

Ductal Carcinoma in Situ: A French National Survey. Analysis of 2125 Patients

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Abstract

This was an analysis of 2125 ductal carcinoma in situ features/treatments from 71 French centers. Mastectomy and breast-conserving surgery was performed in 25% and 75% of cases, respectively; the median tumor size was 15 mm, and the low, intermediate, and high nuclear grade distribution was 12%, 36%, and 47%, respectively. After breast-conserving surgery, 97% underwent whole breast irradiation. This survey reflects the daily ductal carcinoma in situ treatment in France, and the results are in accordance with national guidelines.

Background: Ductal carcinoma in situ (DCIS) represents 15% of all breast cancers in France. The first national survey was conducted in 2003. The present multi-center real-life practice survey aimed at assessing possible changes in demographic, clinical, pathologic, and treatment features. **Material and Methods:** From March 2014 to September 2015, patients diagnosed with DCIS from 71 centers with complete information about age, diagnostic features, and treatment modalities were prospectively included. **Results:** A total of 2125 patients with a median age of 58.6 years from 71 centers were studied. DCIS was diagnosed by mammography in 87.5% of cases. Preoperative biopsy was performed in 96% of cases. The median tumor size was 15 mm. Nuclear grade was low, intermediate, and high in 12%, 36%, and 47% of cases, respectively. Margins were considered to be negative in 83% of cases. Overall mastectomy and lumpectomy rates were 25% and 75%, respectively. The immediate breast reconstruction rate was 50%. Sentinel node biopsy and axillary dissection rates were 41% and 2.6%, respectively. After lumpectomy, 97% of patients underwent radiotherapy, and 32% received a boost dose. Only 1% of patients received endocrine therapy. Compared with our previous survey, the median tumor size remained the same, and the proportion of high-grade lesions increased by 9%. The mastectomy rate decreased by 4%. **Conclusions:** The clinical practice identified in this survey complies with French DCIS guidelines. About 10% of patients with low-grade DCIS may be eligible to participate in treatment de-escalation trials.

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Keywords: DCIS, Mastectomy, Radiotherapy, Sentinel node biopsy, Surgery, Treatment

Introduction

Pure ductal carcinoma in situ (DCIS) now represents about 15% of all breast cancers (BCs) in Western countries,^{1,2} but with different types of lesions characterized by their morphology and prognostic features.³ Prognosis is favorable in most cases, but invasive local recurrences (LRs) can lead to metastasis in

10% to 15% of cases.⁴⁻⁷ The treatment modalities for DCIS have been widely debated for many years, with several major questions concerning the role of mastectomy, sentinel node biopsy (SNB), whole breast radiotherapy (RT) with or without boost after breast-conserving surgery (BCS), and the real impact of tamoxifen.⁸⁻¹⁰

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In order to analyze real-life clinical practice, a first national prospective survey was performed in France from March 2003 to April 2004 to assess the epidemiologic data, diagnosis, and treatment modalities in 1289 patients with pure DCIS.⁸

In late 2004, the national screening program was applied throughout France, and the French DCIS guidelines were published in October 2009 (www.e-cancer).

With the support of the French Society of Senology (SFSPM) and the National Cancer Institute (INCa), we conducted a new national prospective survey to assess any changes in the demographic, radiologic, and clinicopathologic features and treatment options in patients with DCIS treated from March 2014 to September 2015 compared with the previous survey. This study was also designed to analyze compliance with French DCIS guidelines and to compare our results with those reported in other countries. Treatment results will be evaluated at 3, 5, and 10 years.

Materials and Methods

Patient Inclusion

This prospective observational study was conducted from March 2014 to September 2015 in a total of 71 centers comprising comprehensive cancer centres and private clinics, as well as general and/or university hospitals.

Eligibility criteria were female patients with a diagnosis of pure DCIS. Women with microinvasive lesions, previous or synchronous contralateral invasive BC, or other cancers were excluded.

We collected demographic characteristics (age, family history of breast cancer, menopausal status, hormone replacement therapy), clinical or mammographic findings, biopsy procedures, specimen pathology characteristics (tumor subtype, size, grade, excision quality, and hormone receptor status), and treatments: type of surgery for breast \pm axilla, number of surgical procedures, and adjuvant RT with or without boost to the tumor bed, as well as tamoxifen use. The study was approved by the French data protection authority (CNIL).

Statistical Methods

All summaries and statistical analyses were generated using SAS software (version 9.4, SAS Institute Inc, Cary, NC).

The following statistical tests were used to compare 2 groups: the Student *t* test or nonparametric Mann-Whitney test, when the assumption of normality was not met, for continuous data, and the χ^2 test or Fisher exact test for categorical data. When more than 2 groups were compared, we used the χ^2 test for categorical variables and the Kruskal-Wallis test for continuous variables.

All statistical analyses were performed at a limit of significance of 5% using 2-sided tests, except for normality, which was tested at a limit of 1% (Shapiro-Wilk test).

Results

Study Population

A total of 2125 patients (corresponding to 2141 treated breasts) in 71 centers (4 centers included more than 100 patients, another 4 centers included 50-100 patients, 19 centers included 30-50 patients, and 48 centers included less than 30 patients) were prospectively included. Forty-eight percent of patients were treated in comprehensive cancer centers, 33% were treated in private clinics,

11.5% were treated in university hospitals, and 7.5% were treated in general hospitals.

Demographic Data

The median age was 58.6 years (range, 30-93 years); 3% of the women were younger than 40, 20% were between 41 and 50 years, 64% were between 51 and 70 years, and 13% were over 70 years. A family history of BC (first- and/or second-degree relative) was identified in 37.5% of all patients. Young age was significantly correlated with a family history of BC, as follows: 48% in patients younger than 40 and 45% in women aged 41-50 ($P < .0004$).

A total of 1424 (69%) patients were postmenopausal. The median age of menopause was 50 years.

Twenty-eight percent of the study population had received hormone replacement therapy for a median of 8 years.

Mode of Detection

DCIS was diagnosed by mammographic abnormality in 87.5% of cases, whereas 12.5% of the patients presented with clinical symptoms, such as a mass, Paget's disease, serosanguinous nipple discharge, or nipple retraction. Forty-six percent of women under the age of 40 presented clinical symptoms, whereas symptoms were present in 18% of patients between the ages of 40 and 50 years and 18% of patients over the age of 70, and only 8% of women diagnosed between the ages of 50 to 70 years presented clinical symptoms. This difference was statistically significant ($P < .0001$).

Mammographic Features and Preoperative Biopsy

Mammograms were available for 2078 (97%) of the 2141 breasts; 87% showed the presence of microcalcifications, together with round opacity in 7% of cases, increased density in 5% of cases, and other images and/or combinations in 7% of cases.

A total of 1877 mammograms were evaluated according to the Breast Imaging Reporting and Data System from American College of Radiology (BI-RADS) classification¹¹ and were classified as follows: 58 (3.2%) BI-RADS 2, 115 (6%) BI-RADS 3, 1372 (73%) BI-RADS 4, and 327 (17.5%) BI-RADS 5. Multicentricity or multifocality was identified in 14.3% of 1929 evaluable cases, mostly in young patients: 23.8% in patients younger than 40 and 18.3% in patients aged 41 to 50 ($P = .0056$). Preoperative needle biopsy was performed in 96% of patients. Vacuum-assisted needle biopsy (8-11 gauge) was performed in 79% of cases, and stereotactic core-needle biopsy (14-16 gauge) was performed in 21% of cases.

Surgery

Breast Surgery. All patients underwent surgery. Among 71 centers, twenty did not include the patients treated by mastectomy ($n = 350$, all treated by lumpectomy or quadrantectomy). Among the remaining 1781 patients treated for DCIS, primary surgery consisted of lumpectomy or quadrantectomy in 1530 (85.8%) cases, whereas in 165 (9.4%) and 86 (4.8%) cases, simple or subcutaneous mastectomy was performed, respectively.

Owing to incomplete resection or close resection margins and/or multifocal or large lesions, second surgery was performed in 414 (22.6%) of 1781 cases, consisting of second conservative surgery in 278 (68%) cases, simple mastectomy in 101 (24%) cases, and subcutaneous mastectomy in 35 (8%) cases. A third operation was

French National Survey on DCIS in France

performed in 59 of 414 cases: 38 were simple mastectomy, 18 were subcutaneous mastectomy, and only 3 cases were lumpectomy.

The final overall mastectomy rate was 21.7% after the second operation and 24.8% after the third operation.

Residual disease was present at the second operation in 47% of cases. Predictive factors for residual disease were nuclear grade (NG) and tumor size. Low, intermediate, and high NG rates were 33%, 44%, and 53%, respectively ($P = .014$), and 32% of lesions were smaller than 20 mm versus 57% of lesions that were larger than 20 mm ($P = .0001$).

Immediate breast reconstruction was performed in 50% of cases: 44% after simple mastectomy and 86% after subcutaneous mastectomy ($P < .0001$). Various types of implants were used in 52% of cases, followed by musculoglandular flaps in 30% of cases, a combination of the 2 in 8% of cases, and other techniques in 10% of cases.

Axillary Surgery. Sentinel node biopsy (SNB) was performed in 863 (41%) cases, mostly after mastectomy. The SNB rate was significantly influenced by the type of surgery, the mode of detection, and, more particularly, grade and size (Table 1). Axillary dissection (AD) was performed in only 54 (2.6%) patients; 5.2% of cases of mastectomy and 2.2% of cases of conservative surgery ($P = .01$).

Histopathology

The median tumor size of the 1732 evaluable lesions was 15 mm; 66% of tumors were smaller than 20 mm (Table 2). NG was low in 12%, intermediate in 36%, and high in 47% of cases (5% of cases were not evaluable). Low NG was more frequently observed in small lesions and high NGs more frequently observed in larger tumors, especially those larger than 40 mm ($P < .0001$). After BCS, excision was considered to be complete (with margins ≥ 2 mm) in 83% of cases. The detailed tumor-free margin status is shown in Table 2.

RT

Of the 1658 women treated by BCS, 1608 (97.2%) received whole breast irradiation with a median dose of 50 Gy. A 10 to 16 Gy boost was delivered to 32% of patients. Two factors influenced the use of boost radiation: NG (24%, 31%, and 36.5% for low, intermediate, and high grade, respectively; $P = .019$) and margin status (37.5% ≤ 1 mm, 33% 2-9 mm, and 25% ≥ 10 mm, respectively; $P = .021$). Age and tumor size were not significantly associated with boost radiation. Of the 415 patients who underwent mastectomy, 29 (7%) received RT owing to very extensive disease, deep margins ≤ 1 mm, and/or wide multicentricity.

Hormone Therapy

Only 20 (1%) of the 1896 evaluable patients received hormone therapy, mostly tamoxifen.

Discussion

This second national survey provides comprehensive and unselected data on DCIS characteristics and treatment modalities in France. We also compared the results of this survey with those of the first survey⁸ (Table 3) after widespread implementation of the

Table 1 Factors Influencing SNB Use

	n	SNB %	P
Type of surgery (n = 2103)			
Mastectomy	302	75	
Subcutaneous mastectomy	138	87	<.0001
Conservative surgery	1663	31	
Discovery modalities (n = 2073)			
Clinical	262	51	.0003
Radiologic	1811	39	
Grade (n = 1950)			
Low	248	18	
Intermediate	732	29	<.0001
High	970	57	
Tumor size, mm (n = 1728)			
≤ 5	320	23	
6-10	333	29	
11-20	467	41	<.0001
21-40	380	51	
>40	228	68	

Abbreviation: SNB = sentinel node biopsy.

national screening program (late 2004) and publication of the first national DCIS guidelines in October 2009 (www.e-cancer.fr/). These new data were also compared with data from other large

Table 2 Histopathologic Features

Feature	n	%
Tumor size, mm (n = 1733)		
≤ 5	310	19
6-10	340	20
11-20	468	27
21-40	380	21
>40	225	13
Nuclear grade (n = 2094)		
Low	249	12
Intermediate	746	36
High	987	47
Not specified	112	5
Final margins, mm (n = 1536 ^a)		
≤ 1	260	17
2-3	330	21
4-5	224	15
6-9	157	10
≥ 10	324	21
Not specified	241	16
Hormone receptors (n = 343 ^b)		
Positive ER	343	78
Positive PgR	334	64

Abbreviations: ER = estrogen receptor; PgR = progesterone receptor.

^aBreast-conserving surgery.

^bAssessed in only 19% of the cases.

Table 3 Comparison Between 2 French Surveys: Clinicopathologic Features and Treatment Modalities

	2003-2004, %	2014-2015, %	P
Patients, n	1289	2125	
Centers, n	77	71	
Median age, y (range)	56 (30-84)	58.6 (30-93)	<.0001
Family history of BC	30	37.5	<.001
Menopause	63.5	69	.0013
HRT	52	28	<.0001
Diagnosis			
Mammography	88	88	NS
Clinical	12	12	NS
Biopsy (total)	62	96	<.0001
14-16 G	34	21	<.0001
8-11 G	66	79	<.0001
Median tumor size, mm	14.5	15	NS
Grade			
Low	21	13	<.0001
Intermediate	39	38	NS
High	40	50	<.0001
Margins (<1 mm)	12	20	<.0001
Mastectomy	30.5	25.2	<.0001
BCS	7.7	2.8	<.0001
BCS + RT	61.8	72	<.0001
Immediate reconstruction	55	49	.26
SNB	21	41	<.0001
Axillary dissection	10.4	2.6	<.0001
Tamoxifen	13.4	1	<.0001

Abbreviations: BC = breast cancer; BCS = breast-conserving surgery; HRT = hormone replacement therapy; NS = not significant; RT = radiotherapy; SNB = sentinel node biopsy.

studies performed in several countries, especially The Netherlands, the United Kingdom (UK), Canada, and the United States (US).^{2,9,10,12-16}

The overall rate of mammographically detected DCIS in both surveys was identical: 87.5%, in accordance with other series.¹⁷ Microcalcifications remain the major abnormality (87% vs. 82.5% previously). The rate of BI-RADS III/IV classification was also very similar (88.5% vs. 90.8%). On the other hand, we observed a slight increase in the percentage of women presenting

with “clinical symptoms” in women under the age of 40 (46% vs. 39% previously).

The rate of biopsy-proven diagnosis increased dramatically from 61.8% to 96% ($P < .0001$), with a large predominance of vacuum-assisted needle biopsies (8-11 gauge) increasing from 66.4% to 79% of cases ($P < .0001$).

Final tumor size was assessed in 81.5% of cases (82.4% in the initial survey). Median size was not significantly different between the 2 surveys (15 mm vs. 14.5 mm previously); lesions smaller than 10 mm were observed in 29% of our cases. In the UK study, 34.5% of the 7007 patients treated by BCS presented lesions < 10 mm.¹⁰

The low NG DCIS rate decreased significantly (13% vs. 21%; $P < .0001$), whereas the “high grade” rate increased (50% vs. 41%; $P < .0001$). Almost identical results were reported in a recent large-scale Dutch study including 4901 cases of DCIS, showing 13%, 39%, and 48% of low, intermediate, and high NG, respectively.¹⁸ Table 4 shows the NG distribution in other large-scale national studies. The rate of low-grade tumors varied from 8% to 13% and the rate of high-grade tumors varied from 34% to 57%. Several studies have reported discrepancies in grading accuracy between pathologists, partly owing to the frequency of “mixed forms.”^{3,18}

Surprisingly, the rate of “suboptimal excision” with margins < 1 mm increased from 12% to 20% ($P = .0001$). International guidelines¹⁹ define free margins as margins equal to or greater than 2 mm. Less detailed results are reported in the literature for “close” resection margins and focally involved margins. In these cases, most patients received a 16 to 20 Gy boost dose to tumor bed with good local control, as previously reported.²⁰ This practice complies with the American consensus of specific “clinical judgement” in patients with negative margins less than 2 mm.¹⁹ We observed several changes in the treatment strategy between this survey and the previous survey, reflecting the widespread implementation of the national DCIS guidelines (Table 3).

The mastectomy rate decreased significantly from 30.5% to 25% ($P < .0001$). In a very large UK study (Sloane Project) including 9938 women treated from 2003 to 2012, the mastectomy rate was 29.5%.¹⁰ In another study from the US (2007-2011)² and in an older one from Ontario (1994-2003),¹⁵ mastectomy rates were 27% and 35%, respectively. In the series of 12,256 patients collected by the Netherlands Cancer Registry from 1999 to 2012, 44.3% underwent mastectomy (33.5%, 39.3%, and 49.5% for grades I, II, and III, respectively).¹⁶

In our study, the mastectomy rate was 50% in women under the age of 40. Young age is associated with a high risk of LR related to well-known risk factors, such as extensive disease (> 4 cm),

Table 4 Distribution of Nuclear Grade in 5 National Studies

Grade, %	PRACCIS II (Present Study)	UK Sloane Project ¹⁰	NL Cancer Registry ¹⁶	NL Palga Study ¹⁸	Ontario ¹⁵
Low	12	11	12	13	8
Intermediate	36	32	30	39	46
High	47	57	50	48	34
Unknown	5	—	8	—	12

Abbreviations: NL = Netherlands; UK = United Kingdom.

Table 5 Impact of Whole Breast RT on Local Control After Breast-conserving Surgery

	N	LR, %		Absolute Benefit, %	Follow-up, mo
		No RT	RT		
NSABP B-17 ^{5,a}	818	35	20	15	204
EORTC 10583 ^{6,a}	1010	30	17	13	190
SWE-DCIS ^{28,a}	1046	32	18	14	202
UK-ANZ DCIS ^{29,a}	1030	19.5	7	12.5	120
Ontario ^{15,b}	3303	20.8	15.5	5.3	132
Munich ^{30,b}	1048	20	13.5	6.5	88

Abbreviations: LR = local recurrence; RT = radiotherapy.

^aRandomized trials.

^bRetrospective studies.

multicentric and high-grade lesions, and close or positive margins after BCS.^{21,22}

In this study, AD was almost abandoned (2.6% vs. 10.4% in our previous study; $P < .0001$), whereas the SNB rate doubled (41% vs. 21%; $P < .0001$). Although the SNB rate of approximately 80% among patients treated by mastectomy complies with national and international guidelines, the 31% SNB rate in patients treated by BCS appears to be much higher than expected. In a retrospective Swedish study including 753 patients treated by mastectomy (40%) or BCS (60%) with SNB for pure DCIS in 2008 to 2009, only 5 (0.7%) positive SN were found (3 micrometastases and 2 macrometastases).²³ In a large Danish population-based study in 2618 patients with DCIS, SNB was performed in 54% of cases (44% and 86% in the BCS and mastectomy groups, respectively) and, in 24% of cases, SNB did not comply with guidelines.²⁴ In another international survey (ICSN [International Cancer Screening Network]) studying 3831 screened patients between the ages of 50 and 69 years between 2003 and 2008 (30% of mastectomies), the overall AD and SNB rates were 8.4% and 35%, but with marked differences between countries.²⁵

In the US study based on the National Cancer Database including 88,083 patients diagnosed with DCIS between 1998 and 2011, 37% underwent mastectomy and 63% underwent BCS. The overall AD rate in the mastectomy group decreased from 50% in 1998 to 16% in 2011, whereas the SNB rate increased from 24% to 77%. In the BCS group, the AD rate decreased from 13% to 5% and the SNB rate increased from 7% to 39%.²⁶ A recently published literature review and meta-analysis based on 48 articles with a total of 9803 patients concluded that SNB should be routinely considered only in patients with large (> 2 cm) and high-grade DCIS.²⁷

The use of RT after BCS increased from 89% to 96% ($P < .0001$), reflecting good compliance with national guidelines (published in 2004) based on the updated results of 4 randomized trials as well as other large retrospective studies, all of which showed a 50% to 60% reduction of LRs (both invasive and in situ recurrences) related to the use of RT after BCS. Table 5 shows the results of randomized trials and several large retrospective studies confirming the place of RT in reduction of LR rates after BCS.^{5,6,15,28-30}

The meta-analysis showed that approximately 50% of LRs were invasive.³¹ The benefit of RT increases with time, as the overall

absolute LR reduction was 10.5% at 5 years and 15.2% at 10 years (from 28.1% to 12.9%; log rank $P < .0001$). Despite these results, the use of RT after BCS varies considerably between countries. For instance, a study in Japan showed only 41% of RT use after BCS, whereas other series in the UK,¹⁰ Queensland,³² and Munich³⁰ showed 62%, 62%, and 66% rates, respectively, with similar rates in the ICSN multicenter study.²⁵ A study conducted in the Navarra region of Spain reported a 100% RT rate.

In 2 studies including “very low risk” DCIS, omission of RT led to a marked increase in local recurrence rates: in the ECOG (Eastern Cooperative Oncologic Group)-ACRIN (American College of Radiology Imaging Network) E5194 Study, with a 12-year follow-up, LR rates were 14.4% in cohort 1 (DCIS NG 1-2 < 2.5 cm) and 24.6% in cohort 2 (DCIS NG 3 < 1 cm). It should be noted that the median size of DCIS included in these 2 cohorts was only 6 mm, with very wide free margins in 80% of cases.³³ Similar results were observed in the RTOG (Radiation Therapy Oncology Group) 9804 trial, including low or intermediate DCIS (< 2.5 cm) with ≥ 3 -mm free margins. With a 12-year follow-up, LR rates were 2.8% with RT and 11.4% without RT ($P = .0001$).³⁴

In the present study, 32% of patients treated by BCS and whole breast RT received tumor bed boost. In the literature, boost rates are extremely heterogeneous (ranging from 25% to 71%), and boost radiation is mainly used in “high-risk” cases, including high-grade and extensive DCIS, close or focally positive margins, and young age. In a French-Italian study on 819 patients, boost radiation was used in 48% of cases (55% in France and 45% in Italy; $P = .017$).³⁵ In another multicenter study in The Netherlands, boost radiation was used in 59% of 1248 patients, especially in the case of grade III tumors and/or positive or close (≤ 1 mm) margins.³⁶

The role of boost radiation was reported in a large international retrospective study including 4131 patients: boost radiation (performed in 62% of patients) reduced the 15-year LR rate from 12% to 8.4% ($P = .04$).³⁷

A subgroup of patients in which boost radiation is clearly beneficial should be identified in 2 randomized trials that are now closed for accrual.

Besides, in our group of 361 patients (26%) treated by mastectomy, 29 (8%) underwent chest wall irradiation. As in other studies, very extensive disease, with or without multicentricity and/or deep margins ≤ 2 mm were the main indicators for chest wall irradiation.³⁸

Conclusions

Finally, the DCIS prognosis remains favorable, with a breast cancer-specific mortality rate of 3% in a large Dutch study (3.9% and 2% for patients treated by BCS and BCS + RT, respectively, but 5.4% in women under the age of 40).¹² Data derived from real-life clinical practice are very important to detect possible over-treatment or undertreatment. Our study showed several factors associated with SNB use and risk of residual disease, as well as boost use. We confirmed a small percentage (about 10%-12%) of low-grade DCIS, as in other studies (with also a high misinterpretation rate among pathologists).³⁹ Similarly, DCIS smaller than 5 mm represent less than 20% of cases. Consequently, treatment de-escalation studies omitting RT after BCS, especially the “observational strategy,” appear to be suitable for only about 10% of selected patients.

In the future, this very detailed real-life data-based study (with an already planned follow-up at 5 and 8 years) could allow for a better orientation of DCIS treatment modalities. This kind of approach has already been suggested.⁴⁰

Clinical Practice Points

- DCIS represents about 15% of all breast cancers in France, with literature showing a heterogeneous management. A national survey conducted in 71 centers in 2014 to 2015 allowed us to analyze the real radiologic and pathologic features as well as treatments in daily practice without any selection.
- Among 2125 patients, the median age was 58.5 years. The median tumor size was 15 mm; nuclear grade was low, intermediate and high in 12%, 36%, and 47% of cases, respectively. Margins were negative in 83% of cases. Mastectomy and lumpectomy rates were 25% and 75%, respectively. Sentinel node biopsy and axillary dissection rates were 41% and 2.6%, respectively. After lumpectomy, 97% of patients underwent whole breast irradiation (32% with a boost). Only 1% of patients received endocrine therapy.
- These results are in accordance with the French guidelines published in 2009. Overall, less than 10% of DCIS treated in clinical practice seems eligible for “de-escalation” trials.

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Disclosure

The authors have stated that they have no conflicts of interest.

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Appendix

Complementary Investigator List		
Investigator	Center	City
Dr Delphine Antoni	Centre Paul Strauss	Strasbourg
Dr Delphine Argo-Leignel	CH de Bretagne Sud	Lorient
Dr Jean-Sébastien Aucouturier	Groupe Hospitalier La Rochelle	La Rochelle
Dr Sandrine Avigdor	CHR d'Orléans	Orleans
Dr Marc Baron	Clinique Mathilde	Rouen
Dr Isabelle Bartholomot	Clinique Mutualiste de l'Estuaire	Saint-Nazaire
Dr Pierre Baumann	Centre d'Oncologie de Gentilly	Nancy
Dr Deborah Belemsagha	Centre Médical de Forcilles	Ferolles-Attily
Dr Aurélie Bellière-Calandry	Centre Jean-Perrin	Clermont Ferrand
Dr Marc Bollet	Clinique Hartmann	Levallois-Perret
Dr Marie-Christine Bone-Lepinoy	Centre de Radiothérapie du Parc	Dijon
Dr Patrick Bontemps	CHU de Besançon	Besancon
Dr Fatiha Boulbair	Centre hospitalier de Belfort-Montbéliard	Montbéliard
Dr Claire Brunaud	Institut de Cancérologie de Lorraine	Vandoeuvre-les-Nancy
Dr Louis-Michel Caquot	Institut Jean Godinot	Reims
Dr Christian Chevelle	Clinique Pasteur	Toulouse
Dr Vanessa Conri	CHU Bordeaux	Bordeaux
Dr Anne-Catherine Courtecuisse-Degrendel	Centre Joliot Curie	Saint Martin Boulogne
Pr Didier Cowen	Hôpital de la Timone	Marseille
Dr Francesco Del Piano	Hôpitaux du Léman	Thonon les Bains
Dr Elisabeth Deniaud-Alexandre	CH Départemental La Roche-sur-Yon	La Roche sur Yon
Dr Nadine Dohollou	Polyclinique Bordeaux Nord	Bordeaux
Dr Virginie Doridot	Clinique du Sein	Clermont-Ferrand
Dr Patrick Dubé	Clinique de l'Europe	Amiens
Dr Catherine Ferrer	CHU de Nîmes	Nimes
Dr Virginie Fichet	Clinique de l'Ormeau	Tarbes
Dr Alain Fignon	Clinique de l'Alliance	Saint-Cyr-sur-Loire
Dr Alain Fourquet	Institut Curie	Paris
Dr Sophie Girard	Centre Hospitalier Alpes Léman	Contamine sur Arve
Dr Dominique Gouders	CH de Cornouaille	Quimper
Pr Olivier Graesslin	CHU de Reims	Reims
Pr Jean-Michel Hannoun-Levi	Centre Antoine Lacassagne	Nice
Dr Anne Karst	Centre libéral de radiothérapie	Strasbourg
Dr Hortense Laharie-Mineur	Clinique Tivoli	Bordeaux
Dr Julien Langrand-Escure	Institut de cancérologie Lucien Neuwirth	Saint Priest en Jarez
Dr Sandrine Lavau-Denes	CHU de Limoges	Limoges
Dr Julie Leseur	Centre Eugène Marquis	Rennes
Dr Christelle Levy	Centre François Baclesse	Caen
Dr Francis Lipinski	Centre d'Oncologie et de Radiothérapie	Bayonne
Dr Valérie Magnin	CHU La Réunion	Saint Pierre
Dr Jacques Medioni	Hopital Européen Georges Pompidou	Paris
Dr Jacques Mermet	Médipôle de Savoie	Challes-les-Eaux
Dr Eliane Mery	Gustave Roussy	Villejuif
Dr Erik Montpetit	Centre Saint Yves	Vannes
Dr Matthieu Muller	CH de MORLAIX	Morlaix
Dr Lobna Ouldamer	CHU de Tours	Tours
Dr Karine Peignaux	Centre Georges François Leclerc	Dijon
Dr Philippe Quetin	CHR de Metz	Metz
Dr Aurélie Revaux	GH Diaconesses Croix St Simon	Paris
Dr Jean-Louis Reynoard	Centre Clinical	Soyaux

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Continued

Investigator	Center	City
Dr Pascale Romestaing	Centre Radiothérapie Charcot	Sainte Foy les Lyon
Dr Naoum Sader	CH de Saint-Quentin	Saint-Quentin
Dr François Sensenbrenner	Hôpital Privé Drôme Ardèche	Guilherand-Granges
Dr Hélène Simon	CHU de Brest	Brest
Dr Agnès Tallet	Institut Paoli-Calmettes	Marseille
Dr Pierrick Theret	CHU d'Amiens	Amiens
Dr Caroline Toussaint	Centre Hospitalier Marne-la-Vallée-Jossigny	Jossigny
Dr Véronique Vaini-Cowen	Polyclinique du Parc Rambot	Aix-en-Provence
Dr Brigitte Vie	Clinique Armoricaïne	Saint Brieuc
Dr Anne Vincent-Salomon	Institut Curie	Paris
Dr Delphine Weitbruch	Hôpital Pasteur	Colmar
Dr Cécile Zinzindohoué	Clinique Clémentville	Montpellier
Dr Amira Ziouèche	Hôpital de la Croix Rouge Française	Toulon