 ± 170.71	540.60 ± 153.15	557.17 ± 159.08	0.510
Lminor.lean.mean	22.77 ± 8.66	33.06 ± 9.28	17.75 ± 9.34	0.013
Lminor.lean.std	32.95 ± 2.76	28.71 ± 3.73	26.66 ± 2.84	<0.001
Lminor.lean.skewness	-0.25 ± 0.30	-0.82 ± 0.36	-0.71 ± 0.41	<0.001
Lminor.lean.mode	25.98 ± 20.34	46.03 ± 12.43	31.42 ± 13.59	<0.001
Lminor.lean.median	25.28 ± 10.80	38.98 ± 10.17	23.83 ± 11.27	<0.001
Lmajor.CSA	1771.24 ± 571.40	1511.02 ± 497.38	1626.00 ± 614.29	0.001
Lmajor.mean	23.29 ± 16.53	33.87 ± 10.70	22.77 ± 10.99	0.001
Lmajor.skewness	0.21 ± 1.43	-0.68 ± 1.08	-0.56 ± 1.04	<0.001
Lmajor.median	28.07 ± 16.34	41.45 ± 11.10	29.50 ± 11.97	<0.001
Lmajor.lean.CSA	1517.60 ± 505.15	1440.81 ± 494.49	1577.15 ± 598.22	0.838
Lmajor.lean.mean	26.55 ± 9.55	34.84 ± 9.10	24.16 ± 10.03	0.006
Lmajor.lean.std	33.22 ± 2.73	29.70 ± 3.35	27.18 ± 2.72	<0.001
Lmajor.lean.kurtosis	-0.48 ± 0.44	0.53 ± 0.97	0.43 ± 1.08	<0.001
Lmajor.lean.skewness	-0.35 ± 0.32	-0.94 ± 0.35	-0.81 ± 0.44	<0.001
Lmajor.lean.mode	35.01 ± 21.01	48.56 ± 11.84	36.35 ± 13.15	<0.001
Lmajor.lean.median	29.74 ± 11.57	41.52 ± 10.10	30.10 ± 11.47	<0.001
Lsubcufat.CSA	3009.44 ±1584.13	1849.70 ± 995.85	3260.89 ±2146.06	0.004
Lsubcufat.mean	-99.04 ± 11.77	-91.20 ± 16.47	-105.65 ± 9.22	0.571
Lsubcufat.std	41.59 ± 10.98	35.00 ± 10.31	26.05 ± 7.86	<0.001
Lsubcufat.kurtosis	2.90 ± 6.41	2.21 ± 1.71	3.73 ± 2.39	0.946
Lsubcufat.skewness	0.95 ± 0.71	0.89 ± 0.74	1.01 ± 0.80	0.948
Lsubcufat.mode	-110.32 ± 13.53	-103.44 ± 20.54	-114.14 ± 10.81	0.367
Lsubcufat.median	-104.86 ± 10.85	-97.56 ± 17.11	-110.42 ± 8.36	0.484
Lsubcufat.max	102.34 ± 93.93	47.78 ± 40.40	21.91 ± 33.57	<0.001
Rminor.CSA	639.24 ± 185.50	559.60 ± 177.68	586.40 ± 181.12	0.001
Rminor.std	49.36 ± 14.43	38.08 ± 11.71	30.43 ± 5.02	<0.001
Rminor.kurtosis	2.43 ± 5.34	4.70 ± 9.40	0.77 ± 1.06	0.640
Rminor.median	22.50 ± 13.78	37.68 ± 11.06	23.21 ± 15.26	<0.001
Rminor.max	206.09 ± 143.08	187.45 ± 132.85	76.56 ± 18.56	<0.001
Rminor.lean.CSA	553.83 ± 164.53	532.29 ± 175.23	565.12 ± 177.14	0.760
Rminor.lean.mean	22.00 ± 8.74	31.97 ± 9.41	18.22 ± 12.24	0.005
Rminor.lean.skewness	-0.23 ± 0.30	-0.82 ± 0.36	-0.73 ± 0.51	<0.001
Rminor.lean.mode	27.34 ± 20.57	44.23 ± 12.74	31.79 ± 17.09	<0.001
Rminor.lean.median	24.31 ± 10.84	37.78 ± 10.68	24.62 ± 14.59	<0.001
Rmajor.CSA	1768.85 ± 528.63	1543.07 ± 480.48	1720.69 ± 670.08	0.018
Rmajor.mean	24.62 ± 14.63	35.40 ± 11.13	24.77 ± 11.19	<0.001

Rmajor.kurtosis	4.66 ± 9.74	6.86 ± 20.48	6.58 ± 12.35	0.253
Rmajor.mode	37.22 ± 19.65	49.91 ± 12.75	38.05 ± 13.03	<0.001
Rmajor.median	30.05 ± 14.98	42.68 ± 11.51	31.70 ± 12.67	<0.001
Rmajor.max	295.65 ± 180.57	260.06 ± 519.59	205.67 ± 151.44	0.153
Rmajor.lean.CSA	1520.60 ± 473.39	1456.22 ± 469.61	1667.40 ± 660.72	0.514
Rmajor.lean.mean	27.72 ± 8.85	35.75 ± 9.26	26.10 ± 10.27	0.002
Rmajor.lean.std	33.24 ± 2.85	29.73 ± 3.49	27.51 ± 2.55	<0.001
Rmajor.lean.kurtosis	-0.47 ± 0.48	0.63 ± 1.13	0.56 ± 1.33	<0.001
Rmajor.lean.skewness	-0.40 ± 0.30	-0.96 ± 0.37	-0.88 ± 0.50	<0.001
Rmajor.lean.mode	37.30 ± 19.31	49.91 ± 12.75	38.05 ± 13.03	<0.001
Rmajor.lean.median	31.36 ± 10.49	42.52 ± 10.44	32.33 ± 12.06	<0.001
Rmajor.lean.max	89.82 ± 1.11	89.71 ± 1.04	88.40 ± 5.16	0.001
Rsubcufat.CSA	2933.79 ±1661.30	1791.39 ± 985.85	3133.47 ±1951.93	0.003
Rsubcufat.std	44.70 ± 21.46	36.30 ± 13.97	27.17 ± 9.02	<0.001
Rsubcufat.kurtosis	12.29 ± 57.61	3.50 ± 18.86	4.58 ± 6.31	0.060
Rsubcufat.skewness	1.41 ± 2.65	0.92 ± 1.27	0.93 ± 0.88	0.026
Rsubcufat.median	-104.01 ± 10.45	-96.38 ± 17.28	-109.91 ± 8.14	0.478
Rsubcufat.max	189.73 ± 519.73	63.97 ± 216.38	33.00 ± 83.80	0.001
StandardPMA	4822.65 ±1355.81	4183.54 ±1181.50	4513.07 ±1490.28	0.001
LeanPMA	4152.43 ±1204.07	3969.92 ±1173.20	4366.83 ±1461.97	0.960
SFA	5943.23 ±3217.07	3641.08 ±1969.91	6394.36 ±4074.13	0.004
CLE_percent	12.28 ± 14.29	13.08 ± 16.16	2.63 ± 4.38	0.012
PSE_percent	4.58 ± 6.01	4.05 ± 5.12	1.06 ± 1.96	0.001
Emphysema_percent	16.86 ± 19.56	17.12 ± 20.66	3.69 ± 5.73	0.005

Table 13: 3-means clustering clinical variables summary (full cohort, N=414)

	Cluster 1		*Cluster 2*		*Cluster 3*		
	N	*Median (Range)*	*N*	*Median (Range)*	*N*	*Median (Range)*	*Kruskal-Wallis* P-*value*
Age (years)	169	65.0 (50.0, 88.0)	202	66.0 (49.0, 89.0)	43	65.0 (51.0, 82.0)	0.843
BMI	155	29.3 (20.1, 49.4)	185	24.8 (14.0, 66.3)	42	30.4 (15.8, 48.8)	<0.001
Pack year history	162	40.0 (15.5, 155.0)	197	45.0 (2.5, 150.0)	43	45.0 (20.0, 94.5)	0.607
FEV1 (% predicted)	156	71.0 (28.0, 118.0)	190	76.5 (20.0, 129.0)	39	76.0 (42.0, 122.0)	0.278
FEV1 decline (mL/yr)	105	54.5 (-6152.9, 2920.0)	102	20.3 (-1085.1, 713.8)	14	22.5 (-582.1, 280.2)	0.013

	N (%)	*N (%)*	*N (%)*	P-*value for independence (including Not reported/ Unknown data)*	P-*value for independence (excluding Not reported/ Unknown data)*
Gender				0.046	0.046
Female	33 (0.2)	37 (0.2)	15 (0.3)		
Male	136 (0.8)	165 (0.8)	28 (0.7)		
Race				0.932	0.932
White	128 (0.8)	146 (0.7)	31 (0.7)		
Black	26 (0.2)	34 (0.2)	7 (0.2)		
Other	15 (0.1)	22 (0.1)	5 (0.1)		
Ethnicity				0.109	0.074
Hispanic	1 (0.0)	8 (0.0)	1 (0.0)		
Non-Hispanic	157 (0.9)	173 (0.9)	37 (0.9)		
Not reported/Unknown	11 (0.1)	21 (0.1)	5 (0.1)		
BMI				0.001	0.001
Underweight	0 (0.0)	14 (0.1)	2 (0.0)		
Normal	34 (0.2)	84 (0.4)	8 (0.2)		
Pre-obese	50 (0.3)	58 (0.3)	9 (0.2)		
Obese class I	43 (0.3)	24 (0.1)	10 (0.2)		
Obese class II/III	28 (0.2)	5 (0.0)	13 (0.3)		
Not reported/Unknown	14 (0.1)	17 (0.1)	1 (0.0)		

Smoking status				0.134	0.044
Current smoker	60 (0.4)	94 (0.5)	13 (0.3)		
Former smoker	96 (0.6)	95 (0.5)	26 (0.6)		
Not reported/Unknown	13 (0.1)	13 (0.1)	4 (0.1)		
Number of exacerbations per year				0.563	0.307
0	39 (0.2)	38 (0.2)	11 (0.3)		
> 0	78 (0.5)	101 (0.5)	16 (0.4)		
Not reported/Unknown	52 (0.3)	63 (0.3)	16 (0.4)		
Inhaled corticosteroids[1]				0.095	0.169
Yes	66 (0.4)	61 (0.3)	11 (0.3)		
No	99 (0.6)	127 (0.6)	30 (0.7)		
Not reported/Unknown	4 (0.0)	14 (0.1)	2 (0.0)		
FEV1 decline (mL/yr)				<0.001	0.002
≥ 40	62 (0.4)	37 (0.2)	4 (0.1)		
< 40	43 (0.3)	65 (0.3)	10 (0.2)		
Not reported/Unknown	64 (0.4)	100 (0.5)	29 (0.7)		
COPD status[2]				0.102	0.038
Yes	80 (0.5)	106 (0.5)	13 (0.3)		
No	76 (0.4)	84 (0.4)	26 (0.6)		
Not reported/Unknown	13 (0.1)	12 (0.1)	4 (0.1)		
GOLD COPD[2] stage				0.458	0.355
I	14 (0.1)	22 (0.1)	2 (0.0)		
II	46 (0.3)	55 (0.3)	8 (0.2)		
III	18 (0.1)	21 (0.1)	3 (0.1)		
IV	2 (0.0)	8 (0.0)	0 (0.0)		
No COPD[2]	76 (0.4)	84 (0.4)	26 (0.6)		
Not reported/Unknown	13 (0.1)	12 (0.1)	4 (0.1)		

[1] Inhaled corticosteroids within 2 weeks prior to study registration

[2] Calculated COPD status using lower limit of normal

Table 14: 3-means clustering clinical variables summary (subset with RNA sequencing data, N=164)

	Cluster 1		*Cluster 2*		*Cluster 3*		
	N	*Median (Range)*	*N*	*Median (Range)*	*N*	*Median (Range)*	*Kruskal-Wallis P-value*
Age (years)	65	65.0 (50.0, 80.0)	86	66.0 (49.0, 81.0)	13	64.0 (51.0, 82.0)	0.808
BMI	62	28.5 (20.4, 49.4)	76	25.2 (15.8, 35.4)	13	29.5 (19.9, 43.9)	<0.001
Pack year history	65	40.0 (19.5, 155.0)	86	44.5 (20.0, 150.0)	13	40.0 (20.0, 70.0)	0.225
FEV1 (% predicted)	65	73.0 (28.0, 118.0)	86	77.0 (26.0, 115.0)	13	76.0 (44.0, 109.0)	0.668
FEV1 decline (mL/yr)	44	54.4 (-2212.1, 2920.0)	46	20.3 (-1085.1, 561.1)	3	26.6 (0.0, 52.0)	0.215

	N (%)	*N (%)*	*N (%)*	P-*value for independence (including Not reported/ Unknown data)*	P-*value for independence (excluding Not reported/ Unknown data)*
Gender				0.705	0.705
Female	10 (0.2)	16 (0.2)	3 (0.2)		
Male	55 (0.8)	70 (0.8)	10 (0.8)		
Race				0.875	0.875
White	49 (0.8)	61 (0.7)	10 (0.8)		
Black	10 (0.2)	15 (0.2)	1 (0.1)		
Other	6 (0.1)	10 (0.1)	2 (0.2)		
Ethnicity				0.798	0.582
Hispanic	0 (0.0)	2 (0.0)	0 (0.0)		
Non-Hispanic	60 (0.9)	78 (0.9)	12 (0.9)		
Not reported/Unknown	5 (0.1)	6 (0.1)	1 (0.1)		
BMI				<0.001	<0.001
Underweight	0 (0.0)	7 (0.1)	0 (0.0)		
Normal	14 (0.2)	29 (0.3)	3 (0.2)		
Pre-obese	23 (0.4)	30 (0.3)	5 (0.4)		
Obese class I	19 (0.3)	9 (0.1)	1 (0.1)		
Obese class II/III	6 (0.1)	1 (0.0)	4 (0.3)		
Not reported/Unknown	3 (0.0)	10 (0.1)	0 (0.0)		

Smoking status				0.243	0.145
Current smoker	25 (0.4)	43 (0.5)	3 (0.2)		
Former smoker	36 (0.6)	40 (0.5)	9 (0.7)		
Not reported/Unknown	4 (0.1)	3 (0.0)	1 (0.1)		
Number of exacerbations per year				0.154	0.539
0	13 (0.2)	21 (0.2)	4 (0.3)		
> 0	37 (0.6)	55 (0.6)	5 (0.4)		
Not reported/Unknown	15 (0.2)	10 (0.1)	4 (0.3)		
Inhaled corticosteroids[1]				0.027	0.042
Yes	30 (0.5)	21 (0.2)	4 (0.3)		
No	34 (0.5)	57 (0.7)	8 (0.6)		
Not reported/Unknown	1 (0.0)	8 (0.1)	1 (0.1)		
FEV1 decline (mL/yr)				0.003	0.022
≥ 40	26 (0.4)	15 (0.2)	1 (0.1)		
< 40	18 (0.3)	31 (0.4)	2 (0.2)		
Not reported/Unknown	21 (0.3)	40 (0.5)	10 (0.8)		
COPD status[2]				0.475	0.475
Yes	37 (0.6)	46 (0.5)	5 (0.4)		
No	28 (0.4)	40 (0.5)	8 (0.6)		
Not reported/Unknown	0 (0.0)	0 (0.0)	0 (0.0)		
GOLD COPD[2] stage				0.966	0.966
I	6 (0.1)	9 (0.1)	1 (0.1)		
II	22 (0.3)	27 (0.3)	3 (0.2)		
III	8 (0.1)	7 (0.1)	1 (0.1)		
IV	1 (0.0)	3 (0.0)	0 (0.0)		
No COPD[2]	28 (0.4)	40 (0.5)	8 (0.6)		
Not reported/Unknown	0 (0.0)	0 (0.0)	0 (0.0)		

[1] Inhaled corticosteroids within 2 weeks prior to study registration

[2] Calculated COPD status using lower limit of normal

Table 15: Contingency table for the number of cases in each cluster for the 2- and 3-means cluster analyses (full cohort)

	3-means clustering			
2-means clustering	Cluster 1 *n*=	Cluster 2 *n*=	Cluster 3 *n*=	**Total**
Cluster 1 (*n*=)	169	11	1	181
Cluster 2 (*n*=)	0	191	42	233
Total	169	202	43	414

Table 16: Contingency table for the number of cases in each cluster for the 2- and 3-means cluster analyses (subset with RNA sequencing)

	3-means clustering			
2-means clustering	Cluster 1 *n*=	Cluster 2 *n*=	Cluster 3 *n*=	**Total**
Cluster 1 (*n*=)	65	3	1	69
Cluster 2 (*n*=)	0	83	12	95
Total	65	86	13	164