Allocation of Mammographic Predictors from categories BI.RADS ® 4 and 5 and analysis of the positive predictive value (PPV) for the diagnosis of breast cancer.

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Aims and objectives

Mammography is a utility method known to the early detection of breast cancer clinically occult. To assist in the interpretation of the mammogram, the American College of Radiology (ACR) developed a system, the Breast Imaging Reporting and Data System (BI-RADS®), which is based on the use of a common vocabulary standardized, which allows the incorporation of concepts to facilitate the realization of the radiology reports, allowing categorize lesions according to the degree of suspicion of cancer with a certain positive predictive value (PPV).

As well there is a protocol of radiology reading to have greater certainty in the diagnosis without having histological test, because each risk category is associated a PPV of the radiological signs of that category that determines a specific recommendation for action, treatment or follow up.

This system has been updated in 4 editions (1993, 1996, 1998 and 2003). The latest edition adds the BI-RADS category 6, and subdivides the group 4 in three subgroups (4A, 4B and 4C). Recommended to assign the BI-RADS category 4 by exclusion (cases with VPP greater than BI-RADS 3 but less than BI-RADS 5), leaving open the allocation to each subcategory of BI-RADS 4 to the experience of the individual center.

In summary form, the classification BI-RADS ® (2003) is as follows:

- Category 1: negative, normal breast. Recommendation: routine monitoring.

- Category 2: finding benign nodular (fibroadenomas, oval lesions with calcifications or with fat, axillary lymph nodes, etc.) or benign calcifications (calcification in egg shell, vascular calcification, in tubular form (fine, large), dystrophic, of the skin, round or with clear center, rude in corn flakes, suture threads, milk calcium, punctiform and scattered). Recommendation: routine monitoring.

- Category 3: finding probably benign. Suggests short interval follow-up, because your probabilidad of malignancy (PPV) is less than 2 %, but it implies that cancer will appear in the follow-up in any patient. In nodules image would include round, oval, winged, or focal asymmetric density. Calcifications are included in the lobular round calcifications and luminances grouped. Recommendation: Frequent monitoring (unilateral in the breast affects 6 months followed by bilateral one at 12 and 24 months).
- Category 4: suspicious anomalies. Biopsy should be considered due to risk of cancer, with a PPV that goes from 3-94 %. In all the subcategories the recommendation is the histological study.

  - Category 4A: injury that has a low probability of being malignant, which however, are going to biopsy and results are expected of benignancy. PPV should be considered of 3-5 %.
  - Category 4B: intermediate lesions of suspicion of malignancy. The conduct will depend on the correlation radiohistologica when it comes to accepting a diagnosis of benign nature of the sample by puncture, to the least doubt has to resort to surgical biopsy. PPV should be considered of a 6-50 %
  - Category 4C: lesions with moderate to high suspicion of malignancy but without the classic image of malignancy. PPV should be considered a 51-94 %. The monitoring depends on the correlation radiopathologic, so that the expected outcome is of malignancy, if gettin in benign puncture would have to resort to surgical biopsy.

- Category 5: highly suggestive of malignancy. PPV should be considered of greater than or equal to 95 %. Does not define what exactly the predictors, reference is made to the classic signs of malignancy, as nodule of irregular morphology, especulados margins, high density and microcalcifications associated high suspicion. Recommendation: histological study to confirm and characterize the malignancy.

- Category 6: they are called to the cancers already confirmed with biopsy, prior to your treatment defined (surgery, radiation therapy, chemotherapy, hormone therapy). PPV of 100 %.

The objective of this study is to define a few signs to include the mammographic examinations in categories 5 and 4A, B and C. Once included in each category and given that these categories are forced to perform biopsy, are available in all the cases of pathological diagnosis that we rely to calculate the true VPP. It is intended to see the degree of concordance with the VPP of descriptors assigned previously, to assess the appropriateness of the descriptors defined for each category, as they are consistent or not with the VPP required by the ACR.
Methods and materials

It was established mammographic signs for each category:

A. Category 4A. Anomaly suspicious of malignancy, but low suspicion of malignancy. PPV: 3-5 %.

Nodules:

1. Dense nodules that are included in the category 3 by its imaging characteristics, but that are palpable, in women older than 35 years.
2. Nodules dense, included in the category 3, whose size has increased or that have become palpable, in the course of the successive controls.
3. Nodules dense round, oval or lobed margin microlobulado, non-palpable and without microcalcifications in its interior.

Microcalcifications:

1. Microcalcifications that have been included in the category 3 and that do not have remained stable over the course of follow-up.
2. Regular punctiform microcalcifications, heterogeneous rude and amorphous type of aggregate distribution, that is not associated with nodule, area of distortion or asymmetric density.

Asymmetric Densities:

1. Focal asymmetric densities of glandular aspect, that is, densities of irregular shape, margins and imprecise with radiolucencias in its interior, which are palpable, without producing differential image with ultrasound.
2. The presence of asymmetric breast tissue or asymmetries in the glandular distribution, which is associated with palpable abnormalities, without echographic abnormalities.

Areas of parenchymal distortion:
1. The presence of asymmetric breast tissue or asymmetries in the galndular distribution, which is associated with palpable abnormalities, without echographic abnormalities.

**B. Category 4B. Anomaly suspicious of malignancy, but suspected of intermediate malignancy. PPV: 6-50 %**

Nodules:

1. Dense round, oval nodules or lobed margins blurred, palpable and non-palpable, without microcalcifications in its interior.

**Microcalcifications:**

1. Type microcalcifications punctiform, amorphous and heterogeneous rude of linear or segmental distribution, that is not associated with nodule, area of distortion or asymmetric density.

**C. Category 4C. Anomaly suspicious of malignancy, with high suspicion, but are not classical images of malignancy. PPV: 51-94 %**

Nodules:

1. Dense nodules included in category 3, in which there appear microcalcifications punctiform or amorphous, in the course of follow-up.
2. Dense nodules included in category 3, which appears in the distortion of the surrounding tissues, in the course of follow-up.
3. Dense nodules of any form and margin, except the unifocal, punctiform with microcalcifications or amorphous in its interior.
4. Nodules of dense irregular shape with hidden margins, microlobulados or blurry, without microcalcifications in its interior.

**Microcalcifications:**

1. Microcalcifications of pleomorphic type of aggregate distribution, linear, segmental or regional, new-onset or not.

**Asymmetric densities:**
1. Focal asymmetric densities or asymmetries in the glandular distribution, included in the category 3, which have been made palpable or in which they have appeared microcalcifications punctiform, amorphous or epitheloid or which manifest parenchymal distortion, in the course of follow-up.

2. Focal asymmetric densities of new appearance, also called neodensidades, whether or not tangible, while the patient is in hormonal treatment alternative.

Parenchymal distortions:

1. Areas of parenchymal distortion, which do not disappear with localized compression, whether they are palpable as if they are not, or which contain microcalcifications or not, except in cases that matches a scar.

D. Category 5. Finding highly suggestive of malignancy. PPV: >95 %.

Nodules:

1. Isodense or hiperdense nodules whith oval, round or lobed shape, margins or microlobulados blurred, with microcalcifications of pleomorphic type linear or branched in its interior. 2

2. Isodense or hiperdense nodules whith oval, round or lobed shape, with spiculated margins.

3. Nodules of dense irregular shape with hidden margins, microlobulados or blurred, with microcalcifications in its interior or associated with parenchymal distortion.

Microcalcifications

1. Type microcalcifications linear branched thin discontinuous distribution grouped, linear, segmental or regional.

It has been made initially a descriptive longitudinal, observational study followed by a simple analysis of the data obtained, which analyzed the mammograms for all women subjected to study during the years 2011 and 2012 in the Hospital Complex of Caceres, analyzed a total of 350 consecutive breast lesions. To all their explorations, prospectively, were assigned to one of the categories of risk BI-RADS ® 4A/ B/ C or BI-RADS ® 5 and therefore a particular VPP for malignancy, depending on the signs (predictors) selected mammographic we ordered in four groups: nodules, microcalcifications, focal asymmetric densities (DFA) and areas of parenchymal distortions (ADP). Given that the inclusion in these categories implies the realization of a biopsy, in all cases, the ordered the anatomopathological diagnosis after undergoing biopsy (by percutaneous puncture needle 12-14 gauge G or surgical), in which we rely to calculate the PPV real of each
lesion in each category, globally, by subgroups and mammographic signs. Have followed the rules laid down in the Unit of breast pathology for the collection of information, and as the study did not involve experimental performances outside of the usual clinical practice in breast pathology, it was not considered necessary to obtain the permission of the ethics committee of the Hospital. Each case was interpreted by a single Radiologist of a team of 2 dedicated exclusively to breast imaging (diagnostic and screening program) and experience in diagnostic breast of more than 10 years. Prior to the collection of information, a consensus was reached to use descriptors outlined for assigning patients to a single subcategory by injury, considering the characteristics of greater suspicion. Since each case was evaluated by a single doctor, in the context of health care activity over two years, has not been made specific study of variability.

**METHODOLOGY OF ANALYSIS** Data were collected in Excel tables for later analysis.

- Was first discussed the VPP for carcinoma of the subcategories BI-RADS® 4 and 5 in the series: was assigned a probability of carcinoma (VPP) total and by subcategories of prospectively for each type of injury in mammography, following the descriptors elected (not yet defined in detail by the ACR).

- In second place was retrospective study, calculating the VPP for carcinoma once obtained the histological confirmation, for each category and subcategory of globally and mammographic signs depending on the individual.

- Have been finally calculated relative risks (RR) for each type of injury in mammography, taking as reference group the set of lesions that do not meet the condition analyzed (for example, RR of carcinoma when the injury is a nodule on the rest of lesions that do not meet this condition: microcalcifications, DFA and ADP).
Results

CLASSIFICATION AND NUMBER OF LESIONS

The most frequent lesions were nodules (60.85 %, 213/350), followed by the areas of parenchymal distortion (17.71 %, 62/350), the microcalcifications (15.14 %, 53/350) and focal asymmetric density (6.28 %, 22/350). (Figure 1).

ANALYSIS OF THE POSITIVE PREDICTIVE VALUE FOR CARCINOMA OF THE SUBCATEGORIES BI-RADS ® 4 and BI-RADS ® 5.

Of the 350 injuries, 101 were classified as a subcategory BI-RADS ® 4 (28.85 %), 42 as 4 B (12 %), 123 as 4C (35.14 %) and 84 as BI-RADS ® 5 (24 %). It is histologically confirmed a total of 186 carcinomas through biopsy, which involves a PPV of 53.14 % for the whole series (Figure 7).

By subcategories, the VPP real were 12% for 4A, 40% for 4B, 63% for 4C and 95% for 5. In figures 3, 4, 5, 6 and Figure 2 describes the lesions by subcategories with their respective VPP in global and by type of injury.

**Nodules:**

The total VPP was 52% (213/111), (Figure 7).

In the subcategories 4A / B / C and 5 were classified 75 nodular lesions, with a PPV of 5 % (75/4), 30 injuries, with a PPV of 43% (30/13), 40 injuries, with a PPV of 73% (40/29) and 68 injuries, with a PPV of 94% (68/64) respectively, fulfilling in all cases the VPP required by the ACR.

**Areas of parenchymal distortion**

The total VPP was 68% (62/42), (Figure 7).

In the subcategories 4A and B are respectively classified 2 lesions, with a PPV of 50% (2/1) and 2 other injuries, possible calculate the PPV because none of the injuries confirmed malignancy (2/0). In both cases was not met with the VPP required torque the ACR for those subcategories.
In the subcategories 4C and 5 were classified 50 injuries, with a PPV of 66% (50/33) and 8 lesions with a PPV of 100% (8/8) respectively, fulfilling both with the VPP required by the ACR.

**Microcalcifications:**

The total VPP was 49% (53/26), (Figure 7).

In the subcategories 4 A and C were classified 17 lesions with a PPV of 35% (17/6) and 20 lesions with a PPV of 50% respectively (20/10), not complying with both subcategories with the VPP required by the ACR.

In the subcategories 4 B and 5 classified 10 lesions with PPV of 40% (10/4) and 6 lesions, with a PPV of 100% (6/6) respectively, fulfilling both with the VPP required by the ACR.

**Focal asymmetric Densities:**

The total VPP was 36% (22/8), (Figure 7).

In the subcategories 4A/B/C and 5 are respectively classified 7 lesions, with a PPV of 14% (7/1), 0 injuries, not being possible to establish any VPP, 13 lesions with a PPV of 38% (13/5) and 2 lesions with a PPV of 100% (2/2). For this injury, only category 5 met with the VPP required by the ACR.

In summary, by descriptors, the allocation of lesions was adequate in the subcategories 4A for nodules (PPV 5 % ); in the 4B for nodules (43 %) and VVP microcalcifications (PPV 40 %); in the 4 C for nodules (PPV 73 %) and areas of parenchymal distortion (PPV 66 %) and for all the injuries in category 5 (VPP > 95 % ). (Figure 7 and 8).

Therefore, in this series of cases, the majority of the individual descriptors (microcalcifications, DFA and ADP) were within the VPP corresponding to the sub category 4B, not having been appropriately assigned some types of lesions (microcalcifications, DFA and ADP of 4A, which finally corresponded to 4B and the microcalcifications and DFA of 4C that finally corresponded to 4B. ) The exception were the nodules in all categories and the ADP of 4C, that if they were well allocated from the start.
RETROSPECTIVE ANALYSIS OF THE PROBABILITY OF CARCINOMA (RR) OF EACH TYPE OF LESION BY SUBCATEGORIES.

The PPV of the mammographic descriptors are listed in figure 7. The RR calculated for each lesion is reflected in figures 8 and 9. The study of RR has been useful for the identification of the lesions that may be considered risk factors for malignancy (values of RR > 1) as well as low risk in comparison with the rest of lesions and/or descriptors in your same group (RR < 1).

By type of lesion in the mammogram, the nodules present values of RR > 1 in the categories 4B and C, which indicates a probability of carcinoma significantly higher when the injury is classified a nodule in those categories that is a nodule in 4A and 5, where its RR is <1.

With regard to the microcalcifications, presented a RR >1 in the category 4A and 5, thus taking greater probability of carcinoma that when the microcalcifications are classified in 4B and C, where your RR is < 1.

The DFA presented a RR>1 in the category 4A and 5, with more likely to develop a carcinoma that when sorted in 4C (could not be calculated in 4B). However, the ADP in all categories (except in 4B where could not calculate) had a RR >1, indicating greater probability of carcinoma when we find this type of injury compared to the other.
Fig. 1: The number of lesions.

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Fig. 2: Allocation of the prospective lesions to each BI-RADS category @ VPP and end of each category, once obtained the histologic findings.
**Fig. 3:** Number of injury assigned to the category 4A, histologic confirmation and PPV real for malignancy. O. C: goal fulfilled with regard to the VPP marked by the ACR.

**Fig. 4:** The number of injuries to the assigned category 4B, histological confirmation and PPV real for malignancy. O. C: goal fulfilled with regard to VPP marked by the ACR.
Fig. 5: The number of lesions assigned to the category 4C, histological confirmation and PPV real for malignancy. O. C: goal fulfilled with regard to VPP marked by the ACR.

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<table>
<thead>
<tr>
<th>VPP de BI-RADS ® 5: 95-100 %</th>
<th>Total</th>
<th>No Malignos</th>
<th>Malignos</th>
<th>VPP para malignidad (IC 95%)</th>
<th>O. C.</th>
</tr>
</thead>
<tbody>
<tr>
<td>BR 5 General</td>
<td>84</td>
<td>4</td>
<td>80</td>
<td>95 % (90,1-100)</td>
<td>Sí</td>
</tr>
<tr>
<td>BR 5 Nódulos</td>
<td>68</td>
<td>4</td>
<td>64</td>
<td>96% (87,8-100)</td>
<td>Sí</td>
</tr>
<tr>
<td>BR 5 Microcalcificaciones</td>
<td>6</td>
<td>0</td>
<td>6</td>
<td>100 % (91,7-100)</td>
<td>Sí</td>
</tr>
<tr>
<td>BR 5 Densidades focales asimétricas</td>
<td>2</td>
<td>0</td>
<td>2</td>
<td>100% (75-100)</td>
<td>Sí</td>
</tr>
<tr>
<td>BR 5 Áreas de distorsión</td>
<td>8</td>
<td>0</td>
<td>8</td>
<td>100% (93,8-100)</td>
<td>Sí</td>
</tr>
</tbody>
</table>

Fig. 6: Number of lesions assigned to Category 5, histological confirmation and PPV real for malignancy. O. C: goal fulfilled with regard to VPP marked by the ACR.

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<table>
<thead>
<tr>
<th>Número de lesiones/Número malignas (VPP) (IC 95%)</th>
<th>4A</th>
<th>4B</th>
<th>4C</th>
<th>5</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nódulos</td>
<td>75</td>
<td>4</td>
<td>10</td>
<td>13</td>
<td>213</td>
</tr>
<tr>
<td>Microcalcificaciones</td>
<td>7</td>
<td>1</td>
<td>2</td>
<td>1</td>
<td>21</td>
</tr>
<tr>
<td>Densidad focal asimétrica</td>
<td>7</td>
<td>1</td>
<td>1</td>
<td>5</td>
<td>16</td>
</tr>
<tr>
<td>Áreas de distorsión</td>
<td>2</td>
<td>1</td>
<td>2</td>
<td>1</td>
<td>6</td>
</tr>
</tbody>
</table>

Fig. 7: Lesions in mammography: total number and PPV, by subcategories and in combination in the entire series.

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**Fig. 8:** Relative Risk of the different types of lesions.

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<table>
<thead>
<tr>
<th>Tipos de lesiones y su RR (IC 95%)</th>
<th>4A (3-10%)</th>
<th>4B (11-50%)</th>
<th>4C (51-94%)</th>
<th>5 (95-100%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nódulos</td>
<td>0,173 (0,6-0,53)</td>
<td>1,3 (0,53-3,19)</td>
<td>1,25 (0,96-1,63)</td>
<td>0,941 (0,87-1)</td>
</tr>
<tr>
<td>Microcalcificaciones</td>
<td>4,94 (1,81-8,93)</td>
<td>0,98 (0,41-2,34)</td>
<td>0,768 (0,48-1,22)</td>
<td>1,054 (1-1,11)</td>
</tr>
<tr>
<td>Densidad focal asimétrica</td>
<td>1,22 (0,18-8,14)</td>
<td>No aplicable</td>
<td>0,587 (0,29-1,18)</td>
<td>1,051 (1-1,1)</td>
</tr>
<tr>
<td>Áreas de distorsión</td>
<td>4,5 (1,01-20,04)</td>
<td>0</td>
<td>1,095 (0,83-1,44)</td>
<td>1,055 (1-1,11)</td>
</tr>
</tbody>
</table>

**Fig. 9:** Relative Risk of various types of lesions and VPP calculated according to histological results. Between parentheses mark the VPP is required by the ACR for each subcategory. In blue are marked the descriptors that have met the PPV of ACR.

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Conclusion

We were be able to verify the suitability of the majority of the mammographic signs elected on a global basis, therefore, except in the category 4A, in the rest of categories to meet VPP required by the ACR. Although the VPP of these categories justify filiation histological regardless of age or associated clinical, the characterization in 4A/B/C or 5 could be useful in decision-making after the puncture and the modality of treatment to apply. In agreement with these results, we propose the following correlation with the new classification of the category BI-RADS® 4 and 5: BI-RADS® 4A

- Dense nodules that are included in the category 3 by its imaging characteristics, but that are palpable, in women older than 35 years.
- Dense nodules, including in category 3, whose size has increased or that have become palpable, in the course of the successive controls.
- Dense round, oval or lobed margin microlobulate nodule non-palpable and without microcalcifications in its interior.

BI-RADS® 4B

- Nodules dense round, oval or lobed margins blurred, palpable and non-palpable, without microcalcifications in its interior.
- Type microcalcifications punctiform, amorphous and heterogeneous rude of linear or segmental distribution, that is not associated with nodule, area of distortion or asymmetric density.
- Microcalcifications that have been included in the category 3 and not have remained stable in the course of follow-up.
- Regular punctiform microcalcifications, heterogeneous rude and amorphous type of aggregate distribution, that is not associated with nodule, area of distortion or asymmetric density.
- Microcalcifications of pleomorphic type of aggregate distribution, linear, segmental or regional, new-onset or not.
- Focal asymmetric densities of glandular aspect, that is, densities of irregular shape, margins and imprecise with radiolucencias in its interior, which are palpable, without producing differential image with ultrasound.
- The presence of asymmetric breast tissue or asymmetries in the glandular distribution, which is associated with palpable abnormalities, without echographic abnormalities.
- The presence of asymmetric breast tissue or asymmetries in the galndular distribution, which is associated with palpable abnormalities, without echographic abnormalities.
- Focal asymmetric densities or asymmetries in the glandular distribution, including category 3, which have been made palpable or in which they have appeared microcalcifications punctiform, amorphous or epitheloid or in which it manifests itself parenchymal distortion, in the course of follow-up.
• Focal asymmetric densities of new appearance, also called neodensidades, whether or not tangible, while the patient is in hormonal treatment alternative.

BI-RADS® 4C

• Dense nodules included in category 3, in which there appear microcalcifications punctiform or amorphous, in the course of follow-up
• Dense nodules included in category 3, which appears in the distortion of the surrounding tissues, in the course of follow-up.
• Dense nodules of any form and margin, except the unifocal, punctiform with microcalcifications or amorphous in its interior.
• Nodules of dense irregular shape with hidden margins, microlobulados or blurry, without microcalcifications in its interior.
• Areas of parenchymal distortion, which do not disappear with localized compression, whether they are palpable as if they are not, or which contain microcalcifications or not, except in cases that matches a scar.

BI-RADS® 5

• Iso or blade nodules of oval, round or lobed, margins or microlobulados blurred, with microcalcifications of pleomorphic type linear or branched in its interior.
• Iso or blade nodules of round, oval or lobulated espiculados margins.
• Nodules of dense irregular shape with hidden margins, microlobulados or blurred, with microcalcifications in its interior or associated with parenchymal distortion.
• Iso or blade nodules of irregular shape and espiculados margins, with or without microcalcifications in its interior. - Type microcalcifications linear branched thin and discontinuous distribution grouped, linear, segmental or regional.

It would be very beneficial larger studies and propose the descriptors for each category by different researchers, in different centers, so that the ACR could have large databases in order to define the descriptors of each category, providing a better support for the decision-making.
References


