

XXXIII CONGRESSO NAZIONALE AIRO

# AIRO2023

BOLOGNA,  
27-29 OTTOBRE 2023

PALAZZO DEI CONGRESSI

Radioterapia Oncologica: l'evoluzione al servizio dei pazienti



Associazione Italiana  
Radioterapia e Oncologia clinica

## DICHIARAZIONE

Relatore: ***Dott.ssa Damaris Patricia Rojas***

Come da nuova regolamentazione della Commissione Nazionale per la Formazione Continua del Ministero della Salute, è richiesta la trasparenza delle fonti di finanziamento e dei rapporti con soggetti portatori di interessi commerciali in campo sanitario.

- Posizione di dipendente in aziende con interessi commerciali in campo sanitario **NIENTE DA DICHIARARE**
- Consulenza ad aziende con interessi commerciali in campo sanitario **NIENTE DA DICHIARARE**
- Fondi per la ricerca da aziende con interessi commerciali in campo sanitario **NIENTE DA DICHIARARE**
- Partecipazione ad Advisory Board **NIENTE DA DICHIARARE**
- Titolarità di brevetti in compartecipazione ad aziende con interessi commerciali in campo sanitario **NIENTE DA DICHIARARE**
- Partecipazioni azionarie in aziende con interessi commerciali in campo sanitario **NIENTE DA DICHIARARE**
- Altro



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Radioterapia Oncologica: l'evoluzione al servizio dei pazienti

## Un nomogramma per la predizione del rischio di recidiva locale in pazienti con cancro al seno trattate con radioterapia intraoperatoria con elettroni

## A nomogram for predicting local recurrence risk in breast cancer patients treated with intraoperative radiotherapy with electrons

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### Radiation therapy for the whole breast: Executive summary of an American Society for Radiation Oncology (ASTRO) evidence-based guideline

Benjamin D. Smith, MD <sup>a,\*</sup>, Jennifer R. Bellon, MD <sup>b</sup>, Rachel Blitzblau, MD, PhD <sup>c</sup>, Gary Freedman, MD <sup>d</sup>, Bruce Haffty, MD <sup>e</sup>, Carol Hahn, MD <sup>f</sup>, Francine Halberg, MD <sup>g</sup>, Karen Hoffman, MD <sup>h</sup>, Kathleen Horst, MD <sup>h</sup>, Jean Moran, PhD <sup>i</sup>, Caroline Patton, MA <sup>j</sup>, Jane Perlmutter, PhD <sup>k</sup>, Laura Warren, MD <sup>b</sup>, Timothy Whelan, BM, BCh <sup>l</sup>, Jean L. Wright, MD <sup>m</sup>, Reshma Jagsi, MD, DPhil <sup>i</sup>

Practical Radiation Oncology (2018) 8, 145-152 doi.org/10.1016/j.pro.2018.01.012

### How Do the ASTRO Consensus Statement Guidelines for the Application of Accelerated Partial Breast Irradiation Fit Intraoperative Radiotherapy? A Retrospective Analysis of Patients Treated at the European Institute of Oncology

Maria Cristina Leonardi, M.D.,\* Patrick Maisonneuve, Ing.,<sup>†</sup>  
Mauro Giuseppe Mastropasqua, M.D.,<sup>‡</sup> Anna Morra, M.D.,\* Roberta Lazzari, M.D.,\*  
Nicole Rotmensz, M.Sc.,<sup>§</sup> Claudia Sangalli, D.M.,<sup>§</sup> Alberto Luini, M.D.,<sup>§</sup>  
Umberto Veronesi, M.D.,\* and Roberto Orecchia, M.D.\*<sup>||</sup>

Int J Radiation Oncol Biol Phys, Vol. 83, No. 3, pp. 806e813, 2012

### Long term survival and local control outcomes from single dose targeted intraoperative radiotherapy during lumpectomy (TARGET-IORT) for early breast cancer: TARGET-A randomised clinical trial

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Steffi Pigorsch,<sup>5</sup> Michael Alvarado,<sup>6</sup> Michael Douek,<sup>7</sup> Christobel Saunders,<sup>8</sup> Henrik L Flyger,<sup>9</sup>  
Wolfgang Eiermann,<sup>3</sup> Chris Brev-Graves,<sup>1</sup> Norman R Williams,<sup>1</sup> Ingrid Potyka,<sup>1</sup>  
Nicholas Roberts,<sup>1</sup> Marcella Bernstein,<sup>10</sup> Douglas Brown,<sup>11</sup> Elena Sperk,<sup>1</sup> Siobhan Laws,<sup>12</sup>  
Marc Sutterlin,<sup>13</sup> Tammy Corica,<sup>14</sup> Steinar Lundgren,<sup>15,16</sup> Dennis Holmes,<sup>17</sup> Lorenzo Vinante,<sup>18</sup>  
Fernando Bozza,<sup>19</sup> Montserrat Pazos,<sup>20</sup> Magali Le Blanc-Onfroy,<sup>21</sup> Gunther Gruber,<sup>22</sup>  
Wojciech Polkowski,<sup>23</sup> Konstantin J Dedes,<sup>24</sup> Marcus Niewald,<sup>25</sup> Jens Blohmer,<sup>26</sup>  
David McCready,<sup>27</sup> Richard Hoefler,<sup>28</sup> Pond Kelemen,<sup>29</sup> Gloria Petralia,<sup>30</sup> Mary Falzon,<sup>31</sup>  
David J Joseph,<sup>14</sup> Jeffrey S Tobias<sup>32</sup>

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### Intraoperative radiotherapy versus external radiotherapy for early breast cancer (ELIOT): a randomised controlled equivalence trial

Umberto Veronesi, Roberto Orecchia, Patrick Maisonneuve, Giuseppe Viale, Nicole Rotmensz, Claudia Sangalli, Alberto Luini, Paolo Veronesi,  
Viviana Galimberti, Stefano Zurrada, Maria Cristina Leonardi, Roberto Lazzari, Federica Cattani, Oreste Gentilini, Mattia Intra, Pietro Caldarella,  
Bettina Ballardini

Lancet Oncol 2013; 14: [http://dx.doi.org/10.1016/S1470-2045\(13\)70497-2](http://dx.doi.org/10.1016/S1470-2045(13)70497-2)

### Intraoperative irradiation for early breast cancer (ELIOT): long-term recurrence and survival outcomes from a single-centre, randomised, phase 3 equivalence trial

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Federica Cattani, Claudia Sangalli, Alberto Luini, Pietro Caldarella, Marco Venturino, Daniele Sances, Stefano Zurrada\*, Giuseppe Viale,  
Maria Cristina Leonardi†, Mattia Intra†

Lancet Oncol 2021; 22: 597–608 doi.org/10.1016/S1470-2045(21)00080-2

### Intraoperative radiotherapy during breast conserving surgery: a study on 1,822 cases treated with electrons

Umberto Veronesi · Roberto Orecchia · Alberto Luini · Viviana Galimberti ·  
Stefano Zurrada · Mattia Intra · Paolo Veronesi · Paolo Arnone ·  
Maria Cristina Leonardi · Mario Ciocca · Roberta Lazzari · Pietro Caldarella ·  
Nicole Rotmensz · Claudia Sangalli · Daniele Sances · Patrick Maisonneuve

Breast Cancer Res Treat (2010) 124:141–151 DOI 10.1007/s10549-010-1115-5

## Aim

This study aimed to identify a useful tool for predicting local recurrence (LR) in breast cancer (BC) patients treated with intraoperative radiotherapy with electrons (IOERT) as the sole treatment



## Material and Methods

Patients diagnosed with primary breast cancer (BC) treated with intraoperative radiotherapy with electrons (IOERT) at a single institution in the period 2000-2016

Primary outcome:

Local recurrence (LR) rate, including events either in the same quadrant as the primary BC or in other quadrants of the ipsilateral breast, with or without synchronous nodal involvement or distant metastasis

## Material and Methods

Statistically significant predictors were identified at univariate and multivariate (MV) analyses.

A predictive nomogram based on logistic model was developed

The nomogram was internally validated for discrimination and calibration using Hosmer& Lemeshow Goodness of fit method

## Results

### MV analysis, predictors for LR

Variable	Level	N	IBTR	Univariable analysis			Multivariable analysis		
				HR	95% CI	P-value	HR	95% CI	P-value
Age at surgery (y)	>60	1791	101	Ref.	-	-	Ref.	-	-
	50 - 60	1088	96	1.36	1.03-1.80	0.029	1.36	1.03-1.80	0.031
	40 - 50	497	62	1.76	1.27-2.42	<0.001	1.75	1.26-2.45	<0.001
	<40	21	6	3.27	1.36-7.89	0.008	3.08	1.18-8.01	0.021
	In continuous (+5 y)			0.90	0.84-0.97	0.004			
Histology	Ductal	2715	201	Ref.			Ref.		
	Lobular / Mixed ductal and lobular	455	46	1.36	0.99-1.87	0.058	1.64	1.18-2.29	0.004
	Favourable histology	167	8	0.62	0.31-1.24	0.18	1.01	0.46-2.21	0.98
	Other	60	10	2.52	1.37-4.64	0.003	2.49	1.26-4.92	0.008
pT (cm)	<2	3019	217	Ref.	-	-	Ref.	-	-
	≥2	371	46	1.52	1.10-2.11	0.012	1.07	0.75-1.54	0.71
	In continuous (+1 cm)			1.41	1.24-1.61	<0.001			
	Missing	7	2						
pN	0	2590	174	Ref.	-	-	Ref.	-	-
	1mi / 1 / 2 / 3	716	87	1.62	1.24-2.10	<0.001	1.39	1.06-1.82	0.019
	X	91	4						
	I	948	39	Ref.	-	-	Ref.	-	-
Grade	II	1645	125	1.85	1.30-2.64	<0.001	1.56	1.06-2.29	0.025
	III	733	97	3.13	2.16-4.54	<0.001	2.12	1.26-3.57	0.005
	Missing	71	4						
	Both <1%	306	42	Ref.	-	-	Ref.	-	-
ER/PgR	ER ≥1% or PgR ≥1%	3089	223	0.53	0.37-0.74	<0.001	0.85	0.55-1.30	0.45
	Missing	2	0						

Variable	Level	N	IBTR	Univariable analysis			Multivariable analysis		
				HR	95% CI	P-value	HR	95% CI	P-value
Her2 status	Negative	3000	221	Ref.	-	-	Ref.	-	-
	Positive w/o anti-HER2 therapy	90	19	2.19	1.32-3.63	0.002	1.13	0.63-2.02	0.68
	Positive with anti-HER2 therapy	220	16	1.09	0.66-1.81	0.74	0.81	0.48-1.36	0.43
	Missing	87	9						
Ki-67	<20%	2145	123	Ref.	-	-	Ref.	-	-
	≥20%	1244	141	1.98	1.56-2.52	<0.001	1.35	0.96-1.91	0.087
	Missing	8	1						
Subtype	Luminal A	2018	110	Ref.	-	-			
	Luminal B (Ki67≥20%)	761	79	1.95	1.47-2.60	<0.001			
	Luminal B (HER2 positive) w/o anti-HER2 therapy	59	13	2.97	1.61-5.49	<0.001			
	Luminal B (HER2 positive) with anti-HER2 therapy	163	12	1.45	0.80-2.61	0.22			
Subtype	HER2 positive w/o anti-HER2 therapy	31	6	2.97	1.22-7.27	0.017			
	HER2 positive with anti-HER2 therapy	57	4	1.60	0.59-4.36	0.36			
	Triple negative	216	32	2.65	1.76-3.98	<0.001			
	Missing	92	9						



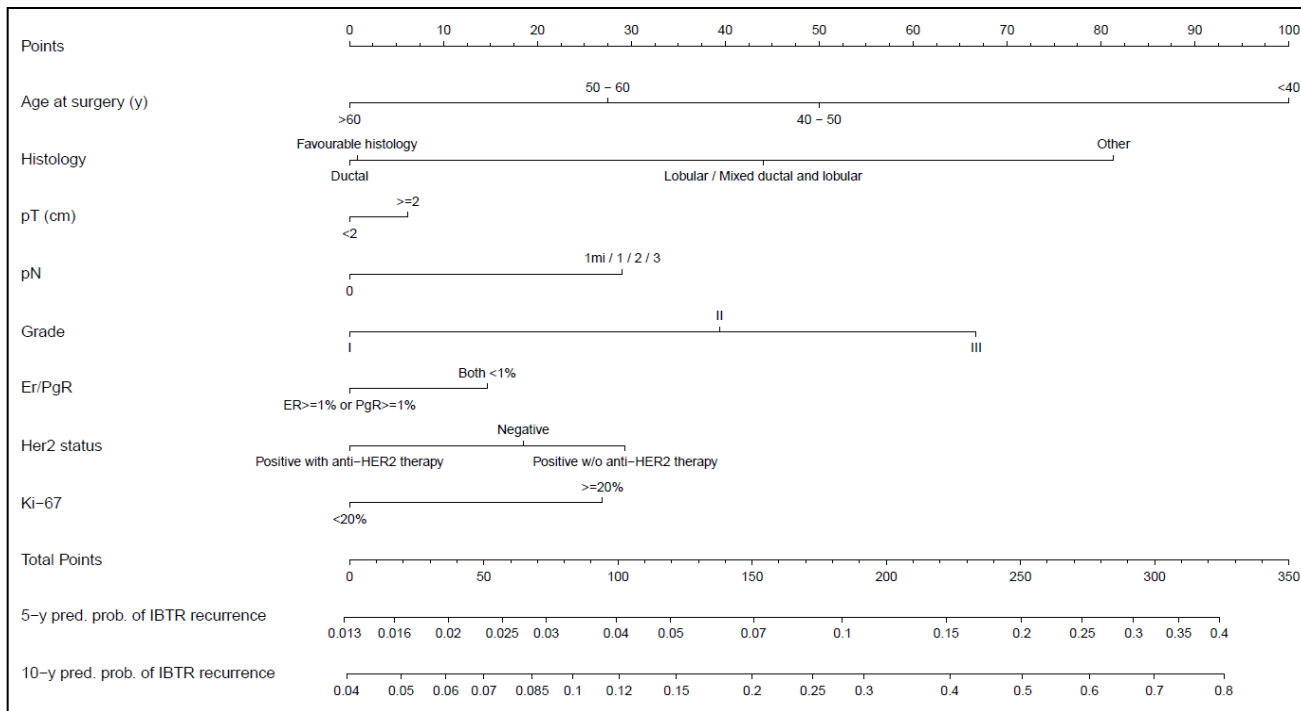
## Results

Data of 3397 patients were analyzed

AT MV analysis, predictors for LR included:

- younger age
- tumor grade 2-3
- histologic subtype
- ER and PR negative status
- tumor size  $\geq 1.5$  cm
- nodal involvement
- molecular subtype other the Luminal A
- HER2 (+) receiving anti-HER2 therapy

## 5-years and 10-years probability of IBTR recurrence, according to the multivariable Fine and Gray regression model



## Results

Median FU: 6.1 years (range 4.3-8.0)

265 local events (7.8%)

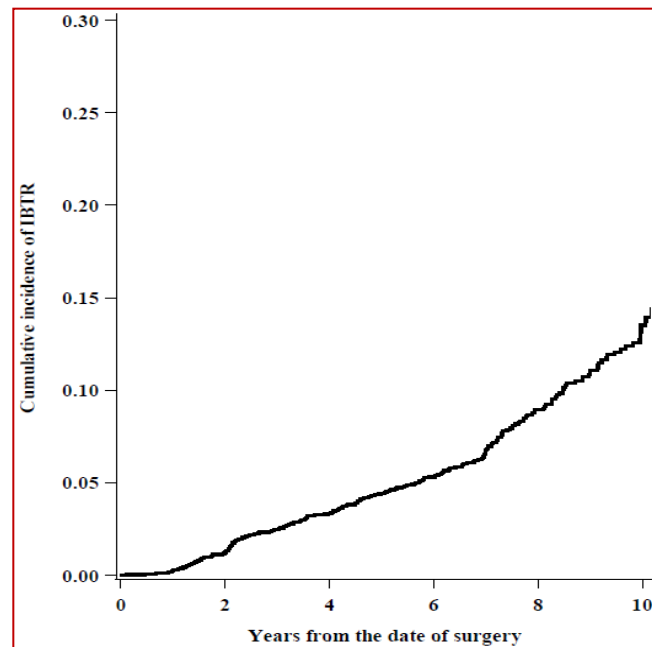
LR cumulative incidence (CIF) of 4.4% ( 95% CI 3.7-5.2) at 5 years and 13.5% (95% CI, 11.7-15.5) at 10 years



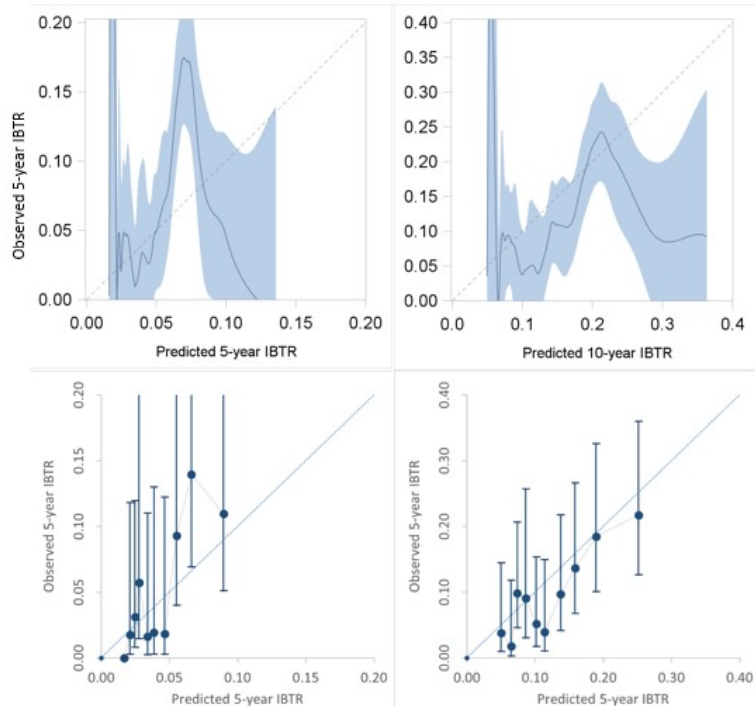
## Results

Cumulative incidence of ipsilateral breast tumor recurrence (IBTR) (N=3397) (Median FU (Q1-Q3) in years: 6.1 (4.3-8.0))

Events	Competing events	Censored	1-y CIF (95% CI)	3-y CIF (95% CI)	5-y CIF (95% CI)	10-y CIF (95% CI)
265 (7.8%)	388 (11.4%)	2744 (80.8%)	0.3 (0.1-0.5)	2.5 (2.0-3.1)	4.4 (3.7-5.2)	13.5 (11.7-15.5)



**Figure 1.** Calibration curves of the nomograms predicting the 5-year and 10-year cumulative incidence of IBTR in 585 patients who received intraoperative radiotherapy in the ELIOT trial (per protocol analysis)



Internal validation was performed on the IOERT arm of the ELIOT phase III randomized trial (585 women)

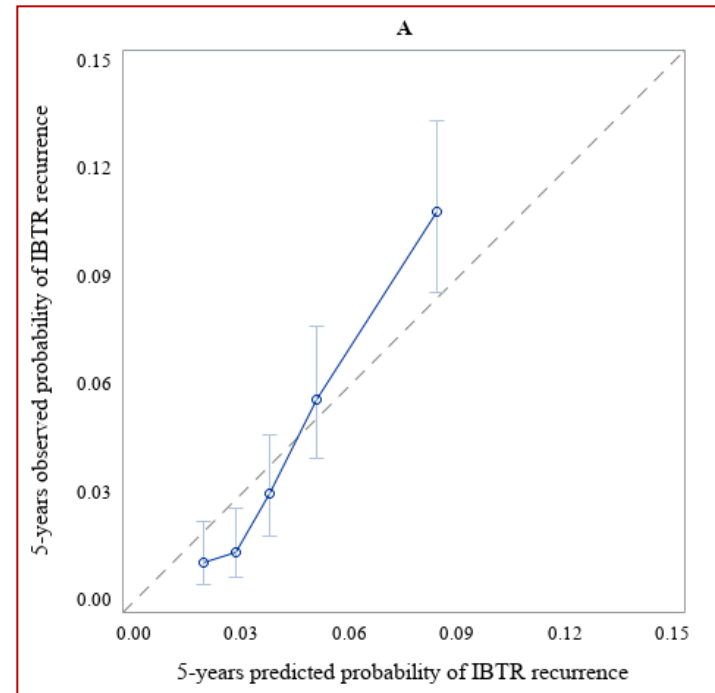
Decile of risk	Observed 5-year IBTR	Predicted 5-year IBTR	Observed 10-year IBTR	Predicted 10-year IBTR
D1 (n=60)	0	1.0	2	3.0
D2 (n=57)	1	1.2	1	3.7
D3 (n=69)	2	1.7	6	5.1
D4 (n=36)	2	1.0	3	3.1
D5 (n=62)	1	2.1	3	6.3
D6 (n=57)	1	2.2	2	6.5
D7 (n=56)	1	2.6	5	7.7
D8 (n=58)	5	3.2	7	9.2
D9 (n=56)	7	3.7	9	10.6
D10 (n=58)	6	5.2	11	14.6
Total (n=569*)	26	23.9	49	69.8
Hosmer & Lemeshow	Chi square = 8.38 with 9 DF (P=0.50)		Chi square = 9.91 with 9 DF (P=0.36)	
Goodness of fit				
*Missing explanatory variables for 16 patients (pT n=2, tumour grade n=12, HER2 n=1, Ki67, n=1)				

**Harrell's c-index: 0.69 (95% CI: 0.66 - 0.73)**

## Results

Calibration plots showed that the observed proportion of LR in the ELIOT arm well fit with the expected proportion as predicted by the logistic models at 5 years ( 26 CIF observed vs 23.9 CIF predicted, Chi square= 8.38 with 9D,  $p= 0.50$ )

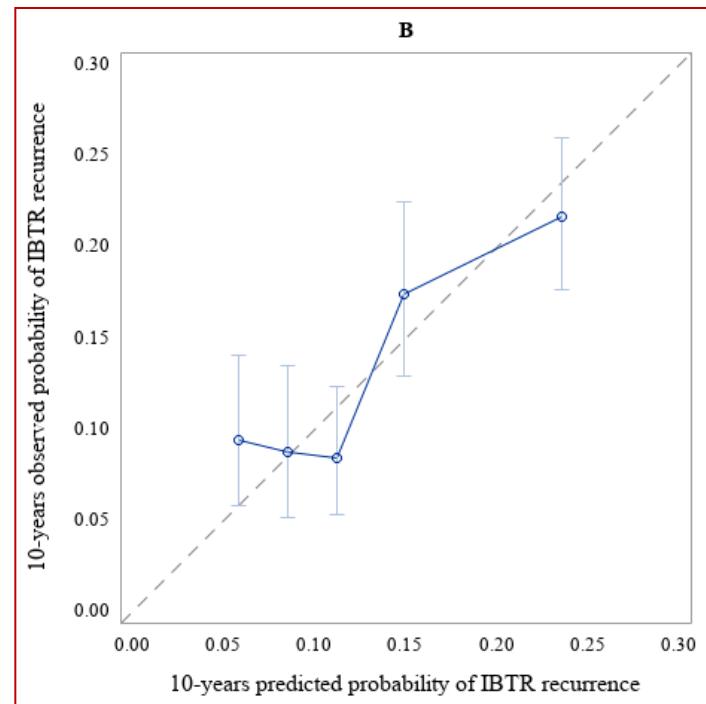
**Harrell's c-index: 0.69 (95% CI: 0.66 - 0.73)**





## Results

At 10 years the estimated probability was not so close to the probability observed in the data, even if the difference was not significant (49 CIF observed vs 69.8 CIF predicted, Chi square= 9.91 with 9 D ,  $p=0.36$ ).



## Conclusion

The nomogram-predicted results were well fitted to the actual outcomes in an internal validation using the ELIOT trial population, with a better risk prediction at 5 years and it can be an useful tool for guiding treatment decision making for patients candidates to IOERT