Can accelerated hypofractionated radiotherapy (AHRT) be an acceptable treatment option in inoperable non-small cell lung cancer Myanmar patients?

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Background and Objective

- The prognosis of lung cancer is poor even if patients can undergo curative treatments such as radical surgery or standard radical radiotherapy treatment (60 Gy in 30 fractions over six weeks with or without concurrent chemotherapy).
- Most lung cancer patients are diagnosed as advanced inoperable stage and majorities are old age, with comorbid diseases or with poor lung/ cardiac function. Therefore, for those patients, shorter course radiation regime such as accelerated or hypofractionated regime should be considered.
- This study was conducted to assess the outcomes of **accelerated hypofractionated radiotherapy (AHRT) (45 Gy in 15 fractions over three weeks by using 3D conformal planning)** in inoperable non-small cell lung cancer (NSCLC) patients who were ineligible for surgery or standard concurrent chemo radiotherapy (CCRT).

Methods

- A hospital based **prospective study** done in Radiotherapy Department, Yangon General Hospital, Myanmar (2018 January- 2019 June)
- A total of **65 patients** with unresectable or medically inoperable non-small cell lung cancer, who were unfit for chemotherapy due to some comorbidities (E.g., poor cardiac, liver or renal function, etc., or old age) were enrolled
- Patients with poor PS (ECOG PS >2), patients with distant metastasis or patients previously treated with thoracic radiotherapy or chemotherapy were excluded.
- They were treated with the regime of **45 Gy in 15 fractions over 3 weeks** by using **3D conformal** RT technique.
- **Locoregional response** was assessed by chest CT before and six weeks after RT. Revised RECIST (Response Evaluation Criteria in Solid Tumours) guideline version 1.1 was used to detect locoregional response [1].
- **Relief of symptoms** such as cough, dyspnoea and chest pain was evaluated before RT, during RT and six weeks after RT.
- **Treatment related acute toxicities** such as dysphagia and radiation dermatitis were observed during and six weeks after RT.
- Common Terminology Criteria for Adverse Events (CTCAE) version 5.0 was used to study these symptoms and toxicities [2].

Results

- **Sixty five** patients with inoperable NSCLC (7 patients with stage II and 58 patients with stage III)
- most common age group was **71-80 years** (36.92%)
- most commonly found cell type was **squamous cell carcinoma** (73.9 %)
- majorities were **male** (69.2%), **smokers** (67.7%), with **PS 1** (44.6%).
- Among them, two patients were lost to follow-up at 12 weeks after RT due to non cancer related death.
- Assessment of locoregional response six weeks after RT showed that **partial response (PR**) was seen in **69.23%** of patients and **stable disease (SD)** was seen in **30.77%** while there was neither complete response (CR) nor progressive disease (PD).
- Associations between baseline characteristics and tumour response were also observed.
- Statistically significant associations were only found between **pre-treatment tumour size vs tumour response and performance status of the patients vs tumour response** (Table 1).
- **Good relief of symptoms** such as cough, dyspnoea and chest pain was found after RT, but **no severe acute toxicities** such as dysphagia and radiation dermatitis (more than grade 3) were resulted at the end of the study (Figure 1 and Table 2).
- Due to time limitation and feasibility reason, late toxicities and survival outcome could not be assessed in this study.

Table 1. Association between tumour response and baseline patients' characteristics

	Partial response Mean ± SD/ No. (%) (n = 46)	Stable disease Mean ± SD/ No. (%) (n = 19)	p
Age (years)	70.46 ± 10.21	68.26 ± 7.60	0.403$^{\#}$
Sex			
Male	31 (67.4)	14 (73.7)	0.617$^{\wedge}$
Female	15 (32.6)	5 (26.3)	
Stages			
IIB	6 (13)	1 (5.3)	0.329$^{\$}$
IIIA	18 (39.1)	4 (21.1)	
IIIB	17 (37)	11 (57.9)	
IIIC	5 (10.9)	3 (15.8)	
Size of tumour (cm)	5.65 ± 1.62	7.73 ± 1.50	0.00001$^{\#***}$
Performance status			
0	8 (17.4)	2 (10.5)	0.010$^{\wedge *}$
1	25 (54.3)	4 (21.1)	
2	13 (28.3)	13 (68.4)	

* - $p < 0.05$, *** - $p < 0.001$, $^{\#}$ - Independent samples t test,
$^{\wedge}$ - Chi-square test, $^{\$}$ - Fisher's exact test

Table 2. Grading of Acute Toxicities during RT and after RT

Acute toxicities	Grades	During RT No. (%) 1st week	2nd week	3rd week	6 weeks after RT No. (%)	12 weeks after RT* No. (%)
Dysphagia	Grade 0	63 (96.92)	60 (92.31)	54 (83.08)	58 (89.23)	60 (92.31)
	Grade 1	2 (3.08)	4 (6.15)	8 (12.30)	5 (7.69)	3 (4.62)
	Grade 2	0 (0.00)	1 (1.54)	3 (4.62)	2 (3.1)	0 (0.00)
Radiation Dermatitis	Grade 0	65 (100.00)	65 (100.00)	62 (95.38)	64 (98.46)	63 (96.92)
	Grade 1	0 (0.00)	0 (0.00)	3 (4.62)	1 (1.54)	0 (0.00)

* = 2 missing values in 12 weeks after RT

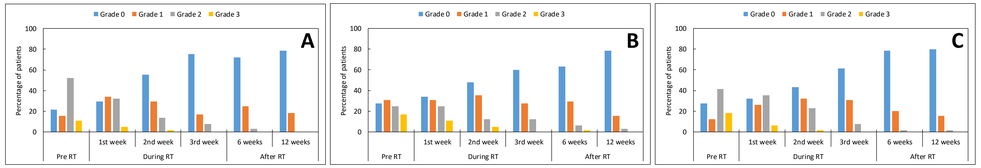

Figure 1. Grading of symptoms at pre-RT, during RT and after RT (n=65). A: cough, B: dyspnea and C: chest pain (2 missing values in 12 weeks after RT)

Conclusions

- The locoregional and symptomatic response of inoperable non-small cell lung cancer patients to this radiotherapy regime (45 Gy in 15 fractions over three weeks) were good with acceptable acute toxicity results.
- As accelerated radiotherapy can decrease treatment time and treatment related costs, this may become an acceptable option for those patients who are unfit for prolonged intensive radical treatment in a resource limiting country like Myanmar.

References

[1] **Eisenhauer EA et al.** New response evaluation criteria in solid tumours: Revised RECIST guideline (version 1.1). *Eur J Cancer* 2008;45:228-47. https://doi.org/10.1016/j.ejca.2008.10.026
[2] **National Cancer Institute (NCI).** *Common Terminology Criteria for Adverse Events (CTCAE) version 5.0.* U.S Department of Health and Human Services, National Institute of health, National Cancer Institute; 2009.