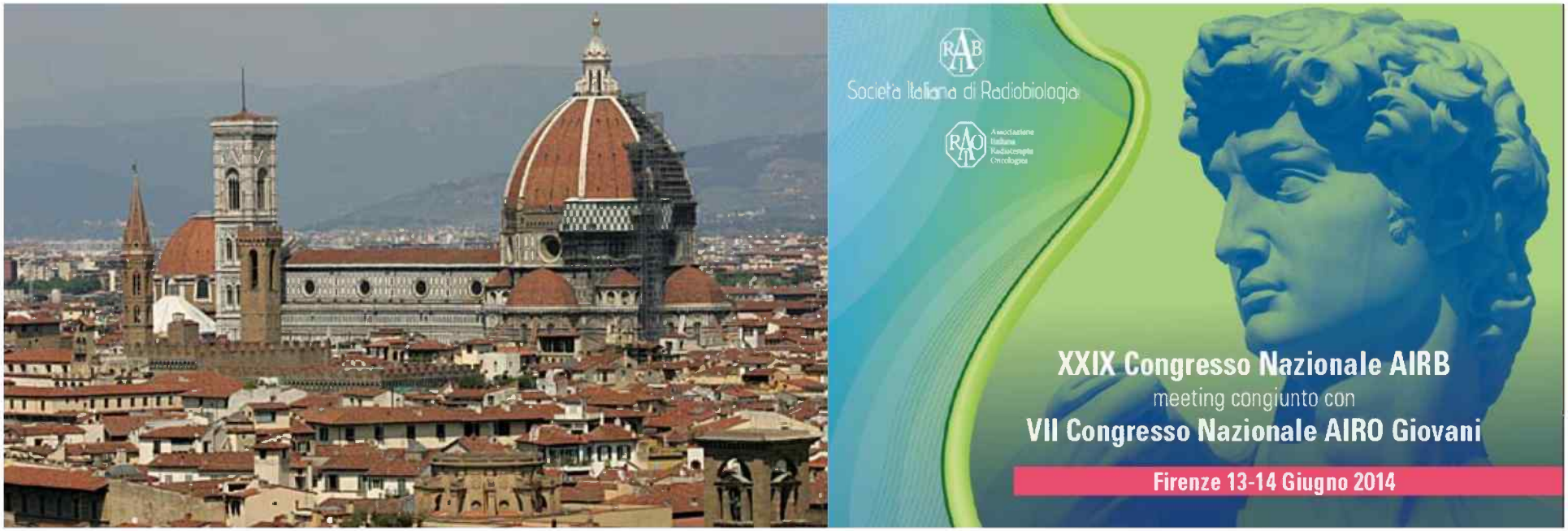

Radioterapia Stereotassica Ablativa "Risk-Adapted" in pazienti affetti da lesione primitiva polmonare.

S. Badellino, A.R. Filippi, A. Guarneri, M. Levis, R. Ragona e U. Ricardi

SC Radioterapia, Dipartimento di Oncologia, Università di Torino

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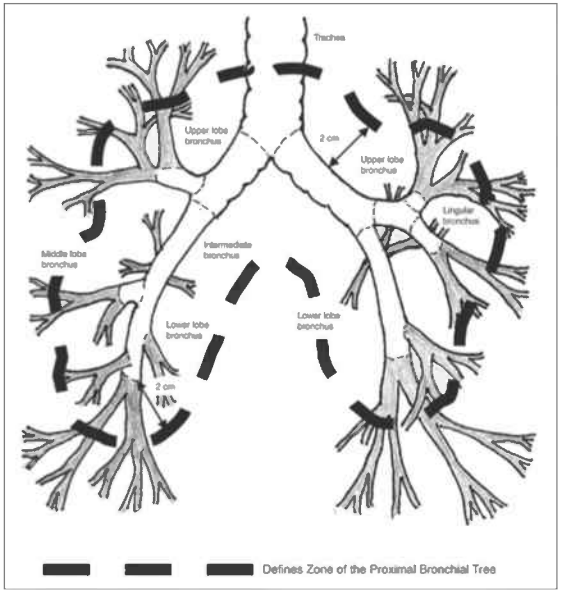
BACKGROUND

VOLUME 24 · NUMBER 30 · OCTOBER 20 2006
JOURNAL OF CLINICAL ONCOLOGY ORIGINAL REPORT

Excessive Toxicity When Treating Central Tumors in a Phase II Study of Stereotactic Body Radiation Therapy for Medically Inoperable Early-Stage Lung Cancer

Robert Timmerman, Ronald McGarry, Constantin Yiannoutsos, Lech Papiez, Kathy Tudor, Jill DeLuca, Marvene Ewing, Ramzi Abdulrahman, Colleen DesRosiers, Mark Williams, and James Fletcher



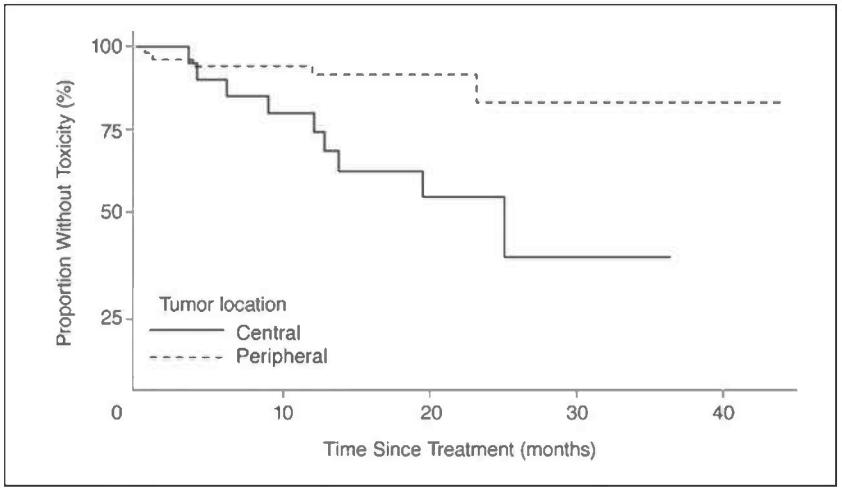


Fig 4. Kaplan-Meier plot of time from treatment until grade 3 to 5 treatment related toxicity comparing patients with tumors in the central (perihilar and central mediastinal) regions from those with more peripheral tumors.

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OUTCOMES OF RISK-ADAPTED FRACTIONATED STEREOTACTIC RADIOTHERAPY FOR STAGE I NON–SMALL-CELL LUNG CANCER

Table 1. Characteristics of patient and tumors

Gender	
Male	n = 115 (56%)
Female	n = 91 (44%)
Median age	73 years
Tumors (n = 219)	
T1	n = 129 (59%)
T2	n = 90 (41%)
Reason for referral	
Medically inoperable	n = 167 (81%)
Refusing surgery	n = 39 (19%)
Pathological confirmation	
Yes	n = 64 (31%)
No	n = 142 (69%)
Histology (n = 64)	
Adenocarcinoma	n = 23 (36%)
Squamous cell carcinoma	n = 19 (30%)
Undifferentiated NSCLC	n = 22 (34%)
Fractionation scheme (n = 219)	
20 Gy × 3	n = 93 (43%)
12 Gy × 5	n = 99 (45%)
7.5 Gy × 8	n = 27 (12%)
GOLD class	
No COPD	n = 36 (18%)
Class I	n = 16 (8%)
Class II	n = 60 (29%)
Class III	n = 75 (36%)
Unknown	n = 19 (9%)

Abbreviations: COPD = chronic obstructive pulmonary disease; NSCLC = non–small-cell lung cancer.

Lagerwaard et al, IJROBP 2008

Conclusions

SBRT is well tolerated in patients with extensive comorbidity with high local control rates and minimal toxicity. In view of patient convenience, such risk-adapted SBRT schedules should be considered treatment of choice in patients presenting with medically inoperable Stage I NSCLC

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PURPOSE

- To evaluate efficacy and tolerability of different SABR fractionation schemes in a series of patients consecutively treated (time interval 2003-2013)

- **Outcome measures: Local-Relapse Free-Survival, Nodal Relapse Free-Survival, Distant Relapse Free-Survival, Cancer-Specific Survival, RTOG toxicity (clinical and radiological)**

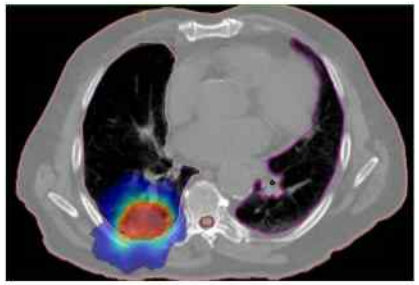
- **Inclusion criteria:**
  - ECOG PS 0-1
  - Stage I NSCLC
  - Pulmonary function (FEV1 and FVC $\geq$ 40%)

MATERIAL AND METHODS

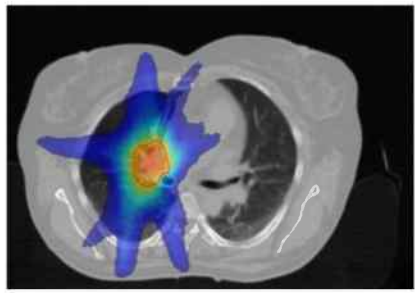
FRACTIONATION SCHEDULE:

15-18 Gy X **3** fractions (80% isodose)
115.5 Gy-151 Gy BED

11 Gy X **5** fractions (80% isodose)
115 Gy BED



7.5 Gy in **8** fractions (80% isodose)
105 Gy BED



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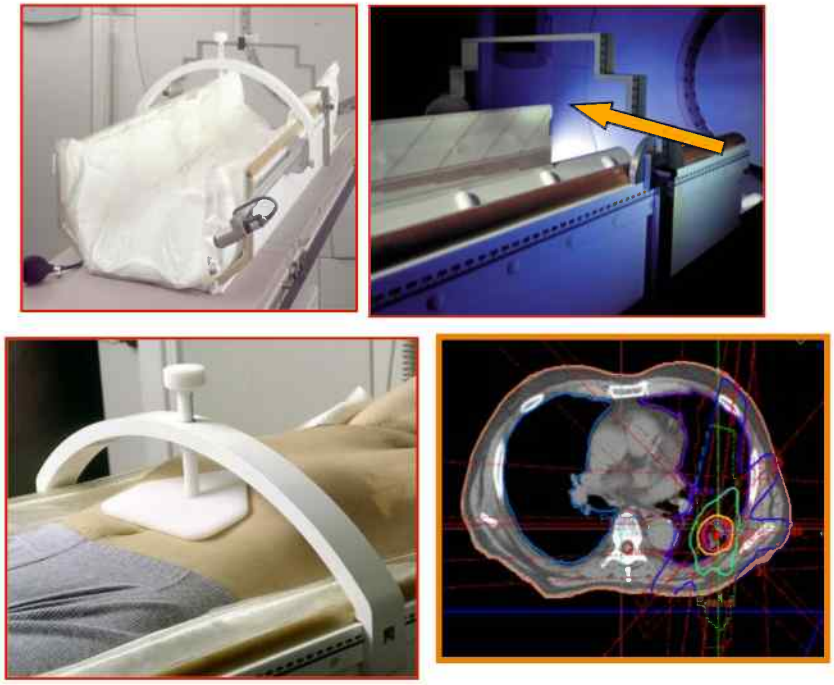
MATERIAL AND METHODS

From 2003…



- Elekta®-Stereotactic Body Frame
- Device for diaphragm compression (breathing tumor movements >10 mm at fluoroscopy)
- Stereotactic coordinates system

- **Slow CT scan**

- Elekta Precise® Linear Accelerator
- 3D conformal technique: 6–8 static non-opposing, non-coplanar shaped fields/ 6–10MV photons

- 0°-90° DPI/ DRRs

PTV = CTV + 5mm margin in the axial plane
10mm margin in longitudinal direction

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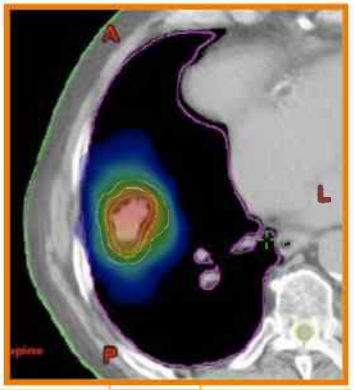
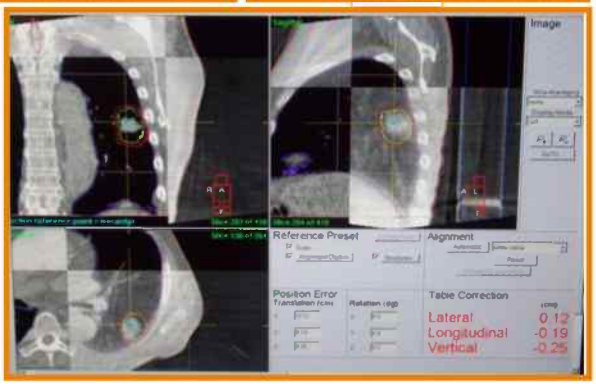
MATERIAL AND METHODS

...to 2010...

- BodyFix ® frameless
- 4D CT simulation
- Monaco®
- Elekta Axesse® Linear Accelerator
- Volumetric-Modulated Arc Therapy (VMAT)
- **Cone Beam CT**:
  - compare volumetric information (3D) with a high resolution and quality
  - KV images





4DCT + IGRT → PTV= ITV + 3 mm isotropic

MATERIAL AND METHODS

• Normal Tissue Constraints

Serial Tissue	Maximal dose	Single fraction		3 fractions		5-8 fractions		Toxicity (≥G3)
		Dose soglia (Gy [Gy/fr.])	Dose max (Gy [Gy/fr.])	Dose soglia (Gy [Gy/fr.])	Dose max (Gy [Gy/ fr.])	Dose soglia (Gy [Gy/ fr.])	Dose max (Gy [Gy/fr.])	
Spinal Cord	<0.35 cc	10	14	18 (6)	21.9 (7.3)	23 (4.6)	30 (6)	Myelite
Esophagel	<5 cc	11.9	15.4	17.7 (5.9)	25.2 (8.4)	19.5 (3.9)	35 (7)	Stenosis/Fistula
Brachial plex	<3 cc	14	17.5	20.4 (6.8)	24 (8)	27 (5.4)	30.5 (6.1)	Neuropathy
Heart/ pericardium	<15 cc	16	22	24 (8)	30 (10)	32 (6.4)	38 (7.6)	Pericarditis
Principle Vassels	<10 cc	31	37	39 (13)	45 (15)	47 (9.4)	53 (10.6)	Aneurisma
Trachea/bronchial	<4 cc	10.5	20.2	15 (5)	30 (10)	16.5 (3.3)	40 (8)	Stenosis/Fistula
Small air	<0.5 cc	12.4	13.3	18.9 (6.3)	23.1 (7.7)	21 (4.2)	33 (6.6)	Stenosi/atelectasia
Rib	<1 cc <30 cc	22	30	28.8 (9.6) 30 (10)	36.9 (12.3) D0,5 cc (costa) <33Gy	35 (7)	43 (8.6)	Pain/fracture
Skin	<10 cc	23	26	30 (10)	33 (11)	36.5 (7.3)	39.5 (7.9)	Ulceration

Benedict et al. Medical Physics 2010 (AAPM 2010)

• Lung Constraints → MLD_{2Gy}< 12 Gy

MATERIAL AND METHODS

Follow-up

- **CT scan total body:** 6-8 weeks after SABR and then after 3 months
- **CT-PET scan:** if clinically indicated after CT scan

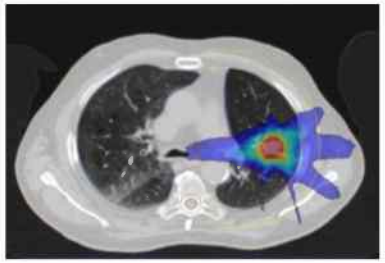
Evaluation of toxicity

- **Acute and late RTOG toxicity scale**

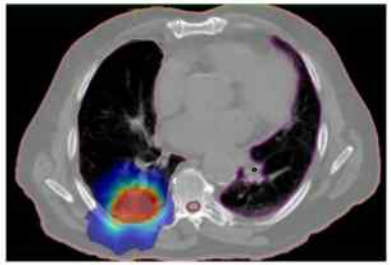
RESULTS

FRACTIONATION SCHEDULE:

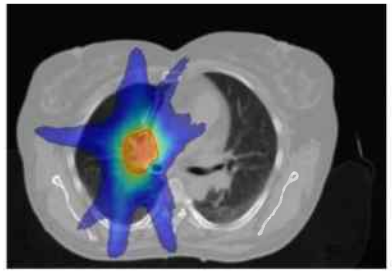
15-18 Gy X **3** fractions (80% isodose) *115.5 Gy-151 Gy BED*



11 Gy X **5** fractions (80% isodose) *115 Gy BED*



7.5 Gy in **8** fractions (80% isodose) *105 Gy BED*



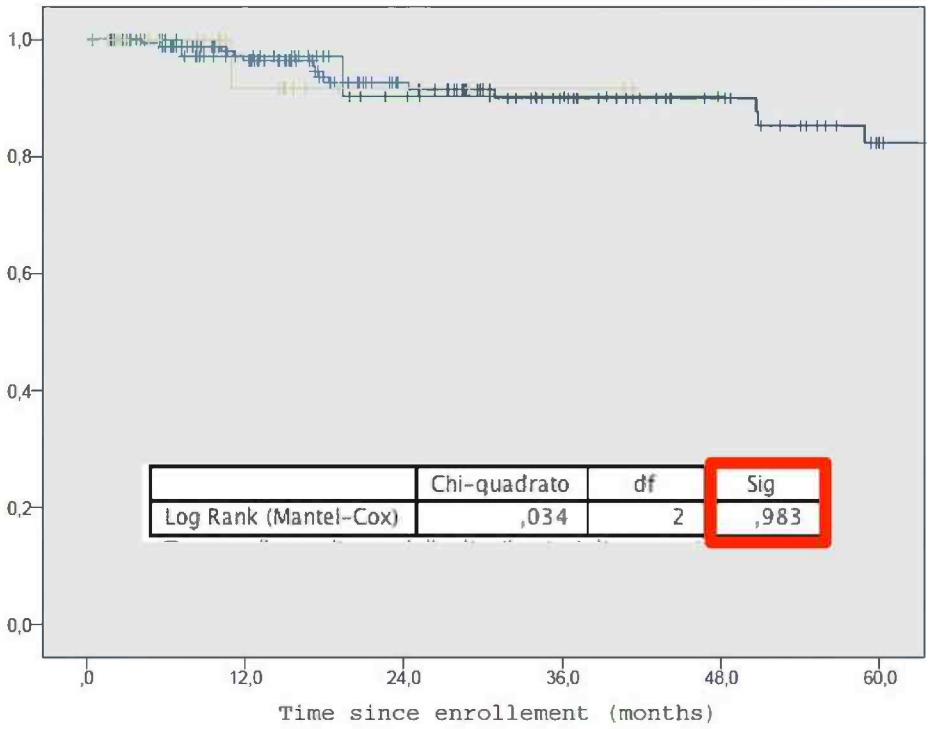
PATIENTS CHARACTERISTICS

N. OF PATIENTS	248
Males	189 (76.2.%)
Male : female proportion	3.2:1
AGE (YEARS)	
Median	76 (53-90)
HISTOLOGY	
NSCLC adenocarcinoma	55 (22%)
NSCLC squamous/other	74 (30%)
Not biopsied	119 (48%)
STAGE	
IA	189 (76.2%)
IB	59 (23.8%)
REASON FOR REFERRAL	
Refusing surgery	25 (10%)
Major pulmonary comorbidities	73 (29%)
Medically inoperable (age, other comorbidities)	150 (61%)
NUMBER OF FRACTIONS	
3	169 (68.1%)
5	50 (20.2%)
8	29 (11.7%)
TECHNIQUE	
3DCRT	130 (52.4%)
IMRT/VMAT	118 (47.6%)
TUMOR SIZE (MM)	
Median	25
Range	10-50

RESULTS

MEDIAN FOLLOW UP: 22 months

3 fr Group: 30 months
5 fr Group: 18 months
8 fr Group: 14 months



3 fr
5 fr
8 fr

LOCAL RELAPSE FREE-SURVIVAL

3 fr	@ 1 year	96.4%
	@ 2 years	91.5%
5 fr	@ 1 year	100%
	@ 2 years	90.2%
8 fr	@ 1 year	100%
	@ 2 years	91.7%

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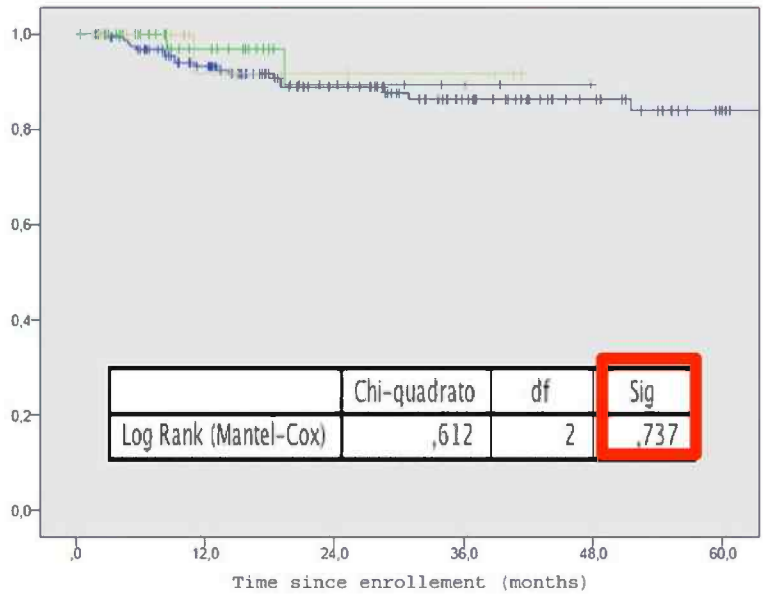
RESULTS



3 fr
5 fr
8 fr

Pattern of progression	n
Local recurrence at SABR site	19
Nodal recurrence	21
New pulmonary metastasis	30
Adrenal Gland Metastasis	5
Liver Metastasis	4
Brain Metastasis	10
Bone Metastasis	9

NODAL RELAPSE FREE-SURVIVAL

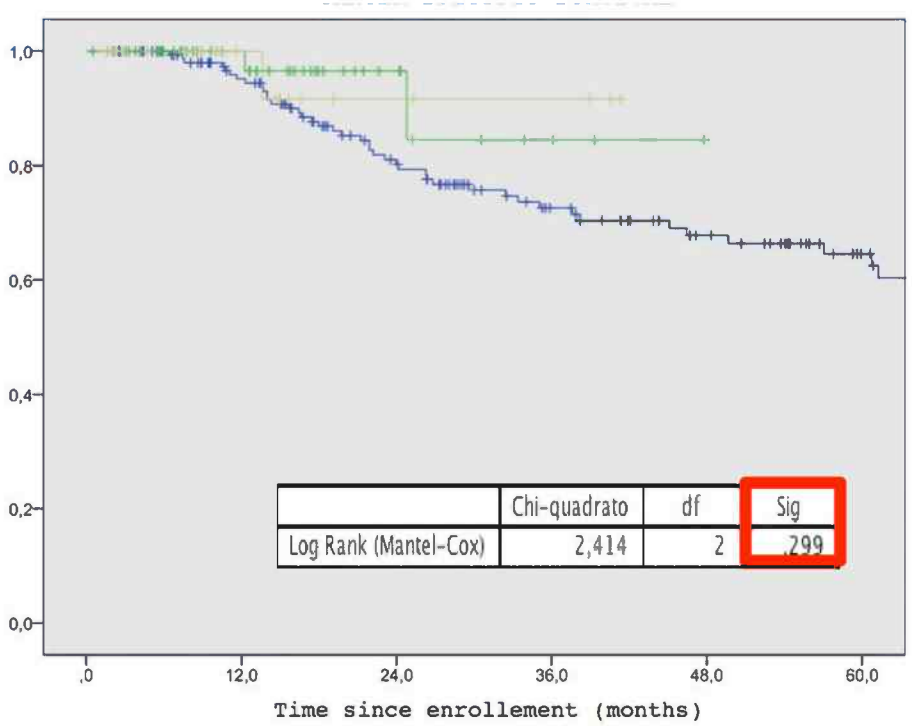
3 fr	@ 1 year	93.3%
	@ 2 years	98.8%
5 fr	@ 1 year	96.9%
	@ 2 years	89.4%
8 fr	@ 1 year	91.7%
	@ 2 years	91.7%

DISTANT RELAPSE FREE-SURVIVAL

3 fr	@ 1 year	87.4%
	@ 2 years	76.3%
5 fr	@ 1 year	77.1%
	@ 2 years	67.4%
8 fr	@ 1 year	87.9%
	@ 2 years	75.4%

RESULTS

Median survival time not reached (MST estimated > 60 months)



3 fr
5 fr
8 fr

CANCER-SPECIFIC SURVIVAL

3 fr	@ 1 year	95.2%
	@ 2 years	80.2%
5 fr	@ 1 year	96.6%
	@ 2 years	84.5%
8 fr	@ 1 year	100%
	@ 2 years	91.7%

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RESULTS

Clinical Acute Toxicity

RTOG	3 fractions	5 fractions	8 fractions
Grade 0-1	95.7%	100%	100%
Grade 2	2.3%	10%	10%
Grade 3-4	2%	0%	8.5%

p = 0,1

Average MLD_{2Gy}: 11 Gy

Clinical Chronic Toxicity

RTOG	3 fractions	5 fractions	8 fractions
Grade 0-1	96%	88%	94.5%
Grade 2	3%	12%	2.5%
Grade 3-4	1%	0%	3%

p = 0,9

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RESULTS

Chronic Radiological Toxicity

RTOG	3 fractions	5 fractions	8 fractions
Grade 0-1	78%	80.5%	71.8%
Grade 2-3	22%	19.5%	28.2%

p = 0,66

- ***Eleven (11) patients (all treated with 3 fractions, except one treated with 5 fractions) experienced chest wall toxicity (rib fracture in 2 cases, chest pain in 9 cases), 2 patients had cutaneous erythema and 1 patient had chronic brachial plexopathy***

CONCLUSIONS

- Clinical outcomes were comparable in terms of local control, nodal relapse free-survival, distant metastasis free-survival and cancer specific survival for all the fractionation schemes.
- Similar results in terms of chronic radiological toxicity profile evaluated according to RTOG lung toxicity scale.
- Higher acute pulmonary toxicity for 8 fractions (below 10%)
- Longer follow-up needed, specially for patients treated with 5 or 8 fractions, to validate these results

Grazie per l'attenzione…

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