

## EP-1202

CBCT in Lung FFF-SABR: predictive parameters of early response

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**Purpose or Objective:** aim of the study was to analyze tumor volume variations, by contouring on cone-beam computed tomography (CBCT) images, to evaluate early predictive parameters of Flattening Filter Free Stereotactic Ablative Radiation Therapy (SABR) treatment response.

**Material and Methods:** the prescribed dose of SABR varied according to the tumor site (central or peripheral) and maximum diameter of the lesions using a strategy of risk-adapted dose prescription with a range of dose between 48 and 70 Gy (3-10 consecutive fractions). For the purpose of the analysis, gross tumor volume (GTV) was re-contoured for each patient at first and last CBCT using two lung levels/window: 1) -600/1000 Hounsfield Units (HU) and 2) -1000/250 HU. Statistical analysis was performed to evaluate correlations between target variations on CBCT, using the two window-levels, and treatment response three months after the end of SABR. The analysis was conducted considering the following variables: number of fractions  $\geq 5$ , BED 95-110, BED > 110 and GTV volume pre-SABR > 6 cc.

**Results:** 41 lung lesions were evaluated. The median follow-up was 14 months (range, 5 - 43 months). For both the CBCT level/windows, GTV shrinkage of at least 20% was associated to the probability of achieving a disease complete response (CR) at 3 months. The probability of CR ranged between 6 and 8 times higher, in respect to the CBCT lung level adopted, comparing to patients without a GTV decrease of 20%. This cut-off value was confirmed for all the variables analyzed.

**Conclusion:** according to current findings, a tumor shrinkage cut-off of at least 20% at last session of SABR is predictable for CR

## EP-1203

Stereotactic radiotherapy for oligometastases or oligorecurrence within a mediastinal lymph node

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**Purpose or Objective:** This study was to evaluate the safety and efficacy of stereotactic radiation therapy (SRT) in the treatment of patients with oligometastases or oligorecurrence within a mediastinal lymph node (MLN).

**Material and Methods:** Between October 2006 and May 2015, patients with oligometastases or oligorecurrence within MLNs originating from different primary tumor were enrolled and treated with SRT at our hospital. The primary end-point was MLN local control (LC). Secondary end-points were: time to symptom alleviation; overall survival after SRT (OS); and toxicity using the Common Terminology Criteria for Adverse Events (CTCAE v4.0).

**Results:** Eighty-five patients with 98 MLN oligometastases or oligorecurrence were treated with SRT. For the entire cohort, the 1-year and 5-year actuarial LC rates were 97.3% and 77.2%, respectively. Symptom alleviation was observed in 28 patients (28/32, 87.5%), with symptomatic lesions after a median of 5 days (range, 3-30 days). The median OS were 27.17 months for all patients and 32.20 months for those with NSCLC. Univariate and multivariate analyses revealed that an interval between diagnosis of primary tumors and SRT and MLN PTV volume were independent prognostic factors for OS in patients with NSCLC. CTCAE v4.0 Grade 3 toxicities occurred in six patients (7.06%), with Grade 5 in three patients (all with radiotherapy history to MLN station 7).

**Conclusion:** SRT is a safe and efficacious treatment modality for patients with oligometastases or oligorecurrence to MLN, except for patients who received radiotherapy history to MLN station 7. Further investigation is warranted to identify the patients who benefit most from this treatment modality.

## EP-1204

Predicting toxicity after lung stereotactic radiation therapy

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**Purpose or Objective:** Lung SBRT has shown excellent local control rates for inoperable patients with early-stage lung cancer without lymph node involvement. The reported toxicity is low, but factors associated with toxicity such as pneumonitis or lung fibrosis have not been well documented.

**Material and Methods:** All inoperable patients treated in our institution between August 2007 and April 2013 with SBRT for peripheral early-stage lung cancer were included. Endpoints of the study were rib fracture, acute pneumonitis, lung fibrosis, hemoptysis. Univariate binary logistic regressions were used to look for statistical associations between binary (eg, gender), ordinal (eg, age, dose per fraction, total dose, number of treatment session, V20, mean lung dose, volumes) or nominal (eg tracking method, previous treatment) variables and the study endpoints. Multivariate logistic regression was to be performed if more than 1 factor was associated with 1 of the outcomes of interest with a P value of less than .2. Treatment fractionation regimens were adapted according to tumor localization.

**Results:** 205 patients with 214 lesions were included in the study (67 central and 147 peripheral). 73 patients (36%) had toxicities: 14 patients (6.8%) had acute pneumonitis and 56 lung fibrosis (27.3%) without clinical effects. Two patients had a rib fracture (1%) and 1 patient had rib cage pains. No other toxicities were observed. In univariate analysis, a lower number of treatment sessions ( $p=0.018$ ) and higher dose per fraction ( $p=0.011$ ) were associated with more toxicity. Longer treatment sessions were associated with more acute pneumonitis ( $p=0.001$ ). Lung fibrosis was associated with a higher dose per fraction ( $p=0.027$ ). Tracking was also associated with a higher rate of lung fibrosis, but patients treated with tracking had bigger tumors (mean diameter : 21.9 mm vs 28 mm). Tumor localization (central vs peripheral) was not a predictive factor of toxicity.

**Conclusion:** A higher dose per fraction and fewer treatment sessions were associated with more toxicity. Tumor localization was not associated with toxicity, suggesting that treatment regimens adapted for central tumors are efficient in minimizing toxicity.

## EP-1205

Resected pN1 non-small cell lung cancer: recurrence patterns and nodal risk factors

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**Purpose or Objective:** To describe the pattern of recurrence in resected pN1 non-small cell lung cancer (NSCLC), aiming to identify clinical, pathological, treatment and nodal factors predicting an increased risk of locoregional recurrence (LR) or distant metastasis (DM), in order to define a selected population who may benefit of postoperative radiotherapy (PORT).

**Material and Methods:** All patients who underwent surgery for NSCLC with pathologically confirmed N1 disease at the Spedali Civili Hospital of Brescia between 2001-2011 were identified. Patients with positive surgical margins, undergoing neoadjuvant treatment or PORT were excluded. LR was defined as first event of recurrence at the surgical bed, ipsilateral hilum or mediastinum, other sites were considered as DM. Kaplan-Meier actuarial estimates of overall survival (OS), progression free survival (PFS), freedom-from LR (FFLR) and freedom-from DM (FFDM) in different subgroups were compared with the log-rank test. The Cox proportional hazard regression model was used for multivariate analysis.

**Results:** Among 285 patients who underwent surgery during the interval, 202 met the inclusion criteria. Clinical pathological, treatment and nodal factors are reported in table 1. Twenty four percent received adjuvant chemotherapy. The median follow-up was 39 months. The total number of recurrences was 118 (64.4%): 44 (24%) and 74 (40.4%) for LR and DM, respectively. 5-year OS and PFS rates were 39,2% and 33,3%, respectively. Patients with recurrences experienced a statistically worse OS than patients without recurrences ( $p < 0.001$ ) and patients with DM had in turn OS rates significantly worse than those with LR (Figure 1). At multivariate analysis, extra capsular extension (ECE) (RR 2.10  $p$  0.01) and lymph nodal ratio (LNR)  $> 0:15$  (RR 1.68,  $p = 0.015$ ) were associated with a worse PFS. ECE and LNR  $> 0,15$  were significantly related to a worst FFLR (RR 3.04 and 4.42, respectively), adenocarcinoma to an unfavorable FFDM (RR 1.97,  $p = 0.013$ ).

Table 1. Clinical pathological (a), treatment (b) and nodal (c) factors

a) Characteristics		N (%)
Sex	Male	171 (84.6%)
Sex	Female	31 (15.4%)
Age	Median	63 (30.9%)
Age	Range	45-86 (22.3%)
Primary tumor	Lung	159 (78.7%)
Primary tumor	Rectum	4 (2.0%)
Primary tumor	Colon	3 (1.5%)
Primary tumor	Breast	2 (1.0%)
Primary tumor	Endometrial	1 (0.5%)
Primary tumor	Prostate	1 (0.5%)
Primary tumor	Other	6 (3.0%)
Treated lesion	Primary tumor	12 (32.4%)
Treated lesion	Nodal metastases	9 (24.3%)
Treated lesion	Distant metastases	16 (49.3%)

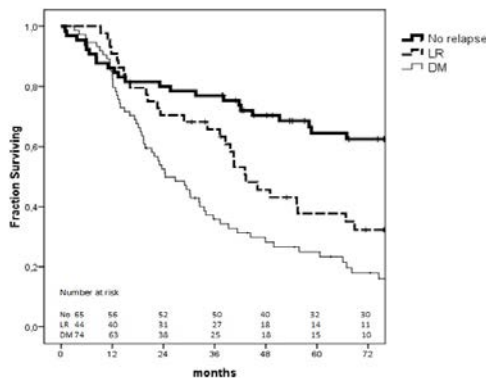
  

b) Characteristics		N (%)
Adjuvant chemotherapy	Yes	49 (24.3%)
Adjuvant chemotherapy	No	153 (75.7%)
PORT	Yes	44 (21.8%)
PORT	No	158 (78.2%)
SBRT	Yes	18 (8.9%)
SBRT	No	184 (91.1%)
SBRS	Yes	18 (8.9%)
SBRS	No	184 (91.1%)

c) Characteristics		N (%)
EC	Yes	27 (13.4%)
EC	No	175 (86.6%)
LNR	$> 0:15$	33 (16.3%)
LNR	$\leq 0:15$	169 (83.7%)
LN	$> 1$	87 (42.6%)
LN	$\leq 1$	115 (57.4%)
LN	$> 1:1$	33 (16.3%)
LN	$\leq 1:1$	136 (66.7%)
LN	$> 2:1$	33 (16.3%)
LN	$\leq 2:1$	136 (66.7%)

Abbreviations: LR: ipsilateral hilum or mediastinum; DM: distant metastases; ECE: extra capsular extension; LN: lymph node ratio; LNR: lymph node ratio



**Conclusion:** LR are common in pN1 NSCLC patients. Nodal factors as high LNR and ECE can predict an increased risk of worse FFLR and PFS. Prospective data on selected patients, treated with modern radiotherapy techniques, need to be collected to re-evaluate the role of radiotherapy.

EP-1206

Adequacy of dose/volume constraints in stereotactic radiotherapy and radiosurgery of thoracic area

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**Purpose or Objective:** To verify adequacy of dose volume constraints reported in literature about stereotactic radiotherapy (SBRT) and radiosurgery of thoracic area. This study is based on the toxicity recorded in organs at risk (OARs) of patients enrolled in dose-escalation trials.

**Material and Methods:** This is a retrospective study evaluating treatment plans of neoplasms in thoracic area. All 55 patients were treated between November 2009 and December 2013 using SBRT (37 pt) or SBRS (18 pt). Prescribed doses were 30-35 Gy in 5 fractions in SBRS treatments and 16-28 Gy in single fraction in SBRS treatments. All patients underwent radiotherapy with V-MAT technique. Main OARs were heart, oesophagus, and ribs with suggested Dmax of 35 Gy, 32.5 Gy and 32.5 Gy in SBRT treatment, respectively, and 22 Gy, 15 Gy and 30 Gy in SBRS treatment, respectively. Plans were evaluated by DVH analysis. Dosimetric data were compared with clinical data on early and late toxicity.

Table 1: Patients' characteristics

	SBRT (N, %)	SBRS (N, %)
N*	37 (67.3)	18 (32.7)
M/F	28/9	6/12
Age (range; media)	45-86; 65	37-75; 56
Primary tumor		
	Lung	19 (51.4)
	Rectum	4 (10.8)
	Colon	3 (8.1)
	Breast	2 (5.4)
	Endometrial	1 (2.7)
	Prostate	1 (2.7)
	Other	6 (16.2)
Treated lesion		
	Primary tumor	12 (32.4)
	Nodal metastases	9 (24.3)
	Distant metastases	16 (43.3)

**Results:** SBRT treatment: considering heart, oesophagus and ribs, Dmax constraints were exceeded in 7/37 patients (18.9%), 4/37 (10.8%) and 16/37 (43.2%) respectively. In these patients results about OARs were as follow: heart Dmax 36.6-50 Gy, V35 0.5-4.7 cc; oesophagus Dmax 35.7-41.3 Gy, V32.5 0.1-0.9cc; ribs Dmax 35.7-52.5 Gy, V32.5 0.1-7.9cc. SBRS treatment: dose on heart and ribs exceeded Dmax constraints in 1/18 patients (5.6%) with a Dmax of 23.3Gy (V22=0.6cc) and 33.6Gy (V30=0.3cc) respectively. With a median follow up of 18 months considering SBRT treatment and 16 months considering SBRS, no Grade  $> 2$  (CTCAE 4.3), early or late toxicity of heart or ribs was reported. In SBRT group, 1 grade 2-oesophagus toxicity in a patient exceeding DMax constraint was registered.

**Conclusion:** Patients irradiated did not develop severe toxicity on heart, oesophagus, and ribs although the administered doses were above constraints proposed in literature. A prolonged follow up and a larger population are needed to confirm the safety of dose-volume constraints