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Breast Microcalcifications: Multivariate Analysis of Radiologic and Clinical Factors for Carcinoma

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Abstract. Screening mammography contributes to the improvement of breast carcinoma survival through early detection and treatment of non-palpable lesions. Microcalcifications are of fundamental importance in this process. The percentage of malignant lesions found in biopsies for microcalcifications varies from 10% to 40%. The purpose of this study was to evaluate the relationship between clinical and radiologic records and the presence of malignant breast diseases. To establish the basis for the study, 211 mammographic files showing clustered microcalcifications from 204 women were prospectively reviewed and clinical records were retrospectively drawn. Definitive pathologic analysis was available for all. The value for cancer of each criterion was investigated by univariate and multivariate analyses. A first analysis was performed on the entire population and a second one was performed with stratification on morphologic subgroups. There were 99 malignant lesions (47%). In the entire group, no clinical criterion was significant. In the univariate analysis, five radiologic variables were significant: morphologic type ($p < 0.0001$), number of calcifications per cluster ($p < 0.0001$), linear or triangular distribution ($p < 0.0002$), diameter of the area ($p < 0.01$), and number of clusters ($p = 0.011$). In the multivariate analysis, two criteria remained significant: morphologic type 4 (irregularly punctiform) or 5 (vermicular) microcalcifications (Le Gal's classification) ($p < 0.0001$) and diameter of the cluster larger than 25 mm ($p = 0.032$). In subgroups, in the multivariate analysis, the "age > 60 years" criterion was statistically significant in the group of regular punctiform microcalcifications (type 2); for irregularly punctiform microcalcifications (type 4), "number of microcalcifications > 20" was significant. The morphologic features of microcalcifications must be the first criterion evaluated. They permit identification of characteristically benign (annular calcifications) or malignant calcifications (vermicular calcifications). For the remainder of the calcification types, other criteria must be taken into account, and their value vary with (according to) the morphologic aspect. These findings have implications for the management of women with microcalcifications and could help breast specialists make treatment decisions.

Mammography is the mainstay of early diagnosis of breast cancer. Although this screening contributes to the reduction in breast cancer mortality, it also increases the detection of non-palpable breast lesions. Microcalcifications are of fundamental importance in early diagnosis, but they are not breast cancer specific. Evaluation of indication for biopsy is a problem of major importance in the everyday practice of a breast surgeon [1, 2]. Systematic excisional biopsies of microcalcifications lead to a positive diagnosis of carcinoma in only a small percentage of cases, but controversies exist about management decisions (follow-up, sterotactic biopsy, surgical biopsy).

The purpose of our study was to evaluate the relationship between clinical and radiologic records and the presence of malignant lesions. From a multivariate analysis of 211 mammographic files prospectively recorded, we examined the independent value of each factor generally reported in different published series. Our study was the first to appreciate the value of each criterion according to the morphologic characteristics of microcalcifications. These features are helpful in determining which breast biopsy technique is appropriate.

Materials and Methods

We reviewed the records of 488 women with microcalcifications who were referred to our institution between 1986 and 1996. We selected, for prospective study, the mammographic files of the 204 patients who underwent surgery for 211 clustered microcalcifications without stellate opacities and without a palpable mass.

The diagnosis of clustered microcalcifications was performed with mediolateral, oblique and craniocaudal views for all patients. Magnifications were available for 154 women (73%). The mammograms were categorized by the radiologists without knowledge of the histologic findings. The eight most important radiologic criteria were recorded [3].

1. Number of clusters
2. Retroareolar location (or not) of the cluster
3. Largest diameter of the area (mm)
4. Total number of microcalcifications in the cluster
5. Density of the cluster: number of microcalcifications within a 4-mm-diameter circle
6. Morphologic aspect of the microcalcifications classified by the Le Gal classification (Fig. 1–6) [4]

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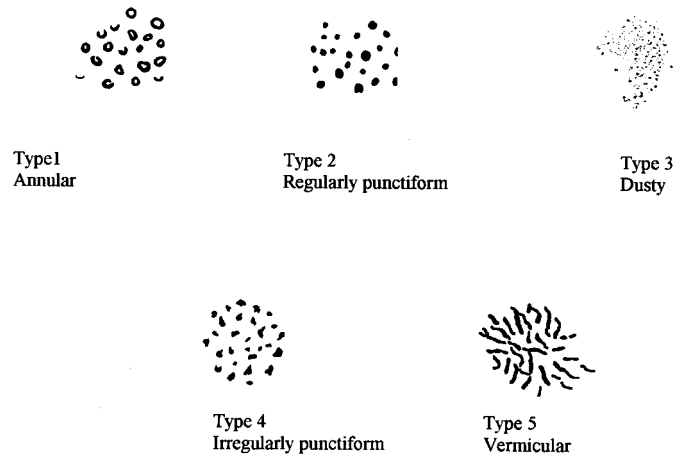


Fig. 1. Description of the morphologic character of the microcalcifications according to Le Gal's classification [4].

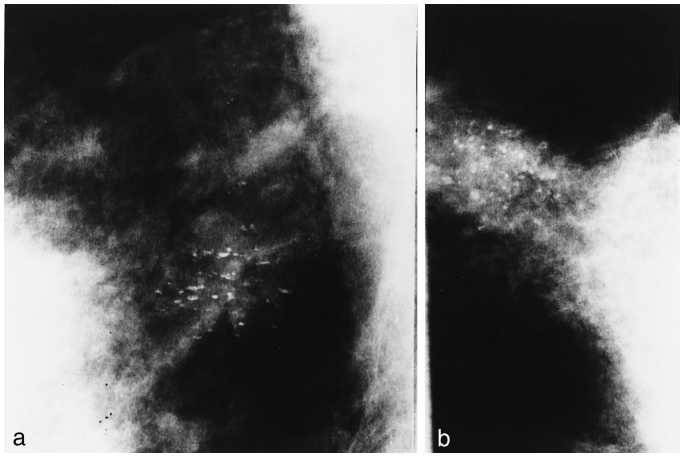


Fig. 2. Type 1 microcalcifications in Le Gal's classification. **a**. oblique view; **b**. craniocaudal view.

7. Heterogeneity when different morphologic aspects were present in the same cluster
8. Linear or triangular distribution pattern (or not)

For each case, the following data were retrospectively drawn from clinical records: patient age, hormonal status, hormonal treatment, parity, breast-feeding, positive personal or family history of neoplasm (breast or others), personal history of benign breast disease.

For all women an open biopsy had been conducted. The procedure was consistent with what is usually advised [5]: preoperative stereotactic hook wire localization, complete excision confirmed by intraoperative radiography of the surgical specimen and by 6-month systematic postoperative mammography.

The definitive pathologic analysis was grouped into two classes:

- Malignant lesions: invasive carcinoma and ductal carcinoma in situ
- Benign lesions: all others

The positive predictive value for cancer of the different criteria was investigated by univariate (chi square, Fisher, or Student tests) analysis. All the variables found to be significant were incorporated stepwise, one by one, into a multivariate logistic regression. Statistical significance of observed differences was set at $p < 0.05$.

Results

Pathologic examination revealed 99 malignant lesions (47%), 55 of which were ductal carcinomas in situ and 44 were infiltrating carcinomas. Of the remainder, 78 were proliferative fibrocystic changes and 12 were lobular carcinoma in situ (Table 1).

The patients ranged in age from 23 to 70 years, with a median age of 52 years.

Entire Group

Univariate Analysis. Table 2 shows the distribution of the studied cases according to histologic diagnosis and clinical records. No difference was statistically significant. Age, menopause status, hormonal treatment, parity, breast-feeding, positive personal or familial history of neoplasm, personal history of benign breast disease were comparable among women with benign and malignant breast lesions.

The following radiologic variables were significantly indicative of malignancy: (1) morphologic aspect, (2) more than one cluster, (3) great number of calcifications per cluster, (4) large diameter of the area, (5) triangular or linear distribution.

The results according to the morphologic aspect of microcalcifications (Le Gal's classification) are recorded in Table 3. This criterion was significantly associated with malignant lesions ($p < 0.0001$): the percentage of malignancy was 27%, 32%, and 65%, respectively, for regularly punctiform (type 2), dusty (type 3), and irregularly punctiform (type 4) microcalcifications. The association was 0% for annular calcifications (type 1) and 100% for vermicular (type 5) microcalcifications.

Table 4 shows the results of the comparison of the other four criteria.

The mean number of calcifications was 24.4 per cluster in the malignant lesions and 16.9 in the benign disease ($p < 0.001$). The "35 or fewer microcalcifications" criterion appeared to be the best level in determining malignancy ($p < 0.0001$).

The diameter of each cluster ranged from 2 to 92 mm. The mean diameter was 17 mm for malignant lesions and 12.7 mm for benign lesions ($p = 0.014$). Twenty-five millimeters was the best level: 44% of malignancy for the clusters smaller than 25 mm and 69% for those larger than 25 mm ($p < 0.01$).

Linear or triangular distribution was statistically associated with malignant lesions ($p < 0.0002$).

Multivariate Analysis. The five significant variables in the univariate analysis were entered into the multivariate analysis: more than one cluster, diameter > 25 mm, linear or triangular distribution of the cluster, number of calcifications > 35 per cluster, and morphologic aspect of microcalcifications. According to the incidence of malignancy, a difference between a group with types 1, 2, 3 (32% or less of malignancy) and a group with types 4 and 5 (65% or more of malignancy) appeared. So, for this analysis and for this criterion, we took the "morphologic type 4 or 5 (or not)" variable into account.

Only two criteria remained statistically significant: the presence

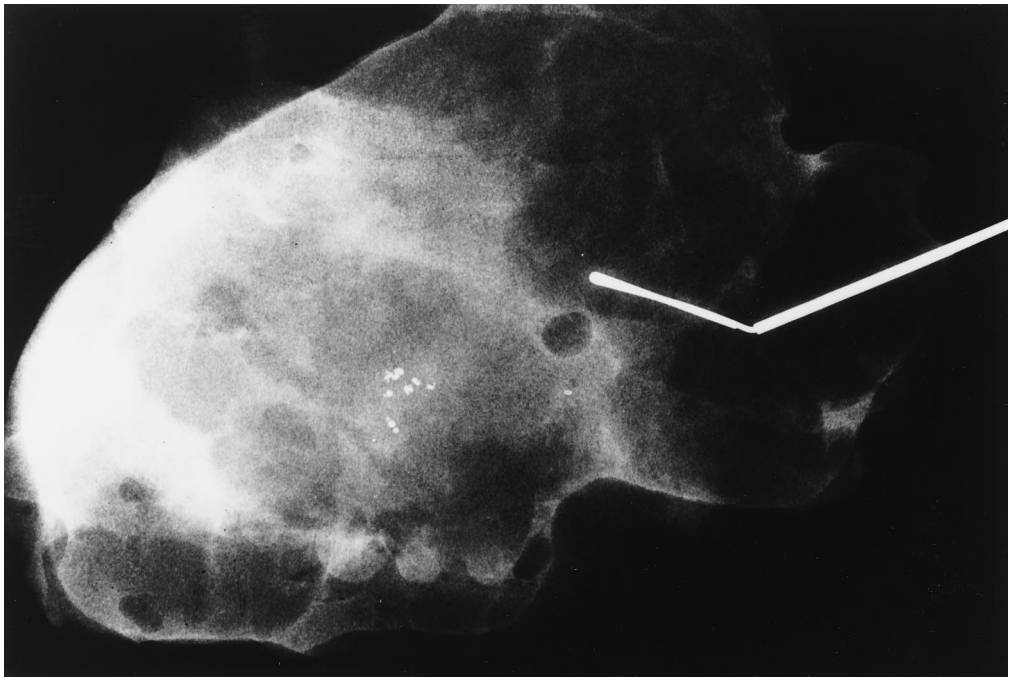
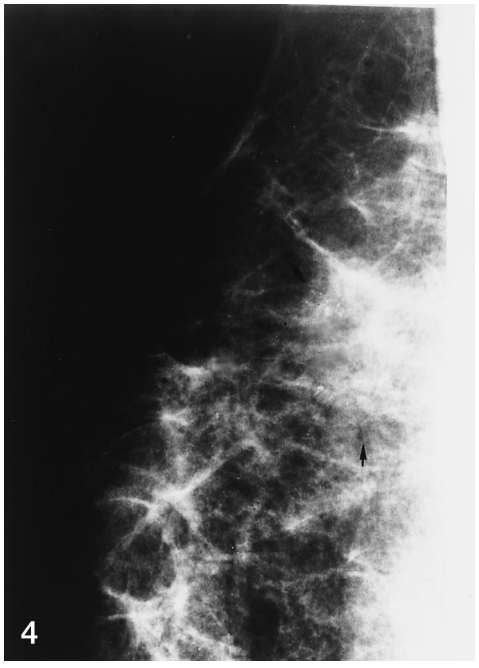
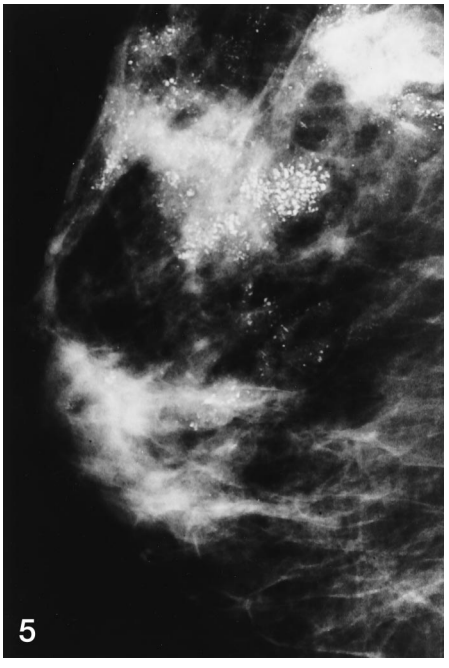


Fig. 3. Type 2 microcalcifications in Le Gal's classification. Radiography of the surgical specimen.





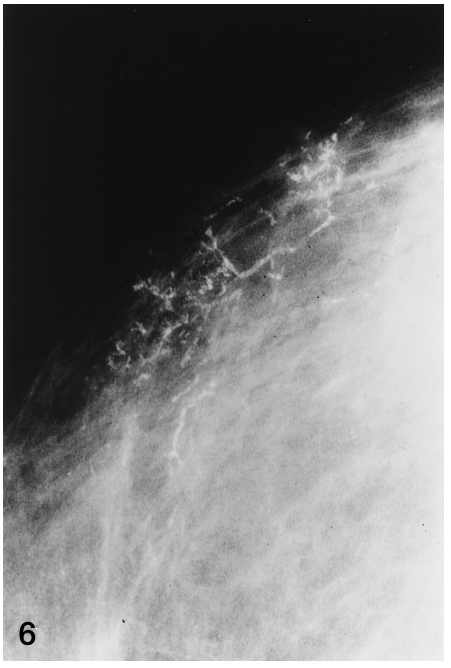


Fig. 4. Type 3 microcalcifications in Le Gal's classification (between arrows).
Fig. 5. Type 4 microcalcifications in Le Gal's classification.
Fig. 6. Type 5 microcalcifications in Le Gal's classification.

of type 4 or 5 microcalcifications (Le Gal's classification) ($p < 0.0001$) and diameter of the cluster >25 mm ($p = 0.032$).

In Subgroups

Because we never found benign lesions in vermicular calcifications (type 5) and never detected cancer in annular calcifications (type 1), we eliminated these two groups, and a second analysis was performed on the remainder of the microcalcification types. We divided the patients into three groups: women with punctiform calcifications, regular (type 2) or irregular (type 4), and those with dusty calcifications (type 3).

Univariate Analysis. For regular punctiform calcifications (type 2), women with malignant tumors were significantly older than women with benign diseases (57.7 vs. 49.2 years, $p = 0.032$) and more often postmenopausal (41 vs. 0%, $p = 0.049$).

For irregular punctiform lesions (type 4), the significant num-

Table 1. Distribution of cases among different pathologic groups.

Malignant	99 (47%)
Intraductal carcinoma	55 (55.5%)
Comedocarcinoma	31
Non-comedocarcinoma	24
Invasive carcinoma	44 (44.5%)
Ductal	41
Lobular	3
Benign	112 (53%)
Fibrocystic dystrophy	78
Lobular carcinoma in situ	12
Adenofibroma	11
Others	11

Table 2. Comparison of risk factors among patients with benign and malignant biopsies.

	Benign	Malignant	*p* value
Age (yr)	51	53	0.107
Breastfeeding (%)			
Yes	50	50	
No	55	45	0.51
Menopausal (%)			
No	59	41	
Yes	50	50	0.32
Postmenopausal hormone (%)			
Yes	50	50	0.6
History of breast cancer (%)			
Yes (27 patients)	37	63	
No	55.5	44.5	0.11
Other histories of carcinoma (%)			
Yes (8 patients)	87.5	12.5	
No	52	48	0.11
Familial history of breast cancer (%)			
Yes	49	51	
No	54	46	0.59

Table 3. Distribution of cases according to Le Gal's classification [4].

Le Gal type	Number of patients	Benign	Malignant	% Malignant
1	4	4	0	0
2	30	22	8	27
3	100	68	32	32
4	52	18	34	65
5	25	0	25	100

ber of calcifications was 20 per cluster (90.5% of malignancy over vs. 46% under, $p = 0.0037$) and the significant cluster diameter was 10 mm (86% vs. 42%, $p = 0.01$). In this subgroup, the density of the cluster appeared significantly related to malignant lesions: 87% of the high-density cluster (> 8 microcalcifications/12.6 mm^2) were malignant compared with 30% of the low-density cluster ($p = 0.0065$).

Neither clinical nor radiologic criteria appeared discriminating for dusty microcalcifications (type 3).

Multivariate Analysis. In the group of type 2 microcalcifications, age > 60 remained the only significant criterion. In women over the age of 60, we found 62.5% malignancy; in younger women, 18% ($p = 0.032$).

In the group of type 4 microcalcifications, number of microcalcifications (> 20) was the only significant criterion: in clusters with fewer than 20 microcalcifications, 51% of the lesions were malignant; in clusters with more than 20 microcalcifications, 90% of the lesions were malignant ($p = 0.004$).

Table 4. Radiologic characteristics statistically significant in univariate analysis.

	Benign (%)	Malignant (%)	*p* value
Number of clusters			
1	58	42	
> 1	37	63	0.011
Number of calcifications/cluster			
≤ 35	58	42	
> 35	17	83	0.0001
Diameter (mm)			
≤ 25	56	44	
> 25	31	69	0.01
Distribution			
Linear, triangular	26	74	
Others	68.5	31.5	0.0002

Table 5. Sensitivity, specificity, and odds ratio of the criteria in the multivariate analysis.

	Sensitivity (%)	Specificity (%)	Odds ratio	95% Confidence interval
Entire population				
Type 4 or 5	58	84	7.18	3.7–13.6
Diameter > 25 mm	18	93	2.8	1.1–6.8
For type 2				
> 60 years	56	86	7.5	1.2–45
For type 4				
Number > 20	59	88	11	2.1–56

The sensitivity, specificity, and odds ratio for each criterion are shown in Table 5.

Discussion

The increase in mammography screening over the years has highlighted more and more non-palpable breast lesions, many of which are benign. Because they may prove to have been unnecessary, invasive procedures (whether stereotactic core biopsy or open biopsy) should be used sparingly. In cases of microcalcifications, indications for biopsy are among the most difficult to establish. The reported incidence of malignant lesions in open biopsies varies from 13% to 45% in different series [6] and was 47% in our series. The purpose of this study was to determine the diagnostic value of clinical or mammographic criteria. Although our object was not the selection of what modality to use for biopsy, it appears that our results could be interesting in that regard as well.

In this series, histopathologic diagnoses were performed on surgical specimens. Our aim was to gain better knowledge of the criteria related to malignancy, and although surgical procedures present disadvantages, they are the "gold standard" against which all other diagnostic techniques should be measured [7]. Inclusion of only surgical biopsy cases in our study ensured histopathologic diagnoses, but it did not enable us to determine the exact frequency of carcinoma in microcalcifications.

The univariate analysis results in our study were consistent with the findings of other series: morphologic aspect, diameter of the area, linear or triangular distribution, number of clusters, number

of calcifications are predictive criteria [6, 8–12]. The last three features disappeared in multivariate analysis, however, because they did not provide independent information. A longitudinal axis of clusters directed toward the nipple can show an intraductal lesion [13]. So alignment of the microcalcifications is often a criterion of suspicion. Our univariate analysis confirmed that linear or triangular aspect was significantly correlated with malignancy. In De Lafontan's multivariate analysis, this criterion remains predictive [6]. This distribution is often found in irregularly punctiform (type 4) and vermicular microcalcifications (type 5), which could explain why this criterion disappeared in our multivariate analysis. Because the morphologic type could be difficult to determine precisely (especially the regularity of the punctiform calcifications), and despite our multivariate analysis results, we think that this feature should help inform a physician's decision to take an aggressive approach. In our study, the "greatest diameter of the cluster $>$ 25 mm" criterion was significant in both the univariate and multivariate analyses for the entire population. This confirms that the average area covered by the malignant lesions was wider than that covered by benign lesions [10]. Certainly, the importance of this criterion explains the disappearance of the "number of calcifications" criterion in the multivariate analysis.

Because the density of ducts behind the nipple is significant, the risk of calcified retroareolar lesions being intraductal seems greater. Thus, this location seems more suspect. Like Franceschi and Le Gal, we did not find a statistically significant correlation between the location of the lesion and the incidence of malignancy [4, 8].

These findings could help breast specialists in that they could perfect the recommendations. Actually, the Breast Imaging Reporting and Data System (BI-RADS) recommended by the American College of Radiology is the most used [14]. Our results showed the importance of Le Gal's classification, which is often used in Europe and which is based on the morphologic aspect of microcalcifications [4]. The lexicon can help physicians if these standardized categories are useful in predicting which lesions are malignant and in determining the best diagnostic protocol. This study supports the importance of these two lexicons (BI-RADS and Le Gal). They permit the identification of characteristically benign or malignant calcifications [15]. Annular, semi-lunar, curvilinear, egg-shell, coarse, or lucent-center forms indicate benign processes [9, 15, 16]. They are classified as type 1 in Le Gal's classification [4] and as BI-RADS category 2 [14]. They do not warrant an aggressive diagnostic approach. Conversely, vermicular or linear forms (type 5 in Le Gal's classification and BI-RADS category 5) are always suspect [8, 17–19]. De Lafontan and coworkers reported a 71% incidence of malignancy in type 5 [6], and we never found benign lesions in such cases. These findings suggest the presence of intraductal lesions, which are more often suspect, particularly comedocarcinomas [20]. Typically, the tumor tissue was necrotic at the center of the duct and later became calcified.

The remainder of the calcifications corresponded to various granular types: more or less regular or dusty; 15% to 40% proved to be linked with cancer [15, 19]. They may be the foci of dystrophic calcification in necrotic tumor cells that have not coalesced to form casts or calcified secretions, or they may result from mucin found in spaces of histologic subtypes other than comedocarcinoma [21]. This group of lesions is often called "indeterminate."

Table 6. Percentage of malignant lesions according to the number of microcalcifications: review of literature.

	Number of calcifications/cluster	% Malignant	*p* value
Franceschi [8]	>15	NP	0.02
De Lafontan [6]	<10	7	
	10	19	
	<20	49	<0.001
Le Gal [4]	>30	56	<0.01
Colbassani [10]	<9	0	
	>30	81	NP
Meunier [30]	3–30	28	
	>30	60	0.01
Avigdor [31]	<30	15	
	>30	73	<0.001
Abbes [32]	<10	9	
	11–50	53	
	>50	100	<0.001
This study	<35	42	
	>35	83	0.0001

NP: not present.

The risk of malignancy varies according to the morphologic aspect as shown by the rate of malignant lesions occurring in relation to Le Gal's typing: 10% for regular (type 2), 19% for dusty (type 3), 28% for irregular (type 4) in De Lafontan's series [6] and 27%, 32%, and 65%, respectively, in our series. These results are not an adequate basis for deciding on a biopsy or for choosing the modality for biopsy. Other criteria are needed which are not useful for types 1 and 5. These microcalcifications correspond to BI-RADS categories 3 and 4, for which recommendations vary from follow-up mammography, to stereotactic biopsy, to open biopsy [22]. The aim of the second part of our study was to question the existence of specific criteria in the group of indeterminate calcifications. As the "morphologic aspect of the microcalcifications" criterion has a binary expression (groups 1, 2, 3 versus groups 4, 5) in the multivariate analysis, a second analysis was performed for types 2, 3, and 4 to specify the particular level of each criterion for each morphologic type.

Two results agree with the assumption that the value of each criterion varies according to the morphologic type. The probability of malignancy seems proportional to the number of calcifications [12, 23], even if it is difficult to define a number under which no cancer is found. In the study of Hallgrimson and co-workers, malignancy could not be ruled out even when the lesion included only a few microcalcifications [12]. Table 6 shows the results for different series. Our study suggests that the number determining malignancy varies with the morphologic aspect of the calcifications. The best level is 35 microcalcifications per cluster for the entire population (predictive value: 83%) and 20 for type 4 only (90.5% malignancy for clusters with more than 20 microcalcifications). Our results are consistent with the French recommendations of the Agence Nationale d'Acréditation et d'Evaluation des établissements et des réseaux de Santé (ANAES) analysis, which categorizes numerous irregular calcifications as BI-RADS category 5 while less numerous calcifications are BI-RADS category 4 [24]. It is generally accepted that biopsy is necessary in the evaluation of irregular microcalcifications, and the French recommendations propose open biopsies for BI-RADS category 5 and percutaneous biopsy for category 4 [24]. Biopsy selection for these two categories could also be based on our results: category 4 for

fewer than 20 calcifications per cluster being suitable for stereotactic biopsy and category 5 for more than 20 calcifications per cluster, suitable for open biopsy.

In the analysis of the entire group, clinical criteria appeared not to be different for the two groups of lesions and so it was not possible to differentiate between them. Although this finding is often presented as justification for biopsy, other studies confirm these indeterminate results [8, 15, 25]. For Harkins and colleagues, this mean that risk factors are high among women referred for open biopsy [9]. Our study does not suggest that clinical risk factors are helpful in decreasing the rate of benign biopsy when considering the entire population of microcalcifications. For regular punctiform microcalcifications (type 2 in Le Gal's classifications and BI-RADS category 3), however, age appears helpful. This finding suggests that a biopsy should be proposed for women over 60 years of age presenting regular punctiform microcalcifications and for whom more than 6/10 biopsies revealed cancer. Our results are consistent with the recommendations that propose stereotactic percutaneous biopsy in BI-RADS category 3 when risk factors are present [24]. These findings can also explain the divergent opinions concerning the interest of this clinical criterion within series where the incidence of this type of microcalcification can differ [25, 26].

From the results in the literature and our results, we propose the following diagnostic and treatment approaches:

- No biopsy for type 1 (BI-RADS 2)
- Systematic surgery for type 5 (BI-RADS 5). (Preoperative stereotactic biopsy can be useful to refine patient information.)
- For type 4, open biopsy for more than 20 microcalcifications (BI-RADS 5); stereotactic biopsy for small clusters with fewer than 20 microcalcifications (BI-RADS 4).
- For regular calcifications, indicative of cancer in 2% to 27% of the cases, first take age into account; stereotactic biopsy for women over 60 (BI-RADS 3 with risk factors). Independent of age, a triangular cluster is suitable for stereotactic biopsy, which may reveal false regular microcalcifications. Otherwise, follow up 6 months later is useful to see if suspect criteria have appeared [27].
- For the dusty calcifications (type 3 and BI-RADS category 4), which are indicative of cancer in 12.5% to 40% of cases, we agree with the recommendation of stereotactic biopsy if the cluster is well identified because we never found specific criteria of malignancy.

These propositions may evolve as new criteria are established with new breast macrobiopsy techniques [28, 29]. Nevertheless, careful management should always be the rule with malignant lesions to avoid unnecessary resections.

Conclusions

This study supports the importance of the morphologic aspect of microcalcifications in the assessment of breast lesions. This must be the first criterion evaluated. Annular calcifications should not be considered indicative of breast cancer. In the presence of vermicular calcifications, an aggressive approach should always be considered. For all other types of microcalcifications, various morphologic criteria must be considered. Our findings have implications for the management of patients with microcalcifications and further studies are needed to confirm our results.

Résumé. Le dépistage par mammographie améliore la survie des cancers du sein grâce à la possibilité de détecter les lésions précoces ainsi que les cancers non-palpables. La mise en évidence d'amas de microcalcifications est d'une importance fondamentale dans ce diagnostic. Le pourcentage de lésions cancéreuses retrouvées sur les biopsies varie de 10 à 40%. Le but de cette étude a été d'évaluer les rapports entre les dossiers cliniques et radiologiques et la présence de lésions malignes du sein. 211 mammographies montrant des microcalcifications chez 204 femmes ont été analysées prospectivement et ensuite on a regardé les dossiers médicaux correspondants. On disposait d'une analyse anatomopathologique définitive pour tous les dossiers. La valeur de chaque critère pour faire le diagnostic de cancer a été analysée en uni- et en multivariée. On a effectué deux analyses: la première sur toute la population, la seconde après stratification selon des sous-groupes morphologiques. Il y avait 99 lésions malignes (47%). Dans la population en général, aucun des critères cliniques n'était significatif. En analyse univariée, cinq critères radiologiques sont sortis significatifs: le type morphologique ($p < 0.0001$), le nombre de calcifications regroupées dans chaque amas ($p < 0.0001$), une distribution linéaire ou triangulaire ($p < 0.0002$), le diamètre de l'amas intéressé ($p < 0.01$), Ie nombre d'amas de microcalcifications ($p = 0.011$). En analyse multivariée, deux critères sont restés significatifs: les microcalcifications de type morphologique 4 (punctiforme irrégulier) ou de type 5 (vermiculaire) selon la classification de Le Gal) ($p < 0.0001$) et le diamètre de l'amas > 25 mm ($p = 0.032$). Dans les analyses multivariées par sous-groupes, l'âge > 60 ans est sorti comme facteur de risque significatif dans le groupe de microcalcifications punctiformes régulières (type 2) et pour les microcalcifications punctiformes irrégulières (type 4), un nombre de calcifications supérieur à 20. L'aspect morphologique des microcalcifications doit être le premier critère qu'on analyse. Il permet l'identification de lésions manifestement bénignes (calcification annulaire) ou manifestement malignes (calcifications vermiculaires). Pour le reste, d'autres critères doivent être pris en compte, avec une détermination spécifique pour les lésions malignes selon l'aspect morphologique. Ces données ont des implications dans la prise en charge des femmes présentant des microcalcifications et pourrait aider des spécialistes du sein, comme les chirurgiens, à prendre leurs décisions.

Resumen. La exploración mamográfica ha aumentado la supervivencia del carcinoma de mama, al permitir detectar y tratar tumoraciones impalpables. En dicho proceso la detección de microcalcificaciones tiene una importancia fundamental. La tasa de lesiones malignas, objetivadas mediante biopsias, en las microcalcificaciones de mama oscila entre el 10 y 40%. El objetivo del presente trabajo fue valorar la relación existente entre la clínica y hallazgos radiológicos con la presencia de lesiones malignas de mama. Se revisaron prospectivamente las historias clínicas obtenidas retrospectivamente de 204 mujeres, en las que las 211 placas mamográficas revelaron agregados microcalcificados. En todas se pudo revisar el diagnóstico anatomopatológico definitivo. El valor de cada factor diagnostico del cáncer de mama se estudió tanto mediante análisis uni como multivariante. El primero, se extendió a toda la población objeto de estudio, el segundo, se realizó tras estratificación morfológica en subgrupos. Se constataron 99 lesiones malignas (47%); ningún criterio clínico fue significativo para toda la población estudiada. Sin embargo, en el análisis univariante se constataron 5 variables radiológicas significativas: las características morfológicas ($p < 0.0001$), el número de calcificaciones por grupo ($p < 0.0001$), la distribución lineal o triangular de las mismas ($p < 0.0002$), el diámetro del área afectada ($p < 0.01$) y el número de agregados microcalcificados ($p = 0.011$). En el análisis multivariante sólo 2 criterios conservaron su significación: las características morfológicas, tipo 4 (microcalcificaciones irregulares puntiformes) y el tipo 5 (disposición vermicular de las mismas), siguiendo la clasificación de La Gal, y el diámetro del agregado > 25 mm ($p = 0.032$). El estudio multivariante por subgrupos demostró que constituía un factor pronóstico estadísticamente significativo la edad > 60 años en el tipo 2 (microcalcificaciones puntiformes regulares) y, en el tipo 4 (microcalcificaciones puntiformes irregulares) el número de microcalcificaciones > 20. El primer criterio diagnóstico que ha de tenerse en cuenta es el aspecto (características) de las microcalcificaciones, pues permite identificar las lesiones benignas (calcificaciones anulares) de las malignas (calcificaciones vermiculares). En los restantes casos deberán tenerse en cuenta otros criterios para determinar el grado específico de malignidad, tales como el aspecto

morfológico de la lesión. Estos hallazgos son importantes tanto para el tratamiento de las mujeres con microcalcificaciones como para las indicaciones quirúrgicas.

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