

XXVI Congresso Nazionale AIRO

A randomized Study of Hypofractionated and
Conventional Breast Irradiation in Early-Stage
Breast Cancer: toxicity and long-term outcome

Dott. Stefano Durante

Background



2002

Randomized Trial of Breast Irradiation Schedules After Lumpectomy for Women With Lymph Node-Negative Breast Cancer

Timothy Whelan, Robert MacKenzie, Jim Julian, Mark Levine, Wendy Shelley, Laval Grimard, Barbara Lada, Himu Lukka, Francisco Perera, Anthony Fyles, Ethan Laukkanen, Sunil Gulavita, Veronique Benk, Barbara Szechtman

2003 – 2006 Pilot Study IEO

270 Pazienti 45 Gy in 20 fr + Boost concomitante 0.25 Gy/ fr

Scheme	Total dose	BED 3	BED 4	BED 10
2 Gy/die x 25 fx	50	83	75	60
+ 2Gy/die x 5 fx (sequential boost)	60	100	90	72
2.25 Gy/die x 20 fx	45	79	70	55
+ 0.25 Gy/die x 20 fx (concomitant boost)	50	92	81	62.5
2,65 Gy/die x 16 fx (Whelan)	42,5	80	71	54



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Materials and Methods

Time: April 2007 – March 2010

Patients: 249 Patients post BCS

Features: T1-T3

N0-N1

HT / Adjuvant CHT \pm HT



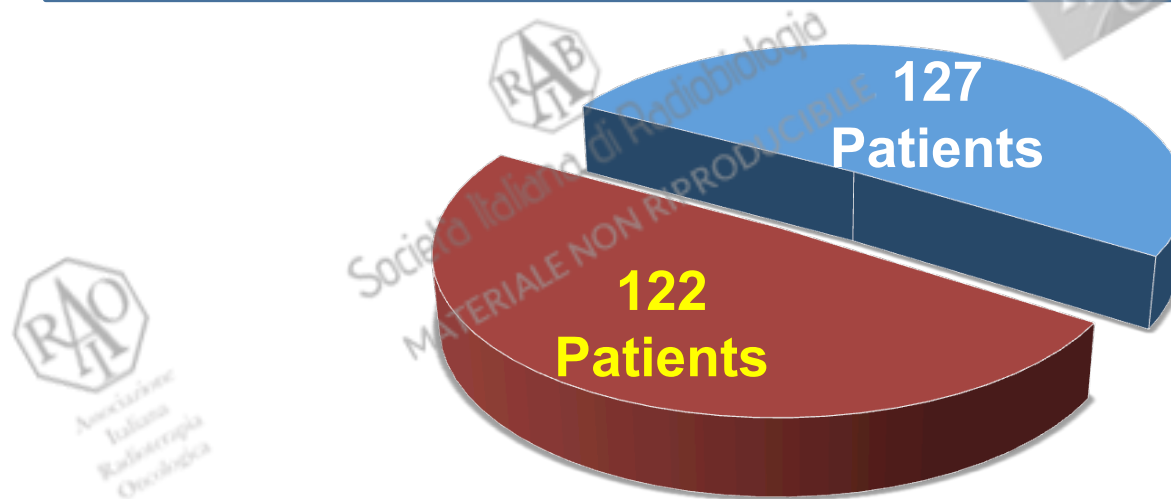
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Materials and Methods

Conventional Scheme

50 Gy/25 fr (2 Gy/fr)

Sequential Boost 10 Gy/5 fr (2Gy/fr)



Hypofractionated Scheme

45 Gy/20 fr (2.25 Gy/fr)

Concomitant electrons Boost 5 Gy/4 fr (1.25 Gy/fr 1/week)

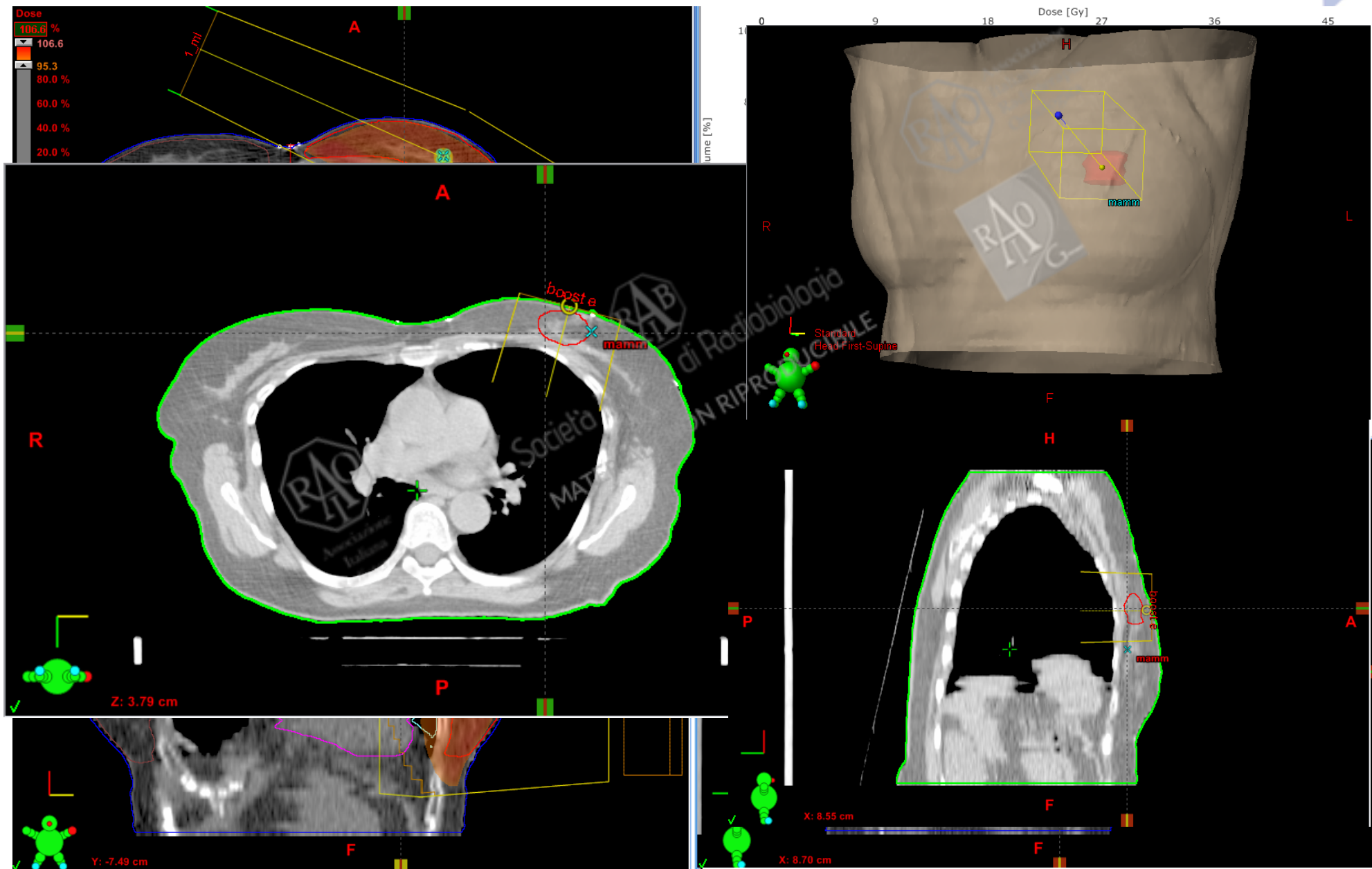


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Study Endpoints

Primary Endpoint:

Acute side effects of CF-WBI vs HF-WBI

Secondary Endpoints:

Compare subjective acute side effects,
early late side effects



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Results: Acute Toxicity (RTOG)



	20 fx (122 pts) n (%)	30 fx (127 pts) n (%)	95% CI difference [RTOG>2]
G0	2 (1.6)	1 (0,8)	
G1	72 (59.0)	33 (26.0)	
G2	48 (39.3)	84 (66.1)	
G3	0 (-)	9 (7.1)	-7.1(-12.4, -1.8)



12 Months Toxicity (LENT-SOMA)



	20 fx n (%)	30 fx n (%)	<i>p</i>
Pain	4 (3.3)	3 (2.4)	0.68
Edema	1 (0.8)	1 (0.8)	0.99
Fibrosis	6 (5)	10 (8.1)	0.32
Retraction	1 (0.8)	1 (0.8)	0.99
Atrophy	3 (2.5)	1 (0.8)	0.30
Telangectasie	1 (0.8)	1 (0.8)	0.3
Lymphoedema	0	0	-



ASTRO recommendation 2010

Appropriate use of hypofractionated regimens

- Women >50 years of age
- pN0
- Tumor size < 5 cm
- Inhomogeneity kept within $\pm 7\%$
- No agreement on boost
- No adjuvant CT





Tailoring therapies – improving the management of early breast cancer: St Gallen International Expert Consensus on the Primary Therapy of Early Breast Cancer 2015

A. S. Coates¹, E. P. Winer², A. Goldhirsch^{3*}, R. D. Gelber⁴, M. Gnant⁵, M. Piccart-Gebhart⁶, B. Thürlimann⁷, H.-J. Senn⁸ & Panel Members[†]

radiation therapy

Radiotherapy courses involving hypofractionation were considered appropriate irrespective of age for patients without prior chemotherapy or clinical lymph node involvement. A bare majority of the Panel would accept hypofractionated radiotherapy for patients with axillary lymph node involvement or prior chemotherapy.



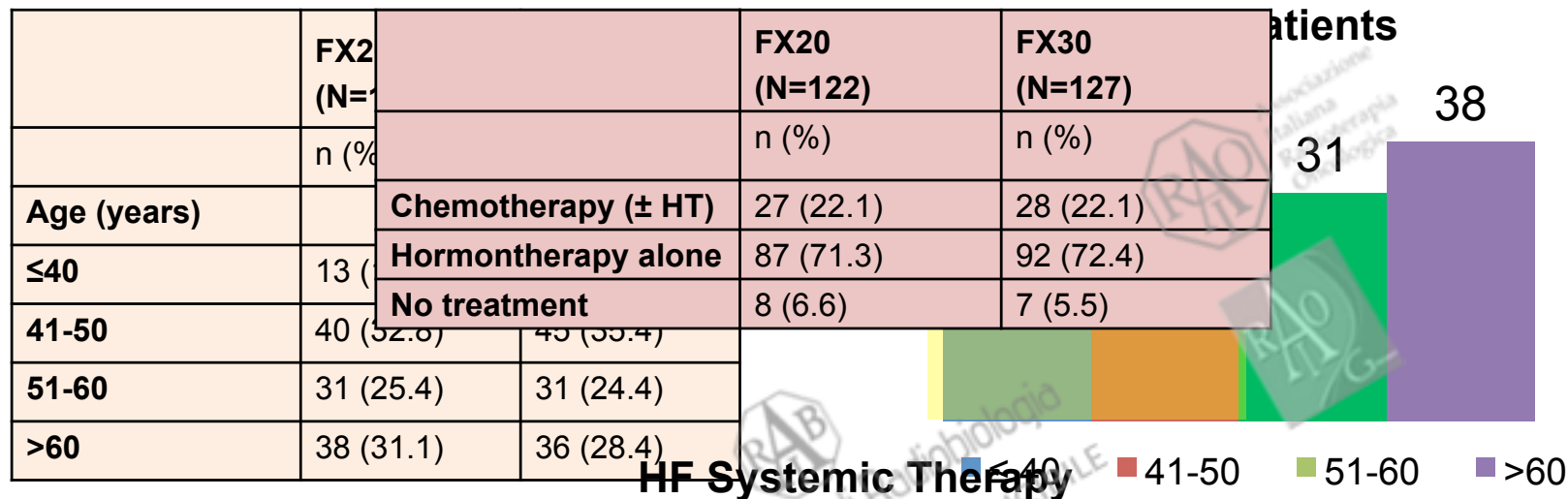
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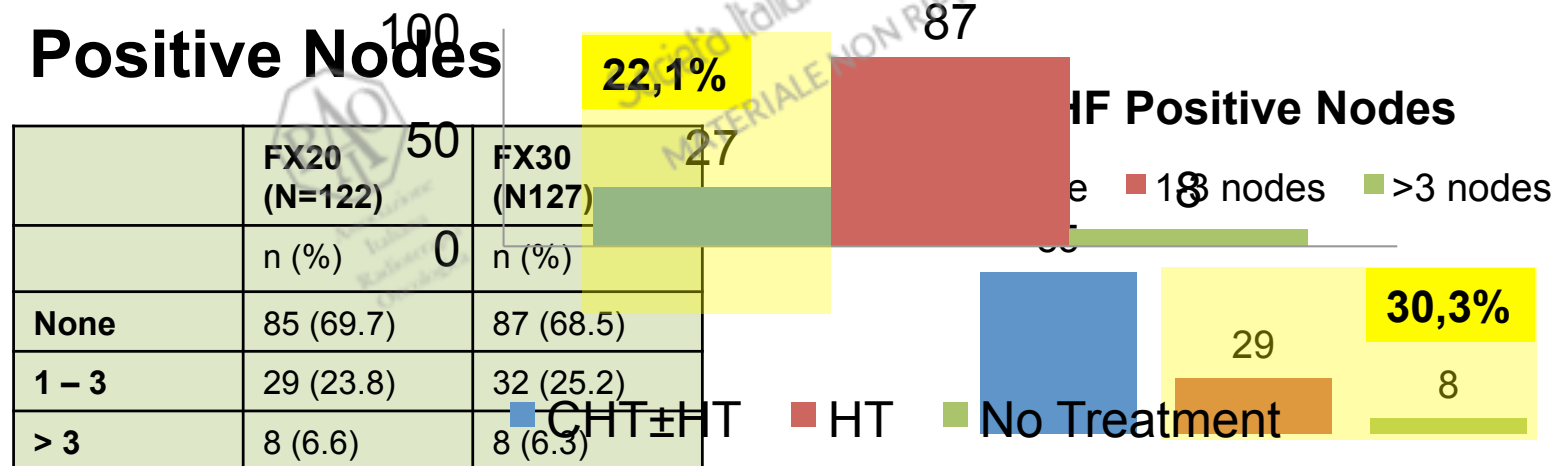
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Age (Years) Systemic Therapy

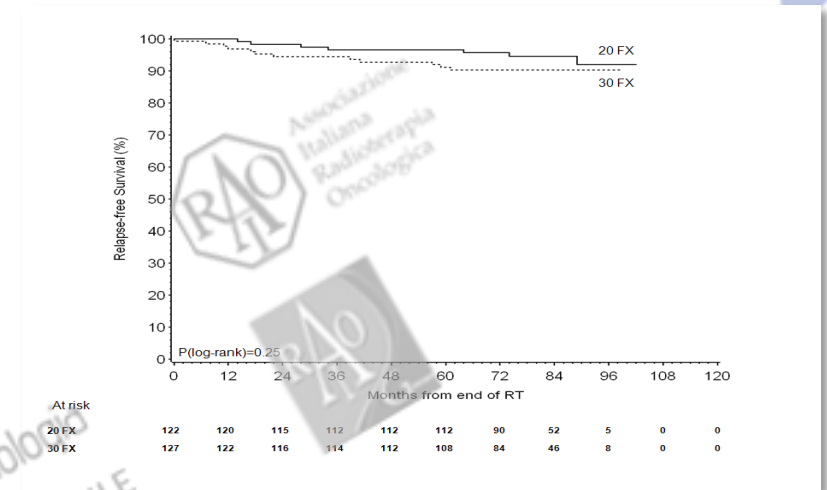


Positive Nodes

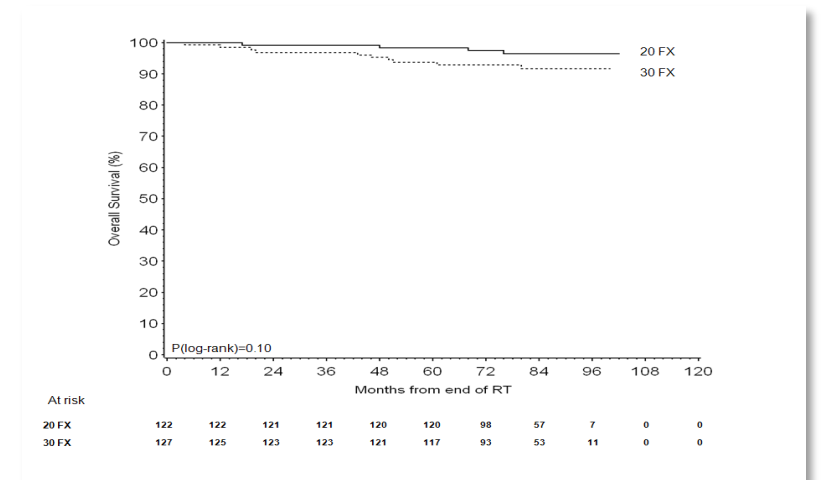


5-Years Survival Rates

	Randomized groups		p-value
	FX20 (N=122)	FX30 (N=127)	
	n (%)	n (%)	
DFS:			
Local	99.1	97.4	0.32
Regional	97.4	99.1	0.31
Distant	98.3	94.3	0.10
Any relapse	96.6	91.1	0.07
OS	98.4	93.7	0.06



Disease-free survival



Overall Survival

The UK Standardisation of Breast Radiotherapy (START) trials of radiotherapy hypofractionation for treatment of early breast cancer: 10-year follow-up results of two randomised controlled trials



Joanne S Haviland, J Roger Owen, John A Dewar, Rajiv K Agrawal, Jane Barrett, Peter J Barrett-Lee, H Jane Dobbs, Penelope Hopwood, Pat A Lawton, Brian J Magee, Judith Mills, Sandra Simmons, Mark A Sydenham, Karen Venables, Judith M Bliss*, John R Yarnold*, on behalf of the START Trialists' Group†

	Events (n/patients; %)	Estimated proportion of patients with event by 5 years (%; 95% CI)	Estimated proportion of patients with event by 10 years (%; 95% CI)	Crude hazard ratio (95% CI)	p value*
Local relapse					
50 Gy	50/1105 (4.5%)	3.3% (2.4–4.6)	5.2% (3.9–6.9)	1.00	..
40 Gy	36/1110 (3.2%)	1.9% (1.2–3.0)	3.8% (2.7–5.2)	0.70 (0.46–1.07)	0.10
Local-regional relapse					
50 Gy	53/1105 (4.8%)	3.5% (2.5–4.8)	5.5% (4.2–7.2)	1.00	..
40 Gy	42/1110 (3.8%)	2.3% (1.5–3.4)	4.3% (3.2–5.9)	0.77 (0.51–1.16)	0.21
Distant relapse					
50 Gy	158/1105 (14.3%)	10.5% (8.8–12.5)	16.0% (13.8–18.5)	1.00	..
40 Gy	121/1110 (10.9%)	7.5% (6.0–9.2)	12.3% (10.3–14.6)	0.74 (0.59–0.94)	0.014
Any breast cancer-related event†					
50 Gy	222/1105 (20.1%)	14.3% (12.3–16.5)	22.2% (19.7–25.0)	1.00	..
40 Gy	182/1110 (16.4%)	10.4% (8.7–12.4)	18.3% (16.0–20.9)	0.79 (0.65–0.97)	0.022
All-cause mortality					
50 Gy	192/1105 (17.4%)	10.9% (9.1–12.9)	19.2% (16.8–21.9)	1.00	..
40 Gy	159/1110 (14.3%)	7.9% (6.4–9.6)	15.9% (13.7–18.4)	0.80 (0.65–0.99)	0.042

* Assessed with log-rank test compared with 50 Gy. † Local, regional, or distant relapse, breast cancer death, contralateral breast cancer.

Table 4: Relapse and mortality according to fractionation schedule in START-B



Conclusion

- ❖ The acute and intermediate toxicity observed in HFS was well tolerated and better than the one observed in CS.
- ❖ No statistical difference of Disease free survival and Overall Survival in HFS scheme vs CS, even though there was a trend of HFS to better OS as we saw in the results of randomized controlled trials START.





Grazie per l'attenzione



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