# **REVIEW**

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# The many MRI faces of invasive lobular carcinoma: a pictorial essay



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# Abstract

**Background** Invasive lobular cancer is the second most common subtype of invasive breast cancer. Due to the wide diversity of histopathological, clinical, and radiological presentations, it can provide diagnostic and therapeutic challenges. Magnetic resonance imaging (MRI) has the highest sensitivity for its detection and the most accurate determination of invasive lobular cancer extent. The aim of our pictorial review was to demonstrate the different presentations of invasive lobular cancer on MRI and thus facilitate the interpretation of imaging findings for radiologists.

**Main body of the abstract** The pictorial essay carefully extracted six different MRI presentations of an invasive lobular cancer with brief histopathological and clinical patient data. We showed that invasive lobular cancer presentation on MRI varied, ranged from a single focus to single and multiple lesions, non-mass enhancements of various distributions, and in some cases with nonspecific enhancement curves.

**Conclusions** This pictorial essay presented a spectrum of MRI findings of invasive lobular cancer, showing the variety of their appearances. Considering the variety of MRI imaging, the radiologist sometimes has to look for other diagnostic methods for the final interpretation of the imaging findings. We believe that the presentation of different cases will educate radiologists and help in making appropriate diagnostic and therapeutic decisions.

Keywords Breast, Cancer, MRI, Diagnosis, Contrast agents

# Background

After invasive ductal carcinoma, invasive lobular carcinoma is the second most prevalent breast malignancy. It forms in the breast milk-producing glands known as lobules, and it is often luminal A intrinsic subtype, estrogen and progesterone receptor positive, and human epidermal growth factor receptor 2 negative [1, 2]. Invasive lobular carcinoma frequently has diffuse, spider web, and irregular growth patterns with minimal or no desmoplastic reaction, thus preserving breast architecture

<sup>3</sup> University Department of Health Studies, University of Split, Rudera Boškovića 35, 21000 Split, Croatia [3, 4]. It can occur multifocally, multicentrically, or bilaterally, with the extent of the disease often being underestimated. Thus, this type of breast cancer is diagnostic challenge due to diversity of its morphological features. Invasive lobular carcinoma displays diverse histologic patterns varying from classical through solid to pleomorphic subtypes, more solid subtypes having better prognosis [5]. In the late twentieth century, researchers even described seven different growth patterns including dissociated growth, single files, trabecular, alveolar, solid, and plexiform growth, and admixed tubules [6]. Therefore, the diverse magnetic resonance imaging (MRI) presentation of invasive lobular carcinoma is not surprising.

Diagnosis and determination of invasive lobular cancer extent are based on imaging methods. The sensitivity of mammography for detecting invasive lobular cancer ranges between 57 and 81% [7, 8], and of ultrasound between 68 and 98% [9]. MRI has the highest overall sensitivity of 93% for detecting invasive lobular cancer



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with, however, lower specificity [10]. MRI is also the most effective technique for the assessment of its local extent, which is important for optimal treatment planning [11]. The correlation between lesion size on different imaging modalities and final tumor size has not been well characterized, even though some research demonstrated MRI to provide a better estimate of tumor size than classic mammography and ultrasound, the size of the tumor on imaging only weakly correlated with pathology [12].

The most common MRI presentation of an invasive lobular cancer is a mass, followed by non-mass enhancement in approximately one-third of cases, but it can present as a focus or even be MRI occult. A mass can be found in a single, multifocal, or multicentric distribution, typically of irregular and spiculated margins, with heterogeneous contrast enhancement, and type III enhancement curve. The possible distribution patterns of invasive lobular cancer presenting as non-mass enhancement are focal, linear, segmental, regional, multiple regions, and diffuse [11–16].

Due to the important role of MRI in the management of invasive lobular cancer and its varied appearance on MRI, we aimed to present the pictorial essay which will illustrate the varied features of invasive lobular cancer on MRI and thus facilitate the interpretation of imaging findings for radiologists. For that purpose, we included MRI case series of different invasive lobular cancer presentations in addition to the histopathological diagnosis.

## Main text

# Imaging protocol

All cases of invasive lobular cancer are scanned with the MRI performed on the Magnetom Avanto 1.5 T, Siemens Healthcare, Erlangen, Germany, with a compatible 15-channel diagnostic breast coil prior to operation or other treatment modalities at Clinical Department of Diagnostic and Interventional Radiology, University Hospital of Split, Croatia. Slice thickness was 1.6 mm. A standard breast dynamic contrast-enhanced MRI protocol included 3-plane localizers, a water-sensitive sequence, an unenhanced T1-weighted image (T1WI), and five contrast-enhanced T1WIs obtained in a dynamic fashion. The sequences can be performed with or without fat suppression, and postprocessing can be used to generate subtraction and maximum intensity projection images. A diffusion-weighted imaging/apparent diffusion coefficient (DWI/ADC) map, indicating restriction diffusion, were included in the protocol. The average scan time was approximately 24 min, within a range of 16–40 min. Image interpretation was performed by assessing the morphology of lesions as well as the vascular kinetics. Vascular kinetic enhancement information for a particular lesion was obtained from the delayed postcontrast T1WIs at various time points. Kinetic curves provided information about speed of contrast uptake and release within particular lesion and are classified into three categories: persistent (type I), plateau (type II), or washout (type III). Finally, the following sequences were done: T1WI and T2WI, DWI, ADC, maximum intensity projection precontrast, postcontrast, and subtraction. Dynamic tests were performed with the administration of contrast agent Dotarem (gadoterate meglumine) at the dose of 0.1 mmol/kg with flow of 3 ml/s, followed by a rinse with 20 ml of NaCl.

The authors carefully searched the database of pathologically confirmed invasive lobular cancers and reviewed their MRI scans. They selected the most representative MRI cases which most clearly demonstrate the different morphologies of invasive lobular cancer morphological MRI subtype. Pathohistological diagnosis of all cases was done within 1 month of an MRI scan for each patient.

## Case series

A 53-year-old female presented with areolar erythema and bloody nipple discharge of the left breast. Following mammography and ultrasound, axial T1WI postcontrast subtracted MRI revealed a 0.4-cm retroareolar focus within the left breast. Focus demonstrated initial rapid enhancement and the washout—kinetic curve type III (Fig. 1). It was of high signal intensity on DWI and low signal on ADC map, indicating a restricted diffusion. Pathohistological analysis of ultrasound-guided core needle biopsy sampled tissue confirmed an invasive lobular cancer, luminal A, with proliferation index (Ki-67) of 6%.

A 75-year-old female presented with a palpable mass located in the left breast. Following mammography and ultrasound, MRI revealed the segmental non-mass enhancement with partially homogeneous and clumped internal enhancement of upper medial quadrant of the left breast on axial postcontrast subtracted T1WI (Fig. 2). The non-mass enhancement demonstrated progressive uptake of the contrast-kinetic curve type I. It was of high signal intensity on DWI and low signal on ADC map, indicating a restricted diffusion. However, within the non-mass enhancement, one homogeneous enhancing spiculated irregular mass and few foci were distinguished. Pathohistological analysis of ultrasound-guided core needle biopsy sampled tissue showed that it was an invasive lobular cancer, luminal B, with proliferation index (Ki-67) of 15%.

An 84-year-old female underwent breast MRI for accurate estimation of newly diagnosed left breast cancer. Axial postcontrast fat-suppressed subtracted T1WI demonstrated three distinguished lesions located in the retroareolar region in the middle and ventral portion of the left breast characterized as irregular spiculated masses



Fig. 1 Breast MRI of a 53-year-old female presenting with areolar erythema and bloody nipple discharge of the left breast showed the 0.4-cm hyperintense focus located in the retroareolar region within left breast on fat-suppressed T2WI (**A**). The focus had high signal intensity on DWI and low signal on ADC indicating a restricted diffusion (**B** and **C**), enhancement on postcontrast T1WI (**D**), maximum intensity projection (**E**), and axial postcontrast subtracted T1WI (**F**). Kinetic curve was type III (**G** and **H**)



Fig. 2 Breast MRI of a 75-year-old female presenting with a palpable mass located in the left breast showed low signal of segmental non-mass enhancement of upper medial quadrant of the left breast on fat-suppressed T2WI (**A**), high signal intensity on DWI and low signal on ADC indicating a restricted diffusion (**B** and **C**), clumped non-mass enhancement on axial postcontrast T1WI (**D**), axial maximum intensity projection (**E**), and sagittal postcontrast subtracted T1WI (**F**). The non-mass enhancement kinetic curve was type I (**G** and **H**)

with intensive enhancement but centrally lucent (indicating necrosis). Skin and subcutaneous tissue were thickened due to marked breast edema. Intramammary and axillary lymph nodes were enlarged and showed heterogeneous enhancement. However, in the right breast, in an architectural retroareolar distortion, a focal non-mass enhancement was revealed, not recognized by previous diagnostic methods. The largest lesion in the left breast demonstrated plateau enhancement (type II), while focal non-mass enhancement of the right breast demonstrated delayed washout (type III curve), Fig. 3. Pathohistological analysis of ultrasound-guided core needle biopsy sampled tissue showed an invasive lobular cancer, luminal B, with proliferation index (Ki-67) of 4.8%.

A 62-year-old female presented with malignancy of the left breast. An irregular mass with spiculated margins and homogeneous enhancement located in the middle portion of the left breast on the border of the lateral quadrants was described on axial postcontrast subtracted T1WI MRI. Mass demonstrated initial rapid enhancement and delayed washout—kinetic curve type III (Fig. 4). The mass showed high signal intensity on DWI



Fig. 3 Breast MRI of an 84-year-old female with newly diagnosed left breast cancer showed showing marked breast edema and thickened skin of the left breast and hypointense retroareolar lesion (one of few lesions was presented) in the middle and ventral portion of the left breast on fat-suppressed T2WI (**A**), high signal intensity on DWI and low signal on ADC indicating a restricted diffusion (**B** and **C**), spiculated centrally lucent mass and few retroareolar focuses within the right breast, focal non-mass enhancement also on the right breast, and enhancement of the thickened skin of the left breast on axial postcontrast T1WI (**D**), maximum intensity projection (**E**), and all mentioned changes in both breast shown on postcontrast subtracted T1WI (**F** and **G**). The largest lesion in the left breast demonstrated kinetic curve type II, while focal non-mass enhancement in the right breast demonstrated kinetic curve type III (**H** and **I**)



Fig. 4 Breast MRI of a 62-year-old female with newly diagnosed left breast cancer showed irregular hypointense mass located in the middle portion of the left breast on the border of the lateral quadrants on fat-suppressed T2WI (**A**), high signal intensity on DWI and low signal on ADC indicating a restricted diffusion (**B** and **C**), irregular mass with spiculated margins and homogeneous enhancement on axial postcontrast T1WI (**D**), maximum intensity projection (**E**), postcontrast subtracted T1WI (**F**), and kinetic curve type III (**G** and **H**)

and low signal on ADC map, indicating a restricted diffusion. Pathohistological analysis of ultrasound-guided core needle biopsy sampled tissue showed an invasive lobular cancer, luminal A, with proliferation index (Ki-67) of 18%.

A 66-year-old female presented with two irregular lesions within the left breast on ultrasound. Axial postcontrast subtracted T1WI MRI showed irregular heterogeneous mass with spiculated margins located in the middle portion of the left breast on the border of the lateral quadrants. Next to, medially, a focal non-mass enhancement with heterogeneous internal enhancement pattern was described. Lesions demonstrated plateau enhancement—kinetic curve type II (Fig. 5). The lesions showed high signal intensity on DWI and low signal on ADC map, indicating a restricted diffusion. Pathohistological analysis of ultrasound-guided core needle biopsy sampled tissue showed an invasive lobular cancer, luminal A, with proliferation index (Ki-67) of 8%.

A 67-year-old female presented with spiculated lesions within the right breast on mammography. Axial postcontrast subtracted T1WI MRI showed large multiregional non-mass enhancement in upper lateral and medial quadrants of the right breast with a partially homogeneous and clumped internal enhancement pattern. Within non-mass enhancement, multiple homogeneously enhancing spiculated masses and multiple foci within the upper quadrants of the right breast were distinguished.



Fig. 5 Breast MRI of a 66-year-old female presenting with two irregular lesions within the left breast on ultrasound showed intermediate signal of focal non-mass in the on the border of the lateral quadrants of the left breast, and a single irregular lesion next to it on fat-suppressed T2WI (**A**), high signal intensity on DWI and low signal on ADC (**B** and **C**), axial postcontrast T1WI (**D**), focal non-mass on maximum intensity projection (**E**), and focal non-mass and single irregular lesion on postcontrast subtracted T1WI (**F** and **G**), both showed kinetic curve type II (**H**, **I**, **J**)

Non-mass enhancement demonstrated initial rapid enhancement and delayed washout—kinetic curve type III (Fig. 6). Pathohistological analysis of ultrasoundguided core needle biopsy sampled tissue showed mixed NOS and invasive lobular cancer, pleomorphic subtype, with proliferation index (Ki-67) of 60%.

# Discussion

The case series showed variability of invasive lobular carcinoma on MRI. Our six women presented as case series were of postmenopausal age, and average age of invasive lobular carcinoma diagnosis is 55 years or older. Histological subtypes of the elected women were very different, almost the same ratio of luminal A and B, although recent research showed that luminal A subtype is more frequent than luminal B, HER2+ or triple-negative subtypes [17]. Different invasive lobular carcinomas presented by this review showed all three types of kinetic curves. Studies showed that kinetic curve type I is the least common finding in invasive lobular carcinoma, compared to curve types II and III, with kinetic curve type III found in more than half cases [18]. Restricted diffusion is generally associated with malignant tumors as a result of their high cellularity, which was showed by our case series as well. It was found in almost all imaging presentation of lobular carcinoma. The most common magnetic resonance imaging presentation of the invasive lobular carcinoma on MRI is a mass, or two or more masses. However, the nonmass enhancement is also relatively common and can be found in combination with masses or foci, as our review showed. Very rarely, the invasive lobular carcinoma can be even MRI occult. Variability in gadolinium uptake and morphology of invasive lobular cancer reflects the tumor histology. Some studies showed some invasive lobular carcinomas to have an infiltrative growth pattern without significant angiogenesis and/or neovascularity. This may



Fig. 6 Breast MRI of a 67-year-old female presenting with spiculated lesions within the right breast on mammography showed multiregional non-mass enhancement in upper lateral and medial quadrants of the right breast, which has low signal on fat-suppressed T2WI (**A**), intermedial signal intensity on DWI (**B**), and high signal on ADC (**C**) indicating no restricted diffusion; within the non-mass enhancement, multiple enhancing spiculated lesions and multiple foci of the upper quadrants of the right breast on axial postcontrast T1WI (**D**), maximum intensity projection (**E**), postcontrast subtracted T1WI (**F**), and non-mass enhancement had kinetic curve type III (**G** and **H**)

be the reason why MRI was reported to be falsely negative on occasion when invasive lobular carcinoma is present [14, 19, 20]. In a small percent of cases, an invasive lobular carcinoma may be presented as a focus. An MRI focus is an enhancing lesion < 5 mm in size, and it is too small to be characterized. It may be benign or malignant, with the estimated risk of malignancy ranging from 0.6 to 37. Multiple scattered foci, a focus stable or decreasing in size, with 100% persistent delayed kinetics or cyst-like morphology can be considered benign. In contrast, a new or enlarged focus or focus showing washout kinetics is suspicious [15, 16, 21]. We presented a patient with focus that showed restriction diffusion and kinetic curve type III (rapid washout), very suggestive to be malignant.

The invasive lobular cancer presents a diagnostic challenge, not only of mammography or ultrasound, but also of MRI. Sometimes, it is very difficult to differentiate it from invasive ductal carcinoma. A study comparing the morphological and dynamic characteristics of invasive lobular cancer and invasive ductal cancer showed that there is a significant morphological overlap between them. They only differed by the presence of perifocal edema, which is more often reported in invasive ductal cancer [22]. This has logical explanation, because it has grown pattern as a mass, while invasive lobular carcinoma grows more infiltratively. Some differences regarding the kinetic curve were also reported. It was found that maximum enhancement of invasive lobular carcinoma is attained at a slower rate than in invasive ductal carcinoma, but the peak enhancement is independent of tumor histology. Moreover, a smaller number of invasive lobular carcinoma show delayed-phase washout in comparison with invasive ductal carcinoma [20, 23-25]. The correlation of an invasive lobular carcinoma with histopathological characteristics was not strong, as the previous research confirmed. The heterogeneity and diversity of histological growth pattern and subtypes of invasive lobular carcinoma make the MRI presentation very different, as our case series showed.

Given that the feature of invasive lobular cancer is multifocality and bilaterality, as was shown by our cases Nr. 3, 5, and 6, MRI shows a high rate of detection of additional focal breast lesions. Research has shown that additional lesions are detected in over 30% of patients undergoing breast MRI and that over three-quarters of lesions are pathohistologically confirmed as malignant [26]. Furthermore, MRI can detect not only the infiltration of underlying muscles that is not visible with classical diagnostic modalities [27], but can also detect changes in regional lymph nodes with almost the same accuracy as axillary ultrasound [28]. Although MRI has emerged as a superior diagnostic method, there is still a certain number of undetected invasive lobular carcinoma. In recent years, the spatial resolution of MRI has increased with the advent of 3 T magnets, which increased the detectability of previously occult tumors [20].

Finally, considering all the positive characteristics of MRI, the question arises whether it should be introduced into the standard diagnostic treatment. Current opinions are conflicting due to false-positive results, which could lead to unnecessary biopsies or mastectomy [26]. However, the majority of evidence still indicates that MRI has a place in the diagnostic workup are younger patients, patients who have dense breasts, poor visualization of breast parenchyma lesions mammographically, patients who have undergone neoadjuvant therapy due to breast cancer, and patients who are considering breast cancer surgery [29]. However, in invasive lobular carcinoma, the role of MRI in its detection, preoperative management, and follow-up is enormous.

The work has some limitations. Only six representative imaging examples were selected for the research; the aim was not to examine the frequency of occurrence of a particular presentation of invasive lobular carcinoma on MRI, and no statistical analysis was performed. In each of the six cases, only basic demographic, clinical, and previous imaging data were briefly listed, without discussing them in detail.

## Conclusions

Although MRI is considered the most accurate imaging method in invasive lobular cancer diagnosis and management, this pictorial essay demonstrated how it can be variable and atypical in MRI presentation. Radiologists interpreting MRI findings must interpret the findings carefully and be aware of the spectrum of invasive lobular cancer imaging presentations. Considering the variety of MRI imaging, the radiologists have to look for other diagnostic methods for the final interpretation of the imaging findings. We believe that the presentation of different cases will educate radiologists and help in making appropriate diagnostic and therapeutic decisions.

#### Abbreviations

- MRI Magnetic resonance imaging DWI Diffusion-weighted imaging
- DWI Diffusion-weighted imaging ADC Apparent diffusion coefficient
- T1WI T1-weighted image
- i i weiginteu image

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#### Author contributions

KJ and IO designed the study. DV extracted data and helped to the draft. DV, DBM, and KJ wrote a draft. IO supervised the study. All authors read and approved the final manuscript.

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#### Availability of data and materials

Upon reasonable request.

## Declarations

#### Ethics approval and consent to participate

Study was approved by Ethical Committee of Split Clinical Hospital Centre, Class 500-03/23-01/101; Nr 2181-147/01/06/LJ.Z.-23-02.

#### **Consent for publication**

Due to a retrospective nature of study, it was waived.

#### **Competing interests**

The authors declare no competing interests.

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