Abbreviated breast MRI combining FAST protocol and ULTRAFAST sequence

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**Aims and objectives**

DCE breast MRI is an advanced imaging technique used to diagnose breast cancer with a reported sensitivity of 95-99% and specificity values of 72% in meta-analysis (1). However, breast MRI is a complex time-consuming examination for acquisition time.

Since 2014, new breast MR protocols named FAST protocols have been developed, characterized by only one acquisition after contrast administration.

Many studies have demonstrated that these protocols have a similar sensitivity compared to conventional MRI protocols to detect breast cancer (2-7). Nevertheless the realization of conventional enhancement curves is not possible with these protocols although using dynamic information has been demonstrated to improve breast MRI specificity (8). More recently, some authors described new dynamic characteristics of breast lesions using an ULTRAFAST sequence oversampling the first minute after contrast administration, and reported a correlation between early enhancement semi-quantitative parameters and lesion malignancy (9-15).

Our objective was to test a FAST protocol compared to a conventional protocol; and then to test the diagnostic performance of an additional ULTRAFAST sequence oversampling the first minute after contrast administration to improve lesion classification while decreasing acquisition time.
Methods and materials

Population

120 women (mean age = 55 years old (28-88)) who underwent breast MRI between July 18th 2016 and March 31th 2017 in whom an abnormal enhancing lesion was identified with subsequent pathological analysis (n=179: 69 benign, 7 borderline, 103 malignant lesions) were retrospectively and consecutively included, regardless of MRI indication.

MR acquisition (Fig.1)

Patients were imaged in prone position on a 1.5 T GE Optima MR 450w GEM system using a dedicated 8-channel breast array coil (GE, Milwaukee, USA).

T1 and T2-weighted non fat-saturated axial sequences were acquired before contrast administration. Dynamic contrast-enhanced T1-weighted fat-saturated gradient-echo sequences (VIBRANT, GE) were acquired before and four times after bolus injection of Gadolinium chelate. The ULTRAFAST sequence named DISCO (Differential Subsampling with Cartesian Ordering ; T1W Gradient-echo sequence undersampling k-space) sequence was performed before the first phase of the T1 VIBRANT sequence. DISCO sequence acquisition began simultaneously to the contrast injection; eleven temporal DISCO ranks were thus acquired during 1 min 18 sec (7.7 sec each rank) in order to assess early lesion enhancement.

Reading protocols (Fig2)

Full standard protocol

The two readers, blinded to clinical and pathological data, were asked to classify lesions according to the Bi-rads MR lexicon based on morphology and enhancement characteristics (obtained from curves type 1,2,3).

FAST protocol

A month later, readers were asked to read the FAST protocol consisted in T2-W, T1-W and the first T1-W fat-saturated VIBRANT after contrast injection. They were ask to classify lesions according to Bi-rads classification, blinded thought from any dynamic enhancement parameters.

Abbreviated protocols
Readers were asked to determine in which of the leven ranks on the ULTRAFAST sequence the lesion beacame first visible.

Then, to perform semi-quantitative analysis, Region of Interest (ROI) were drawn on the ULTRAFAST sequence in each lesion detected. Enhancement curves were extracted from AW server sofware by a research engineer (GE, Milwaukee, USA).

The following parameters were extracted from curves : Enhancement integral (EI,%) ; Maximal Slope of Increase (MSI, %/sec) ; Maximim of Enhancement (Rmax, %) ; Time of Maximum of Enhancement (Rmax Timing, sec) ; Wash-in Rate (WIR, sec) ; EA (Enhancement Amplitude, %) ; Time of Half Rising (THR, sec)

Statistical analysis

Analysis was performed on statistics sofware MedCalc (Ostend, Belgium). Descriptive anlysis was performed using a non-parametric Mann-Whitney test for non-continuous variables. To determine whether ‘continuous values’ could differentiate malignant from benign lesions, thresholds were determined by constructing a receiver operating characteristic (ROC) curve. We calculated odds ratios (OR) for predicting malignancy with 95% confidence intervals and p-values for each of the predictor variables for malignancy. Quadratic # coefficients were calculated to assess intraobserver agreements for lesion characterization between the two protocols (FAST and Full protocol), regardless of dynamic data. Quadratic # coefficients were calculated to assess interobserver agreement for enhancement rank determination on ULTRAFAST acquisition. Univariate analysis was used to calculate odds ratios for each of the predictor variables for malignancy. Then, step by step logistic regression analysis was performed to determine which criteria was significantly associated with malignancy. A receiver operating (ROC) curve analysis was performed to compare the results of interpretations based on the full gold standard protocol versus the abbreviated protocol.
**Fig. 1:** MR acquisition protocol acquired for each patient Consisted in T1W, T2W non fat matured sequence; followed by a contraste injection; Ultrafast sequence directly acquired after injection; 5 'traditional' T1W sequences after contrast injection.

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**Fig. 2:** Reading protocols

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Results

Lesion description

The lesion was a mass in 70% (125/179), a NME in 27.3% (49/179) and a focus in 2.7% (5/179). The average lesion size was 18 mm (3-85 mm). The size of 45/179 (25.1%) lesions was inferior to 10 mm; 49/179 (27.4%) lesions size ranged from 10 to 20 mm, and 85/179 (47.5%) lesions were larger than 20 mm.

Bi-RADS performance on FULL and FAST protocol readings

All cancers were detected on FAST protocol. FAST protocol showed lower diagnostic performance (AUROC: 0.802) compared to FULL protocol (AUROC: 0.834) (p<0.01) with a higher number of cancers rated BI-RADS 3 (PPV of malignancy of 27.5% (8/29) in FAST versus 18.7% (3/16) in FULL protocol (Fig 3). Inter reader agreement of BI-RADS classification for FAST protocol was excellent with a Kappa value equal to 0.801 (0.715-0.887).

ULTRAFAST sequence analysis

171/179 (95.5%) lesions were visible on the ULTRAFAST sequence only. Reading only the ULTRAFAST sequence, we did not identify 8/179 (4.5%) lesions including 5/76 (3.9%) benign lesions and 3/103 (2.9%) breast cancers. The 3 undetected cancers were 2 small intra ductal carcinoma (size =7mm), 1 papillary carcinoma that appeared as a NME smaller than 1cm. All visible lesions on ULTRAFAST sequence enhanced within the 7 first ranks (earlier than 1min after injection). Inter reader agreement to determine the first ULTRAFAST rank to detect the lesion was good with a kappa value of 0.651 (0.535-0.768)

The wide majority of cancers (84%, 87/103) enhanced within the first four ranks (i.e 31sec after injection). Malignant lesions were 5.6 times more likely to be associated with early enhancement (within the first four ranks, with mean a Time To Enhancement (TTE) < 31 sec) rather than delayed (after the four rank) with an OR = 5.6 (IC 95%: 3.3 - 20.4; p < 0.0001) (Fig 4.). Independently from size, an earlier first rank of lesion detection was correlated with malignancy.

All semi-quantitative parameters were significantly different between benign and malignant lesions (except Rmax timing). Malignant lesions displayed a higher enhancement integral, a higher enhancement amplitude, a shorter time of half rising, a steeper maximal slope, a higher maximal slope of increase, a higher wash-in rate, and a higher maximum enhancement rate (R Max).
Building the abbreviated protocol

A multivariate analysis including all significant features issued from ULTRAFAST analysis (TTE <31 sec or rank 1-2-3-4, EA, EI, THR, MS, MSI, RMax, WIR), only TTE <31 sec was significantly associated to malignancy (p<0.0001 OR= 3.9).

Thus, readers reclassified BI-RADS 3, BI-RADS 4a, BI-RADS 4b using the data issued from the ultrafast sequence (i.e early enhancement (TTE <31 sec or rank 1-2-3-4) as following: BI-RADS 3 lesions with a suspicious early enhancement (TTE < 31s) were upgraded as BI-RADS 4a. BI-RADS 4a and 4b lesions with a non-suspicious late enhancement (TTE > 31 s) were downgraded as BI-RADS 3. No change was performed on BI-RADS 4c or BI-RADS 5 lesions. Predictive positive values as well as positive likelihood ratio for each BI-RADS category determined for each protocol are summarized in Figure 6 and percentage of malignant lesions in each reading protocols represented in Figure 7.

Performances of the ABBREVIATED PROTOCOL

Abbreviated protocol (combining FAST and ULTRAFAST data) had better diagnostic performance (AUROC = 0.826) compared to FAST protocol (AUROC = 0.802) (p<0.01) and no significantly different performance compared to the FULL standard protocol (AUROC = 0.834).

Abbreviated protocol could have avoided unnecessary biopsies in 8.9% of lesions (16/179) rated BI-RADS 4a and 4b on FAST protocol and confirmed benign (p=0.0139) and 10.6% (19/179) of lesions incorrectly rated on FULL protocol (p=0.0034)(Figure 8). Inter reader agreement for BIRADS performance of abbreviated protocol was excellent with a Kappa values equal to 0.889 (0.840-0.938)
Images for this section:

<table>
<thead>
<tr>
<th>PPV / LR+</th>
<th>FULL</th>
<th>FAST</th>
<th>ABBREVIATED</th>
</tr>
</thead>
<tbody>
<tr>
<td>BI-RADS 3</td>
<td>18.7% (3/16)</td>
<td>27.6% (8/29)</td>
<td>12.8% (5/39)</td>
</tr>
<tr>
<td></td>
<td>0.17 (0.05-0.58)</td>
<td>0.28 (0.13-0.60)</td>
<td>0.11 (0.04-0.26)</td>
</tr>
<tr>
<td>BI-RADS 4a</td>
<td>21.2% (7/33)</td>
<td>18.2% (4/22)</td>
<td>41.7% (10/24)</td>
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<tr>
<td></td>
<td>0.20 (0.09-0.43)</td>
<td>0.16 (0.06-0.46)</td>
<td>0.53 (0.25-1.12)</td>
</tr>
<tr>
<td>BI-RADS 4b</td>
<td>37.5% (12/32)</td>
<td>41.4% (12/29)</td>
<td>52.9% (9/17)</td>
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<tr>
<td></td>
<td>0.44 (0.23-0.85)</td>
<td>0.52 (0.26-1.02)</td>
<td>0.83 (0.34-2.05)</td>
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<tr>
<td>BI-RADS 4c</td>
<td>69.8% (30/43)</td>
<td>66.7% (30/45)</td>
<td>66.7% (30/45)</td>
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<td>1.70 (0.95-3.04)</td>
<td>1.48 (0.86-2.54)</td>
<td>1.48 (0.86-2.54)</td>
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<tr>
<td>BI-RADS 5</td>
<td>92.7% (51/55)</td>
<td>90.7% (49/54)</td>
<td>90.7% (49/54)</td>
</tr>
<tr>
<td></td>
<td>9.41 (3.55-24.91)</td>
<td>7.23 (3.03-17.28)</td>
<td>7.23 (3.03-17.28)</td>
</tr>
</tbody>
</table>

PPV: Predictive Positive Value (number/total number)
LR+: Positive Likelihood Ratio

**Fig. 3:** Table illustrating the evaluation of the clinical of malignancy for each BIRADS classification for the different protocols tested

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**Fig. 4:** Comparison between benign and malignant lesions related to the first rank of visibility. Most of malignant lesions enhance early, within the first four ranks (Time to Enhancement < 31sec), whereas benign lesions have a more normal low distribution. N.E. : Non enhanced lesions

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**Fig. 5:** Integration of ULTRAFAST TTE <31sec (early enhancement) to FAST protocol

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<table>
<thead>
<tr>
<th>Performance</th>
<th>FULL</th>
<th>FAST</th>
<th>FAST+ULTRAFAST</th>
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<tbody>
<tr>
<td>True-positive result, n</td>
<td>100</td>
<td>95</td>
<td>98</td>
</tr>
<tr>
<td>False-negative result, n</td>
<td>3</td>
<td>8</td>
<td>5</td>
</tr>
<tr>
<td>True-negative result, n</td>
<td>13</td>
<td>21</td>
<td>34</td>
</tr>
<tr>
<td>False-positive result, n</td>
<td>63</td>
<td>55</td>
<td>42</td>
</tr>
<tr>
<td>Sensitivity (95% CI)</td>
<td>0.97 (0.93–1)</td>
<td>0.92 (0.87–0.97)</td>
<td>0.95 (0.91–0.99)</td>
</tr>
<tr>
<td>Specificity (95% CI)</td>
<td>0.17 (0.89–0.93)</td>
<td>0.27 (0.17–0.37)</td>
<td>0.45 (0.33–0.56)</td>
</tr>
<tr>
<td>Positive likelihood ratio (95% CI)</td>
<td>1.17 (1.05–1.30)</td>
<td>1.27 (1.10–1.48)</td>
<td>1.72 (1.40–2.12)</td>
</tr>
<tr>
<td>Negative likelihood ratio (95% CI)</td>
<td>1.17 (0.05–0.58)</td>
<td>0.28 (0.13–0.60)</td>
<td>0.11 (0.04–0.26)</td>
</tr>
<tr>
<td>Positive predictive value (95% CI)</td>
<td>0.61</td>
<td>0.63</td>
<td>0.70</td>
</tr>
<tr>
<td>Negative predictive value (95% CI)</td>
<td>0.81</td>
<td>0.72</td>
<td>0.87</td>
</tr>
<tr>
<td>Accuracy (95% CI)</td>
<td>0.63</td>
<td>0.65</td>
<td>0.73</td>
</tr>
</tbody>
</table>

**Fig. 6:** Comparison of diagnostic performance of the different reading protocol

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**Fig. 7:** Percentage of malignant lesions in the new BI-RADS classification with the abbreviated protocol (combining FAST protocol and ULTRAFAST sequence) compared to FAST protocol alone and FULL protocol

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**Fig. 8:** A 42 y.o. high-risk woman referred for breast cancer screening. Vibrant and Disco focal enhancement that corresponds to a mass, enhancing according to a Time intensity curve type 2. According to FULL protocol, this lesion was rated Bi-rads 3. According to FAST protocol, missing dynamic criteria, the lesion would be rated either Bi-rads 3 or 4a. Adding ULTRAFAST criteria (lesion visible before 31 sec (before rank 4), this lesion was classified as Bi-rads 4a. A second look ultrasonography allowed to perform a percutaneous biopsy that revealed an invasive lobular carcinoma.

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Conclusion

Our study demonstrates that ultrafast sequence is useful to distinguish malignant from benign lesions with a shorter time to enhancement for breast carcinoma: a lesion that enhances within the first 31 seconds after injection has 5.6 times more risk to be a cancer. Theses results are in line with those previously published (8,10).

ULTRAFAST sequence can not be used alone as 3 breast cancers were missed (2 intraductal carcinoma and 1 papillary carcinoma) because of a good but not optimal spatial resolution; explaining why we included a conventional low temporal but high spatial resolution T1W sequence.

Adding the parameter time to enhancement (TTE < 31s) derived from ultra-fast sequence to FAST sequence improves diagnostic value of the BI-RADS classification on abbreviated protocol to reach values issued from full standard protocol with half less acquisition time (7 min 48 sec versus 13 min 54 sec).

In conclusion, an abbreviated breast MRI protocol combining a FAST protocol and an ULTRAFAST acquisition is a performant method that could lead to better availability of MR imaging. An ULTRAFAST sequence provide information on early enhancement characteristic (Time To Enhancement < 31sec), which is a useful parameter for lesion characterization, decreasing unnecessary biopsies.
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