Is a breast MRI possible and indicated in case of suspicion of breast cancer during lactation?

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Abstract The paper tries to answer two questions: the safety of the injection of gadolinium during breastfeeding; the value of a breast MRI in the nursing mother if breast cancer is suspected. Recent Anglo-Saxon publications are in favour of continued breastfeeding following the injection of gadolinium. In fact, only a minute quantity of contrast product passes into the mother’s milk, much less than the threshold recommended in paediatrics in the infant. However, a suspension of lactation for 24 h after the injection of gadolinium chelate is still recommended in France. The literature is poor as regards the contribution of the MRI during lactation, although the data indicates that the MRI is contributory, in spite of the physiological changes in the breast during this period. In fact, all of the lesions have been visualised and correctly classified according to the BI-RADS classification by the ACR. However, the semiology is specific and has to be known.

Pregnancy-associated breast carcinoma (PABC) occurs during a period ranging from the beginning of a pregnancy to one year after delivery. It is not rare and strikes between 0.2 and 3% of all breast cancers [1], or 350 to 750 women per year in France [2,3]. The frequency of PABC is increasing, in part due to a later first pregnancy (mean of 29.8 years in 2007 versus 24 years in 1970 in France). The prognosis of these cancers is often poor as they are detected at a more evolved stage with only 30% of the tumours under 2 cm and 61% N+ (versus 50% and 28% respectively in a control population of the same age) [3]. A recent article examined the impact of pregnancy on breast cancers occurring before the age of 35. The tumours of the patients pregnant during the year following the diagnosis were larger, more often with an invasion of the lymph glands [4].

KEYWORDS Breast MRI; Breastfeeding; Pregnancy-associated breast cancer; Gadolinium chelate

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The negativity of the hormonal receptors, the positivity of HER 2/neu, the SBR II or III grade of these tumours is also frequent. It is difficult to determine whether these prognostic factors are only related to the young age of the patients or whether the pregnancy favours them [2,3].

With lactation, the breast acquires its final differentiation and these changes are also visible in the different imaging usually used in sonology. Sonography, the reference examination during pregnancy and breastfeeding, remains efficient in the diagnosis of masses [5]. In addition to their diagnosis and the characterisation, it allows for indispensable guided biopsies or the monitoring of their evolution during neoadjuvant chemotherapy. The sonographic semiology of the masses does not seem to change during lactation. This technique is currently the gold standard in the exploration of breast anomalies in the nursing woman. The decreased sensitivity of the mammography is known during this period. The increased density makes masses more difficult to detect. However, the often-associated microcalcifications, skin changes, axillary adenopathies and density asymmetries indicate the diagnosis of a malignant lesion. In an article published in 2003 on 22 patients presenting a pregnancy-associated cancer, 13 of the 15 mammographies (86.7%) were positive although only eight of them presented masses [6]. Two other studies, in 1994 and 2006, found a positive mammography in 78% and 90% of the cases, respectively, in spite of the dense breasts (BI-RADS 3 and 4) [7,8].

The MRI with injection is not currently recommended in pregnancy-associated breast cancers. Only an unquestionable indication with a calculated benefits-risk ratio indicates an MRI in this context [9]. The question is whether or not this technique has any value during lactation and whether the injection of gadolinium chelate represents a risk. This question also subsists during the weeks following the end of lactation. In fact, the involution of the histological changes mainly occurs during the 3 months after the suspension of breastfeeding [1,10]. Although no study has yet determined the evolution of the imaging after the suspension of breastfeeding, we can assume that the changes in the imaging are correlated with that of the anatomopathology.

Analysis of the literature

Injection of gadolinium chelate and breastfeeding

Both radiologists and patients are reticent about an MRI during lactation. The women worry about the suspension of breastfeeding and the doctors about the futility of this examination. However, two recent articles confirm the possibility of continuing breastfeeding without any specific precautions after the injection of gadolinium chelate [11,12]. In fact, only 0.04% of the injected dose passes into the milk. This is a very low dose and less than one hundredth of the permissible dose in the infant (200 μm/kg) [13]. A third article appearing in 2007 backed up this idea, calculating the absorption of gadolinium at 0.2% of the administrable dose in pediatrics (0.1 mmol/kg) for an infant weighing 3 kg and its 70 kg mother [12]. Therefore, this data has led the American College of Obstetricians and Gynaecologists to confirm the safety of breastfeeding immediately after the examination [11,12]. However, as opposed to the European and American recommendations, the French recommendations continue to suspend breastfeeding for 24 h after the administration of gadolinium [14].

MRI during breastfeeding

It is acknowledged that this examination is limited during lactation, thereby accounting for the few articles dealing with this subject.


In 2003, an article reported the case of a young 36-year-old nursing mother presenting a clinical anomaly with a negative standard assessment. The MRI then carried out did not detect any focal anomaly although major glandular changes, with dense breasts, presented diffuse and heterogeneous contrast enhancement. The flow extraction (FE) increased (over 25) in a great many zones (the flow extraction is a parameter assessing the permeability, flow and the vessels and is expressed in millilitres of blood, 100 mg of tissue/minute. An increase indicates a possible malignant lesion). In view of the negativity of all of the explorations, a biopsy-exeresis was carried out. This confirmed the benign histology. The authors then wondered, if the lesion was malignant, would it have been objectified or, on the contrary, would it have masked the physiological modifications [7]?

First study: 2005 [16]

In 2005, a study was published on this question [8]. Three readers carried out a retrospective analysis of breast MRIs on 7 women 27—42 years of age (mean age: 36 years) who had nursed between 5 days and 22 months. Four women continued breastfeeding and three stopped during the MRI (a maximum of 12 days before). The MRI indications were five cases of an assessment of the extension of histologically-proven breast cancer, one case of screening in a woman with a high genetic risk and one case of a suspicion of breast angiosarcoma after a skin biopsy (Appendix I). The protocol was standard, including one T1 SE, fast-SE T2 sequence with Fat Sat, dynamic sequences in T1 EG, and one high resolution T1 sequence. Different parameters were assessed concerning the breast (density, signal in T2 compared with the pectoral muscle, morphological appearance and dynamics of the enhancement), and the focal lesions detected (morphology, enhancement and dynamics of the contrast enhancement).

Physiological modifications of the breast in MRI

The following were found in the normal breast: an increase in the density in T1 weighting, super-imposable over that of the mammography, a T2 hypersignal related to an increase in the free water and a dilation of the galactophoric channels related to the milk production. After injection, as previously described, the breast presents diffuse, heterogeneous enhancement, attesting to the hypervascularisation related to this state. The dynamic curve carried out on the breast reveals a fast initial and then progressive secondary contrast enhancement of variable intensity in most cases. Only one patient presented a wash-out. The existence of little distinct enhancement of the retroareolar channels was noted.
This has never been described in the literature before. Two hypotheses are available to account for this: enhancement of the wall or excretion of gadolinium in the milk. All of these physiological modifications therefore are due to the histological modifications resulting from lactation.

Neoplasia
As regards the detection of tumoral lesions, the study also demonstrates the value of the T2 Fat Sat sequence during this period. In fact, the glandular hypersignal indicates the hyposignal of infiltrating ductile carcinomas and in certain cases, the lineal hyposignal of cancers in situ. After the injection of gadolinium, in spite of the diffuse glandular enhancement, infiltrating ductile carcinomas are well individualised since they are enhanced even sooner and much more intensely than the adjacent parenchyma (153% versus 60%), in most cases with a wash-out. An annular enhancement, a criterion of malignity, is described in two of the five cases. The in situ ductile carcinomas described in this study present a segmental or more diffuse contrast, but are only objectified in two patients (versus four infiltrating ductile carcinomas in anatomopathology). As regards the suspicion of angiosarcoma, neither the surgical biopsy nor the MRI was able to prove the malignity in this patient. The 18-month monitoring was also found to be negative. Finally, the MRI of the patient with a high genetic risk did not detect a tumour.

Second study: 2007 [17]
A second study, concentrating more on the performance of the different techniques (sonography, mammography and MRI) in the exploration of masses palpated during lactation appeared in 2007 in Clinical Imaging. Among the 27 lactating patients, nine MRI were carried out. The results obtained demonstrate the good radio-histological correlation since all of the masses classified BI-RADS 4 or 5 in MRI corresponded to infiltrating ductile carcinomas. The MRI also allowed for a reclassification as BI-RADS 1 or 2 for images classified as 3 in the standard assessment (mammography/sonography). This was proven exact (histological proof). Finally, in one case, the clinical bifocal nature was confirmed (Appendix II).

Limits and biases
The two studies described contradict the idea that the MRI is less efficient during lactation. However, they include a number of biases and limits. First, the very limited number of patients renders the results non statistically significant. However, the MRI indications remain present, in particular in the assessment before and during neoadjuvant chemotherapy in these large tumours. Second, they are retrospective studies or involve large known lesions. The radiologists are therefore oriented: what is the situation for infra-clinical lesions? The question of the screening of women with a high genetic risk is raised since the examination is often suspended during a considerable period of time, during a period favourable for the development of tumours. Finally, the masses studied are always ductile, the most frequent histology. According to the literature, the distribution of the histological sub-types does not change during pregnancy or lactation. However, lobular neoplasia, although more rare, is also more difficult to diagnose. The morphologies and enhancement curves in MRI are variable [18,19] and the diagnosis may prove to be difficult outside of any context. This difficulty is most likely increased during a period of lactation. However, are these lobular cancers occurring during lactation unexplainable by this technique?

The radio-histological comparison is also insufficient. In the first study on five neoplasias, only two analyses immediately after the examination were recovered (among the three anatomopathological studies, one was carried out in another centre, the other two after neoadjuvant chemotherapy). Therefore, it was only possible to compare the estimated size in sonography and MRI with the real size of the tumour in one case. A significant difference in the size of the masses is noted between the two techniques in one patient: 6.7 cm in MRI versus 3.4 cm in sonography without anatomopathology to make sure of the real correspondence.

Conclusion
In conclusion, these studies are imperfect. However, they back up the idea that MR imaging is not void of value during lactation. The MRI has its own semiology during lactation, related to the physiological changes. Even so, it remains efficient, allowing for the satisfactory detection according to the BI-RADS classification of tumours by the ACR. The MRI and the injection of gadolinium chelate also seem to be risk free during breastfeeding both for the mother and the child. However, the suspension of breastfeeding for 24h after the injection remains recommended in France.

Disclosure of interest
The authors declare that they have no conflicts of interest concerning this article.
Appendix I. Details on the five patients presenting breast cancer in the 2005 study [16].

<table>
<thead>
<tr>
<th>Anatomopathology</th>
<th>Patient 1</th>
<th>Patient 2</th>
<th>Patient 3</th>
<th>Patient 4</th>
<th>Patient 5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type</td>
<td>CCI</td>
<td>CCI</td>
<td>CCI</td>
<td>CCI</td>
<td>CCI</td>
</tr>
<tr>
<td>Size (cm)</td>
<td>NC</td>
<td>NC²</td>
<td>1,2</td>
<td>1,9</td>
<td>NC²</td>
</tr>
<tr>
<td>Multifocality</td>
<td>NC</td>
<td>NC²</td>
<td>No</td>
<td>Yes</td>
<td>NC²</td>
</tr>
<tr>
<td>Associated CCIS</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Sonography (hypoechoic mass)</td>
<td>3.4</td>
<td>2</td>
<td>NC</td>
<td>1.5</td>
<td>3.2/1.2/3.1</td>
</tr>
<tr>
<td>Multifocality or extensive tumour</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>MRI Description of the mass</td>
<td>Heterogeneous enhancement</td>
<td>Annular enhancement</td>
<td>Annular enhancement</td>
<td>Homogeneous enhancement of the mass</td>
<td>Heterogeneous of half of the breast</td>
</tr>
<tr>
<td>Size (cm)</td>
<td>1.2</td>
<td>NC</td>
<td>1.2</td>
<td>8</td>
<td></td>
</tr>
</tbody>
</table>

²Anatomopathological analysis carried out in another establishment, data missing.

a Initial size not known (adjuvant chemotherapy).

Appendix II. Details on the nine patients in the 2007 study [17].

<table>
<thead>
<tr>
<th>Age</th>
<th>Palpable mass</th>
<th>BI-RADS sonography</th>
<th>BI-RADS mammography</th>
<th>MRI</th>
<th>Decision</th>
<th>Histology</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient 1</td>
<td>33</td>
<td>Left</td>
<td>5</td>
<td>5</td>
<td>4</td>
<td>Surgery</td>
</tr>
<tr>
<td>Patient 2</td>
<td>32</td>
<td>Right</td>
<td>3</td>
<td>3</td>
<td>5</td>
<td>Cytopuncture and Surgery</td>
</tr>
<tr>
<td>Patient 3</td>
<td>33</td>
<td>Left</td>
<td>3</td>
<td>4</td>
<td>4</td>
<td>Cytopuncture and Surgery</td>
</tr>
<tr>
<td>Patient 4</td>
<td>35</td>
<td>Left</td>
<td>4</td>
<td>3</td>
<td>4</td>
<td>Surgery</td>
</tr>
<tr>
<td>Patient 5</td>
<td>33</td>
<td>Left</td>
<td>2</td>
<td>3</td>
<td>3</td>
<td>Biopsy</td>
</tr>
<tr>
<td>Patient 6</td>
<td>32</td>
<td>Left</td>
<td>2</td>
<td>3</td>
<td>3</td>
<td>Cytopuncture</td>
</tr>
<tr>
<td>Patient 7</td>
<td>41</td>
<td>Right</td>
<td>3</td>
<td>1</td>
<td>3</td>
<td>Biopsy</td>
</tr>
<tr>
<td>Patient 8</td>
<td>35</td>
<td>Right</td>
<td>2</td>
<td>1</td>
<td>1</td>
<td>Monitoring</td>
</tr>
<tr>
<td>Patient 9</td>
<td>31</td>
<td>Right</td>
<td>3</td>
<td>1</td>
<td>2</td>
<td>Biopsy</td>
</tr>
</tbody>
</table>

References

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