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Masses in mammography: What are the underlying anatomopathological lesions?

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Abstract The semiological description of masses in mammography is based on the BI-RADS system provided by the American College of Radiology. The contour is the most discriminating morphological criterion between benign and malignant masses. Most circumscribed masses are benign. Nevertheless, due to specific histological characteristics, certain malignant lesions or lesions with a risk of malignancy may appear in the mammography in this falsely reassuring form. An indistinct contour in the mammography is suspicious and requires a tissue sample. The positive predictive value of malignancy varies according to the morphology of the contour. It is lower for microlobulated contours, increases for masked, then indistinct contours and reaches 96% for spiculated contours. However, in rare cases, certain benign lesions may appear in the form of spiculated masses. In these specific cases, a correlation between the histological results with the imaging data is essential in order to avoid failing to recognise an underlying malignant lesion that the biopsy may have underestimated.

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In mammography, a mass is defined as a space-occupying lesion, visible in two different projections, characteristic by its shape and contour. The asymmetry of the density, as opposed to the mass, corresponds to a localised asymmetric aspect of the mammary gland, without a defined contour. The mass should be measured and located. For this, a profile view, in addition to the external anterior posterior and oblique views is recommended. The mammogram with localised compression allows for a more precise analysis of the shape, contour and density of the mass. It is also useful to distinguish an image obtained by superposition of the mammary gland from a real mass.

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According to the BI-RADS system (Breast Imaging Reporting and Data System) by the American College of Radiology (ACR), a mass is characterised by [1]:

- the shape: round, oval, lobulate or irregular;
- the contour: circumscribed, microlobulated, masked, indistinct, spiculated;
- the density with respect to normal fibroglandular tissue: high, medium or low density or containing fat;
- the association with other anomalies: micro or macrocalcifications, skin retraction, skin thickening, architectural distortion, etc.;
- the evolution over time when past mammograms are available.

The contour is the most discriminating morphological criterion between benign and malignant masses. The positive predictive value (PPV) for malignancy ranges from 2% for circumscribed masses to 96% for spiculated masses [2].

Circumscribed masses

A circumscribed mass in mammography is a mass where the contour is clearly defined along at least 75% of its surface. The remaining 25% may, at most, be masked by the adjacent gland.

Circumscribed masses first indicate benign lesions. In mammography, circumscribed masses of typically benign appearance, placed in category 2 of the BI-RADS system by the ACR, have to be distinguished from “probably” benign lesions, placed in category 3, as they require short-term monitoring (in general after 4 months, then 1 year, then 2 years).

Typically benign masses: BI-RADS 2

In the mammogram, the semiology of certain masses is characteristic, thereby allowing them to be classified as benign with certainty. Therefore, knowledge of the semiology is essential so as not to prescribe useless radiological controls for lesions that are certainly benign, and also not to place images in this category where the benign nature is doubtful and will then not be monitored.

The typically benign masses in mammography are:

- circumscribed masses with macrocalcifications (fibroadenomas and calcified cysts);
- masses of fatty or mixed density;
- circumscribed masses corresponding to cysts in the sonography.

Calcified fibroadenomas

A fibroadenoma is a benign fibroepithelial proliferation distinct from the adjacent mammary parenchyma. The distribution of the epithelial structures is homogenous on the surface of the tumour and is balanced with the connective component.

"Juvenile" (or "cellular") fibroadenomas are rare lesions characterised by mixed epithelial and connective hyperplasia with sectors of hypercellularity of the stroma but without an imbalance between the two components. They are generally faster growing and larger. The fibroadenoma is an oval or lobulate tumour, with well defined contours due to the existence of a peripheral pseudocapsule formed by "compressed" connective tissue, accounting for the circumscribed contour in mammography [3] (Fig. 1). Since the growth of the fibroadenoma is hormone sensitive, the natural evolution after menopause is the hyalinisation and appearance of coral-shaped ("pop-corn") calcifications, pathognomonic in mammography (Fig. 1d).

Calcified cysts

Breast cysts are unilocular formations corresponding, in histology, to a liquid distension of the lobular acini. In mammography, they are masses with a distinct contour and homogenous density. They may contain "milk of calcium" that sediments in the profile view and produces the characteristic "teacup" appearance of the intracystic microcalcifications. In mammography, the macrocalcifications of the cysts are typical, due to their arcuate appearance related to the calcification of the walls of the cyst. When all of the walls are calcified, this creates the classic image of rounded macrocalcification with a light centre.

Masses containing fat

Lymph node
In mammography, the axillary lymph node is characteristic in the form of a round or oval mass, with a circumscribed contour or radiotransparent peripheral indentation, the peripheral density corresponding to the cortex and the radiotransparent zone to the fatty hilum (Fig. 2a).

Oily cyst
The oily cyst is a post-traumatic lesion (whether or not iatrogenic). The initial trauma leads to destruction of adipocytes in the breast that release their lipid content in the interstitium, provoking the liquification of the fatty acids and the formation of a fibrous capsule formed by the saponification of the fats. Therefore, in mammography, the oily cyst characteristically appears in the form of a round or oval, well circumscribed mass of oily density, surrounded by a thin peripheral capsule (Fig. 2b). The calcium may precipitate along this capsule and form macrocalcifications that have a typical "eggshell" appearance in mammography.

Hamartoma
A hamartoma is a well-circumscribed pseudo-tumoral lesion, formed by a heterogeneous blend of different components of normal breast tissue.

Therefore, variable proportions of fibrous tissue, glandular tissue and fats are found. In the mammography, this composition accounts for the well-circumscribed, round or oval mass, containing fibroglandular tissue and radiotransparent fat, in certain cases associated with a peripheral pseudocapsule, histologically corresponding to the compression of the adjacent normal tissue. This is the classic image of a "breast within a breast" (Fig. 2c).

Lipoma
A lipoma is a benign tumour formed from mature adipocyte tissue, surrounded by a pseudocapsule formed by the compression of normal breast tissue. For this reason, in the mammography, the lipoma typically appears as a well-circumscribed, round or oval, totally radiotransparent mass, exerting a mass effect on the adjacent tissue. Necrosis may
be at the origin of rearrangements, with the appearance of arcuate macrocalcifications.

**Galactocele**
A galactocele is a retention cyst containing milk, resulting from the occlusion of a milk duct. In the mammography, the density of the galactocele depends on the composition of the milk in the cyst, consisting of variable proportions of proteins and lipids. In the profile view, there may be a liquid/fat level that is then pathognomonic. In certain cases, it is possible to find a liquid/calcium level or even arcuate calcifications, related to fat necrosis.

**Probably benign masses: BI-RADS 3**
In mammography, they are well-circumscribed, round, oval or lobulated masses and are not calcified or liquid in sonography. The vast majority of these masses correspond to benign lesions such as a fibroadenoma or cyst with thick contents. However, it is necessary to monitor these lesions on a short-term basis, even though the positive predictive value is very low (<2%) since certain types of cancers or lesions comprising a risk may present in this falsely reassuring form. In case of a morphological modification or an increase in the size of a circumscribed mass, a histological sample should be taken. In a woman with a high risk of breast cancer, this biopsy is
indicated as soon as the mass is discovered, due to the higher rate of cancer with a reassuring mammography/sonography.

Lesions involving a risk

**Phyllode tumour**
A phyllode tumour is a proliferation with a double epithelial and a connective component that is well circumscribed with respect to the adjacent breast parenchyma. The distribution of the epithelial structures is heterogeneous within the stroma, which is predominant and characterised by its hypercellularity and expansive nature. The interface between the lesion and the adjacent breast tissue may be regular with ‘pushing’ or even more invasive aspects. Most, although not all, phyllode tumours are benign (grade 1) (75%), with a non-negligible proportion of borderline (grade 2) (8%) and malignant (grade 3) (17%) lesions [4]. By mammography or histology, phyllode tumours are difficult to distinguish from fibroadenomas (Fig. 3). The differential diagnosis with a fibroadenoma, in particular of the ‘cellular’ type, may be difficult with simple biopsy samples.

These lesions are fast growing and the indication for the biopsy of a circumscribed mass is in general raised due to the growth of the lesion between two controls. A size exceeding 3 cm may also result in a biopsy due to the higher rate of malignancy for large lesions [5].

**Papilloma**
A papilloma is an intra-ductal lesion consisting of an epithelial proliferation developed around fibrovascular stalks. The central papilloma, more often solitary and close to the nipple is distinguished from the peripheral papilloma, more often multiple and smaller. Papillomas, mainly of the peripheral type, may be associated with atypical ductal hyperplasia lesions, ductal carcinoma *in situ*, or even invasive carcinoma. In mammography, a papilloma is rarely found due to its small size. When visible, it may appear in the form of a round mass with a circumscribed contour, in general corresponding to walls of the dilated lactiferous duct, more or less associated with polymorphous microcalcifications.

**Malignant tumours**

**High grade invasive ductal carcinoma**
Common high grade, invasive ductal carcinoma (no special type or NST according to the WHO) [6] may, in certain cases, occur in the form of a mass with a circumscribed contour. This specific presentation is related to the very rapid proliferation of the lesion, at the origin of concentric growth of the mass and thereby its round or oval form, as well as the absence of stroma reaction around the lesion, accounting for the sudden interface with the normal adjacent breast tissue and therefore its regular contour (Fig. 4).

**Medullary carcinoma**
Medullary carcinoma is a specific histological sub-type of invasive ductal carcinoma, corresponding to a high-grade proliferation with a high mitotic index, large syncitial cells, associated with lymphoid infiltration and not very abundant fibrous stroma. In mammography, it usually presents as an oval, round or lobulated mass, with a contour that may be circumscribed. This well-circumscribed contour is due to the mass effect that the tumour has on the adjacent mammary gland without really invading it (‘pushing’ effect), and to the very limited nature of the essentially inflammatory stroma reaction at the interface.

**Mucinous carcinoma**
Mucinous or colloid carcinoma is also a specific sub-type of invasive carcinoma. This tumour is highly differentiated, characterised by the existence of a large quantity of extracellular mucins within which carcinomatous structures float. In mammography, it may present as a dense, well-circumscribed mass, especially in the pure forms [7]. The well-circumscribed nature is again related to the pushing of the normal tissue by the tumour and the absent or weak stoma reaction (Fig. 5).

**Papillary carcinoma**
The “encapsulated” variant of papillary carcinoma is characterised by the branching of fibrovascular stalks lined with tumoral epithelial cells of low to moderate nuclear grade, surrounded by a well-circumscribed fibrous capsule observed in mammography. These stalks and the periphery of the lesion are in most cases without a base of myoepithelial cells [6].

![Figure 3](image_url)

Figure 3. Grade 1 phyllode tumour: a: histology: fibro-epithelial lesion with polylobate contours (HES); b: histology: cellular richness of the connective component deforming the epithelial structures (HES); c: mammography: oval mass with a partly circumscribed and partly masked contour.
Rare tumours
Other, much more rare, malignant tumours may present in mammography by a well-circumscribed mass. These are intramammary metastases of cancer of another origin (melanoma, pulmonary carcinoma, ovarian, carcinoid tumours, etc.) (Fig. 6), metastatic nodes and lymphomas.

Non-circumscribed masses: BI-RADS 4 or 5
In mammography, the existence of a non-circumscribed contour, whether microlobulate, masked or indistinct, justifies a biopsy for histological examination. The aetiologies of non-circumscribed masses are extremely varied and include benign lesions (complicated cysts, fibroadenomas, adenosis, etc.) as well as lesions involving a risk (phylloide tumour, papilloma, etc.) or even malignant lesions of all histological types.

However, the risk of malignancy differs according to the morphology of the contour: the microlobulate contour is associated with a 17% risk of cancer, the masked contour with a 33% risk of cancer and the indistinct contour with a 44% risk of cancer [8].

At the microscopic level, microlobulation is related to a microinvasion of the stroma. The indistinct contour follows infiltration by the tumour of the adjacent...
Masses in mammography: What are the underlying anatomopathological lesions?

In mammography, spiculated (or stellar) masses correspond to opacities formed by a dense centre from which arise multiple radial prolongations called spicules. They differ from architectural distortions by the presence of a dense centre. The mammography aspects vary and depend on the thickness, length and distribution of the spicules around the mass. The PPV of malignancy in mammography of a spiculated mass is very high, about 96%.

Malignant spiculated masses

Malignant spiculated masses, in the vast majority of cases, correspond to invasive carcinomas. The spiculate nature of the contours is preferentially found for slow growth lesions that will generate a major and progressive stroma reaction, leading to the formation of the spicules.

Common invasive ductal carcinoma (or NST carcinoma)

NST invasive carcinoma accounts for 75% of all breast cancers [6]. The mammography presentation in the form of a stellar mass is present in 72% of the low-grade lesions, but in only 24% of the high grade [9].

Macroscopically, the stellar lesion consists of a dense central mass surrounded by peripheral spicules. The histological analysis of the dense centre detects a fibroelastoidoed stroma containing a low proportion of tumoral cells (mean cell/stroma ratio = 1/3). The contours of the dense centre are irregular due to the presence of retractile spicules. These spicules correspond to connective tissue consisting of variable proportions of fibrosis and elastosis, responsible for the retractile nature and therefore the stellar aspect in the imaging (Fig. 7). The spicules may contain tumoral cells (invasive or in situ lesions) that are more abundant at the base of the spicule and more rare at the end. Very fine spicules are generally related to a fibrous reaction whereas short and thick spicules probably follow the infiltration of the connective tissue by tumoral cells [10]. Nevertheless, in mammography, it is not possible to distinguish tumoral spicules from non-tumoral spicules and it is therefore essential to specify the size of the dense centre as well as the totality of the stellar lesion, including spicules. In addition, this latter measure is better correlated with the clinical size [11] than only measurement of the dense centre.

In mammography, the stellar mass is sometimes surrounded by a light peripheral halo whose outer limit corresponds to the end of the spicules. The hypothesis used to account for this radiological aspect is dehydration of the peritumoral fatty tissue [12].

Invasive lobular carcinoma

Invasive lobular carcinoma accounts for 5 to 15% of the invasive breast carcinomas [6]. Histologically, it corresponds to a proliferation of non-cohesive monomorphous small cells distributed in “Indian file” or concentrically around lobules that may be the seat of lobular neoplasm. The stroma reaction is generally moderate. Therefore, the tumour may invade a large proportion of the breast tissue without modifying the architecture and thereby making it difficult to detect in the imaging. The most frequent mammography presentation of invasive lobular carcinoma is an asymmetry of density [13]. Nevertheless, in about one third of the cases, invasive lobular carcinoma presents in the form of a spiculate mass, especially when the evolution is long (Fig. 8).

Tubular carcinoma

Tubular carcinoma is a sub-type of invasive carcinoma, formed by highly differentiated tubules consisting of a single layer of regular cubo-cylindrical cells, arranged within an abundant fibrous and elastoidosic stroma. In mammography, the classic appearance is that of a small spiculated mass, in 50% of the cases associated with microlacifications [14]. Tubular carcinoma is a slow growing lesion with a good prognosis. This is why the mammography image may sometimes appear to be stable for several years. Therefore, the stability of a stellar image over time isn’t a criterion of benignity.

Figure 7. Invasive ductal carcinoma, spiculated form: a: mammography: oval mass with short peripheral spicules; b: histology: alternation of lobular contours and sometimes coalescent short spicules rich in tumoral cells invading the peripheral fatty breast tissue. Post-biopsy scar in the centre (HES).
Benign spiculated masses

Benign spiculated masses are rare (<4%). In case of a benign result for the biopsy of a stellar mass, it is essential to make sure of the radiohistological concordance and, with the slightest doubt, take another biopsy with a larger calibre needle (macrobiopsy by suction) or complementary surgery. The aetiologies of benign spiculated masses are varied, essentially consisting of lesions presenting a predominant fibrous component.

Post-surgical scars

Post-surgical scars may appear in the form of a stellar mass, especially in case of post-surgical complications such as haematoma or infection. The dense centre is usually small or absent. Since the scar has a 2D structure, the appearance of the stellar mass may change on the orthogonal view where the scar then appears in the form of a linear image. The stable nature of the scar over time after partial surgery for breast cancer is a basic element in the monitoring, and any change in the mammography should trigger suspicions of a recurrence.

Inflammatory pseudotumours

All inflammatory lesions responsible for a fibrous or chronic granulomateous reaction may present in the form of a stellar mass. This category includes diverse aetiologies such as abscess, cytosteatonecrosis, granulomateous mastitis, tuberculosis, sacoidosis and focal fibrosis.

Sclerosing adenosis

Sclerosing adenosis is a proliferative lesion corresponding to an increase in the number and/or size of the lobules, associated with sclerosis of the interstitium, responsible for the distortion of the lobules. In spite of the distortion, the lobules remain separated by a layer of collagen and the architecture in double epithelial and myoepithelial base is preserved and is better revealed after immunohistochemical study with a myoepithelial marker. These histological elements are basic in order to distinguish sclerosing adenosis from cancer.

Fibromatosis

Breast fibromatosis is a rare benign lesion, corresponding to the proliferation of fibroblastic and myofibroblastic fusiform cells with little or no atypia and low mitotic activity. It consists of a poorly defined invasive lesion of the breast parenchyma in periphery, in the form of “digiform” prolongations that cover the pre-existing lobular and ductal structures, at the origin of the spiculated contours (Fig. 9).

Conclusion

The analysis of masses in mammography is standardised, based on the BI-RADS system by the ACR. This lexicon proposes the procedure required as a function of the morphology of the masses, since the probability of malignancy highly depends on this factor, and in particular on the contour of the mass. Histologically, a circumscribed mass is more readily benign than a more suspect irregular or even spiculated contour, indicating a biopsy. However, certain malignant lesions may present in a falsely reassuring form and inversely benign lesions may present in a suspect form in mammography. In view of these elements, the senologist radiologist should, when faced with a mass in mammography, always consider the basic elements of the semiological analysis that will determine the procedure required. In particular, there are four key points:

- the radiologist should be familiar with and master the semiology of typically benign lesions that will not lead to any specific control or sampling;
- they should be careful to well analyse the semiology of masses and, in particular, the contours, in order to differentiate masses with a benign aspect requiring only short-term monitoring (ACR3), from masses immediately requiring a histological sample (ACR4);
- the short-term monitoring of masses with a circumscribed contour is of particular use to “catch” cancers with an unusual presentation (high grade, mucinous, medullary, etc.);
- in case of a benign result after the biopsy of a spiculated mass, the radiologist should make sure of the radio-histological concordance. For this, they should be familiar with the benign lesions likely to present as stellar masses in mammography and make sure of the good representativeness of the samples taken. With the slightest doubt, continued explorations with a new and larger

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Figure 8. Invasive lobular carcinoma: a: mammography: irregular mass with a spiculated contour; b: histology: long fibrous spicules of variable cell richness (HES); c: histology: proliferation of little cohesive cells invading the fat and (small) fibrous peripheral spicules (HES).
calibre biopsy, surgery or complementary MRI is indispensable in order to avoid missing an underlying malignant lesion that would have been underestimated.

The latter point emphasises the importance of multi-disciplinary meetings to determine the level of radio-pathological concordance of the samples taken and define, in correlation with the clinical data, the subsequent adapted procedure required: stop the investigations (benign concordant), monitoring, MRI, new biopsy or even diagnostic surgery (benign of uncertain concordance of non concordant) or surgical treatment (lesion involving a risk or malignant).

Case report

Ms. R., 76 years old, consults for swelling of the left breast noted over the last 6 months. Clinically, there are two palpable masses, the first 5 cm internal peri-nipple and the second 3 cm from the upper outer quadrant. Flat skin is associated at the union of the lower quadrants as is slight nipple retraction. A bilateral mammography is carried out. The images are normal on the right. The images of the left breast are presented in Fig. 10.

Figure 9. Fibromatosis: a: mammography: spiculated mass BI-RADS 5; b: histology: spiculated peripheral contours (HES); c: histology: long fibrous spicules with “digiform” invasion of the fat (HES); d: histology: fasciculated proliferation consisting of fibroblasts without atypia (HES).

Questions

1. Describe and classify the mammography images according to the BI-RADS system.
2. A complementary sonogram (Fig. 11) finds, in correspondence with the central mass, an irregular mass with angular and indistinct contours (BI-RADS 5) and opposite the mass of the union of the external quadrants, a complex cyst with a focally thickened wall at 8 mm (BI-RADS 4). An ultrasound-guided biopsy is carried out on both lesions. The report on the histological analysis concludes as to a papillary carcinoma for one and a grade III invasive ductal carcinoma for the other (Fig. 12). Which mass corresponds to which histological result and why?
3. What treatment do you propose?

Answers

1. There are two mammography masses:

**TAKE-HOME MESSAGES**

Masses with a circumscribed contour
- Typically benign masses (BI-RADS 2) do not require specific monitoring:
  - Circumscribed masses with macrocalcifications (hyalinised fibroadenomas or calcified cysts)
  - Masses of fatty or mixed density (lymph node, oily cyst, hamartoma, lipoma, galactocele)
  - Circumscribed masses that correspond to simple cysts in sonography
- Probably benign masses (BI-RADS 3) requiring short-term monitoring:
  - They are mainly benign (98%)
  - Certain lesions involving a risk may present in this form:
    - Phyllode tumour
    - Papilloma

Figure 10. Mammography of the left breast: a: AP view; b: external oblique view; c: profile view.
Certain types of cancers may present in the form of a circumscribed mass due to an absent or limited stroma reaction or inflammatory and non-fibrous mass:
- High grade invasive ductal carcinoma,
- Medullary carcinoma,
- Pure mucinous carcinoma,
- Papillary carcinoma.

Masses with a non-circumscribed contour
- The cancer PPV varies according to the type of contour:
  - Microlobulate contour: PPV = 17%,
  - Masked contour: PPV = 33%,
  - Indistinct contour: PPV = 44%,
  - Spiculated contour: PPV = 96%.

Masses with a spiculated contour
- They are mainly malignant (96%).
- The spicules result from a major stroma reaction that preferentially develops around slow-growing lesions.
- The most common spiculated cancers are:
  - Invasive ductal carcinoma (most often low grade)
  - Invasive lobular carcinoma
  - Tubular carcinoma
- Benign spiculated masses are very rare.
- The correlation between the histological and radiological data is indispensable in case of the benign result of a biopsy of a spiculated mass and further exploration is indispensable with the slightest doubt as to the representativeness of the samples.

- The 1st located in central and internal position corresponds to a lobulate, high-density mass with indistinct contours, associated with slight nipple retraction and very probable invasion of the pectoral muscle that has retracted due to the tumor. It measures 50 mm. It is classified BI-RADS 5 (high probability of cancer). The clinically described flat skin is visible in mammography at the union of the lower quadrants.
- The second, located in the upper outer quadrant corresponds to a round mass with circumscribed contours (less than 25% of the mass is masked by the 1st lesion), of average density. It measures 30 mm. The morphological appearance in mammography corresponds to a BI-RADS 3 mass (probably benign).

2. The central mass corresponds to a grade III invasive ductal carcinoma. This is a high-grade carcinoma, accounting for the lobular form (centric growth), the indistinct contours (invasion of the adjacent parenchyma faster than the stroma reaction) and high density (strong cellularity). The slight nipple retraction follows the invasion of the back nipple region and distinct lactiferous lesions of the breast parenchyma at the interface. The infiltration of the pectoral muscle is confirmed on the mastectomy tissue (Fig. 12a). The mass of the upper outer quadrant corresponds to papillary carcinoma. This is an intracystic lesion accounting for the well-circumscribed contour and the average density (Fig. 12b).

3. This is a multicentric carcinoma of the left breast. A total mastectomy with left axillary node dissection was carried out. The lesions were classified as pT3 N0 (tumour size > 5 cm without metastatic adenopathy). Complementary radiotherapy of the thoracic lining was carried out due to the histological grade, the size of the tumour and the multifocal nature of the tumour. Since the hormone receptors were positive, adjuvant hormone therapy was prescribed. Adjuvant chemotherapy was not proposed in view of the N- nature and the age of the patient.

Figure 11. Breast sonography.

Figure 12. Histology of the total mastectomy tissue: a: central tumour: grade III invasive ductal carcinoma, invading the pectoral muscle (HES); b: central tumour: invasion of the muscle fibres of the pectoral by the tumour (stronger magnification) (HES); c: tumour of the upper outer quadrant: carcinoma with intracystic (or encapsulated) papillary component (HES).
Disclosure of interest

The authors declare that they have no conflicts of interest concerning this article.

References


