Dépistage en IRM mammaire

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UNIVERSITÉ DE LORRAINE

Ecole Doctorale BioSE (Biologie-Santé-Environnement)

Thèse

Présentée et soutenue publiquement pour l'obtention du titre de

DOCTEUR DE L'UNIVERSITE DE LORRAINE

Mention : « Sciences de la Vie et de la Santé »

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Le 19/12/2017

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INTRODUCTION

En France, le cancer du sein est le premier cancer féminin en termes de fréquence avec plus de 50 000 nouveaux cas estimés en 2008. L'âge médian au diagnostic est de 61 ans. Le cancer du sein représente plus du tiers de l'ensemble des nouveaux cas de cancer chez la femme et une part importante des patients en affection de longue durée (ALD 30). Ainsi près de 17 % des personnes prises en charge au titre d'une ALD 30 en 2006 l'ont été pour un cancer du sein. Son incidence a augmenté de manière constante entre 2000 et 2005 (évolution du taux d'incidence standardisé de + 2,1 % par an en moyenne). Parallèlement, sa mortalité était en diminution sur cette même période (diminution de 1,3 % par an en moyenne). Ces évolutions inverses s'expliquent en partie par le dépistage organisé ayant amené à des diagnostics plus précoces, mais aussi par l'amélioration de l'efficacité des traitements disponibles. Des données publiées en 2008 à partir de la base de données des ALD du régime général de l'Assurance maladie suggèrent une diminution depuis 2005 de l'incidence du cancer du sein possiblement liée aux diminutions de prescriptions des traitements hormonaux de la ménopause. Le cancer du sein bénéficie d'un pronostic à long terme favorable, d'autant plus qu'il est diagnostiqué et pris en charge de plus en plus tôt. La survie moyenne à 5 ans est estimée à près de 85 %.

Sa détection précoce est un élément clé dans la prise en charge de cette pathologie pour améliorer le pronostic et en diminuer la morbi-mortalité.

Cette détection précoce repose en majorité sur les examens d'imagerie que sont la mammographie, l'échographie et l'imagerie par résonance magnétique mammaire.

L'IRM mammaire a été largement acceptée comme outil de diagnostic essentiel. En outre, elle joue un rôle dominant et de plus en plus important dans l'imagerie mammaire, en particulier pour le dépistage des femmes à risque élevé de développer un cancer du sein, dans le bilan

d’extension mammaire du cancer du sein, dans l'évaluation après la chimiothérapie néoadjuvante et en cas d’adénopathie axillaire sans lésion mammaire visible en mammographie et en échographie (1-3). Ses indications sont bien connues: le dépistage des femmes à haut risque de cancer du sein, le bilan d’extension mammaire (à la fois homolatéral et controlatéral), l'évaluation après chimiothérapie néoadjuvante, la recherche de complication des implants mammaires, le bilan d’adénopathie axillaire sans primitif mammaire diagnostiqué sur le bilan standard, les récidives locales présumées, la résolution de problèmes (résultats équivoques à la mammographie / échographie) lorsqu'une biopsie ne peut être effectuée et le bilan d’écoulement mammelonnaire (4). Cependant, les examens qui respectent les recommandations de bonnes pratiques de la Société européenne des spécialistes du cancer du sein (EUSOMA) nécessitent 30 minutes pour leur réalisation (5). Cela comprend une acquisition pondérée en T1 et une en pondération T2, suivies par des séquences de moins de 90 secondes répétées avant et après l'injection d’un produit de contraste et une acquisition tardive à 7 minutes. Le temps total prend également en compte le temps d'installation et de désinstallation de la patiente dans l’IRM. L'IRM mammaire a donc des coûts directs et indirects élevés qui limitent son utilisation plus large, d'autant plus que les protocoles actuels d'IRM mammaire nécessitent un temps considérable pour l'acquisition et l'interprétation (6-12). En outre, comme c'est le cas dans certains pays européens tels que la France, le nombre d’IRM est insuffisant pour répondre aux indications croissantes de l'IRM mammaire, y compris le dépistage annuel d'un nombre croissant de femmes à haut risque pour le cancer du sein et des ovaires. Malgré la disponibilité limitée de l'IRM, les indications pour les examens d'IRM augmentent de façon exponentielle (13). Entre 2000 et 2009, la demande d'IRM mammaire a augmenté d'un facteur supérieur à 20 (14). Par exemple, les recommandations de l’INCa de septembre 2009 préconisaient la réalisation d’une IRM annuelle systématique dès 35 ans chez les femmes identifiées comme porteuses d’une mutation génétique (BRCA 1 et

BRCA 2). 340 femmes porteuses d'une mutation BRCA 1 ou 2 ont été identifiées en Lorraine. L'INCa estime à 2 femmes pour 1000 le nombre de porteuses de mutation dans la population générale. A l'échelle de la Lorraine qui compte 1 202 655 femmes en 2009 selon l'INSEE, cela pourrait concerner 2405 femmes porteuses du gène BRCA 1 ou 2. L'Institut de Cancérologie de Lorraine a répondu avec le CHU à l'appel à projet de l'INCa portant sur la «Prise en charge multidisciplinaire des personnes prédisposées héréditairement au cancer ». Un suivi structuré et individualisé des personnes identifiées par les structures d'oncogénétique comme porteuses de gène de prédisposition, mais également des « personnes sans mutation identifiée mais présentant des antécédents médicaux, personnels et familiaux, très évocateurs d'une prédisposition au cancer » a été mis en place. Le référentiel ONCOLOR-CAROL dans sa révision interrégionale Grand Est de 2012 préconise également de réaliser une IRM annuelle chez les femmes à risque génétique chez lesquelles aucune mutation n'a été identifiée. L'élargissement de la file active aux femmes dont la recherche de mutation est restée non informative et à leur famille va augmenter les besoins en IRM de sein, réalisées sur un rythme annuel sans limite d'âge préconisée à ce jour. L'unité d'Oncogénétique ICL-CHU rapporte pour la Lorraine une population de 1350 femmes dont la recherche de mutation BRCA a été réalisée et est restée non informative. Recommander la réalisation d'une IRM mammaire annuelle aux patientes concernées et à leurs apparentées (filles, sœurs, mère) multiplierait ce chiffre par un facteur 6, avec un potentiel de 8000 femmes concernées par une surveillance par IRM pour la Lorraine.

Compte tenu de ces éléments, il est apparu primordial de pouvoir réaliser des examens plus rapides permettant d'augmenter le nombre d'examens pour répondre à ces différentes problématiques tout en conservant une sensibilité et une spécificité élevées identiques à celles obtenues par le protocole standard.

Actuellement, l'IRM mammaire est réalisée en position couchée de procubitus ce qui soulève un certain nombre de problèmes comme par exemple les corrélations topographiques entre l'IRM, l'échographie et la chirurgie ou l'inconfort généré par cette position pour les patientes.

Compte tenu de ces différents éléments, nous avons distingué trois parties principales à notre travail incluant l'ensemble des articles publiés ou en cours d'évaluation que nous avons réalisés.

Le premier chapître concerne le travail sur le positionnement des patientes (procubitus et décubitus) et l'évaluation de ce positionnement par les patientes en terme de confort, de gêne, de sensation d'oppression notamment. Il se déclinera en plusieurs sous-parties reposant sur différentes études cliniques impliquant des volontaires et des patientes.

Il comportera les articles suivants :

- Feasibility of supine breast MRI with volunteers. Cet article est en cours d'évaluation pour publication dans le journal *Japanese journal of radiology.*
- Prone-to-supine tumor displacement in the breast : an investigation with prone MRI and supine ultrasound . Cet article est en cours d'évaluation pour publication dans le journal *Breast Disease.*
- Feasibility study of supine breast MRI : comparison with prone MRI and comfort assessment. Cet article est en cours d'évaluation pour publication dans le journal *Iranian journal of radiology.*

Le deuxième chapître traitera des moyens d'amélioration du temps d'acquisition et de leur évaluation. Il se présentera sous forme de différentes études qui porteront sur l'amélioration de la résolution temporelle, sur la diminution du temps d'acquisition et sur l'évaluation de ces différentes données en terme d'efficacité diagnostique de l'examen ainsi qu'en analyse des données lésionnelles obtenues.

Il comportera les articles suivants :

- Optimized breast DCE MRI protocol: a pseudo-random k-space trajectory design for the flexible reconstruction of both standard and accelerated images in fat-suppressed breast DCE-MRI. Cet article est en cours d'évaluation pour publication dans le journal *BioMed Research International*.

- Abbreviated breast magnetic resonance protocol: Value of high-resolution temporal dynamic sequence to improve lesion characterization. Cet article a été publié dans *European Journal of Radiology*.
- Does use of an abbreviated protocol for breast magnetic rensonance imaging alter the BI-RADS classification ? Cet article a été accepté dans *Diagnostic and Interventional Radiology*.
- The usefulness of high temporal resolution with breast MRI sequences : A case report. Cet article a été accepté dans *La Presse Médicale*.
- Comparison of morphology, margin and enhancement analysis of breast carcinomas between the abbreviated and full diagnostic MRI protocol. Cet article est en cours d'évaluation pour publication dans le journal *Japanese journal of radiology*.

- Protocole d'IRM abrégée pour le diagnostic et le dépistage du cancer du sein. Sollicitation d'article par la revue *Oncologie.*

Enfin le troisième chapitre présentera les projets en cours et notamment celui soumis à l'appel à projet du Programme Hospitalier de Recherche Clinique cancer (PHRC K) 2017.

Chapitre 1 : Etude du positionnement en IRM mammaire

Ce chapitre est constitué de trois articles traitant des modifications topographiques entre le procubitus et le décubitus.

Actuellement, l'IRM mammaire est réalisée en position couchée de procubitus ce qui soulève un certain nombre de problèmes. En effet, tout d'abord la corrélation avec le bilan conventionnel mammographique et échographique ainsi que le repérage des lésions pré opératoires peut être complexe puisque l'échographie et la chirurgie se réalisent en position couchée de décubitus et la mammographie en position debout. Or le sein est un organe mobile et si l'on compare uniquement les examens faits en position couchée, la topographie des lésions est déjà modifiée entre le procubitus et le décubitus(15). Ainsi, certaines lésions non retrouvées en échographie post-IRM faite en procubitus peuvent être visualisées en échographie après une IRM en décubitus (16). Cette modification de la topographie et des rapports anatomiques a également été avancée pour expliquer dans l'essai COMICE le fait que l'IRM n'ait pas montré son utilité dans la diminution des marges positives et dans la nécessité de reprise chirurgicale (17). En effet, la position en décubitus est plus fidèle à la position opératoire (18).

Par ailleurs, la position en procubitus est souvent jugée inconfortable par les patientes notamment par l'appui sternal, l'installation peut être difficile chez les patientes âgées, voire impossible chez les patientes obèses car les seins sont surélevés et donc cela réduit la taille de l'anneau. Elle augmente l'angoisse des patientes claustrophobes. De plus, la taille de l'antenne est identique quelque soit la taille de la poitrine ce qui entraine des modifications de la forme des seins pour les poitrines volumineuses moulant la forme de l'antenne et rendant difficile la comparaison d'un examen à l'autre compte tenu d'un positionnement variable du sein dans l'antenne. Enfin, le design des antennes actuelles surélève les patientes de façon significative rendant l'examen impossible pour certaines patientes corpulentes dans des anneaux classiques de 60 cm.

Il y a toutefois peu de données dans la littérature sur l'IRM mammaire en décubitus (19-21) et un certain nombre de difficultés existent comme par exemple l'absence d'antenne dédiée, les mouvements plus importants notamment respiratoires, la diminution du volume des seins secondaire à la pesanteur et la chute latérale des seins. Il n'y a par ailleurs pas d'information concernant une meilleure tolérance de ce positionnement par rapport au procubitus.

Article 1 : Feasibility of supine breast MRI with volunteers.

Les objectifs de cet article sont de savoir si la position en décubitus en IRM mammaire est mieux tolérée par les patientes, de résoudre les problèmes d'étalement latéral des seins et de compression par l'antenne et d'analyser la qualité d'image.

Il s'agit d'une étude prospective consécutive sur 10 volontaires sains avec réalisation pour chaque personne d'acquisitions en procubitus avec antenne sein et en décubitus avec antenne cardiaque. Un questionnaire d'évaluation du confort était rempli par les volontaires à la fin de l'examen. Les rapports signal sur bruit (RSB) et contraste sur bruit (RCB) ainsi que la qualité image étaient analysés tout comme le maintien latéral et l'aplatissement des seins.

Les résultats montrent que 70% des volontaires ont préféré le décubitus. Il était jugé plus confortable, le contact avec le matériel était moins douloureux et il y avait moins de gêne ressenti pendant l'examen. Le RSB était meilleur en procubitus ainsi que la qualité image mais il n'y avait pas de différence pour le RCB. Le maintien latéral des seins était jugé comme correct et l'utilisation de cales latérales évitait l'aplatissement des seins.

Cette étude confirme la faisabilité de l'IRM en décubitus en proposant notamment un maintien latéral des seins et en évitant l'aplatissement des seins par l'antenne. Elle montre que le décubitus est préféré au procubitus par les patientes. Il existe toutefois certains points à améliorer avec notamment la nécessité de correction des mouvements respiratoires et d'antenne mammaire dédiée pour le décubitus.

Feasibility of supine breast MRI with volunteers

Guillaume Oldrini, Julie Poujol, Julia Salleron, Philippe Henrot, Frédéric Marchal

Article soumis à *Japanese Journal of Radiology*

ABSTRACT

Purpose: To determine whether a supine position breast MRI is better tolerated by patients and suitable for quality image analysis.

Methods: It is a prospective study of 10 healthy volunteers who underwent prone acquisition with a breast coil and supine acquisition with a cardiac coil. A post-examination questionnaire assessing comfort was completed. The signal-to-noise ratio (SNR) and contrast-to-noise ratio (CNR) as well as the quality of the images were analyzed, as were the lateral displacement and flattening of the breasts.

Results: Seventy percent preferred the supine position because it was more comfortable, contact with the equipment was less painful, and the examination was found less obtrusive. The SNR was better with the prone position, as was image quality; there was no difference in the CNR. The lateral displacement was deemed to be indiscernible and the use of side supports avoided flattening of the breasts.

Conclusion: This study confirmed the feasibility of supine MRI, with lateral displacement and flattening of the breasts by the coil to be avoided in particular. Patients preferred being in a supine rather than a prone position. There are several aspects that warrant improvement, such as correction for respiratory motion and availability of a coil specific for breast imaging in the supine position.

Keywords: Breast, MRI, Supine, Prone

INTRODUCTION

Breast magnetic resonance imaging (MRI) has a prominent and an increasingly important role in breast imaging, particularly for screening of women at high risk of breast and ovarian cancer, for loco-regional assessment of breast cancers, for evaluation following neoadjuvant chemotherapy, or for assessment of axillary adenopathy when no primary can be found by breast ultrasound [1-3].

Breast MRI is currently performed lying down in a proneposition, which gives rise to several issues. First of all, the correlation with conventional mammograms and ultrasound imaging, as well as pre-operative location of lesions, can be complex since the ultrasound and the surgery take place in a supineposition while mammograms are taken when standing upright. Yet the breast is a mobile organ and even when just examinations done lying down are considered, the topography of the lesions is altered even between prone and supine positions [4]. Thus, some lesions that cannot be found by ultrasound post-MRI in a prone position can be visualized by ultrasound following an MRI in a supine position [5].This change in the topography and the anatomical relations was pointed out in the COMICE trial so as to explain the fact that MRI has not been shown to be useful for decreasing the level of positive margins and the need for renewed surgery

[6].Indeed, the supine position more accurately matches the surgical position [7].

Furthermore, theproneposition is often deemed to be uncomfortable by the patients, particularly due to pressure on the sternum, while getting into the correct position can provetroublesome for elderly patients and even impossible for obese patients since their breasts are raised and this hence reduces the space available in the bore of the MRI device.It increases anxiety in claustrophobic patients. Furthermore, the size of the coil is the same regardless of the size of the breasts.With large busts, it is hard to reproduce the positioning from one examination to the next since the breasts are molded in the coil in an uncontrollable manner. Lastly, the current design of coils significantly elevates patients to the point where an examination becomes impossible for particularly corpulent patients who cannot fit into the bore of an MRI device for which the diameter is usually 60 or 70 cm.

There is, however, little data in the literature in regard to breast MRI in the supine position [8-10],and it is associated with several problems such as, for example, the lack of dedicated coils, significant respiratory motion in particular, the decrease in the volume and the lateral displacement of the breasts secondary to the weight. There is also no information regarding better tolerance of this positioning relative to being in the prone position. Preliminary tests on mammography phantoms allowed us to validate the feasibility of using a cardiac coil for breast examinations by making comparisons of the signal with the two coils.

This study hence had several aims: determination of whether a supine position is better tolerated by patients than a prone position, attempting to provide a solution to problems caused by this position such as lateral displacement of the breasts and their compression by the coil in particular, and lastly to analyze the quality of the images taken lying face up compared to those taken lying face down.

MATERIALS AND METHODS

Population

This prospective study was conducted on 10 consecutive volunteers between the11th of Marchand the 2nd of May 2014. The examinations were performed on a 3T GE MRI (type, Milwaukee, USA).The volunteers provided their informed written consent. This study was conducted in full accordance with the World Medical Association Declaration of Helsinki, and was approved by the local ethics committee (ClinicalTrials.govIdentifier: NCT02887053). All volunteers gave written informed consent.

Following an acquisition with an eight-channel cardiac coil while lying on their back (i.e. supine), each participant underwent an acquisition with a dedicated eight-channel breast coil while lying on their stomach (i.e. prone). The order in which the two positionings were performed was randomized. The sequences, in both cases, were 3DFast Spoiled Gradient-Echo (SPGR) sequences without fat signal suppression (3D SPGR without), with standard saturation of the fat signal (3D SPGR cla),and specialized saturation of the fat signal (3D SPGR spe) sagittaly on the left breast with and without RF and an axial T2 sequence (Table 1).

The prone position was the standard position for a breast MRI witha dedicated breastcoil.For the supine position, to resolve the problem of lateral displacement of the breasts and their compression by the coil, several supports were used: a surgical bra for the first volunteer, then a sling with slatted side panels for the second and the third volunteers (Fig.1) and finally, for the

last seven volunteers cardboard lateral side panels between the arms and the torso on each side with the cardiaccoilresting on the panels without it being in direct contact with the chest (Fig.2).

Figure 1

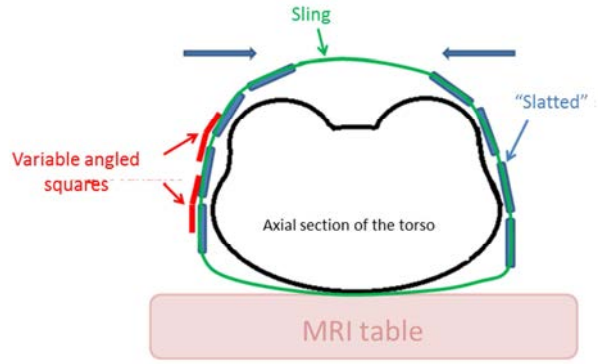


Fig 1.Schematic outline of the set-up with the slatted side plates.The slatted side plates are mounted on a sling that goes around the patient so as to provide lateral support responsible for a degree of flattening of the chest.

Figure 2

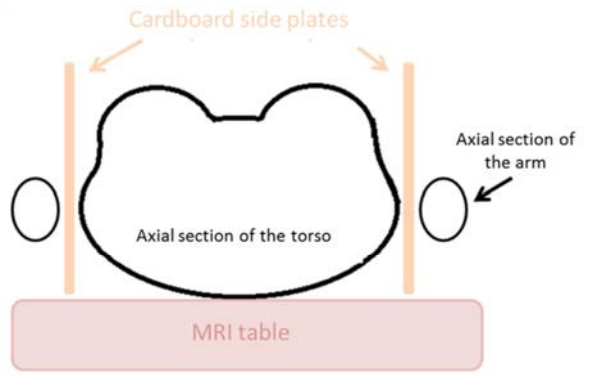


Fig 2.Schematic outline of the set-up with cardboard side plates.The cardboard side plates are placed on both sides of the volunteer between their arms and their chest to re-center the breasts and to avoid lateral displacement. Thus the coil comes to rest on the side plates without it pushing against the chest so as to avoid squashing the breasts.

At the end of the acquisitions, the volunteers had to complete a questionnaire in regard to the level of comfort during the examination and to indicate their preferred positioning (Appendix 1).

Data analysis

An analysis of the compression of the breasts was performed for each restraining technique by assigning a score of 0 if the restraint by the coil resulted in a flattening of the breasts, and 1 if this was not the case. The extent of sideways displacement was assessed subjectively by a radiologist with four years of experience with breast MRI in two ways: indiscernible or noticeable.

A study of the signal to noise ratio (SNR) in the fat and in the gland was performed in each sequence and in each position while resuming identical anatomical areas for the two positionings (Fig.3), taking the average of the SNRs for the gland and the fat for each position. The contrast-to-noise ratio (CNR) between the fat and the gland was also calculated for each acquisition. This amounted to the difference in the value of the fat divided by the standard deviation of the noise.

Figure 3

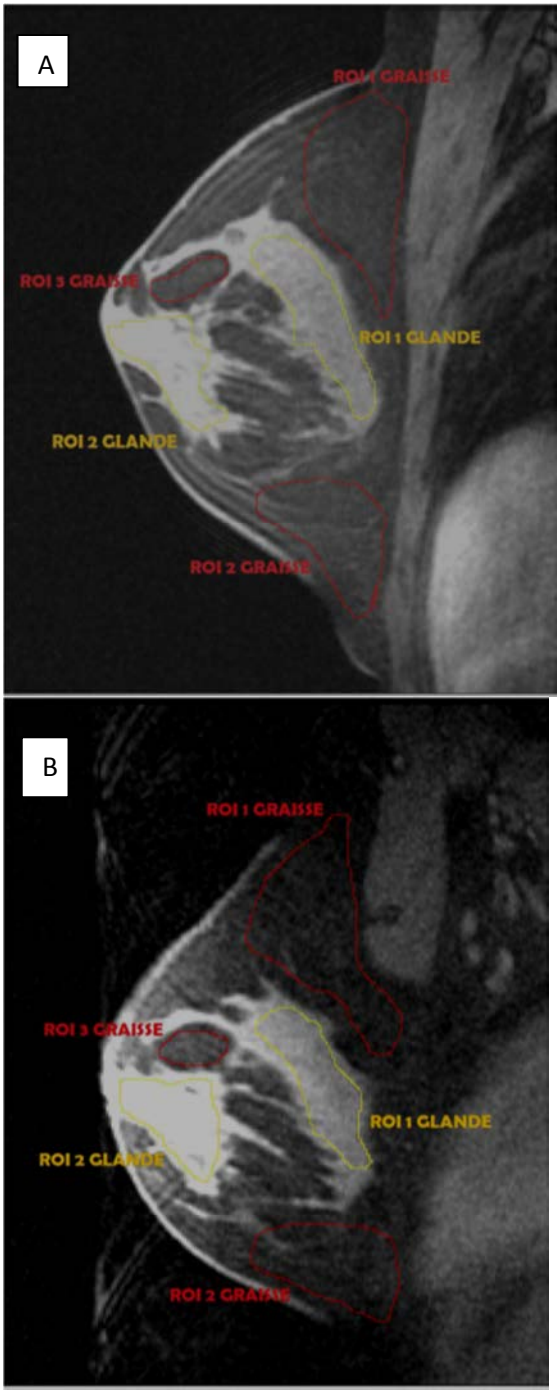


Fig 3.Regions of interest for calculation of the SNR in supine and prone positions. 3D SPGR acquisition of the signal from the fat in the prone (A) versus supine (B) position. The regions of interest were placed in the same anatomical areas on the prone and the supine acquisitions.

Lastly, the radiologist reviewed each examination, and for each positioning they assigned a quality score subject to the examination as a function of the homogeneity of the fat signal saturation, the quality of the signal, and the artefacts (e.g. movements and phantom images in particular).This score was based on five categories designated from 1to 5. A score of 1 corresponded to an uninterpretable examination, a 2 to a poor quality examination but uninterpretable, a 3 to an average quality examination but interpretable, a 4 to a good quality examination, and a 5 to a very high quality examination.

Statistical analyses

The qualitative parameters were described as a percentage and confidence interval at 95%. The numerical parameters were expressed as medians and ranges. Normality was verified by a Shapiro-Wilks test. The comparison of supine and prone parameters was performed by the Student's t-test for matched samples in case of normality, and by the Wilcoxon test otherwise. The threshold for significance was set at 5%. The analyses were performed using SAS version 9.3 software (SAS Institute Inc., Cary, NC 27513 USA).

RESULTS

The median age of the volunteers was 25 years, ranging from 23 to 61 years of age, while their median weight was 58.5kg, ranging from 40 to 82 kg.

For seven volunteers, there was no flattening of the breasts (lateral side panels) with a score of 1.In three other cases (surgical bra and slatted side panels), the displacement or the coil led to a loss of the breast contour with a score of0. Lateral support was deemed to be adequate among the 10 volunteers.

The examinations took less time when lying face down (25 min [14;38]) than

when lying face up (30min[24;50]) (p=0.031).

Seventy percent [35%–93%] of the volunteers preferred the face up position.

Thus, the face up position was deemed to be more comfortable (p=0.037). When lying on one's back, contact with the equipment was less painful (p=0.035) and the examination was found to be less obtrusive (p=0.031).

The feeling of confinement or oppression and anxiety during the examination was less for the supine position than for the prone position (p=0.060 and 0.071, respectively).

The median subjective quality score was 4[3;5] lying face down, and 3[2;4] lying face up (p= 0.031).

The values for the SNR and the CNR are shown in Table 2. There was a significant difference, with less high SNRs for supine compared to prone acquisitions (p= 0.016) for each sequence. These results were found for the fat as well as for the gland. By contrast, there was no significant difference in the CNRs, with better values obtained with the breast coil without reaching statistical significance.

DISCUSSION

Seventy percent of the volunteers preferred the supine position. It was deemed to be more comfortable, contact with the equipment was less painful, and the examination was found to be less obtrusive. Lateral support using cardboard side platesallowed lateral displacement and flattening of the breasts by the coil to be avoided, unlike the other two supports that were used. The SNR was better with the proneposition, as was the image quality, while there was no difference in the CNR.

The face up position offers several advantages relative to being face down. The patients found it to be more comfortable and less painful, even though the examination lasted longer with the supineversus the proneposition, and it was preferred over the latter, even when taking into account the low number,as the confidence interval remained high.The impetus for providing a better tolerated positioning is that it allows for a higher level of compliance and a better adherence to screening, since the patients who benefit most from screening by MRI are often those with an elevated genetic risk for which this examination has now been available for several decades. It is hence paramount to make this examination less obtrusive for them by taking note of their preferences, which also allows for kinetic artefacts to be reduced that can compromise the interpretation. Indeed, the interpretation of breast MRIs is, to a large extent, based on dynamic injected series and on subtracted images performed using the mask without injection. If the patient moves however between the injected and the non-injected series, the subtracted images are of lower quality and the contrast images less clear, less amenable to analysis, and potentially masked [11]. Notably, in their study, Paage et al. did not identify technical deficiencies in MRI examinations that failed to pick up breast cancer [11].Furthermore, in this study, the median age was fairly low, which made it relatively easy to get the volunteers into the correct position. For the population monitored by MRI, the medianage of the patients is above that of the volunteers of this study. It is readily apparent that the ease of getting properly positioned for a supine relative to prone acquisition could be another advantage for elderly individuals who tend to have considerably reduced mobility. Furthermore, with obese patients, the prone positioning in the coil elevates the thorax and does not allow entry into an MRI bore, for which the diameter is 60 or 70 cm depending on the instrument. With these patients the supine

positioning allows the examination to be performed.

A supine examination should also allow for a better topographical matching of the lesions withthe ultrasound and the surgery. Carbonaro et al. determined the average displacement in the three spatial planes to be between 3 and 6 cm between prone and supine positioning [8]. In essence, aside from lesions of the lower inner quadrant which has little mobility, the topographical alterations of breast lesions between proneandsupinepositions are hard to predict and they are variable, which makes it difficult to determine the topography of a lesion in the perioperative supineposition based on a preoperativebreast MRI in the prone position [4]. Some studies have examined the displacement of lesions and the breast deformations between the two positions using physical modeling [12, 13],but this cannot readily be applied in clinical practice or to guide surgery [4]in light of its complexity.Furthermore, there is greater movement of the breast when the size of the breast increases[14],or as a function of the proportion of fat in the breast [4].

Use of cardboard lateral side plateshas proven to be effective for lateral support of the breasts, and it has also served as support for the cardiaccoil, thereby avoiding additional flattening of the chest (as opposed to a surgical bra and a sling with slats), which has allowed images of suitable quality to be obtained (Fig. 4) that in some cases are as good as images obtained in the prone position (Fig.5).

Figure 4

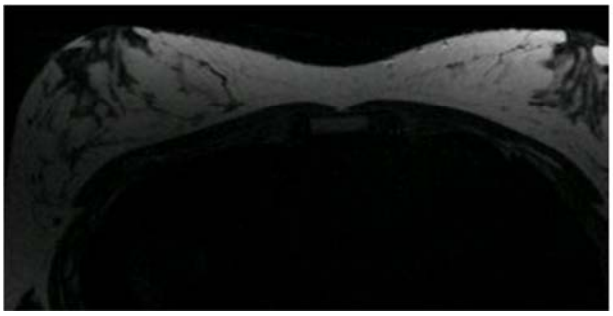
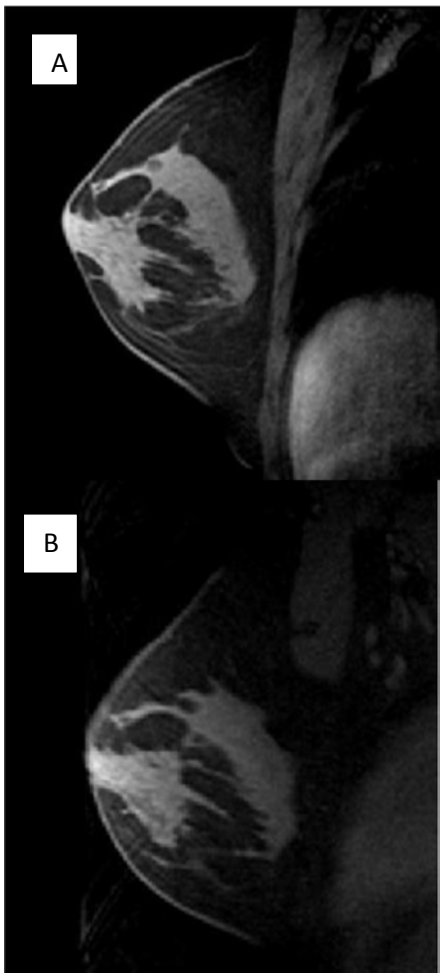


Fig 4.Axial T2 image in the supine position with lateral support of the breasts by cardboard side plates. The lateral support of the breasts by lateral side plates allows lateral displacement of the breasts to be avoided. Furthermore, flattening of the breasts by the coil is avoided since the coil is supported by the side pates.

Figure 5



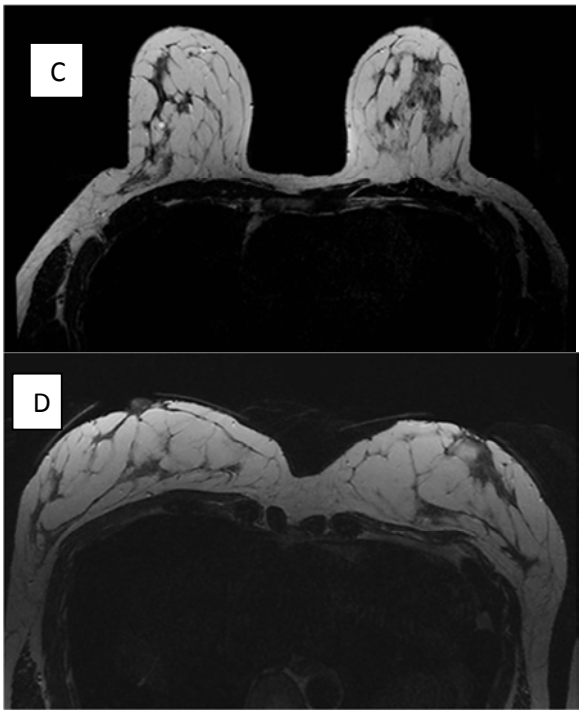


Fig 5.Comparison between prone and supine position for axial T2 (A prone, B supine) and 3D SPGR acquisitions (C prone, D supine). Good maintenance of the breast outline upon acquisition in the supine position with good visualization of the glandular structures compared to acquisition in the prone position.

There are nonetheless several limitations. While only the aesthetic quality of the images was considered and not their informative nature in light of the absence of a breast lesion, and injection of contrasting agent, supine MRI was deemed to be less good mainly due to kinetic artefacts with the presence of phantom images (Fig.6) secondary to respiratory motion. These artefacts are enhanced when the volunteer subject is anxious[10]and hence breathing more deeply. We are currently working on a procedure to correct for motion that should allow us to overcome this issue.

Figure 6

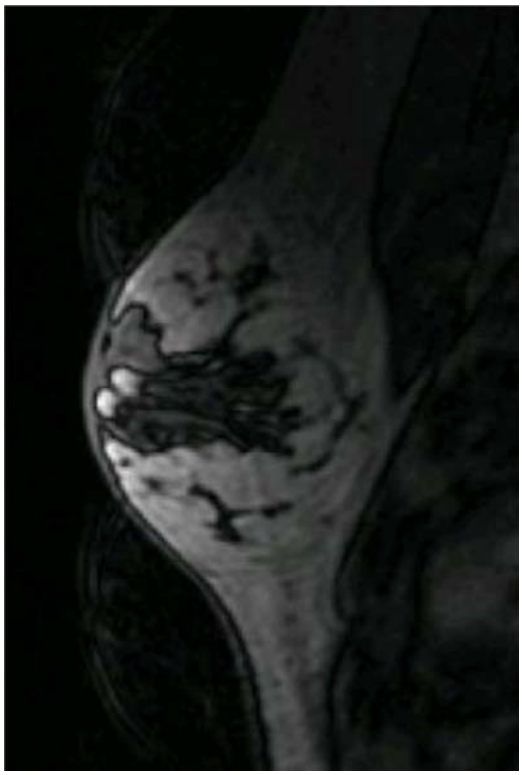


Fig 6.Sagittal acquisition of the left breast by 3D SPGR without fat saturation. In the supine position, with the lateral side plates and the cardiac coil resting on the plates without contacting the breast, the breast maintains its correct outline. Phantom images due to respiratory motion can be seen.

Otherwise, the SNR has proven to be less good in the supine position, but not the CNR. This can probably be explained by the fact that although the two coils comprisedeightchannels, with the breast coil there were fourchannels per breast while with the cardiac coil there were fourchannels for the back and fouron the chest and hence the number per breast was twoinstead of four. This can readily be improved by using cardiac coils with more channels.Furthermore, Ziegler et al. have shown in their study that the SNR was more homogenous with a breastcoil and that in the supine position the SNR decreased when the distance to the coil increased[10].This underscores the need to use a dedicated breast coil for the supine position. In addition to a dedicated coil, it is important to have the same sequences

available on just the breast coil, and to work with suitable fields of view.

Lastly, other limitations of this study were the low number of subjects and the use of different restraints on the first several volunteers. It was however a feasibility study, aimed at obtaining preliminary results in regard to comfort and image quality. Further investigation with a greater number of subjects will have to be performed.

In conclusion, this study confirms the feasibility of MRI in the supineposition, which offers lateral support for the breasts and avoids flattening of the breast by the coil in particular. It appears that the volunteers preferred the supine position over the prone position. There are nonetheless several items that could be improved,particularly in terms of the requirement for correcting for respiratory motion and use of a dedicated breast coil for the supine position.

MAIN POINTS

- Breast MRI is currently performed lying down in a prone position. Our study confirmed that the supine position was preferred by 70% of patients.
- The majority of patients deemed the supine position as more comfortable, contact with the equipment was less painful, and the examination was found to be obtrusive.
- The supine position offers lateral support for the breasts and avoids flattening of the breast by the coil in particular.
- No difference was observed in the contrast to noise ratio for the supine versus prone position.The MRI image quality and signal to noise ratio was better for the prone position.

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TABLES

Table 1: Parameters of the sequences used.

Name of the sequence	Echo Time(msec)	Repetition Time (msec)	Thickness of the sections (mm)	Bandwidth	Matrix	Number of excitations
Axial T2 prone	120	7970	3	62.5	480x320	1
3D SPGR without prone	min		2.2	62.5	224x224	1
3D SPGR cla prone	min		2.2	62.5	224x224	1
3D SPGR spe prone	min	TI auto	2.2	62.5	224x224	1
Axial T2 supine	120	4831	3	62.5	480x320	1
3D SPGR without supine	min		2.2	62.5	224x224	1
3D SPGR cla supine	min		2.2	62.5	224x224	1
3D SPGR spe supine	min	TI auto	2.2	62.5	224x224	1

SPGR: 3D Fast Spoiled Gradient-Echo sequences; 3D SPGR without: SPGR without fat signal suppression; 3D SPGR cla: SPGR with standard saturation of the fat signal;3D SPGR spe: SPGR with specialized saturation of the fat signal; prone: in prone position; supine: in supine position

Table 2: Outcomes for the questionnaire and the values of the signal-to-noise ratio (SNR) and contrast-to-noise ratio (CNR).

Variable	Supine	Prone	Difference	p
Duration of the examination	25.5 [14 ; 38]	30 [24 ; 50]	4 [-12 ; 30]	0.239
Comfort	3.4 [0.5 ; 7.7]	0.9 [0 ; 4.2]	-1.3 [-6.8 ; 1]	0.037
Ease of positioning	2.15 [0.1 ; 6.1]	1.05 [0 ; 6]	-0.35 [-4.8 ; 2.7]	0.230
Discomfort from equipment contact	2.8 [0.1 ; 6.8]	1.5 [0.1 ; 4.3]	-0.65 [-6.7 ; 2]	0.112
Pain from equipment contact	2.3 [0 ; 8.5]	0.15 [0 ; 4.8]	-2.15 [-8.4 ; 2.6]	0.035
Obtrusiveness of the examination	1.9 [0 ; 10]	0.05 [0 ; 2]	-1.4 [-10 ; 0]	0.031
Pain during the examination	0 [0 ; 10]	0 [0 ; 5.7]	0 [-4.3 ; 0]	0.500
Hindered breathing	0.4 [0 ; 3.9]	1.8 [0 ; 5]	0 [-1.8 ; 3.8]	0.162
Pain due to hindered breathing	0.3 [0 ; 3.6]	0.35 [0 ; 2.4]	0 [-2.6 ; 1.9]	0.875
Confinement or oppression	4.1 [0 ; 10]	0.05 [0 ; 6.7]	-2.9 [-10 ; 5]	0.060
Anxiety	3.2 [0 ; 7.2]	0.05 [0 ; 6.5]	-2.1 [-7.2 ; 4.7]	0.071
Image quality score	4 [3 ; 5]	3 [2 ; 4]	-1 [-2 ; 1]	0.031
SNR Gland spe	36.73 [12.56 ; 53.38]	63.57 [36.81 ; 127.1]	-17.20 [-91.82 ; -2.99]	0.016
SNR Fat spe	12.12 [6.24 ; 15.44]	26.77 [18.3 ; 54.69]	-13.19 [-48.45 ; -9.09]	0.016
SNR Gland cla	57.25 [21.07 ; 67.24]	74.27 [61.13 ; 111.45]	-14.43 [-84.23 ; -1.29]	0.016
SNR Fat cla	17.87 [10.07 ; 23.72]	30.21 [25.47 ; 37.87]	-12.78 [-27.79 ; -5.83]	0.016
CNR spe	24.27 [6.52 ; 38.36]	34.25 [12.31 ; 83.73]	-9.41 [-49.24 ; 8.64]	0.078
CNR cla	37.91 [11.22 ; 48.76]	46.15 [32.62 ; 76.91]	-3.29 [-51.11 ; 6.66]	0.375

The results are expressed as the median and the range. SNR Gland cla: signal-to-noise ratio of gland with standard fat suppression SNR Fat spe: signal-to-noise ratio of gland with

specialized fat suppression; CNR spe: contrast-to-noise ratio with specialized fat suppression; CNR cla: contrast-to-noise ratio with standard fat suppression.

Appendix1: Questionnaire assessing the examination.

7 Did the examination impede your breathing?

8) In case of impeded breathing, was this:

9) During the examination, did you feel confined or restricted?

10 During the examination, were you anxious?

11) If you had to redo this examination, would you do it while on your back or on your stomach? (circle your response)

On my stomach On my back

Why this choice? .....

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Do you have any other comments or suggestions regarding this examination?.....

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Article 2 : Prone-to-supine tumor displacement in the breast : an investigation with prone MRI and supine ultrasound .

Le but de cette étude est de déterminer le déplacement des lésions mammaires entre le procubitus et le décubitus en se basant sur les données d'IRM en procubitus et des échographies en décubitus.

Il s'agit d'une étude retrospective réalisée sur 57 lésions chez 47 patientes présentant un cancer du sein. Pour chaque lésion, la distance au mamelon, le quadrant lésionnel et le rayon horaire étaient déterminés pour l'IRM et l'échographie.

Les résultats montrent que le quadrant était identique entre les deux positionnements pour 64.9% des lésions et dans 43.9% pour le rayon horaire. La distance au mamelon n'était pas reproductible entre les deux positionnements.

Cet article met en évidence le déplacement substantiel des lésions entre le procubitus et le décubitus. Il apparaît donc nécessaire d'améliorer la concordance topographique des lésions entre l'IRM et l'échographie ainsi que la chirurgie.

Prone-to-supine tumor displacement in the breast: an investigation with prone MRI and supine ultrasound

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Article soumis à Breast Disease

ABSTRACT

Background: The aim of the present study was to determine the prone-to-supine displacement of breast lesions using prone MRI and supine ultrasound (US) data.

Methods: A retrospective study was performed of 57 lesions in 47 breast cancer patients. For each lesion, the distance to the nipple, the affected quadrant, and the clock position were determined by MRI and by US.

Results: The breast quadrant was the same with these two imaging modalities for 64.9% of the lesions, while the clock position was the same for 43.9% of the lesions. The distance to the nipple was not reproducible.

Conclusions: The lesions underwent a substantial degree of displacement between a prone and a supine position. Improving the correlation of breast MRI with sonography and surgery is hence warranted.

Keywords: breast MRI, cancer, sonography, prone, supine, displacement

Background

MRI has increasingly become the norm for breast imaging [1-3]. Due to its high level of sensitivity, breast MRI is superior to more commonly used imaging modalities (e.g. mammography, sonography). Breast MRI has proven useful for assessing local disease extension and multicentric or synchronous bilateral breast cancers. In the study by Lafaye-Carré et al. [4], it improved local staging in close to 9% of the patients.

However, the low specificity [5] of this imaging procedure requires a systematic validation of the detected lesions by ultrasound-guided biopsy prior to surgical planning [6]. Indeed, in light of the large number of false positives, there is a lack of consensus in regard to indications for preoperative breast MRI [7]. A recent study performed by Nam et al. [8] highlights the importance of second-look breast ultrasound (US). At present, breast MRI is performed in a prone position, and this can give rise to a number of problems. The correlation with the ultrasound assessments, as well as the location of the pre-operative lesions with wire localization, can be complex since the ultrasound and the surgery are performed in a supine position. The topography of lesions can readily become altered between a prone and a supine position because breast is a mobile organ [9]. The inability of MRI-based detection to reduce repeat operation rates, as reported in the COMICE study, might be due to the need for the surgeon to make allowances for the patient's position when interpreting the imaging data [10, 11]. With a prone MRI, the breast is in a different position than when the patient is lying down in the operating room [10, 12]. Indeed, supine MRIs more accurately replicate the surgical position [10]. One of the challenges with the clinical use of preoperative breast

MRIs relates to the transfer of prone MRI information to the supine position [7]. If the spatial displacement of breast lesions in the supine position could be predicted, it could be used as a guide for second-look ultrasound. However, the physical models created to predict tumor displacement as the finite element method [13-15] are very complicated and they cannot be used clinically [7].

As these displacements have not been investigated in detail, further evaluation of the extent of these displacements is warranted in order to guide second-look US. The aim of the present study is to determine the prone-to-supine displacement of breast lesions using preoperative prone MRI and supine second-look ultrasound data.

Methods

Study population

A retrospective review was performed using the imaging records of 47 breast cancer patients who had undergone preoperative breast MRI and second-look ultrasound between January 2014 and January 2015 at our institution. The inclusion criteria were being a woman with breast lesions whose assessment involved breast MRI and ultrasound at our institution. There were no exclusion criteria. All of the patients were 33 to 75-year-old females (mean age: 64.12 years). A total of 57 breast lesions (9 bilateral; 50 malignant; 7 benign) were included in this study.

MRI and US protocols

Breast MRIs were performed with an MRI 3 Tesla General Electric device (HDX Twinspeed, Milwaukee, U.S.A.) with a dedicated 8-channel phased-array bilateral breast coil. Patients were examined using a standard clinical MRI protocol in a prone position with both arms placed above the head. Our breast MRI protocol included an axial T2-weighted acquisition, sagittal 3D EG T1 dynamic Vibrant acquisitions: one before and five after injection (each phase duration was 90 seconds) of gadolinium, and one axial Vibrant high resolution acquisition (Table 1). Images subtracted from the first three series after injection, and images of the maximum intensity projection (MIP) of these subtractions, were also available. Prior to administration of the contrasting agent, axial bilateral images were acquired using a T2-weighted fast spin-echo sequence MRI.

For dynamic contrast-enhanced MRI, gadoterate meglumine (DOTAREM®) was administered intravenously using a power injection at a dose of 0.2 mmol/kg of body weight and a flow rate of 2 mL/s, followed by flushing with 20 mL of a saline solution.

Second-look ultrasonography was performed by using a Toshiba ultrasound device. Patients were instructed to lie in a supine position, with their hands behind their heads.

Image measurements

All of the breast MRI and US examinations were reviewed by a resident specialized in radiology and a radiologist specialized in breast imaging who had 6 years of experience. The junior radiologist reported on the images and performed the measurements. The senior radiologist together with the junior then reviewed the reports and validated those measurements without modification. All lesions were mass on MRI.

For each lesion, the distance to the nipple, the size of the lesion, the affected quadrant of the breast, and the clock position were determined by MRI and by US. The width of a breast ultrasound transducer is around of 2 cm. We decided this measurement could be use as margin of error to distance to the nipple. So, the distance to the nipple was deemed to be different when the difference in the measurements from the two imaging modalities was greater than 2 cm. In regard to the MRI data, the quadrant and the clock position of the breast were determined using maximal intensity projections. For the distance from the nipple to the detected lesion, we used multi-planar reconstruction in a frontal plane (Fig. 1). It

corresponds to the distance between the nipple and skin projection of the lesion as in US. Indeed, due to compression by the probe, it is the only measurement possible. So, we do not study distance to skin or pectoral major because these measurements cannot be easily measured on US due to compression by the probe. The examiner evaluated the US data using a ruler and the radial technique. The secondary factors were the age of the patients, their menopause status, being on hormone replacement therapy, the breast density (categorized as either low (BI-RADS A and B) or high density (BI-RADS C and D)), and the malignancy of the lesion (categorized as malignant or benign, based on the anatomopathological diagnosis).

Statistical analysis

Qualitative parameters were described in terms of the frequency and the percentage; quantitative parameters in terms of the mean and standard deviation. Reproducibility of the size measurements and distances to the nipple between MRI and US were assessed with the intra-class correlation coefficient according to the Fleiss method [16]. A value greater than 0.8 was deemed to represent a good level of agreement. The clinical factors that could explain the concordance of the clock position between MRI and US were investigated with the Chi-squared or Fisher's exact test for qualitative parameters, and with the Mann-Whitney U-test for quantitative parameters. The statistical analysis was performed using SAS version 9.2 software (SAS Institute, Cary, NC 25513). A p-value of < 0.05 was considered statistically significant.

Results

The average age was 64.12 years (±10.4), and ranged from 33 to 75 years of age. The low breast density group comprised 23 patients, and the high breast density group comprised 24 patients.

Thirty-two patients (68.10%) were menopausal, and 15 of these 32 patients received a hormone replacement therapy on the day of the examination.

These 47 patients exhibited 57 lesions that were studied, of which 32 (56.1%) were in the right breast and 25 (43.9%) were in the left breast. The average size of the lesions was 16.1 mm (± 9.3) as determined by ultrasonography, and 18.4 mm (± 10.5) as determined by MRI ($p < 0.001$). The size measurements were reproducible between the MRI and the US imaging modalities, with an intra-class correlation coefficient of 0.83 (Table 2). Details according to histopathological data are available in Table 2. The average distances to the nipple were 3.4 cm (± 1.4) and 5.8 cm (± 2.0), respectively. Fifty lesions (87.7%) were malignant.

In regard to MRI, 20 (35.1%) of the lesions were located in the upper outer quadrant (UOQ), 4 (7%) in the lower outer quadrant (LOQ), 3 (5.3%) in the lower inner quadrant (LIQ), 11 (19.3%) in the upper inner quadrant (UIQ), 3 (5.3%) at the union of the outer quadrants, 8 (14%) at the union of the lower quadrants, 4 (7%) at the union of the inner quadrants, and 4 (7%) at the union of the upper quadrants.

The breast quadrant involved was the same for both imaging modalities for 64.9% [95% confidence interval: 52.5%; 77.3%] of the lesions. The clock position was the same for both imaging modalities for 43.9% [31%; 57%] of the lesions. There was one clock position of difference for 49.1% of the lesions (Fig. 1) and two clock positions of difference for 7% of the lesions.

In the high breast density group, the clock position was the same for 53.3% of the lesions versus 34.6% of the lesions in the low breast density group ($p = 0.16$). In regard to the group with malignant lesions, the clock position was the same for 48% of the lesions versus 14.3% of the lesions in the group with benign lesions ($p = 0.12$). The menopause status, the size of the lesion, the distance to the nipple, and the

side of the lesion had no influence on the concordance of the clock position (with *p*-values > 0.2). The distance to the nipple was not reproducible between the two imaging modalities (Fig. 2): the intra-class correlation coefficient was 0.24 and 0.28 in case of an identical clock position between the two imaging modalities.

Discussion

The present study indicates that the magnitude of prone-to-supine breast lesion displacements is often quite considerable. Indeed, the clock position was different in more than half of the cases. Even the breast quadrant differed in more than a third of the cases. Satake et al. were also able to demonstrate that changing from a prone to a supine position can change a lesion's quadrant [7]. This presents a problem for second-look sonography, since if the correlation between the two examinations is not sufficient, it can be difficult to find additional lesions that have been detected by MRI. Moreover, surgery is performed in a supine position. Thus, surgeons can also often have difficulty with evaluating the position of lesions detected by MRI. The use of supine MRI may hence allow tumors to be excised with greater precision [10].

The second element accounting for the location of tumors is the distance from the nipple. It is indeed an important element because it allows the lesion to be properly located. While it is a relative distance based on the spatial separation between the tumor and the nipple [7], it is practical measure and it is easy to use. Although Carbonaro et al. have suggested that the distance of the lesion to the nipple is the most reliable measurement [6], it was found to not be reproducible between the two examinations and the two positions from an overall point of view as well as in case of a corresponding and discordant clock position. The study by Satake et al. [7] showed that the direction of the tumor displacement depends on the tumor location, and that lesions tended to move in the inner-lower quadrant of the breast with a prone-to-supine change in the patient's position. They determined a prone-to-supine projection ratio which appears to be an indicator of breast mobility. Moreover, the displacement distance differed based on the quadrant of the tumor's location, with a more accurate prediction of displacements for lesions in the inner-lower quadrant [7]. This notion could not be investigated in our study due to the low number of lesions in these internal quadrants.

The clock position seems to be more concordant between MRI- and US-based measurements in the high breast density group and in the malignant lesions group. The correlation of the lesion's location between MRI-detected lesions and second-look US was variable, and it appeared to depend on the breast density and the nature of the lesion, although the difference was not significant due to the limited size of the patient population. Indeed, fat is less rigid than fibroglandular tissue, so an increased level of breast mobility may correlate positively with the amount of fat [7]. We have not studied this point but probably that size of the lesion, for this same reason, affects the difference of topography between US and MRI. Indeed, large lesions could be more fixed as malignant lesions. Concerning the apparent size of the lesions, they were significantly greater with MRI-based imaging.

Although previous studies have already reported in regard to deviations in the nipple-to-tumor distance [6], our study has shown that in one case out of three, the displacement is in regard to the breast quadrant; and in one case out of two, the displacement amounts to a change of at least one clock position.

Second-look US is the best option for management of MRI-detected lesions. Although use of MRI-guided biopsies is increasing, US-guided biopsy is a less expensive and a faster navigation technique that is more readily accepted by patients. The positive results with biopsies are of note, although proper detection of the lesions and reconstruction of their spatial

positions based on prone MRI versus supine US depends on the skill of the US technician. This level of displacement could have an impact on the detection of breast lesions in second-look US.

Improving the correlation in locating breast lesions by MRI, sonography, and surgery is hence warranted. In order to improve the accuracy with which this is achieved, it may be worth investigating the relative merit of MRI in a supine position to evaluate the extent to which the location of breast lesions differs with the two techniques. Although supine MRI is known to be less accurate for breast cancer diagnoses than prone MRI, which is the standard MRI technique for breast evaluation, the use of real-time supine MRI navigated US has been shown to significantly increase the detection rate of breast tumors [5]. Although Pons et al. have shown a good correlation between supine MRI and US in regard to the detection of breast lesions, other studies indicate that the correlation using prone MRI may be quite limited [5, 17]. Supine MRI-optical scans can also be used to define tumor size and location [10].

Breast MRI in a supine position could be a way to increase the rate of positive second-look US-guided biopsies. Indeed, it has been reported to have a better correlation with tumor extension [5, 18-20]. However, respiration causes breast motion in the supine position [12].

Our study has several limitations. First, it was a retrospective study. Second, the patient population was limited, particularly in terms of inner quadrant lesions. Moreover, as the correlation between prone MRI and supine sonography is limited, further investigation of the correlation between prone and supine MRI appears to be warranted.

Conclusions

The difference in the location of breast lesions in the prone versus supine position was found to be quite substantial in terms of the distance to the nipple, the clock position, and the breast quadrant. This was particularly so for cases with low breast densities. Improving the correlation of breast MRI with sonography and surgery is hence clearly warranted.

Declarations

Ethics approval and consent to participate

This retrospective study was conducted according to the Declaration of Helsinki's "Ethical Principles for Medical Research Involving Human Subjects". As it is a monocentric retrospective study, informed contentment was waived.

Consent for publication

Not applicable

Availability of data and materials

All data generated or analyzed during this study are included in this published article [and its supplementary information files].

Competing interests

The authors declare that they have no competing or conflicting interests.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Authors' contributions

GO performed manual measurements, drafted the manuscript, and conceived the study.

GD performed manual measurements, helped on conceived the study. JS performed statistical analysis, helped on conceived the study. FM and PH helped on conceived the study. GO, JS, GD, PH, FM contributed to the design of the study. Further, all authors contributed with intellectual discussion. All authors have revised the manuscript and approved the final version.

Acknowledgements
Not applicable.

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Tables

Table 1. Breast MRI protocol

	Axial T2 SE	Sagittal Vibrant	Axial Vibrant HD
Flip angle degrees	90	10	10
Repetition time (msec)/ Echo time (msec)	7723/120.12	4.89/2.10	9.59/4.25
Field of view (cm)	34 x 37.4	22 x 24.2	29 x 31.9
Matrix	320 x 480	224 x 224	416 x 512
Section thickness (mm)	3	2.2	1.8
Number of excitations	1	0.5	0.71

		(± 6.8)	(± 6.7)		
Malignant	50	16.9 (± 9.4)	19.5 (± 10.6)	2.6 (± 5.7)	0.81

Table 2. Reproducibility of size of the lesions based on ultrasonography (US) and based on MRI in all population and according to histopathological data.

	N	US	MRI	Difference (MRI-US)	Intra-class correlation coefficient
All	57	16.1 (± 9.3)	18.4 (± 10.5)	2.3 (± 5.5)	0.83
Benign	7	10.9	10.7	-0.1 (± 0.9)	0.99

Figures

Figure 1: breast carcinoma on US and MRI

a) Hypo echogenic lesion (blue line) on US. Clock position is 12 o'clock and distance to nipple is 3cm

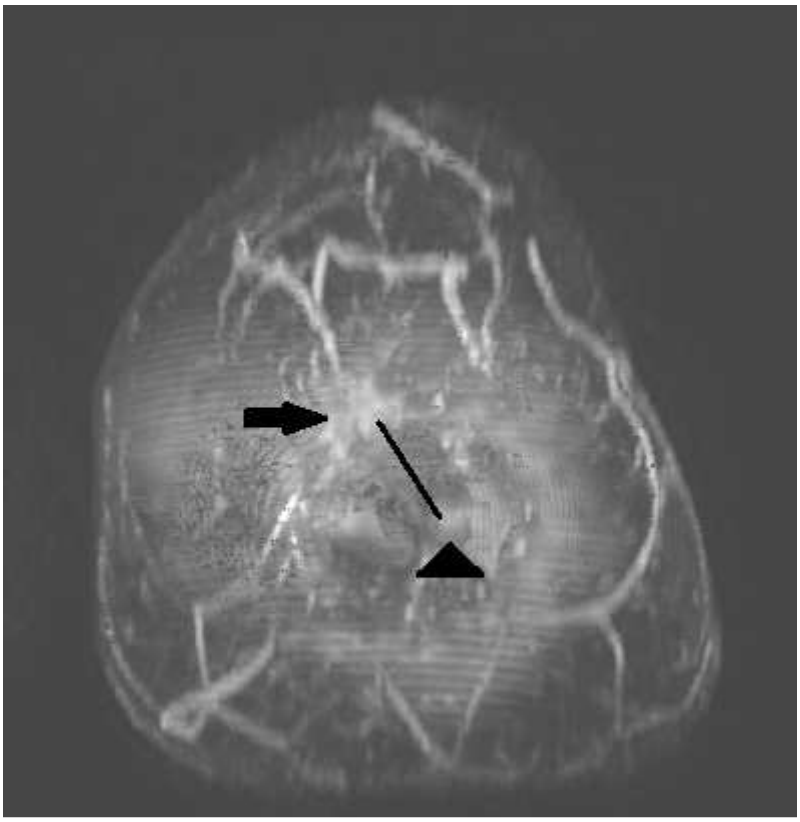

Figure 1: breast carcinoma on US and MRI
b) Lesion (black arrow) on frontal Maximum Intensity Projection view to determine clock position. Clock position is 11 o'clock and distance to nipple (black arrowhead) is 3cm

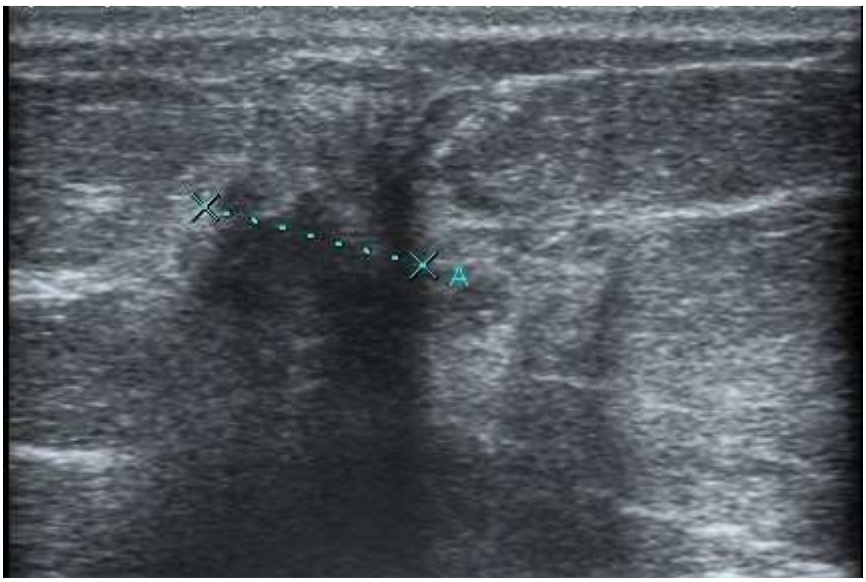

Figure 2: breast carcinoma on US and MRI
a) Hypo echogenic lesion on US. Clock position is 6 o'clock and distance to nipple is 5cm

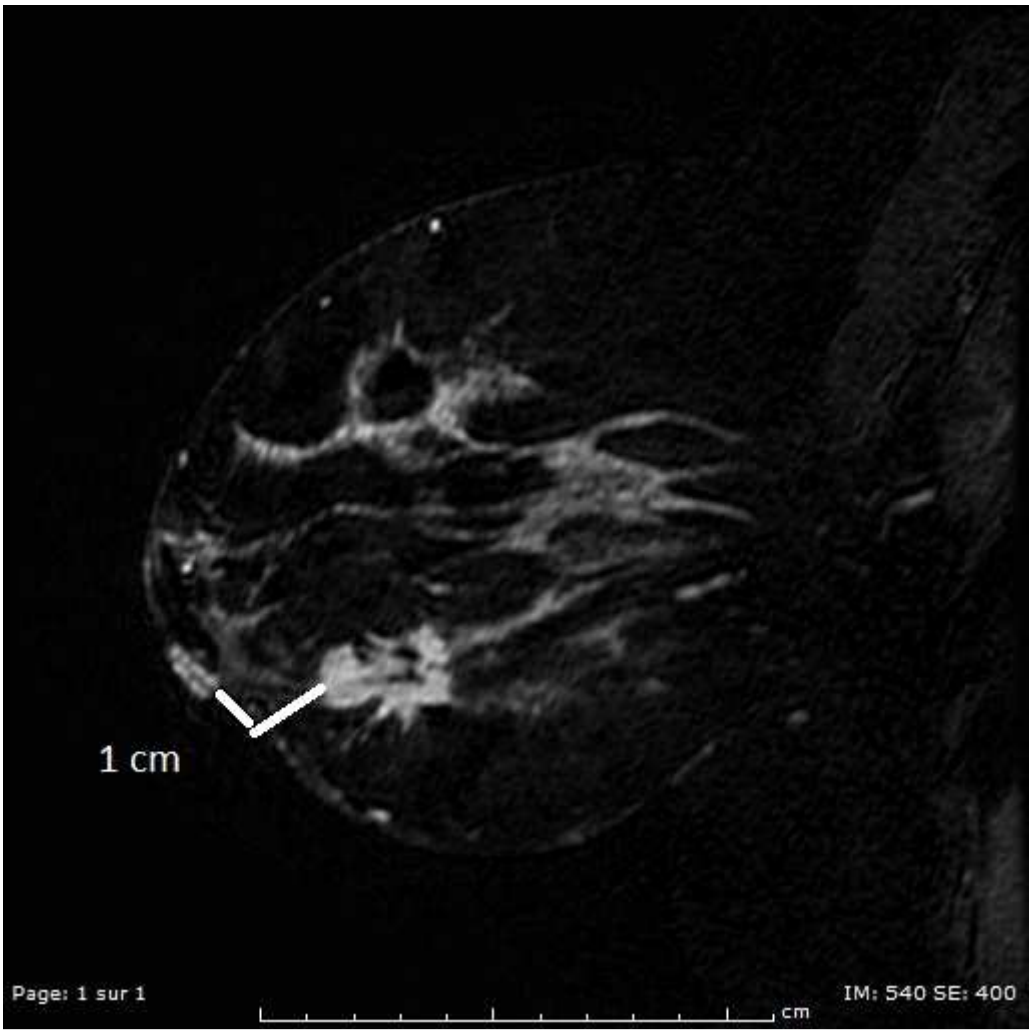

Figure 2: breast carcinoma on US and MRI

b) Lesion is at 6 o'clock but distance to the nipple is 1cm on sagittal view on MRI

Article 3: Feasibility study of supine breast MRI: comparison with prone MRI and comfort assessment

L'IRM mammaire est habituellement réalisée en procubitus. Les objectifs de ce travail sont de déterminer quel positionnement est le mieux toléré par les patientes entre le procubitus et le décubitus et de mettre en évidence les changements topographiques des lésions entre les deux positionnements en IRM et avec l'échographie en décubitus.

Il s'agit d'une étude prospective monocentrique approuvée par le CPP EST III et enregistrée sur clinical trial (NCT02865239). Les patientes ont signé un consentement. 15 patientes prises en charge pour un carcinome mammaire ou pour une lésion suspecte du sein ont bénéficié d'une échographie mammaire et d'une IRM mammaire standard en procubitus suivie d'une IRM en décubitus. A la suite de ces examens, les patientes ont répondu à un questionnaire de confort. Nous avons également analysées les changements topographiques entre les trois examens.

Les patientes ont préféré le décubitus (60%). De plus, la corrélation topographique est plus élevée entre l'IRM en décubitus et l'échographie qu'entre l'IRM en procubitus et l'échographie (Kappa respectivement à 1 et 0,3293). En comparaison avec l'échographie, il y avait une différence significative entre les deux IRM en terme de topographie des lésions (p=0,0027) et de rayon horaire (p=0,0047).

En comparaison avec l'IRM en procubitus, l'IRM en décubitus montre une meilleure corrélation de la topographie des lésions avec l'échographie. Ces éléments pourraient permettre une détection plus efficace et plus simple des lésions au cours de l'échographie post-IRM et ainsi réduire les biopsies sous IRM. Enfin, les patientes trouvent le décubitus

plus confortable et moins angoissant ce qui pourrait permettre un meilleur degré de compliance dans le cadre du dépistage au long cours des patientes à haut risque.

Feasibility study of supine breast MRI: comparison with prone MRI and comfort assessment

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Article soumis à *Iranian Journal of Radiology*

Abstract

Background: Breast magnetic resonance imaging (MRI) has an important role in breast imaging, particularly for the screening of women at high risk of breast cancer. Breast MRI is currently performed lying down in a prone position.

Objectives: To determine if the supine or prone breast MRI position is better tolerated by patients and to highlight changes in lesion topography between prone and supine breast MRI in comparison to supine ultrasonography (US).

Methods: The institutional review board approved this monocentric prospective study. All patients signed an informed consent form. Fifteen patients who were referred for a follow-up of a breast carcinoma or a suspicion of breast carcinoma participated in the study. For each patient, we performed a supine breast US, a standard prone breast MRI, and then a supine breast MRI. The patient was then asked to answer a questionnaire on comfort. We analyzed changes in lesion topography between the three exams.

Results: Patients preferred the supine position (60%). Moreover, a higher lesion topography correlation was demonstrated for supine US (Kappa=0.3293 for prone MRI and 1 for supine MRI). With respect to the US, there was a statistically significant difference between the prone and supine MRI in terms of lesion topography (p=0.0027) and hourly radius (p=0.0047).

Conclusion: Compared to prone breast MRI, supine breast MRI showed a higher correlation in lesion topography to supine US. These findings should allow for easier and more effective detection of lesions on second-look US and consequently reduce MR-guided biopsies. Moreover, patients preferred the more comfortable and less obtrusive supine position which may promote a higher level of compliance and a better acceptance of long-term screening in high risk women.

Keywords: Magnetic Resonance Imaging, Breast, Diagnostic Imaging, Ultrasonography, Breast Neoplasms, Early Detection of Cancer.

Background

Breast magnetic resonance imaging (MRI) has a prominent and an increasingly important role in breast imaging, particularly for the screening of women at high risk of breast and ovarian cancer, the locoregional assessment of breast cancers, the evaluation following neoadjuvant chemotherapy, and for the assessment of axillary adenopathy when no primary can be found by breast ultrasound [1-3].

Breast MRI is currently performed lying down in a prone position, which gives rise to several issues. Firstly, the topographic correlation with conventional mammograms and ultrasound imaging, as well as pre-operative location of lesions, can be complex since the ultrasound and the surgery take place in a supine position while mammograms are taken when standing upright. The breast is a mobile organ and even when examinations are done lying down, the topography of the lesion is altered between prone and supine positions [4]. Thus, some lesions that cannot be found by ultrasound post-MRI in a prone position can be visualized by ultrasound post-MRI in a supine position [5]. This change in the topography and the anatomical relations was pointed out in the COMICE trial (Comparative effectiveness of MR Imaging in breast cancer) as an explanation to the fact that MRI has not been shown to be useful for decreasing the level of positive margins and the need for renewed surgery [6]. Indeed, the supine position more accurately matches the surgical position [7].

The prone position is often deemed uncomfortable by patients, particularly due to pressure on the sternum. In addition, it can increase anxiety in claustrophobic patients. Getting into the correct position can prove troublesome for elderly patients and for obese patients, as their breasts are longer, reducing the space available in the bore of the MRI device. Moreover, the size of the coil is the same regardless of the size of the patient's breasts. With large busts, it is hard to reproduce the positioning from one examination to the next since the breasts are molded in the coil in an uncontrollable manner. Lastly, the current coil designs significantly elevate patients, making it impossible for corpulent patients to fit into the bore of an MRI device for which the diameter is usually 60 or 70 cm.

There is, however, little data in the literature on breast MRI in the supine position [4, 5, 7-13]. The supine position is associated with several problems such as the lack of dedicated coils, significant respiratory motion, decrease of breast volume, and lateral displacement of the breasts. There is also no information regarding better tolerance of this positioning relative to that of the prone position.

This study hence had several aims, including to determine if the supine position is better tolerated by patients than the prone position, and to highlight lesion topography modification between prone and supine MRI in comparison to supine ultrasonography (US).

Methods

Written informed consent was obtained from all participants. The study was approved by the institutional review board. The study was registered under clinical trial (NCT02865239).

Population

The study population included 15 outpatients who had been evaluated with MRI. The scanning protocol was prospectively applied during an 18-day period (from 02 October 2015 to 20 October 2015) to a population of patients referred for the follow-up of a breast carcinoma or a suspicion of breast carcinoma. Patients were eligible for the study if they were 18 years of age or older

and had an ECOG performance status ≤ 3. Exclusion criteria included the presence of claustrophobia and contraindication to the injection of contrast medium Gadoline.

Population characteristics were the following: mean age 52.9 years (range from 36 to 64 years), including 8 menopausal women (53.3%). In this population, 2 women had a family history of breast cancer without context of high risk (13.33%).

MR acquisition

MRI sequences were acquired on a 3 T GE MR scanner using a dedicated phased array breast coil. Patients were imaged in the prone position. Dedicated breast coils covering both breasts were used. For dynamic MRI, gadoterate meglumine (DOTAREM) was administered intravenously using a power injection at a dose of 0.2 mmol/kg of body weight and a flow rate of 2 mL/s, followed by flushing with 20 mL of saline solution. At the end of the standard protocol (Axial T2-weighted, sagittal Vibrant dynamic and axial Vibrant HR), patients were then placed in the supine position. An acquisition with an eight-channel cardiac coil was achieved. To resolve the problem of lateral displacement of the breasts and their compression by the coil, we used lateral cardboard panels between the arms and the torso on both sides such as to have the cardiac coil resting on the panels and not being in direct contact with the chest. A sagittal 3D Fast Spoiled Gradient-Echo (SPGR) T1-weighted acquisition with fat saturation was obtained.

At the end of the acquisitions, the patients completed a questionnaire on the level of comfort during the examination and indicated their preferred positioning (Appendix 1). All resulting MR images were reviewed on a Picture Archiving and Communication System (PACS) workstation (Agfa HealthCare, a division of Agfa-Gefaert Group, Belgium).

Supine US acquisition

Each patient had a supine US breast examination in standard conditions with arms behind the head. This examination could be performed before or after the MRI depending on the patient's care schedule.

MR and supine ultrasound data analysis

A first reading was carried out by a senior radiologist with 6 years of experience in breast MR imaging. The reader analyzed both MR acquisitions (prone and supine) and supine US for all patients. On each acquisition, the lesions to be studied were marked to ensure that they were analyzed on subsequent readings. Only lesions greater than 10 mm seen on ultrasound and classified ACR 4 or 5 in accordance with the Breast Imaging Reporting and Data System (BI-RADS) of the American College of Radiology (ACR) were marked.
The radiologist then performed the readings of each imaging modality in the following order: prone acquisitions, supine acquisitions, and supine US, observing a two-week interval between each imaging modality group. Information on the women’s past clinical history including reason for referral, respective risk level, and prior imaging studies was withheld from the reader. Imaging from the other two modalities was equally withheld from the reader at the time of reporting.
The following parameters were measured for prone and supine MRI acquisition: distance to nipple, distance to the pectoralis major muscle, projection of the lesion to the skin with respect to the nipple, breast quadrant, and hourly radius. Image quality was assessed on a four level graduated scale: Uninterpretable for medical diagnostic; poor quality, making interpretation difficult; average quality but interpretable; good quality.

For supine US acquisition, the distance of the lesion projection to the skin with respect to the nipple, breast quadrant, and hourly radius were recorded for each lesion. The

primary objective of the study was to compare the topography of the lesions according to prone and supine MRI with supine US. The topography of lesions was considered to be the same if the hourly radius was identical and the difference in distance of skin projection with respect to the nipple was less than 2 cm between the different examinations.

Statistical analysis

Quantitative variables were described with mean and standard deviation; qualitative variables by frequency and percentage. The normality of the distribution was assessed with the Shapiro-Wilk test. The comparison of parameters with respect to MRI positioning was performed with the paired student T-test or a Wilcoxon U test for paired samples. The comparison of the rate of difference according to MRI position was investigated by McNemar's test.

All statistical analyses were performed using SAS version 9.3 (SAS, Cary, NC, USA). The significance level was set at 0.05.

Results

The 15 patients enrolled presented with 16 lesions (one patient presented with two lesions). On supine US examination, 7 (43.6%) were in outer quadrants, 6 (37.6%) in inner quadrants, and 3 (18.8%) were central. The mean size lesion was 17.31 mm with a SD of 10.89 mm.

The results of distance to nipple and to pectoralis major muscle, and skin projection with respect to the nipple reported from both breast MRI positions are presented in Table 1. The description of the location of the lesions for the three imaging protocols are presented in Table 2.

Comparison of supine US and prone MRI

The lesion topography differed in 11 cases (68.75%): 4 lesions (25%) showed a greater than 2 cm difference in the distance of skin projection with respect to the nipple between the two imaging modalities and 8 lesions (50%) were reported to have a different hourly radius between both modalities (1 lesion with both).

Comparison of supine US and supine MRI

The hourly radius was the same in all cases. Skin projection with respect to the nipple was different for 2 lesions (12.5%) and lesion topography was different for 2 lesions (12.5%).

Difference between prone and supine MRI with respect to US

There was a statistically significant difference in lesion topography (p=0.003) and hourly radius (p=0.005) (Table 2). There was no difference in skin projection with respect to the nipple (p=0.414).

Image quality

For prone MRI, 8 images (53.33%) were of average quality but interpretable and 7 images (47.67%) were of good quality. For supine MRI, 1 image (6.67%) was uninterpretable for medical diagnostic, 12 (80%) were of poor quality, making interpretation difficult, and 2 (13.33%) were of average quality but interpretable.

Questionnaire analysis

The results of the patient questionnaire for the 15 patients are available in Table 3. In the prone position, contact with the equipment during breast MRI was more uncomfortable (p=0.039), more painful (p=0.010), discomfort was more continuous (p=0.038), and breathing was more difficult (p=0.039) and painful (p=0.001).

Nine patients preferred the supine position (60%; 95% confidence interval from 35.1 to 87.2), 4 preferred the supine position (26.7%), and for 2 patients, both positions were equivalent (13.3%).

Discussion

The supine MRI position was preferred by patients. Moreover, it demonstrated a better correlation with supine US.

The supine position offers several advantages relative to the prone position. The patients found it to be more comfortable and less painful, and it was preferred over the latter, even when taking into account the low number of enrolled patients, as the confidence interval remained high. The impetus for providing a better tolerated positioning is that it allows for a higher level of compliance and a better adherence to screening. This is particularly relevant to patients with a genetically elevated risk of developing breast malignancy as screening implies multiple and regular MRI exams over several decades. It is hence paramount to make this examination less obtrusive for patients by taking note of their preferences. This also allows for kinetic artefacts to be reduced which could otherwise compromise the interpretation. Indeed, the interpretation of breast MRIs is, to a large extent, based on dynamic contrast enhanced series and on subtracted images performed using the mask before administration of an intravenous (i.v.) contrast medium. If the patient moves between the injected and the non-injected series, the subtracted images are of lower quality and the contrast images less clear, less amenable to analysis, and potentially masked [14]. Notably, in their study, Pages et al. did not identify technical deficiencies in MRI examinations that failed to pick up breast cancer [14]. It is readily apparent that the ease of getting properly positioned for a supine relative to prone acquisition could be another advantage for elderly individuals who tend to have considerably reduced mobility. Furthermore, with obese patients, the prone positioning in the coil elevates the thorax and does not allow entry into an MRI bore, for which the diameter is 60 or 70 cm depending on the equipment. Supine positioning allows the examination to be performed on elderly and obese patients.

A supine examination should also allow for a better topographical matching of the lesions with ultrasound and surgery. Carbonaro et al. determined the average displacement in the three spatial planes to be between 3 and 6 cm between prone and supine positioning [8]. In essence, besides lesions of the lower inner quadrant with little mobility, the topographical alterations of breast lesions between prone and supine positions are hard to predict and are variable, which makes it difficult to determine the topography of a lesion in the surgical supine position based on a preoperative breast MRI in the prone position [4]. Some studies have examined the displacement of lesions and the breast deformations between the two positions using physical modeling [15, 16], but this cannot readily be applied in clinical practice or to guide surgery [4] in light of its complexity. Furthermore, there is greater movement of the breast when the size of the breast increases [17], or when the fat content of the breast increases [4]. In our study, we found a perfect correlation in topographic lesion between supine US and MRI contrary to supine US and prone MRI. These findings should allow for easier and more effective detection of lesions on second-look US and consequently reduce MR-guided biopsies.

Our study has several limitations. Firstly, the number of patients is small and a prospective study with a greater number of patients is required to confirm the results of this feasibility study. However, the differences observed remain statistically significant. Secondly, MRI image quality is lower in the supine position. This can probably be explained by the fact that although the two coils comprised eight channels, the breast coil bears four channels per breast while the cardiac coil has four channels for the back and four on the chest, hence two coils per breast rather than four.

This can readily be improved by using cardiac coils with more channels. Furthermore, Siegler et al. have shown that the SNR was more homogenous with a breast coil and that the SNR decreased in the supine position when the distance to the coil increased [10]. Moreover, there was no supplementary administration of contrast medium during the supine acquisition, which led to a poor enhancement of lesions given the delayed time between the administration of i.v. contrast media and the supine acquisition. Furthermore, due to the lack of infusion of an additional contrast media before the execution of magnetic resonance imaging in the supine position, we introduced a bias because only lesions greater than 10 mm could be analyzed.

Correlation in lesion topography to supine US is better with supine MRI than with prone MRI. This should facilitate the detection of lesions on second-look US. Moreover, the supine position is preferred by patients, especially for comfort, which can bring about a higher level of compliance and a better adherence to long-term screening in high risk women.

Acknowledgements

The authors declare that they have no competing interests. No specific funding was received for this study.

Authors' contributions

GO included patients, performed manual measurements, drafted the manuscript, and conceived the study. JS performed statistical analysis, helped on conceived the study. EH, FM and PH helped on conceived the study. GO, JS, EH, PH, FM contributed to the design of the study. Further, all authors contributed with intellectual discussion. All authors have revised the manuscript and approved the final version.

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Tables

Table 1. Different measurements according to MRI position.

	Distance to nipple (mm)	Distance to pectoral (mm)	Skin projection according to nipple in up-down (mm)	Skin projection according to nipple in left-right (mm)
Prone MRI	43.19	34.81	23.81	9.69
Supine MRI	26	14.31	23	18.88

Table 2. Description of the location of the lesions for the three imaging protocols and comparison of the differences MRI with Supine US.

	Supine US	Prone MRI	Supine MRI	p-value
Hourly radius				
1	1 (6.25%)	1 (6.25%)	1 (6.25%)	
2	1 (6.25%)	1 (6.25%)	1 (6.25%)	
3	2 (12.5%)	2 (12.5%)	2 (12.5%)	
4	0	0	0	
5	2 (12.5%)	1 (6.25%)	2 (12.5%)	
6	0	0	0	
7	0	1 (6.25%)	0	
8	1 (6.25%)	2 (12.5%)	1 (6.25%)	
9	0	0	0	
10	2 (12.5%)	1 (6.25%)	2 (12.5%)	
11	4 (25.0%)	3 (18.75%)	4 (25.0%)	
12	3 (18.75%)	4 (25.0%)	3 (18.75%)	
Difference with Supine US	-	8 (50%)	0	0.005
Distance of skin projection according to the nipple	38.7+/-22.7	32.4+/-25.3	36.2+/-24.0	
Difference with Supine US (≥2 cm)	-	4(25.0%)	2 (12.5%)	0.414
Difference of topography with Supine US*	-	11 (68.75%)	2 (12.5%)	0.003
Location				
Ext	7 (43.75%)	8 (50%)	7 (43.75%)	
Inf	6 (37.5%)	3 (18.75%)	6 (37.5%)	
Union	3 (18.75%)	5 (31.25%)	3 (18.75%)	
Difference location with Supine US	-	7 (43.75%)	0	0.008

Table 3. Questionnaire analysis.

Question	Position	Mean (0–10)	Standard deviation	p
1	Prone	4.07	2.48	0.1367
	Supine	2.85	2.35	
2	Prone	2.55	1.98	0.1432
	Supine	1.73	1.87	
3	Prone	2.77	1.80	0.0393
	Supine	1.65	1.08	
4	Prone	2.45	2.31	0.0098
	Supine	0.86	0.87	
5	Prone	3.01	2.60	0.0376
	Supine	1.27	1.34	
6	Prone	1.54	1.97	0.8828
	Supine	1.07	1.58	
7	Prone	3.43	2.75	0.0396
	Supine	1.45	1.90	
8	Prone	2.41	1.99	0.0015
	Supine	0.93	1.37	
9	Prone	3.29	3.16	0.6469
	Supine	2.88	3.06	
10	Prone	3.69	2.93	0.1582
	Supine	2.50	2.23	

Conclusion du chapitre 1 :

Ces différents articles mettent en évidence l'importance du positionnement des patientes pendant l'acquisition des images en IRM. Ainsi, elles montrent les modifications topographiques importantes entre le procubitus et le décubitus et mettent en évidence une meilleure corrélation de la topographie des lésions entre l'IRM et l'échographie quand elle est réalisée en décubitus. Cela pourrait permettre de faciliter les échographies post-IRM et ainsi d'éviter certaines macrobiopsies sous IRM. De plus, que ce soient les volontaires ou les patientes, le décubitus est préféré par les patientes en ce qui concerne le confort et le caractère anxiogène de l'examen. Toutefois, il reste à développer une antenne dédiée pour le décubitus afin de permettre d'améliorer la qualité des images.

Chapitre 2 : Etude des moyens d'amélioration du temps d'acquisition et de leur évaluation.

Il est composé de 6 articles qui étudient les moyens d'amélioration de la résolution temporelle des acquisitions et le protocole abrégé en IRM mammaire.

En effet, comme nous l'avons vu, il est nécessaire de diminuer le temps d'examen global mais également d'augmenter la résolution temporelle des séquences. Il existe désormais des séquences à haute résolution temporelle mais qui ont une résolution spatiale moindre que les séquences de type 3DT1 telle que Vibe® ou Vibrant®. Il nous a apparu intéressant dans un premier temps de travailler sur des moyens de codage tels que le compressed sensing pour améliorer la résolution temporelle de ces séquences commerciales tout en conservant leur résolution spatiale élévée. Ce travail est présenté dans l'article Optimized breast DCE MRI protocol: a pseudo-random k-space trajectory design for the flexible reconstruction of both standard and accelerated images in fat-suppressed breast DCE-MRI. Dans un deuxième temps, nous nous sommes consacrés à des études visant à évaluer l'utilisation du protocole abrégé en IRM mammaire avec et sans l'adjonction de séquences à haute résolution temporelle de type TRICKS® ou TWIST®. Pour ce faire, nous l'avons toujours comparé au protocole complet. Nous avons également étudié ces conséquences en terme de classement BI-RADS mais également son retentissement sur l'analyse lésionnelle : forme, contours, rehaussement interne.

Dans la littérature, dans les différentes études sur les protocoles abrégés, il n'est jamais fait mention de la manière dont sont classées les lésions. En effet, l'étude de la cinétique de rehaussement décrite dans le lexique BI-RADS n'étant pas possible pour le protocole abrégé, il paraît très important de définir la manière de classer les lésions à contours lisses pour pouvoir expliciter les calculs de sensibilité et spécificité. Nous avons clairement défini ce classement BI-RADS adapté au protocole abrégé pour rendre ce protocole moins subjectif.

Article 1: Optimized breast DCE MRI protocol: a pseudo-random k-space trajectory design for the flexible reconstruction of both standard and accelerated images in fat-suppressed breast DCE-MRI.

L’objectif de cette étude est d’évaluer la faisabilité d'une acquisition cartésienne randomisée compatible avec la suppression de la graisse spectrale pour fournir une reconstruction à haute résolution temporelle.

Une acquisition entièrement aléatoire dans les directions de phase et de coupe a été générée en premier dans une séquence d'écho de gradient avec suppression de la graisse pour permettre une reconstruction sous-échantillonnée. Pour garantir une suppression efficace de la graisse, les lignes kz les plus centrales doivent être acquises à un moment optimal après les impulsions d'inversion spectralement sélectives. Par conséquent, l'échantillonnage aléatoire initial a été modifié avec un schéma de réordonnancement kz. La séquence modifiée a été testée sur fantôme et sur volontaire pour évaluer l'efficacité de suppression de graisse. Une étude portant sur 12 patients a été réalisée pour évaluer l'effet de l'échantillonnage aléatoire sur la prise de contraste. Enfin, les reconstructions accélérées et conventionnelles ont été comparées sur un fantôme mammaire de lésion maligne.

Le schéma d'échantillonnage avec réorganisation kz fournit une suppression efficace de la graisse. Les différences de contraste obtenues à partir des séquences conventionnelles et modifiées dans les lésions, le cœur, les muscles et les ganglions n'étaient pas significatives différentes (valeur p de 0,057 à 0,987). La reconstruction accélérée avec une reconstruction de détection compressée adéquate a amélioré la précision des paramètres semi-quantitatifs. Le fantôme dynamique de lésions mammaires a été correctement classé comme type III avec reconstruction accélérée mais mal classifié comme type II avec reconstruction classique.

Cette étude a démontré qu'une acquisition randomisée intelligente de l'espace k combinée à une reconstruction par détection compressée peut améliorer la performance de la séquence conventionnelle du sein en termes de résolution temporelle.

A k-space trajectory design for the flexible reconstruction of both standard and accelerated images in fat-suppressed DCE-MRI of breast

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Article soumis à *BioMed Research International*

Purpose: To assess the feasibility of a randomized Cartesian acquisition compatible with spectral fat suppression to provide high temporal resolution reconstruction for quantitative breast dynamic contrast-enhanced MRI.
Materials and Methods: A fully random acquisition in phase and slice directions was first generated in a fat suppressed 3D gradient echo sequence to allow undersampled reconstruction. To guarantee an efficient fat suppression, the most central k_z lines need to be acquired at an optimal time following the spectrally selective inversion pulses. Therefore the initial random sampling was modified with a k_z reordering scheme. The modified sequence was played out on phantom and on volunteer to assess the fat suppression efficiency. A study involving 12 patients was performed to evaluate the effect of the randomized sampling on contrast uptake. Finally, accelerated and conventional reconstructions were compared on a malignant dynamic lesion breast phantom.
Results: The sampling scheme with k_z reordering provides an efficient fat suppression. Differences in contrast uptakes obtained from the conventional and modified sequences in lesions, heart, muscles and ganglions were not significant (p-value from 0.057 to 0.987). Accelerated reconstruction with an adequate compressed sensing reconstruction improved the accuracy and precision of semi-quantitative parameters (time-to-peak…). The dynamic breast lesion phantom was correctly classified as type III with accelerated reconstruction but misclassified as type II with conventional reconstruction.
Conclusion: This study has demonstrated a smart randomized acquisition of k-space combined with compressed sensing reconstruction can improve the performance of the breast conventional sequence in terms of temporal resolution without impacting quantitative uptake rates.

Keywords: dynamic contrast enhancement; fast breast MRI; spectral fat suppression; accelerated reconstruction

INTRODUCTION

During the last three decades, Dynamic Contrast Enhanced MRI (DCE-MRI) has never stopped improving thanks to technical breakthroughs allowing images with good SNR, high spatial and relatively high temporal resolution. Especially in the breast cancer screening field, DCE-MRI has been demonstrated to be a very sensitive (sensitivity between 90% and 100%) imaging modality to detect breast cancer in high risk women population [1–6]. Since 2007, international guidelines have thus recommended the systematically use of MRI as an adjunct to mammography for screening the high-risk women population [7, 8] as it provides increased sensitivity compared to other imaging modalities [9]. However, DCE-MRI specificity for breast cancer detection and characterization is more controversial due to highly variable specificity reported in the literature: from 60% to 100% [10–14]. While the lack of standardization and interpreting skills certainly contribute to the low specificity of breast DCE MRI, the intrinsic limitation of breast DCE-MRI, in particular its low temporal resolution, may also impact the diagnosis specificity.

A conventional breast DCE-MRI protocol consists in 3D fat-suppressed T_1-weighted Fast Gradient Echo sequences covering the whole chest and six successive acquisitions are performed during a Gadolinium-based Contrast Agent (CA) injection. Conventional accelerations techniques such as parallel imaging and partial Fourier are used to achieve the highest feasible temporal resolution but the latter is still limited to approximately 90 seconds. Enhancing lesions are identified in the subtracted images and contrast uptake curves are extracted by drawing Regions of Interest (ROIs) in the lesion and by normalizing enhancement rates with respect to baseline lesion signal intensity (image acquired before CA injection). Diagnoses of enhancing breast lesions are based on both contrast agent uptakes (using qualitative [10] and semi-quantitative parameters [15]) and morphology analysis [16, 17].

Quantitative analysis of perfusion using tracer kinetic model to improve the exam specificity [18, 19] is the expected outcome of DCE-MRI. In 1998, Henderson et al have done computer simulations of breast enhancing lesions and have concluded a temporal sampling between 5 seconds and 15 seconds is needed for tracer kinetics modeling in breast [20].

Therefore many developments have been done to increase temporal resolution in breast DCE-MRI acquisitions. Time-resolved MR sequences and their derivatives initially developed for qualitative interpretation of angiography images such as TRICKS (GE), TWIST (Siemens), have been applied to breast DCE-MRI [21, 22]. These methods all have their origins in a method know as *keyhole imaging* [23]. Although the details of theses vendor-specific sequences vary, all are based on the assumption that the center of the k-space contains contrast information while edges and details are encoded in the periphery. All sequences have in their core a 3D based fast Gradient-echo acquisition with thin slices (1-2 mm), very short TEs and TRs. They all begin with a total acquisition of the Fourier domain before Contrast Agent injection. During the spreading of the contrast bolus, the k-space center is sampled much more frequently than the periphery. Combining the data

from the center and the periphery with a view-sharing technique, these sequences can provide a series of time-resolved images combined with high spatial resolution. As with the conventional sequence, the original non-contrast images can be subtracted from the injected ones to improve lesion conspicuity. Clinical evaluation of theses sequences have been published [21, 22, 24–29]. Although they showed promising results, none of them fully satisfies the conditions for achieving high quality breast MRI. Radial acquisitions [24] can lead to image blurring and distortion related to B_0 inhomogeneity and gradient non linearity [30]. Some studies used no fat suppression [21], used water-only excitation [22, 26] needing a very homogeneous B_0 field or used the more time-consuming DIXON technique to reconstruct both water and fat images [27–29]. Finally, all these sequences need view-sharing technique to fill the k-space when the data are not acquired to accelerate the acquisition. This view-sharing technique works well for relatively big spherical homogeneous lesions but for those which have complicated morphology, errors can be noticeable in the uptake curves as signals from the core and the rim interfere with each other [31] and the morphology can be distorted [32].

To avoid the bias introduced by view sharing, another type of reconstruction has emerged to obtain good quality images from under-sampled k-space data. This technique known as compressed sensing (CS) reconstruction has been introduced to the MRI field in 2007 by Lustig et al [33]. This reconstruction exploits the sparsity of MR images either in space domain (angiogram for example) or in a transform domain (e.g. spatial-finite differences or wavelet domain). By enforcing sparsity constraints in such domains, the CS algorithm can remove artifacts due to under-sampling in the Fourier domain. Some studies can be found applying CS reconstruction but like the other sequences described earlier, none of them fully satisfies high quality breast MRI acquisition: one breast acquired [34], no fat suppression [35]; or they were only simulation studies using retrospectively under-sampled k-spaces [32, 36, 37].

The aim of this study is to design and validate a random under-sampling strategy suitable for CS reconstruction that also fulfills the requirements for high-quality breast MRI [38] (both breast coverage, fat suppression and high spatial resolution). The proposed sequence involves a modification of the k-space sampling in the conventionally used Cartesian 3D gradient echo sequence with fat suppression covering both breasts. Therefore the raw data can be used to reconstruct the conventional images (without CS acceleration, 90 s temporal resolution) and higher temporal resolution images (CS acceleration factor of 6 meaning 15 s temporal resolution). This time flexible reconstruction will allow complementary information from fast (pharmacokinetic analysis) and slow imaging (BI-rads classification : lesion morphology and contrast kinetic uptakes) for an improved performance of breast DCE-MRI [39].

The sequence was validated in three steps: (i) the compatibility of the proposed k-space reordering scheme with spectral fat suppression was assessed in a fat/water phantom and in a volunteer; (ii) we applied both the conventional and proposed sequences in a pilot study with 12 female patients in order to compare morphology

and quantitative enhancement ratios measured in numerous regions of interest including breast lesions (without CS acceleration); (iii) we applied the proposed sequence to a time-controlled dynamic injection phantom with known enhancement curves and evaluated the impact of temporal resolution (with and without CS acceleration) on semi-quantitative parameters derived from the enhancement curves.

MATERIALS AND METHODS

All MRI developments and experiments were performed with a 3T system (Signa HDx 3.0T, General Electric, Milwaukee, USA) using the dedicated conventional 8 channel breast coil.

DCE-MRI pulse sequence with spectral fat suppression

We designed our study based on the breast DCE-MRI clinical protocol used in our center. In this clinical protocol, DCE acquisitions were performed in a sagittal plane with a breast specific 3D fast spoiled Gradient Echo sequence (vendor's name : VIBRANT- Volume Imaging for Breast AssessmeNT). The parameters were as follows: TR/TE = 4.9/2.1 msec, flip angle = 10°, 128 slices with 2.2 mm slice thickness, 22 cm field of view and a programmed acquisition matrix = 224 x 224 resulting in 1x1x2.2 mm^3 of spatial resolution. To prevent wrap-around artifacts from the head, phase oversampling ("No phase wrap") was used meaning doubling the number of k-space phase lines acquired. Parallel imaging with an accelerated factor of two was chosen in the slice direction (right-left); and partial Fourier in both phase and frequency directions were intrinsically implemented by the constructor. The actual (asymmetric) acquisition matrix in the Fourier domain was therefore 256 x 184 x 64 (k_y x k_x x k_z) and the duration of one VIBRANT sequence was approximately 90 seconds.

To obtain fat suppressed images, the conventional spectral fat suppression available on the vendor's scanner was used. This spectral fat suppression – named "SPECIAL – SPEctral Inversion At Lipids" [40] provides an efficient fat suppression with a spectrally selective chemical inversion technique. To apply the fat suppression, the VIBRANT sequence uses a segmented acquisition scheme. Before the acquisition of each segment, the frequency-selective inversion pulse is applied to the fat protons in the whole active volume of the transmitting coil, followed by crusher gradients to dephase any signal produced in the transverse plane by inaccuracies in the 180° pulse. To maximize lipid-suppression efficiency, k-space data should be acquired at TI = TI_{null} (i.e when longitudinal fat magnetization equal to zero) so this time is typically reserved for the acquisition of the central k-space lines of the segment because the contrast is predominantly determined by those lines [40]. For the conventional VIBRANT sequence, the vendor designed a centric acquisition which only affects the ordering of slice encodes, whereas phase encodes are acquired in a linear fashion.

Modified sampling scheme allowing fat suppression and CS acceleration

To achieve a prospective random sampling of the Fourier domain in both phase and slice directions, we modified the VIBRANT sequence within the General Electric pulse sequence programming environment (EPIC®, DV23 software version).

First, we generated a random Cartesian sampling of Fourier domain by random

permutation of all k-space samples in both slice and phase directions. As in the conventional sequence described earlier, this scheme has to be modified to account for the fat suppression. Given the desired CS acceleration factor (AF) selected by the operator, the random sampling allows the raw data to be equally split into AF frames. Each frame is thus equivalent to an undersampled Fourier domain containing data uniformly distributed in phase and slice directions (Figure 1-a). Within each undersampled frame, the (k_y,k_z) pairs are sorted according to their distance to the central kz plane (as it is done in the conventional sequence) and separated into N groups T_1 to T_N (Figure 1-a) – Example of an undersampled frame with N=16), where N is the number of k-space lines acquired per segment, i.e. between two inversion pulses. After a fat inversion pulse is applied, (k_y,k_z) pairs are picked up from groups T_1 to T_{16} of the initial random selection (with T_8 being the group of most central k-space lines) as shown in Figure 1-b.

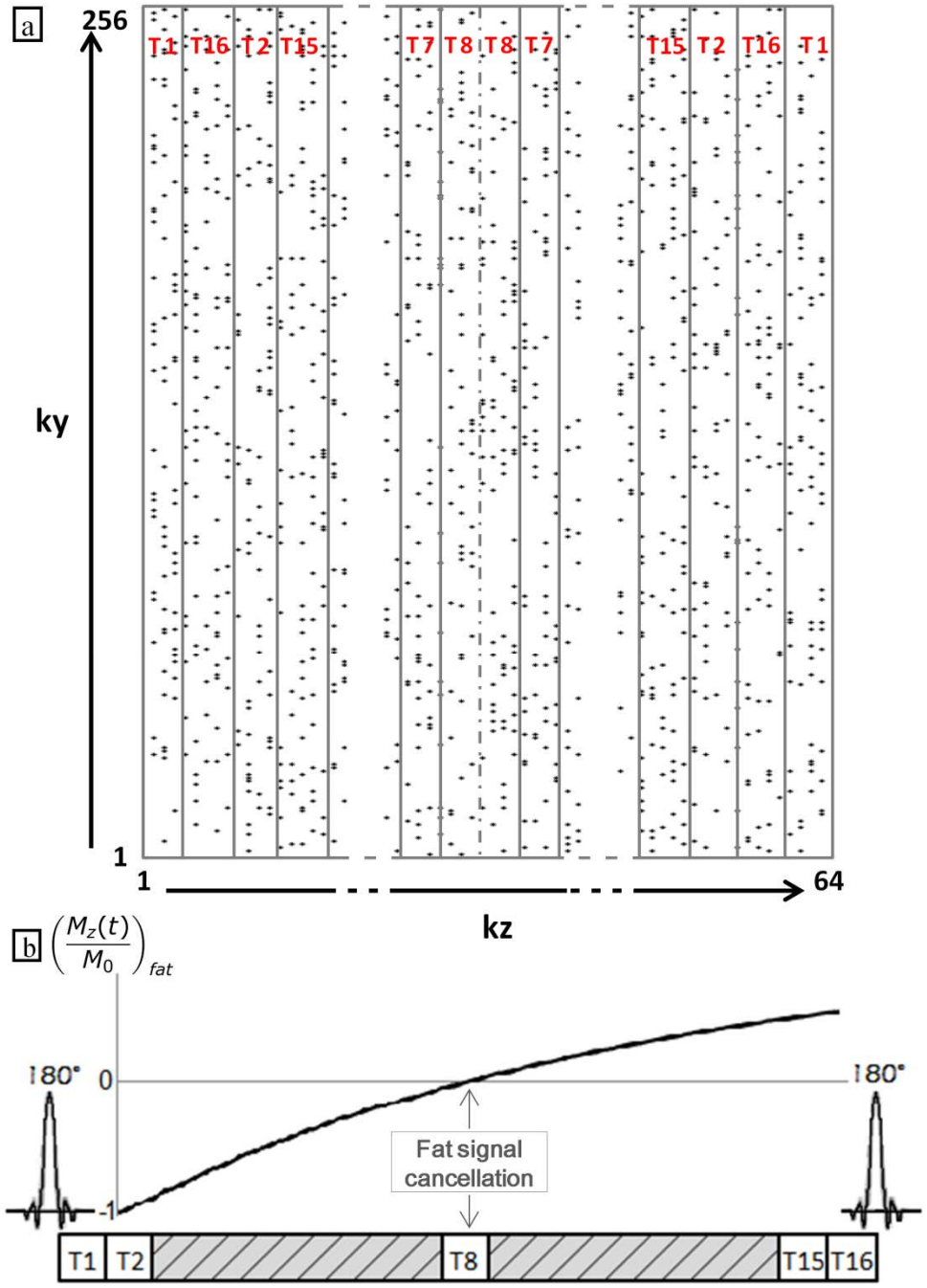

Figure 1: *Implementation of Cartesian random acquisition compatible with spectral fat suppression. a) Initial selection of a uniform random under-sampling for a frame of interest (256 phase lines and 64 slices) ; samples from this frame are split into 16 regions (segments) according to their distance to the most central kz line (i.e. kz=32 here). b) Sketch of the segmented acquisition: after a fat inversion pulse is played out, N=16 (ky,kz) lines are picked up from region T1 to T16, so that data in region T8 (most central k-space lines) are acquired when the fat signal is minimized (b)*

Note that the AF selected by the operator is the maximal possible acceleration that can be applied at the reconstruction stage. All divisors of AF can be used for the reconstruction as they also provide a uniform random splitting of the k-space. For instance, if the conventional sequence has a temporal resolution of 90 s and if the user selects AF=12 at the console, it is possible to reconstruct images with

acceleration rates of 12 (7.5 sec), 6 (15 sec), 4 (22.5 sec), 3 (30 sec), 2 (45 sec) and 1 (90 sec).

Assessment of fat suppression accuracy

Acquisitions were performed on a phantom made of bowls filled with water and commercial sunflower oil and on one healthy volunteer to assess the efficiency of fat suppression. Healthy volunteer acquisitions were approved by an ethical committee (ClinicalTrials.gov Identifier: NCT02887053). In both cases, the modified VIBRANT sequence was used with a fully random sampling in both phase and slice directions; or with the above-mentioned slice (k_z) reordering scheme. Images acquired with the proposed sampling were reconstructed without CS acceleration, i.e. using only conventional acceleration techniques (partial Fourier and 2-fold accelerated parallel imaging). Conventional reconstruction was applied using SENSE [41] for parallel imaging combined with homodyne reconstruction [42] for partial Fourier.

Impact of random sampling on morphology and quantitative DCE-MRI

A prospective pilot study was performed involving 12 patients who underwent MRI as part of their standard care pathway. The study was approved by the Research Ethics Board of our institution (ClinicalTrials.gov Identifier: NCT02826369) and all volunteers gave written informed consent. The imaging protocol was based on the conventional breast DCE MRI protocol used in clinical routine. Bolus injection of 0.1 mmol/kg bodyweight gadoterate meglumine (Dotarem, Guerbet) followed by a 20-mL saline flush was performed. In addition of the six successive conventional VIBRANT sequences performed during CA injection (one acquisition before injection and five after), three scans with our modified VIBRANT sequence were inserted: one before injection, one at 4.5 min (T_{middle}) after injection and one after the last clinical sequences (T_{final}) (see Figure 2). Image reconstruction from the modified VIBRANT sequence was performed using conventional acceleration only (SENSE and partial Fourier) as it is done for the clinical sequence.

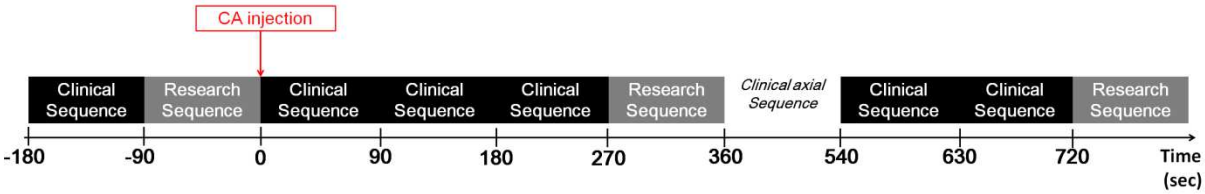

Figure 2: *Imaging protocol used for the pilot clinical study. The contrast uptake follow-up is done using Sagittal 3D FSPGR sequence. Our research sequences (gray colored on the scheme) are inserted inside the conventional clinical protocol before and after the Contrast Agent injection.*

For each patient, enhanced ROIs were tracked and manually delineated in each pre- and post-injection image. Numerous ROIs were picked up in several enhancing anatomical regions, including those used for clinical assessment (ganglions, benign or malignant lesions) and others for control (pectoral muscle, heart, mammary artery or veins). We chose control ROIs in order to characterize our research sequence with a

wide range of enhancement curves, both in terms of shape and intensity, distributed in the whole field of view covering both breasts. A total of 86 enhancing ROIs including 22 breast lesions were delineated by a radiologist. ROI sizes were highly variable, from 2.71 mm^2 (small lesions) to 735.06 mm^2 (muscle and heart ROIs), with an average of 157.54 mm^2 (all sizes are listed in Table 1). Enhancement rates were calculated from the clinical and research sequences using the following formula:

$$R(t)_{clinical/research} = \frac{S(t)_{clinical/research} - Sbaseline_{clinical/research}}{Sbaseline_{clinical/research}} * 100$$

First, we evaluated qualitatively the enhancement curves by visualizing both clinical and research data in the same graph to check the consistency of the results. Error bars on enhancement curves were calculated applying error propagation theory on enhancement rates: $\Delta R(t)=R(t)*\sqrt{\left(\frac{\Delta S(t)}{S(t)}\right)^2+\left(\frac{\Delta S_{baseline}}{S_{baseline}}\right)^2}$ which explains no error bars for null enhancement rates before CA injection**.** Secondly, to assess research data reliability, we interpolated the clinical enhancement rates at the time points (T_{middle} and T_{final}) when the research sequences were played out using a cubic fit. We used a Wilcoxon test for each class of anatomical regions and each time point to test whether the differences between clinical and research sequences were statistically significant.

Qualitative morphological evaluations were performed on each patient focusing on breast lesions and ganglions. As our research sequence allows reconstructing images without acceleration using all the data acquired for one image, these images can be used for the conventional diagnosis using BI-rads classification. For that purpose we also need to ensure that the pseudo-random sampling in our sequence does not impact morphologic analysis.

High temporal resolution compressed sensing reconstruction using a dynamic phantom acquisition

A dynamically enhanced breast lesion phantom was designed for this study inspired from Freed et al [43]. The dynamic phantom was time-controlled and was calibrated to reproduce a given injection pattern, so that the reconstructed contrast uptake curve can be compared to the ground truth injection command. Figure 3 shows the lesion phantom combined with the dedicated injecting system.

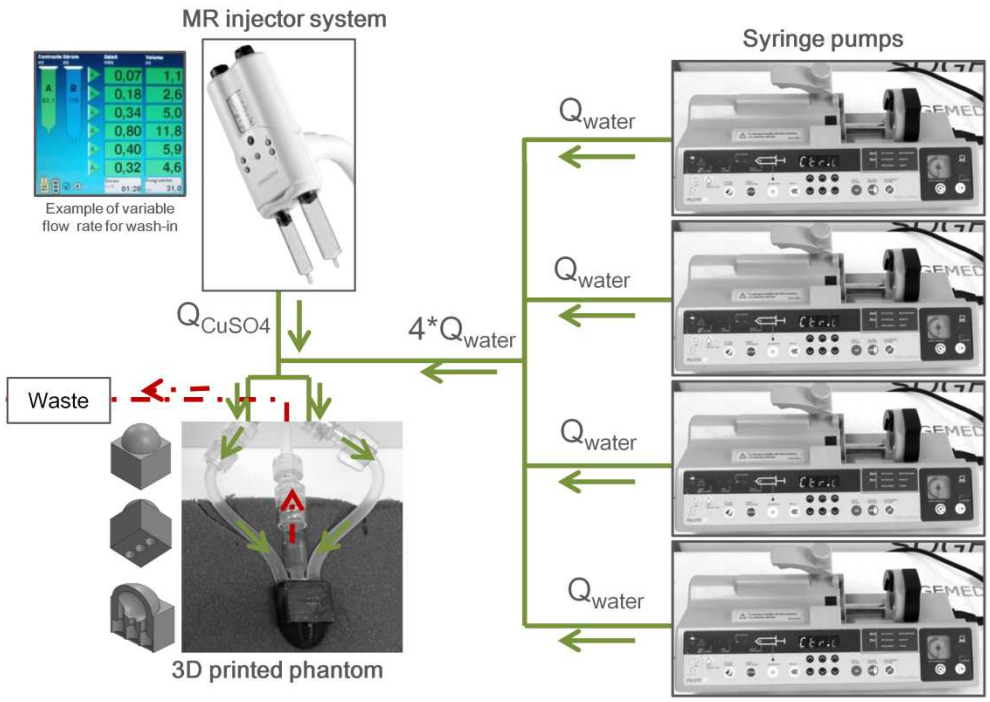

***Figure 3**: 3D printed phantom and its associated injecting system. Green and red arrows represent fluid circulation direction. The four syringe pumps are placed outside the MR room and deliver a constant water flow (358.7 mL/h). The MR injector system is placed near the scanner and delivers a variable flow rate of copper sulfate solution with 15 seconds of temporal resolution. Two inlets were used to inject the solution into the phantom to ensure more homogeneous distribution inside and one outlet was connected to a waste box*

The phantom consists in a 1 cm diameter printed sphere manufactured with a *Printrbot Simple Metal* printer (Printrbot Inc, Lincoln, USA). The phantom was connected through medical tubing to an injecting system made with a combination of an automated MR injector system (Spectris Solaris EP, MEDRAD UK Ltd) and four syringe-pumps placed outside the MRI scanner room. In order to mimic a contrast enhancement in the phantom, a variable concentration of $CuSO_4$ solution is injected into it. The four syringe-pumps are filled with distilled water which continuously inject during the acquisition with a constant flow rate of Q_{water}=358.7 mL/h. The automated MR injector allows the $CuSO_4$ flow rate (Q_{CuSO4}) to be varied during the acquisition and thus the $CuSO_4$ solution concentration to be varied according to the following equation: $C_{phantom} = C_{CuSO_4} \frac{Q_{CuSO_4}}{Q_{CuSO_4}+4*Q_{water}}$. The phantom filled with water is used as the pre-injection reference for contrast uptake curves plot. In a preliminary study, we calibrated our system by imaging several Copper sulfate solutions with fixed concentration with our modified sequence. The relation between enhancement rate and CuSO4 concentration was established. This allowed the right concentration to be injected into the phantom in order to achieve a desired enhancement. To model a malignant lesion acquired with high temporal resolution images, we chose rapid arbitrary enhancement rates based on a qualitative

analysis of a type III curve as described by Kuhl et al [10].

3D acquisitions with our modified VIBRANT sequence were performed on the dynamic breast lesion phantom for 6 minutes. One sequence of 90 seconds was performed before the Copper sulfate injection and three sequences were performed afterwards. Reconstruction using conventional acceleration only (SENSE and Partial Fourier) was tested (providing a temporal resolution of 90 seconds), as well as a CS accelerated reconstruction using an AF equal to 6, meaning the temporal resolution was 15 seconds.

For the CS accelerated reconstruction we used a Compressed Sensing algorithm coupled with a SENSE reconstruction presented in Ref.[44] which consists of minimizing the following cost function: $\hat{\rho} = \arg\min \|\boldsymbol{E}\rho - s\|_2^2 + \lambda\|\boldsymbol{S}\rho\|_1 + \alpha\|\boldsymbol{G_t}\rho\|_2^2$ with λ=1 and α=0.01. **S** is the transform operator from image domain to the chosen sparsity domain (temporal Fourier transform after subtraction of the baseline image) needed for compressed sensing reconstruction. **E** is the MR acquisition operator (Coil sensitivities multiplication followed by Fourier transformation and random undersampling), ρ the 3D+T phantom to be reconstructed and s the under-sampled acquired data. An additional constraint based on the temporal gradient of the image ($\mathbf{G_t}$) was added to impose temporal regularity in the uptake curves. This scheme was shown to provide better results in that study [44].

To evaluate the feasibility and the benefit of high temporal resolution acquisition, we compared the command of the injector (ground-truth) expressed in enhancement rate with enhancement rates from CS accelerated and conventional reconstructions.

RESULTS

Assessment of fat suppression accuracy

A comparison of the full data reconstruction with different k-space reordering strategies is shown in Figure 4. All images are windowed and leveled to highlight fat artifacts.

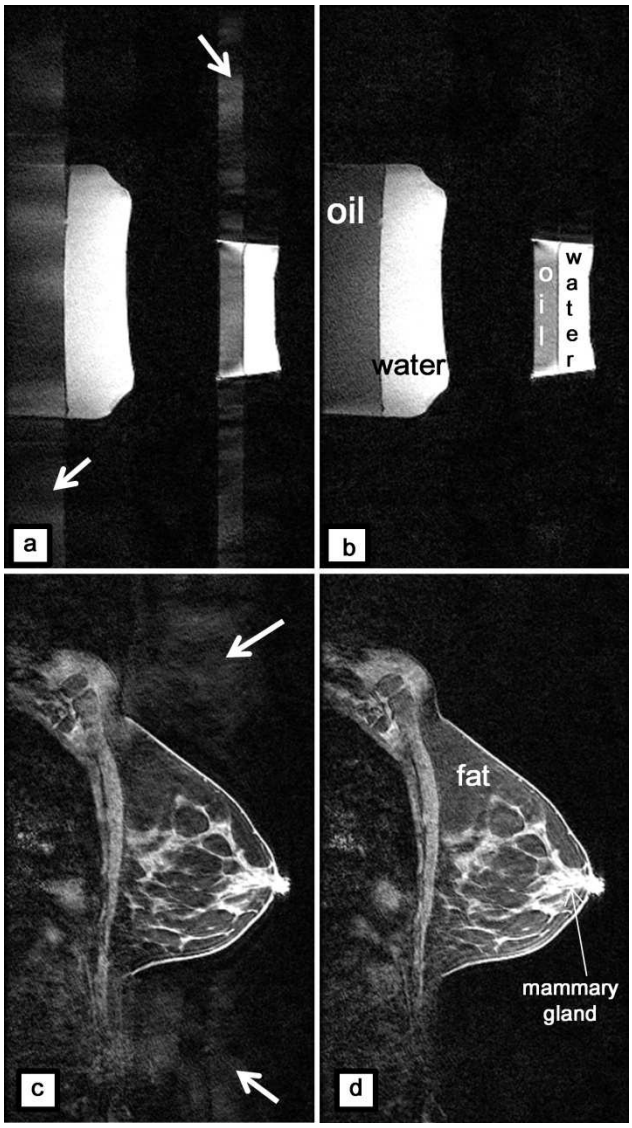

***Figure 4**: Effect of k-space reordering on fat suppression efficiency. The upper row images (a-b) show results for a water/oil phantom, while the bottom row images (c-d) show result for a female volunteer. The left column show images acquired without k-space reordering meaning a totally random acquisition in both phase and slice directions; while the right column shows images acquired with the slice reordering mentioned above. Arrows indicate fat artifacts in both phantom and volunteer acquisitions which are not present in the acquisition with the slice reordered research sequence*

The images in the top panel represent data acquired on the static phantom and those in the bottom are from the healthy female volunteer acquisition. In the left column, the results with a fully random (without the proposed slice reordering) acquisition in both ky and kz directions are presented. In both phantom and volunteer acquisitions, fat aliasing spreading into phase and slice directions can be observed when a naïve random sampling in both phase and slice directions is applied. Conversely, in the right column no fat artifacts can be seen when the proposed reordering in the slice direction (kz) is applied.

Impact of random sampling on morphology and quantitative DCE-MRI

Figure 5 shows four representative uptakes curves of our ROI database. Enhancement rates from the clinical VIBRANT sequence were plotted with black circles and the ones obtain with the modified VIBRANT sequence were plotted with gray triangles. Both points with 0% enhancement rates and negative time abscissa are images acquired before contrast agent injection and used as baseline for contrast uptake evaluation.

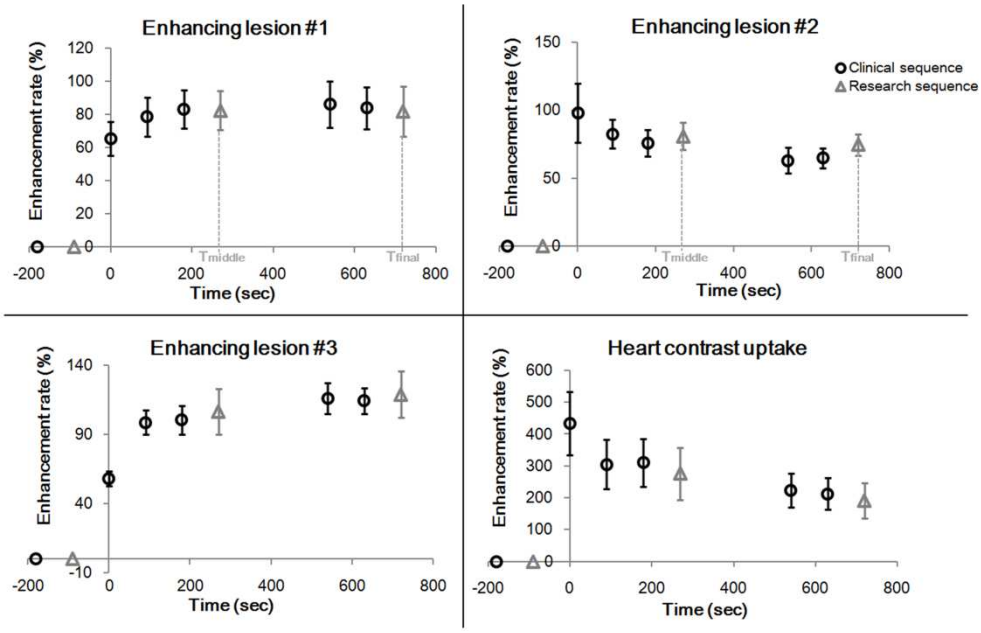

Figure 5: *Four contrast uptake curves acquired with both clinical (dark circles) and research sequences (gray triangle). A good agreement between enhancement rates obtained with the clinical sequence and those obtained with our research sequence can be observed.*

Enhancement rates obtained with the random VIBRANT sequence are visually consistent with those obtained with the standard sequence.

Table 1 summarizes the quantitative comparisons between clinical and research enhancement rates. No significant differences were observed between enhancement rates obtained with the conventional VIBRANT sequence and our modified VIBRANT sequence for ROIs drawn in heart, ganglions, mammary lesions and pectoral muscles (p-values ranging from 0.057 to 0.987) taking both acquisition times into account (T_{middle} and T_{final}). However significant differences can be observed for ROIs picked up in mammary vessels with p-values equal to 0.040 and 0.032 for T_{middle} and T_{final} respectively.

Table 1: *Quantitative evaluations of enhancement rates for each class of enhancing region and each research data acquisition time. A Wilcoxon test was used to determine p-value for each case*

			Tmiddle			Tfinal		
	Number	**Size (mm²)**	**Clinical enhancement**	**Research enhancement**	**p-value**	**Clinical enhancement**	**Research enhancement**	**p-value**
Ganglions	8	61.38 (±68.88)	123.85 (± 49.24)	128.92 (± 50.20)	0.313	91.85 (± 40.72)	91.31 (± 46.46)	0.742

Mammary lesions	22	8.49 (±4.84)	114.79 (± 44.39)	118.29 (± 43.81)	0.306	106.12 (± 44.06)	106.15 (± 43.92)	0.987
Mammary vessels	24	71.13 (±72.60)	191.81 (± 38.33)	201.35 (± 36.41)	**0.040 ***	159.27 (± 37.33)	167.74 (± 30.44)	**0.032 ***
Heart	12	434.34 (±159.25)	215.27 (± 36.85)	215.44 (± 41.13)	0.791	170.21 (± 22.93)	170.62 (± 24.71)	0.910
Pectoral muscle	20	293.68 (±175.17)	41.22 (±15.45)	45.20 (± 12.30)	*0.057*	38.21 (± 15.19)	37.06 (± 13.79)	0.478

Figure 6 shows examples on one breast lesion and one ganglion both acquired with clinical and unaccelerated research sequences.

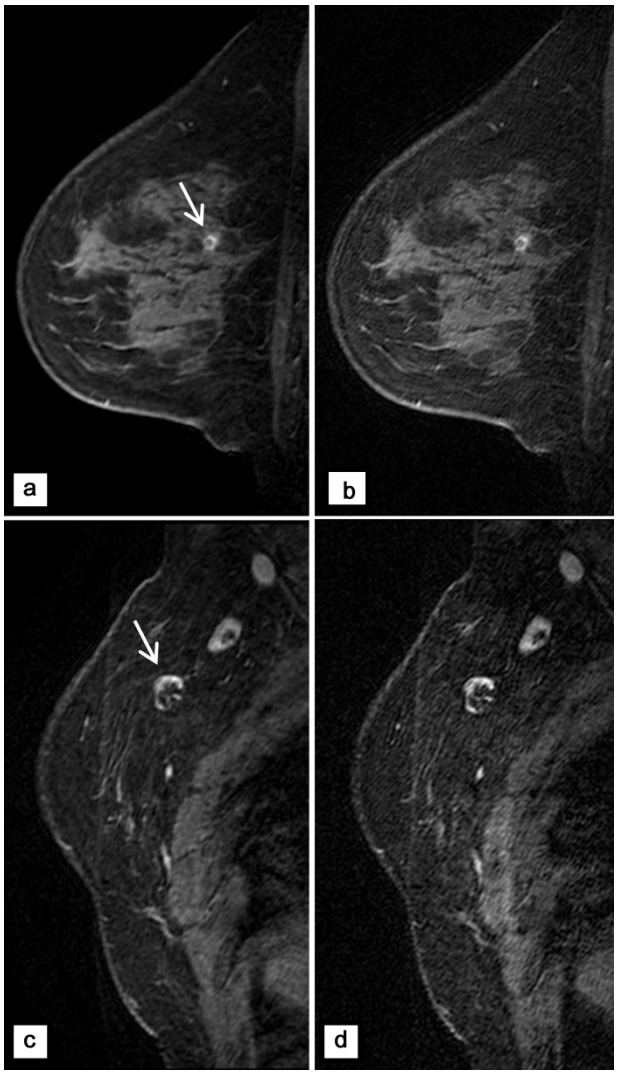

Figure 6: *Effect of pseudo-random sampling on breast lesion and ganglion morphology. The upper row images (a-b) show acquisition on a breast lesion, while the bottom row images (c-d) show acquisition on a ganglion. No morphological differences can be observed between clinical (left column) and research (righ column) sequence*

The images on the left are acquisitions with the clinical sequence and those on the right with our research sequence. The breast lesion and the ganglion are respectively in the top and the bottom panel. Morphology seemed to be well preserved in the research

sequence. All lesions annotated on the clinical sequences were able to be identified easily in the research sequences and no alteration of the morphology was observed.

High temporal resolution compressed sensing reconstruction using a dynamic phantom acquisition

Our modified VIBRANT sequence combined with the adequate compressed sensing reconstruction allows the visualization of contrast uptake with 15s temporal resolution (Figure 7-a)). No undersampling artifacts have been noticed on the images. In Figure 7-b) we plotted the enhancement rates on the lesion phantom obtained with the accelerated reconstruction (dark gray triangles) and the conventional reconstruction (light gray crosses). Theoretical enhancements (black circles) calculated from calibration curves and the command of the injector are also displayed on the graph.

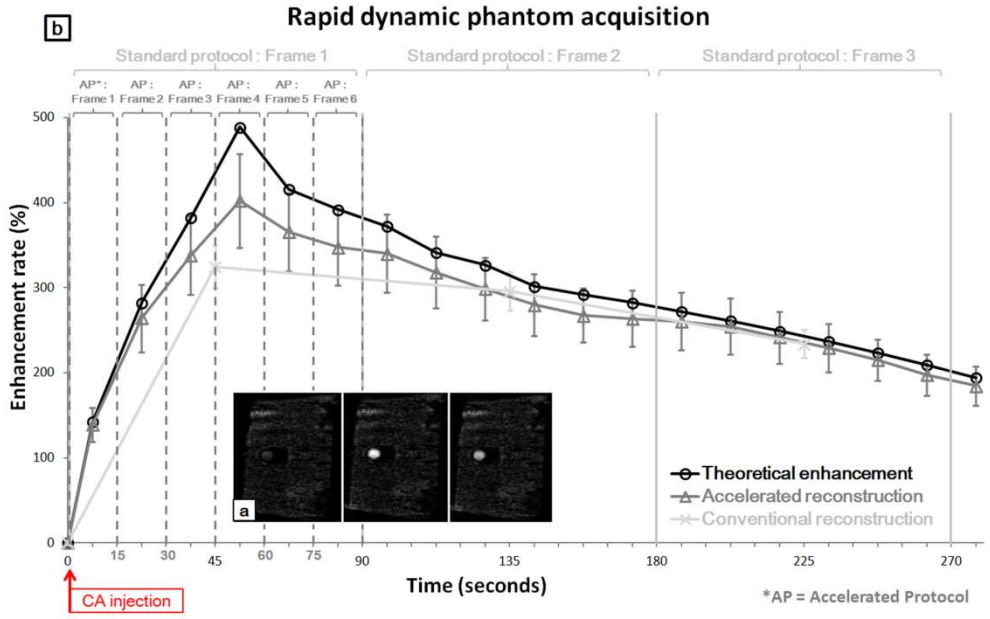

Figure 7: *Data acquired on a dynamic breast lesion phantom with the modified VIBRANT sequence. a) Image reconstructions with a compressed-sensing based algorithm – Contrast uptake visual follow-up on one slice centered in the phantom b) Contrast uptake curves – error bars represent the standard deviation in the enhancement ROI. Temporal resolutions were respectively 90 sec and 15 sec for conventional and accelerated reconstructions*

Table 2 summarizes semi-quantitative analysis commonly used in clinical routine for helping diagnosis such as maximum enhancement rate, Time To Peak (TTP), Wash-in and Wash-out. We defined Wash-in as the slope of enhancement curve between the pre-injection image and the first post-injection image. Wash-out was defined as the slope right after reaching the maximum enhancement rate i.e. the slope measured between the image with the maximum enhancement rate and the following one.

Table 2: *Semi-quantitative analysis on contrast-uptake curves – comparison between theoretical, accelerated and conventional reconstructions enhancements*

	Temporal	Maximum	Time To Peak (sec)	Wash-in (%/sec)	Wash-out (%/sec)

	resolution (sec)	enhancement rate (%)			
Theoretical enhancement	15	488.43	52.5	18.98	- 4.88
Accelerated reconstruction	15	402.18 (± 55.03)	52.5 (± 7.5)	18.51	-2.45
Conventional reconstruction	90	324.27 (± 24.75)	45 (± 45)	7.21	-0.69

The predicted maximum enhancement rate was 488.43% and those obtained respectively with accelerated and conventional reconstruction were 402.18% and 324.27%. The underestimation of the maximum enhancement rate reached 17.7% for accelerated reconstruction and 33.6% for conventional reconstruction. This maximum enhancement rate occurred at TTP = 52.5 ± 7.5 second for accelerated reconstruction and at TTP= 45± 45 seconds for conventional reconstruction while theoretical Time To Peak was 52.5 seconds. The predicted wash-in (18.98 %/sec) is almost reached in the accelerated reconstruction (18.51 %/sec i.e. 2.5% of error) whereas it is half-reduced in the conventional reconstruction (7.21 %/sec i.e. 62% of error). With regards to wash-out, the predicted value of -4.88 %/sec is underestimated by both reconstructions: -2.46 %/sec for accelerated reconstruction (error: 49.6%) and -0.69 % for conventional reconstruction (error: 85.9%).

DISCUSSION

This study has shown the feasibility of acquiring randomized Cartesian data in a way compatible with a spectral fat suppression. The proposed sampling scheme for random Fourier domain subsampling allows a good fat suppression. For a segmented sequence, if a spectral fat suppression is used, the k-space phase and slice lines cannot be acquired in a naïve and fully random way. We have shown in a phantom and in a volunteer that a naïve random sampling of k-space induces severe fat artifacts. Our k-space trajectory design with reordering in the slice direction makes randomized Cartesian k-space acquisition techniques compatible with spectral fat suppression. We chose that fat suppression technique because this technique provides a good compromise between rapidity and fat suppression efficiency.

With the proposed sequence, random acquisition of the k-space does not impact the contrast of enhancing anatomical regions including breast lesions. Most of the contrast uptakes were found to be consistent between the clinical sequence acquired with linear view ordering and our modified VIBRANT sequence. The inconsistent contrast uptakes mostly came from regions of interest drawn into pectoral muscle which is a highly heterogeneous region (made of vessels, different muscle components etc.) or from mammary vessels. Indeed, it was often difficult to track small and tortuous structures like vessels with millimetric thickness and which were very difficult to visualize on images before injection. Moreover all of the 12 patients of the study moved during and between each VIBRANT sequence acquisition leading to kinetic blurring, structure deformation and slice change (certain lesions moved from one slice to another between acquisitions). We decided not to apply 3D non rigid registration (we manually tracked ROIs instead) because it might impact the image signal intensity and we wanted to evaluate the performance of our modified VIBRANT

sequence only. In addition to the variability due to manual segmentation, the differences between enhancement rates obtained with the clinical and our modified VIBRANT sequence can also be explained by slight differences between our reconstruction pipeline and the vendor's one (proprietary implementation of regularization, coil weighting, post-reconstruction filters etc…). Random acquisition of the k-space also does not impact lesion and ganglion morphologies which are key radiofindings for the diagnosis.

The proposed protocol allows a flexible use of the acquired data at the reconstruction stage. On the one hand, we can choose to reconstruct the images from the non-CS-accelerated k-space data, as the sequence described in clinical guidelines for DCE-MRI of breast. This reconstruction should be used to perform BI-rads classification as usual and obtain the minimal information for diagnosis. On the other hand, a high-temporal resolution dataset can be reconstructed using Compressed Sensing after a simple splitting of the k-space into a chosen number of frames (chosen before starting the sequence). This accelerated reconstruction should be used for tracer kinetic modeling to improve the diagnosis specificity.

The dynamic phantom experiments showed the benefit of reconstructing data with a higher temporal resolution (Acceleration Factor = 6 for this study). Kuhl et al [11] formalized the questions a radiologist needs to answer to diagnose breast cancer : "**How strongly does the lesion enhance?**", "**How fast does the lesion enhance**?", "**When does the lesion start to enhance?**" and "**What happens after the initial signal increase?**". Answers provided by the radiologist are directly correlated with their interpretations of Maximum enhancement rate, Wash-in and Wash-out. The conventional sequence recommended by international guidelines cannot provide accurate measurements for these values as it has been shown for the dynamic breast lesion which mimicked a typical physiological enhancement profile for a type III lesion. Early contrast uptake can be missed with the conventional reconstruction with a 90 sec temporally resolved acquisition and the curve obtained with it could be misclassified as a type II whereas for the accelerated reconstruction, a type III curve seems to be more suitable. Although both reconstructions underestimate the maximum enhancement rate, the 17.6% underestimation for accelerated reconstruction is accountable to the compressed sensing based algorithm reconstruction as it has been shown in [44]. This also applies for the underestimation of wash-out for accelerated reconstruction because it is directly linked to the maximum enhancement rate underestimation. Improvements concerning this compressed sensing reconstruction will be the scope for future work. Possible improvements include in particular adapting the weight of the temporal regularization term (α). Alternative constraints such as low rank models [45] may also be investigated.

We chose to develop a random Cartesian acquisition because it was based on the 3D fat-suppressed T1-weighted Fast Gradient Echo sequence described in International guidelines for breast MRI. Radial or stack-of-stars sequences which have been used in some studies to perform accelerated breast MRI are also of interest. When combined with fat suppression, they will also need to use a segmented acquisition scheme and

therefore will also be sensitive to fat artifacts. Therefore a reordering strategy such as the one we have proposed should be implemented. Since compressed-sensing reconstruction techniques have the property to remove incoherent aliasing in images, such fat artifacts (which also look like incoherent artifacts) could remain unnoticed when working with under-sampled images only, however they might introduce a bias in the quantitative DCE-MRI analysis. One advantage of the proposed Cartesian sequence is that the flexible reconstruction can provide from the same acquired data both the standard clinical images and accelerated images. This sequence can be implemented on basic scanners and does not replace the reference sequence that radiologists use to diagnose breast cancer.

A limitation of the study is that we did not apply the proposed sequence during the entire time course of the injection for the 12 patients. This would have allowed the accelerated CS reconstruction to be performed in the patients as well. The interleaved protocol shown in Fig. 2 was chosen for the submission to the ethical committee because this preliminary step was necessary in order to demonstrate that the proposed sequence would not impact the clinical diagnosis for the patient. This is why the clinical sequence was used immediately after Gadolinium injection which is the most important for diagnosis. In future work the proposed sequence will be used during the entire course of injection, so that images with both high spatial resolution (1x1x2.2 mm^3) and high temporal resolution (at least 15 seconds per frame) can be reconstructed using a CS based algorithm like the one mentioned earlier. Quantitative analysis on injected images could then be applied using tracer modeling. We could extract, from the high temporal resolved uptakes curves, quantitative parameters which reflect lesions pathophysiology (tissue perfusion, capillary permeability, interstitial and plasma volume fraction) to obtain a more accurate diagnosis of the lesions. Moreover, in the cases where non-rigid or rigid motions occur during the follow-up of the injection, motion compensated reconstruction can be integrated into the CS algorithm [46–48].

CONCLUSION

This pilot study has proven the feasibility of developing a randomized Cartesian sequence compatible with (i) the basic hardware available in most MRI scanners, (ii) the widely used spectral fat suppression and (iii) allowing high temporal resolution, compressed sensing based reconstruction. The proposed k-space sampling scheme allows both non-CS accelerated and CS-accelerated images to be reconstructed. The non-CS accelerated images showed good agreement with the conventional clinical sequence in terms of quantitative contrast uptake rates, while the 6-fold CS accelerated reconstruction has shown the potential to recover semi-quantitative parameters such as time-to-peak, maximum peak enhancement rate, wash-in and wash-out with improved accuracy and precision.

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Article 2: Abbreviated breast magnetic resonance protocol: Value of high-resolution temporal dynamic sequence to improve lesion characterization.

L'objectif de cette étude est d'évaluer la valeur ajoutée de la séquence ULTRAFAST (TRICKS®) à un protocole abrégé (FAST) par rapport au protocole standard (FULL) pour distinguer les lésions bénignes des lésions malignes mammaires.

Il s'agit d'une étude rétrospective sur un total de 70 patientes présentant 106 lésions histologiquement prouvées (58 malignes et 48 bénignes) et ayant bénéficié d'une imagerie par résonance magnétique mammaire. Deux lecteurs ont évalué les examens des différents protocoles (ULTRAFAST, FAST et FULL). La sensibilité, la spécificité, les valeurs prédictives positives et négatives et l'éfficacité diagnostique ont été calculées pour chaque protocole et comparées avec un test de McNemar.

Pour tous les lecteurs, le protocole FAST-ULTRAFAST combiné a considérablement amélioré la lecture avec une spécificité améliorée par rapport au protocole FAST et FULL sans modification de la sensibilité. En ajoutant le protocole ULTRAFAST au protocole FAST, les lecteurs 1 et 2 ont réussi à modifier correctement le diagnostic dans 22,9% (11/48) et 10,4% (5/48) de lésions bénignes, sans faux négatif supplémentaire. L'interprétation et les temps d'acquisition d'image pour le protocole combiné FAST-ULTRAFAST et le protocole FAST ont été plus courts en comparaison au protocole FULL ($p < 0,001$).

Comparativement au protocole FULL, l'ajout des séquences ULTRAFAST au protocole FAST améliore la spécificité, principalement en reclassifiant correctement les masses bénignes et réduit les temps d'interprétation et d'acquisition, sans diminuer la sensibilité.

Abbreviated breast magnetic resonance protocol: Value of high-resolution temporal dynamic sequence to improve lesion characterization

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Article accepté dans *European Journal of Radiology*

ABSTRACT

Purpose: To evaluate the added value of ULTRAFAST-MR sequence to an abbreviated FAST protocol in comparison with FULL protocol to distinguish benign from malignant lesions in a population of women, regardless of breast MR imaging indication.

Materials and Methods: From March 10th to September 22th, 2014, we retrospectively included a total of 70 consecutive patients with 106 histologically proven lesions (58 malignant and 48 benign) who underwent breast MR imaging for preoperative breast staging (n=38), high-risk screening (n=7), problem solving (n=18), and nipple discharge (n=4) with 12 time resolved imaging of contrast kinetics (TRICKS) acquisitions during contrast inflow interleaved in a regular high-resolution dynamic MRI protocol (FULL protocol). Two readers scored MR exams as either positive or negative and described significant lesions according to Bi-RADS lexicon with ~~a~~ TRICKS images (ULTRAFAST), an abbreviated protocol (FAST) and all images (FULL protocol). Sensitivity, specificity, positive and negative predictive values, and accuracy were calculated for each protocol and compared with McNemar's test.

Results: For all readers, the combined FAST–ULTRAFAST protocol significantly improved the reading with a specificity of 83.3% and 70.8% in comparison with FAST protocol or FULL protocol, respectively, without change in sensitivity. By adding ULTRAFAST protocol to FAST protocol, readers 1 and 2 were able to correctly change the diagnosis in 22.9% (11/48) and 10.4% (5/48) of benign lesions, without missing any malignancy, respectively. Both interpretation and image acquisition times for combined FAST-ULTRAFAST protocol and FAST protocol were shorter compared to FULL protocol ($p<0.001$).

Conclusion: Compared to FULL protocol, adding ULTRAFAST to FAST protocol improves specificity, mainly in correctly reclassifying benign masses and reducing interpretation and acquisition time, without decreasing sensitivity.

Keywords: MRI, Breast, Tricks, Abbreviated protocol, Diagnosis

INTRODUCTION

Breast magnetic resonance imaging (MRI) is the most sensitive imaging method to detect breast cancer available at this time, and it is superior to both mammography and ultrasonography[1–3]. Thus, breast MRI indications have increased during the last decade, including screening of high risk women, problem solving, pre-operative staging, implant integrity evaluation and nipple discharge.[4, 5]. However, breast MRI presents high direct and indirect costs which limits its wider use. This is primarily because current breast MRI protocols are time-consuming to acquire and interpret, with acquisition times of 20

to 25 minutes [4] following the recommendations of good practice of the European Society of Breast Imaging (EUSOBI) [6]. Furthermore, in the current conditions, for many European countries, the number of MR scanners is insufficient to absorb the increasing indications of breast MRI, including the yearly screening of an increasing number of women at high risk for breast or ovarian cancer.

Kuhl et al. first showed the use of an abbreviated protocol (FAST protocol) as a valid alternative protocol for MR imaging, without compromising sensitivity nor specificity, in a population of women undergoing screening[7]. The use of an abbreviated protocol allows for not only shortened examination time but also faster interpretation for the radiologist[7, 8]. Thus, several authors published on this popular topic and confirmed the ability of an abbreviated MR protocol to detect breast cancer in populations of high risk screening as well as in women with proven breast cancers[8–11]. However, the main limitation of an abbreviated protocol is its lack of specificity due to the absence of dynamic enhancement criteria, which is especially useful for the classification of small mass-like lesions[12–15]. In this regard, Mann et al. suggested the use of high temporal resolution sequences using TWIST sequence (ULTRAFAST protocol) that would help characterize breast lesions by fitting a time intensity curve obtained during the first minute[16].

Thus, our purpose was to evaluate the added value of ULTRAFAST MR sequence to an abbreviated FAST protocol in comparison with FULL protocol to distinguish benign from malignant lesions in a population of women, regardless of breast MR imaging indication.

MATERIAL AND METHODS

Institutional ethic committee approved the study and granted a waiver of informed consent.

Population

Between March 10th and September 22th, 2014, our MR imaging database was retrospectively queried to identify women who had undergone breast MR with high temporal resolution sequences (n = 166). Women with normal examinations (ACR BI-RADS 1 or 2) were excluded (n=79). We also excluded women treated with neoadjuvant chemotherapy (n=3), lesions without pathological analysis (n=13), and those with technical problems related to Picture Archiving Computer System (PACS) (n=1). The final cohort consisted of 70 women (mean 53 years, range 24 to 77 years), including 38 menopausal women (54.3%) and 32 premenopausal women (45.7%).

Indications for MRI were preoperative breast cancer staging (n=38; 54.2%), high-risk screening (n=7; 10%), problem-solving, such as radiological discordance between mammography and ultrasonography or radiopathological discordance (n=18;25.7%), nipple discharge (n=4;5.4%). Overall, 7 women had a personal history of breast cancer (10%), 5 women were high risk women with proven genetic susceptibility (7%), and 27 women had a family history of breast cancer without context of high risk (38.6%). Finally, 5 women underwent surgery for benign lesions (7.1%).

MR Acquisition

MRI sequences were acquired on a 1.5 T GE MR scanner using a phased array dedicated 8-channel breast coil. Patients were imaged in the prone position. Dedicated breast coils covering both breasts were used. We interleaved 12 time resolved imaging of contrast kinetics (TRICKS) acquisitions (TR=3.5, TE=min, Matrix=256x192, FOV 35, Slice thickness=2) during contrast inflow in a regular high-resolution dynamic MRI protocol between axial T1 weighted acquisition before injection and axial

dynamic contrast-enhanced T1-weighted fat-saturated gradient-echo sequences (Figure 1).

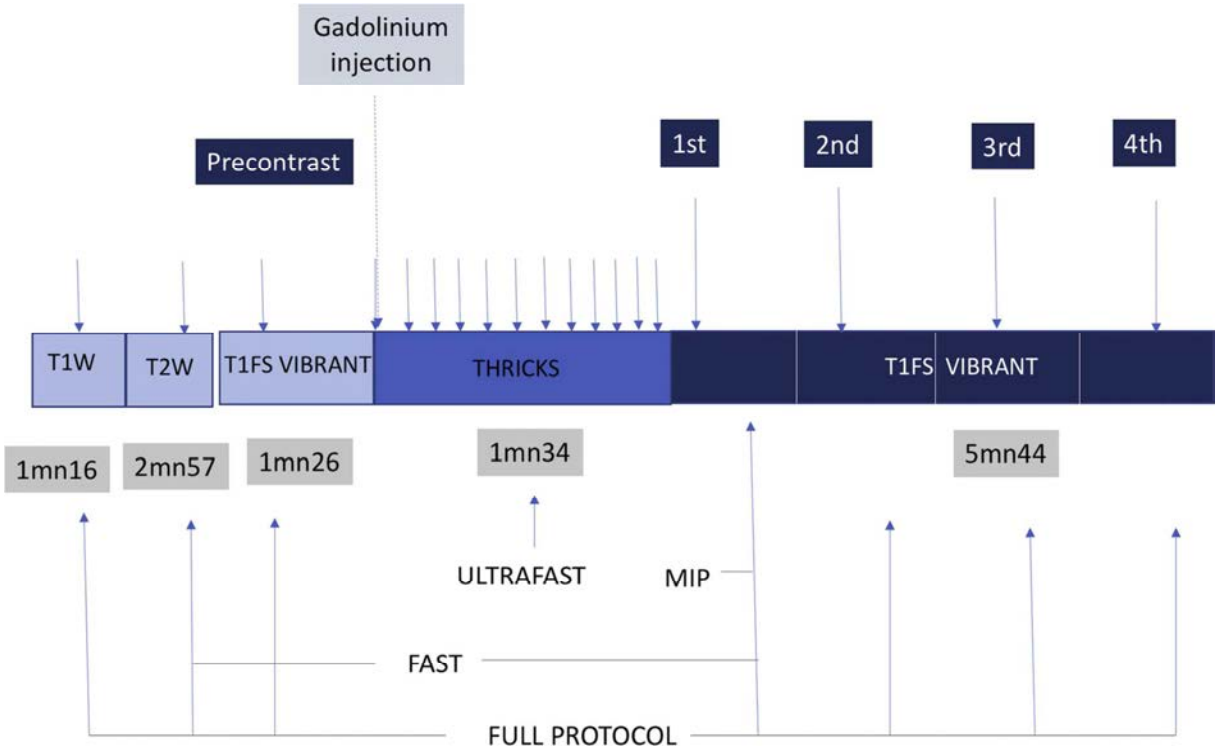

Figure 1: MR protocol.

The acquisition time for a single TRICKS acquisition was 7.8 seconds. TRICKS is a dynamic contrast-enhanced 3D FGRE technique with segmentation of 3D k-space in 4 concentric regions. The central region is fully sampled at each phase and provides angiographic temporal information. The three peripheral regions are under sampled (sampled only once every three phases) and provide spatial resolution. In each phase, the closest neighbor was used for reconstruction. The regular protocol included an axial T2-weighted acquisition (TR=9789, TE=102, Matrix=416x320, FOV 35, Slice thickness=2, Nex=1), an axial T1-weighted acquisition (TR=6.5, TE=3.1, Matrix=380x360, FOV 35, Slice thickness=2), axial dynamic contrast-enhanced T1-weighted fat-saturated gradient-echo sequences (VIBRANT), and acquisitions before and after injection of gadolinium (TR=6.5, TE=4, Matrix=368x360, FOV 35, Slice thickness=2). Vibrant sequences were acquired once before and four times after bolus injection of Gadolinium chelate (Dotarem; GuerbetFrance) (0.1 mmol.kg–1 body weight), given via a power injector (Medrad, Maastricht, The Netherlands) at a rate of 2 ml.s–1, followed by 20 ml saline flush. Post-processing consisted of subtracted images from the dynamic sequence and Maximum Intensity Projection (MIP) reconstructions. All MR images were reviewed on a Picture Archiving and Communication System (PACS) workstation (Carestream).

MR Data Analysis

Two radiologists, with 5 and 6 years of experience in breast MR imaging, respectively, independently reviewed MR images in five sessions, separated by at least two weeks in order to limit a memory bias. The readers were blinded to any clinical or prior imaging information. Moreover, the reading of a protocol was blinded to that of the other protocols in order to limit recall bias. All lesions were identified by their size and position to ensure that they were the same between the five readings. The details of each reading protocol are presented below:

In the first session, the MIP protocol (consisting only of the fusion of subtracted images of the first post contrast VIBRANT acquisition) was evaluated. The readers simply categorized the MR exam as either positive or negative on the basis of the detection of any significant enhancement.

In the second session, the FAST protocol (consisting of the native images of the first post contrast VIBRANT acquisition and the corresponding subtracted images and T2W) was analyzed. Breast density and background glandular enhancement were assessed according to the BI-RADS lexicon [17]. Then, the readers classified each enhancing lesion into one of 6 categories: BIRADS 1or2, BIRADS 3, BIRADS 4A, BIRADS 4B, BIRADS 4C, and BI-RADS 5. Readers excluded time intensity curve criteria as follows: Non-enhanced masses were rated BI-RADS 2. Enhanced masses with smooth margins, round or oval shape, and homogeneous enhancement were classified as BI-RADS 3 in the absence of available time intensity curve. Other masses were classified BI-RADS 4 or 5 according morphological criteria. For non-masses and foci, as the time intensity curve has no impact on BI-RADS classification, the same criteria as the FULL protocol were used.

In the third session, the ULTRAFAST protocol (consisting of MIP TRICKS and native TRICKS images) was analyzed. The readers were asked to identify any enhancement and the presence of afferent vessels and to report the presence of artifacts that limit interpretation and to classify each MRI exam as positive of negative on the basis of the detection of any significant enhancement on MIP TRICKS and native TRICKS images

In the fourth session, a combined abbreviated protocol consisting of the addition of FAST and ULTRAFAST protocol was analyzed. The following algorithm was applied to combine the reading of first subtracted and native VIBRANT images (FAST protocol) with native TRICKS images (ULTRAFAST protocol). If no lesion was visible on the first subtracted and native VIBRANT images, readers concluded there was no lesion. If a lesion was visible on the first VIBRANT images but not visible on the TRICKS images, readers considered there was no lesion except if the lesion was in the upper outer quadrant (frequent artifacts). In all other cases, lesions were rated according to the classification given on the FAST protocol.

In the fifth and last session, readers read the FULL protocol (T2W, T1W, DCE MR sequence). Breast density and background glandular enhancement were assessed according to BI-RADS lexicon [17]. Then, the readers classified each visible lesion according to BI-RADS MR lexicon into the 6 categories as detailed above.

The order of sessions was random to limit the recall bias.

Finally, the time duration of the reading sessions (FULL protocol, FAST protocol, combined FAST-ULTRAFAST protocol) was measured, beginning when reader opened the folder to analyze the

images and finishing when a BI-RADS conclusion was given. Acquisition times were also noted and included only the time for imaging acquisition, excluding patient installation.

Reference Standard

Pathological analysis was available in 106 lesions either due to detection on prospective MR analysis (n=100) or to supplementary lesions detected on histology of mastectomy (n=6). The diagnoses were established by percutaneous biopsy (50/106) (47.1 %) or by surgical pathology (56/106) (52.9%). Histopathological findings included 48 benign lesions (45.3%) and 58 (54.7%) malignant tumors. Malignancies consisted in 8 (13.8%) ductal carcinoma in situ (DCIS), 4 (6.9%) invasive ductal carcinoma with DCIS, 26 (44.9%) pure invasive ductal carcinoma (IDC), 16 (27.6%) invasive lobular carcinoma (ILC), 1 (1.7%) angiosarcoma, 1 (1.7%) Paget's disease, 1 (1.7%) metastasis of ovarian cancer, and 1 (1.7%) intraparenchymal metastatic adenopathy.

Statistical analysis

Size was assessed by maximal diameter and was described by mean and standard deviations, while qualitative parameters were described by number of events and percentage. Comparison of the time duration of the reading sessions and acquisition time for the three reading protocols was performed with a Mann-Whitney test. A receiver operating characteristic (ROC) curve analysis was performed to compare the results of interpretations based on full diagnostic protocol versus FAST protocol and combined FAST-ULTRAFAST protocol. The discriminant power of the BI-RADS classification to detect a cancer was assessed with the Area Under the Curve (AUC) for each protocol. The AUC of different protocols were then compared using a non-parametric approach. For statistical analysis, we consider an MRI to be positive if ACR BI-RADS was equal to or greater than 4. The values of sensitivity and specificity of different protocols were compared by a McNemar test. The diagnostic accuracy was expressed as a proportion of correctly classified subjects (TP+TN) among all subjects (TP+TN+FP+FN).

The inter-reader reliability and the reliability between the different reading protocols were assessed using the intra-class correlation coefficient (ICC). Based on the terminology proposed by Landis and Koch[18], an ICC value from 0.6 to 0.8 indicated substantial agreement, and from 0.8 to 1.0 almost full agreement.

A p-value of less than 0.05 was considered to indicate a statistically significant difference. Statistical analyses were performed using the following MedCalc software (www.medcalc.be, Belgium).

RESULTS

General MR findings

Breast density was higher in women with benign lesions that in women with malignant lesions (p=0.03 for R1 and p=0.01 for R2) (Table 1).

Table 1: MR characteristics of breast parenchyma

	Reader 1	**Reader 2**
Breast density		
Type A	8.6% (6)	8.6% (6)
Type B	47.1% (33)	40.0% (28)
Type C	24.3% (17)	38.6% (27)

Type D	20% (14)	12.9% (9)
Background glandular enhancement		
Type 1	51.4% (36)	45.7% (32)
Type 2	28.6% (20)	34.3% (24)
Type 3	14.3% (10)	12.9% (9)
Type 4	5.7% (4)	5.7% (4)

This is probably due to a significant difference in the age of patients between the women with benign (average 48 years old, range 33-77, n=27) and malignant tumors (average 57 years old, range 24-76, n=43) (p=0.006). No significant difference in background glandular enhancement was found between women with benign lesions and those with malignant lesions.

The size, type, and morphologic features of lesions are summarized in Table 2.

Table 2: MR descriptive analysis

	Reader 1		**Reader 2**	
Histology	Benign (n=48)	Malignant (n=58)	Benign (n=48)	Malignant (n=58)
Size (mm)	8.1 [3-25]	20.8 [3-80]	10.8 [3-100]	25.9 [5-100]
Type of lesion				
Mass	52.1% (25)	75.9% (44)	62.5% (30)	74.2% (43)
NML	10.3% (5)	15.6% (9)	10.3% (5)	17.3% (10)
Focus	18.8% (9)	5.1% (3)	8.4% (4)	3.4% (2)
No lesion	18.8% (9)	3.4% (2)	18.8% (9)	5.1% (3)
Shape (mass)				
Round or oval	22	22	25	11
Others	3	19	5	32
Margin (mass)				
Smooth	68% (17)	6.8% (3)	73.3% (22)	2.3% (1)
Non-Smooth	32% (8)	93.2% (41)	26.7% (8)	97.7% (42)
Internal enhancement (mass)				
Homogeneous	32% (8)	25% (11)	76.7% (23)	11.6% (5)
Heterogeneous	56% (14)	63.6% (28)	23.3% (7)	60.5% (26)
Rim	12% (3)	11.4% (5)	-	27.9% (12)
Afferent vessels (on TRICKS)	2%(1)	25.9% (15)	-	18.9%(11)

NML: Non-mass lesion.

Malignant tumors appeared more frequently as a mass than a non-mass lesion (75.9% for R1 and 74.2% for R2). Poorly-circumscribed margin and irregular shape were significantly associated with malignancy for both readers ($p<0.05$). The presence of afferent vessels on TRICKS sequence was correlated with malignancy for both readers (p=0.03) (OR = 26.3). Afferent vessels were present in 16 women and 11 women, according to readers 1 and 2, with a malignancy rate of 93.7% (15/16) for R1 and 100% (11/11) for R2 (Figure 2).

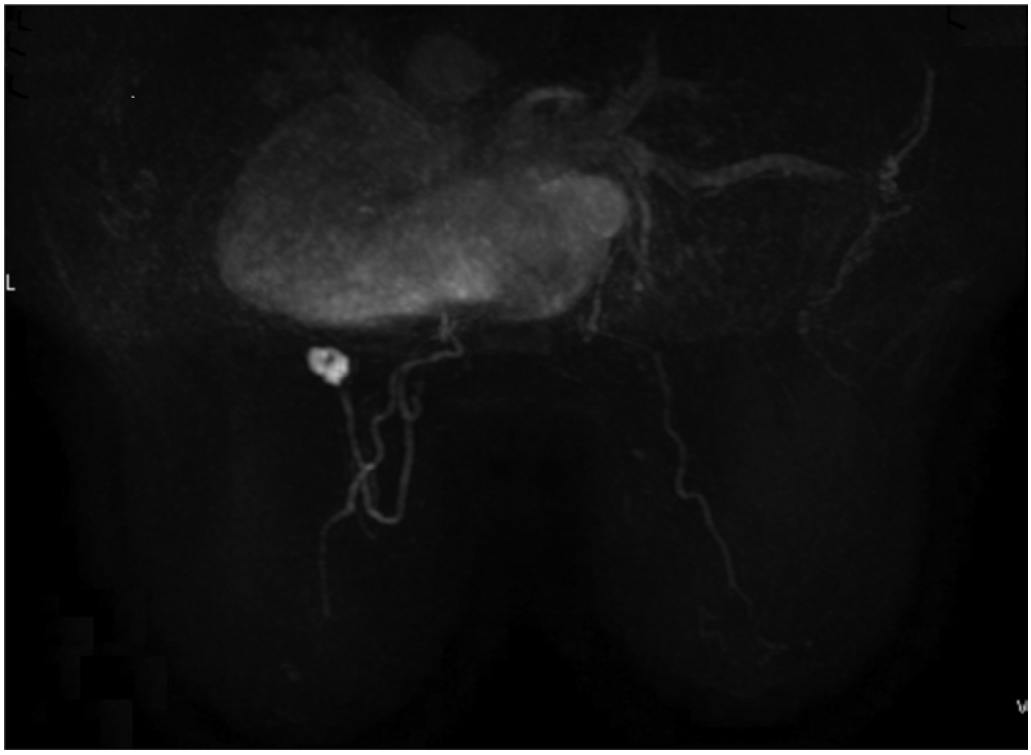

Figure 2: Axial TRICKS sequence performed during the first minute after gadolinium injection showing an invasive ductal carcinoma in the inner part of the left breast with afferent vessels and rim enhancement.

Non-smooth margin was the most accurate sign to predict malignancy with an odds ratio of 26.9 (5.98-177.8) for R1 and 104.5 (13.5-4711.4) for R2.

Diagnostic performance

There was no significant difference in lesion sensitivity for either reader across imaging protocols (Table 3).

Table 3: Comparison of different imaging protocols

	MIP protocol		FAST protocol		ULTRAFAST protocol		FAST-ULTRAFAST protocol		FULL complete protocol	
	R1	R2	R1	R2	R1	R2	R1	R2	R1	R2
TP (No.)	54	55	54	54	52	52	54	54	54	54
TN (No.)	13	11	29	29	30	28	40	34	29	28
FP (No.)	35	37	19	19	18	20	8	14	19	20
FN (No.)	4	3	4	4	6	6	4	4	4	4
Sensitivity (%)	93.1	94.8	93.1	93.1	89.7	89.7	93.1	93.1	93.1	93.1
Specificity (%)	27.1	22.9	60.4	60.4	62.5	58.3	83.3	70.8	60.4	58.3
PPV (%)	60.7	59.8	74	74	74.3	72.2	87.1	79.4	74	73
NPV (%)	76.5	78.6	87.9	87.9	83.3	82.4	90.9	89.5	87.9	87.5
Accuracy (%)	63.2	62.3	78.3	78.3	77.4	75.5	88.7	83	78.3	77.4

TP = true positive, TN = true negative, FP = false positive, FN = false negative, PPV = positive predictive value, NPV = negative predictive value. No. = total number of lesions

For the 58 carcinomas, across all protocols (MIP, FAST, ULTRAFAST, combined FAST-ULTRAFAST or FULL protocol) and both readers, sensitivity was

equal to or higher than 89.7% (52/58). Sixty-six percent of cancers missed by ULTRAFAST protocol (4/6) were located in the upper outer breast quadrant in relation with frequent artifacts of the TRICKS sequence (n=16/70 in this series).

For both readers, there were 4 false negative cases with the FULL protocol which were 3 DCIS (2 low grade and one high grade) and 1ILC. One DCIS was discovered on the surgical pathology for Paget's disease and the two other DCIS measuring 4 and 5 mm at surgical pathology. For the ILC, surgical pathology revealed a tumor measuring 6mm and there was an intense background glandular enhancement that masked the lesion on MR imaging. The two additional false negatives with ULTRAFAST protocol were the same for both readers: one IDC and one ovarian carcinoma metastasis. These two lesions were located in the upper outer quadrant where strong artifact was noticed.

ROC analysis

ROC curves for the three protocols (FULL protocol, FAST protocol and combined FAST-ULTRAFAST protocol) are presented in figure 3.

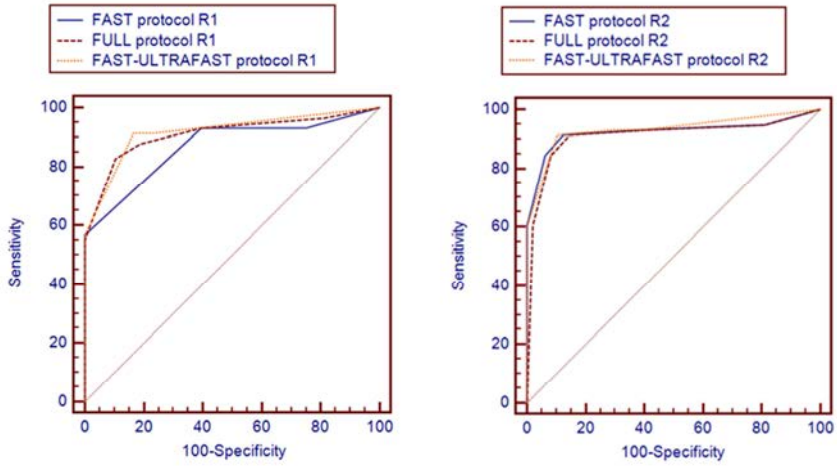

Figure 3: Comparison of diagnostic performance of different imaging protocols according to the reader. FULL protocol, FAST protocol, and combined FAST-ULTRAFAST protocol) are presented with AUROC of 0.911 (0.840-0.958), 0.865 (0.784-0.923) and 0.918 (0.849-0.963) for reader 1 and 0.911 (0.840-0.958), 0.924 (0.856-0.967) and 0.932 (0.867-0.972) for reader 2, respectively.

For reader 1, there was a significant difference between AUROC of FAST protocol and FULL protocol (p=0.0138) and between combined FAST-ULTRAFAST protocol and FAST protocol (p=0.0039). No significant difference was found between FULL protocol and combined FAST-ULTRAFAST protocol (p=0.69) for reader 1. For reader 2, there were no significant difference between AUROC of different protocols (p>0.05).

Inter-observer variability

There was almost perfect agreement for lesion characterization between R1 and R2, regardless of the protocol considered (κ = 0.907 for FULL protocol, 0.800 for FAST protocol and 0.876 for combined FAST-ULTRAFAST protocol).

Accuracy of MR sequences (Table 3)

The combined FAST–ULTRAFAST protocol significantly improved the specificity of the reading for both readers, with a specificity of 83.3% and 70.8%, respectively, compared to

FAST protocol (60.4% for both readers) and FULL protocol (60.4% for reader 1 and 58.3% for reader 2). No change in sensitivity was noticed.

For the two readers, the accuracy of the combined FAST-ULTRAFAST protocol was higher than that of FULL protocol for benign masses (*P* =0.001 for R1 and P= 0.03 for R2) but not for malignant masses (*P* =1) for both readers (Table 4). The addition of ULTRAFAST protocol to FAST protocol increased the correct diagnosis in 10.4% (11/106) and 5.7% (6/106) for readers 1 and 2, respectively (Table 4). Thus, the diagnosis was correctly changed in 22.9% (11/48) and 10.4% (5/48) of benign lesions without any malignant tumors misclassified for readers 1 and 2, respectively. No diagnosis was incorrectly changed for both readers (Figures 4 and 5).

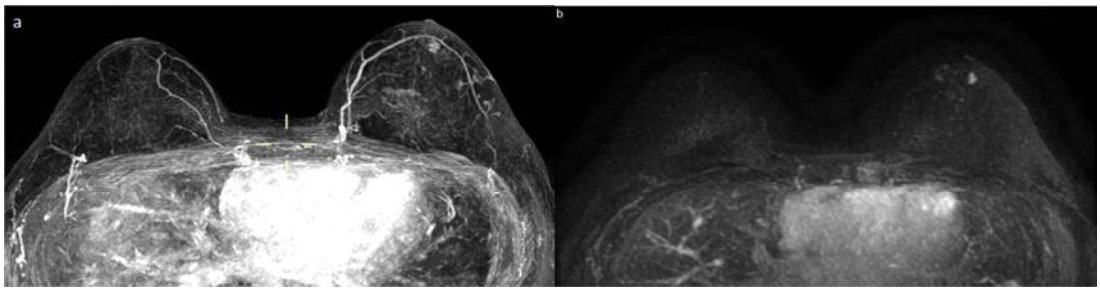

Figure 4: Malignant tumor corresponding to an invasive Ductal Carcinoma located behind the left nipple visible on the MIP VIBRANT performed with the 1st subtraction (a) and also visible on the TRICKS sequence (b).

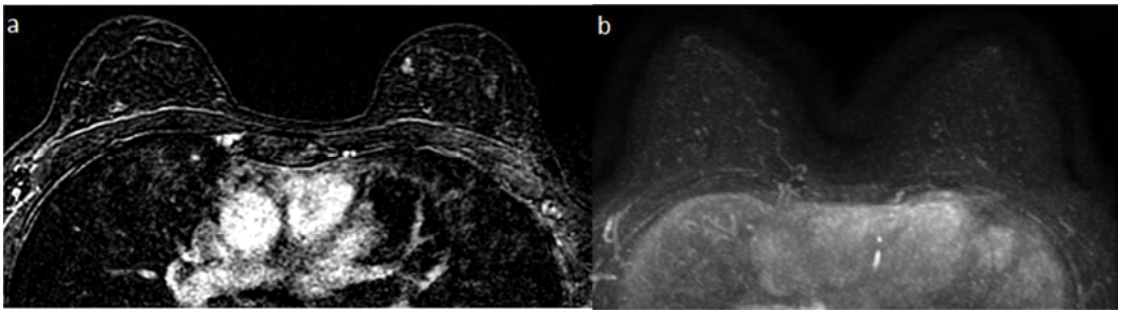

Figure 5: Benign lesion corresponding to a Pseudoangiomatous Stromal Hyperplasia(PASH) located in the inner quadrant of the left breast visible on early SUB VIBRANT sequence (a) and not visible on the TRICKS sequence (b).

For the two readers, the accuracy of the combined FAST-ULTRAFAST protocol was higher than that of FAST protocol for benign masses (*P* =0.001) but not for malignant masses (*P*=1) for reader 1 (Table 4).

Table 4: Comparison of value of the combined FAST-ULTRAFAST protocol with FULL diagnostic protocol and FAST protocol according to Reader Experiment

			FULL diagnostic protocol			FAST diagnostic protocol		
			No. correct	No. misclass	Total	No. correct	No. misclass	Total
Reader 1	FAST+ ULTRAF	No. correct	$83_{(29+54)}$	$11_{(11+0)}$	$94_{(40+54)}$	$83_{(29+54)}$	$11_{(11+0)}$	$94_{(40+54)}$
		No. misclass	$0_{(0+0)}$	$12_{(8+4)}$	$12_{(8+4)}$	$0_{(0+0)}$	$12_{(8+4)}$	$12_{(8+4)}$

Reader 2	FAST+ ULTRAFAST	Total	$83_{(29+54)}$	$23_{(19+4)}$	$106_{(48+58)}$	$83_{(29+54)}$	$23_{(19+4)}$	$106_{(48+58)}$
		No. correct	$82_{(28+54)}$	$6_{(6+0)}$	$88_{(34+54)}$	$83_{(29+54)}$	$5_{(5+0)}$	$88_{(34+54)}$
		No. misclass	$0_{(0+0)}$	$18_{(14+4)}$	$18_{(14+4)}$	$0_{(0+0)}$	$18_{(14+4)}$	$18_{(14+4)}$
		Total	$82_{(28+54)}$	$24_{(20+4)}$	$106_{(48+58)}$	$83_{(29+54)}$	$23_{(19+4)}$	$106_{(48+58)}$

misclass = misclassified. Numbers shown represent the total $_{(benign+malignant)}$

Only a trend toward similar results was noted for reader 2 for benign lesions (p=0.06). The addition of ULTRAFAST protocol to FAST protocol increased the correct diagnosis in 10.4% (11/106) and 4.7%% (5/106) for readers 1 and 2, respectively (Table 4). Thus, the diagnosis was correctly changed in 22.9% (11/48) and 10.4% (5/48) of benign lesions, without any malignant tumors misclassified for readers 1 and 2, respectively. No diagnosis was incorrectly changed for both readers.

False positive results with FAST protocol that were correctly reclassified with the combined FAST-ULTRAFAST protocol due to the absence of enhancement on TRICKS sequence were:7 fibroadenomas (63.6%), 2 cases of adenosis (18.2%), and 2 cases of fibroglandular tissue (18.2%). These lesions corresponded to 10 masses (90.9%) and 1 NME (9.1%) (1). All these masses were round or oval, with 5 masses having circumscribed margins (50%) and one displaying homogenous enhancement (20%). Thus, only one mass with a round shape, smooth margin, and homogeneous enhancement on FAST sequence was classified BI-RADS 4A due to contralateral cancer.

There was no significant difference between the accuracy of FULL protocol and FAST protocol.

Interpretation Time

Median reading time was 9 minutes (min-max =5-18) across all protocols, and was 5.4min (3-9) for FULL protocol, 2min (1-4) and 1.5min (1-4) for FAST protocol, 4min (2-9) and 3min (2-7) for the combined FAST-ULTRAFAST protocol for readers 1 and 2, respectively. Interpretation time for FAST protocol or combined FAST-ULTRAFAST protocol was shorter than for FULL protocol ($p<0.001$).

Acquisition time duration

Median acquisition time was 15min (min-max =14-17) for FULL protocol, 5.8min (5.6-6) for FAST protocol, 5.8min (5.6-6) for the combined FAST-ULTRAFAST protocol. Time duration for FAST protocol or combined FAST-ULTRAFAST protocol was shorter than for FULL protocol ($p<0.001$).

DISCUSSION

Our study demonstrates that the addition of ULTRAFAST sequence to FAST, or even FULL protocol, helps to increase the overall specificity, with improved classification of previously false positive benign lesions. Moreover, the combined FAST-ULTRAFAST protocol allows detection of an equal number of cancers compared to the FULL protocol with a significant reduction in both interpretation time and acquisition time.

Several studies have evaluated various abbreviated protocols in the literature. However, most of these studies have evaluated the ability to detect breast cancer in a context of screening on populations of high-risk women

(calculation of sensitivities), but very few have published the ability to characterize breast lesions regardless of breast MR imaging indication (calculation of specificities) (Table 5).

Table 5: Literature review

	Nb event *	Nb cancer	Pure DCIS	Size	Abbreviated protocol					FULL protocol				
					Se	Spe	PPV	NPV	Read time duration	Se	Spe	PPV	NPV	Read time duration
Kuhl et al (2014)	606	1.8% (11)	4	8.4	100	94.4	31.4	100	28s	100	94.9	33.3	100	-
Mango et al (2015)	100	100% (100)	21	22	96	-	-	-	44s	-	-	-	-	-
Grimm etal. 2015	48	25% (12)	3	-	86 89	52 45	-	-	178s	95	52	-	-	175s
Bickelhaupt et al. (2015)	48	50% (24)	1	NA	85	90	89	87	29s	92	92	92	92	
Moschetta et al (2016)	478	15.7% (75)	0	-	92	92	68	98	120s	89	91	64	98	360s
Harvey et al (2016)	505	1.4% (7)	2	-	100	96.1	24.1	100	93s	-	-	-	-	385s
Heacock et al (2016)	107	100% (107)	13	19	98	-	-	-	25s	-	-	-	-	-
Machida et al (2016)	91	34% (31)	9	25.1	87 93.5	83. 91.7	-	-	-	87.1 96.8	89.7 90.3	-	-	-
Oldrini et al.	106	54.7% (58)	8	22	93.1 93.1	83.3 70.8	87.1 79.4	90.9 89.5	240s 180s	93.1 93.1	60.4 58.3	74 73	87.9 87.5	540s 324s

Nb event: Number of lesion + Number of patients without any lesion; DCIS: ductal carcinoma in situ; Se: sensibility; Sp: specificity; PPV: positive predictive value; NPV: negative predictive value

Adding ULTRAFAST to FAST protocol, we obtained a very accurate protocol with an accuracy higher than that of FAST protocol especially due to the better characterization of benign masses (*P* =0.001). Indeed, many benign lesions were visible on MIP and even on FAST protocol with 18 lesions for R1 and 20 lesions for R2 rated as false positive. For both readers, the number of false positives was clearly decreased (up to 5 and 14).In comparison with previous publications [7, 9, 19], our study reveals a lower specificity of FAST protocol. Specificity is strongly correlated with the prevalence of disease. Most studies reporting on the performance of abbreviated protocols were conducted on populations of high-risk women where the prevalence of cancer is low (i.e. high number of true negative) [7, 9]. In our study, the prevalence of malignancy was very high, about 55%,and specificities are in line with Grimm et al., where the same number of malignant and benign lesions were present [20].

Our study demonstrates that the discriminant power of BI-RADS classification was very good for all FULL and abbreviated reading protocols, although FAST protocol appeared to be less performant than FULL protocol. We hypothesize this may be due to the lack of time intensity curves, which are helpful to characterize masses with benign morphological appearance [14]. Indeed, one third of the lesions we analysed were masses with smooth margins (33/106), underlining this frequent issue in clinical practice. Our results suggest that including a high resolution- dynamic MR protocol during the first minute after injection named TRICKS (similar to TWIST and 4D-TRAK depending on MRI scanner vendors) could be a solution to improve specificity without increasing acquisition time.

MR technical improvements in the last decade have led to the development of ultrafast sequences that capture the inflow of contrast in breast lesions. These methods under-sample the outer part of k-space but share data points between successive time points to increase the obtained spatial resolution to diagnostic quality, as in other sequences such as TWIST [16].Few studies have been conducted with ultrafast sequences[16, 21, 20],and this is the first report regarding the results of TRICKS sequences in breast MR imaging. Our results demonstrate its ability to detect breast cancer with a high sensitivity (89.7%), but with a lower sensitivity than MIP, FAST or FULL diagnostic protocol due to the presence of artifacts, especially in the upper outer quadrant mostly because of decreased signal-to noise ratio. We also observed a new MR sign in this sequence, namely the presence of afferent vessels, which is a direct illustration of the dynamic enhancement of breast cancer due to tumoral neoangiogenesis [22]. Indeed, enhancement of breast cancer is faster than glandular enhancement and benign lesions. When present, this sign may help to improve specificity: the risk of cancer is 26 times greater when afferent vessels are identified. However, this sign was only present in 16 women and 11 women according to readers 1 and 2.

DCE breast MR imaging is well known to be the most sensitive modality to detect breast cancer [2, 23, 24]. Our study confirms that MIP, FAST and FULL protocols are similar and very accurate in terms of their sensitivity for the diagnosis of breast cancers [7, 8, 10, 11, 21, 20]. In contrast with previous reports, we noted an

increased number of missed cancers in both FAST and FULL protocol. This may be partly explained by a higher prevalence of cancer, especially pure DCIS (3/4 missed cancer corresponded to pure DCIS in our study) compared to previous studies [7]. Second, in the studies of Mango et al. [8] and Heacock et al. [10], readers were aware that all imaged patients had breast cancer. Heacock et al. [10] showed that sensitivity is positively affected by the knowledge of prior imaging or clinical history; these data were not available for readers in our study.

We noted that time of interpretation was significantly reduced by the use of an abbreviated protocol in comparison with FULL protocol, as previous studies demonstrated [7, 9]. The addition of UTRAFAST protocol did not increase significantly time interpretation in comparison with FAST protocol, keeping a 3 minutes time analysis, similar to times reported in previous studies [7]. As multiple lesions could be analyzed in one patient, our study does not allow for the comparison of time duration between different MR lesion morphology as Heacock et al. did[10].

The long radiologist interpretation time is not the only limitation to the widespread utilization of breast MRI; it is also limited by overall length of exam. Our study showed that abbreviated protocol decreases interpretation time in comparison with FULL protocol as previously demonstrated[9]. Moreover, the use of abbreviated protocol including TRICKS sequence also decreased time acquisition in regard to FULL protocol with a scan time decreased nearly by a factor of two, as in the literature (decrease of time acquisition of 18.8 minutes)[12].This is a main issue with the increasing of MR indications and its usefulness as a screening test in a high-risk population. Reducing both acquisition and interpretation times are crucial for the future of breast MRI.

Our study presents several limitations. First, this study is a retrospective unicentric study with only proven histological lesions analyzed, which may overestimate the cancer rate. Second, the mean tumor size of malignant lesions was higher than 2cm; the paucity of small cancers may limit our evaluation of the ability of the different reading protocols to correctly detect all cancers. In Heacock's study [10], the only cancer missed measured less than 1cm. However, this limit was also present in most previous studies[8, 10, 21].Thirdly, we decided not to use information issued from time intensity curve built with TRICKS sequence. This could decrease the added value of ULTRAFAST protocol, but we wanted to have criteria that were very reproducible between readers, regardless of the MR unit used. Finally, we did not test the value of diffusion weighted sequence, which is another method to obtain a shortened acquisition in breast MR imaging [25, 26].Reporting on 50 women at intermediate / high risk of cancer, Bickelhaupt et al. described similar performance of an abbreviated protocol using DW Imaging and compared the value of abbreviated protocol (localizer, T2W) and MIP from DWIBS, MIP from first subtracted and full diagnostic protocol[27]. In the future, a study combining ULTRAFAST protocol with DW sequence would be interesting.

In conclusion, an abbreviated protocol including FAST and ULTRAFAST protocol could be useful not only for screening but also for

characterization of breast lesions. ULTRAFAST sequence improves specificity without any significant impact either on acquisition time or interpretation time. Further studies are necessary to confirm these preliminary results.

FUNDING:

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

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Article 3: Does use of an abbreviated protocol for breast magnetic rensonance imaging alter the BI-RADS classification ?

Le but de cette étude est de comparer l'efficacité diagnostique d'un protocole abrégé (comprenant l'acquisition pré et la première série après injection et les images dérivées (images soustraites)) au protocole complet en terme de classification Bi-RADS dans les conditions réelles d'interprétation d'un examen d'IRM mammaire quelque soit l'indication de l'examen.

Nous avons réalisé une étude rétrospective sur 90 patientes. Nous avons inclus 30 examens de trois groupes de classification Bi-RADS à partir du compte-rendu initial: 30 examens bénins (ACR1 ou 2), 30 examens ACR3 et 30 examens nécessitant une preuve histologique (ACR4 ou 5). Deux lecteurs ont relu le protocole complet et le protocole abrégé dans les conditions cliniques habituelles (connaissance des examens antérieurs et de l'indication de l'examen)

Le temps d'interprétation était inférieur pour le protocole abrégé par rapport au protocole standard (différence moyenne : 84 sec, 95% CI [67;101] pour le sénior et 83 sec, 95% CI [70;95] pour le junior; $p<0.001$). La concordance de la classification BI-RADS entre les deux protocoles était très bonne avec un coefficient de corrélation de 0,89 pour le junior et de 0,98 pour le sénior. La concordance inter-observateur était de 0,94 pour le protocole complet et de 0,90 pour le protocole abrégé. Pour le sénior, la sensibilité était de 100% pour les deux protocoles et la spécificité de 95,1% pour le protocole abrégé et 94,4% pour le complet.

L’utilisation d’un protocole abrégé permet de diminuer le temps d’interprétation en conservant une sensibilité et une spécificité élevées. La concordance par rapport au protocole complet est excellente.

Does use of an abbreviated protocol for breast magnetic resonance imaging alter the BI-RADS classification?

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Article accepté dans *Diagnostic and Interventional Radiology*

ABSTRACT

Purpose: The purpose of this study was to compare the diagnostic accuracy and interpretation time of an abbreviated protocol relative to the complete protocol of breast magnetic resonance imaging (MRI) with the use of breast imaging reporting and data system (BI-RADS). Between-reader and between-protocol variability for BIRADS classification and influence of reader expertise on diagnostic accuracies were also evaluated.

Methods: We conducted a retrospective reader study in 90 women who underwent breast MRI: 30 benign examinations (American College of Radiology [ACR]1 or 2), 30 ACR3 and 30 examinations requiring a histological proof (ACR 4 or 5). Two radiologists independently reviewed the protocols. The reference standard was 24 months for imaging follow-up (66.6%, n=60), percutaneous biopsy at the12 month imaging follow-up (5.5%, n=5), and breast surgery (27.9%, n=25). Analysis was done on a per-breast basis. There were 26 cancers in 168 breasts (15.1%)

Results: Interpretation time was higher for complete protocol (mean difference: 84sec, 95% CI [67;101] for senior and 83 sec, 95% CI [70;95] for junior reader; $p<0.001$) . The reliability of BI-RADS classification between both protocols was very good with intra-class correlation coefficient of 0.89 for junior and 0.98 for senior reader; the inter-reader reliability was respectively 0.94 and 0.90 for complete and abbreviated protocol. For senior reader, the specificities were 95.1% and 94.4% for abbreviated and complete protocols and sensitivities were 100 % for both.

Conclusion: Our data provide corroborating evidence that abbreviated protocols decrease interpretation time without compromising sensitivity or specificity. There was a high level of concordance between the abbreviated and the complete protocol and between the two readers.

INTRODUCTION

Breast magnetic resonance imaging (MRI) has a dominant and increasingly important role in breast imaging, particularly for screening of women at high risk of developing breast cancer, in the staging of breast cancers, in the evaluation after neoadjuvant chemotherapy, and for axillary lymph nodes when a primary cannot be found by mammography (1–3). At present, it takes about 30 to 40 minutes

to perform a breast MRI (4) in accordance with the good practice guidelines of the European Society of Breast Cancer Specialists (EUSOMA) This length of time is relatively long, and the examination also presents high direct and indirect costs that limit its wider use (5–11).

Recently, Kuhl et al. (4) showed that in high risk women, the use of an abbreviated protocol is a suitable option that does not compromise the sensitivity or the specificity relative to the conventional complete protocol, thanks to specific characteristics of breast cancers that occur in high risk women. Mango et al. (12) also demonstrated a high sensitivity with an abbreviated protocol for detection of known cancers. Moreover, the use of an abbreviated protocol including the pre-contrast T1-weighted sequence with fat saturation and single early post-contrast imaging with post-processing to generate first post-contrast subtraction and subtraction of maximum intensity projection (MIP) sequences allows the time of interpretation to be reduced in addition to decreasing the duration of the examination itself (4, 12). Thus, several authors published on this popular topic and confirmed the ability of an abbreviated MR protocol to detect breast cancer in populations of high risk screening as well as in women with proven breast cancers. However, few studies have evaluated the specificity of an abbreviated protocol in a non-high risk population (13).

Thus, in this reader study on a selected patient population, our aim was to compare the diagnostic accuracy of an abbreviated protocol relative to the complete protocol in terms of the breast imaging reporting and data system (BI-RADS) classification for interpretation of breast MRIs regardless of the indication of the examination. Moreover we evaluated between-reader variability and influence of reader expertise.

METHODS

From January to June 2013, we retrospectively queried our database to identify the first consecutive 90 MRIs that were classified as American College of Radiology (ACR) category 1 or 2 (n=30), ACR category 3 (n=30), and ACR category 4 or 5 (n=30) in the initial reports. The worst BI-RADS score for both breasts was retained to make the selection.

Our appropriate institutional review board approved the study. Informed contentment was waived. This retrospective study was conducted according to the Declaration of Helsinki's "Ethical Principles for Medical Research Involving Human Subjects."

Exclusion criteria were the absence of a pathological correlation or the absence of follow-up that reached at least 24 months after the MR examination date in the absence of a percutaneous biopsy, or 12 months after the MR examination following a percutaneous biopsy. The mean patient age was 50.4 years (ranging from 27 to 76 years). The indication for breast MR imaging was the breast cancer staging in 19% (n=17), high risk women without BRCA 1 or 2 mutations in 37.7% (n=34), women with BRCA 1 or 2 mutations in 19% (n=17), nipple discharge in 1.1% (n= 1), lesional characterization in 13.2% (n=12), and being ACR category 3 in 10% (n=9).

In our center, a complete breast MRI protocol included an axial T2-weighted acquisition, sagittal 3D EG T1 dynamic Vibrant acquisitions: one before and five after injection (each phase duration was 90

sec) of gadolinium and one axial Vibrant high resolution acquisition on an MRI 3Tesla General Electric device (HDX Twinspeed, Milwaukee, USA) (Table 1).

Table 1. Breast MRI protocol

	Axial T2 SE	**Sagittal Vibrant**	**Axial Vibrant HD**
Flip angle degrees	90	10	10
Repetition time/Echo time (msec)	7723/120.12	4.89/2.10	9.59/4.25
Field of view (cm)	34x37.4	22x24.2	29x31.9
Matrix	320x480	224x224	416x512
Section thickness (mm)	3	2.2	1.8
Number of excitations	1	0.5	0.71

Images subtracted from the first three series after injection and images of MIP of these subtractions were also available. The abbreviated protocol consisted of only the sagittal sequence Vibrant acquisition before injection, the first sagittal series Vibrant acquisition after injection, and the subtracted images (Fig. 1). We did not use axial T2-weighted acquisition and MIP images.

Fig.1 Sagittal Vibrant® image of an invasive breast carcinoma

Two radiologists (a junior physician with 6 months of breast MRI experience, and a senior physician with 5 years of experience) individually reviewed the images in two stages separated by at least two weeks with randomization so as to limit all bias. Abbreviated and complete protocols were mixed in the two stages. For both stages, the readers had access to the previous examinations; to the clinical information, but not to the later examinations; to the current breast MRI report; and to the later possible anatomopathology analysis or imaging follow-up. For every reader, the order of the two stages was randomized and the reading of the abbreviated protocol was blinded from the reading of the complete protocol. For each breast, the readers indicated the size, the quadrant, the type of lesion in case of anomaly, and the ACR BI-RADS classification. The time taken for the readings was also noted. The BI-RADS classifications were then compiled according to the implication on the care: the benign group not requiring specific care (ACR 1 and 2), the surveillance group (ACR 3), and the group requiring histological proof (ACR 4 and 5).

At the end of the reading, in case of discordance with regard to the lesion location, a consensus was sought between the two readers to ensure that it was the same lesion in the three cases (two for the study and the prospective clinical reading). If the lesion differed from the one for the prospective clinical reading, it was considered to be a false positive.

Statistical analysis

The quantitative parameters are described as the mean ±standard deviation and the qualitative parameters as frequency ± percentage. For each reader, the comparison of the reading time according to the two reading protocols was performed with a paired Student's t-test. The inter-reader reliability and the reliability between the two reading protocols were assessed using the intra-class correlation coefficient (ICC). For the inter-reader reliability, according to McGraw and Wong (1996) Convention (14), a two-way random effects Model, absolute agreement, single rater/measurement (ie ICC (2,1) (15)) was performed. For intra-rater reliability, a two-way mixed-effects model - absolute agreement, single measurement- was computed. Based on the terminology proposed by Landis and Koch (16), an ICC value from 0.6 to 0.8 indicated substantial agreement, and from 0.8 to 1.0 indicated almost full agreement. The discriminant power of the BI-RADS classification to detect a cancer was assessed with the area under the curve (AUC) for each protocol. The AUCs for both protocols were then compared using a non-parametric approach (17). The BI-RADS classification was then dichotomized (1, 2, or 3 vs. 4 or 5), and the sensitivity and specificity for each protocol were computed. Sensitivities were then compared using a McNemar's test in the sub-population of breasts for which a cancer was diagnosed. Specificities were compared using a McNemar's test in the sub-population of breasts without a malignant lesion.

Thirty patients were included for each group corresponding to a total sample size of 168 breasts analyzed. It allowed having 80% power to detect a change in sensitivity from 0.9 to 0.99 using a two-sided binomial test, and having 85% power to detect a change in specificity from 0.8 to 0.9 using a two-sided binomial test.

All analyses were performed using SAS software version 9.3 (SAS Institute Inc., Cary, NC 27513 USA). The level for significance was set at $p< 0.05$.

RESULTS

Our population consisted of 90 patients, of whom 12 had a personal history of breast cancer with unilateral mastectomy. Thus, ACR ratings were made for 168 breasts. The gold standard was assessed by a follow-up of 24 month for 137 breasts (81.5%), by percutaneous biopsy with at least a 12 month imaging follow-up for 5 breasts (3%), and breast surgery for 26 breasts (15.5%). Out of the total of 168 breasts, breast cancer was present in 26 breasts (26/168, i.e. 15%). There were 25 (96%) that were invasive and 1 (4%) that was purely a ductal carcinoma in situ (DCIS). Among the 25 invasive breasts cancer, there were 18 (72%) non-specific carcinomas (i.e. invasive ductal carcinoma) and 7 (28%) lobular carcinomas. The histology grades were I for 4 lesions (16%), II for 19 lesions (76%), and III for 2 lesions (8%). 22 (88%) were estrogen receptor positive (ER+) and 3 (12%) were $HER2^{+}$. There were five benign lesions: one adenoma, one fibroadenoma, one papilloadenoma, one breast dystrophy, and one radial scar.

For both readers, the reading time was significantly lower with the abbreviated protocol than with the complete protocol. The average reading time for the junior reader was 247 ± 65 seconds with the abbreviated protocol and 329 ± 84 seconds with the complete protocol (mean difference 83 sec, 95% CI [70;95] $p<0.001$), while for the senior reader these were 59 ± 34 seconds and 143 second ± 72 seconds, respectively (mean difference 84sec, 95% CI [67;101], $p<0.001$).

Lesion characterization

The BI-RADS classifications for the 168 breasts for each reader and each protocol are presented in Table 2 and Fig. 2.

Table 2. The BI-RADS classifications for the 168 breasts for each reader and each protocol.

		Junior		Senior	
Group	**BI-RADS**	**Abbreviated**	**Complete**	**Abbreviated**	**Complete**
Benign	1-2	57.2% (96)	58.3% (98)	54.2% (91)	54.8% (92)
ACR3	3	20.2% (34)	19.1% (32)	26.2% (44)	25.0% (42)
Biopsy	4-5	22.6% (38)	22.6% (38)	19.6% (33)	20.2% (34)

BI-RADS: breast imaging reporting and data system; ACR: American College of Radiology

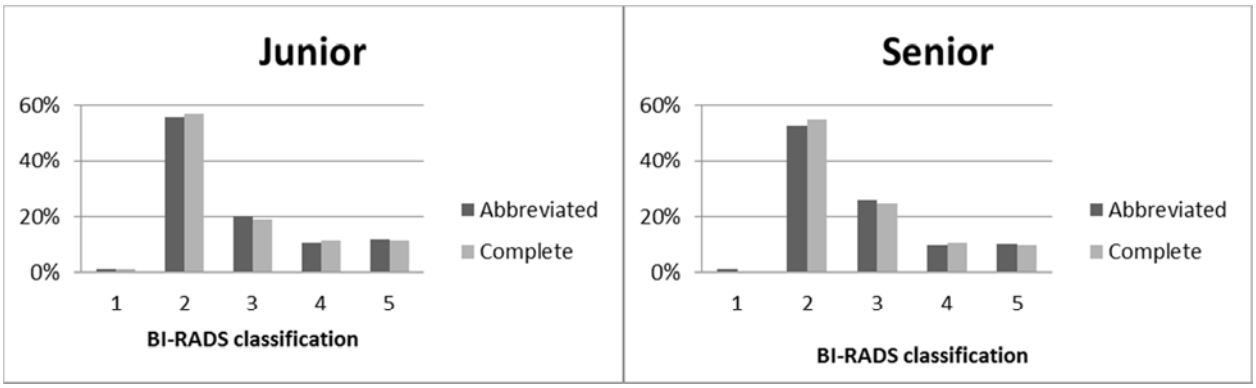

Fig. 2 The BI-RADS classifications for the 168 breasts for the two readers (junior and senior) and each protocol for the five levels of BI-RADS classification.

Considering BI-RADS classification, the inter-reader reliability was 0.941 [0.920–0.956] for the complete protocol and 0.903 [0.871–0.927] for the abbreviated protocol. The reliability between both protocols was 0.895 [0.861–0.922] for the senior and 0.982 [0.975–0.986] for the junior reader.

By pooling the two readers, 14 lesions were classified as “benign” with the complete protocol out of the 78 classified “ACR 3” with the abbreviated protocol (18%).

Regardless of the reader, the AUC of the BI-RADS classification to detect a cancer was not significantly different between the two protocols (Table 3). For both readers, all cancers were in the group “Biopsy required” with both protocols (sensitivity 100 %).

Table 3. Comparison of the performance of BI-RADS classification according to complete and abbreviated protocols. The gold standard is the diagnosis of cancer. Area under the curve (AUC) was computed by considering the five levels of BI-RADS classification. Sensitivity and specificity were computed by considering BI-RADS 4/5 against 1/2/3.

	Junior			**Senior**		
	Abbreviated	**Complete**	**p-value**	**Abbreviated**	**Complete**	**p-value**
AUC	0.985	0.983	0.33	0.987	0.989	0.69
Sensitivity*	100%(26)	100%(26)	1.00	100%(26)	100%(26)	1
Specificity◊	91.5%(130)	91.5%(130)	1.00	95.1%(135)	94.4%(134)	0.71
False positive rate◊	8.4%(12)	8.4%(12)	-	4.9%(7)	5.6%(8)	-

BI-RADS: breast imaging reporting and data system; AUC: area under the curve; *Computed on 26 malignant lesions; ◊computed on 142 breasts without malignant lesions

For the senior reader, out of the 142 breasts without malignant lesions, 135 were classified as “benign” or “ACR 3” with the abbreviated protocol (specificity 95.1 %) versus 134 (specificity 94.4 %) with the complete protocol (p=0.71). For the junior reader, 130 (specificity 91.5 %) were classified “benign” or “ACR 3,” regardless of the protocol.

DISCUSSION

In our study, we showed that there was a clear decrease in the reading time for the examination when the abbreviated protocol was used. There was a high level of agreement between the complete and abbreviated protocols for BI-RADS category. The level of sensitivity and specificity was high with the abbreviated protocol and did not differ significantly from ~~the~~ complete protocol.

The use of an abbreviated protocol, stopping at the first series after injection, allows the duration of the examination to be substantially reduced, with an acquisition time of 3 minutes (4) and an occupation time for the scan that varied from 10 (13) to 15 minutes (12). With the complete protocol, the average acquisition time varies from 30 to 60 minutes (4, 12, 18, 19), which does not allow for more than two patients to be processed per hour in the reference centers (20). Use of the abbreviated protocol may lead to improvements in breast MRI screening since it should allow for a substantial reduction in indirect costs. Thus, it would allow the rate of breast MRIs that can be performed to be substantially increased by at least a factor two over the current rate of two examinations per hour in the reference centers (20).

With the abbreviated protocol, the reading time was also significantly reduced for both readers relative to the complete protocol. With the abbreviated protocol, reading times for the senior physician were about 60 seconds, as opposed to reading times of 60 to 120 seconds for a typical mammography screening (4, 21, 22). Interpretation time significantly decreased with the abbreviated protocol, allowing for innovative reading options, such as double reading and real-time interpretation (23). In our study, interpretation time is far longer than that published by other abbreviated protocols. It is probably due to the fact that we did not use MIP images and made an interpretation with standard sequence. Indeed, contrary to Kuhl et al (4) who used only MIP images for the interpretation of abbreviated protocol, we did not use MIP images because we think that it is necessary to make no differences between interpretation of abbreviated and complete protocols. So, we used native images and substracted images for both interpretations of abbreviated and full protocols.

In our study, there was nearly complete inter-observer agreement for junior and senior readers, both with the complete or the abbreviated protocol. The use of an abbreviated protocol was hence not detrimental in terms of the reproducibility of the interpretation and the ensuing care.

There was also nearly complete concordance (above 0.80) between both protocols for both readers. Moreover, the sensitivity and the specificity were high for both readers, and they were comparable for both reading protocols. The abbreviated protocol did not influence the sensitivity and the specificity of the examination. We provide corroborating evidence for the equal diagnostic utility of abbreviated versus full multiparametric breast MRI.

Indeed, this is in keeping with the findings of Kuhl et al. (4), who demonstrated that the use of an abbreviated protocol for breast screening by MRI is feasible without compromising the sensitivity and the specificity of the examination relative to a complete protocol. It also fits with the findings of Mango et al. (12) who were able to demonstrate a high level of sensitivity for detection of cancers with an abbreviated protocol. Moreover, these results are in agreement with the study by Moschetta et al. (24) who found that abbreviated protocol is a tool with the same diagnostic potential as the standard protocol in patients undergoing breast MRI for screening, problem solving, or preoperative staging. In standard clinical situations, the care provided based on findings from an abbreviated protocol corresponded with what was provided when a standard protocol was used. When an abbreviated protocol was used, both readers still detected all of the cancers. No study previously addressed the concordance between the two protocols and the few studies published on abbreviated protocols did not evaluate specificity. Moreover, our study demonstrates that the abbreviated protocol might be used by a junior reader without any impact on the sensitivity and specificity values of the examination.

The percentage of ACR 3 cases with the abbreviated protocol that were reclassified as ACR 2 with the complete protocol was 18 % versus 37.7 % in the study by Kuhl et al. (4). The utility of the late additional sequences for characterization of the lesion appears to be less clear in our study because there are lower cases ACR 3 with the abbreviated protocol reclassified as ACR2 with the complete protocol. Moreover, we did not find a loss of specificity with abbreviated protocol although late Vibrant acquisitions were not used.

Our study has several limitations. First of all, it was a retrospective study. Secondly, as the readers were cognizant of the indication for the examination, in 17 cases the cancer was hence known to the readers. This could limit the value of the 100% sensitivity that we encountered in our study with the abbreviated protocol. However, with the exception of the tumor staging, detection of all of the cancers was the same regardless of the examination. Furthermore, detection matched the usual clinical conditions for interpretation of breast MRI, which is integrated into the complete breast imaging process for the patient. Indeed, our goal was to evaluate the impact of standard contextual information in the context of an abbreviated protocol, as done by Heacock et al. (11). In our study, there was only one DCIS, which could have led to an overestimation of the sensitivity due to a better sensitivity for invasive carcinoma than for DCIS. Indeed, diagnosing DCIS on MRI represents the single major diagnostic challenge.

Our study indicates that the use of an abbreviated protocol maintained a high level of sensitivity and specificity with decreased examination and reading times. It provides corroborating evidence that abbreviated protocols could be a new diagnostic tool for radiologists instead of full breast MR protocol.

MAIN POINTS

Use of the abbreviated protocol resulted in decreased interpretation time.

There was no difference of sensitivity and specificity between complete and abbreviated protocols.

There was a high level of concordance between the abbreviated and the complete protocol.

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Article 4: The usefulness of high temporal resolution with breast MRI sequences : A case report.

Il s'agit d'un cas clinique mettant en évidence l'intérêt de l'utilisation des séquences à haute résolution temporelle. En effet dans ce dossier, seules les séquences à haute résolution temporelle (Twist®) permettent de démasquer le carcinome lobulaire infiltrant au sein d'un rehaussement matriciel de grade 4 alors que la période de réalisation de l'IRM est adéquate dans la période du cycle. En effet la lésion se rehausse plus précocement que le rehaussement matriciel de fond. Ce différentiel de cinétique de rehaussement n'est pas visible sur la séquence Vibe® standard réalisée dans les 90 premières secondes après injection. Ce cas clinique est en faveur de l'utilisation des séquences à haute résolution temporelle dans la phase de rehaussement initial des lésions c'est-à-dire la première minute après injection. Dans cet exemple, la résolution temporelle du Twist® était de 8 secondes.

The usefulness of high temporal resolution breast MRI sequences: A case report

G. Oldrini, A. Bedri, E. Happi Ngankou, F. Marchal, P. Henrot

Article accepté dans *La Presse Médicale*

Breast MRI bears and ever more important role in the characterisation of breast lesions [1-3]. However, its high negative predictive value can be hampered by background parenchymal enhancement (BPE), masking breast lesions.

We report on the case of a 39 years old patient referred upon discovery of a suspicious lesion in the lower outer quadrant (LOQ) of the left breast. Despite being scheduled with optimal timing on the 8th day of the menstrual cycle, the breast MRI exam with typical sequences showed marked BPE (Fig. 1). It was impossible to single out any lesion from within the LOQ of the left breast. We performed high temporal resolution dynamic sequences (TWIST®) within the first minute after administration of intravenous contrast (acquisition time per sequence: 8 seconds). Analysis of these sequences allowed us to depict an 8mm mass within the LOQ of the left breast bearing an intense enhancement, distinguishing it from the BPE (Fig. 2). A needle core biopsy of the lesion was performed as follow up and yielded a lobular invasive carcinoma.

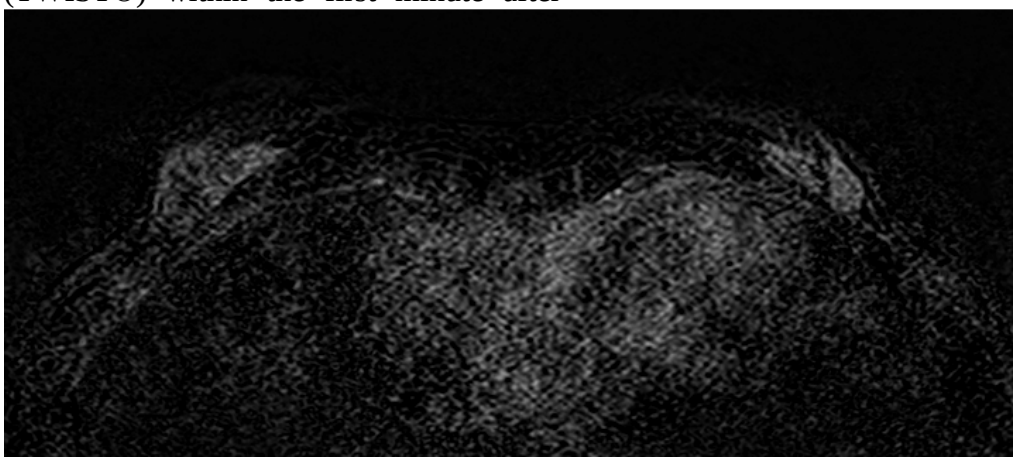

Figure 1: Axial MRI subtracted with standard sequence: lesion of left breast is not visible because of the BPE

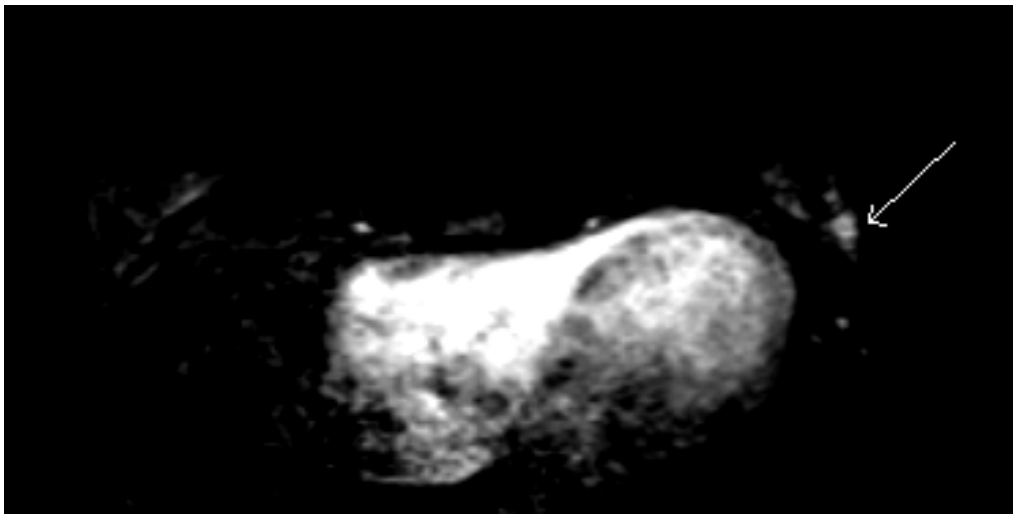

Figure 2: Axial MRI subtracted with TWIST®: lesion of left breast is visible with higher signal intensity than BPE (white arrow)

Discussion

This case highlights the usefulness of new sequences in breast MRI. It would have been impossible to unmask the cancerous lesion in this patient without the help of the high temporal resolution sequences. In the same manner that suspicious lesions can be obscured on a mammogram by dense fibroglandular tissue, BPE does not allow for affirmative conclusions to be drawn on the presence or absence of a suspicious lesion. In such cases, breast MRI fails to uphold its high negative predictive value. Given their lower acquisition times (5 to 10 seconds) [4] compared to more classical sequences (90seconds), these novel high temporal resolution sequences allow for dynamic contrast-enhanced acquisitions at much earlier phases of tumoral enhancement where malignant lesions are known to display earlier enhancement than benign lesions. International and French national guidelines along with the BI-RADS lexicon of the American College of Radiology [5] recommend assessment of late enhancement at 7 minutes and of the wash out as the parameters for distinguishing malignant from benign lesions. Mann et al. [4] demonstrated that though the analysis of enhancement patterns within the first minute after administration of IV contrast was not possible due to the prolonged acquisition times, it was as discriminating as the assessment of kinetic curves. This would lead to shorter exam times and greater specificity than with the shortened protocols [6] presently under assessment. Furthermore, like in the case reported here, sensitivity would be increased when faced with complex diagnostic situations in the setting of background parenchymal enhancement.

Conflict of interest: none

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Article 5: Comparison of morphology, margin and enhancement analysis of breast carcinomas between the abbreviated and full diagnostic MRI protocol.

Le but de cette étude est de comparer la corrélation des protocoles abrégé et complet en terme de morphologie, d'analyse des contours et de rehaussement interne des lésions ainsi que le reproductibilité des deux protocoles.

Il s'agit d'une étude rétrospective sur 50 patientes atteints d'un cancer du sein. Un radiologue a examiné indépendamment les images en quatre séances, séparées par au moins deux semaines, en analysant deux fois chaque protocole: le protocole abrégé et le protocole complet. Pour chaque lecture, le radiologue a enregistré la taille et l'emplacement de la lésion. La morphologie des lésions, les contours et le rehaussement interne ont été rapportés en utilisant le lexique BI-RADS.

Pour la morphologie et le rehaussement interne, la corrélation était parfaite pour les quatre lectures (2 pour le protocole complet et 2 pour l'abrégé). Pour les contours lésionnels, le coefficient kappa entre les deux protocoles était de 0,929 [0,832: 1] pour la lecture 1 et de 0,719 [0,536: 0,903] pour la lecture 2.

Le protocole abrégé présente une forte corrélation avec le protocole complet pour l'évaluation des contours de lésion malignes. De plus, il existe une concordance parfaite entre les deux protocoles pour la morphologie et le rehaussement interne des lésions.

Comparison of morphology, margin and enhancement analysis of breast carcinomas between the abbreviated and full diagnostic MRI protocol

Guillaume Oldrini, Julia Salleron, Emmanuel Happi Ngankou, Philippe Henrot, Frédéric Marchal

Article soumis à *Japanese Journal of Radiology.*

ABSTRACT

Purpose: The aim of this study is to compare the correlation of abbreviated and full complete protocols of breast MRI on shape, margin analysis and lesion enhancement as well as their reproducibility for both protocols.

Materials and methods: This retrospective study was conducted on 50 patients with breast cancer and breast MRI. One radiologist independently reviewed MR images in four sessions, separated by at least two weeks, analyzing two times each protocol: the FAST protocol and the FULL protocol. For each reading, the radiologist recorded lesion size and location. Lesion morphology, margins and internal enhancement were reported using the BI-RADS lexicon.

Results: For lesion shape and internal enhancement, the agreement was perfect across the four readings (2 for the full protocol and 2 for the abbreviated one). For lesion margins, the kappa value between the two protocols was 0.929 [0.832:1] for reading 1 and 0.719 [0.536:0.903] for reading 2.

Conclusion: The FAST protocol exhibits a high correlation with the full protocol for the assessment of malignant lesion margins. In addition, there is perfect concordance between both protocols for lesion shape and assessment of internal lesion enhancement.

Key words: Breast, MRI, Abbreviated protocol, Margin, Morphology

INTRODUCTION

Breast MRI holds an important place in breast imaging.[1-3] As shown by the studies by Kuhl et al.[4] on the use of an abbreviated breast MRI protocol and those by Mann et al.[5] on high temporal resolution allowing for analysis of initial tumor enhancement, it is evident that the abbreviated protocol has been the hottest topic in breast imaging. The growing numbers of publications in this area center mainly around the sensitivity values of the abbreviated protocol.[6-13] Some studies found sensitivity values equivalent to those of the full diagnostic protocol,[7, 9-11, 13] clearing any doubts regarding the

abbreviated protocols performance for lesion assessment.[4]

Despite this growing number of publications, the correlation with clinical follow up and with the BI-RADS categories has not been sufficiently studied. Panigrahi et al.,[14] who recently compared the BI-RADS categories between both imaging protocols, found the abbreviated MRI protocol to be as effective as the full diagnostic protocol. This supports the proposal for the abbreviated protocol as a substitute to the full protocol recommended by international reference bodies such as the European Society of Breast Cancer Specialists (EUSOMA), not only for high-risk screeningm as suggested by Kuhl et al.,[4] but for all indications. Lesion shape, contour, and internal enhancement characteristics bear a major role not only in the BI-RADS classification system for mammography but also for MRI. To the best of our knowledge, the correlation between both protocols on the different criteria of the BI-RADS lexicon has not been studied yet. We thought it important for it to be.

The aim of this study is to compare the correlation of both protocols on shape, margin analysis and lesion enhancement, as well as their reproducibility for both protocols.

MATERIALS AND METHODS

Population

This retrospective study is on 50 consecutive patients (mean age 53 years, range 24 to 77 years) who had undergone a breast MRI with a mass lesion and a breast carcinoma diagnostic between September 3rd, 2016 and February 23rd, 2017 in our institution. There were 27 menopausal women (54%) and 23 premenopausal women (46%).

Five women had a personal history of breast cancer (10%), 1 woman was high-risk with a proven genetic predisposition (2%), and 19 women had a family history of breast cancer without context of high risk (38%).

This retrospective study was conducted according to the Declaration of Helsinki's "Ethical Principles for Medical Research Involving Human Subjects." Our institutional review board approved the study and informed contentment was waived.

MR acquisition

In our center, a complete breast MRI protocol included an axial T2-weighted acquisition and axial 3D EG T1 dynamic Vibe acquisitions: one before and five after injection (each phase duration was 90 seconds) of gadolinium on a 1.5 Tesla Siemens MRI device (Magnetom Aera) (Table 1). Images subtracted from the first three series after injection and images of MIP of these subtractions were also made available. The abbreviated protocol consisted of only the axial Vibe sequence acquisition before injection, the first axial series Vibe acquisition after injection, and the subtracted images and corresponding MIP. All of the MR images were reviewed on a Picture Archiving and Communication System (PACS) workstation.

Table 1: Breast MRI protocol

	Axial T2 SE	Axial VIBE
Flip angle degrees	170	10
Repetition time/Echo time (msec)	9650/128	5.29/2.66
Field of view (cm)	23x40.25	24x36.72
Matrix	320x256	256x204
Section thickness (mm)	2	1
Number of excitations	1	1

MR data analysis

On each acquisition, the lesion to be studied was marked to ensure that it was analyzed on subsequent readings by one radiologist, with eight years of experience in breast MR imaging. Then the reader analyzed each protocol twice: the FAST protocol (consisting in the native images of the pre- and the first post-contrast VIBE acquisition and the corresponding subtracted images) and the FULL protocol (T2W, DCE MR sequences). The reader reviewed MR images in four sessions, separated by at least two weeks, and each reading was performed blindly of the others. For each reading, the radiologist recorded lesion size in millimeter and location in breast (quadrant). Lesion morphology (round, oval, or irregular shape), margins (circumscribed, irregular, or speculated) and internal enhancement (homogenously, heterogeneously or rim enhancement) were reported using the BI-RADS lexicon.

Statistical analysis

Reproducibility of size measure between the abbreviated protocol and the full protocol was assessed with the intra-class correlation coefficient according to the Fleiss method[16] and compare thanks to Mann-Whitney U test. A Cohen kappa statistic was calculated to determine the agreement of the abbreviated protocol and the full protocol according to lesion shape, margins and internal enhancement. A value greater than 0.8 was considered as a good agreement. Statistical analysis was performed using SAS software (SAS Institute Inc., Cary, NC, USA). A p-value <0 .05 was considered statistically significant.

RESULTS

Twenty-six of the 50 analyzed lesions were located in the external quadrants (52%), 17 were found in the internal quadrants (34%), and 7 were centrally located (14%).

Most lesions were carcinomas of non-specific type (n=38, 76%). There were 12

invasive lobular carcinomas (24%). All lesions presented as masses on MRI.

Median size of the lesions was 13 mm (range: 6-24mm) for the abbreviated protocol and 12.5mm (range: 6-23mm) for the full protocol. The mean size did not differ significantly between the protocols (p=0.191) and the inter-protocol reproducibility was excellent at 0.987. Setting the first reading of the full protocol as reference, 30 lesions had an irregular shape (60%), 13 were oval (26%) and 7 were round (14%). Twenty-six lesions showed irregular margins (52%), 4 were smooth (8%), and 20 were spiculated (40%). There were 10 rim enhancement lesions (20%), 28 heterogeneously enhancing lesions (56%), and 12 homogenously enhancing lesions (24%).

Comparing lesion shape

Intra-reader kappa value was 1 between the two readings of the full protocol and between both readings of the abbreviated protocol. The kappa value between the full and abbreviated protocols was equally 1, showing a perfect agreement.

Comparing lesion margins

Intra-reader reproducibility for full protocol

The intra-reader kappa value was 0.894 ([0.776:1] 95% CI). There were three differences; two lesions with irregular margins on the first reading were reported as having spiculated margins on the second reading and 1 spiculated lesion was reported as irregular.

Intra-reader reproducibility for abbreviated protocol

The intra-reader kappa value was 0.895 ([0.779:1] 95% CI). There were 3 differences. Three lesions with irregular margins on the first reading were reported as having spiculated margins on the second reading.

Agreement between the abbreviated and full protocols

Taking into consideration the first reading of each protocol, the kappa value was 0.929 [0.832:1]. There were two differences in lesion margins between both readings (an irregular lesion on the abbreviated protocol reported as spiculated on the full protocol and vice versa). Taking into consideration the second reading of each protocol, the kappa value was 0.719 [0.536:0.903]. There were eight differences in lesion margins between both readings (five irregular on the full protocol reported as spiculated on the abbreviated protocol and three spiculated on the full protocol reported as irregular on the abbreviated protocol).

Comparing lesion enhancement

Intra-reader kappa value was 1 between the two readings of the full protocol and between both readings of the abbreviated protocol. The kappa value between the full and abbreviated protocols was equally 1, showing a perfect agreement.

DISCUSSION

This study highlights the excellent correlation on size, shape, margin assessment and internal enhancement of malignant breast lesion between the abbreviated protocol and the full protocol.

The abbreviated MRI protocol has been extensively studied these past three years.[4,7,9,12,17-21] Its contribution to screening and its sensitivity are now well

known. Its specificity values for lesion characterisation appear to be equivalent to the full protocol.[7, 9-10] However, Panigrahi et al.[14] remain the only ones to have reported on the BI-RADS categorisation of lesions. We deemed it was important to assess lesion characteristics. These criteria are used for the ACR categorisation and hence clinical management.

As showed by Panigrahi et al.,[14] review of sequences included in the full protocol resulted in a change in the final BI-RADS assessments in 3.4% of the cases, the majority of which did not change clinical management with respect to biopsy. Our study confirms this data. Indeed, the agreement between the two protocols is high for the shape, the margins, and the internal enhancement of the lesions. These are major elements of the BI-RADS lexicon. The use of the abbreviated protocol therefore does not seem to alter the results of the MRI with regard to the BI-RADS classification and so the care. This is an additional argument in favour of using the abbreviated protocol instead of the full protocol. In our study, we assessed the correlation between protocols and also intra-protocols, to ensure the reproducibility of results obtained from each protocol. The abbreviated protocol yielded reproducible results on the outcomes of lesion shape, margin and enhancement assessment. These fundamental criteria used to categorise lesions in the BI-RADS lexicon then showed a strong correlation with the full protocol which stands as the reference method for lesion assessment as per international guidelines. This has not been evaluated in the scientific literature. In order to propose the abbreviated protocol as a substitute to the full protocol, these parameters must be verified.

These were three contentious cases for both protocols. The discordance was exclusively on lesion margin assessment between irregular or spiculated. Distinguishing both margin types may be highly subjective, especially with spiculations on small lesions or focal spiculations (Figure 1). However, if margin assessment yielded discordant results between lesions, it was no more concordant between the two readings of the full protocol. On the first reading, two lesions and on the second reading, eight lesions yielded discordant results of lesion margin assessment (spiculated or irregular) between the full protocol and the abbreviated protocol. There persists a high concordance which goes in favour of the abbreviated protocol as a substitute for the full protocol.

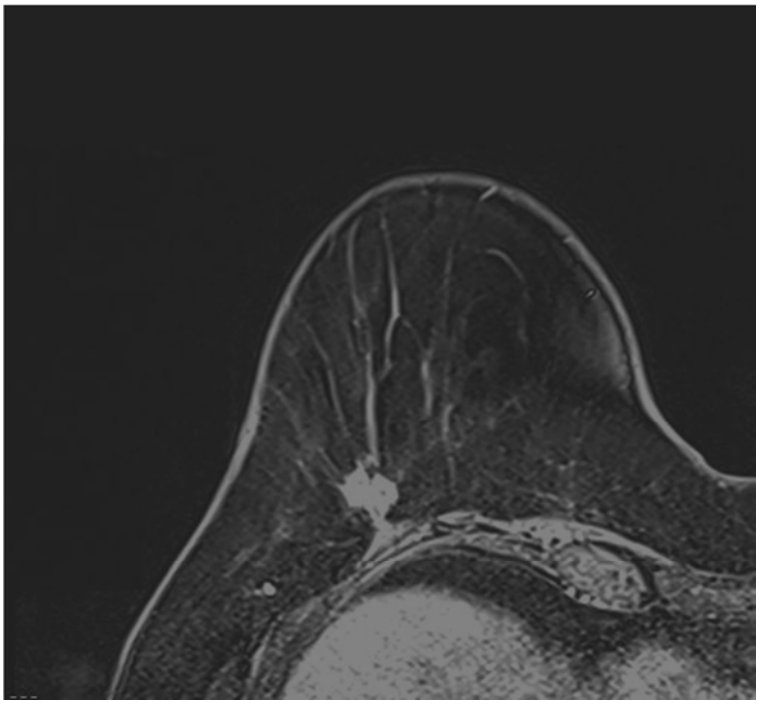

Figure 1: Axial Vibe sequence after injection. Deep carcinoma of right breast. It is subjective to decide if margins are irregular of focally spiculated. It was one of discordant cases between readings.

Our study has several limits. Firstly, it is retrospective and monocentric in design. Moreover, our small sample size necessitates larger scale studies. Finally, only malignant lesions were assessed. It would be of value to extend this study into a more sizeable cohort including benign and malignant lesions.

CONCLUSION

The abbreviated protocol exhibits a high correlation with the full protocol for the assessment of malignant lesion margins. In addition, there is perfect concordance between both protocols for lesion shape and assessment of internal lesion enhancement, which builds a supplemental argument for the abbreviated protocol as a substitute of the full breast MRI protocol.

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Article 6 : Protocole d'IRM abrégée pour le diagnostic et le dépistage du cancer du sein

Il s'agit d'un article commandé par la revue *Oncologie* pour un numéro spécial sur le cancer du sein. Cet article traite du protocole abrégé en IRM mammaire.

Protocole d'IRM abrégée pour le diagnostic et le dépistage du cancer du sein

Abbreviated breast MRI for diagnostic and screening of breast carcinoma

Guillaume Oldrini, Philippe Henrot, Frédéric Marchal

Résumé

Le cancer du sein est le 1er cancer féminin France et sa détection précoce est indispensable. L'IRM mammaire est un élément de choix dans son diagnostic mais il présente des coûts directs et indirects élevés notamment du fait de sa durée qui ralentit son utilisation plus large. Compte tenu de ses éléments, l'utilisation d'un protocole abrégé se développe pour palier à ces inconvénients. Les premières données de la littérature tendent à penser que cet examen plus rapide permet également une durée d'interprétation plus courte. De plus, la sensibilité et la spécificité de l'examen ne sont pas inférieures à celle du protocole complet. Cet article explique ce nouveau concept et son intérêt, le compare au protocole complet et évoque les perspectives futures et notamment à l'adjonction de séquences à haute résolution temporelle.

Mots clés : IRM, protocole abrégé, cancer du sein

Abstract

Breast cancer is the 1st female cancer in France and its early detection is essential. Breast MRI is an element of choice in its diagnosis but it has high direct and indirect costs because of its duration which slows down its wider use. Given its elements, the use of an abbreviated protocol develops to overcome these disadvantages. Early literature data suggests that this faster examination also allows for a shorter interpretation time. In addition, the sensitivity and specificity of the examination are not inferior to that of the complete protocol. This article explains this new concept and its interest, compares it to the complete protocol and evokes the future prospects and in particular the addition of sequences with high temporal resolution.

Keywords: MRI, abbreviated protocol, breast carcinoma

Introduction

Le cancer du sein est le 1er cancer féminin en France. Sa détection précoce est un élément clé dans la prise en charge de cette pathologie pour améliorer le pronostic et en diminuer la morbi-mortalité.

Cette détection précoce repose en majorité sur les examens d'imagerie que sont la mammographie, l'échographie et l'imagerie par résonance magnétique (IRM) mammaire.

L'IRM mammaire a été largement acceptée comme outil de diagnostic essentiel du cancer du sein. En outre, elle joue un rôle dominant et de plus en plus important dans l'imagerie mammaire, en particulier pour le dépistage des femmes à risque élevé de développer un cancer du sein, dans le bilan d'extension mammaire du cancer du sein, dans l'évaluation après chimiothérapie néoadjuvante et en cas d'adénopathie axillaire sans lésion mammaire visible en mammographie et en échographie (1-3). Ses indications sont bien connues: le dépistage des femmes à haut risque de cancer du sein, le bilan d'extension mammaire (à la fois homolatéral et controlatéral), l'évaluation après chimiothérapie néoadjuvante, la recherche de complication des implants mammaires, le bilan d'adénopathie axillaire sans primitif mammaire diagnostiqué sur le bilan standard, les récidives locales présumées et la résolution de problèmes (résultats équivoques à la mammographie / échographie) lorsqu'une biopsie ne peut être effectuée et dans le bilan d'écoulement mammelonnaire (4). Cependant, les examens qui respectent les recommandations de bonnes pratiques de la Société européenne des spécialistes du cancer du sein (EUSOMA) nécessitent 30 minutes pour leur réalisation (5). Cela comprend une acquisition pondérée en T1 et une en pondération T2, suivies par des séquences de moins de 90 secondes répétées avant et après l'injection d'un produit de contraste et une acquisition tardive à 7 minutes. Le temps total prend également en compte le temps d'installation et de désinstallation de la patiente dans l'IRM. L'IRM mammaire a donc des coûts directs et indirects élevés qui limitent son utilisation plus large, d'autant plus que les protocoles actuels d'IRM mammaire nécessitent un temps considérable pour l'acquisition et l'interprétation (6-12). En outre, comme c'est le cas dans certains pays européens tels que la France, le nombre d'IRM est insuffisant pour répondre aux indications croissantes de l'IRM mammaire, y compris le dépistage annuel d'un nombre croissant de femmes à haut risque pour le cancer du sein et des ovaires. Malgré la disponibilité limitée de l'IRM, les indications pour les examens d'IRM augmentent de façon exponentielle (13). Entre 2000 et 2009, la demande d'IRM mammaire a augmenté d'un facteur supérieur à 20 (14).

Compte tenu de ces éléments, il est apparu primordial de pouvoir réaliser des examens plus rapides permettant d'augmenter le nombre d'examens pour répondre à ces différentes problématiques tout en conservant une sensibilité et une spécificité élevées identiques à celles obtenues par le protocole standard.

Protocole abrégé en IRM mammaire

Kuhl et al. (5) ont été les premiers à montrer que l'utilisation d'un protocole abrégé (le protocole «FAST») ne compromet pas la sensibilité ou la spécificité par rapport au protocole

conventionnel dans une population de femmes dépistées par IRM. Le protocole FAST est une version abrégée du protocole complet qui se termine après la première série dynamique suite à l'injection. Il comprend une séquence pondérée T1 pré-contraste avec saturation en graisse et une seule série d'imagerie post-contraste précoce avec post-traitement pour générer une soustraction et une vue de projection d'intensité maximale (MIP). Le différentiel de réalisation des séquences entre le protocole abrégé et le protocole standard est illustré dans la figure 1.

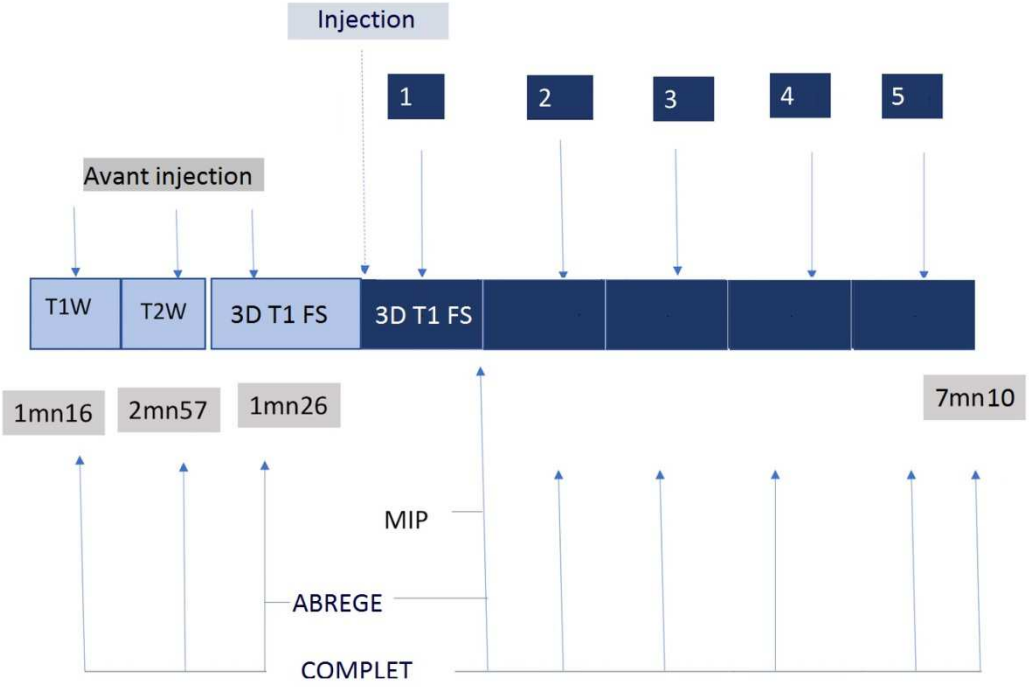

Figure 1. Schéma des protocoles abrégé et complet en IRM mammaire. Le protocole abrégé se limite à une séquence avant et après injection de produit de contraste.

Dans notre institution cela permet par exemple de diminuer le temps d'examen de 12 minutes 49 secondes à 2 minutes et 52 secondes. L'utilisation d'un protocole abrégé permet non seulement un temps d'examen plus court, mais aussi une interprétation plus rapide par le radiologue (5, 15). En outre, un protocole abrégé est bénéfique pour les patients, car il réduit leur temps de présence dans l'IRM (16). Cela pourrait permettre une meilleure compliance des patientes et diminuer les artéfacts cinétiques, ce qui entraînera une meilleure qualité d'image. Cet avantage

sera plus grand pour les patients qui ont des difficultés à tolérer l'IRM mammaire, comme par exemple les patientes qui souffrent de claustrophobie ou d'inconfort lors du positionnement en IRM (16). Mango et al. (15) ont également démontré qu'un protocole abrégé présente une sensibilité élevée pour la détection de cancers connus. Ainsi, plusieurs auteurs ont publié sur ce sujet et ont confirmé la capacité d'un tel protocole à détecter les cancers du sein chez les femmes à haut risque génétique ainsi que chez les femmes atteintes d'un cancer du sein prouvé. Cependant, peu d'études ont évalué la spécificité du protocole abrégé dans une population à risque non élevé ou normal (17). Plusieurs publications ultérieures ont souligné la capacité d'un protocole abrégé à détecter le cancer du sein dans certaines indications particulières, y compris dans le cas de résultats équivoques à la mammographie / échographie, ou en dépistage des patientes à haut risque. Certaines études comprenaient des images pondérées en T2 (12, 18, 19), STIR (18) et des deuxièmes séries après injection (19). Cependant, les séquences pondérées en T2 prennent du temps et Heacock et al. (12) montrent que ces séquences n'ont pas permis d'améliorer la détection du cancer, même si les trois lecteurs ont déclaré qu'une acquisition pondérée T2 était utile dans l'évaluation des lésions.

Comparaison avec le protocole complet

Le tableau 1 résume les principales données concernant le protocole abrégé dans la littérature et notamment les valeurs de sensibilité, spécificité et le temps de lecture. Ce tableau met en évidence les disparités entre les différentes études et montrent que les comparaisons avec le protocole standard ne sont pas systématiques. De plus, le protocole abrégé ne se résume pas à un protocole unique. En effet, la principale disparité concerne le maintien des séquences en pondération T2 avant injection de produit de contraste.

	Nb cancer	CCIS	Taille	Protocole abrégé					Protocole complet				
				Se	Spe	VPP	VPN	Temps de lecture	Se	Spe	VPP	VPN	Temps de lecture
Kuhl et al (2014)	1.8% (11)	4	8.4	100	94.4	31.4	100	28s	100	94.9	33.3	100	-
Mango et al (2015)	100% (100)	21	22	96	-	-	-	44s	-	-	-	-	-
Grimm etal. 2015	25% (12)	3	-	86 89	52 45	-	-	178s	95	52	-	-	175s
Bickelhaupt et al. (2015)	50% (24)	1	NA	85	90	89	87	29s	92	92	92	92	
Moschetta et al (2016)	15.7% (75)	0	-	92	92	68	98	120s	89	91	64	98	360s
Harvey et al (2016)	1.4% (7)	2	-	100	96.1	24.1	100	93s	-	-	-	-	385s
Heacock et al (2016)	100% (107)	13	19	98	-	-	-	25s	-	-	-	-	-
Machida et al (2016)	34% (31)	9	25.1	87 93.5	83. 91.7	-	-	-	87.1 96.8	89.7 90.3	-	-	-
Oldrini et al.	54.7% (58)	8	22	93.1 93.1	83.3 70.8	87.1 79.4	90.9 89.5	240s 180s	93.1 93.1	60.4 58.3	74 73	87.9 87.5	540s 324s

Nb cancer: nombre de cancer; CCIS: carcinome canalaire in situ; Se: sensibilité; Sp: spécificité; VPP: valeur prédictive positive, VPN: valeur prédictive négative

Dans notre service, les différentes études que nous avons menées n'incluent pas ces séquences T2 dans le protocole abrégé puisqu'elles ne nous semblent pas utiles comme indiqué par Heacock et al (12) et elles sont surtout très consommatrices de temps. Quoiqu'il en soit, quand un comparatif est réalisé entre le protocole complet et le protocole abrégé est réalisé, il n'est pas mis en évidence de différence significative des valeurs de sensibilité et de spécificité des deux protocoles. De plus, le temps d'interprétation est également diminué passant de plusieurs minutes pour le protocole complet à moins d'une minute pour le protocole abrégé. Ainsi, le protocole abrégé devrait avoir un impact considérable sur l'interprétation des images et devrait devenir le protocole de référence dans un futur proche (20).

Son interprétation même si elle est plus rapide que celle du protocole standard pose toutefois un certain nombre de problème. Le point essentiel concerne le fait que le lexique BI-RADS d'interprétation de l'American College of Radiology (ACR) ne prend pas en compte ce nouveau protocole. Ainsi, dans le lexique, la cinétique de rehaussement tumoral est prise en compte pour le classement des lésions (lésion bénigne/lésion à contrôler/ lésion à biopsier). Or cette cinétique n'est pas accessible dans le protocole abrégé puisqu'elle nécessite des acquisitions tardives à 7 minutes. Il s'agit là d'un écueil du protocole abrégé qui n'est quasiment

pas abordé dans la littérature puisqu'un seul article décrit la manière de classer ces lésions (21). Cela est toutefois indispensable pour éviter une certaine subjectivité dans ce classement.

Ainsi malgré ces nombreuses publications sur le sujet, la concordance en terme de prise en charge et de classement BI-RADS a été peu étudiée dans la littérature. Récemment, Panigrahi et al (22) et Oldrini et al (23) ont étudié le classement BI-RADS lésionnel entre les deux protocoles d'IRM. Il n'a pas été mis en évidence de différence entre les deux protocoles ce qui conforte l'idée que le protocole abrégé pourrait se substituer au protocole standard défini par les référentiels internationaux comme celui de the European Society of Breast Cancer Specialists (EUSOMA), et ce quelque soit les indications de l'examen et non exclusivement pour le dépistage des patientes à haut risque comme proposé initialement par Kuhl et al (4).

Conclusion et Perspectives

Le protocole abrégé en IRM devrait permettre de réduire les coûts et les délais d'attente d'IRM mammaire ce qui pourrait à terme augmenter les indications de cet examen dans le cadre du dépistage notamment. Cela nécessite toutefois des études prospectives à plus large échelle.

De plus, l'avènement des séquences à haute résolution temporelle devrait permettre, en adjonction du protocole abrégé, d'étudier le rehaussement initial des lésions dans les 45 premières secondes après injection.

Ainsi, Mann et al (17) ont suggéré que ces séquences pourraient permettre d'aider à caractériser les lésions par l'obtention de courbe cinétique tumorale pendant la première minute. De plus, Oldrini et al (21) ont également montré un bénéfice à l'utilisation de ces séquences en complément du protocole abrégé pour augmenter sa spécificité.

Cela nécessite toutefois des études ultérieures pour confirmer ces premières données.

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Conclusion du chapitre 2 :

Ces différents articles mettent en évidence l'intérêt de l'amélioration de la résolution temporelle des séquences en IRM et de la diminution du temps d'examen total. Le protocole abrégé semble donc un outil robuste pour remplacer à terme le protocole standard dans les recommandations des sociétés savantes nationales et internationales. Toutefois il nécessite encore des études prospectives à plus large échelle pour valider définitivement son utilisation en routine clinique.

Dans cette optique, nous avons prolongé ce travail de thèse par un dépôt de dossier à l'appel à projet PHRC-K 2017 qui fait l'objet du chapitre 3.

Chapitre 3 : Perspectives

Suite à ces différents travaux, nous avons déposé une lettre d'intention à l'appel à projet PHRC-K 2017 sous le titre **BREAST01 Validation de l'utilisation du protocole abrégé en IRM mammaire.**

Cette lettre d'intention a été retenue pour le deuxième tour et nous avons déposé le dossier le 11 septembre 2017. Il s'agit d'une étude prospective multicentrique française proposant d'inclure 1400 patientes et ayant pour objectif de montrer une non infériorité du protocole abrégé par rapport au protocole standard. Ce projet est détaillé dans le dossier ci-dessous.

Appel à projets national en cancérologie PHRC-K 2017

Programme hospitalier de recherche clinique en Cancérologie

Programme for Hospital Clinical Research in Cancer

Dossier de candidature /Full project

Le projet doit être rédigé en anglais

Date limite de soumission en ligne : 11 septembre 2017 minuit

http://www.e-cancer.fr/Institut-national-du-cancer/Appels-a-projets/Appels-a-projets-en-cours/PHRC-K-2017

Titre du projet :	
BREAST01 **Validation de l'utilisation du protocole abrégé en IRM mammaire.**	
Project title :	
BREAST01 **Validation of the use of an abbreviated BREAST MRI protocol**	
Mots clés *Keys words* **:**	**Breast MRI, Cancer**
Discipline, spécialité du projet *Project area* :	**Radiology**
Organe, localisation anatomique de la tumeur *Organ, tumor location :*	**Breast**
Nombre de patients *Patient number*	**1,400**

Autre (libre) *Other* :	

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Fonction et spécialité *Position and specialty :*	**Radiologist**
Service ou département *Unit or department* :	**Imaging department**
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Montant demandé arrondi au millier d'€ *Funding requested*	**536 K euros** Actualisation du financement prévisionnel de l'étude suite à la finalisation du projet

Résumé: (max. 700 mots)

Rationnel

L'imagerie par résonance magnétique (IRM) mammaire est devenue un outil diagnostique essentiel et largement accepté. Cependant, les examens respectant les recommandations de bonnes pratiques de la Société européenne des spécialistes du cancer du sein (EUSOMA) durent 30 minutes. Ainsi, l'IRM mammaire a des coûts directs et indirects élevés qui limitent son utilisation plus large, d'autant plus que les protocoles actuels d'IRM mammaire nécessitent un temps considérable pour l'acquisition et l'interprétation. En outre, comme c'est particulièrement le cas dans certains pays européens comme la France, le nombre d'IRM est actuellement insuffisant pour répondre à ses indications croissantes.

Kuhl et al. ont été les premiers à montrer que l'utilisation d'un protocole abrégé (le protocole «FAST») est réalisable sans compromettre la sensibilité et la spécificité par rapport au protocole conventionnel (le protocole «FULL») dans une population de femmes dépistées par IRM. Le protocole 'FAST' correspond au protocole 'FULL' qui s'arrête après la première série après injection. Alors que le protocole 'FULL' comprend plusieurs acquisitions avant injection qui nécessitent beaucoup de temps (acquisitions pondérées T2 et T1 et acquisitions 3D tardives), le protocole 'FAST' est limité au masque (3DT1 avant injection) et à un 3DT1 après injection qui permet de diminuer fortement le temps d'acquisition de 12 min 49 secondes à 2 min 52 secondes. L'utilisation d'un protocole 'FAST' permet non seulement un temps d'examen plus court, mais aussi une interprétation plus rapide par le radiologue. Ce protocole 'FAST' promet d'avoir un impact considérable sur l'interprétation et peut devenir le standard pour le dépistage du cancer du sein dans un proche avenir.

Plusieurs publications concernant cette question importante ont souligné la capacité d'un protocole abrégé à détecter les cancers dans certaines indications particulières (bilan local de cancer, discordance mammo-échographique ou dépistage des patientes à haut risque). Il y a peu d'études sur le protocole abrégé pour les indications d'IRM mammaire habituelles. En outre, dans les études publiées rétrospectivement, le gold-standard est basé uniquement sur les lésions prouvées histologiquement ce qui conduit à un biais de sélection. Le suivi systématique prospectif évitera un tel biais.

Objectifs
L'objectif principal de cette étude est de démontrer une non-infériorité de la sensibilité du protocole 'FAST' par rapport au protocole 'FULL'.
Les reproductibilités intra et inter-lecteurs seront évaluées pour les deux protocoles.

Une composante médico-économique évaluera les avantages d'un protocole abrégé s'il était appliqué dans la pratique réelle. Un modèle d'événements discrets sera développé pour évaluer l'augmentation de la capacité de réalisation d'IRM due au protocole 'FAST' dans les centres de cancérologie. Les informations recueillies seront également utiles pour effectuer un calcul des coûts du protocole 'FAST' par rapport à l'IRM classique.

Population
Toutes les femmes de plus de 18 ans ayant une indication d'IRM mammaire quelle que soit l'indication pourront être incluses.

Conception
Il s'agit d'une étude multicentrique prospective sur 1400 patientes dans les centres spécialisés français d'IRM mammaire. Chaque centre est un centre expert en France en IRM mammaire et les radiologues sont membres de la société française d'imagerie de la femme (SIFEM).
Chaque IRM sera effectuée dans chaque centre selon le protocole habituel (c'est-à-dire le protocole 'FULL'). Les soins aux patientes ne seront pas modifiés par l'étude puisque la lecture de l'IRM mammaire, pour l'étude, se fera en dehors des soins standards. Les patientes seront surveillées selon la pratique clinique habituelle.
La lecture des deux protocoles (c'est-à-dire le «FULL» et le «FAST») sera effectuée dans chaque centre par un radiologue expérimenté, de manière indépendante et dans un ordre aléatoire avec au moins un délai de deux mois entre les deux lectures.
Toutes les patientes seront contactées par téléphone à 12 et 24 mois après la réalisation de l'IRM par une infirmière de recherche clinique pour déterminer si les patientes ont réalisé d'autre(s) imagerie(s) mammaire(s), quels en étaient les résultats et si elles présentent des pathologies mammaires.

Centres participants
Cette étude concerne 7 centres français experts en IRM mammaire. Tous les investigateurs principaux sont membres de la SIFEM. Dans ces 7 centres, 53 IRM mammaires sont effectuées en moyenne par mois et par centre, ce qui permet ce niveau de recrutement (6600 patients incluables pendant la durée d'inclusion de 18 mois).

Abstract: (max. 700 words)

Rationale
Breast magnetic resonance imaging (MRI) has gained widespread acceptance as an essential diagnostic tool. However, examinations that adhere to the good practice recommendations of the European Society of Breast Cancer Specialists (EUSOMA) currently require 30 minutes for completion. Breast MRI has high direct and indirect costs that limit its wider use, especially since current breast MRI protocols require considerable time for acquisition and interpretation. Furthermore, in some European countries such as France, the number of MR scanners is currently insufficient to accommodate the rising demand for breast MRI.
Kuhl et al. were the first to show that use of an abbreviated MRI protocol (the 'FAST' protocol) does not compromise the sensitivity or the specificity in comparison to the conventional MRI protocol (the 'FULL' protocol) in a population of women undergoing breast cancer screening. Whereas the 'FULL' protocol includes several time-consuming acquisitions before contrast injection (T2 and T1 weighted

acquisitions) and late 3DT1 acquisitions, the 'FAST' protocol is limited to just the mask (3DT1 precontrast) and one 3DT1 sequence after contrast injection, which allows for a sharp decrease in acquisition time from 12 minutes 49 seconds to 2 minutes 52 seconds. The use of the 'FAST' protocol allows not only for a shorter examination time but also for a faster interpretation by the radiologist. Moreover, the 'FAST' protocol promises to have a considerable impact on image interpretation and may become the standard for breast cancer screening in the near future.
Several publications regarding this novel 'FAST' protocol have underscored the ability of an abbreviated MR screening to be useful for breast cancer staging, high-risk screening, and in the case of equivocal mammography/ultrasound findings. However, in general there have been few studies of the abbreviated protocol for all breast MRI indications. Additionally, the gold standard in retrospective published studies is based on histological proof, which can lead to selection bias. The use of systematic follow-up will avoid such bias.

Objectives
The main objective of this study is to demonstrate a non-inferiority of the sensitivity of the 'FAST' breast MRI protocol compared to 'FULL' breast MRI protocol.
Reproducibility between intra and inter-readers will be evaluated for both protocols.
A medico-economic component will evaluate the benefits of an abbreviated protocol if it were to be applied in real-life practice. A discrete events model will be developed to assess the increase in breast MRI capacity if the FAST protocol were to be implemented in cancer centres. The information gathered will also be useful for conducting micro costing of the FAST protocol compared to conventional breast MRI.

Population
Women over 18 with any indication for breast MRI may be included.

Design
This is a prospective multicentre study to be undertaken in French expert centres of breast MRI on 1400 patients. Each centre is an expert centre in France of breast MRI and all radiologists taking part in the study are members of the SIFEM (French society of woman imaging).
Each MRI protocol will be done in each centre according to the normal protocol (i.e. the 'FULL' protocol). Patient care will not be affected by study. Indeed, a reading of the breast MRI outside the study will be done in standard clinical practice for patient care. Patients will be monitored according to standard clinical practices.
Reading of the two protocols (i.e. 'FULL' and 'FAST' protocols) will be carried out at each medical centre by an experienced radiologist. Further, readings will be performed independently, in a random order, with at least two months between them.
All patients will be contacted by phone 12 and 24 months after their breast MRI by a clinical research nurse to determine whether patients i) underwent further breast imaging, and if so what the results were, and ii) to enquire regarding the presence of clinical mammary problems.

Participating Centres
This study involves seven leading French centres in breast MRI. All principal investigators are members of the SIFEM (French society of woman imaging). An average of 53 breast MRIs are performed each month in these 7 centres, for a theoretical pool of 6600 patients during the inclusion period of 18 months.

SYNOPSIS

Title	Validation of the use of an abbreviated BREAST MRI protocol
Acronyme	BREAST01
Sponsor	Institut de Cancérologie de Lorraine
Study	Prospective multicenter study in French expert centers of breast MRI.
Center	7 French centers
Coordinator	Dr Guillaume OLDRINI
Co-Coordinators	Dr Corinne BALLEYGUIER
Main objective	The main objective of this study is to demonstrate a non-inferiority of the sensitivity of the abbreviated (FAST) breast MRI protocol compared to the complete regular (FULL) breast MRI protocol.
Secondary Objectives	• To assess the specificity and diagnostic performance of the FAST protocol compared to the FULL protocol. • To assess the agreement between the FAST and FULL protocols. • To assess the sensitivity, specificity and diagnostic performance at the lesion level for the two protocols. • To assess inter- and intra-observer reproducibility for the FAST and FULL protocols. • To evaluate the interpretation time for each protocol. • To evaluate the addition of a high temporal resolution acquisition (ULTRAFAST protocol) to the FAST protocol (no funding is requested for this objective).
Inclusion Criteria	• Women with an indication for breast magnetic resonance imaging (MRI), regardless of the type of the indication • More than 18 years of age
Non Inclusion Criteria	• Contraindication for breast MRI • Contraindication for MRI contrast agent media
Primary End Point	The primary endpoint will be the sensitivity of the FAST and FULL protocols to detect breast cancer. The histological findings and 24 month follow up will be used as the reference standard. Specifically, the sensitivity of each protocol corresponds to the number of women with at least one lesion classified on the BI-RADS scale as a 4, 5 or 6 (women requiring histological proof) out of the total number of women having a breast cancer diagnosis in the same breast within 24 months after imaging.
Estimated Enrollment	1400 patients
Planned Schedule	• Duration of project : 42 months • Duration of participation of each patient : 24 months • Duration of recruitment : 18 months
Design	This is a prospective multicentre study in French expert centres of breast MRI on 1400 patients. Each centre is expert centre in France of breast MRI and radiologists are members of the SIFEM (French society of woman imaging). Each MRI will be done in each centre according to routine protocol which is called FULL protocol. Included patient care will not be changed by study. Indeed, a reading of breast MR outside the study will be done in routine clinic for patient care. A reading of every MRI will be performed according to two protocols (i.e. the FULL protocol and the FAST protocol) at each medical centre by an experienced radiologist and will be performed independently, in a random order with at least two months between two readings. All patients will be contacted by phone at 12 and 24 months after MRI realization by a

	clinical research nurse to determine whether patients underwent further breast imaging, what the results of these were, and to enquire regarding the presence of clinical mammary problems. A reproducibility study on 60 MRI will be carried out to assess intra and inter reading reproducibility for both protocols.
Statistical Analysis	The sensitivities of FAST and FULL protocol will be computed. The difference between the sensitivities will be calculated (FULL minus FAST). The 95% intervals of this difference between these two sensitivities will be computed. If the upper bound of this 95% confidence is less than 5 (the non-inferiority margin), the FAST protocol will be non-inferior as the FULL in term of sensitivity. If the upper bound of this 95% confidence is less than 0, the P value associated with a Mac Nemar test will be performed to evaluate the superiority of the FAST protocol. The specificities, the diagnostic accuracy, the positive and negative predictive values of each protocol will be computed with their 95% confidence interval. The specificities will be compared between the both protocols by a Mac Nemar test.

Conclusion

L'IRM est un élément essentiel de l'arsenal d'imagerie mammaire. Sa place a augmenté au fur et à mesure des années et de son développement. Il persiste un certain nombre de points à améliorer. Dans le 1er chapitre, nous avons vu que le décubitus avait un certain nombre d'avantages par rapport au positionnement standard d'un point de vue médical avec une meilleure corrélation avec l'échographie mais également du point de vue des patientes avec une meilleure tolérance. Pour son développement à plus large échelle, il nécessite des antennes dédiées pour améliorer la qualité des images et la mise au point de technique de correction des mouvements respiratoires et cardiaques.

Le développement encore plus important de l'IRM dans l'imagerie mammaire pourrait être accéléré par le protocole abrégé. En effet, il présente de nombreux avantages dans différents aspects. Il diminue le temps d'examen pour les patientes et la collectivité ; Son temps d'interprétation est également plus court. Enfin, il ne semble pas inférieur en terme de sensibilité, de spécificité et d'efficacité diagnostique avec le protocole complet alors que le temps d'acquisition est réduit par un facteur 5. L'adjonction de séquences à haute résolution temporelle devrait également permettre d'améliorer sa spécificité qui pourrait ainsi être meilleure que celle du protocole complet et ainsi diminuer les biopsies de lésion finalement bénignes.

Ces différents éléments nécessitent toutefois des études à plus large échelle et le dossier soumis à l'appel à projet PHRC-K 2017 devrait permettre de conforter ces données.

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Résumé

L'IRM mammaire a une place prépondérante dans l'imagerie mammaire. Son utilisation plus large est limitée notamment par son coût et le nombre limité de machines. Nous avons travaillé sur plusieurs aspects de cette problématique. Dans un premier temps, nous avons modifié le positionnement en passant du procubitus au décubitus. Ceci a permis de montrer que le décubitus permettait une meilleure corrélation topographique des lésions avec l'échographie et était mieux toléré par les patientes. Dans un deuxième temps, nous avons étudié les facteurs de réduction du temps d'acquisition par l'intermédiaire des séquences à haute résolution temporelle et d'un protocole abrégé. Ces changements devraient permettre de faciliter l'accessibilité de l'IRM aux patientes, de réduire son coût tout en conservant les mêmes valeurs de sensibilité et spécificité que le protocole standard.

Mots-clés : IRM mammaire, cancer, dépistage, protocole abrégé, positionnement

Abstract

Breast MRI has a prominent place in breast imaging. Its wider use is limited in particular by its cost and the limited number of machines. We have worked on several aspects of this problem. In a first step, we changed the positioning from procubitus to decubitus. This showed that the decubitus allowed a better topographic correlation of the lesions with the ultrasound and was better tolerated by the patients. In a second step, we studied the factors of reduction of the acquisition time via the sequences with high temporal resolution and an abbreviated protocol. These changes should make it easier for patients to access MRI, reduce costs while maintaining the same sensitivity and specificity values as the standard protocol.

Keywords: Breast MRI, cancer, screening, abbreviated protocol, positionning