Associations between dose-volume, quality of life and clinical toxicity after lung SBRT

Suneetha Devpura, PhD, Indrin J Chetty PhD, Stephen L. Brown, PhD, Samuel Rusu, MS, Essa Mayyas, PhD, Richard Araj, MS, Joshua Kim, PhD, Junwen Liu, MS, Chang Liu, PhD, Zhen Sun, PhD, Diane Snell, Sean Vance, MD, Munther Ajlouni, MD, Salim M Siddiqui, MD, PhD, Benjamin Movsas, MD

Department of Radiation Oncology, Henry Ford Health System, Detroit, Michigan

Introduction and Objectives

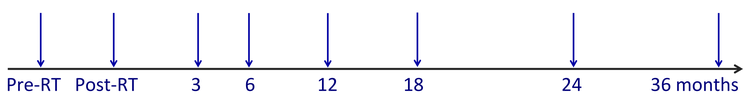
- For patients with non-small cell lung cancer (NSCLC) treated with stereotactic body radiotherapy (SBRT), patient reported quality of life (QOL) may provide a useful secondary endpoint
- This work measures the effect/correlation of the following parameters of NSCLC patients up to 36 months after SBRT
  - ✓ Dosimetric parameters
  - ✓ Prospectively acquired patient reported quality of life (QOL)
  - ✓ Clinical toxicity (provider-reported)

Methods

- Under an IRB-approved protocol, 122 NSCLC patients receiving 12Gy x 4 were evaluated
  - ✓ Dosimetric parameters included the mean lung radiation dose (MLD) and the volume of normal lung receiving at least 5, 10, 13 or 20 Gy (V_5, V_{10}, V_{13}, and V_{20}), esophagus receiving at least 5 Gy, maximum and mean dose (E_V5, E_Dmax, and E_Dmean)
  - ✓ Quality of life was determined using the previously-validated Functional Assessment of Cancer Therapy-Trial Outcome Index (FACT-TOI)[1,2] lung questionnaire which incorporated three subscale endpoints: lung subscale (LSC), physical well-being (PWB) and functional well-being (FWB)
  - ✓ Clinical Toxicity, graded from zero to five, followed the Charlson comorbidity and toxicity index[3]
- Pearson correlation and t-test analyses were used to measure correlations between radiation dose metrics with QOL and clinical toxicities.

Methods: Quality of Life

- Functional Assessment of Cancer Therapy-Trial Outcome Index (FACT-TOI) questionnaire was used to collect QOL data up to 36 months:



- Standardized QOL scores [range: 0-84] were determined by 21 questions related to the following 3 subscales, and baseline-corrected by subtracting pre-treatment QOL data
  - ✓ Lung subscale (LSC)
  - ✓ Physical well-being (PWB)
  - ✓ Functional well-being (FWB)
  - ✓ Trial outcome index: TOI = LSC + PWB + FWB

Methods: Clinical toxicities

- Charlson comorbidity and toxicity scoring was used to evaluate the toxicities of the following subcategories corrected for baseline pre-treatment toxicity levels[3]
  - ✓ respiratory, thoracic, and mediastinal disorders
    - ❖ Cough, dyspnea, pleuritic pain, and pneumonitis
  - ✓ gastrointestinal and general disorders
    - ❖ Esophagitis, esophageal pain, and fatigue
  - ✓ cardiac disorders, and injury, positioning and procedural complications
    - ❖ Pericarditis, pericardial effusion, and dermatitis

Results: QOL correlations to dose/volume/toxicity

- Based on the absolute magnitude of the observed Pearson correlation coefficient, the interpretation is as follows[4];
  - ✓ 0.10 - 0.39: Weak correlation
  - ✓ 0.40 - 0.69: Moderate correlation
  - ✓ 0.70 - 0.89: Strong correlation
  - ✓ 0.90 - 1.00: Very Strong correlation

Stage	Pearson (r value)	p value	No. of patients	Correlations
Stage I&II	-0.551*	0.012	20	TOI-36m vs V5
	-0.532*	0.016	20	PWB-36m vs V5
	-0.528*	0.017	20	FWB-36m vs V5
	-0.247*	0.030	77	PWB-3m vs V10
	-0.326*	0.043	39	TOI-24m vs V10
	-0.407*	0.010	39	LSC-24m vs V10
	-0.521*	0.019	20	TOI-36m vs V10
	-0.634**	0.003	20	PWB-36m vs V10
	-0.253*	0.026	77	PWB-3m vs V13
	-0.377*	0.018	39	TOI-24m vs V13
	-0.415**	0.009	39	LSC-24m vs V13
	-0.370*	0.021	39	PWB-24m vs V13
	-0.548*	0.012	20	TOI-36m vs V13
	-0.676**	0.001	20	PWB-36m vs V13
	-0.707**	**0.000**	**20**	**TOI-36m vs V20**
	-0.543*	0.013	20	LSC-36m vs V20
	-0.657**	0.002	20	PWB-36m vs V20
	-0.655**	0.002	20	FWB-36m vs V20
	-0.637**	0.003	20	TOI-36m vs MLD
	-0.608**	0.004	20	PWB-36m vs MLD
	-0.606**	0.005	20	FWB-36m vs MLD
	0.329*	0.041	39	TOI-24m vs Total lungs
	0.501*	0.025	20	PWB-36m vs Total lungs
	-0.333**	0.010	59	TOI-12m vs Pleuritic pain
	-0.344**	0.008	59	FWB-12m vs Pleuritic pain
	-0.418**	0.004	46	TOI-18m vs Pleuritic pain
	-0.492**	0.001	46	FWB-18m vs Pleuritic pain
	0.317**	0.005	77	FWB-3m vs Dyspnea
Stage III	-0.604*	0.029	13	LSC-3m vs E_Dmax
	0.858**	**0.006**	**8**	**LSC-12m vs Total Lungs**
Stage IV	-0.467*	0.021	24	TOI-3m vs Fatigue
	-0.632**	0.002	24	LSC-3m vs Fatigue
	-0.503*	0.012	22	FWB-3m vs Fatigue
	-0.449*	0.036	22	LSC-6m vs Fatigue
	-0.460*	0.031	22	PWB-6m vs Fatigue
	-0.606**	0.003	22	FWB-6m vs Fatigue
	-0.459*	0.032	22	TOI-6m vs Dyspnea
	-0.486*	0.048	17	TOI-12m vs Pericard
	-0.696**	0.002	17	PWB-12m vs Pericard
	0.484*	0.049	17	TOI-12m vs Total lungs
	-0.461*	0.031	22	LSC-6m vs Pneumonitis

* p<0.05 ** p<0.01

Table 1: A summary of Pearson correlations of QOL (Total outcome index-TOI or subscales: Lung subscale-LSC, physical well-being-PWB, or functional well-being-FWB) and clinical toxicities with dose/volume. Negative Pearson values represent inverse correlations. E_V5, E_Dmean and E_Dmax represent, volume of esophagus receiving at least 5 Gy, and mean and maximum (at 0.035 cc) dose to the esophagus

Results: QOL clinically meaningful change

- Stage I&II and stage III data did not show clinically meaningful change. Stage IV data showed clinical meaningful improvement at 18, 24 and 36 months after radiation as shown in Table 2.
- A 2-3 point difference on the LCS subscale and 5-6 point difference on the TOI are associated with a meaningful difference in clinical indicators[1,2].

Stage IV	Baseline	Change at follow-up timepoints					
		3 months	6 months	12 months	18 months	24 months	36 months
TOI	n=25	n=24	n=22	n=17	n=11	n=11	n=7
Mean	58.28	1.18	0.31	2.84	**10.72**	**10.99**	**14.29**
Std Dev	13.63	17.54	17.42	16.94	10.17	7.63	4.35
effect size		0.05	0.01	0.13	0.63	0.70	1.00
p value (2 tail)		0.79	0.95	0.55	**0.03**	**0.02**	**0.01**
LSC							
Mean	19.68	0.70	-0.36	0.38	2.50	2.68	3.75
Std Dev	5.50	5.49	4.96	6.19	4.29	2.50	2.51
effect size		0.09	-0.05	0.05	0.36	0.44	0.62
p value (2 tail)		0.66	0.81	0.84	0.19	0.13	0.09
PWB							
Mean	22.44	-0.77	-0.89	-0.50	2.56	1.92	3.42
Std Dev	4.87	7.24	6.30	5.49	2.79	3.14	1.57
effect size		-0.09	-0.11	-0.07	0.46	0.33	0.67
p value (2 tail)		0.66	0.59	0.76	0.11	0.24	0.08
FWB							
Mean	16.16	0.88	1.43	2.90	**5.48**	**6.11**	**7.13**
Std Dev	7.51	7.26	8.02	6.32	5.54	4.43	2.81
effect size		0.08	0.13	0.30	0.59	0.70	0.89
p value (2 tail)		0.68	0.53	0.20	**0.04**	**0.02**	**0.02**

Table 2: Stage IV QOL scores (TOI, LSC, PWB, and FWB) over time

Results: Clinical toxicity

- The percentages of patients with ≥ grade 3 clinical toxicities were less than 2%. No toxicity with grade ≥ 4 was observed. Cumulative incidences of toxicities at each follow-up time point are shown in Table 3

Toxicity	Number of patients				Number of patients (%)			
	Grade 0	Grade 1	Grade 2	Grade 3	Grade 0	Grade 1	Grade 2	Grade 3
Cough	64	49	8	0	52.9%	40.5%	6.6%	0.0%
Dyspnea	60	52	9	0	49.6%	43.0%	7.4%	0.0%
Pleuritic pain	104	14	3	0	86.0%	11.6%	2.5%	0.0%
Pneumonitis	113	7	1	0	93.4%	5.8%	0.8%	0.0%
Esophagtis	116	5	0	0	95.9%	4.1%	0.0%	0.0%
Esophageal Pain	110	10	1	0	90.9%	8.3%	0.8%	0.0%
Fatigue	52	55	12	2	43.0%	45.5%	9.9%	1.7%
Pericarditis	119	2	0	0	98.3%	1.7%	0.0%	0.0%
Pericardial effusion	117	3	0	1	96.7%	2.5%	0.0%	0.8%
Dermatitis	114	6	1	0	94.2%	5.0%	0.8%	0.0%

Table 3: Cumulative incidence of toxicities over the follow-up time points, 3, 6, 12 and 18 months from pre-treatment baseline, shown for each toxicity grade

- The correlations between dose/volume and clinical toxicity are presented in Table 4.

Stage	Pearson (r value)	P value	No. of patients	Correlations
Stage I&II	-0.223*	0.047	80	Pleuritic pain vs Total lungs
	0.220*	0.050	80	Dyspnea vs V10
	0.243*	0.030	80	Pneumonitis vs V20
	0.222*	0.047	80	Pneumonitis vs MLD
Stage III	0.564*	0.029	15	Esophagitis vs E_V5
	0.713**	0.003	15	Esophagitis vs E_Dmean
Stage IV	0.672**	0.000	26	Esophagitis vs PTV
	0.413*	0.036	26	Esophageal Pain vs PTV
	0.431*	0.028	26	Dyspnea vs V20

* p<0.05 ** p<0.01

Table 4: A summary of clinical toxicity with dosimetric parameters

Stage I & II: TOI at 36 months vs lung V20

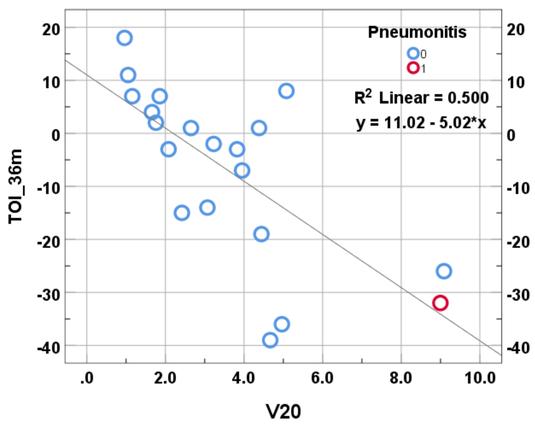


Figure 1 shows a linear correlation between TOI at 36 months and lung V20. 3.2% change in V20 makes a clinically meaningful 5 point decline in QOL.

Figure 1: A plot of stage I &II, TOI at 36 months vs lung V20

Conclusions

- Lung SBRT treatment for patients with NSCLC, using a 12 Gy x 4 dose regimen, was well tolerated.
- Unique QOL data (not previously reported) and clinical toxicities at up to 36 months follow up showed correlations with lung dose and subvolumes for different stages.

Limitations and Future Directions

- Despite promising preliminary conclusions, more patients with longer follow-ups are recommended to improve the predictive capability and increase the correlations between QOL and dosimetric parameters.

References

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Acknowledgement: Work supported in part by Varian Medical Systems, Palo Alto, CA

Author contact info: Suneetha Devpura, PhD, sdevpur1@hfhs.org