



Determination of Optimized Phase through 4DCT Analysis in Lung SBRT

Eun Jeong Heo^{1,2}, Hyeon Seo Yu^{1,3}, Kyung Hwan Chang⁴, Kwang Hyeon Kim⁵

Jang Bo Shim⁶, Chun Gun Park⁷, Min Seok Kim⁷, Chul Yong Kim¹, Suk Lee^{1,*}

¹Department of Radiation Oncology, College of Medicine, Korea University, Seoul, Republic of Korea

²Department of Bio-medical Science, Graduate School of Korea University, Sejong, Republic of Korea

³Program in Bio-medical Science, Graduate School of Korea University, Sejong, Republic of Korea

⁴Department of Radiation Oncology, Yonsei Cancer Center, Yonsei University College of Medicine, Seoul, Republic of Korea

⁵Department of Neurosurgery, Ilsan Paik Hospital, College of Medicine, Inje University, Goyang, Republic of Korea

⁶Department of Radiation Oncology, Guro Hospital, Korea University Medical Center, Seoul, Republic of Korea

⁷Department of Mathematics, Kyonggi University, Gyeonggi, Republic of Korea

Motivation

- ✓ Gated radiotherapy (Plan GAT) could potentially allow a reduction of mean dose and volume in normal tissue
- ✓ Values correlations are significant ($p < 0.05$) for all comparisons except for intestine parameters and V_{5Gy} for the kidney with respect to GITV4D to GTVGAT and PTV volume reduction

Table 2
Normal tissue dose-volume assessments.

	Plan 4D	Plan GAT	p-Value	Reduction		Range	
	Mean (range) (%)	Mean (range) (%)		Mean	SD	Min	Max
D mean liver	9.3 (2.2–17.9)	7.9 (1.9–17.2)	<0.0001	1.5	1.1	0.2	4.2
V_{5Gy} liver	46.8 (11.2–83)	40.3 (10.7–81.5)	<0.0001	6.5	5.0	0.1	17.1
V_{10Gy} liver	32.5 (7.1–63.4)	27.2 (6.2–61.4)	<0.0001	5.4	4.0	0.2	14.6
V_{15Gy} liver	23.9 (4.8–53.2)	19.4 (4–49.8)	<0.0001	4.5	3.4	0.6	13
V_{21Gy} liver	17 (3.4–40)	13.5 (2.6–37.5)	<0.0001	3.4	2.8	0.6	11
D mean kidney	3.9 (0–10.9)	2.3 (0–9.1)	<0.0001	1.6	1.9	0	8.0
V_{5Gy} kidney	24.2 (0–77)	15.1 (0–64.6)	0.0002	9.1	7.9	0	29.2
V_{10Gy} kidney	11 (0–43.9)	5.6 (0–41)	0.0004	5.4	6.8	0	25.8
V_{15Gy} kidney	7.8 (0–35.4)	3.7 (0–30.4)	0.004	4.1	6.4	0	23.8
V_{21Gy} kidney	5.3 (0–27.2)	2.1 (0–15.4)	0.004	3.2	5.6	0	21.3
V_{5Gy} cord	11.1 (0–37)	8.3 (0–35.4)	<0.0001	2.8	3.0	0	11.3
D max cord	8.4 (0.3–19.4)	7.9 (0.2–16.4)	0.0005	0.5	0.9	0	3.5
V_{5Gy} intestine	3.1 (0–17.9)	1.7 (0–10.6)	<0.0001	1.4	1.8	0	7.3
D max intestine	15.8 (0.8–36.7)	11.9 (0.3–35.5)	0.0002	3.9	5.4	0.2	24

Abbreviations: D mean liver, mean dose to the liver; D max cord and intestine, maximum dose to the spinal cord and intestine – values are presented as a % of the prescribed (36 Gy); V_{5Gy} , V_{10Gy} , V_{15Gy} , V_{21Gy} : % of organ volume receiving specific dose.

Plan 4D: Full phase planning
Plan GAT: Selected specific one phase planning

Table 3
The correlation coefficients values. Values correlations are significant ($p < 0.05$) for all comparisons except for intestine parameters and V_{5Gy} for the kidney with respect to GITV4D to GTVGAT and PTV volume reduction.

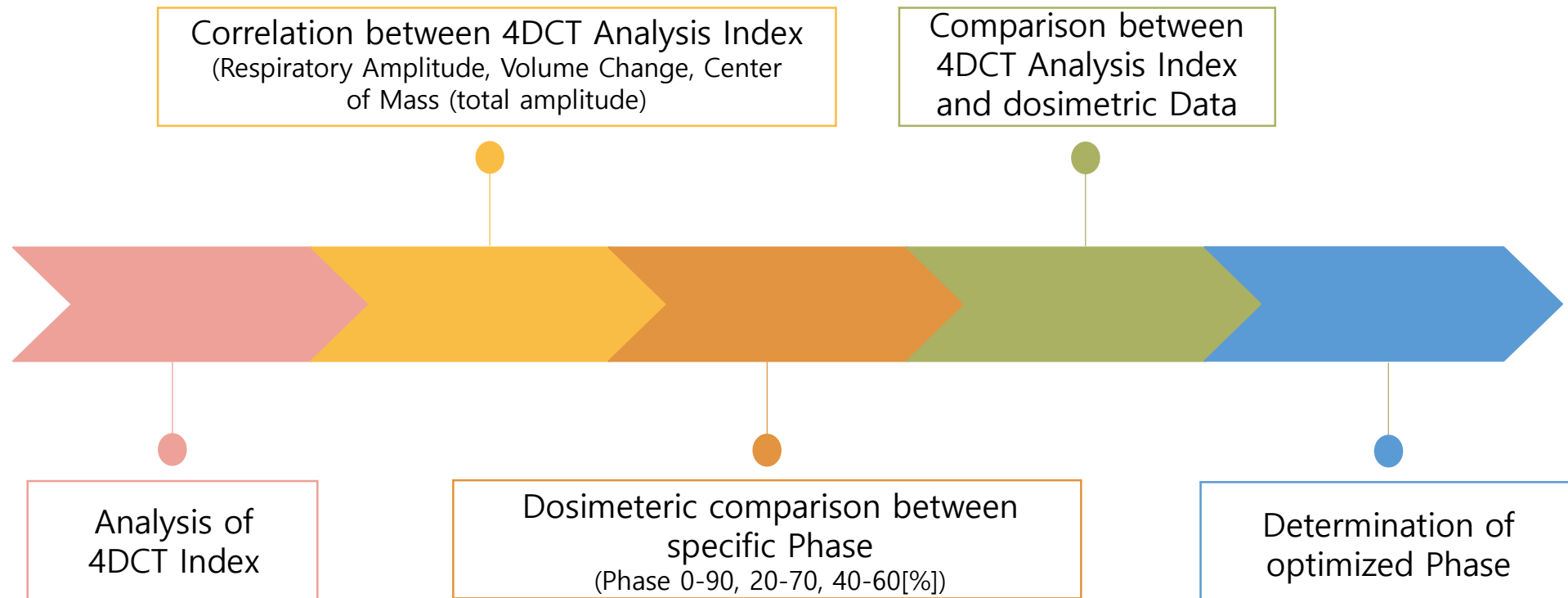
	Coefficient		
	GTV motion	GITV4D to GTVGAT reduction	PTV4D to PTVGAT reduction
D mean liver	0.69	0.72	0.74
V_{5Gy} liver	0.64	0.62	0.65
V_{10Gy} liver	0.69	0.68	0.70
V_{15Gy} liver	0.64	0.72	0.74
V_{21Gy} liver	0.60	0.77	0.78
D mean kidney	0.60	0.56	0.55
V_{5Gy} kidney	0.50	0.37 (NS)	0.39 (NS)
V_{10Gy} kidney	0.53	0.51	0.50
V_{15Gy} kidney	0.46	0.53	0.52
V_{21Gy} kidney	0.48	0.55	0.54
V_{5Gy} cord	0.62	0.69	0.69
V_{5Gy} intestine	0.29 (NS)	0.15 (NS)	0.18 (NS)

Abbreviations: GTV, gross target volume; GITV, gross internal target volume; PTV, planning target volume; D mean, mean dose to the organ; V_{5Gy} , V_{10Gy} , V_{15Gy} , V_{21Gy} : % of organ volume receiving specific dose.

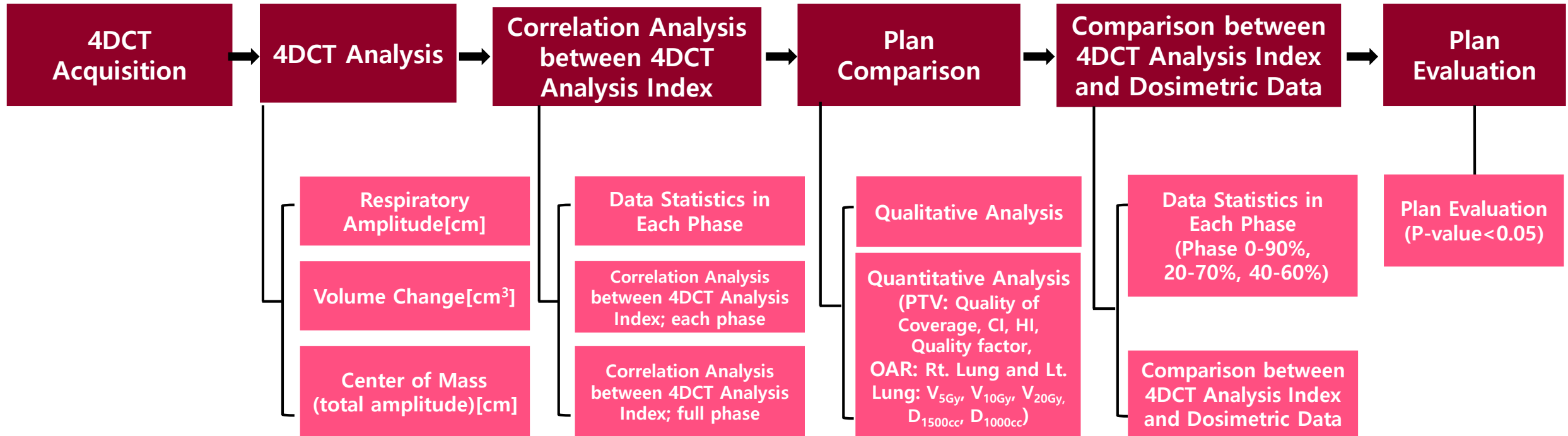
Reference: *Dosimetric comparison of liver tumour radiotherapy in all respiratory phases and in one phase using 4DCT, Radiotherapy and Oncology, 2011*

Purpose

- Determination of Optimized Phase through 4DCT Analysis in Lung SBRT



Scheme of Block Diagram of Study



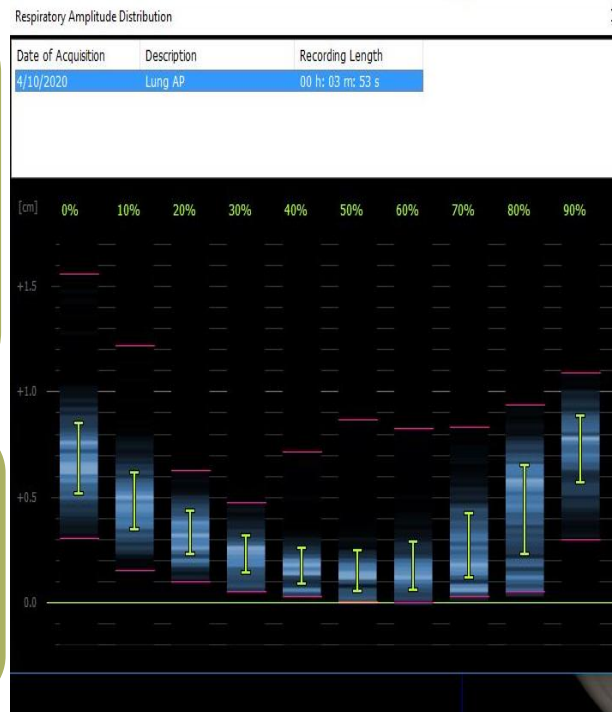
Acquisition of 4DCT Analysis index

Patient Selection

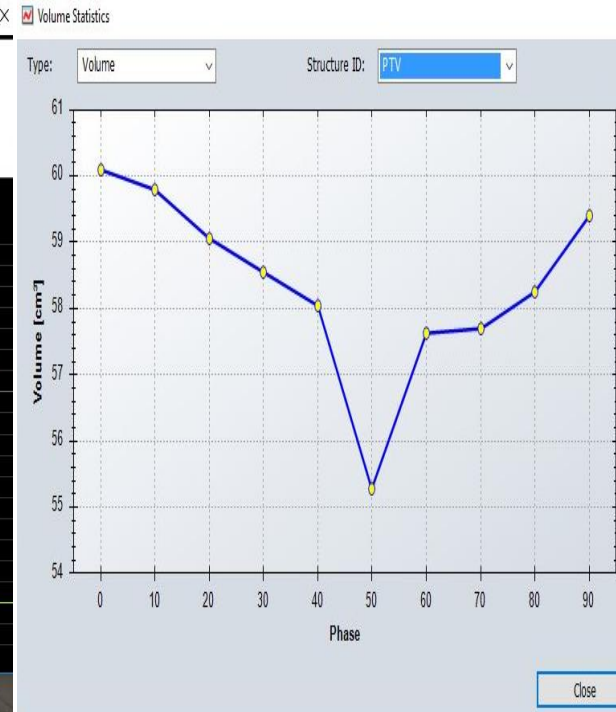
Patients: Total of 33 patients in lung cancer. Patients treated with stereotactic body radiation radiotherapy (SBRT) and simultaneous integrated boost (SIB), Volumetric modulated arc therapy (VMAT)

Target volume delineation: European Organization for Research and Treatment of Cancer (EORTC) (Radiotherapy and Oncology, 2017)

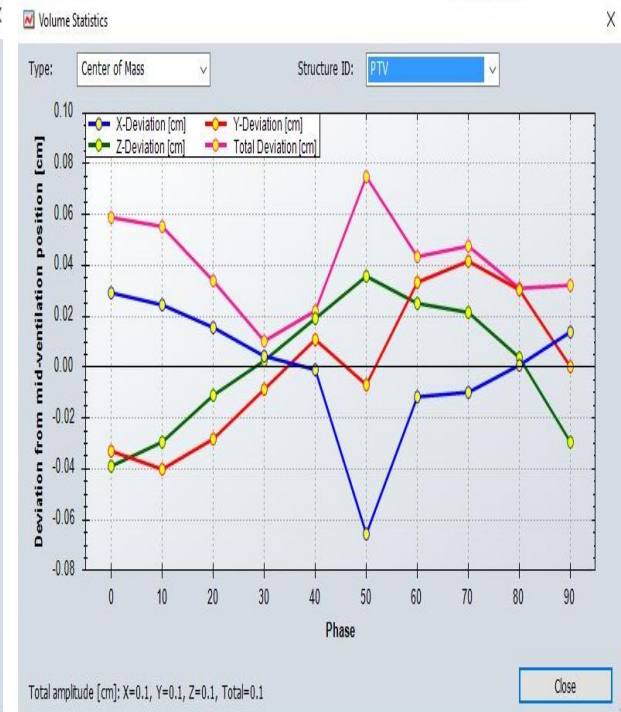
Respiratory Amplitude[cm]



Volume Change for PTV, ITV, Rt. Lung and Lt. Lung[cm³]



Center of mass for PTV, ITV, Rt. Lung and Lt. Lung[cm]



Plan condition and Dose constraints

◆ Plan condition

Patients	10 patients in lung cancer
Target Definition	European Organization for Research and Treatment of Cancer (EORTC) (Radiotherapy and Oncology, 2017)
Prescription Dose	PTV: 56 Gy/ 4 fx ITV: 60 Gy/ 4 fx
Treatment Technique	SBRT(SIB), VMAT, 4DRT
Phase[%]	0-90, 20-70, 40-60

◆ Dose constraints

Structures	Plan Quality Analysis Index	Reference
PTV	Target Coverage $\text{Quality of coverage} = I_{\min}/RI$ $I_{\min}$: Minimal isodose surrounding the target RI : Reference isodose	ICRU62
	Conformity Index $CI = PIV/TV$ PIV : Prescription isodose volume TV : Target volume	RTOG
	Homogeneity Index $HI = D_{\max}/PD$ $D_{\max}$: Maximum dose PD : Prescription dose	RTOG
	Quality Factor $QF = [2.718 \exp(-\sum_{i=1}^N W_i X_i)]$ W_i : Weighting factor X_i : All PTV indices	Pyakuryal A , JACMP, 11-1, 2010
OAR	Esophagus $V_{18.8\text{Gy}} < 5 \text{ cc}$, $D_{\max} < 30 \text{ Gy}$	RTOG 0915
	Heart $V_{28\text{Gy}} < 15 \text{ cc}$, $D_{\max} < 34 \text{ Gy}$	RTOG 0915
	Spinal Cord $V_{20.8\text{Gy}} < 0.3 \text{ cc}$, $V_{13.6\text{Gy}} < 1.2 \text{ cc}$, $D_{\max} < 26 \text{ Gy}$	RTOG 0915
	Lung (Right/Left) $V_{5\text{Gy}}$, $V_{10\text{Gy}}$, $V_{20\text{Gy}}$, $D_{1000\text{cc}} < 12.4 \text{ Gy}$ $D_{1500\text{cc}} < 11.6 \text{ Gy}$	RTOG 0915

Correlation Analysis

Correlation Analysis between 4DCT Analysis Index in full phase

◆ Spearman Correlation Coefficients

- ✓ A nonparametric measure of rank correlation
- ✓ Using a monotonic function

$$r_s = \rho_{rg_X, rg_Y} = \frac{\text{cov}(rg_X, rg_Y)}{\sigma_{rg_X} \sigma_{rg_Y}}$$

Evaluation

- ◆ Wilcoxon rank-sum test (P<0.05)

Correlation Analysis between 4DCT Analysis Index in each phase

◆ Pearson Correlation Coefficients

- ✓ A measure of the linear correlation
- ✓ The covariance of the two variables divided by the product of their standard deviations

$$r_{XY} = \frac{\sum_i^n (X_i - \bar{X}) (Y_i - \bar{Y})}{\sqrt{\sum_i^n (X_i - \bar{X})^2} \sqrt{\sum_i^n (Y_i - \bar{Y})^2}}$$

Evaluation

- ◆ Wilcoxon rank-sum test (P<0.05)

◆ Interpreting the size of a correlation coefficient

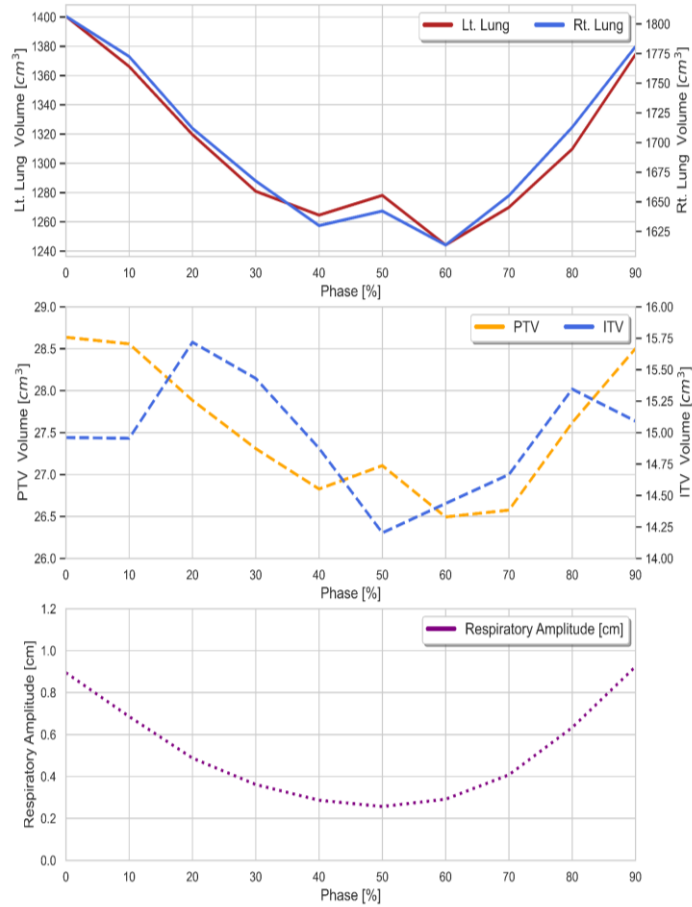
Size of Correlation	Interpretation
0.90 to 1.00 (-0.90 to -1.00)	Very high positive (negative) correlation
0.70 to 0.90 (-0.70 to -0.90)	High positive (negative) correlation
0.50 to 0.70 (-0.50 to -0.70)	Moderate positive (negative) correlation
0.30 to 0.50 (-0.30 to -0.50)	Low positive (negative) correlation
0.00 to 0.30 (0.00 to -0.30)	Negligible correlation

Reference: Mukaka, MM. 'A guide to appropriate use of correlation coefficient in medical research', Malawi Medical Journal, 2012

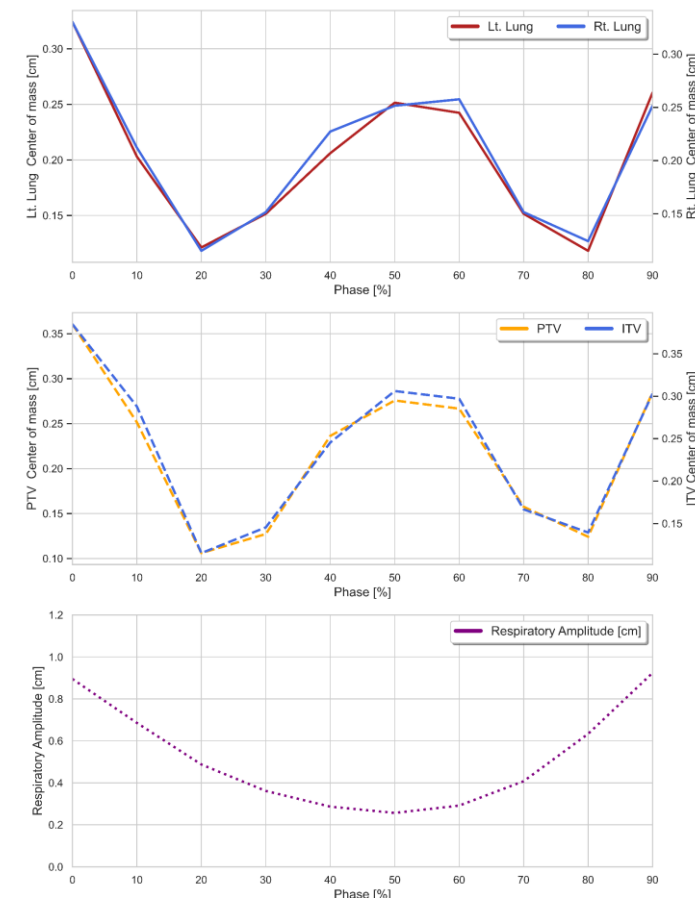
Results

1-1. 4DCT Analysis Index Data in Each Phase (33 Patients)

- ◆ 4DCT analysis index between **respiratory amplitude** and **volume change** of target and OARs in each phase



- ◆ 4DCT analysis index between **respiratory amplitude** and **center of mass (total amplitude)** of target and OARs in each phase



1-2. 4DCT Analysis Index Data in Each Phase (33 Patients)

(Unit: Mean ± SD)											
4DCT Analysis index		Phase[%]									
		0	10	20	30	40	50	60	70	80	90
Respiratory Amplitude [cm]		0.8952±0.3528	0.6858±0.2578	0.4876±0.1921	0.3615±0.1591	0.2867±0.1401	0.2567±0.1359	0.2915±0.1483	0.4079±0.1855	0.6333±0.2679	0.9239±0.3746
Volume Change [cm ³]	PTV	28.63±20.04	28.55±19.82	27.88±19.17	27.30±19.02	26.82±18.76	27.10±18.59	26.49±18.15	26.57±18.49	27.61±19.46	28.50±19.83
	ITV	14.96±11.96	14.95±11.77	15.71±12.47	15.43±12.27	14.87±11.49	14.20±11.22	14.43±11.38	14.66±11.59	15.34±12.06	15.09±11.72
	Rt. Lung	1806±501.0	1772±493.5	1711±489.5	1667±478.8	1629±484.0	1642±482.3	1613±473.9	1655±469.0	1712±478.4	1780±490.1
	Lt. Lung	1400.±390.5	1366±389.6	1319±376.9	1280±372.0	1264±366.3	1278±376.6	1244±358.5	1269±357.3	1309±370.1	1374±385.6
Center of Mass (total amplitude) [cm]	PTV	0.3606±0.2235	0.2515±0.1661	0.1061±0.07470	0.1273±0.1039	0.2364±0.1617	0.2758±0.1751	0.2667±0.1831	0.1576±0.09690	0.1242±0.1062	0.2848±0.2181
	ITV	0.3848±0.2360	0.2879±0.1691	0.1152±0.08700	0.1455±0.1201	0.2455±0.1563	0.3061±0.1819	0.297±0.1944	0.1667±0.1080	0.1394±0.1088	0.3030±0.2257
	Rt. Lung	0.3303±0.1357	0.2121±0.1023	0.1152±0.050800	0.1515±0.08340	0.2273±0.1153	0.2515±0.1121	0.2576±0.1146	0.1515±0.075500	0.1242±0.08300	0.2515±0.1121
	Lt. Lung	0.3242±0.1733	0.2030±0.1075	0.1212±0.060000	0.1515±0.07550	0.2061±0.1144	0.2515±0.1228	0.2424±0.1347	0.1515±0.090600	0.1182±0.08080	0.2606±0.1413

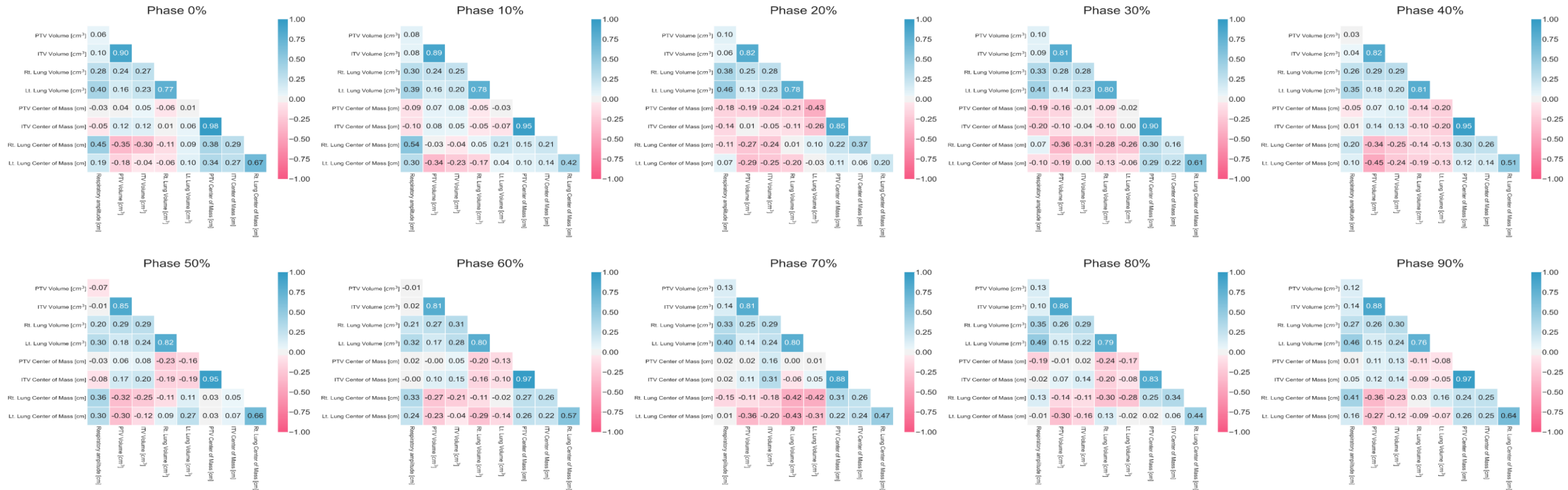
2-1. Pearson correlation matrix between 4DCT Analysis Index in each phase (33 Patients)

Correlation Analysis between 4DCT Analysis Index in each phase

◆ Pearson Correlation Coefficients

- ✓ A measure of the linear correlation
- ✓ The covariance of the two variables divided by the product of their standard deviations

$$r_{XY} = \frac{\sum_i^n (X_i - \bar{X})(Y_i - \bar{Y})}{\sqrt{\sum_i^n (X_i - \bar{X})^2} \sqrt{\sum_i^n (Y_i - \bar{Y})^2}}$$



2-2. Spearman correlation matrix between 4DCT Analysis Index in full phase (33 Patients)

Correlation Analysis between 4DCT Analysis Index in full phase

◆ Spearman Correlation Coefficients

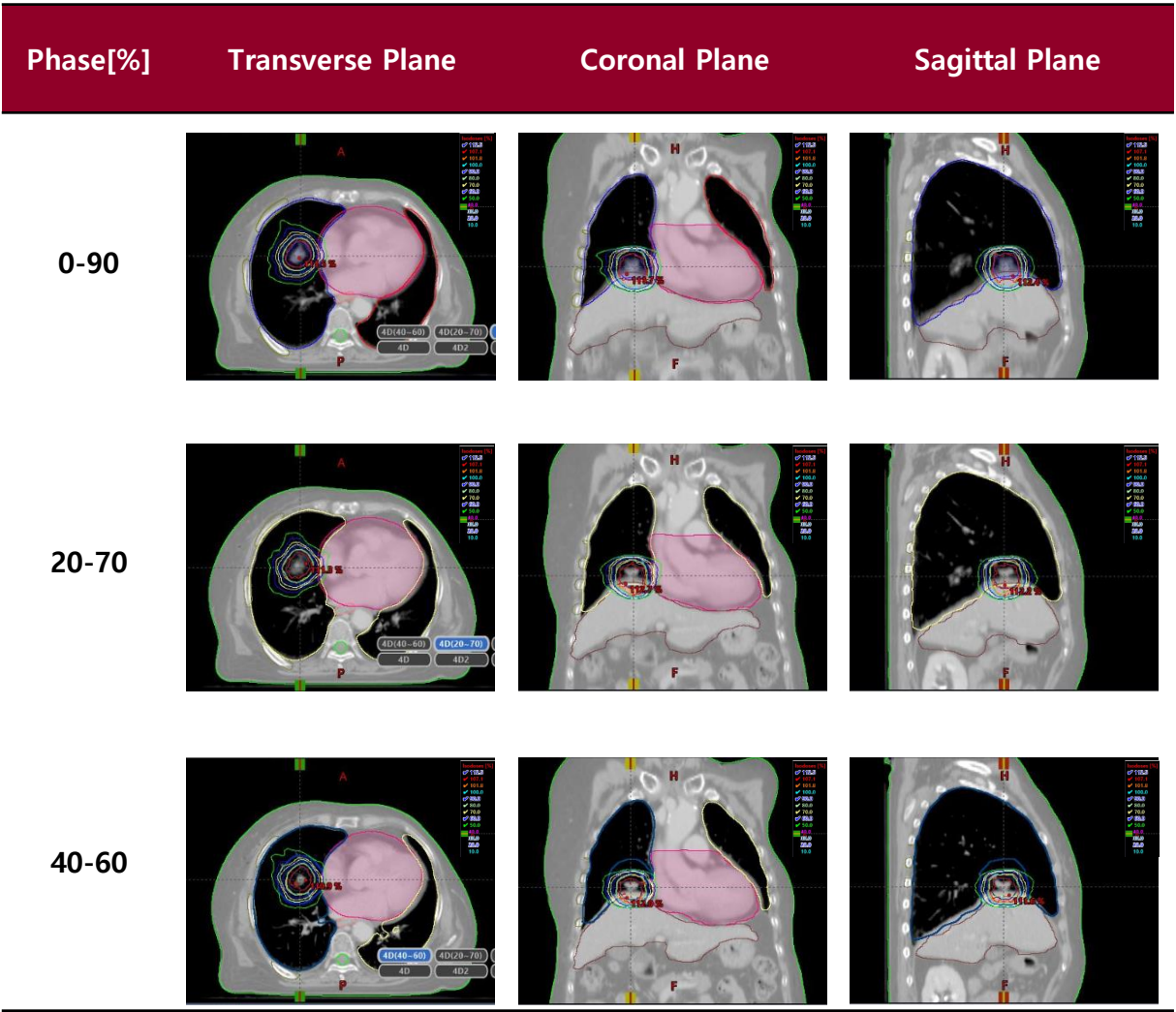
- ✓ A nonparametric measure of rank correlation
- ✓ Using a monotonic function

$$r_s = \rho_{rg_X, rg_Y} = \frac{\text{cov}(rg_X, rg_Y)}{\sigma_{rg_X} \sigma_{rg_Y}}$$

4DCT Analysis index		Respiratory Amplitude[cm]	Volume change[cm ³]				Center of Mass(total amplitude)[cm]			
			PTV	ITV	Rt. Lung	Lt. Lung	PTV	ITV	Rt. Lung	Lt. Lung
Respiratory Amplitude [cm]		1	0.8061	0.5273	0.9273	0.8667	0.2000	0.09091	0.06079	0.1094
Volume Change [cm ³]	PTV	0.8061	1	0.5515	0.9394	0.9758	0.2364	0.1879	0.06079	0.1945
	ITV	0.5273	0.5515	1	0.5636	0.5636	-0.5152	-0.5879	-0.5410	-0.4681
	Rt. Lung	0.9273	0.9394	0.5636	1	0.9758	0.2242	0.1515	0.03647	0.1459
	Lt. Lung	0.8667	0.9758	0.5636	0.9758	1	0.2606	0.2000	0.06687	0.2128
Center of Mass (total amplitude) [cm]	PTV	0.2000	0.2364	-0.5152	0.2242	0.2606	1	0.9879	0.9483	0.9726
	ITV	0.09091	0.1879	-0.5879	0.1515	0.2000	0.9879	1	0.9362	0.9605
	Rt. Lung	0.06079	0.06079	-0.5410	0.03647	0.06687	0.9483	0.9362	1	0.9512
	Lt. Lung	0.1094	0.1945	-0.4681	0.1459	0.2128	0.9726	0.9605	0.9512	1

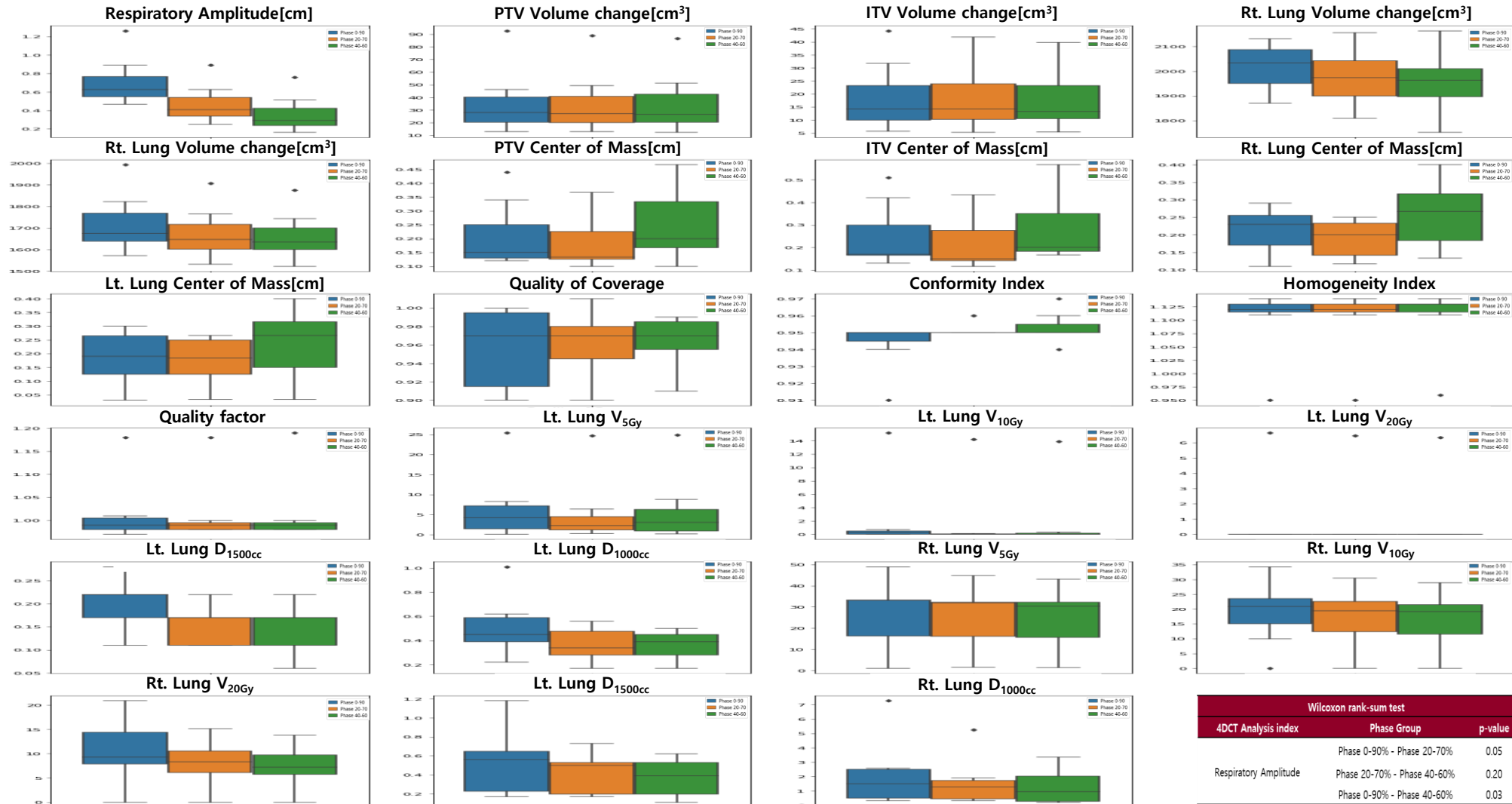
3. Dosimetric Comparison: Qualitative and Quantitative analysis (10 Patients)

(Unit: Mean ± SD)



Structure	Index	Phase[%]		
		0-90	20-70	40-60
PTV	Quality of Coverage	0.9597±0.04104	0.9603±0.03988	0.9596±0.03041
	Conformity index	0.9501±0.004716	0.9512±0.005157	0.9500±0.008742
	Homogeneity index	1.122±0.01198	1.125±0.001508	1.104±0.06219
	Quality factor	0.9890±0.01374	0.9864±0.01113	0.9963±0.02323
Rt. Lung	V _{5Gy}	21.23±15.85	20.44±14.81	20.14±14.30
	V _{10Gy}	14.32±11.96	12.98±10.82	12.42±10.30
	V _{20Gy}	7.873±7.201	6.092±5.236	5.596±4.830
	D _{1000cc}	1.6800±2.153	1.198±1.556	0.9800±1.129
	D _{1500cc}	0.4032±0.3490	0.2968±0.2560	0.2744±0.2277
Lt. Lung	V _{5Gy}	11.07±13.31	9.207±11.85	8.644±12.73
	V _{10Gy}	6.183±9.912	5.027±8.313	4.275±1.523
	V _{20Gy}	3.173±5.488	2.322±3.883	2.145±4.570
	D _{1000cc}	0.4480±0.2532	0.3248±0.1557	0.3111±0.1430
	D _{1500cc}	0.1512±0.09536	0.1064±0.08115	0.1008±0.08264

4-1. Comparison between 4DCT Analysis Index and Dosimetric Data



4-2. Comparison between 4DCT Analysis Index and Dosimetric Data

(Unit: Mean ± SD)

Phase [%]	Respiratory Amplitude [cm]	4DCT Analysis Index										Dosimetric Data											
		Volume Change[cm ³]					Center of Mass[cm]					PTV				Lt. Lung				Rt. Lung			
		PTV	ITV	Rt. Lung	Lt. Lung		PTV	ITV	Rt. Lung	Lt. Lung	Quality of Coverage	CI	HI	QF	V _{5Gy} [%]	V _{10Gy} [%]	V _{20Gy} [%]	D _{1000cc} [Gy]	D _{1500cc} [Gy]	V _{5Gy} [%]	V _{10Gy} [%]	V _{20Gy} [%]	D _{1000cc} [Gy]
0-90	0.5230 ±0.2491	27.55 ±0.8207	14.97 ±0.4596	1699 ±68.48	1311 ±53.16	0.2191 ±0.08508	0.2391 ±0.09120	0.2073 ±0.06960	0.2030 ±0.06758	0.9597 ±0.04104	0.9501 ±0.004716	1.122 ±0.01198	0.9890 ±0.01374	11.07 ±13.31	6.183 ±9.912	3.173 ±5.488	0.4480 ±0.2532	0.1512 ±0.09536	21.23 ±15.85	14.32 ±11.96	7.873 ±7.201	1.6800 ±2.153	0.4032 ±0.3490
20-70	0.3486 ±0.08779	27.03 ±0.5194	14.89 ±0.5840	1653 ±34.33	1276 ±24.94	0.1949 ±0.07384	0.2126 ±0.08129	0.1924 ±0.06044	0.1874 ±0.05374	0.9603 ±0.03988	0.9512 ±0.005157	1.125 ±0.001508	0.9864 ±0.01113	9.207 ±11.85	5.027 ±8.313	2.322 ±3.883	0.3248 ±0.1557	0.1064 ±0.08115	20.44 ±14.81	12.98 ±10.82	6.092 ±5.236	1.198 ±1.556	0.2968 ±0.2560
40-60	0.2783 ±0.01885	26.81 ±0.3065	14.51 ±0.3416	1629 ±14.36	1262 ±17.07	0.2596 ±0.02062	0.2828 ±0.0326	0.2455 ±0.01602	0.2333 ±0.02401	0.9596 ±0.03041	0.9500 ±0.008742	1.104 ±0.06219	0.9963 ±0.02323	8.644 ±12.73	4.275 ±1.523	2.145 ±4.570	0.3111 ±0.1430	0.1008 ±0.08264	20.14 ±14.30	12.42 ±10.30	5.596 ±4.830	0.9800 ±1.129	0.2744 ±0.2277

Conclusion and Discussion

- ✓ It was found that optimized phase is feasible through 4DCT and dosimetric analysis in Lung SBRT
- ✓ Need to correlation analysis between 4DCT Analysis Index and dosimetric data
- ✓ Need to correlation analysis between 4DCT Analysis Index and target margin

KUMP Lab



Thank you

