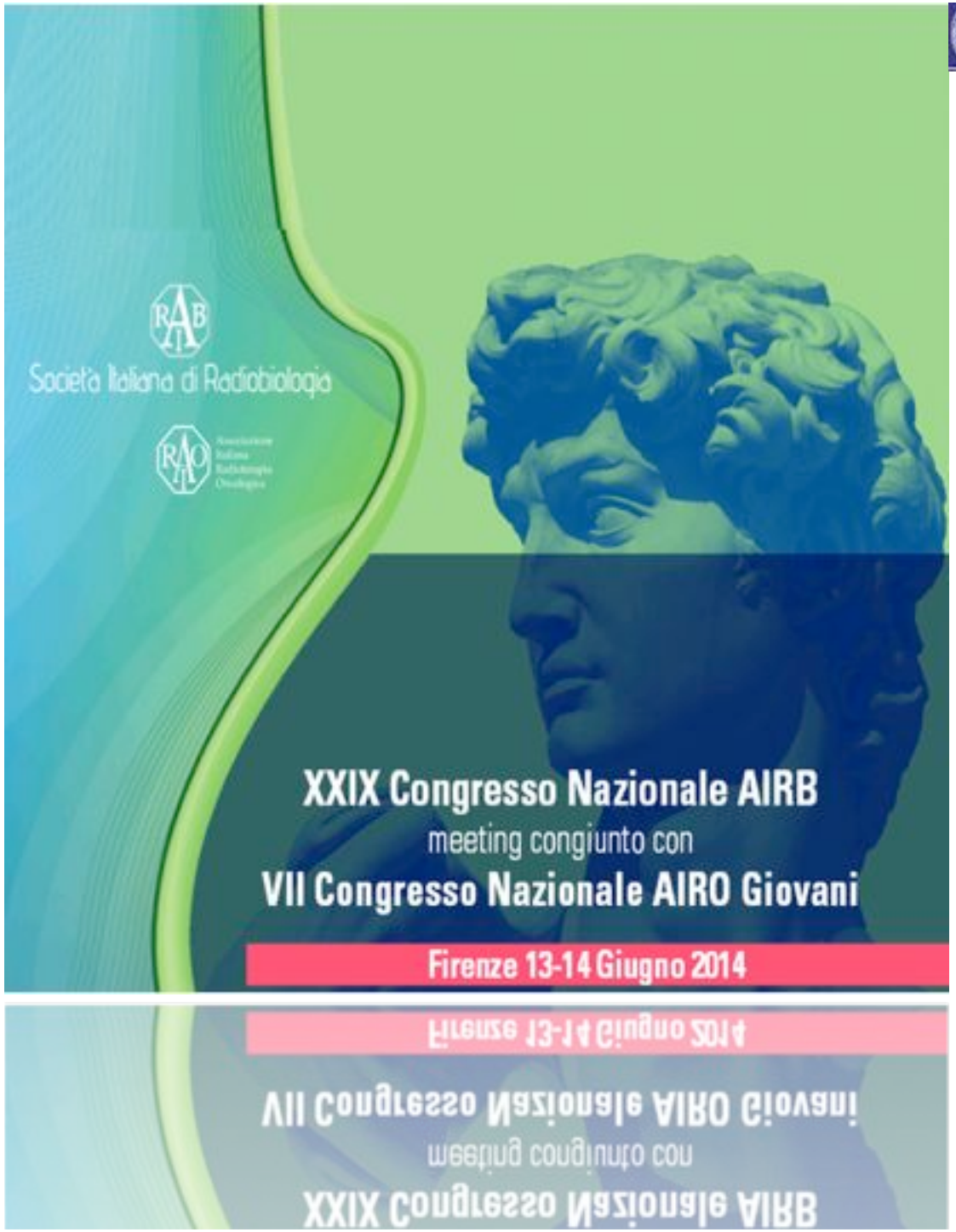

Università degli Studi di Firenze

ANALISI RETROSPETTIVA DI 134 PAZIENTI AFFETTI DA CARCINOMA POLMONARE NON A PICCOLE CELLULE (NSCLC) NON OPERABILI, IN STADIO I, SOTTOPOSTI A TRATTAMENTO STEREOTASSICO PRESSO LA RADIOTERAPIA DELL'UNIVERSITA' DI FIRENZE

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Background

Table 1. Results of retrospective studies of stereotactic body radiotherapy for mainly inoperable patients with T1-3N0M0 non-small-cell lung cancer

Author	Pt. no	Age min–max (median)	Dose Gy/fraction (fx)	Median follow-up (months)	Overall survival rate	Local control	Toxicity
Uematsu (14)	50	54–86 (71)	50–60 Gy/5–10 fx	36	66% (at 3 year)	94%	Rib fracture: 2%
Wulf (15)	20	58–82 (68)	26–37.5 Gy/1–3 fx	11	32% (at 2 year)	92%	No complications > RTOG grade 2
Onishi (16)	35	65–92 (71)	60 Gy/10 fx	13	64% (at 2 year)	88%	NCI-CTC (V2) grade 3 penumonia: 9%
Onimaru (12)	28	52–85 (76)	48 Gy/4 fx	27	IA 82% IB 32% (at 3 year)	64%	NCI-CTC (V3.0) grade 3 pneumonia: 4%
Takeda (17)	63	56–91 (78)	50 Gy/5 fx	31	IA 90% IB 63% (at 3 year)	95%	NCI-CTC (V3.0) grade 3 pneumonia: 3%

- Controllo locale > 80% nella maggior parte degli studi pubblicati
- Tossicità G2 < 10%

Hiroshi Onishi, JJCO, 2013

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Background

Table 2. Results of prospective Phase II trials of stereotactic body radiotherapy for mainly inoperable patients with Stage I non-small-cell lung cancer

Author	Pt. no	Age min–max (median)	Dose Gy/fraction (fx) (prescription)	Median follow-up (months)	Three-year overall survival rate	Three-year local control	Toxicity
Nagata (19)	42	51–87 (77)	48/4 (tumor center)	30	IA 83%, IB 72%	98%	NCI-CTC (V2) grade 2 pneumonia: 4%
Timmerman (20)	70	51–86 (70)	60–66 Gy/3 fr	17	55% (at 2 year)	95% (at 2 year)	NCI-CTC (V2) grade 3–5: 20% grade 5: 8.5%
Zimmermann (21)	68	59–92 (76)	37.5 Gy/3–5 fx (60% isodose)	18	53%	94%	RTOG grade 3 pneumonia: 6% rib fracture: 3%
Fakiris (22)	70	not shown	T1: 60 Gy/3 fx T2: 66 Gy/3 fr (80% isodose)	50	43%	94%	peripheral; NCI-CTC (V2) grade 3–5: 10% central; NCI-CTC (V2) grade 3–5: 27%
Baumann (23)	57	59–87 (75)	45 Gy/3 fx (67% isodose)	35	60%	92%	NCI-CTC (V2) grade 3: 28%
Timmerman (24)	55	48–89 (72)	60 Gy/3 fx (D95)	34	56%	98%	grade 3 NCI-CTC (V3.0): 12.7% grade 4 NCI-CTC (V3.0): 3.6%
Ricardi (25)	62	53–83 (74)	45 Gy/3 fx (80% isodose)	28	57%	92%	pneumonia > RTOG grade 3: 3% rib fracture 2%

I risultati in termini di LC e tossicità sono confermati negli studi di fase 2

Hiroshi Onishi, JJCO, 2013

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Materiali e Metodi

- **134** pazienti trattati dal 2004 a oggi
- Maschi: 58; Femmine: 33
- Età media: **77 anni** (48-87)

Operabilità	**Istologia**	**Dimensioni lesione**
•Operabili: 5 •Non operabili:129	•Adenok (n=42) •NSCLC (n=14) •Squamoso (n=21) •NA (n=57)	• <20 mm (n=41) • 20-30 mm (n=48) • 30-40 mm (n=28) • >40 (n=17)
Stadio	**Localizzazione**	**PS**
•Ia 41 •Ib 93	•Centrale 47 •Periferica 87	• 0: 25 • 1: 65 • 2: 44

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Materiali e Metodi

Schemi di Frazionamento	BED
20-27 Gyx1	60-99.9Gy
28-30 Gy x1	106,4-120 Gy
10-13 Gyx3	60-89.7 Gy
15-20 Gyx3*	112.5-180 Gy
12 Gyx4	106 Gy
6-8 Gy x5	48-72 Gy
10-12 Gy x5*	100-132 Gy
7.5 Gy x 8*	100 Gy

Parametri Tecnici e di simulazione	
Free-breath	55
ABC	49
4D TC	30
SBRT campi statici	113
SBRT VMAT/HT	21
BED>100	62
BED<100	72

* *Lagerwaard FJ IJROBP 2008*

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Risultati

Median FU	ORR	LRR	DRR	OS	1 y DFS	Toxicity
9.6 months	46%	26.3%	21.9%	80.2%	78.3%	G1-G2:4% G3: 0%

- ✓ **DFS BED>100 Gy :96.2%**
- ✓ **DFS BED< 100 Gy: 68.0%**

(p=0.037)

survival 90 Days: 100%

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Background

CANCER October 1, 2004 / Volume 101 / Number 7

Stereotactic Hypofractionated High-Dose Irradiation for Stage I Nonsmall Cell Lung Carcinoma

Clinical Outcomes in 245 Subjects in a Japanese Multiinstitutional Study

RESULTS. During follow-up (median, 24 months; range, 7–78 months), pulmonary complications of National Cancer Institute-Common Toxicity Criteria Grade > 2 were observed in only 6 patients (2.4%). Local progression occurred in 33 patients (14.5%), and the local recurrence rate was 8.1% for BED ≥ 100 Gy compared with 26.4% for < 100 Gy ($P < 0.05$). The 3-year overall survival rate of medically operable patients was 88.4% for BED ≥ 100 Gy compared with 69.4% for < 100 Gy ($P < 0.05$).

BED >100Gy sono correlate a miglioramento del LC e della OS

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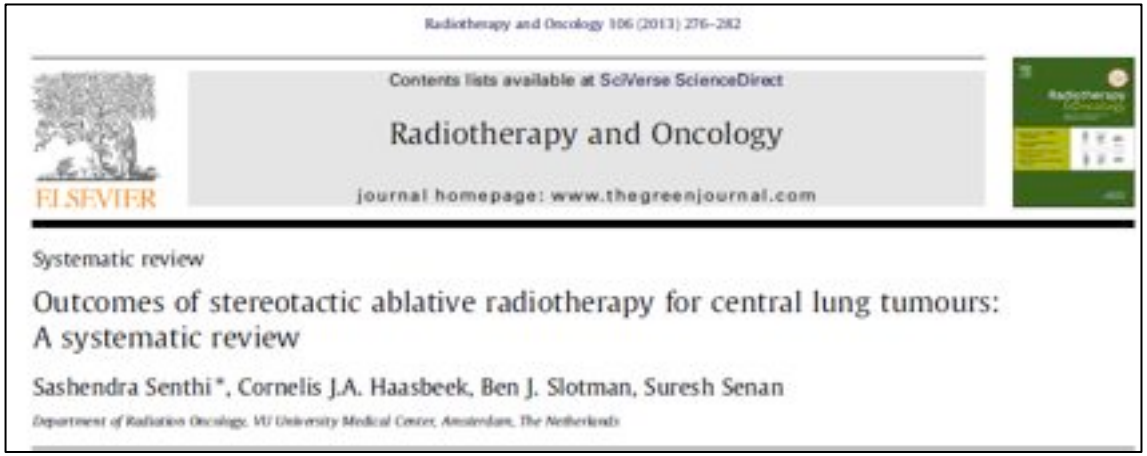
Discussione: Trattamento lesioni centrali (1)



Radiotherapy and Oncology 106 (2013) 276–282

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Systematic review

Outcomes of stereotactic ablative radiotherapy for central lung tumours: A systematic review

Sashendra Senthi*, Cornelis J.A. Haasbeek, Ben J. Slotman, Suresh Senan

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Results: Twenty publications met the inclusion criteria, reporting outcomes for 563 central lung tumours, including 315 patients with early-stage NSCLC. There was heterogeneity in the planning, prescribing and delivery of SABR and the common toxicity criteria used to define toxicities (versions 2.0–4.0). Tumour location (central versus peripheral) did not impact overall survival. Local control rates were ⩾85% when the prescribed biologically equivalent tumour dose was ⩾100 Gy. Treatment-related mortality was 2.7% overall, and 1.0% when the biologically equivalent normal tissue dose was ⩽210 Gy. Grade 3 or 4 toxicities may be more common following SABR for central tumours, but occurred in less than 9% of patients.

Conclusions: Post-SABR survival for early-stage NSCLC is not affected by tumour location. SABR achieves high local control with limited toxicity when appropriate fractionation schedules are used for central tumours.

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Discussione: Trattamento lesioni centrali (2)

Table 3
Treatment-related mortality and severe toxicity.

Author (year published)	Follow-up (months)	Central tumours (n)	Central early-stage NSCLC (n)	Central tumours eligible for RTOG 0813	BED_3 (Gy)	GTV size (range)[a]	Grade 5 toxicity (clinical details if provided)	Grade 3–4 toxicity (clinical details if provided)	Grading system
Onimura [15] (2003)	18	9[a,b]	Not specified	No[f]	144	Max < 60 mm	1 × Oesophageal ulcer (5 months. Max dose BED_3 154 Gy)	None	–
Xia [22] (2006)	27	9	9	Unclear	133	Max < 100 mm	None	None	–
Chang [26] (2008)	17	27	13[c]	No[f]	258	Max < 40 mm	None	*	–
Song [14] (2009)	27	9	9	Yes	240 [g]	Median 23 mm (12–45)	1 × Bronchial stricture (max dose 48 BED_3 240 Gy)	2 × Bronchial stricture (Max dose 40/4 both, BED_3 173 Gy)	CTC (v2)
Milano [27] (2009)	10	63[a]	7	Yes	217[d]	Median 10 cc (0.5–277)	1 × Haemoptysis, 3 × dyspnoea (at median 6.3 months. All patients with stage II–III NSCLC and received multiple courses of SABR)	1 × Pneumonia, 1 × pericarditis	CTC (v3)
Fakiris [24] (2009)	50	22	22	Yes	460	Max < 70 mm	3 × Pneumonia, 1 × haemoptysis, 1 × dyspnoea (median 12.5 months, 4 in central tumours)	1 × Apnoea, 1 × pneumonia, 2 × pleural effusion, 1 × anxiety (At median 7.6 months, 2 in central tumours)	CTC (v2)
Guckenberger [40] (2009)	14	22	6	Unclear	144	Max < 256 cc	None	*	–
Unger [28] (2010)	10	20	3	Yes	147	Median 73 cc (23–324)	1 × Bronchial fistula (max dose 49 Gy BED_3 209 Gy)	1 × pneumonitis	CTC (v3)
Ohtiro [29] (2010)	20	21	1	Yes	217[d]	Median 28 mm (10–40)	1 × Haemoptysis (second course BED_3 250 Gy)	1 × Bronchial stricture (BED_3 180 Gy), 1 × dyspnoea (BED_3 217 Gy)	CTC (v3)
Raba [35] (2010)	26	29	29	Unclear	258	Max < 55 mm	None	*	–
Bradley [33] (2010)	18	8	8	No[f]	180	Max < 51 mm	None	*	–
Andratschke [34] (2011)	21	24	24	Yes	117	Max < 203 cc	None	*	–
Haasbeek [32] (2011)	35	63	63[c]	No[f]	210	Median 36 mm (15–74)	None	Acute 1 × chest wall pain. Late 2 × dyspnoea, 1 × rib fracture, 1 × chest wall pain (occurred in 5 patients)	CTC (v3)
Bral [23] (2011)	16	17	17	Yes	360	Max < 60 mm	1 × Bronchial stenosis/haemoptysis	Acute 2 × pneumonitis, 2 × cough, 1 × pneumonia. Late 3 × pneumonitis, 1 × pneumonia (occurred in 4 patients)	CTC (v3)
Olsen [38] (2011)	11	15	15[c]	No[f]	217	Not specified	None	*	–
Stauder [39] (2011)	16	47[a,b]	Not specified	Yes	240	Max < 60 mm	1 × Bronchial stricture (7.5 months)	1 × dyspnoea	CTC (v3)
Rowe [37] (2012)	11	51[a,c]	30	No[f]	258[d]	Median 31 mm (11–57)	1 × Haemoptysis (10.5 months. Max dose 54 Gy BED_3 297 Gy)	3 × Dyspnoea, 1 × pneumonitis	CTC (v4)
Nuyttens [30] (2012)	23	58[a]	39	No[f]	300[d]	Median 41 mm (12–105)	None	Acute 4 × pneumonitis. Late 6 × pneumonitis. (3 were clearly SABR-related, 7 were more likely felt to be COPD exacerbation).	CTC (v3)
Taremi [25] (2012)	19	20	20	Unclear	210	Max < 57 mm	None	*	–
Jansen [31] (2012)	14	29[b]	Not specified	Unclear	144	Max < 142 cc	None	None	–

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Conclusioni

✓ La SBRT è un trattamento fattibile ed efficace per pazienti con NSCLC in stadio I non operabili o che rifiutano l'approccio chirurgico

✓Le attuali tecnologie permettono di somministrare dosi singole per frazione elevate

✓BED_{10} superiori ai 100 Gy sono correlate ad outcome migliori in termini di DFS e controllo di malattia

✓La tossicità rimane accettabile anche per lesioni centrali con un approccio risk adaptive, la mortalità si riduce in maniera significativa se la BED_3 rimane sotto i 210 Gy

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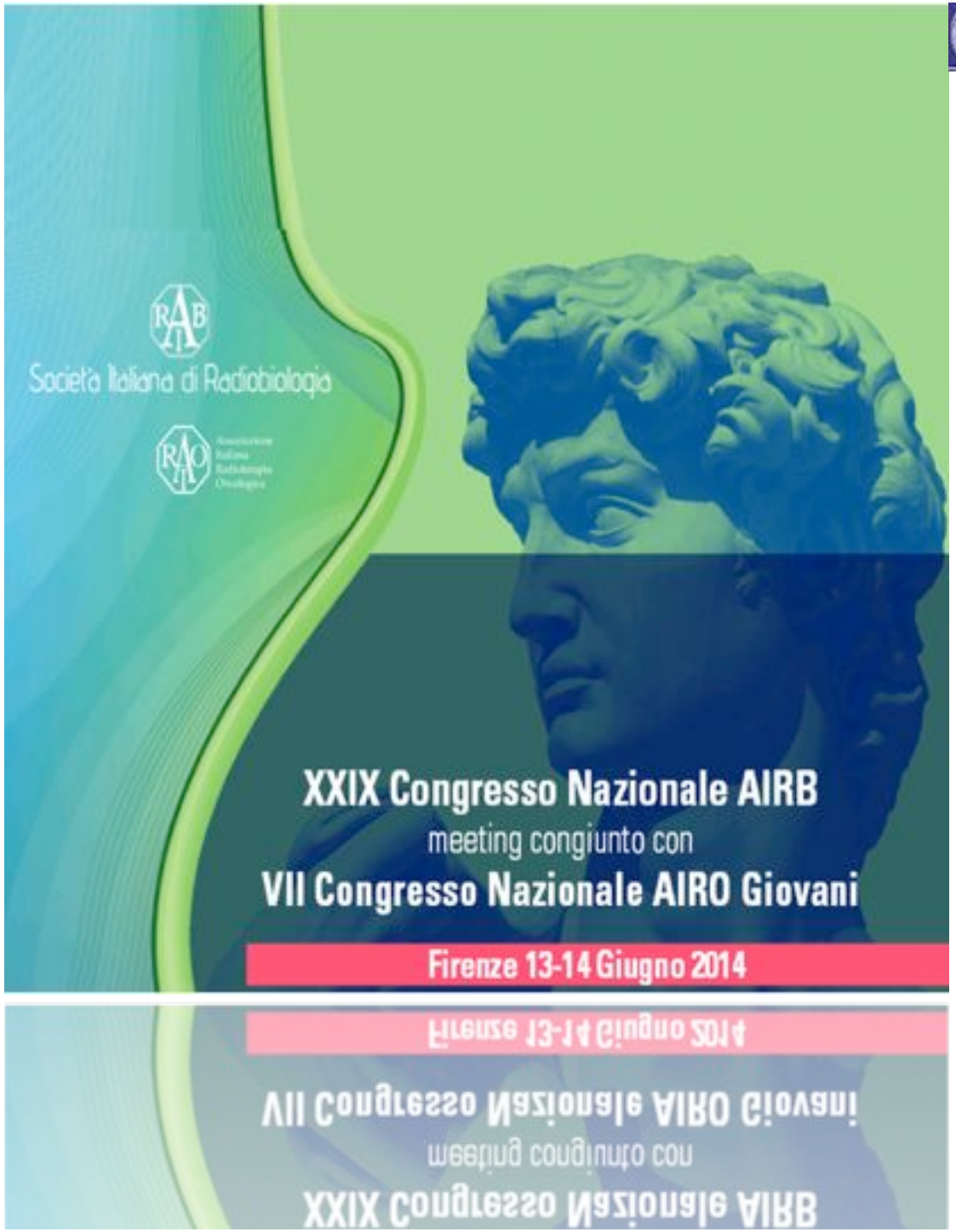

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Grazie per l'attenzione