Breast Oncology: Techniques, Indications, and Interpretation

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Linda Moy
To my parents, Fee and Helen, who taught me to persevere and pursue my dreams
To my children, Cindy and Ethan, who fill my life with joy and laughter
To my husband, Dale, who is a wonderful partner
To Dan Kopans who nurtured a passion for breast imaging
To Hildegard Toth for her unwavering support

Samantha L. Heller
Thank you to my wonderful colleagues—I am so very lucky to work with you.
Raj, Kannon, and Dashiell, this is for you—with love and a bottle of pie.

Foreword

Magnetic resonance imaging (MRI) has become a standard breast imaging tool. Breast MRI is widely accepted as a suitable screening exam for women at high risk for breast cancer and is often invaluable in the diagnostic setting. Yet despite an overall increase in understanding of the strengths and applications of breast MRI and despite increasingly nuanced and evidence-based guidelines, breast MRI techniques, protocols, and indications are not static and may vary from practice site to practice site. In addition, breast MRI has some limitations: it is an expensive exam with the potential to impact on overall health-care costs. As well, false-positive findings generated through the MRI exam can lead to additional imaging and biopsy.

Because the field of breast MR continues to evolve, we hope to introduce the reader to emerging breast MRI techniques and applications even as we offer a complete and thorough review of current breast MRI practice and guidelines. Because the stakes are high surrounding appropriate MR interpretation, we have also aimed to provide a book presenting practical tips regarding optimal MR technical parameters and pearls regarding study evaluation.

To accomplish these goals, we have organized our book into three themed sections. The first section focuses on MRI techniques with the goal of detailing the parameters of breast MRI from standard sequences to up-to-date, cutting-edge techniques. The second section reviews accepted indications for breast MRI and analyzes the available evidence-based support for these indications. The third section focuses on specific MRI findings, interpretation strategies, and management of breast MRI findings. Throughout this book, the authors contextualize controversies and debates within the field. The chapter authors provide both national and international perspective on these topics.

New York, NY, USA — Samantha L. Heller and Linda Moy

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Part I
Techniques

Chapter 1
Breast MRI Technique

Habib Rahbar, Roberta M. Strigel, and Savannah C. Partridge

Abstract Although there is no single standard protocol for breast MRI acquisition, high quality breast MRI generally requires use of a dedicated breast MRI coil and adequate (≥ 1.5 T) magnetic field strength. Currently, breast MRI requires gadolinium contrast agent administration for cancer detection and a dynamic acquisition (dynamic contrast enhanced, or DCE, MRI) using a method that allows for homogenous fat suppression. In order to maximize sensitivity and sensitivity, MRI protocols must balance spatial and temporal resolution so that important morphologic and kinetic enhancement features can be readily identified. In addition, it is important to develop an approach that attains consistency, addresses technical challenges, and minimizes artifacts. Finally, advanced approaches, such as use of higher magnetic field strength (e.g. 3 T) scanners, diffusion weighted imaging, and MR spectroscopy present unique opportunities and challenges that must be considered and addressed prior to adoption in routine clinical practice.

Keywords Breast MRI • Technique • Acquisition • Protocol • Spatial resolution • Temporal resolution • Artifacts • 3 T • Dynamic contrast enhanced • Fat suppression

1.1 Introduction

Breast MRI was initially proposed for breast cancer detection in the 1970s [1] using pre-contrast intrinsic signal properties related to differences in longitudinal (T1) and transverse (T2) relaxation times exhibited by abnormal breast tissue when compared to normal tissue in vitro [2]. However, MRI use did not gain wide clinical acceptance until it was demonstrated that breast cancers exhibit higher signal on

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T1-weighted images after the administration of intravenous gadolinium-based contrast [3]. Breast MRI is now commonly used for a variety of clinical indications, which are covered in greater detail in Section II of clinical indications for breast MRI. In order to maximize the clinical utility of breast MRI, one must carefully balance patient and equipment factors in order to develop a breast MRI program that provides consistent, high quality images with superior sensitivity for breast cancer detection. This chapter discusses the technical considerations that are central to the performance of quality breast MRI for a variety of clinical indications.

1.2 General Breast MRI Technique Considerations

Despite the increasing utilization of breast MRI for a variety of clinical indications, there is currently no single standard protocol for image acquisition. Both the American College of Radiology (ACR) and the European Society of Breast Imaging (EUSOBI) have set minimum standards for acquisition of breast MRI. However, each of these guidelines allow for much flexibility in how images are acquired and what equipment is used. As reflected in these guidelines, there is consensus that high quality breast MRI acquisition should employ a high spatial resolution dynamic contrast-enhanced (DCE) protocol with bilateral acquisition that provides complete coverage of the breasts and axillae using a dedicated breast MRI coil. The clinical images should include key pulse sequences with appropriate spatial and temporal resolution for assessment of lesion morphologic and kinetic information and be free of significant artifacts. Such an approach allows for effective morphologic and semi-quantitative enhancement kinetic feature assessment of breast lesions, as described in the standardized American College of Radiology (ACR) Breast Imaging-Reporting and Data System (BI-RADS) MRI lexicon [4].

1.2.1 Patient Positioning and Comfort

Breast MRI should be performed with the patient positioned prone in the MRI scanner with the breasts pendant in the dedicated breast coils. This allows the breast tissue to be optimally imaged and findings to be accurately localized by stretching out the normal fibroglandular tissue elements away from the chest wall. This approach also has the advantage of increasing the distance of breast tissue from the heart and lungs, which helps to minimize cardiac and respiratory motion artifacts. Most commonly, the patient's arms are raised above her head in order to avoid wrap artifact; however, some coil designs allow the arms to remain at the patient's side yet posterior to the breasts.

Proper positioning with attention to patient comfort and clear communication allows breast MRI to be performed efficiently and without the aid of cardiac or respiratory gating. Maximizing patient comfort can decrease the likelihood of significant intra- and inter-scan motion. Common points of discomfort are the face, ribs, elbows, and sternum, which can be relieved with appropriate placement of vendor-supplied pads to support the sternum, head, and outer edge of the chest and cushions and/or pillows to support the hips, and elbows. It may be preferable to image patients feet first (in the bore of the magnet) rather than head first to decrease claustrophobia. Patients who have limited range of motion at the shoulder joint may require imaging with their arms at their sides (along the torso). In such cases, it may be useful to wrap the arms so that they are fixed in position and increase the field of view to include the arms to minimize the potential for wrap-around artifacts. Finally, specific yet concise instructions and communication allows patients to anticipate what they will experience while in the scanner, which improves compliance.

1.2.2 Magnetic Field Strength

Breast MRI should not be performed at low magnetic field (B_0) strength and ideally should be performed with a 1.5 tesla (T) or greater magnet. Higher field strength allows for increased signal to noise ratio (SNR), which can facilitate acquisition of MR images that meet general spatial and temporal resolution standards. Over the past decade, breast MRI is increasingly being acquired clinically at higher field strength (e.g. 3 and 7 T), which can allow acquisition of high spatiotemporal resolution images with improved contrast resolution that simply cannot be achieved at 1.5 T. Higher field strength imaging also can decrease scan times; however, there are technical, physical, and safety challenges posed by 3 T and higher field strength imaging that need to be addressed. These challenges are discussed further at the end of the chapter (Imaging at Higher Field Strengths).

1.2.3 Coils

In order to maximize signal, breast MRI should be performed using only dedicated breast surface coils, and preferably using coils with a high number of coil elements. Having a high number of coil elements allows for parallel imaging, which is particularly efficient for breast imaging because it can facilitate high spatial resolution acquisitions in less scan time [5]. Newer MRI systems typically support 32 or more simultaneous radiofrequency (RF) channels, with 16-channel phased-array breast coils commercially available [6]. The breasts should be

stabilized within the coil in the lateral-to-medial direction (for axial acquisitions) to minimize the effects of motion, such as ghosting artifacts, and degradation of the subtraction images [7].

1.2.4 Contrast Agent

Although non-contrast MRI techniques, such as diffusion weighted imaging and MR spectroscopy, have shown early promise for breast cancer detection and characterization, all clinical breast MRIs performed for cancer detection or characterization currently require the administration of a gadolinium contrast agent. Chelated gadolinium has paramagnetic properties that result in decreased T1, T2, and T2* relaxation times [8]. Thus, fluid-sensitive imaging, such as T2-weighted series, should be acquired prior to the administration of contrast. Since the decrease in relaxation from injection of the gadolinium chelate is greatest for T1-weighted sequences, DCE MRI is performed with T1-weighting. For breast imaging, the gadolinium chelate should be injected intravenously at a dose of 0.1 mmol/kg body weight followed by a 20 mL saline flush at a rate of approximately 2 mL/s using a power injector. This method both ensures contrast quickly reaches the intravascular space and allows for consistency in contrast enhancement timing across examinations.

1.2.5 Primary Imaging Acquisition Plane and Bilateral Imaging

One of the first decisions when building a breast MRI protocol is to decide on the primary acquisition plane, which may be the only image orientation acquired during the exam. Coronal, sagittal, and axial acquisition planes are all acceptable, particularly because high-quality multi-planar reformats can be reconstructed from imaging at or near isotropic resolution. Primary sagittal and axial acquisitions offer more intuitive orientations of the breast when compared to primary coronal acquisitions. Because the breast is organized anatomically into segments that extend anteroposteriorly from the nipple, both sagittal and axial acquisitions allow optimal visualization of these segments since the full anteroposterior span of the breast is presented on each image. Furthermore, the full plane of the sagittal images closely correlates with standard mediolateral oblique (MLO) and medial-lateral (ML) views obtained on x-ray mammography, whereas the full plane of axial images closely correlates with standard craniocaudal (CC) views. An additional benefit of a primary axial acquisition plane when compared to sagittal is that it allows for more natural side-by-side comparison of the breasts on each image. The authors' practices perform a primary axial acquisition plane for this reason, with multi-planar reformats generated in coronal and sagittal

planes. Primary coronal acquisition is rarely performed because it provides the least intuitive orientation and thus is not considered further in this chapter.

Regardless of plane of acquisition, bilateral imaging is favored over unilateral imaging for several reasons. First, bilateral imaging is clinically desirable because it allows for evaluation of both breasts at an identical post-contrast injection time point. Bilateral scanning also allows for assessment of symmetry of enhancement, which is useful for discriminating unique foci and non-mass enhancement lesions from normal background parenchymal enhancement (BPE). There are also technical reasons to perform bilateral imaging rather than unilateral imaging for breast MRI. Because the phase-encoding gradient is typically applied in the left—right direction to minimize the effects of cardiac motion, images acquired in the axial plane with unilateral acquisition are more prone to wrap-around artifacts from the non-imaged contralateral breast [7].

1.2.6 Field-of-View

The appropriate field-of-view (FOV) used for breast MRI depends on the primary acquisition plane. In general, the smallest FOV necessary to include the entire breast and both axillae is recommended in order to maximize in-plane spatial resolution for the same matrix size. For a bilateral axial acquisition plane, the FOV must be large enough to cover both breasts and axilla in the right—left direction. The appropriate FOV for a sagittal primary acquisition plane must account for the entire breast and axilla in the superior—inferior direction.

1.3 Key Breast MRI Pulse Sequences

A standard breast MRI examination includes multiple acquired sequences, which typically comprise the following (Fig. 1.1):

(i) Scout or localizer obtained in all three perpendicular planes.
(ii) T2-weighted (bright fluid) sequence, most commonly with fat suppression.
(iii) Non-fat suppressed T1-weighted sequence.
(iv) Multi-phase T1-weighted sequences performed before and multiple times after contrast administration.
(v) Silicone sensitive sequence (if silicone implants are present).

Of the above sequences, the 3-plane localizer, T2-weighted sequence, and T1-weighted multi-phase (DCE) sequences (including a pre-contrast and an early and delayed post-contrast series) are required by the ACR Breast MRI Accreditation Program [9]. Although optional from an ACR accreditation standpoint, most complete breast MR examinations also include a non-fat suppressed T1-weighted sequence. Furthermore, a silicone sensitive sequence should also be obtained in

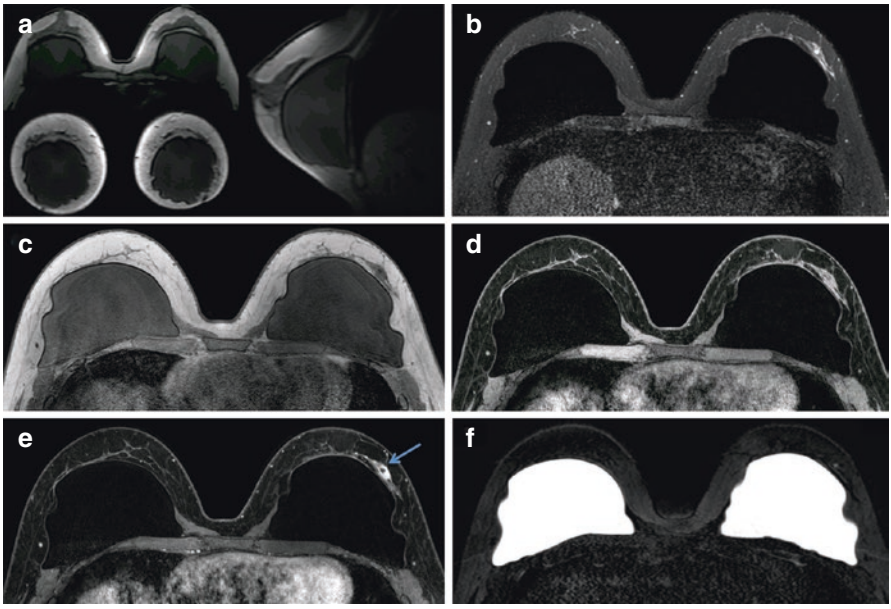

Fig. 1.1 Key breast MRI pulse sequences. Thirty-nine year old woman presents for breast MRI to evaluate extent of disease for known invasive ductal carcinoma of the left breast (*arrow*). Basic sequences include three-plane localizer sequence (**a**), fluid-sensitive sequence (in this case, fast spin echo T2-weighted image with fat saturation) (**b**), non-fat suppressed T1- weighted sequence (**c**), multiphase dynamic contrast-enhanced T1-weighted series with representative pre-contrast (**d**) and first post-contrast (**e**) images presented. Note the enhancing mass (*arrow*), which represents the biopsy-proven invasive ductal carcinoma, with susceptibility artifact within, representing a biopsy marker clip. A silicone-weighted series (**f**) was also obtained in this woman with pre-pectoral silicone implants

women with silicone breast implants. The role and optimization of each individual sequence is discussed in detail below.

For all sequences except the three-plane localizer, the frequency encoding gradient is applied in the anterior-posterior (AP) direction to minimize artifacts due to cardiac motion that would project into the breasts and simulate or obscure suspicious enhancement if the phase encoding direction was AP [10]. Thus, for sagittal acquisition the preferred phase encoding direction is superior—inferior and for axial acquisition the preferred phase encoding direction is left–right.

1.3.1 Three-Plane Localizer

A scout or three-plane localizer is required on all systems to localize the breasts. This allows the technologist to select the appropriate FOV for the patient's anatomy and scan acquisition plane (FOV considerations are discussed in more detail above).

1.3.2 T2-Weighted (Fluid-Sensitive) Sequence

A fluid-sensitive, typically T2-weighted, sequence is important for improved characterization of lesions and benign findings in the breast. For example, simple cysts, lymph nodes, and some fibroadenomas have high signal on the T2-weighted images. There are multiple acceptable sequence types for fluid-sensitive imaging. The most common are spin echo (SE), fast spin echo (FSE), and short tau inversion recovery (STIR) with an inversion time selected to null fat. These sequences are typically acquired as multi-slice 2D acquisitions because of the long repetition times required for T2-weighting and resulting longer acquisition times, which are more prohibitive for three dimensional (3D) imaging [10]. Thus, the T2-weighted images are typically unable to achieve spatial resolution equivalent to the T1-weighted sequences in a reasonable scan time with adequate SNR. Most protocols utilizing SE or FSE technique for T2-weighted imaging also perform fat suppression in order to readily differentiate bright fluid signal from fat. However, others choose to perform T2-weighted images without fat suppression because it can allow for acquisition of higher spatial resolution images and/or decreased scan times.

1.3.3 Non-fat Suppressed T1-Weighted Sequence

If active fat suppression is used for the DCE sequences (discussed below), it is recommended to perform an additional T1-weighted sequence without fat suppression prior to the multi-phase T1-weighted sequences. The sequence is fast, provides an overview of breast anatomy, can aid in assessing the amount of fibroglandular tissue in the breast, and is helpful in distinguishing fat from water-based tissues (such as fibroglandular tissue, breast lesions, etc.). Additionally, this sequence can aid in the identification of fat containing lesions, which is important because lesions containing fat (e.g. fat necrosis) are typically benign. This sequence should be performed with similar parameters and spatial resolution as the multi-phase T1-weighted sequences (as described below), but without active fat suppression, which allows for comparison of lesion characteristics across all the T1-weighted sequences.

1.3.4 Multi-phase T1-Weighted Sequences

The pre-and post-contrast multi-phase T1-weighted MRI images sequences are the most important images for identifying and characterizing lesions. It is imperative that identical scan parameters be used for the multi-phase T1-weighted images so that image registration can be performed, the pre-contrast images can be subtracted from the post-contrast images, and signal differences between sequences can be directly compared. Subtraction images are particularly useful for identifying signal

from gadolinium contrast agents and are mandatory if active fat suppression is not utilized so that contrast-enhancement can be readily differentiated from the bright signal of fat (described further below).

The multi-phase T1-weighted images are used for lesion detection, assessment of lesion morphology, and evaluation of lesion contrast enhancement over time. Characterizing lesion morphology, such as shape, margin, and internal enhancement pattern, requires high spatial resolution images with in-plane resolution of ≤1 mm to depict fine features, such as lesion margins. Through-plane slice thickness should be ≤3 mm; however, thinner slices that approach in plane resolution size (i.e. closer to isotropic) decrease volume averaging in the through-plane direction, which can increase the contrast of small lesions compared with background tissue. Additionally, thin slices facilitate higher quality image reformats, eliminating the need to acquire additional images in different planes (discussed further below). Conversely, voxel size should not be so small that SNR suffers.

A 3D GRE pulse sequence is preferred for multi-phase T1-weighted imaging with a short TR. The GRE pulse sequence should be spoiled to avoid any confounding T2 contrast [11]. There are no consensus guidelines for the number of post-contrast acquisitions or total acquisition time for the multi-phase T1-weighted sequences, although at least two post-contrast sequences should be performed in order to allow for the most basic assessment of contrast enhancement kinetic features. Invasive cancers typically enhance early, peaking in enhancement approximately one to two minutes after contrast injection. Although breast cancers more frequently exhibit initial fast enhancement (increase in signal from pre-contrast to first post-contrast series of >100 %) and delayed washout (decrease in signal from first post-contrast to final post-contrast series of >10 %) than benign findings, there remains substantial overlap in the kinetics of malignant and non-malignant lesions of the breast [12]. The multi-phase T1-weighted MRI protocol should be constructed so that one of the early-phase post-contrast sequences will sample the high frequency data at the center of k-space (which defines image contrast) between one and two minutes. This is important to potentially capture the peak enhancement of invasive cancers, but also to differentiate lesions from benign BPE, which typically increases over time (Fig. 1.2). For the majority of Cartesian sequences with rectilinear k-space sampling, the center of the sequence captures the high frequency data. However, Cartesian sequences with elliptical centric k-space sampling and other k-space sampling trajectories, such as radial, may acquire the center of k-space near the beginning of the sequence. Knowledge of the sampling pattern is thus important to properly time the post-contrast sequences.

1.3.5 Silicone Implants

Silicone, like water, has a longer T2 relaxation time than fat. Thus, on a standard T2-weighted sequence without fat suppression, water will be brighter than silicone, which is brighter than fat [13]. For evaluation of silicone implant rupture, it is often