

SOCIÉTÉ FRANÇAISE DE SÉNOLOGIE
ET DE PATHOLOGIE MAMMAIRE

Les récurrences loco-régionales

Y-a-t-il une place pour une 2^{ème} irradiation ?

Jean-Michel Hannoun-Levi

Pôle de Radiothérapie – Centre Antoine Lacassagne - NICE

Congrès SFPM 2013 - 13 au 15 novembre 2013 - Corum - Montpellier

Taux d'incidence du cancer du sein
 $\approx 22/100.000$



<http://www.livestrong.com/article/55159-statistics-breast-cancer-recurrence/>

Taux d'incidence du cancer du sein

≈ 22/100.000



Taux d'incidence de rechute locale homolatérale (RLH)

≈ 1.3 à 1.7% entre la 2^{ème} et la 7^{ème} année

≈ 0.4%/an @ 10 ans

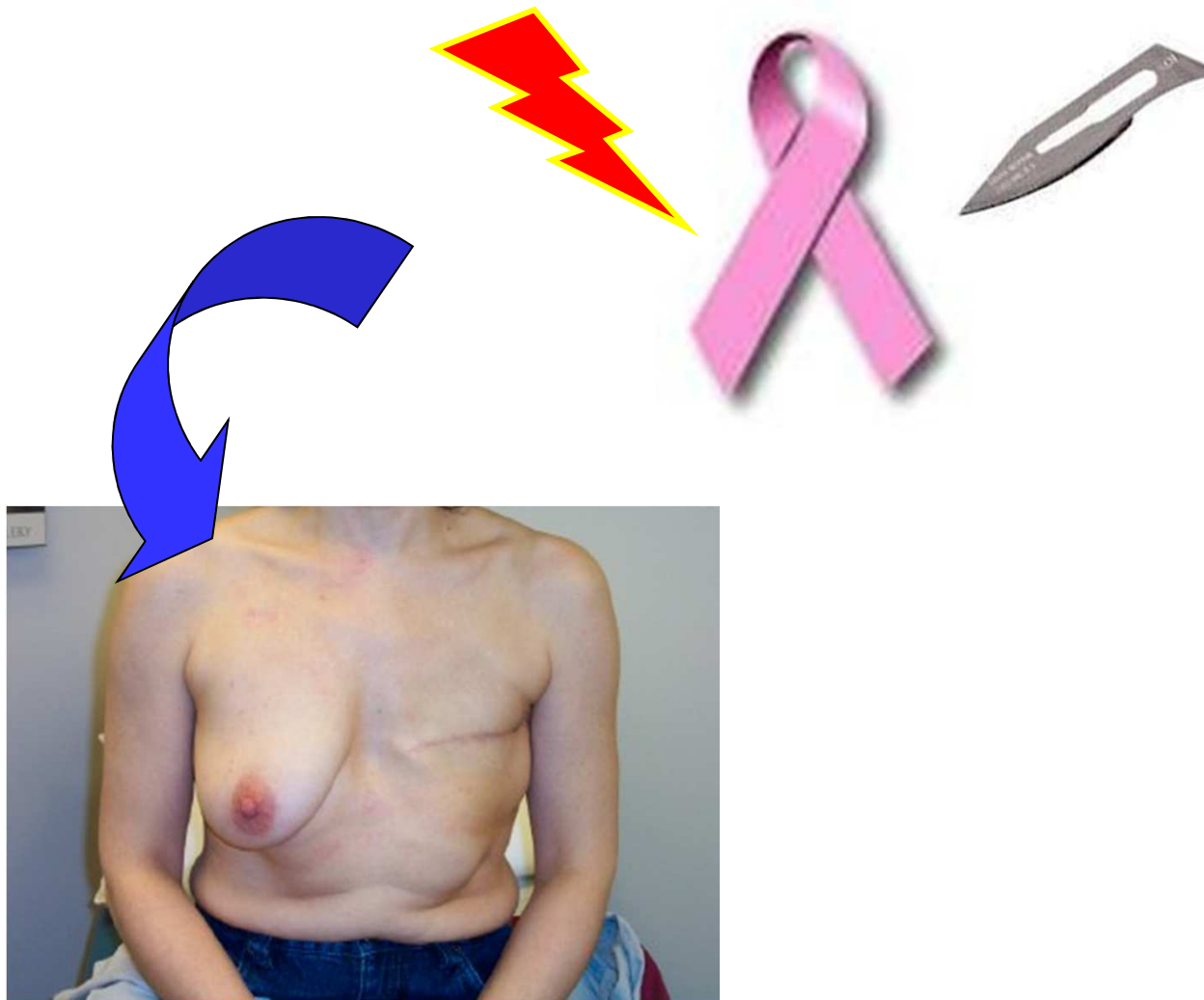
<http://www.livestrong.com/article/55159-statistics-breast-cancer-recurrence/>

Quel traitement local pour une RLH?

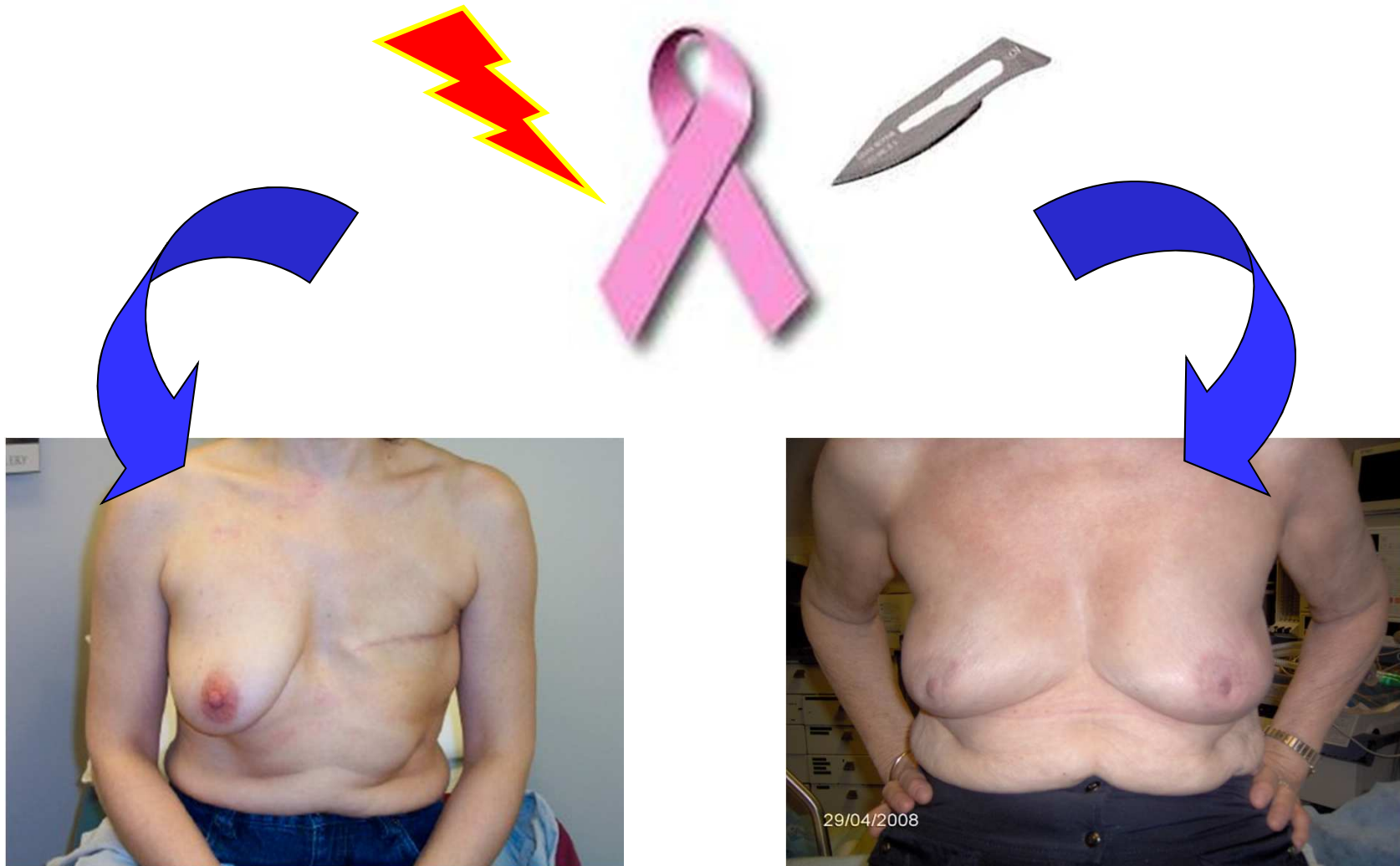
Quel traitement local pour une RLH?



Quel traitement local pour une RLH?



Quel traitement local pour une RLH?

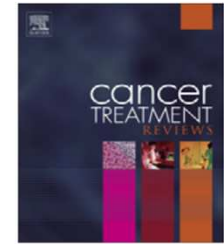




Contents lists available at SciVerse ScienceDirect

Cancer Treatment Reviews

journal homepage: www.elsevierhealth.com/journals/ctrv



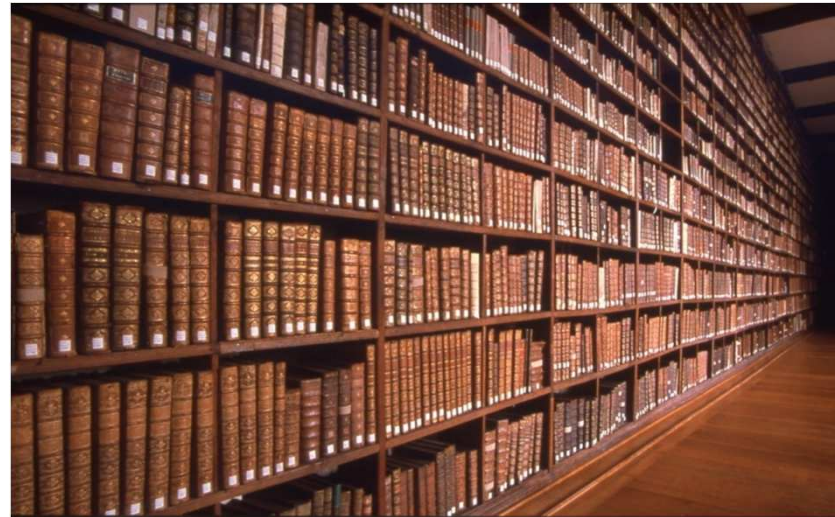
Anti-tumor treatment

Local treatment options for ipsilateral breast tumour recurrence

Jean-Michel Hannoun-Levi ^{a,*}, Tarik Ihrai ^b, Adel Courdi ^a

^a Department of Radiation Therapy, Antoine Lacassagne Cancer Center, University of Nice-Sophia, Nice, France

^b Department of Surgical Oncology, Antoine Lacassagne Cancer Center, University of Nice-Sophia, Nice, France





Mastectomie

	# pts	MFU (months)	2 nd LR (%)	5-year DMFS (%)	5-year DFS (%)	5-year CSS (%)	5-year OS (%)
Kurtz 1988	66	84	12	-	-	-	-
Fowble 1990	52	25	-	-	59	-	84
Osborne 1992	46	28	15	-	55	-	76
Cajucoum 1993	25*	52	32	-	51	-	65
Abner 1993	123	39	6	-	41	-	-
Voogd 1999	266	60	25	47	≈ 10%	-	61
Salvadori 1999	134	-	4	55 (4-y)	-	-	70
Doyle 2001	112	44	3	47 (10-y)	-	-	69 (10-y)
Huang 2002	126	-	12	45 (10-y)	-	62 (10-y)	58 (10-y)
Alpert 2005	116	244	7	32 (10-y)	-	73 (10-y)	66 (10-y)
Chen 2008	568	-	-	-	-	-	78



Tumorectomie

Authors	# pts	MFU (months)	2 nd LR (%)	DMFS (%)	10-year CSS (%)	10-year OS (%)
Kurtz 1988/1991	50	51	32	-	64	42
Abner 1993	16	39	31	-	-	-
Dalberg 1998	17	-	12.5	-	-	-
Salvadori 1999	57	-	19	80 (4-y)	-	85 (5-y)
Alpert 2005	30	244	7	24 (10-y)	61	58
Chen 2008	179	-	-	-	-	57

≥ 20%



Tumorectomie + re-irradiation

Authors	# pts	MFU (months)	IT	Dose (Gy)	2 nd LR (%)	5-year DFS (%)	5-year OS (%)	G3-4 tox (%)	Exc/Gc CR (%)
Maulard 1995	15	48	ILB	30	26	31	61	8	53
	23	36	ILB*	60-70	17	41	50		
Deutsch 2002	39	63	e- TB	50	21	68	78	-	69
Hannoun-Levi 2004	24	50	ILB	30	25	69	92	10	-
	45		ILB	46	11				-
Chadha 2008	15	36	ILB	30-45	7	-	100 (3-y)	0	100
Trombetta 2008/2009	25	38	ILB/MHB	45-50/34	4	-	-	14	92
Guix 2010	36	89	IHB	30	3	64 (10-y)	97 (10-y)	0	-
Hannoun-Levi 2010	42	21	IHB	34	2	-	-	3	97
Kauer-Dorner 2012	39	57	IPB	56	7	77	87	7	37

≈ 10%

* Without 2nd lumpectomy



Tumorectomie + re-irradiation

Authors	# pts	MFU (months)	IT	Dose (Gy)	2 nd LR (%)	5-year DFS (%)	5-year OS (%)	G3-4 tox (%)	Exc/Gc CR (%)
Maulard 1995	15	48	ILB	30	26	31	61	8	53
	23	36	ILB*	60-70	17	41	50		
Deutsch 2002	39	63	e- TB	50	21	68	78	-	69
Hannoun-Levi 2004	24	50	ILB	30	25	69	92	10	-
	45		ILB	46	11				-
Chadha 2008	15	36	ILB	30-45	7	-	100 (3-y)	0	100
Trombetta 2008/2009	25	38	ILB/MHB	45-50/34	4	-	-	14	92
Guix 2010	36	89	IHB	30	3	64 (10-y)	97 (10-y)	0	-
Hannoun-Levi 2010	42	21	IHB	34	2	-	-	3	97
Kauer-Dorner 2012	39	57	IPB	56	7	77	87	7	37

* Without 2nd lumpectomy



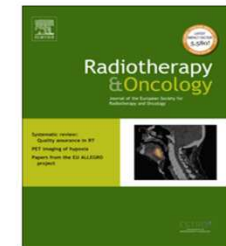
ESTRO



Contents lists available at SciVerse ScienceDirect

Radiotherapy and Oncology

journal homepage: www.thegreenjournal.com



Original article

Accelerated partial breast irradiation with interstitial brachytherapy as second conservative treatment for ipsilateral breast tumour recurrence: Multicentric study of the GEC-ESTRO Breast Cancer Working Group

Jean-Michel Hannoun-Levi^{a,*}, Alexandra Resch^b, Jocelyn Gal^c, Daniela Kauer-Dorner^b, Vratislav Strnad^d, Peter Niehoff^e, Kristina Loessl^f, Gyoergy Kovács^g, Erick Van Limbergen^h, Csaba Polgárⁱ,
On behalf of the GEC-ESTRO Breast Cancer Working Group

^aDepartment of Radiation Oncology, Antoine Lacassagne Cancer Center, University of Nice-Sophia, France; ^bDepartment of Radiotherapy and Radiobiology, University of Vienna, Austria; ^cBiostatistic Unit, Antoine Lacassagne Cancer Center, Nice, France; ^dDepartment of Radiation Oncology, University Hospital Erlangen; ^eDepartment of Radiotherapy, City Hospital Cologne, Germany; ^fDepartment of Radiation Oncology, Bernes, Switzerland; ^gInterdisciplinary Brachytherapy Unit, University of Luebeck, Germany; ^hDepartment of Radiation Oncology, University Hospital Gasthuisberg, Leuven, Belgium; ⁱCenter of Radiotherapy, National Institute of Oncology, Budapest, Hungary

GEC-ESTRO Breast Cancer WG study

✓ Période d'étude : 09/00 – 09/10

GEC-ESTRO Breast Cancer WG study

- ✓ Période d'étude : 09/00 – 09/10
- ✓ # pts RLH : 217

GEC-ESTRO Breast Cancer WG study

- ✓ Période d'étude : 09/00 – 09/10
- ✓ # pts RLH : 217



GEC-ESTRO Breast Cancer WG study

- ✓ Période d'étude : 09/00 – 09/10
- ✓ # pts RLH : 217



Matériel & Méthode - Patients

✓ Age médian (years):

– primaire (P)	50	[19 - 83]
– rechute (R)	61	[28 - 85]

Matériel & Méthode - Patients

✓ Age médian (years):

– primaire (P) 50 [19 - 83]

– rechute (R) 61 [28 - 85]

✓ Interval: 9.4 [1.1 - 35.4]

[P - R] (ans)

Matériel & Méthode - Tumeurs

Characteristic	Primary		IBTR		
	#	Median % [range]	#	Median % [range]	
#Patients			217		
Age (years)		50.3 [19–83]		60.6 [28–85]	
Time to IBTR (years)				10.1 [1.1–35.3]	
IBTR site	ITB		111	51.2	
	Close to ITB		35	16.1	
	Other quadrant		45	20.7	
	Unknown		26	12.0	
pT size (mm)		15.4 [1–60]		12.4 [1–55]	
pLN status	Negative	141	65.0	59	27.2
	Positive	35	16.1	8	3.7
	Unknown	41	18.9	150	69.1
HG	1	36	16.6	34	15.7
	2	60	27.6	81	37.3
	3	40	18.4	58	26.7
	Unknown	81	37.3	44	20.3
HR status	Positive	93	42.9	158	72.8
	Negative	34	15.6	43	19.8
	Unknown	90	41.5	16	7.4
Her2 status	Negative	39	18.0	122	56.2
	+	7	3.2	28	12.9
	++	9	4.1	13	6.0
	+++	11	5.1	28	12.9
	Unknown	151	69.6	26	12.0
Hormonal therapy	Yes	84	38.7	141	65.0
	No	103	47.5	71	32.7
	Unknown	30	13.8	5	2.3
Chemotherapy	Yes	76	35.1	43	19.8
	No	137	63.1	171	78.8
	Unknown	4	1.8	3	1.4
Trastuzumab	Yes	3	1.4	4	1.8
	No	214	98.6	213	98.2
WBI dose (Gy)		56.0 [30–69.6]			

Matériel & Méthode - Tumeurs

Characteristic	Primary		IBTR	
	#	Median % [range]	#	Median % [range]
#Patients			217	
Age (years)		50.3 [19-83]		60.6 [28-85]
Time to IBTR (years)				10.1 [1.1-35.3]
IBTR site				
	ITB		111	51.2
	Close to ITB		35	16.1
	Other quadrant		45	20.7
	Unknown		26	12.0
pT size (mm)		15.4 [1-60]		12.4 [1-55]
pLN status				
	Negative	141	59	27.2
	Positive	35	8	3.7
	Unknown	41	150	69.1
HG				
	1	36	34	15.7
	2	60	81	37.3
	3	40	58	26.7
	Unknown	81	44	20.3
HR status				
	Positive	93	158	72.8
	Negative	34	43	19.8
	Unknown	90	16	7.4
Her2 status				
	Negative	39	122	56.2
	+	7	28	12.9
	++	9	13	6.0
	+++	11	28	12.9
	Unknown	151	26	12.0
Hormonal therapy				
	Yes	84	141	65.0
	No	103	71	32.7
	Unknown	30	5	2.3
Chemotherapy				
	Yes	76	43	19.8
	No	137	171	78.8
	Unknown	4	3	1.4
Trastuzumab				
	Yes	3	4	1.8
	No	214	213	98.2
WBI dose (Gy)		56.0 [30-69.6]		

Matériel & Méthode - Tumeurs

Characteristic	Primary		IBTR		
	#	Median % [range]	#	Median % [range]	
#Patients			217		
Age (years)		50.3 [19–83]		60.6 [28–85]	
Time to IBTR (years)				10.1 [1.1–35.3]	
IBTR site	ITB		111	51.2	
	Close to ITB		35	16.1	
	Other quadrant		45	20.7	
	Unknown		26	12.0	
pT size (mm)		15.4 [1–60]		12.4 [1–55]	
pLN status	Negative	141	65.0	59	27.2
	Positive	35	16.1	8	3.7
	Unknown	41	18.9	150	69.1
HG	1	36	16.6	34	15.7
	2	60	27.6	81	37.3
	3	40	18.4	58	26.7
	Unknown	81	37.3	44	20.3
HR status	Positive	93	42.9	158	72.8
	Negative	34	15.6	43	19.8
	Unknown	90	41.5	16	7.4
Her2 status	Negative	39	18.0	122	56.2
	+	7	3.2	28	12.9
	++	9	4.1	13	6.0
	+++	11	5.1	28	12.9
Unknown	Unknown	151	69.6	26	12.0
	Yes	84	38.7	141	65.0
	No	103	47.5	71	32.7
Unknown	Unknown	30	13.8	5	2.3
	Yes	76	35.1	43	19.8
	No	137	63.1	171	78.8
Unknown	Unknown	4	1.8	3	1.4
	Yes	3	1.4	4	1.8
	No	214	98.6	213	98.2
WBI dose (Gy)		56.0 [30–69.6]			

Matériel & Méthode - Tumeurs

Characteristic	Primary		IBTR	
	#	Median % [range]	#	Median % [range]
#Patients			217	
Age (years)		50.3 [19–83]		60.6 [28–85]
Time to IBTR (years)				10.1 [1.1–35.3]
IBTR site	ITB		111	51.2
	Close to ITB		35	16.1
	Other quadrant		45	20.7
	Unknown		26	12.0
pT size (mm)		15.4 [1–60]		12.4 [1–55]
pLN status	Negative	141	59	27.2
	Positive	35	8	3.7
	Unknown	41	150	69.1
HG	1	36	34	15.7
	2	60	81	37.3
	3	40	58	26.7
	Unknown	81	44	20.3
HR status	Positive	93	158	72.8
	Negative	34	43	19.8
	Unknown	90	16	7.4
Her2 status	Negative	39	122	56.2
	+	7	28	12.9
	++	9	13	6.0
	+++	11	28	12.9
	Unknown	151	26	12.0
Hormonal therapy	Yes	84	141	65.0
	No	103	71	32.7
	Unknown	30	5	2.3
Chemotherapy	Yes	76	43	19.8
	No	137	171	78.8
	Unknown	4	3	1.4
Trastuzumab	Yes	3	4	1.8
	No	214	213	98.2
WBI dose (Gy)		56.0 [30–69.6]		

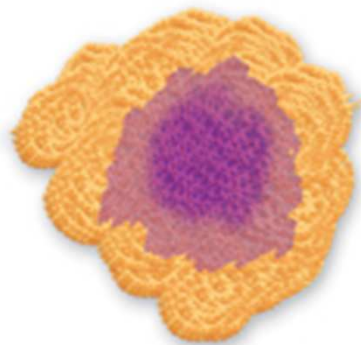
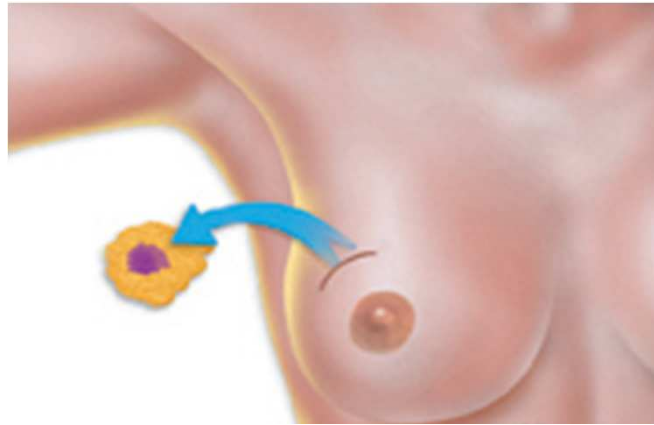
Matériel & Méthode - Tumeurs

Characteristic	Primary		IBTR	
	#	Median % [range]	#	Median % [range]
#Patients			217	
Age (years)		50.3 [19–83]		60.6 [28–85]
Time to IBTR (years)				10.1 [1.1–35.3]
IBTR site				
	ITB		111	51.2
	Close to ITB		35	16.1
	Other quadrant		45	20.7
	Unknown		26	12.0
pT size (mm)		15.4 [1–60]		12.4 [1–55]
pLN status				
	Negative	141	59	27.2
	Positive	35	8	3.7
	Unknown	41	150	69.1
HG				
	1	36	34	15.7
	2	60	81	37.3
	3	40	58	26.7
	Unknown	81	44	20.3
HR status				
	Positive	93	158	72.8
	Negative	34	43	19.8
	Unknown	90	16	7.4
Her2 status				
	Negative	39	122	56.2
	+	7	28	12.9
	++	9	13	6.0
	+++	11	28	12.9
	Unknown	151	26	12.0
Hormonal therapy				
	Yes	84	141	65.0
	No	103	71	32.7
	Unknown	30	5	2.3
Chemotherapy				
	Yes	76	43	19.8
	No	137	171	78.8
	Unknown	4	3	1.4
Trastuzumab				
	Yes	3	4	1.8
	No	214	213	98.2
WBI dose (Gy)		56.0 [30–69.6]		

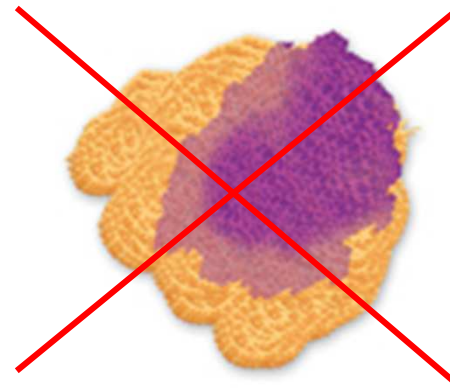
Matériel & Méthode - Tumeurs

Characteristic	Primary			IBTR	
		#	Median % [range]	#	Median % [range]
#Patients				217	
Age (years)			50.3 [19–83]		60.6 [28–85]
Time to IBTR (years)					10.1 [1.1–35.3]
IBTR site	ITB			111	51.2
	Close to ITB			35	16.1
	Other quadrant			45	20.7
	Unknown			26	12.0
pT size (mm)			15.4 [1–60]		12.4 [1–55]
pLN status	Negative	141	65.0	59	27.2
	Positive	35	16.1	8	3.7
	Unknown	41	18.9	150	69.1
HG	1	36	16.6	34	15.7
	2	60	27.6	81	37.3
	3	40	18.4	58	26.7
	Unknown	81	37.3	44	20.3
HR status	Positive	93	42.9	158	72.8
	Negative	34	15.6	43	19.8
	Unknown	90	41.5	16	7.4
Her2 status	Negative	39	18.0	122	56.2
	+	7	3.2	28	12.9
	++	9	4.1	13	6.0
	+++	11	5.1	28	12.9
	Unknown	151	69.6	26	12.0
Hormonal therapy	Yes	84	38.7	141	65.0
	No	103	47.5	71	32.7
	Unknown	30	13.8	5	2.3
Chemotherapy	Yes	76	35.1	43	19.8
	No	137	63.1	171	78.8
	Unknown	4	1.8	3	1.4
Trastuzumab	Yes	3	1.4	4	1.8
	No	214	98.6	213	98.2
WBI dose (Gy)			56.0 [30–69.6]		

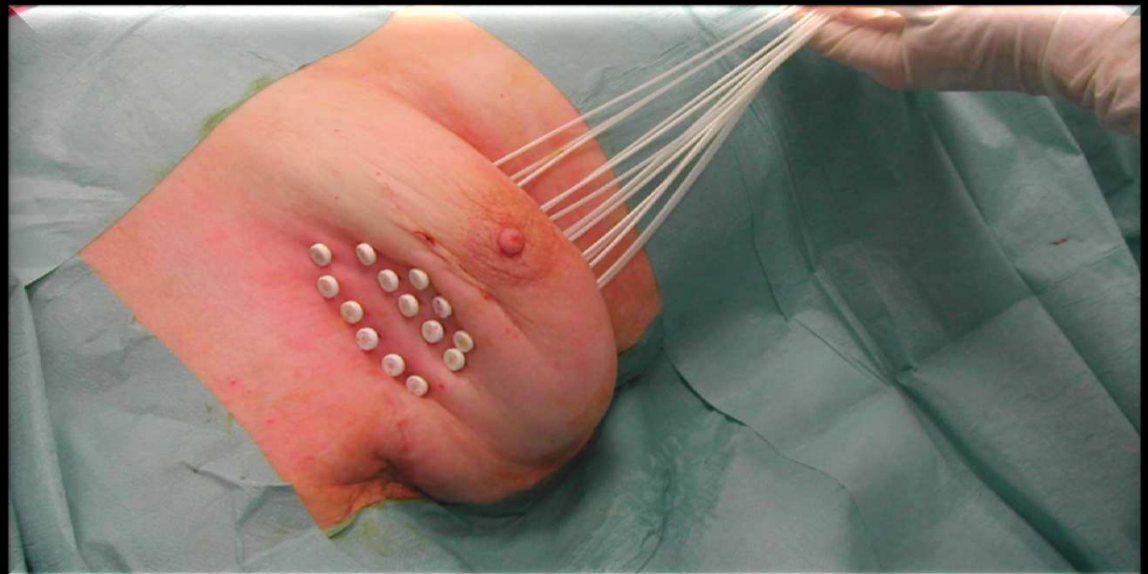
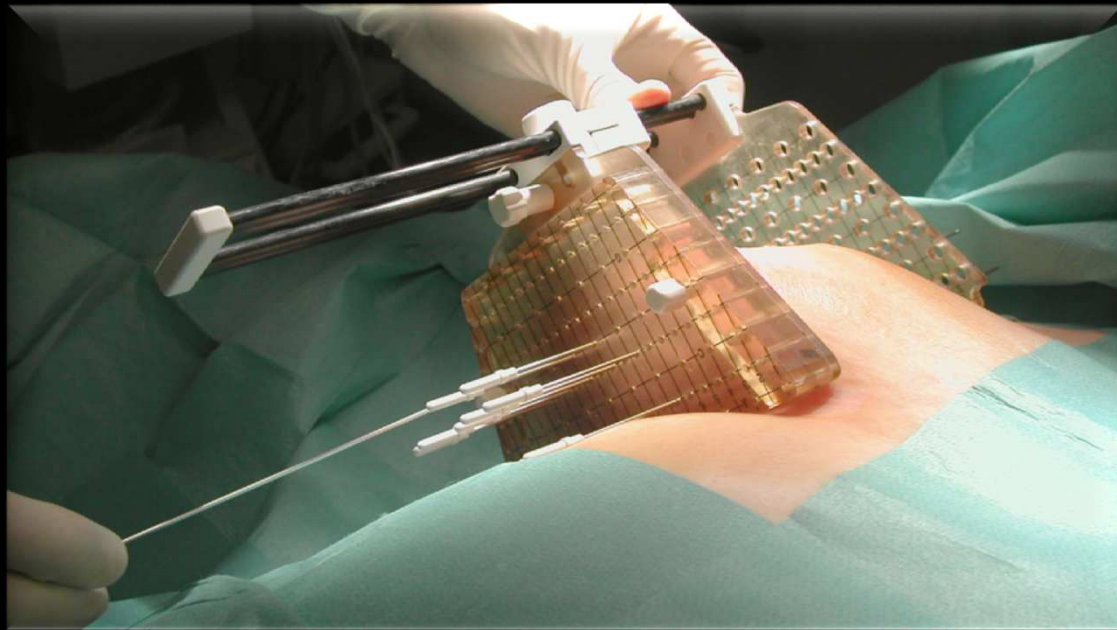
Matériel & Méthode – Traitements

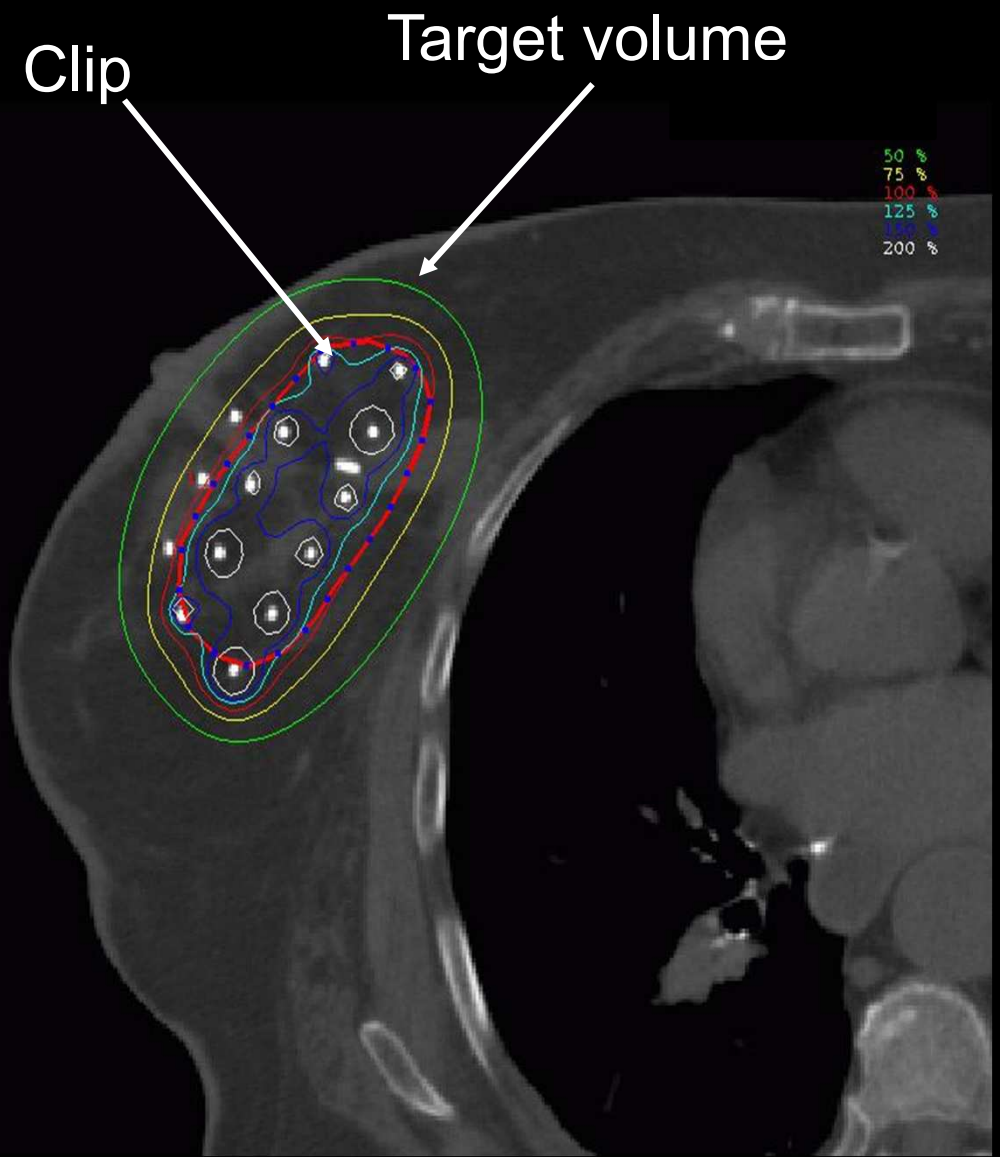


Clear margins



Dirty margins





34 Gy en 10 fractions et 5 j
HDJ



Resultats cliniques

- ✓ Suivi médian (ans):
 - de la tumeur primaire 14.5 [3.5 – 38.2]
 - de la rechute 3.9 [1.1 – 10.3]

Resultats cliniques

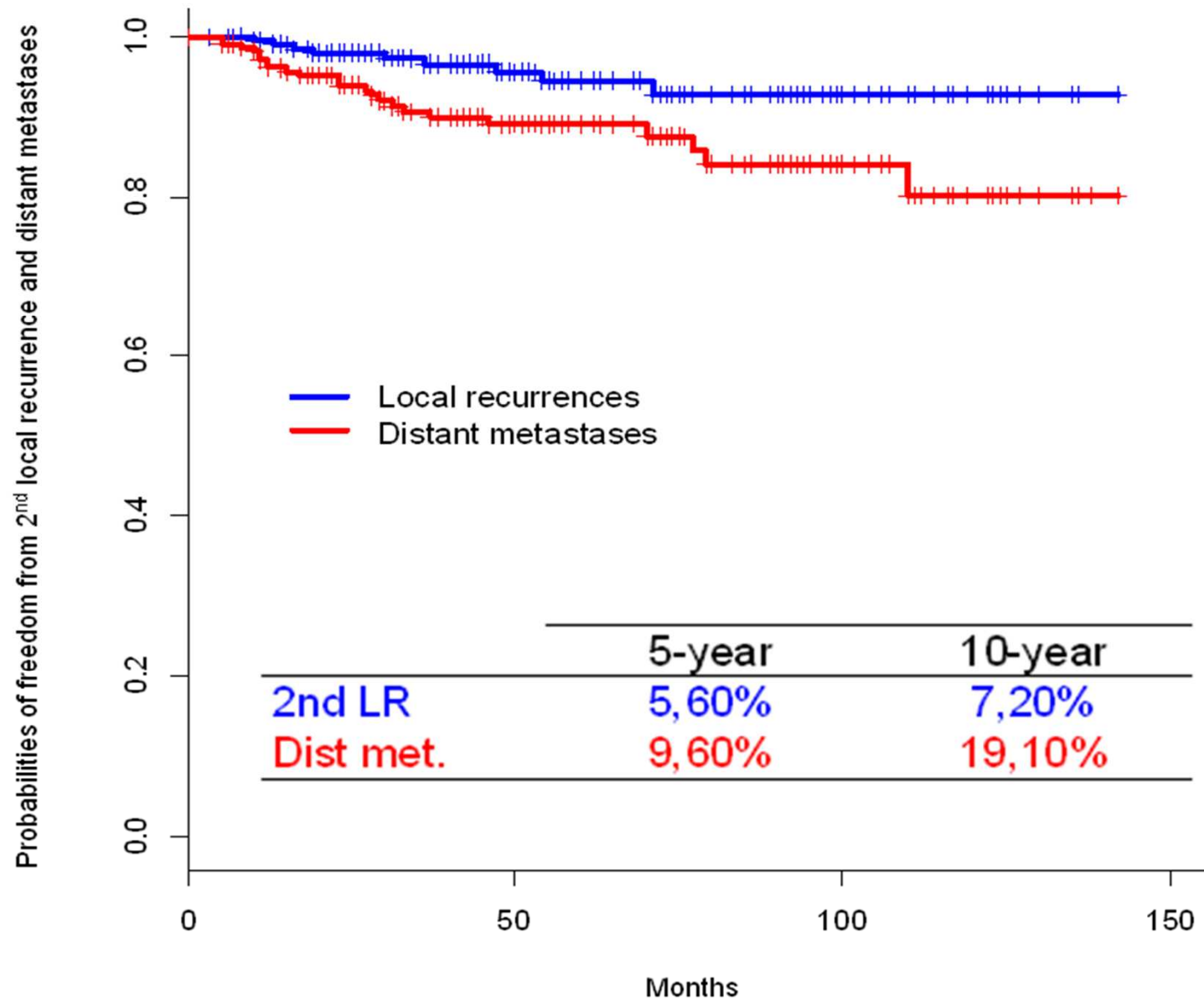
- ✓ Suivi médian (ans):
 - de la tumeur primaire 14.5 [3.5 – 38.2]
 - de la rechute 3.9 [1.1 – 10.3]

✓ 2nd rechute locale: 9 pts 4.1%

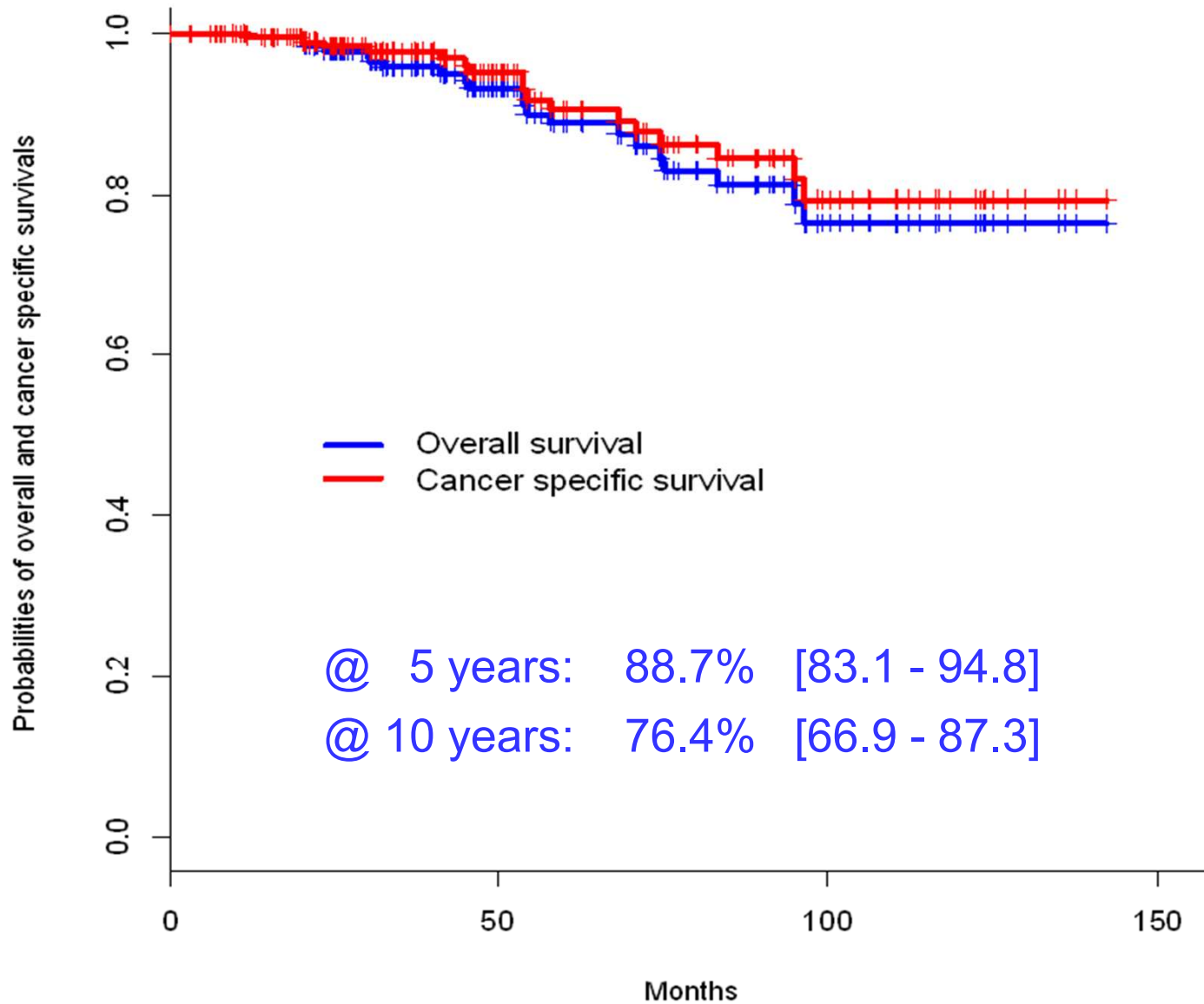
✓ Rechute regionale : 1 pt 0.5%

✓ Metastases: 22 pts 10.1%

Actuarial 2nd local recurrence & distant met. rates



Actuarial overall & cancer specific survival rates



MVA result summary

	UVA			MVA		
	IBTR data		<i>p</i> Value	IBTR data		<i>p</i> Value
2nd LR	Age (years)	>55	0.035			
	HG	III	0.0003	HG	III	0.008
	HR	HR–	0.001			
DM	pT (mm)	>20	0.03	pT	>20	0.03
OS	pT (mm)	>20	0.007			
	HG	III	0.009	HG	III	0.02
	HR	HR–	0.01			

UVA: univariate analysis; MVA: multivariate analysis; 2nd LR: second local recurrence; DM: distant metastases; OS: overall survival; pT: pathological tumour size (mm); HG: histological grade; HR: hormonal receptor status (HR– = ER–/PR–).

MVA result summary

	UVA			MVA		
	IBTR data		<i>p</i> Value	IBTR data		<i>p</i> Value
2nd LR	Age (years)	>55	0.035			
	HG	III	0.0003	HG	III	0.008
	HR	HR–	0.001			
DM	pT (mm)	>20	0.03	pT	>20	0.03
OS	pT (mm)	>20	0.007			
	HG	III	0.009	HG	III	0.02
	HR	HR–	0.01			

UVA: univariate analysis; MVA: multivariate analysis; 2nd LR: second local recurrence; DM: distant metastases; OS: overall survival; pT: pathological tumour size (mm); HG: histological grade; HR: hormonal receptor status (HR– = ER–/PR–).

MVA result summary

	UVA			MVA		
	IBTR data		<i>p</i> Value	IBTR data		<i>p</i> Value
2nd LR	Age (years)	>55	0.035			
	HG	III	0.0003	HG	III	0.008
	HR	HR–	0.001			
DM	pT (mm)	>20	0.03	pT	>20	0.03
OS	pT (mm)	>20	0.007			
	HG	III	0.009	HG	III	0.02
	HR	HR–	0.01			

UVA: univariate analysis; MVA: multivariate analysis; 2nd LR: second local recurrence; DM: distant metastases; OS: overall survival; pT: pathological tumour size (mm); HG: histological grade; HR: hormonal receptor status (HR– = ER–/PR–).

MVA result summary

	UVA			MVA		
	IBTR data		<i>p</i> Value	IBTR data		<i>p</i> Value
2nd LR	Age (years)	>55	0.035			
	HG	III	0.0003	HG	III	0.008
	HR	HR–	0.001			
DM	pT (mm)	>20	0.03	pT	>20	0.03
OS	pT (mm)	>20	0.007			
	HG	III	0.009	HG	III	0.02
	HR	HR–	0.01			

UVA: univariate analysis; MVA: multivariate analysis; 2nd LR: second local recurrence; DM: distant metastases; OS: overall survival; pT: pathological tumour size (mm); HG: histological grade; HR: hormonal receptor status (HR– = ER–/PR–).

Resultats – Effets tardifs

✓ Effets tardifs : 141 pts (65%)
193 complications

Resultats – Effets tardifs

✓ Effets tardifs : 141 pts (65%)
193 complications

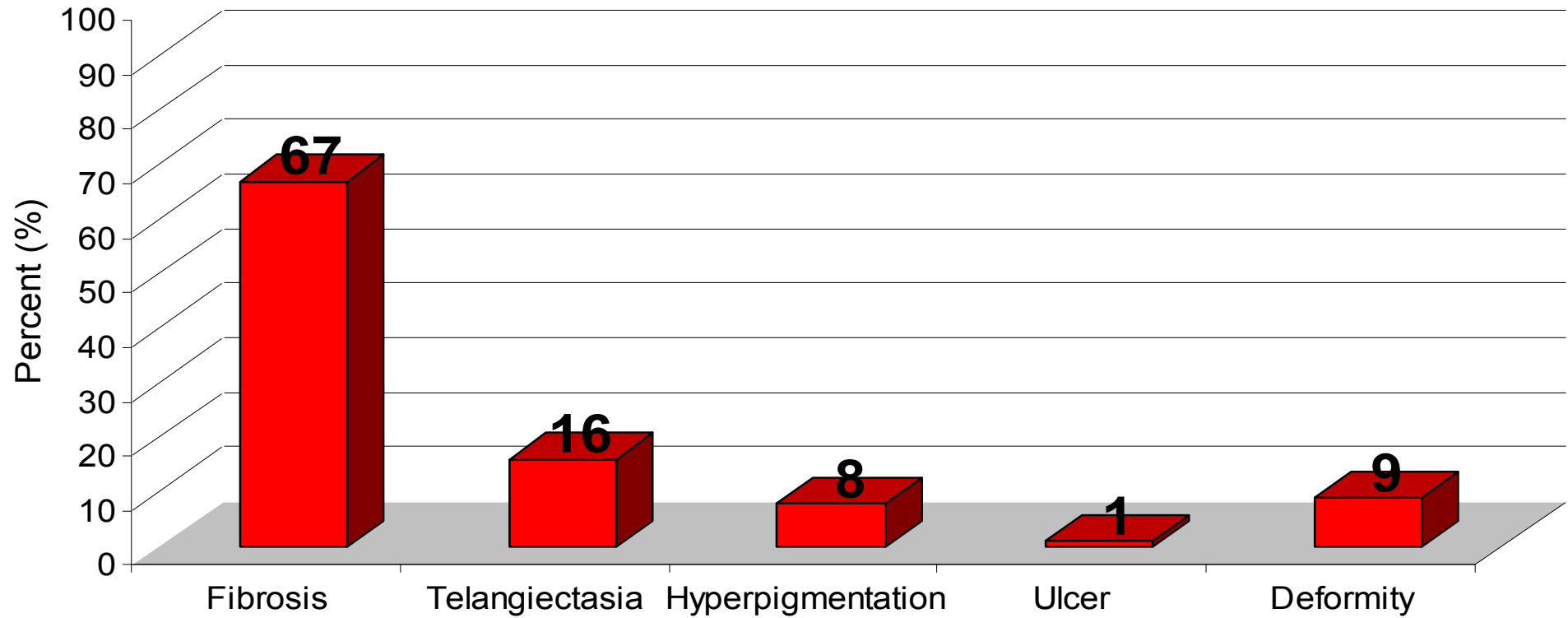
✓ Types

✓ Grades

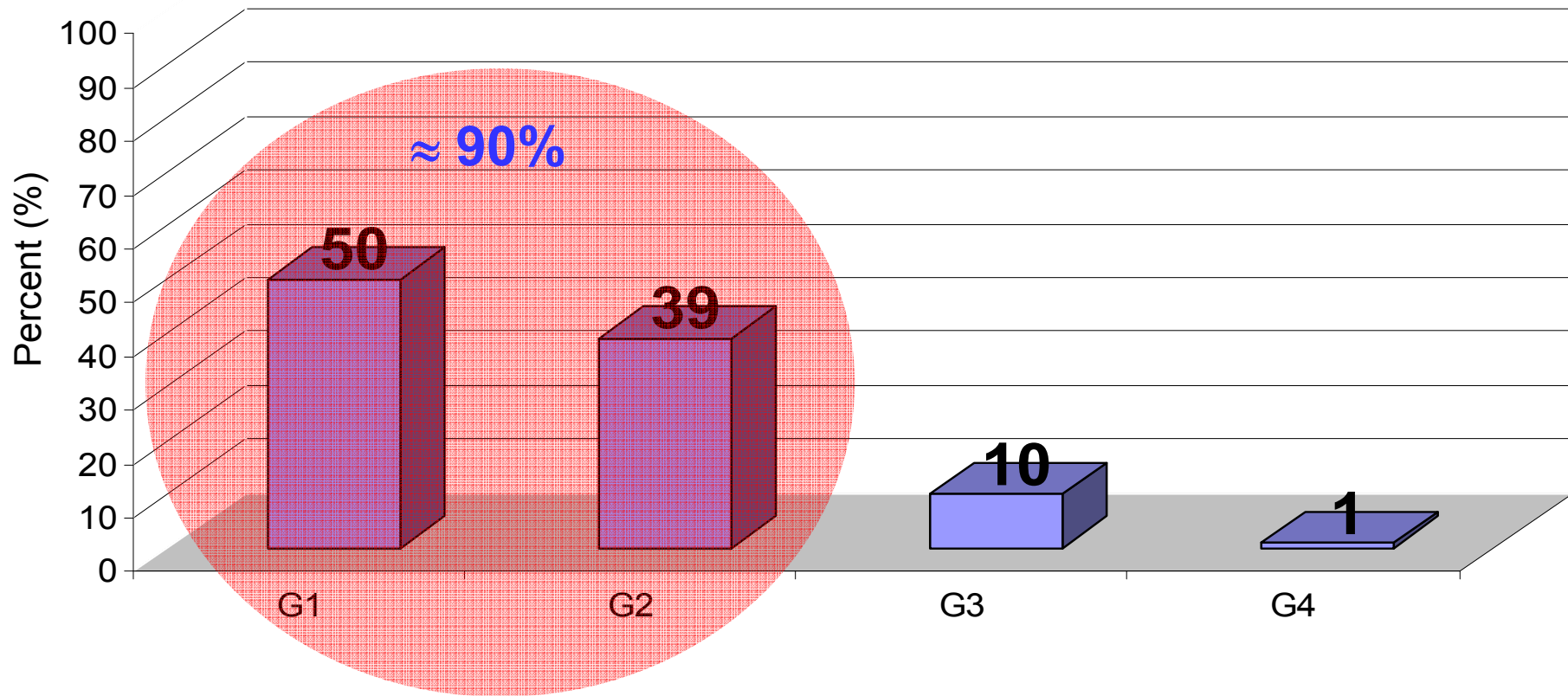
✓ Résultats cosmetiques (109 pts)

Wazer D. et al IJROBP 2002

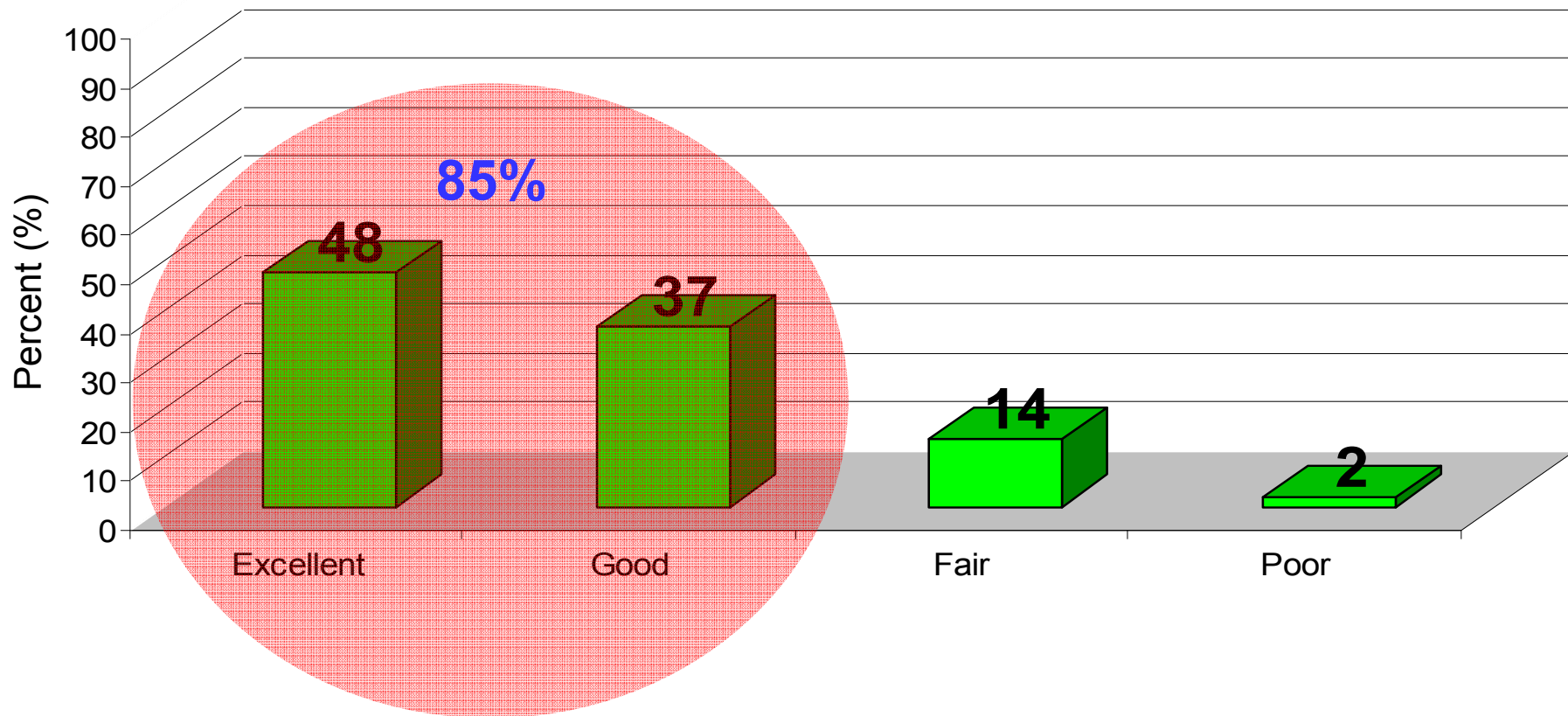
Resultats – Types



Resultats – Grades



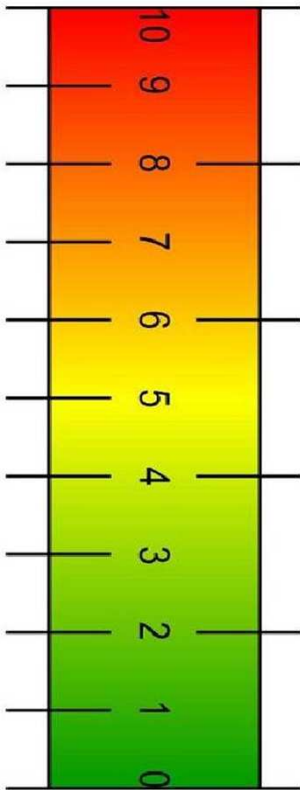
Resultats cosmetiques (109 pts)



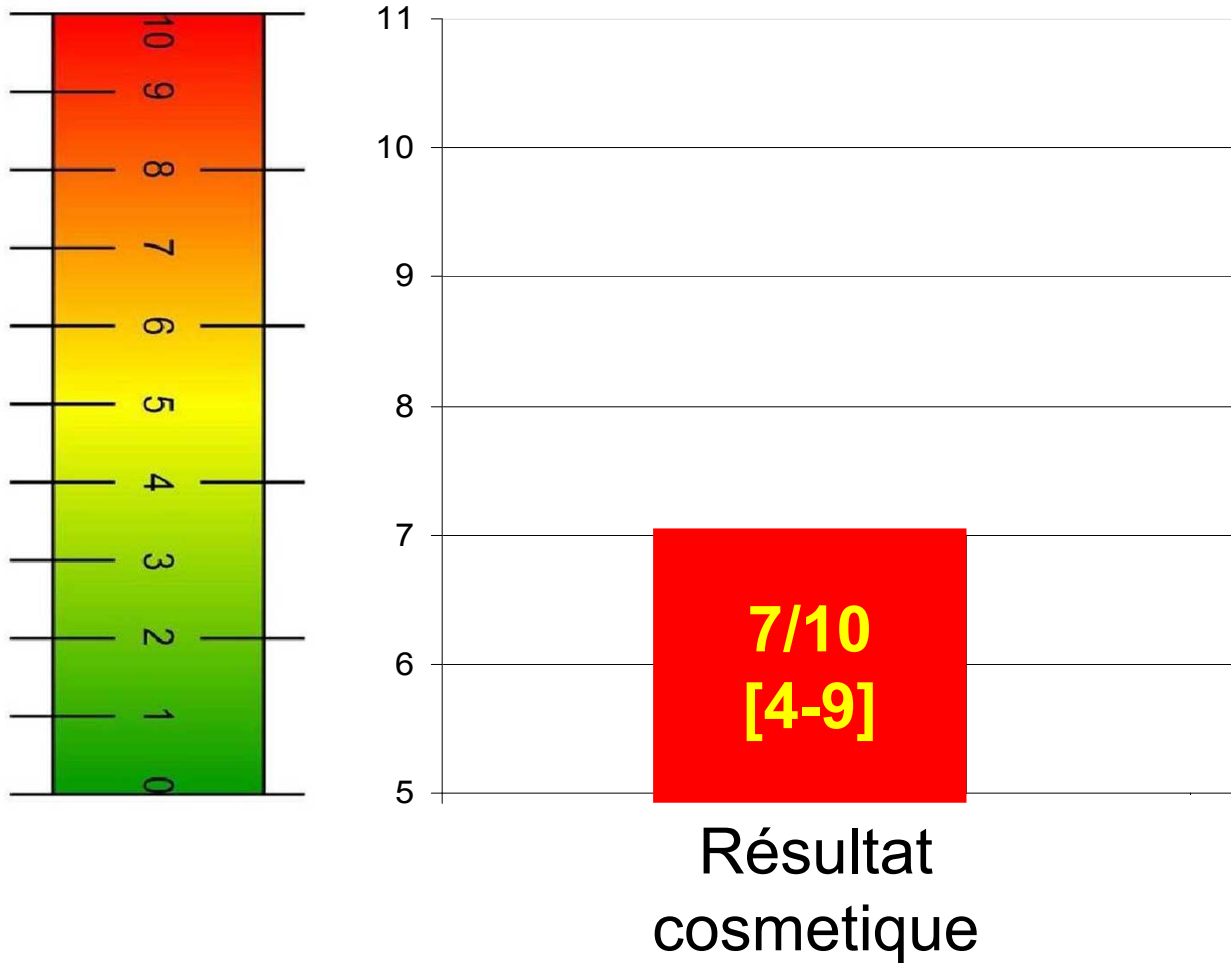




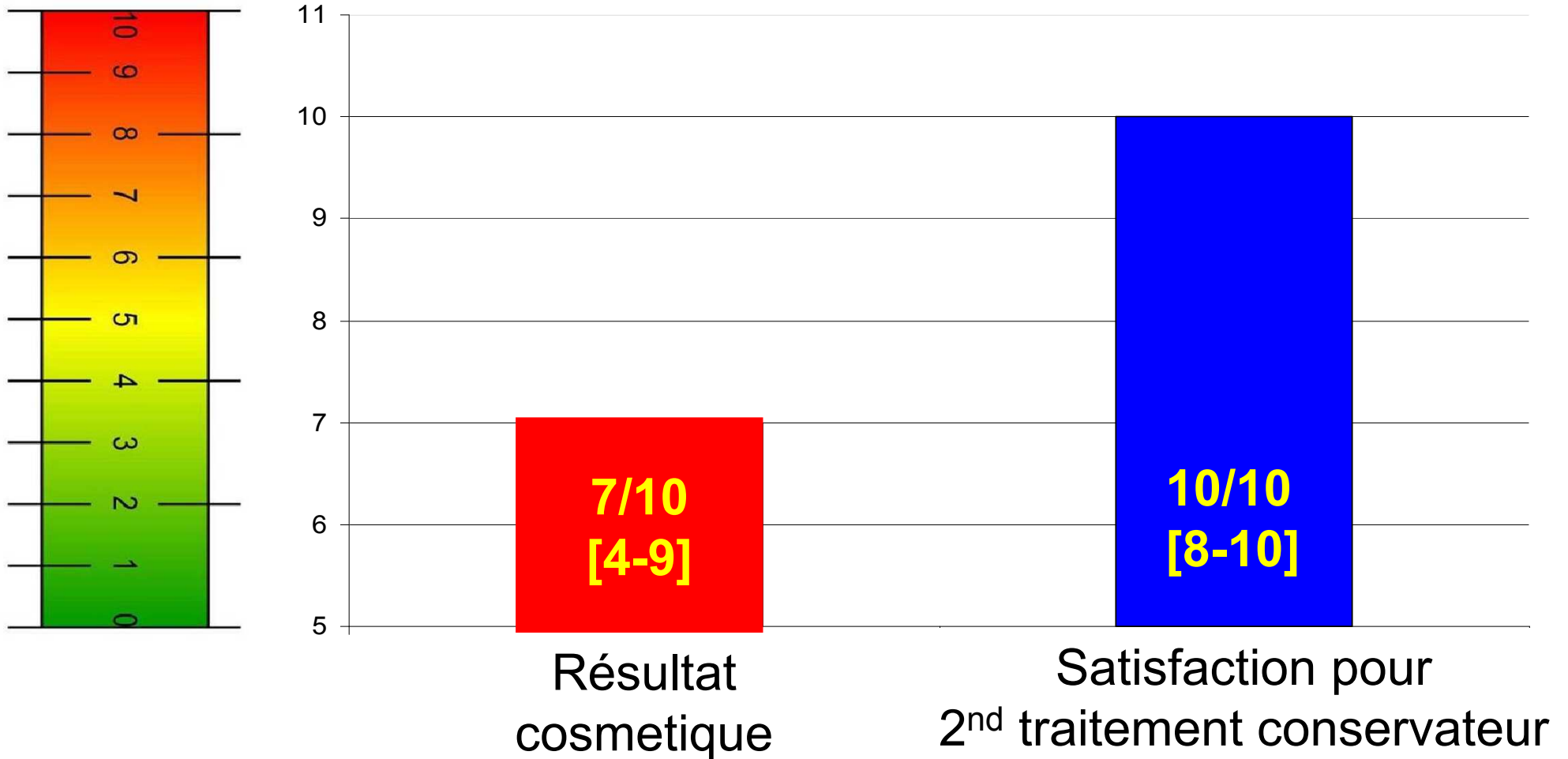
Analyse par la patiente du résultat comsétique (EVA)

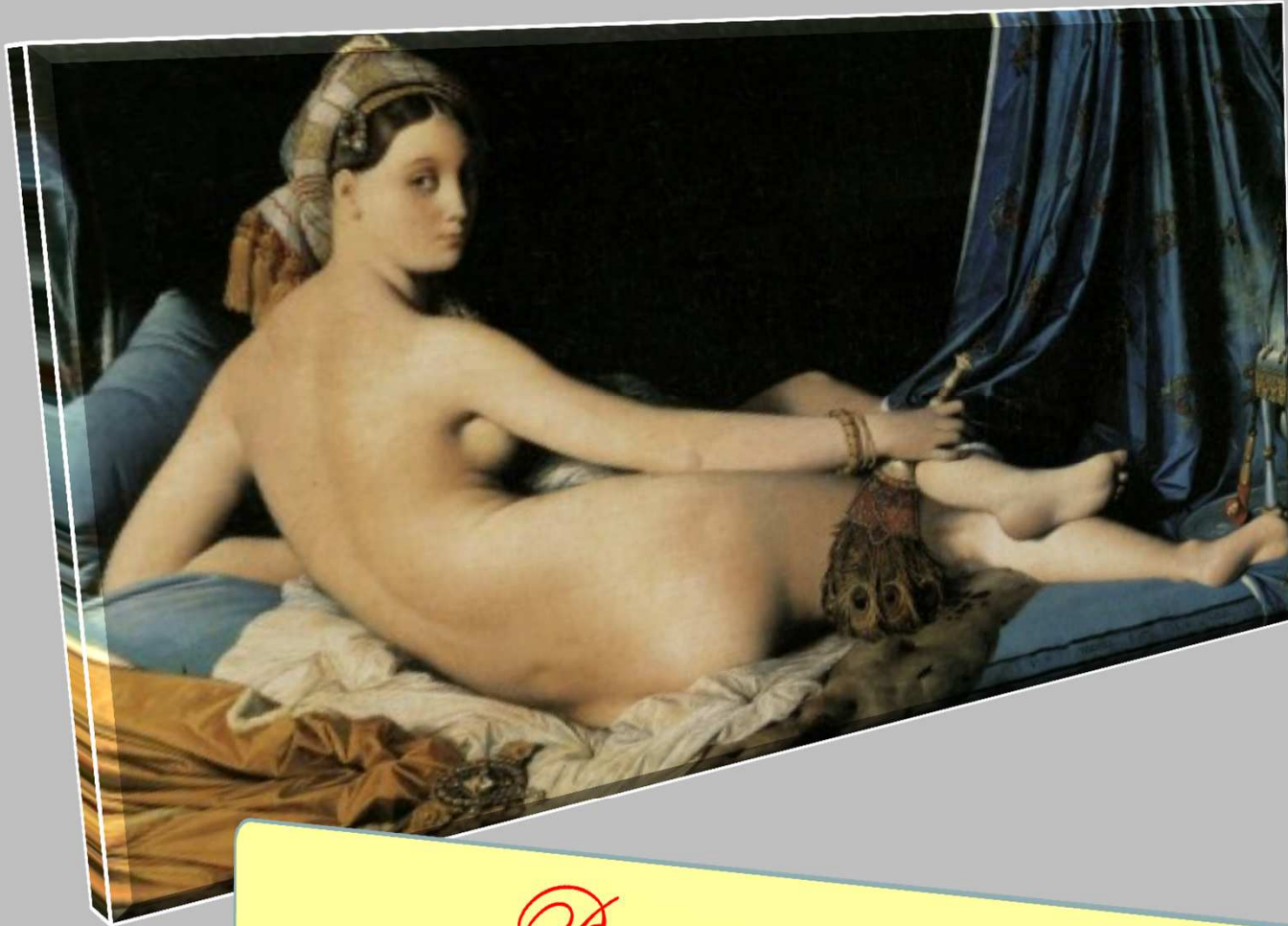


Analyse par la patiente du résultat comsétique (EVA)



Analyse par la patiente du résultat comsétique (EVA)





Perspectives

Protocol Info

Forms

Regulatory Resources

Broadcasts

Contact Personnel

Clinical Trials > Protocol Table > Study Details

RTOG 1014 Protocol Information

A Phase II Study of Repeat Breast Preserving Surgery and 3D-Conformal Partial Breast Re-Irradiation (PBRI) for Local Recurrence of Breast Carcinoma

Protocol Documents

Protocol

Current Version Date: 12/1/2011

Informed Consent

Summary of Changes

Track Amendments/ Update

Case Credits/Reimbursement Info

Principal Investigator: Douglas W. Arthur, MD



**GEC-ESTRO
Workshop**

22 November, 2013 | Brussels, Belgium



GEC-ESTRO BCWG Phase II trial for 2nd breast conservative treatment

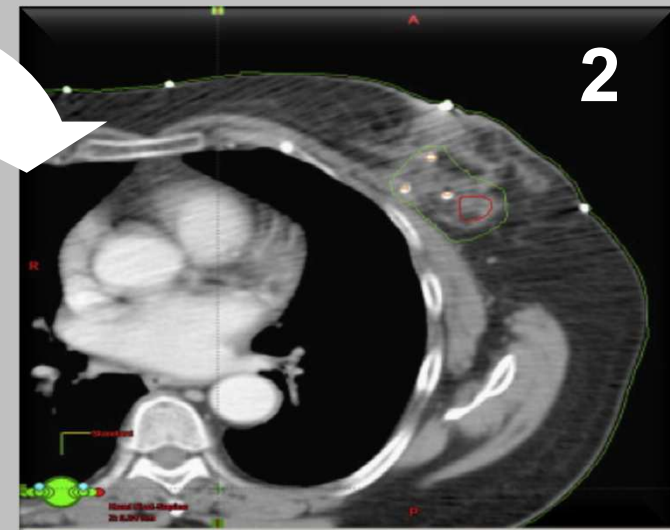
Conclusions

En pratique

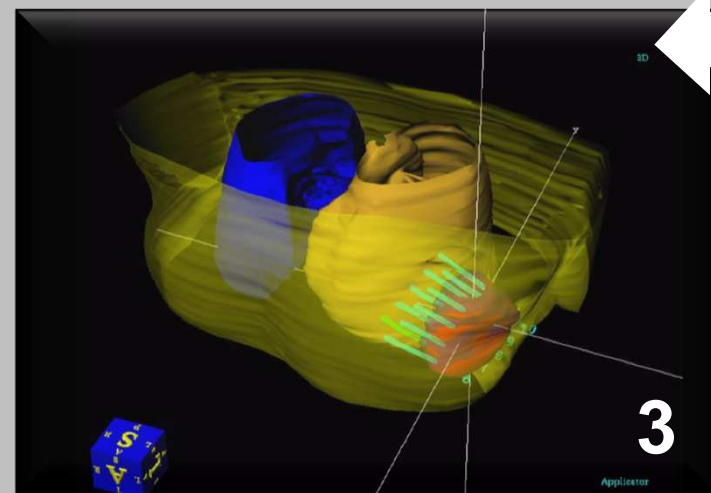
En pratique



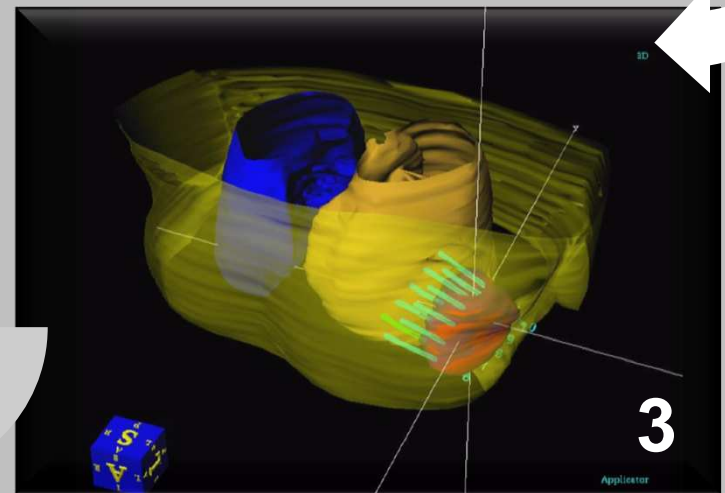
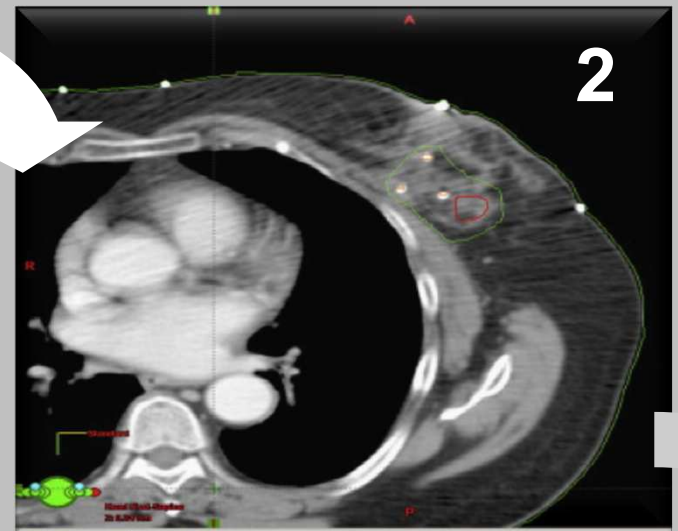
En pratique



En pratique



En pratique



Conclusions



Pas de traitement standard

Conclusions



Pas de traitement standard



Conclusions



Pas de traitement standard

Information benefice-risque

Conclusions



Pas de traitement standard

Information benefice-risque

Age, grade, pT & HR status

Conclusions



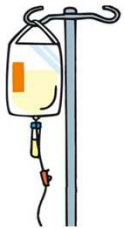
Pas de traitement standard



Information benefice-risque



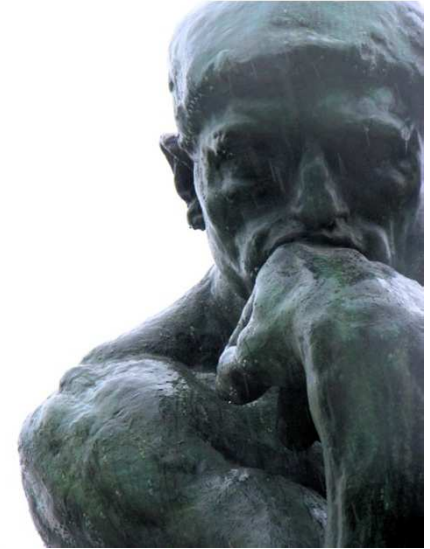
Age, grade, pT & HR status



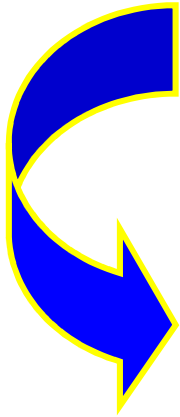
Traitements systemiques

Conclusions

TTT RLH \neq TTT primaire ?



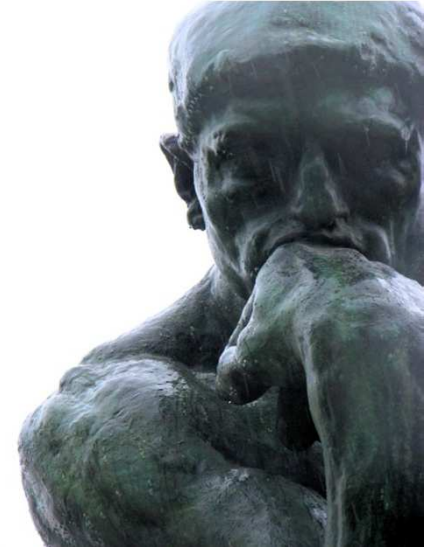
Conclusions



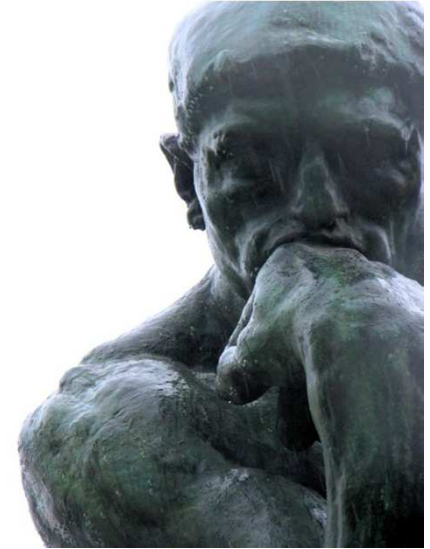
TTT RLH \neq TTT primaire ?

Mêmes buts:

- ✓ Contrôle local
- ✓ Survie globale
- ✓ Résultats cosmétiques



Conclusions



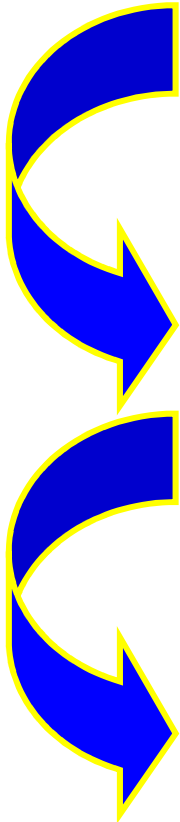
TTT RLH \neq TTT primaire ?

Mêmes buts:

- ✓ Contrôle local
- ✓ Survie globale
- ✓ Résultats cosmétiques

Impact du:

- ✓ 2nd évènement sur évolution clinique (VR ou NT)
- ✓ TTT initial sur TTT de la rechute





Merci de votre attention