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BREAST RADIOLOGY
*SENOLOGIA*

# Correlation between breast density in mammography and background enhancement in MR mammography

# *Correlazione tra densità mammaria in mammografia e background enhancement in risonanza magnetica della mammella*

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**Abstract**
***Purpose.*** We aimed to analyse the influence of mammographic breast density on background enhancement (BE) at magnetic resonance (MR) mammography in pre- and postmenopausal women. In addition, we questioned predictability of contrast-enhancement dynamics of normal fibroglandular tissue (NFT) at MR mammography according to mammographic breast density.
***Materials and methods.*** Twenty-six patients (mean age 51.54±11.5 years; range 37–79 years) who underwent both MR mammography and conventional mammography were included in this retrospective study. Fourteen patients were premenopausal and 12 were postmenopausal. The ethics committee of our institution approved the study. The mammograms were retrospectively reviewed for overall breast density according to the four-point scale (I–IV) of the Breast Imaging Reporting and Data System (BI-RADS) classification. Two radiologists, who were unaware of the clinical data, separately assessed the MR mammography images. Images were assessed for enhancement kinetic features (enhancement kinetic curve and the early-phase enhancement rate) and BE. MR mammography and conventional mammography findings were compared according to BI-RADS breast density category and menopausal status.
***Results.*** Percentage of increased signal intensity values during the first minute did not change according to mammographic breast density, and the mean early-phase enhancement rate scores were similar among breast density groups ($p$=0.942). There was no significant difference between pre- and postmenopausal groups. Enhancement

***Riassunto***
***Obiettivo.*** *Scopo del nostro studio è analizzare l'influenza della densità mammografica del seno sul background enhancement in risonanza magnetica, considerando donne in pre e post-menopausa.*
*È stata inoltre valutata la prevedibilità delle dinamiche di contrast-enhancement del tessuto fibroghiandolare normale (NFT) in RM, in rapporto alla densità mammografica del seno.*
***Materiali e metodi.*** *In questo studio retrospettivo sono state incluse 26 pazienti (media di età 51,54±11,5; range 37–79 anni), sottoposte sia a RM sia a mammografia convenzionale. Quattordici pazienti erano in pre-menopausa e dodici in post-menopausa. Lo studio è stato approvato dal comitato etico del nostro istituto. Gli esami sono stati analizzati retospettivamente per valutare la densità complessiva del seno, in accordo con la scala di quattro punti (I-IV) basata sulla classificazione BI-RADS (Breast Imaging Repotring and Data System).*
*Due radiologi, senza conoscere i dati clinici, separatamente, hanno valutato le immagini RM.*
*Sono state analizzate le caratteristiche cinetiche di enhancement (curva della cinetica di enhancement e velocità della fase precoce di enhancement) e il background enhancement.*
*I rilievi ottenuti in RM e in mammografia convenzionale sono poi stati comparati con la classificazione BI-RADS, e lo stato menopausale.*
***Risultati****. La percentuale di valori con intensità del segnale aumentato durante i primi minuti non è risultata variare in rapporto alla densità mammografica del seno, e i valori*

kinetic features of the different groups based on BI-RADS breast density category and menopausal status were similar. There was no correlation between breast density and BE in either premenopausal ($p$=0.211) or in postmenopausal ($p$=0.735) groups.
***Conclusions.*** We determined no correlation between mammographic breast density and so-called BE in MR mammography in either premenopausal or postmenopausal women. NFT at MR mammography cannot be predicted on the basis of mammographic breast density.

**Keywords** Breast · Breast density · Mammography · Magnetic resonance imaging

*medi di velocità di enhancement in fase precoce sono risultati simili tra i gruppi di densità del seno (p=0,942). Non sono emerse differenze significative tra gruppi pre e post-menopausa.*
*Le cinetiche di enhancement dei differenti gruppi basati sulla classificazione di densità del seno (BI-RADS) e sullo stato menopausale, sono risultati simili. Non è stata evidenziata correlazione tra densità mammaria e background enhancement nei gruppi premenopausa (p=0,211),o postmenopausa (p=0,735).*
***Conclusioni****. Non abbiamo rilevato correlazione tra la densità del seno in mammografia e il cosiddetto background enhancement in risonanza magnetica, né per quanto riguarda donne in pre-menopausa, né in post-menopausa. Il tessuto fibroghiandolare in RM non può essere correlato alla densità mammaria mammografica.*

***Parole chiave*** *Seno · Densità mammaria · Mammografia · Immagini di risonanza magnetica*

## Introduction

Radiographically, the breast consists mainly of two component tissues: fibroglandular tissue and fat. Fibroglandular tissue (fibrous connective tissue and glandular epithelial cells) forms mammographic density [1]. Mammographic density has been shown to be a strong independent risk factor for the development of breast cancer [2–5]. High breast density decreases the sensitivity of detecting breast cancer on conventional mammography [6]. In such cases, in addition to conventional mammography, ultrasonography and contrast-enhanced magnetic resonance (MR) mammography can be performed [7].

MR mammography for detecting cancer is the most sensitive of all imaging techniques and has been used for two decades. It is a problem-solving modality when conventional mammography and ultrasonography findings are inadequate [8–11]. It is different from the other breast-screening modalities (conventional mammography and ultrasonography) in that it adds functional information to the morphological data on normal fibroglandular tissue (NFT) [12]. At MR mammography, tissue perfusion and enhancement kinetics of NFT and breast lesions can be evaluated. Recent studies have investigated the characteristics of NFT enhancement kinetics. These studies also discuss factors such as age, menstrual or menopausal status and hormone replacement therapy, which may affect NFT enhancement kinetics [13–16].

Fibroglandular parenchyma enhances at MR mammography. The term background enhancement (BE) refers to NFT enhancement [13]. It is usually bilateral and symmetrical. Intensely enhancing NFT may obscure underlying malignancy. Background enhancement at MR mammography decreases the technique's sensitivity and increases false positives, as does breast density at conventional mammography [12, 17, 18]. To our knowledge, no published study to date has investigated the relationship between breast density on conventional mammography and BE in MR mammography. This study aimed to analyse the influence of mammographic breast density on BE at MR mammography in pre- and postmenopausal women. In addition, we questioned the predictability of NFT contrast-enhancement dynamics at MR mammography according to mammographic breast density.

## Materials and methods

### Patients

Seventy-nine patients who underwent both MR mammography and conventional mammography at our institution were included in this retrospective study. We excluded women who were in the perimenopausal period (n=2), in the third or fourth week of their menstrual cycle (n=14), had an irregular cycle (n=12), were postmenopausal and on hormone replacement therapy at the time of the study and/or within the previous 6 months (n=12) and who had received chemotherapy within the previous 6 months. Twenty-six patients remained in the study, which was approved by the ethics committee of our institution.

Mean patient age was 51.54±11.5 (range 37–79) years.

Fourteen patients were premenopausal and 12 were postmenopausal. In premenopausal women, both imaging modalities were performed on the same day of the same or subsequent cycle. As premenopausal women usually undergo breast MR imaging and conventional mammography between the fifth and 12th day after the start of the menstrual cycle, the same time frame was used [13, 19, 20].

MR mammography indications were different, as ten patients had proven breast cancer. Patients with breast cancer underwent MR mammography for preoperative staging (n=3), for evaluating the remaining breast after mastectomy (n=4) and for examining both breasts after conservative breast surgery (n=3). In patients with breast cancer, evaluations were performed on the other breast, which was not affected by cancer or radiation therapy. Patients without breast cancer underwent MR mammography as a problem-solving tool to characterise lesions detected at ultrasonography and conventional mammography. In these cases, evaluation was not performed on the breast with suspicious lesions but on the contralateral breast. With the criteria described above, only one breast for each patient was included in the study.

## MR mammography

Breast MR imaging was performed on a 1.5-T imager (Intera, Philips Medical Systems, Best, The Netherlands) with a dedicated double-breast surface coil and bilateral scans. Before the examination, a needle for intravenous administration of contrast agent was placed in a cubital vein and the patient placed in a comfortable prone position. A transverse three-dimensional high-resolution T1-weighted fast gradient echo fat-suppressed sequence [TE/TR 2.4/4.6 ms; inversion delay spectral presaturation attenuated by inversion recovery (SPAIR) 90 ms; flip angle 10°; FOV 360×360 mm$^2$, acquired voxel size 0.9×0.9×2.5 mm$^3$, reconstructed voxel size 0.83×0.83×2.50 mm$^3$, total acquisition time 60 s] was performed before administration of contrast agent, followed by repeat performance of this same sequence at 0, 1, 2, 3, 4, 5, and 6 min after administration of contrast agent. An additional transverse T2-weighted fat suppressed spin echo sequence (TE/TR 110/7548 ms; inversion delay SPAIR 80 ms; flip angle 90°; FOV 380×380 mm$^2$, acquired voxel size 1.06×1.74×3.0 mm$^3$, reconstructed voxel size 0.94×0.94×3.00 mm$^3$, total acquisition time 242 s) was performed before administration of contrast material. Postcontrast three-dimensional T1-weighted fast gradient-echo dynamic MR images were acquired after administration 0.1 mmol/kg gadolinium diethylenetriamine pentaacetic acid (Gd-DTPA).

## Image interpretation

One author (BN) retrospectively reviewed the conventional mammography results for overall breast density according to the four-point scale (I–IV) of the Breast Imaging Reporting and Data System (BI-RADS) classification [21]. The density scoring system has four categories: BI-RADS 1 indicates a predominantly fatty breast, BI-RADS 2 scattered fibroglandular densities, BI-RADS 3 heterogeneous density

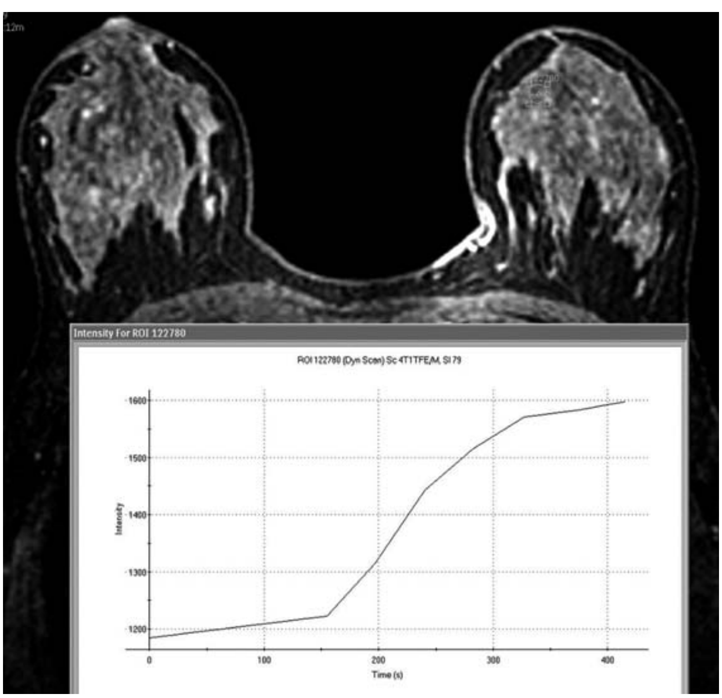


**Fig. 1** Enhancement of normal fibroglandular tissue (NFT) in a normal breast: NFT enhances gradually during the initial phase but continues to enhance persistently in the late phase.

***Fig. 1*** *Enhancement del tessuto fibroghiandolare normale in un seno normale: il tessuto si impregna gradualmente durante la fase iniziale, ma continua anche nelle fasi successive.*

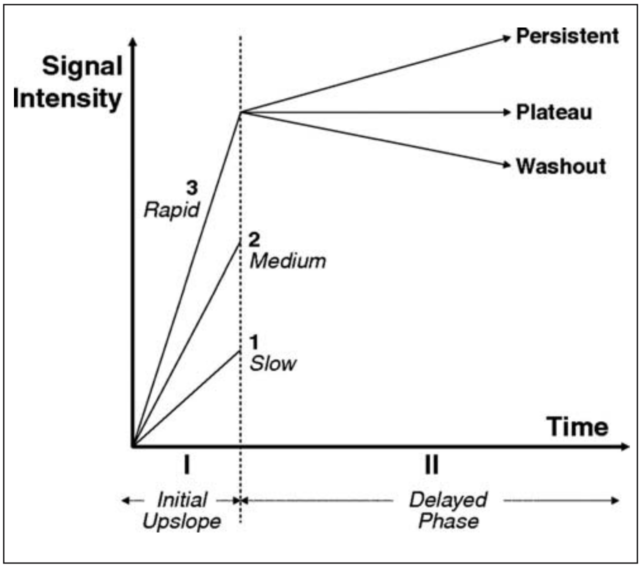


**Fig. 2** Time-signal intensity curves of dynamic contrast enhancement based on enhancement kinetic features according to the American College of Radiology BI-RADS MRI lexicon.

***Fig. 2*** *Curva tempo-intensità del segnale della dinamica contrastografica, basata sulle caratteristiche cinetiche di impregnazione in RM secondo l'American College of Radiology Brest Imaging Reporting end Data System - BI-RADS -.*

and BI-RADS 4 extremely dense breast tissue.

MR images were interpreted by two radiologists experienced in breast MR imaging, who were blinded to the mammographic breast density. Two authors (RC, NT) with 4 and 7 years' experience, respectively, reading breast MR images reviewed the studies to reach a consensus regarding the findings. Before BE assessments NFT, enhancement kinetic features (enhancement curve, early-phase enhancement rate) were measured in a region of interest (ROI) containing entirely NFT to evaluate contrast-medium enhancement at 0–6 min after gadopentetate dimeglumine injection. ROI size less than three pixels was avoided (Fig. 1). Thus, we obtained quantitative/semiquantitative data about the enhancement kinetic features of breast parenchyma on which we performed visual assessments for BE. MR imaging diagnosis was based on enhancement kinetic features according to the American College of Radiology BI-RADS MRI lexicon (Fig. 2). Enhancement kinetic curve evaluation was based on the initial phase (within the first 2 min or when the curve began to change) and the late phase (after 2 min or after the change). The initial enhancement phase is further categorised into fast, medium, slow. The late enhancement phase is described as persistent, plateau and washout [21]. The early-phase enhancement rate (percentage of 1-min signal intensity increase) was quantified by an ROI-based determination of the signal intensity of normal glandular tissue before and after injection of gadopentetate dimeglumine. To assess the early-phase increase in signal intensity, we calculated the enhancement for the first postcontrast image. The early-phase enhancement rate was calculated according to the enhancement formula [(SI post- SI pre/SI pre)]×100% (SI pre: baseline signal intensity, SI post: signal intensity after contrast injection).

At dynamic MR mammography, BE was evaluated visually in all the postcontrast series of the same breast of each patient and enhancement kinetic features were analysed. Patients were divided into four subgroups according to BE [12]. If NFT enhanced strongly and diffusely, it was categorised as severe BE; slight or no enhancement (even in the late postcontrast phase) was defined as absent or minimal BE. According to the criteria above, "mild and moderate BE" was subjectively classified intermediate.

### Statistical analysis

Statistical Package for the Social Sciences (SPSS vs 11.0) was used for statistical analysis. As the data was not normally distributed, we used nonparametric tests. To compare pre- and postmenopausal patients, we used the Mann–Whitney *U* test, and to compare BI-RADS breast-density groups (2, 3 and 4) we used the Kruskal–Wallis test. To compare the relationship between breast-density groups and contrast pattern (initial- and late-enhancement phases) and BE, e used the chi-square test.

## Results

At conventional mammography, there were 11 cases (42%) with BI-RADS breast density category 2, nine (35%) with BI-RADS category 3 and six (23%) with BI-RADS category 4. Patients with BI-RADS 4 were all in the premenopausal period, and the age range was 37–49 years. No patient was considered to have fatty breast parenchyma (Table 1). Mean breast density score was 3.3±0.7 in the premenopausal group and 2.3±0.5 in the postmenopausal group. The difference between the two groups was statistically significant ($p$=0.001) (Table 2)

During enhancement kinetic curve assessment, two cases (8%) were had medium contrast enhancement at the initial phase, whereas slow enhancement was determined in the remaining 24 cases (92%). At the late-enhancement phase, all cases had persistent curves. There were no cases with plateau or washout-type enhancement curve (Table 1). Early-phase enhancement rates varied between 13% and 58%. The percentage of first-minute signal intensity increase values did not change according to mammographic breast density, and mean early-phase enhancement rate

**Table 1** Summary of imaging findings and patient data in 26 patients
***Tabella 1*** *Sommario degli aspetti all'imaging e delle caratteristiche dei 26 pazienti*

| Patient No. | Age | Menopausal status | BI-RADS breast density category | 1-minute signal intensity increase | Background enhancement | Initial enhancement phase | Late enhancement phase |
|---|---|---|---|---|---|---|---|
| 1 | 37 | Premenopausal | 4 | 35 | Severe | Slow | Persistent |
| 2 | 37 | Premenopausal | 4 | 24 | Moderate | Slow | Persistent |
| 3 | 40 | Premenopausal | 3 | 42 | Severe | Slow | Persistent |
| 4 | 37 | Premenopausal | 4 | 46 | Severe | Slow | Persistent |
| 5 | 49 | Premenopausal | 3 | 13 | Moderate | Slow | Persistent |
| 6 | 44 | Premenopausal | 2 | 13 | Moderate | Slow | Persistent |
| 7 | 43 | Premenopausal | 2 | 30 | Severe | Slow | Persistent |
| 8 | 48 | Premenopausal | 4 | 27 | Severe | Slow | Persistent |
| 9 | 41 | Premenopausal | 3 | 26 | Moderate | Slow | Persistent |
| 10 | 47 | Premenopausal | 4 | 27 | Severe | Slow | Persistent |
| 11 | 49 | Premenopausal | 4 | 13 | Severe | Slow | Persistent |
| 12 | 43 | Premenopausal | 3 | 38 | Moderate | Slow | Persistent |
| 13 | 43 | Premenopausal | 3 | 47 | Moderate | Slow | Persistent |
| 14 | 45 | Premenopausal | 3 | 27 | Severe | Slow | Persistent |
| 15 | 79 | Postmenopausal | 2 | 19 | Moderate | Slow | Persistent |
| 16 | 58 | Postmenopausal | 2 | 25 | Moderate | Slow | Persistent |
| 17 | 54 | Postmenopausal | 2 | 13 | Moderate | Slow | Persistent |
| 18 | 64 | Postmenopausal | 3 | 18 | Moderate | Slow | Persistent |
| 19 | 62 | Postmenopausal | 3 | 16 | Mild | Slow | Persistent |
| 20 | 56 | Postmenopausal | 2 | 14 | Moderate | Slow | Persistent |
| 21 | 57 | Postmenopausal | 2 | 33 | Mild | Slow | Persistent |
| 22 | 59 | Postmenopausal | 2 | 52 | Mild | Medium | Persistent |
| 23 | 54 | Postmenopausal | 2 | 19 | Mild | Slow | Persistent |
| 24 | 75 | Postmenopausal | 2 | 58 | Mild | Medium | Persistent |
| 25 | 49 | Postmenopausal | 3 | 20 | Moderate | Slow | Persistent |
| 26 | 70 | Postmenopausal | 2 | 33 | Moderate | Slow | Persistent |

*BI-RADS,* Breast Imaging Reporting and Data System

**Table 2** Breast Imaging Reporting and Data System (BI-RADS) breast density categories according to menopausal status
***Tabella 2*** *Categorie di densità mammaria secondo il Breast Imaging Reporting and Data System (BI-RADS) in relazione allo stato menopausale*

| Menopausal status | BI-RADS breast density category | | |
|---|---|---|---|
| | Mean | Standard deviation | Mean standard error |
| Premenopausal (n=14) | 3.2857 | 0.72627 | 0.19410 |
| Postmenopausal (n=12) | 2.2500 | 0.45227 | 0.13056 |

scores were similar among breast-density groups ($p$=0.942) (Table 3). Mean early-phase enhancement rate scores in the premenopausal group were 29.14±11.48 and in the postmenopausal group 26.66±14.78 ($p$=0.455). There was no significant difference between pre- and postmenopausal groups (Fig. 3). With these results, we concluded that enhancement kinetic features of the different groups, which were created according to BI-RADS breast density category and menopausal status, were similar.

BE values were mild in five cases (19%), moderate in 13 (50%) and severe in eight (31%). Absent or minimal BE was not determined. In 14 premenopausal cases, moderate enhancement was defined in six and severe enhancement in eight, whereas 12 postmenopausal cases showed moderate (n=7) or mild (n=5) enhancement (Table 1). There was no correlation between breast density and BE in either the premenopausal ($p$=0.211) or postmenopausal ($p$=0.735) group.

## Discussion

High mammographic density not only increases breast cancer risk but also decreases the detection rate of breast

**Table 3** Relationship between the early-phase enhancement rate and Breast Imaging Reporting and Data System (BI-RADS) breast density category
***Tabella 3*** *Relazione tra la fase iniziale di enhancement e le categorie di densità del seno secondo BI-RADS*

| BI-RADS breast density category | 1-min signal intensity increase (%) | | | |
|---|---|---|---|---|
| | Minimum | Maximum | Mean | Standard deviation |
| 2 (n=11) | 13.00 | 58.00 | 28.0909 | 15.31962 |
| 3 (n=9) | 13.00 | 47.00 | 27.4444 | 12.20769 |
| 4 (n=6) | 13.00 | 46.00 | 28.6667 | 11.07550 |

cancer at mammography, especially in the premenopausal population [22–26]. MR mammography is frequently used as an auxiliary modality in patients with dense breast pattern. In this study, we investigated the effect of breast density on BE in MR mammography. We also questioned the predictive value of mammographic density for the NFT contrast enhancement pattern. NFT shows highly variable contrast enhancement that depends on hormonal status [12, 18]. NFT enhances gradually but persistently after contrast-medium injection. In MR mammography, all patients showed this contrast enhancement pattern regardless of their breast density and menopausal status.

The percentage of first-minute increase in signal intensity indicted the early-phase enhancement rate, which allows calculation of the amount of initial enhancement. After the contrast-medium injection, in the early few minutes, breast cancer shows a contrast enhancement peak because of its highly vascularised structure, which helps delineate its borders on NFT in this particular phase. Later on, the affected area loses its signal and the contrast between NFT and the cancer region decreases. This rapid decrease in signal intensity is referred to as washout. However, sometimes, NFT may enhance quickly and intensely in the initial phase and may mask the underlying cancer [8, 12, 17]. Therefore, initial studies in the 1990s claimed that MR mammography had low sensitivity, especially in women with secretory diseases, inflammatory processes, proliferating changes or who were premenopausal [27, 28]. Nonetheless, recent studies have shown that for detecting breast cancer, MR imaging has the greatest sensitivity of all imaging techniques [9, 11, 25]. Especially in cases of diffusely growing invasive cancers or in medullar cancers with benign morphological appearance, MR mammography has greater sensitivity compared with conventional mammography [29–32]. In our study, mammographic breast density or menopausal status had no significant effect on the early-phase enhancement rate. Our results are consistent with previous studies. This study also confirms that MR mammography is an effective imaging method in premenopausal women. Compared with the postmenopausal group, higher mammographic breast density in premenopausal women may cause difficulties in detection or may obscure the cancer in conventional mammography [24]. In our study, the breast densities of premenopausal women were significantly higher than those of postmenopausal women. Yet the early-phase enhancement rate did not change according to breast densities in either group.

The term BE refers to NFT enhancement at MR mammography. BE does not always correspond to mammographic density [12]. In other words, extremely dense breasts may show absent or mild BE, whereas mildly dense breasts may have moderate or marked BE on MR mammography. Subjectively and volumetrically, BE is usually categorised into four groups: absent or minimal, mild, moderate and marked or severe [12, 18]. Moderate and severe BE may hide the underlying breast cancer. Teifke et al., in their study of 354 patients, reported 41 missed cancers. Among them, quick and intense enhancement of the surrounding NFT caused false negative results in three cases [17]. In our study, we found no relationship between BE and breast density in either the premenopausal or postmenopausal group. Despite the significant difference shown on mammography between breast densities of these two groups, BE was not affected by menopausal status. This was consistent with previous studies. BE is more prominent at the luteal phase of the cycle in premenopausal women [13, 20]. In our study, to equalise the hormonal factors affecting BE, MR mammography and conventional mammography were performed between the fifth and 12th day of the menstrual cycle in all premenopausal cases. We excluded women with irregular cycles or receiving hormone replacement therapy. High breast density, which decreases the sensitivity of conventional mammography, does not correlate with BE in MR mammography. Therefore, MR mammography is thought to have higher diagnostic value in dense breasts [6, 12, 17, 18, 25, 26]. The authors of recent review articles recommend that BE should be written on MR mammography reports and that it should be included in updates of the BI-RADS MRI lexicon [12, 18]. Furthermore, these authors report that radiologists should note moderate or marked BE on MR mammography reports to inform physicians about the sensitivity of the examination. We believe that our study with homogenously selected patients may contribute to this topic by revealing that menopausal status has no significant effect on BE.

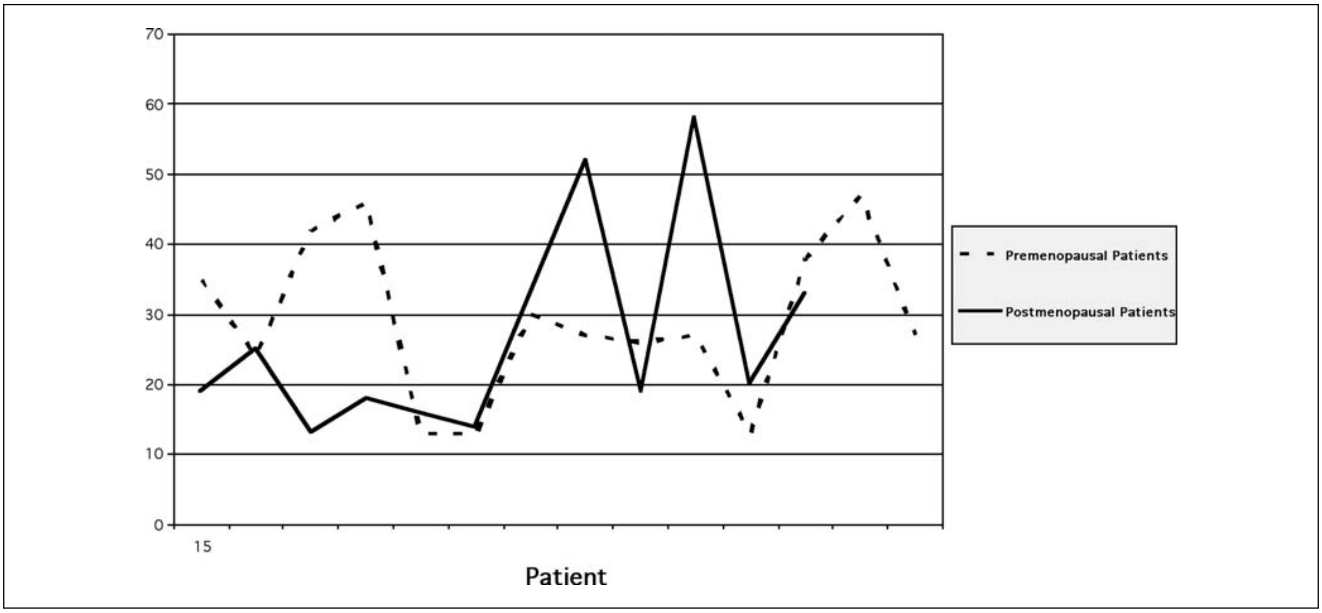


**Fig. 3** Comparison of mean early-phase enhancement rates in pre- and postmenopausal women.
***Fig. 3*** *Confronto tra valori medi di enhancement in fase precoce in donne in pre e post-menopausa.*

This study had a limited number of subjects because it is difficult to recruit patients who underwent both conventional and MR mammography during the same period of their cycle. Moreover, patients undergoing both examinations tend to be complex cases with a history of radiation therapy or chemotherapy or both, and these were our exclusion criteria. In our study, we had no women with American College of Radiology type 1 breast density, which may be perceived as a limitation. However, with very rare exceptions, breasts with complete fatty involution can be easily evaluated with conventional mammography without the need for MR mammography.

In conclusion, we determined no correlation between mammographic breast density and so-called BE in MR mammography in either premenopausal or postmenopausal women. NFT at MR mammography cannot be predicted on the basis of mammographic breast density. MR mammography is a reliable technique that can be used in patients with high breast density regardless of menopausal status.

**Conflict of interest** None

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