Multifocal tumor : oncologic questions

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Breast cancers are defined as multifocal when there is more than one distinct tumour within the same quadrant of the breast and multicentric when multiple cancers develop in different quadrants of the breast
MF/MC breast cancers have been reported with an incidence of 40–70% in serial-sectioning studies of mastectomy specimens

- Pathological characteristics of tumors in multifocal breast cancer.
- Prognosis

Pathological characteristics

Most guidelines recommend assessing biological markers only on the largest tumor in the case of multifocal breast cancers.

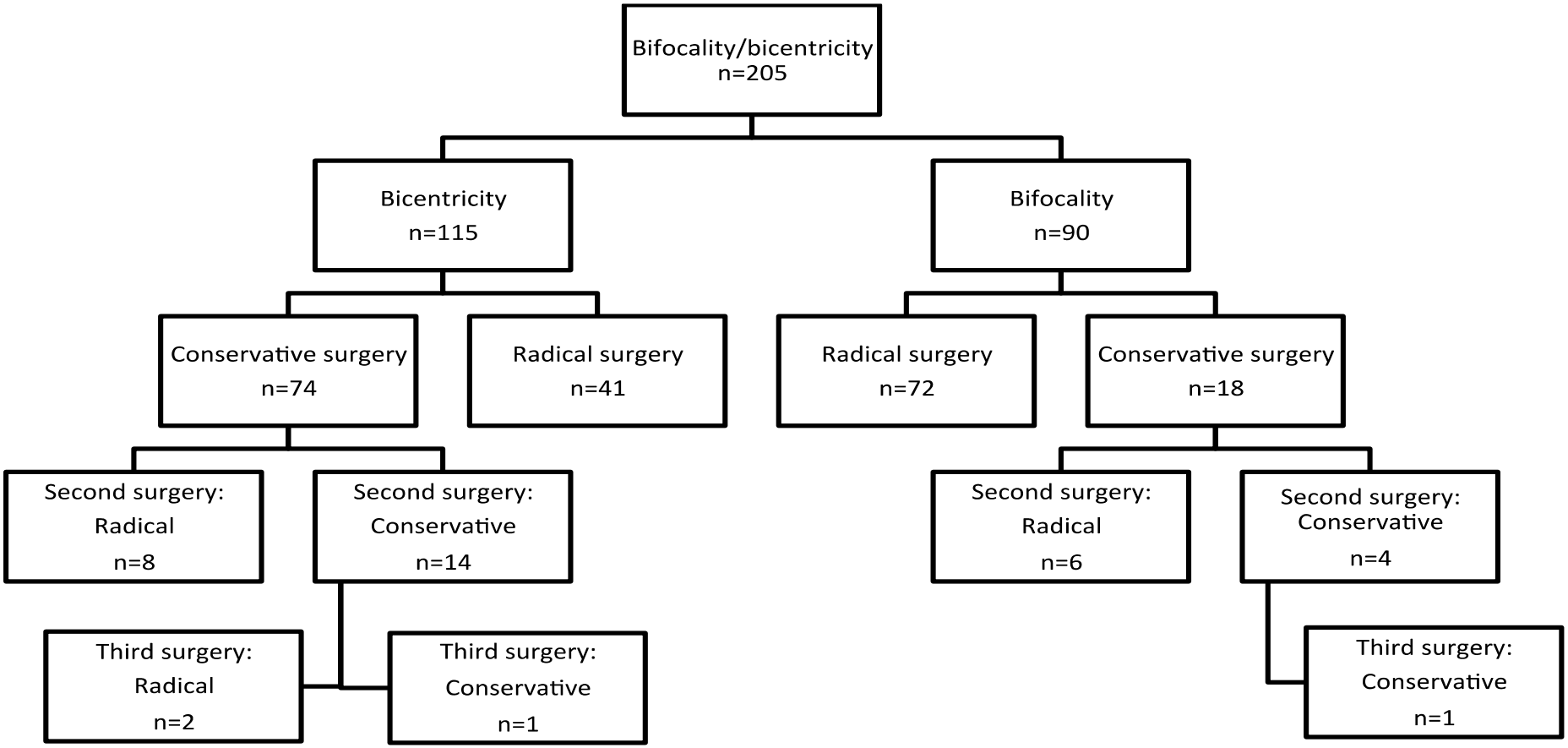
The objective of our study was to describe the biological characteristics of each lesion in bifocal/bicentric breast cancer and to assess differences in molecular subtype classification between foci.

Material and pethods

We retrospectively reviewed the charts of 205 patients diagnosed with BF/BC breast cancer.

The degree of concordance between the 2 malignant lesions in terms of histological type, tumor grade, ER, PR and HER2 status, and Ki67 rates were assessed using Pearson product-moment correlation coefficients.

Surgical management of the studied population



Pathological characteristics of both tumors in BF/BC breast cancers

	Tumor 1		Tumor 2		p
Clinical diagnosis, n, %	130	63.4%	41	20.0%	<0.05
Hitology, n, %					NS
Invasive ductal carcinoma	128	62.5%	124	60.5%	
Invasive lobular carcinoma	28	13.7%	28	13.7%	
Invasive ductal+lobular	35	17.1%	32	15.6%	
in situ ductal carcinoma	9	4.4%	13	6.3%	
*others**	5	2.4%	8	3.9%	
Histological size in mm, median (intervalle)	17	(3-80)	9.6	(1-40)	<0.05
Tumour grade, n, % (missing n=13 and n=20)					NS
I	40	20.8%	40	21.6%	
II	84	43.8%	79	42.7%	
III	68	35.4%	66	35.7%	
Lymphovascular embols, n, % (missing n=10 and n=13)	57	29.2%	57	29.7%	NS

*mucinous, micropapillary

Mismatches in biological features between T1 and T2

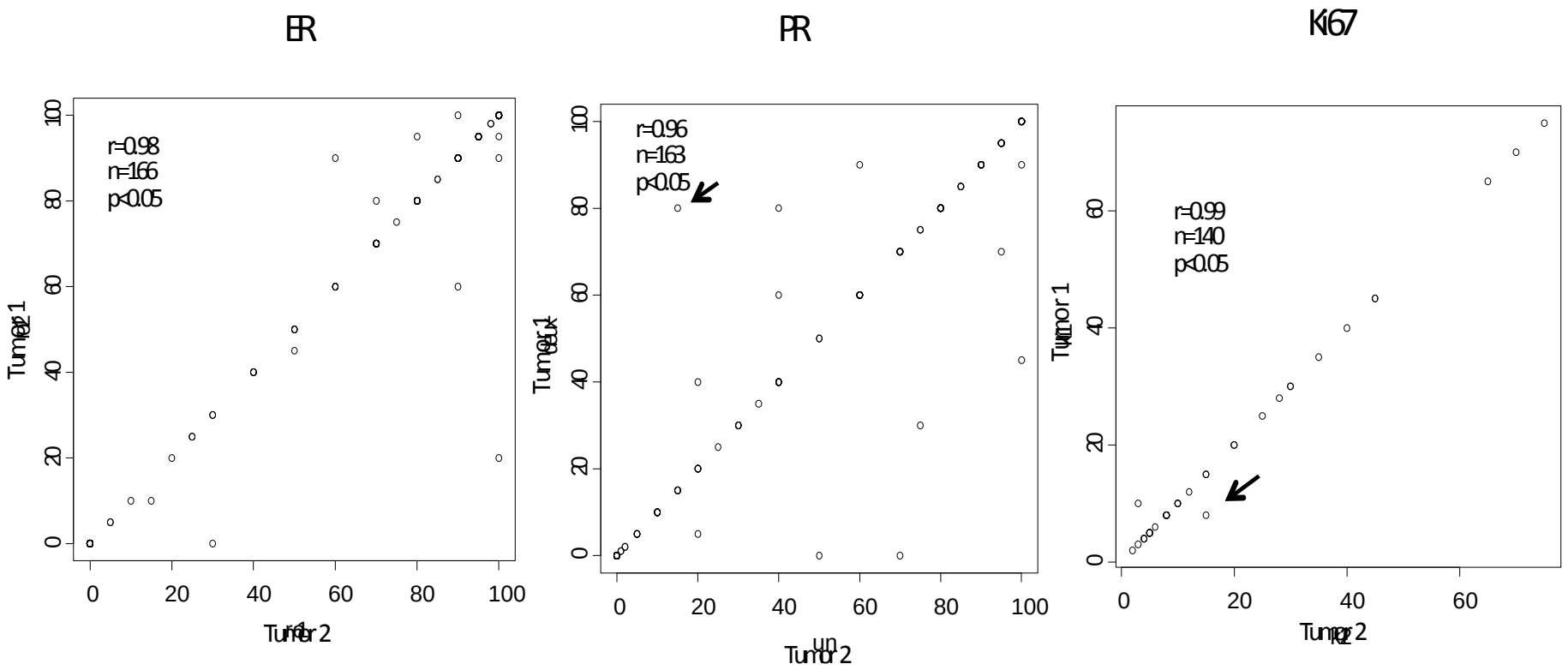
	Mismatches in biological characteristics among tumours, n, %	
Histologic type, N=203	21	(10.3)
Histologic grade (1 verus 2), N=184	6	(3.3)
Estrogen receptors, N=168	9	(5.4)
Progesterone receptors, N=165	12	(7.3)
Ki67, N=42	2	(4.8)
HER2, N=177	0	0

N: number of patients with data available for both lesions

Discordance between foci in MF/MC breast cancers in literature

			Discordance between foci (%)						
References	Year	Number of patients	Histotype	Grade	ER status	PR status	HER2 status	Ki67	molecular subtypes
Middleton et al. (120)	2002	32	38%	0%	0%	0%	0%	6%	NA
Garimella et al. (121)	2007	18	0%	17%	12%	12%	NA	NA	NA
Boros and al. (122)	2012	91	12%	10%	NA	NA	NA	NA	NA
Choi et al. (123)	2012	65	37%	12%	3%	11%	6%	NA	8%
Buggi et al. (124)	2012	113	NA	18.6%	4.4%	15.9%	9.7%	15%	NA
Pekmezci et al. (125)	2013	51	12%	13.7%	7.8%	7.8%	2%	NA	NA
Bethune et al. (126)	2013	246	11.8%	NA	2.8%	2.8%	6.5%	NA	NA
Pekar et al. (127)	2014	110	14.6%	5.5%	NA	NA	NA	NA	10-12%
Our results	2014	205	10.3%	3.3%	5.4%	7.3%	0%	4.8%	2.4%

Degree of concordance between Tumor 1 and Tumor 2 for percentage of ER, PR and Ki67.



Main findings

Both tumors displayed the same histological type in 182 patients (89%).
The same grade was found in both tumors in 178 of the cases (96.7% and 100% for grade 3 lesions).
Immunohistochemical concordance between the two tumors was excellent with correlation coefficients of 0.98, 0.96 and 0.99 for estrogen receptors (RE), progesterone receptors (RP) and Ki67, respectively.
HER2 status was available for both tumors in 177 cases (86%) with a perfect concordance (151 negative-negative and 26 positive-positive).
We did not find significant difference in molecular subtype between tumor foci.

Conclusion

This retrospective study of 205 BF/BC breast cancers revealed very similar histological characteristics and immunohistochemistry results between the two foci of the cancer.

Therefore, it is sufficient to perform immunohistochemistry analysis on the main tumor alone.

PROGNOSIS

Background

Indeed, the biological and clinical significance of MF/MC breast cancer is still controversial.

In the literature, few studies have investigated the prognosis of MF/MC cancers, and they have produced contrasting results: some investigators have not found any influence on long-term survival while other recent series have reported a worse outcome for MF/MC breast cancers.

Background

Therefore, it remains unclear whether MF/MC breast cancers should be considered a separate category with a potentially unfavourable impact on prognosis and whether these lesions require specific treatment with more extensive surgery or committed adjuvant therapies.
The present study was directed to analyse, in a large retrospective series of breast cancer patients treated at a single institution, the impact of MF/MC breast cancers on the long-term survival in relation to other known pathological and clinical factors and to the type of treatment received.

Methods

32257 women operated on for a breast cancer were included in this retrospective study; clinical and pathological data were obtained from the institutional database of the Institut Curie

Period of treatment 1981 – 2008

The impact of MF/MC breast cancers on patterns of recurrence and breast cancer specific survival (BCSS) was investigated in relation to the type of surgical treatment.

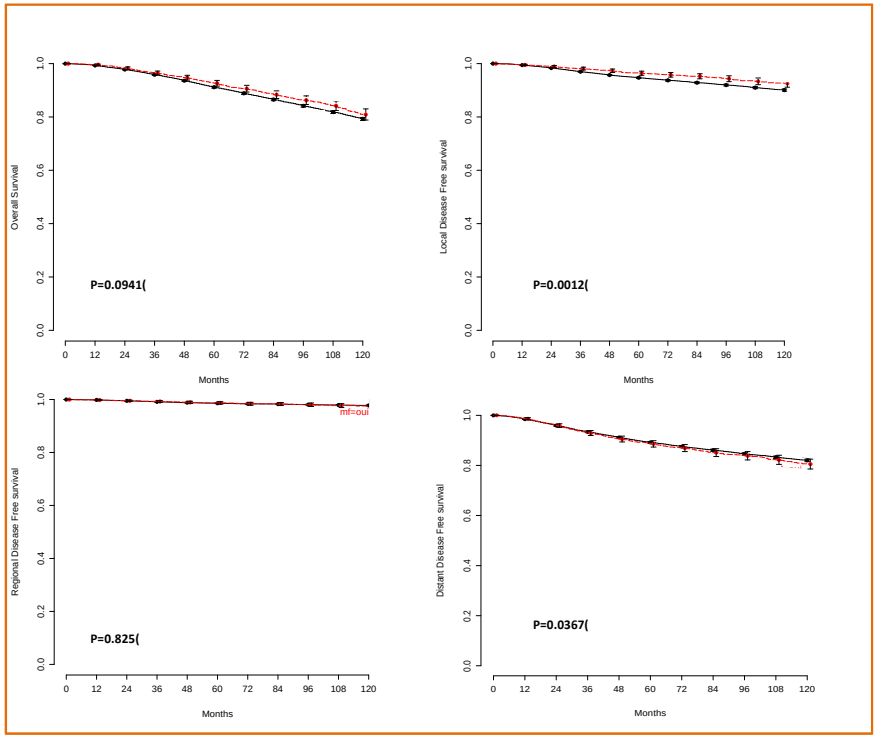
Characteristics and treatment

		Multifocal BC, n=2823		Unifocal BC, n=29434		
		n or median	% or range	n or median	% or range	p
Age at diagnosis (years)		54	(27-100)	58	(21-95)	<0.005
Menopause status						<0.005
	Postmenopausal	1559	55,2%	17635	59,9%	
	Premenopausal	940	33,3%	7535	25,6%	
	Unknown	324	11,5%	4264	14,5%	
In Situ						<0.005
	Yes	1239	43,9%	4449	15,1%	
	No	182	6,4%	1317	4,5%	
	Unknown	140	5,0%	23668	80,4%	
Histological grade						<0.005
	I	675	23,9%	8322	28,3%	
	II	1161	41,1%	12376	42,0%	
	III	908	32,2%	7852	26,7%	
	Unknown	79	2,8%	884	3,0%	
Emboli						
	Yes	610	21,6%	3334	11,3%	0.0566
	No	841	29,8%	4114	14,0%	
	Unknown	1372	48,6%	21986	74,7%	
Estrogen receptors status						0.0121
	Positive	2173	77,0%	21550	73,2%	
	Negative	425	15,1%	4839	16,4%	
	Unknown	225	8,0%	3045	10,3%	
Progesteron receptor status						0.2315
	Positive	1485	52,6%	16469	56,0%	
	Negative	679	24,1%	7982	27,1%	
	Unknown	659	23,3%	4983	16,9%	
HER2 status						<0.005
	Overexpressed	309	10,9%	1308	4,4%	
	Non-overexpressed	1189	42,1%	9206	31,3%	
	Unknown	1325	46,9%	18920	64,3%	
Ki67 (%)		15	(0-90)	13	(0-100)	0.0872

	Multifocal BC, n=2823		Unifocal BC, n=29434		
	n or median	% or range	n or median	% or range	p
Type of breast surgery					<0.005
Radical	1851	65,6%	9650	32,8%	
Conservative	972	34,4%	19784	67,2%	
Type of lymph node surgery					<0.005
Sentinel procedure	331	11,7%	4376	14,9%	
Sentinel procedure followed by lymphadenectomy	186	6,6%	1514	5,1%	
Axillary lymphadenectomy	2224	78,8%	22263	75,6%	
Unknown	82	2,9%	1281	4,4%	
Axillary lymph node status					<0.005
Positive	1216	43,1%	9790	33,3%	
Negative	1527	54,1%	18074	61,4%	
Unknown	80	2,8%	1570	5,3%	
Adjuvant hormone therapy					<0.005
Yes	1706	60,4%	14758	50,1%	
No	1117	39,6%	14676	49,9%	
Unknown					
Adjuvant chemotherapy					<0.005
Yes	1184	41,9%	8966	30,5%	
No	1639	58,1%	20468	69,5%	
Radiotherapy					
Breast/chest					<0.005
Yes	1827	64,7%	22816	77,5%	
No	270	9,6%	810	2,8%	
Unknown	726	25,7%	5808	19,7%	
Axillary Lymph nodes					<0.005
Yes	579	20,5%	8665	29,4%	
No	1510	53,5%	14922	50,7%	
Unknown	734	26,0%	5847	19,9%	
Internal chain and/or subclavicular lymph nodes					<0.005
Yes	730	25,9%	2184	7,4%	
No	459	16,3%	3088	10,5%	
Unknown	1634	57,9%	24162	82,1%	
Follow-up (months)	90	(0-281)	70	(0-248)	<0.005

Results

COURBES DE SURVIES GLOBALE (a), SANS RECIDIVE LOCALE (b), SANS RECIDIVE REGIONALE (c) ET SANS RECIDIVE A DISTANCE DES (d) CANCERS DU SEIN UNIFOCAUX (____) ET MUTIFOCAUX (____)



→ **Survie globale à 10 ans**
Pas de différence UF/MF (79,2% vs 80,9%, p=0,0941)

→ **Survie sans récidive locorégionale à 10 ans**
Meilleure en cas de cancer MF/MC (96,4% vs 92,6%, p=0,001)
Mais en analyse multivariée, MF/MC n'était pas retrouvée comme facteur indépendant de survie sans récidive locorégionale

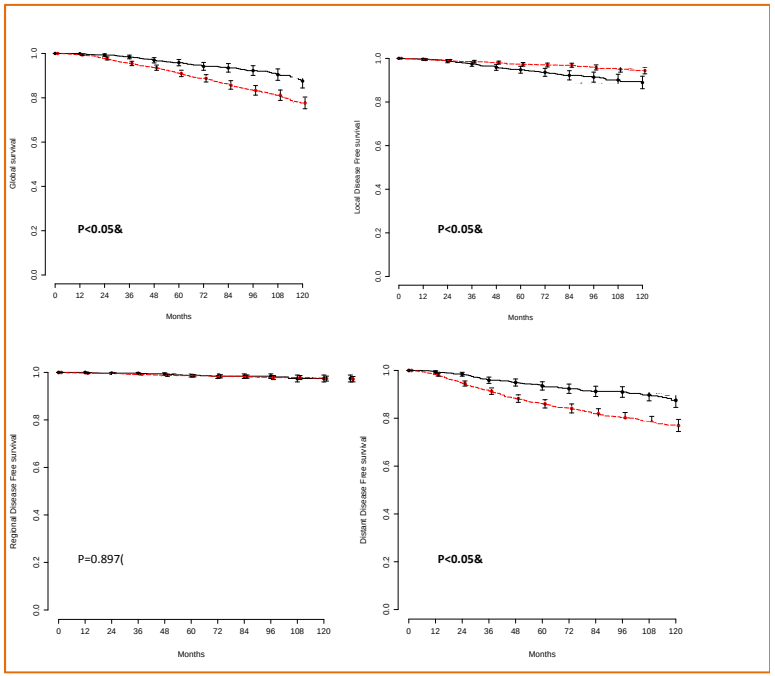
→ **Survie sans récidive à distance à 10 ans**
La MF/MC semble être un facteur pronostique indépendant (HR=0,72; IC95% [0,5278 -0,9996]; p=0,049)

Results

Caractéristiques et traitements des cancers unifocaux et multifocaux

	Radical surgery, n=1851		Conservative surgery, n=972		
	n or median	% or range	n or median	% or range	p
Age at diagnosis (years)	53	(27-89)	56	(25-100)	0.134
Menopause status					**<0.005**
Postmenopausal	979	52,9%	580	59,7%	
Premenopausal	657	35,5%	283	29,1%	
Unknown	215	11,6%	109	11,2%	
In Situ					**<0.005**
Yes	736	39,8%	503	51,7%	
No	74	4,0%	108	11,1%	
Unknown	1041	56,2%	361	37,1%	
Histological grade					**<0.005**
I	363	19,6%	312	32,1%	
II	769	41,5%	392	40,3%	
III	666	36,0%	242	24,9%	
Unknown	53	2,9%	26	2,7%	
Emboli					
Yes	436	23,6%	174	17,9%	**<0.005**
No	439	23,7%	402	41,4%	
Unknown	976	52,7%	396	40,7%	
Estrogen receptors status					0.0656
Positive	1405	75,9%	768	79,0%	
Negative	295	15,9%	130	13,4%	
Unknown	151	8,2%	74	7,6%	
Progesteron receptor status					0.1155
Positive	976	52,7%	509	52,4%	
Negative	470	25,4%	209	21,5%	
Unknown	405	21,9%	254	26,1%	
HER2 status					**<0.005**
Overexpressed	226	12,2%	83	8,5%	
Non-overexpressed	737	39,8%	452	46,5%	
Unknown	888	48,0%	437	45,0%	
Ki67 (%)	15	(0-90)	6	(1-85)	**<0.005**
Type of lymph node surgery					**<0.005**
Sentinel procedure	63	3,4%	268	27,6%	
Sentinel procedure followed by lymphadenectomy	75	4,1%	111	11,4%	
Axillary lymphadenectomy	1680	90,8%	544	56,0%	
Unknown	33	1,8%	49	5,0%	
Axillary lymph node status					**<0.005**
Positive	935	50,5%	281	28,9%	
Negative	901	48,7%	626	64,4%	
Unknown	15	0,8%	65	6,7%	
Adjuvant hormone therapy	1182	63,9%	524	53,9%	**<0.005**
Adjuvant chemotherapy	874	47,2%	310	31,9%	**<0.005**
Radiotherapy					
Breast/chest	1170	63,2%	951	97,8%	**<0.005**
Axillary Lymph nodes	471	25,4%	108	11,1%	**<0.005**
Internal chain Lymph nodes	521	28,1%	209	21,5%	**<0.005**
Follow-up (months)	71	(0-348)	68	(0-324)	0.7025

COURBES DE SURVIES GLOBALE (a), SANS RECIDIVE LOCALE (b), SANS RECIDIVE REGIONALE (c) ET SANS RECIDIVE A DISTANCE DES CANCERS DU SEN MULTIFOCAUX AVEC TRAITEMENT CHIRURGICAL CONSERVATEUR (____) ET RADICAL (____)



→ *Après ajustement sur tous les facteurs associés en analyse univariée, aucune différence de survie en analyse multivariée entre traitement chirurgical conservateur ou radical des cancers MF/MC*

Conclusion

Our results indicate that MF/MC cancers do not have a negative impact on prognosis but are associated with pejorative characteristics

No impact of surgical treatment: MF/MC should not be considered as a contra-indication of conservative surgery

The challenge is the biological behavior