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Associazione  
Italiana  
Radioterapia  
Oncologica

XXV CONGRESSO NAZIONALE

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## Irradiazione locoregionale con schema ipofrazionato in pazienti con ricostruzione mammaria immediata: valutazione della tossicità acuta e a medio termine

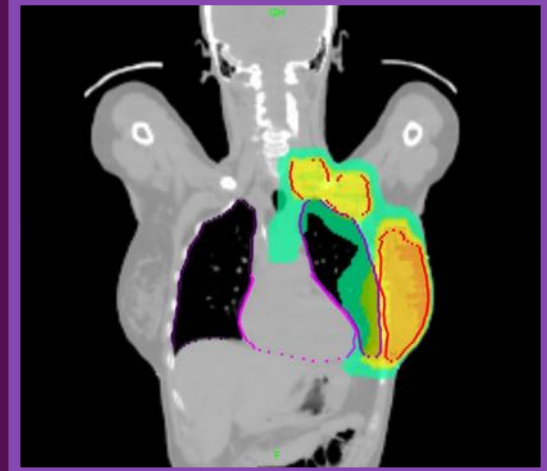
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**Dr.ssa Damaris Patricia Rojas**



# BACKGROUND



## The UK Standardisation of Breast Radiotherapy (START) Trial B of radiotherapy hypofractionation for treatment of early breast cancer: a randomised trial

**Interpretation** A radiation schedule delivering 40 Gy in 15 fractions seems to offer rates of local-regional tumour relapse and late adverse effects at least as favourable as the standard schedule of 50 Gy in 25 fractions.

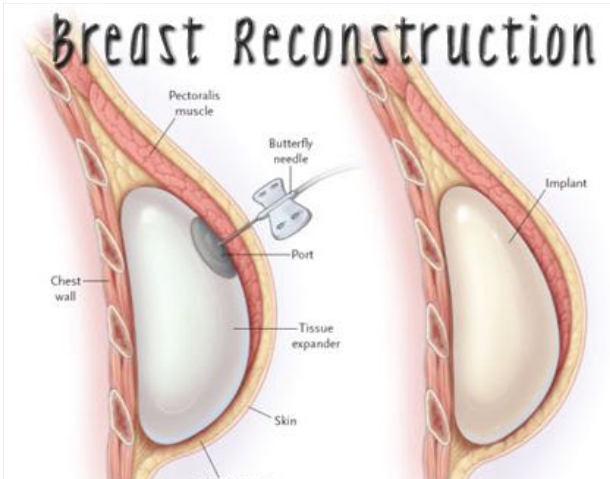
[Radiother Oncol.](#) 2009 Jan;90(1):141-7. doi: 10.1016/j.radonc.2008.09.023. Epub 2008 Nov 1.

### **Incidence of severe capsular contracture following implant-based immediate breast reconstruction with or without postoperative chest wall radiotherapy using 40 Gray in 15 fractions.**

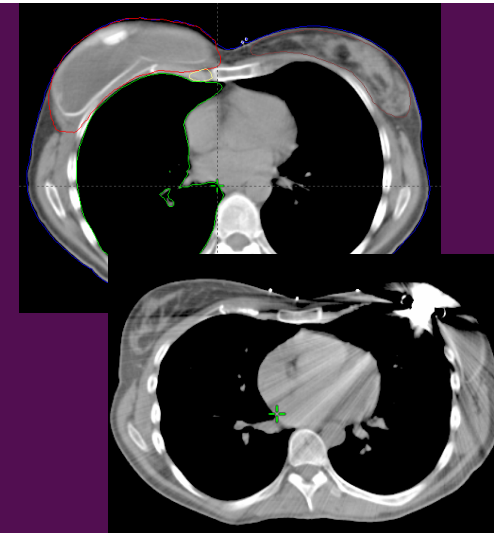
[Whitfield GA](#)<sup>1</sup>, [Horan G](#), [Irwin MS](#), [Malata CM](#), [Wishart GC](#), [Wilson CB](#).

**CONCLUSIONS:** This series showed a significantly higher rate of severe CC with postoperative RT. This finding has important clinical implications, when counselling patients for immediate breast reconstruction.

Importantly for other centres employing the short 3 week RT fractionation schedule (40 Gy in 15 fractions), the rates of severe CC appear comparable to those with 5 week schedules.



# BACKGROUND



[Int J Radiat Oncol Biol Phys. 2003 Sep 1;57\(1\):136-42.](#)

## Radiotherapy and immediate two-stage breast reconstruction with a tissue expander and implant: complications and esthetic results.

[Tallet AV<sup>1</sup>, Salem N, Moutardier V, Ananian P, Braud AC, Zalta R, Cowen D, Houvenaeghel G.](#)

**CONCLUSION:** Immediate breast reconstruction with an expander/implant can be considered even for patients requiring adjuvant treatment. However, the complication and failure rates are three times higher after postexpander radiotherapy.

## The influence of radiotherapy on capsule formation and aesthetic outcome after immediate breast reconstruction using bidimensional anatomical expander implants.

[Behranwala KA<sup>1</sup>, Dua RS, Ross GM, Ward A, A'hern R, Gui GP.](#)

## Complication Rates of Radiation on Tissue Expander and Autologous Tissue Breast Reconstruction

[Tiffany Berry, MD<sup>1,2</sup>, Suzanne Brooks, MD<sup>1</sup>, Nicole Sydow, MD<sup>1</sup>, Risal Djohan, MD<sup>3</sup>, Benjamin Nutter, MD<sup>4</sup>, Joanne Lyons, MD<sup>1</sup>, and Jill Dietz, MD<sup>1</sup>](#)

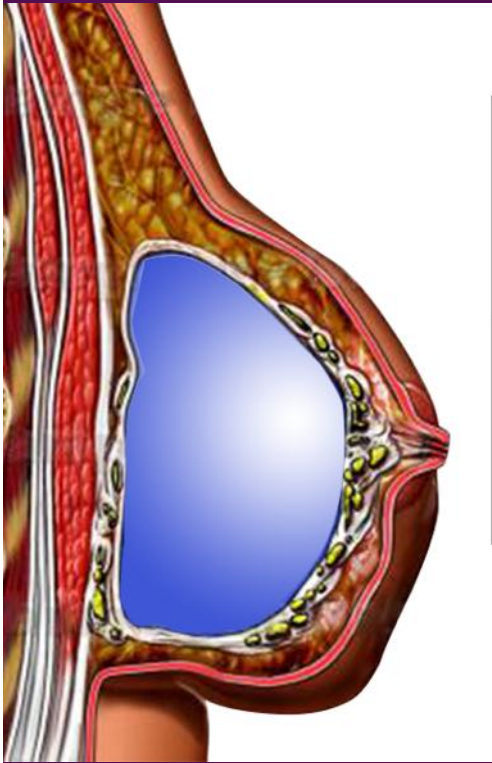
## Risk Factors for Complications of Radiation Therapy on Tissue Expander Breast Reconstructions

[Suzanne Brooks, MD,\\* Risal Djohan, MD,† Rahul Tendulkar, MD,‡ Benjamin Nutter, MS,§ Joanne Lyons, BSN RN,\\* and Jill Dietz MD\\*](#)



## Fattori di rischio per complicanze dopo RT in ricostruzione con protesi/espansore

- IPA
- DM
- BMI (Body Index Mass)
- Fumo



## ENDPOINTS

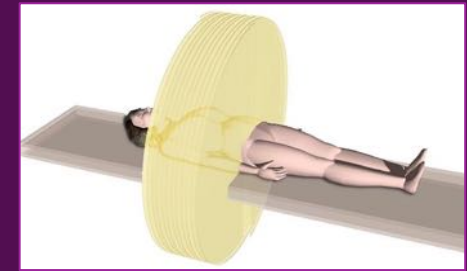
### Endpoint primario:

- Incidenza di contratture capsulari richiedenti una chirurgia maggiore (sostituzione della protesi) con valutazione a 4 anni di follow-up.

### Endpoint secondari:

- Tossicità acuta (scala RTOG)
- Tossicità cronica ( scala SOMA-LENT)
- Controllo locoregionale di malattia
- Sopravvivenza globale

Attualmente valutabili solo gli endpoints secondari di tossicità ,  
per questo sono l'oggetto dell'abstract



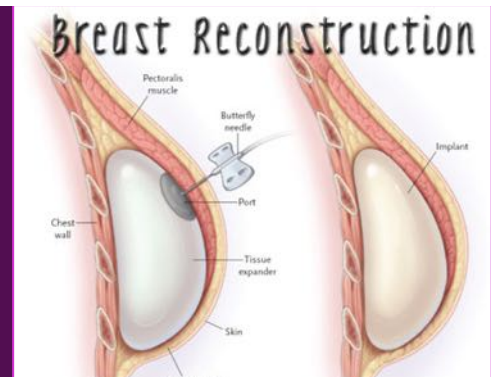
- Studio di fase II
- Totale pazienti: 124 (2012 – 05/2015)
- Espansore: 57
- Protesi: 67
- BMI (Body Mass Index)
- Gruppo CHT: 109 / 124 pazienti
- Gruppo HT: 15/124 pazienti
- Chirurgia-RT: Media = 6.2 mesi, Mediana = 6.7 mesi (Range = 1.8-10.2 mesi)
- Follow-up mediano: 14.5 mesi (range 5.8-35.3 mesi)

**Table 5.** Classification of capsular contracture after prosthesis breast reconstruction (Spear, S. L., & Baker Jr, J. L. (1995))

Class IA	Absolutely natural, cannot tell breast was reconstructed
Class IB	Soft, but implant is detectable by physical examination or inspection because of mastectomy
Class II	Midly firm reconstructed breast with an implant that may be visible and detectable by physical examination
Class III	Moderately firm reconstructed breast. The implant is readily detectable, but the result may be still acceptable
Class IV	Severe capsular contracture with a unacceptable aesthetic outcome and/or significant patient symptoms requiring surgical intervention



## Inclusion/Exclusion Criteria



INCLUSION	EXCLUSION
Diagnosi istologica di ca mammella	Malattia residua macroscopica o microscopica
Tumore localmente avanzato (qualsiasi N3, qualsiasi T4, qualsiasi N2, T3 N1)	Pregressa RT toracica
Rischio intermedio (T3 N0, 1-3 linfonodi positivi con caratteristiche di alto rischio)	Chemioterapia concomitante
Mastectomia con ricostruzione immediata (espansore o protesi)	Malattie connettive
Recidive in pregressa mastectomia	Gravi malattie sistemiche
No metastasi sincrone	Gravidanza
Età > 18 anni	Carcinoma infiammatorio
Trastuzumab (permesso)	
Terapia ormonale (permessa)	
Chemioterapia neoadiuvante (permessa)	

# FRAZIONAMENTO

- 40.05 Gy in 15 Frazioni
- Dose frazione: 2.67 Gy/fr in 3 settimane (5fr/sett)
- IMRT con HELICAL Tomotherapy
- Contouring (Linee guida AIRO)
- Bolus di 0.5 cm per 1/3 o metà del trattamento

	Limite mediale	Limite Laterale	Limite craniale	Limite Caudale	Limite in superficie	Limite Profondo
CTV mammario	Limite palpabile / Giunzione sterno-clavare	Limite palpabile / Linea medio-ascellare, fino al muscolo latissimo del dorso escluso	Limite palpabile / inserzione della II costa	Limite palpabile / limite del tessuto ghiandolare su immagini TC	Cute esclusa (cute compresa in caso di infiltrazione)	Esclusi muscoli pettorali, muscoli della parete toracica e coste
Parete toracica	Giunzione sterno-clavare	Linea medio-ascellare, fino al muscolo latissimo del dorso escluso	Bordo caudale della testa della clavicola	Limite palpabile / limite del tessuto ghiandolare contralaterale su immagini TC	Cute compresa. Cicatrice chirurgica inclusa intesmente	Interfaccia parete-pleura. Inclusi muscoli pettorali, muscoli della parete toracica e coste

	Linfonodi sovraclavari	Linfonodi infraclavari
Craniale	Limite caudale della cartilagine cricoide	Limite superiore del muscolo piccolo pettorale
Mediale	Margine laterale della trachea (escludendo la ghiandola tiroide) - superficie mediale dell'arteria carotide e della vena giugulare interna	Angolo laterale della clavicola, bordo laterale del muscolo succlavio
Laterale	Superficie laterale del muscolo scaleno anteriore e scaleno medio, clavicola (includendo la vena giugulare esterna)	Superficie mediale del muscolo piccolo pettorale
Ventrale	Superficie dorsale del muscolo sternocleidomastoideo	Superficie profonda del muscolo grande pettorale
Dorsale	Superficie ventrale e laterale del muscolo scaleno anteriore e medio, bordo ventrale dell'arteria succlavia	Bordo ventrale e laterale del muscolo succlavio, arteria succlavia - ascellare
Caudale	Inserzione della clavicola nel manubrio sternale	Inserzione della clavicola nel membro clavale

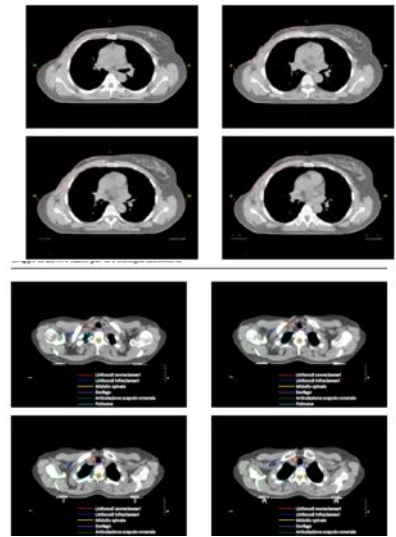


Table 4. Plan evaluation parameters for OARs

OARs	Dose/volume constraints	Treatment plan parameters
Heart	D <sub>0.5cc</sub> < 8 Gy	Gy
	D <sub>0.1cc</sub> < 6 Gy	Gy
	D <sub>max</sub> < 5 Gy (5Gy CMI)	Gy
LAD	D <sub>max</sub> < 10.5 Gy	Gy
	D <sub>0.1cc</sub> < 17.6 Gy	Gy
Ipsilateral lung	D <sub>0.1cc</sub> < 31 Gy	Gy
	D <sub>0.1cc</sub> < 26.4 Gy	Gy
	D <sub>0.1cc</sub> < 17.6 Gy	Gy
Contralateral lung	D <sub>0.1cc</sub> < 13 Gy	Gy
	D <sub>0.1cc</sub> < 10.6 Gy	Gy
Lungs	D <sub>0.1cc</sub> < 9 Gy	Gy
	D <sub>0.1cc</sub> < 10 Gy	Gy
Contralateral Breast	D <sub>0.1cc</sub> < 17.6 Gy	Gy
	D <sub>0.1cc</sub> < 9 Gy	Gy
	D <sub>0.1cc</sub> < 6 Gy	Gy
Brachial plexus	D <sub>0.1cc</sub> < 4.4 Gy	Gy
	D <sub>0.1cc</sub> < 39.6 Gy	Gy
Thyroid	D <sub>0.1cc</sub> < 17.7	Gy
Spinal cord	D <sub>0.1cc</sub> < 17 Gy	Gy
PRV spinal cord	D <sub>0.1cc</sub>	Gy
Liver	V <sub>10</sub> < 10 %	%
	D <sub>0.1cc</sub> < 4.4 Gy	Gy
Stomach	D <sub>0.1cc</sub> < 10 Gy	Gy
Esophagus	D <sub>0.1cc</sub> < 3 Gy	Gy
	D <sub>0.1cc</sub> < 10 Gy	Gy
Humeral head	D <sub>0.1cc</sub> < 30 Gy	Gy

Table 3. PTV dose distribution

Chest wall /IMC		Supraclavicular node	
Ideal	Acceptable	Ideal	Acceptable
V <sub>95%</sub> ≥ 90%	V <sub>90%</sub> ≥ 90%	V <sub>95%</sub> ≥ 85%	V <sub>90%</sub> ≥ 80%
V <sub>90%</sub> ≥ 95%	V <sub>90%</sub> ≥ 90%	V <sub>90%</sub> ≥ 95%	V <sub>90%</sub> ≥ 85%
D <sub>mean</sub> ≥ 99%	D <sub>mean</sub> ≥ 95%	D <sub>mean</sub> ≥ 95%	D <sub>mean</sub> ≥ 90%
D <sub>0.03cc</sub> ≤ 110%	D <sub>0.03cc</sub> ≤ 115%	D <sub>0.03cc</sub> ≤ 110%	D <sub>0.03cc</sub> ≤ 115%
V <sub>107%</sub> ≤ 30%	---	V <sub>107%</sub> ≤ 30%	---



**Tab 1 - Summary Acute toxicity (summary)**



Eventi	N (%)	Max grade≥2
<b>Any toxicity</b>		
0	11 (8.9)	
1	70 (56.4)	
2	43 (34.7)	43 (34.7)
<b>Eritema</b>		
0	16 (12.9)	
1	93 (75.0)	
2	15 (12.1)	15 (12.1)
<b>Epiteliolisi</b>		
0	112 (90.3)	
1	12 (9.7)	
2	0 (-)	0 (-)
<b>Edema</b>		
0	91 (73.4)	
2	33 (26.6)	33 (26.6)
<b>TOTAL</b>	<b>124 (100)</b>	



Tab 2 - Any acute toxicity\*

	G0-G1	≥G2	Total	p-value
<b>Device</b>				
<b>Espansori</b>	41 (61.2)	26 (38.8)	67 (100.0)	
<b>Protesi</b>	40 (70.2)	17 (29.8)	57 (100.0)	0.29
	81	43	124	

\*Massimo grado tra tossicità

## Tab 3 - Any acute Toxicity (Grade≥2) by Subgroups

Characteristics	Any toxicity			Espansori			Protesi			Interaction test*
	N	Events (%)	p-value	N	Events (%)	p-value^	N	Events (%)	p-value^	
<b>AGE (YEARS)</b>			.73^			.47^			.24^	.12
<45	58	21 (36.2)		32	10 (31.2)		26	11 (42.3)		
45-54	41	14 (34.1)		25	12 (48.0)		16	2 (12.5)		
55-64	16	5 (31.2)		5	2 (40.0)		11	3 (27.3)		
>=65	9	3 (33.3)		5	2 (40.0)		4	1 (25.0)		
<b>BMI (kg/m2)</b>			.08^			.28^			.16^	.95
Underweight (<18.5)	3	0 (-)		2	0 (-)		1	0 (-)		
Normal weight (18.5-24.99)	88	30 (34.1)		45	18 (40.0)		43	12 (27.9)		
Overweight (25-29.99)	22	7 (31.8)		15	5 (33.3)		7	2 (28.6)		
Obese (≥30)	9	6 (66.7)		4	3 (75.0)		5	3 (60.0)		
<b>CHEMOTHERAPY</b>			.58			.66			.50	.50
HT alone	15	4 (26.7)		5	1 (20.0)		10	3 (30.0)		
AC (± HT)	21	6 (28.6)		13	5 (38.5)		8	1 (12.5)		
Altra CT (± HT)	88	33 (37.5)		49	20 (40.8)		39	13 (33.3)		
<b>BOLUS</b>			.48			.42			.83	.50
No	119	42 (35.3)		66	26 (39.4)		53	16 (30.2)		
Yes	5	1 (20.0)		1	0 (-)		4	1 (25.0)		
<b>HYPERTENSION</b>			.49			.64			.35	.33
No	109	39 (35.8)		63	24 (38.1)		46	15 (32.6)		
Yes	15	4 (26.7)		4	2 (50.0)		11	2 (18.2)		
<b>SURGERY</b>			.67			.14			.44	.71
Mastectomy	4	0 (-)		1	0 (-)		3	0 (-)		
Mastectomy +BLS	3	0 (-)		0	0 (-)		3	0 (-)		
Mastectomy +DA	72	22 (30.6)		44	14 (31.8)		28	8 (28.6)		
Mastectomy +BLS+DA	36	18 (50.0)		22	12 (54.6)		14	6 (42.9)		
Altro	9	9 (33.3)		0			9	3 (33.3)		
<b>All</b>	<b>124</b>	<b>43 (34.7)</b>		<b>67</b>	<b>26 (38.8)</b>		<b>57</b>	<b>17 (29.8)</b>		

## Tab 4 - Edema [acute toxicity] (Grade≥2) by Subgroups

Characteristics	Edema			Espansori			Protesi			Interaction test*
	N	Events (%)	p-value	N	Events (%)	p-value^	N	Events (%)	p-value^	
<b>Age (years)</b>			.93^			.58^			.68^	.50
<45	58	16 (27.6)		32	8 (25.0)		26	8 (30.8)		
45-54	41	10 (24.4)		25	8 (32.0)		16	2 (12.5)		
55-64	16	4 (25.0)		5	1 (20.0)		11	3 (27.3)		
>=65	9	3 (33.3)		5	2 (40.0)		4	1 (25.0)		
<b>BMI (kg/m2)</b>			.01^			.09^			.06^	.90
Underweight (<18.5)	3	0 (-)		2	0 (-)		1	0 (-)		
Normal weight (18.5-24.99)	88	21 (23.9)		45	12 (26.7)		43	9 (20.9)		
Overweight (25-29.99)	22	6 (27.3)		15	4 (26.7)		7	2 (28.6)		
Obese (≥30)	9	6 (66.7)		4	3 (75.0)		5	3 (60.0)		
<b>Chemotherapy</b>			.51			.90			.17	.22
HT alone	15	3 (20.0)		5	1 (20.0)		10	2 (20.0)		
AC (± HT)	21	4 (19.0)		13	4 (30.8)		8	0 (-)		
Altra CT (± HT)	88	26 (29.6)		49	14 (29.6)		39	12 (30.8)		
<b>Bolus</b>			.73			.52			.98	.54
No	119	32 (26.9)		66	19 (28.8)		53	13 (24.5)		
Yes	5	1 (20.0)		1	0 (-)		4	1 (25.0)		
<b>Hypertension</b>			.99			.32			.58	.27
No	109	29 (26.6)		63	17 (27.0)		46	12 (26.1)		
Yes	15	4 (26.7)		4	2 (50.0)		11	2 (18.2)		
<b>Surgery</b>			.36			.76			.32	.38
Mastectomy	4	0 (-)		1	0 (-)		3	0 (-)		
Mastectomy +BLS	3	0 (-)		0	0 (-)		3	0 (-)		
Mastectomy +DA	72	18 (25.0)		44	12 (27.3)		28	6 (21.4)		
Mastectomy +BLS+DA	36	13 (36.1)		22	7 (31.8)		14	6 (42.9)		
Altro	9	2 (22.2)		0			9	2 (22.2)		
<b>All</b>	124	33 (26.6)		67	19 (28.4)		57	14 (24.6)		

# RISULTATI

Tab 1 - SOMA LENT any toxicity (summary)

Eventi	All patients N (%)	Espansori N (%)	Protesi N (%)	p-value
<b>Dolore</b>				<b>0.05</b>
0	61 (82.4)	35 (92.1)	26 (72.2)	
1	10 (13.5)	2 (5.3)	8 (22.2)	
2	3 (4.1)	1 (2.6)	2 (5.6)	
<b>Fibrosi</b>				<b>0.005</b>
0	52 (70.3)	33 (86.8)	19 (52.8)	
1	12 (16.2)	2 (5.3)	10 (27.8)	
2	6 (8.1)	3 (7.9)	3 (8.3)	
3	4 (5.4)	0 (-)	4 (11.1)	
<b>Ipopigmentazione</b>				<b>0.009</b>
0	68 (91.9)	38 (100.0)	30 (83.3)	
1	6 (8.1)	0 (-)	6 (16.7)	
<b>Iperpigmentazione</b>				<b>0.46</b>
0	62 (83.8)	33 (86.8)	29 (80.6)	
1	12 (16.2)	5 (13.2)	7 (19.4)	
<b>Linfedema braccio*</b>				<b>0.10</b>
0	57 (85.1)	32 (91.4)	25 (78.1)	
1	9 (13.4)	2 (5.7)	7 (21.9)	
3	1 (1.5)	1 (2.9)	0 (-)	
<b>Contrattura capsulare*</b>				<b>&lt;0.001</b>
IA	9 (13.0)	8 (21.6)	1 (3.1)	
IB	9 (13.0)	6 (16.2)	3 (9.4)	
II	31 (44.9)	18 (48.6)	13 (40.6)	
III	17 (24.6)	5 (13.5)	12 (37.5)	
IV	3 (4.3)	0 (-)	3 (9.4)	
<b>TOTAL</b>	<b>74 (100)</b>	<b>38 (100)</b>	<b>36 (100)</b>	

## Tab 2 - SOMA LENT toxicity ( $\geq G2$ )

Eventi	All patients	Espansori	Protesi	p-value
	N (%)	N (%)	N (%)	
<b>Dolore</b>				0.52
<b>G0-G1</b>	71 (95.9)	37 (97.4)	34 (94.4)	
<b>G2-G3</b>	3 (4.1)	1 (2.6)	2 (5.6)	
<b>Fibrosi</b>				0.15
<b>G0-G1</b>	64 (86.5)	35 (92.1)	29 (80.6)	
<b>G2-G3</b>	10 (13.5)	3 (7.9)	7 (19.4)	
<b>Ipopigmentazione</b>				-
<b>G0-G1</b>	74 (100.0)	38 (100.0)	36 (100.0)	
<b>Iperpigmentazione</b>				-
<b>G0-G1</b>	74 (100.0)	38 (100.0)	36 (100.0)	
<b>Linfedema braccio*</b>				0.33
<b>G0-G1</b>	66 (98.5)	34 (97.1)	32 (100.0)	
<b>G2-G3</b>	1 (1.5)	1 (2.9)	0 (-)	
<b>Contrattura capsulare*</b>				0.002
<b>I/II</b>	49 (70.9)	32 (86.4)	17 (53.1)	
<b>III/IV</b>	20 (28.9)	5 (13.5)	15 (46.9)	
<b>TOTAL</b>	74 (100)	38 (100)	36 (100)	

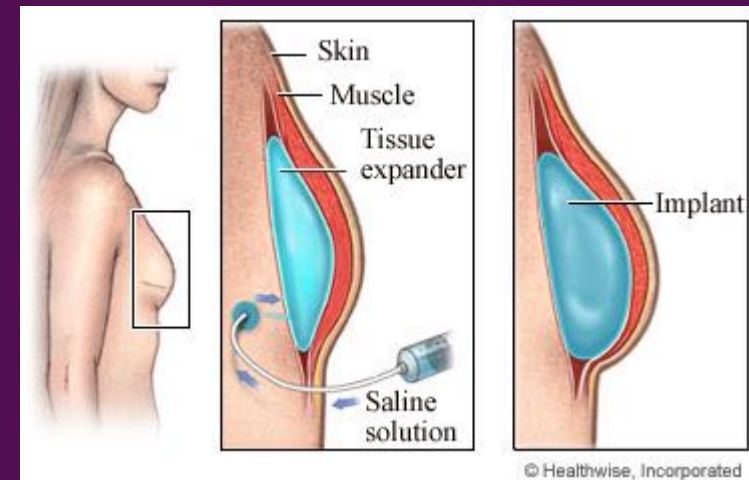
# CONCLUSIONI

Si conferma fattibilità dell'ipofrazionamento nelle pazienti sottoposte a mastectomia con ricostruzione immediata (espansore/protesi):

- Tossicità acuta soddisfacente
- Nessun fattore (età, BMI, CT, bolus, ipertensione, chirurgia ) risulta essere associato alla tossicità acuta nella popolazione generale , né nei due sottogruppi
- Edema di grado  $\geq 2$  aumenta all'aumentare dell'indice di massa corporea

# CONCLUSIONI

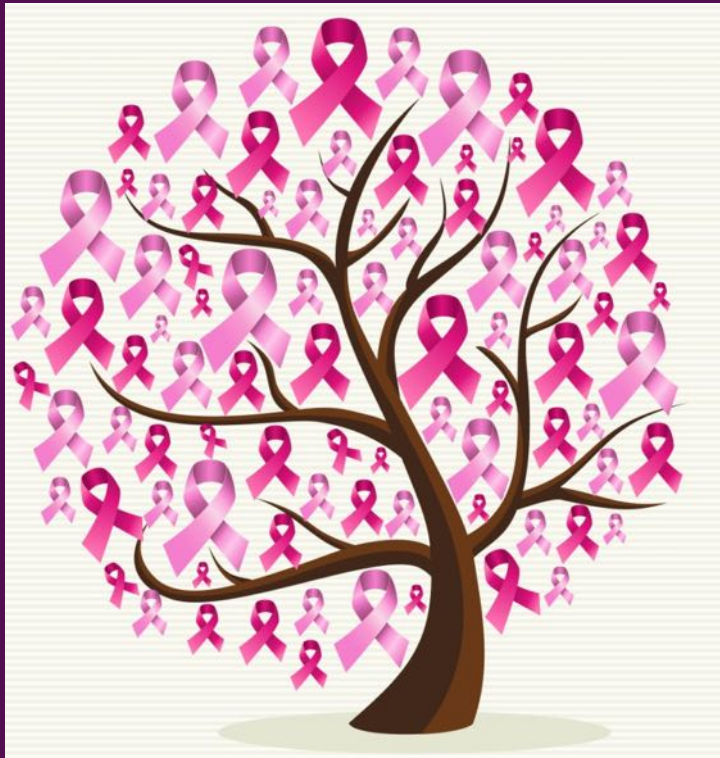
- Tossicità intermedia parzialmente valutabile
- Tossicità cronica SOMA-LENT (espansore < protesi)
- Gruppo protesi > contratture severe (15/36; 46.9%) vs (5/38; 13.5%).
- Numeri molto bassi.







Lo studio prosegue fino al raggiungimento della dimensione campionaria e del follow-up adeguato



**Grazie**