MRI of Breast Lesions

Magnetic Resonance Mammography (MRM) has evolved in the last 17 years as a powerful tool for diagnosing breast lesions. The tomographic aspect of imaging and a high soft tissue contrast without radiation proved to have the highest sensitivity in detecting especially small invasive breast lesions. Some major advantages of MRM are the detection of multifocality/multicentricity; differentiation between scar and tumor; delineation of breast implants; analysis of "surprising" lesions in the contralateral breast; search for primary tumor in a CUP syndrome (Cancer of Unknown Primary) after having detected malignant lymph nodes in the axillary region; and early analysis of response to chemotherapy. Several unanswered questions remain, including: the varying specificities reported in the literature, depending on the technical and methodological variations and problems; MRM's high price; the lack of detection of microcalcification and some cases of DCIS (Ductal Carcinoma in situ); the need for contrast and sophisticated data evaluation as well as delineation of hormonal aspects; and a broad variety of technical pitfalls.

For differentiating between malignant and benign lesions, a high spatial as well as temporal resolution is of utmost importance. Therefore, a so-called dynamic technique (i.e., the repetitive imaging of the same slices before and in short time intervals after the injection of contrast medium), is essential to detect the differences in initial enhancements between malignant and benign lesions which are reflected by the tumorangiogenetic vascular network of malignant lesions. This network results not only in an increased number of vessels, but also and especially in a changed vascular architecture consisting of primitive membranes, including defects in basal membranes, which are responsible for an increased interstitial space and AV-shunts, which might explain the so-called wash-out effect, i.e., the decrease of signal intensity after the initial rise in the first 1 to 2 min after contrast agent injection. The protocols given here focus on dynamic techniques at high field strength (1.5 T), where the majority of experience has occurred in MR Mammography in the last decade.

DYNAMIC MR MAMMOGRAPHY

BASIC PROTOCOL

Magnetic Resonance Mammography was mainly evaluated at field strengths of 1.0 T and 1.5 T. There is only little experience at mid-field (0.5 T) or low field (0.2 T and lower). At low field strength some compromises have to be made, for example, increase of contrast medium, decrease of repeat time, and increase of flip angle in order to compensate the relatively low decrease of T_1 relaxation time induced by gadolinium based contrast agents compared with high fields. The sequences described herein are based on the author's experience with a Philips 1.5 T ACS II and a Siemens 1.5 T Vision Scanner, but are expected to be equally applicable to devices from other manufacturers.

The following technical advice is given to the technologist and radiologist, who, especially in the field of dynamic MR Mammography, have to work together as an effectively coordinated team in order to make the examination successful.

Dynamic MR Mammography can be performed either as a multi-slice 2-D or a dynamic 3-D sequence. The 3-D sequence offers higher through-plane resolution than the 2-D sequence; however, some machines and coils still lack sufficient signal homogeneity in 3-D techniques. In these cases, the critical subtraction images can be deteriorated by artifacts. Most machines can perform multi-slice 2-D gradient echo sequences in a sufficient homogeneity over a wider range of field of view, which is especially important

Contributed by Werner A. Kaiser

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Table A21.1.1 Equipment Parameters for Dynamic MR Mammography

Coil type	Bilateral circularly polarized breast coil (or phased array double breast coil, if available)
Gradient coil strength	15-25 mT/m (or whatever the system permits)
Cardiac gating	No
Peripheral gating	No
Respiratory gating	No
Oxygen	Usually not
Motion cushions	Very useful
Subtraction software	Very useful
Automatic tuning	Yes, but no additional tuning after the first pre-contrast scan ("switched off" or "offline" technique)
Fast dynamic technique	Yes
Automatic image subtraction	Yes
Signal intensity versus time curves	Very useful
Use of contrast agent	Yes

in imaging of both breasts in transverse or coronal orientation and for a later analysis of lesions in subtracted images.

Table A21.1.1 lists the hardware necessary to perform the procedure along with the major appropriate parameters. The double breast coil is essential in order to evaluate both breasts simultaneously. This is especially important to compare enhancement of both breasts, i.e., in cases of in-flow phenomena, DCIS, inhomogeneities, and detection of lesions in either one or both breasts simultaneously. Once the contrast medium is injected, the simultaneous examination of both breasts is strongly recommended.

Patients having any ferromagnetic metal should be excluded from the examination, e.g., ferromagnetic particles, pacemakers, etc. This should be clarified by phone, before the MR examination is scheduled.

The currently available MR breast coils and MR machines have relatively limited space because of the space taken up by the doublebreast coil. In our experience, patients weighing more than 95 kg cannot be put in today's machines, and so patients should be screened by phone in advance. Patients taking hormones (i.e., hormone replacement therapy after menopause) should be advised to stop taking the hormones for ~3 months before MRM examination. Patients in the menstrual cycle can normally be examined. However, the progesterone effect in the second half of the menstrual cycle usually induces a slightly increased contrast uptake, which might be a problem for inexperienced readers. Therefore, an MR examination in the first half of the menstrual cycle, at least between day 7 and 20, is advisable but not necessary.

Besides pacemakers or ferromagnetic parts, other exclusion criteria are: previous allergies to gadolinium (Gd); unclear implants; clip implantations (especially in arteries or in the breast); psychiatric conditions, or claustrophobia. If there is any doubt about the possibility of some unclear implants, please contact the website *http://www.mrisafety.com*, for further information.

Since many technical and methodological pitfalls can occur, it is strongly advised to perform an MRM examination only if sufficient experience in analyzing the images is available.

There are two major disadvantages of low field strength. These are, first, the reduced signal-to-noise, and, second, a smaller decrease in T_1 induced by gadolinium based contrast agents as a result of the initially low T_1 values of the tissue (for example, 600 msec at 0.5 T, 900 msec at 1.5 T). However, these disadvantages can be compensated at mid field by additional use of strong gradients (≥15 mT/m) and high slew rates (≥15 to 25 T/m/sec). We also recommend increasing sensitivity towards Gd at low field by making the sequence more T_1 dependent (shortening of repeat time, increase of contrast medium dose, etc.).

Besides the exclusion criteria listed above, we advise that one rigorously select for strong indications for MR Mammography. Today, one should perform this relatively expensive and time-consuming technique only if high-quality X-ray mammography and ultrasound examinations still leave some doubts about the presence or absence, the malignancy or benignancy of a lesion, and/or the multicentricity or multifocality of lesions.

Sequence overview in dynamic MRM (1.5 T)

Table A21.1.2 gives an overview of the sequences used in the complete dynamic MR examination at 1.5 T (for example, a Philips 1.5 T ACS II machine). After a short scout sequence, a coronal T_1-weighted gradient-echo and a transverse T_2-weighted turbo-spin-echo sequence follow. The key part of this dynamic procedure is a T_1-weighted gradient-echo sequence *before* and 7 times *after* injection of contrast agent. Finally, the T_1-weighted coronal sequence is repeated so that a complete pre- and post-contrast image data set is available in two orientations. In special patients (see Critical Parameters and Troubleshooting) a dynamic examination in coronal orientation is advised; in these cases the orientations of the sequences outlined in Table A21.1.2 are listed in parentheses.

Materials

Normal saline (0.9% NaCl), sterile
Extravascular contrast agent (e.g., Magnevist, Omniscan, or Prohance)

NOTE: Be sure that technicians and nurses have immediate access to any emergency equipment that may be relevant to a given study, or that may be needed for a particular patient, such as crash carts or oxygen.

Set up equipment and patient

1. Interview (screen) the patient to ensure that she has no contraindications such as cardiac pacemakers or other implants containing ferromagnetic materials. Also, determine if the patient has any health conditions that may require the presence of

Table A21.1.2 Dynamic MRM Examination at 1.5 T[a]

Sequence	Time
1. Scout (transverse + coronal)	37 sec
2. Coronal (transverse) T_1-weighted gradient echo	1 min, 47 sec
3. Transverse (coronal) T_2-weighted turbo spin echo	3 min, 12 sec
4. Transverse (coronal) T_1-weighted gradient echo	1 min, 0 sec
Injection of contrast agent: 0.1 mmol/kg Gd-DTPA intravenous (or 0.2 ml/kg per dose)	
5. Transverse (coronal) T_1-weighted gradient echo (7 repetitions)	1 min, 0 sec per scan (total 7 min)
Automatic image subtraction (between sequences 5 and 4)	
6. Coronal (transverse) T_1-weighted gradient echo	1 min, 47 sec

[a]Total scanning time of these sequences is 15 min and 23 sec.

special emergency equipment during the scanning procedure, or if she will need sedation medication necessitating the use of appropriate monitoring equipment. Use sedation only if it cannot at all be avoided. If you are unsure about the presence of any ferromagnetic materials, please contact the referring physician or the web site *http://www.mrisafety.com*.

The presence of any ferromagnetic metals may be a health hazard to the patient when she is inside the magnet, and will also affect the imaging. If in doubt as to the exact composition of the items, it is best to exclude patients with any metal implants; see also Shellock (1996) for discussion of what implants may be safely scanned using magnetic resonance.

Patients may be accompanied into the magnet room by a friend or family member, who can sit in the room during the scan and comfort the patient as needed. This companion must be screened as well to ensure the absence of loose metal objects on the body or clothing. It is strongly advised that this accompanying person does not talk to the patient during the examination to avoid any movements.

2. Clarify that the patient has had no previous allergy to or contraindications against Gd. Explain the examination in detail and have the patient sign any necessary consent form.
3. Have the patient remove all jewelry and change into a gown to eliminate any metal that might be found in clothing.
4. Have the patient wash off any mascara and other makeup to avoid local tissue heating and image artifacts. Especially look for metallic rings in any body parts.
5. Inform the patient about what will occur during the procedure, what she will experience while in the magnet, and how to behave, including the following:
   a. If earphones or headphones are used to protect the ears from the loud sounds produced by the gradients, the patient will be asked to wear these, but will be able to communicate with you at any time during the imaging.
   b. The patient will be given a safety squeeze-bulb or similar equipment to request assistance at any time (demonstrate how this works).
   c. Explain to the patient that movement of the head or coughing deteriorates image quality. For good results the patient should not talk, and should avoid or minimize swallowing or other movement during each scan—i.e., as long as the banging sounds continue. Between scans, talking and swallowing are allowed in most cases, but should be avoided when comparative positional studies are being performed; the patient will be informed when this is the case.
   d. Nevertheless, the patient may call out any time if she feels it necessary.
6. Help the patient mount onto the table and stand beside the patient during positioning in the magnet. Either before or right after the patient lies down, set up any triggering devices or other monitoring equipment that is to be used.
7. If the patient is nervous, calm her and talk to her as much as possible before positioning her into the machine. After having positioned her, explain that you will not talk to her in order to avoid any motion, unless communication is necessary.
8. Insert the plastic cannula into the cubital vein, fix it and connect a plastic tube before putting the patient into the machine. After positioning the patient in the machine, connect the plastic tube with the automatic injector filled with a sufficient dose of contrast medium and a bolus of sodium chloride (physiological concentration).
9. Place patient's breasts in the coil.

Be sure that each breast is not deformed within the coil, since a later description of the exact position of a lesion in the breast is performed by describing the breast as a half-spherical mass with a nipple at the top and the lesion being positioned as xyz mm medially, laterally, cranially, caudally or dorsally in relation to the nipple.

10. Be sure that the patient has stretched arms along the body and not bent arms crossed over the head, in order to guarantee constant influx of the contrast medium.

    Injection of contrast medium is performed in the magnet without moving the patient out of the magnet.

11. If needed, place a pillow or other support under the knees to make the examination more comfortable for the patient. Have the patient cushioned as comfortably as possible in order to let her relax and to obtain images without motion artifacts.

12. Use the centering light to position the middle of the breast coil (this should coincide with the middle of the breast at the level of the nipple) and to put her into the isocenter of the magnet.

13. If the patient is very nervous, try to calm her or bring her out of the magnet after a few seconds and talk to her. In most cases this is sufficient.

    Try to avoid any medical sedation, as that reduces the possibility of exchanging information or of detecting an allergy, and it may induce a paradoxic reaction.

Sequence 1: Rapid two-plane positioning pilot

14. To validate the patient's position, run the system's pilot (or scout) scan to ensure correct location of the breast in two dimensions, using the imaging sequence given in Table A21.1.3 or similar parameters. This sequence usually consists of two orthogonal planes to allow localization.

Sequence 2: T_1-weighted gradient echo

15. Run sequence 2 according to Table A21.1.4.

    This coronal T_1-weighted sequence allows the complete examination of the axillary region. The slice thickness in this and all following sequences depends on breast size and varies

Table A21.1.3 Primary Clinical Imaging Parameters for Pilot Scan (Sequence 1)

Patient position	Prone
Scan type	Spin echo (multi-slice, half-Fourier)
Imaging plane (orientation)	Transverse and coronal
Central slice or volume center	Middle of the breast (usually at the nipple)
Echo time (T_E)	13 msec
Repeat time (T_R)	121 msec
Flip angle (FA)	90°
Fields of view (FOV_x, FOV_y)	450 mm, 450 mm
Resolution (Δx, Δy)	2.53 mm, 1.76 mm
Number of data points collected (N_x, N_y)	178, 256
Slice thickness (Δz)	5 mm
Number of slices	5 in each orientation
Slice gap	3 mm
Number of acquisitions (N_{acq})	1
Scan time	37 sec

between 3 and 5 mm; correspondingly, the gap between the slices varies between 0.1 and 1.0 mm, depending on breast size. Slice thickness and slice gaps are kept constant throughout the whole examination of the patient.

Sequence 3: T_2-weighted turbo spin echo (TSE)

16. Run sequence 3 according to Table A21.1.5.

The additional evaluation of signal intensity in T_2-weighted images is important for the delineation of fluid cysts, myxoid fibroadenomas, edema, blood, abscesses, septations in the lesion, etc.

Table A21.1.4 Primary Clinical Imaging Parameters for T_1-Weighted Gradient Echo (Sequences 2 and 6)

Patient position	Prone
Scan type	T_1-weighted 2-D gradient echo
Imaging plane (orientation)	Coronal
Central slice or volume center	Middle of the breast
Echo time (T_E)	5 msec
Repeat time (T_R)[a]	100 msec
Flip angle (FA)	80°
Fields of view (FOV_x, FOV_y)	350 mm, 315 mm
Resolution (Δx, Δy)	1.37 mm, 1.53 mm
Number of data points collected (N_x, N_y)	256, 206
Slice thickness (Δz)	3–5 mm (depending on breast size)
Number of slices[b]	24
Slice gap	0.1–1.0 mm (depending on breast size)
Number of acquisitions (N_{acq})	2
Scan time	1 min, 47 sec

[a] T_R is 100 msec for the Philips ACSII-1.5 T-machine or 240 msec for the Siemens Vision 1.5T machine.
[b] 3 slabs of 8 slices each for the Phillips machine or 1 slab of 24 slices for the Siemens machine.

Table A21.1.5 Primary Clinical Imaging Parameters for T_2-Weighted Turbo Spin Echo (TSE; Sequence 3)

Patient position	Prone
Scan type	T_2-weighted turbo spin echo
Imaging plane (orientation)	Transverse
Central slice or volume center	Middle of the breast
Echo time (T_E)	300 msec
Echo train length (ETL)	35
Repeat time (T_R)	4000 msec
Flip angle (FA)	90°
Fields of view (FOV_x, FOV_y)	315 mm, 350 mm
Resolution (Δx, Δy)	1.64 mm, 1.37 mm
Number of data points collected (N_x, N_y)	192, 256
Slice thickness (Δz)	3–5 mm
Number of slices	24
Slice gap	0.1–1.0 mm
Number of acquisitions (N_{acq})	1
Scan time	3 min, 12 sec

Sequence 4: Transverse T_1-weighted gradient echo (pre-constrast scan)

Since a variety of pitfalls can occur, this dynamic scan procedure has to be carefully checked at three different checkpoints (see Fig. A21.1.1). Checkpoint I is just before the precontrast scan. At this point, define the exact position of the breast in the coil by analyzing the scout scan and correct any deformation or malpositioning of the nipple. The orientation of the dynamic slices is checked (see below), the phase encoding direction is optimized (see below), and the scan parameters are finally controlled.

17. Perform checkpoint I.
18. Run sequence 4 according to Table A21.1.6.
19. After running sequence 4, checkpoint II of the dynamic scan is reached. At this point, i.e., after the precontrast scan and before the injection of contrast medium (see Fig. A21.1.1), evaluate the homogeneity of the coil by observing how constant the fat signal is across both breasts. This is to ensure that the placement of the coil is

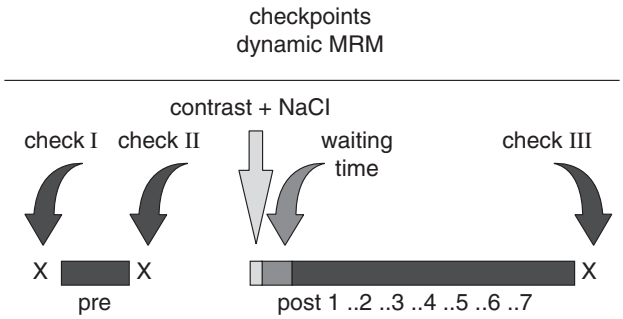

Figure A21.1.1 Special sequential performance of the scans in the dynamic MRM (sequences 4 to 6). There are 3 "checkpoints" where the examiner has to control the performance: before the pre-contrast scan (checkpoint I), after the pre-contrast scan (checkpoint II), and after the last post-contrast scan (checkpoint III; see text).

Table A21.1.6 Primary Clinical Imaging Parameters for T_1-Weighted Gradient Echo (Pre-Contrast) Scan (Sequence 4)

Patient position	Prone
Scan type	T_1-weighted 2-D gradient echo
Imaging plane (orientation)	Transverse
Central slice or volume center	Middle of the breast
Echo time (T_E)	5 msec
Repeat time (T_R)[a]	100 msec
Flip angle (FA)	80°
Fields of view (FOV_x, FOV_y)	315 mm, 350 mm
Resolution (Δx, Δy)	1.23 mm, 1.37 mm
Number of data points collected (N_x, N_y)	256, 256
Slice thickness (Δz)	3–5 mm
Number of slices[b]	24
Slice gap	0.1–1.0 mm
Number of acquisitions (N_{acq})	1
Scan time	1 min, 0 sec

[a] T_R is 100 msec for the Philips ACSII-1.5 T-machine or 240 msec for the Siemens Vision 1.5T machine.
[b] 3 slabs of 8 slices each for the Phillips machine or 1 slab of 24 slices for the Siemens machine.

appropriate and no tuning artifacts occurred and that the complete breast parenchyma is included in the dynamic scans. Be sure that the automatic adjustment is switched off for the following post-contrast scans in order to ensure an identical adjustment position in pre- and post-contrast scans. Look for and analyze possible artifacts (e.g., metals, clips). If the patient had shown any motion, advise her not to move and in that case, the pre-contrast scan is repeated once again.

Sequence 5: Transverse T_1-weighted gradient echo (post-contrast scan)

20. Leaving the patient in the magnet, inject a dose of 0.1 mmol/kg (= 0.2 ml/kg) Gd-DTPA at a bolus of 3 ml/sec followed by a sodium chloride bolus (physiological concentration) of 20 ml (if the position is in the cubital vein) or 30 ml (if the position is at the lower arm or hand vein).
21. After the end of the sodium chloride injection, wait 20 sec before beginning the first post-contrast scan, in order to let the contrast medium flow in and to be able to compare the results with previously published dynamic procedures. This waiting time also makes it possible to avoid artifacts from interleaved data acquisitions of different slices during the post-contrast scans.
22. After that waiting time, repeat without interruption seven post-contrast acquisitions with identical measurements and sequence parameters as the pre-contrast scan. The total scan time is 7 min (Table A21.1.7).

Automatic image subtraction

23. The software will perform an automatic image subtraction as soon as data points have been measured; this automatic image subtraction is finished shortly after the end of sequence 5.
24. Data evaluation begins at the monitor as soon as images are displayed on the screen (see Table A21.1.2). As soon as the dynamic scan is finished, an automatic subtraction allows for a complete fat subtraction and a quick detection of enhancing lesions among these "innumerable" images. The subtraction images also allow the detection of possible motions or inhomogeneities (Fig. A21.1.2 and Fig. A21.1.3). The auto-

Table A21.1.7 Primary Clinical Imaging Parameters for T_1-Weighted Gradient Echo (Post-Contrast) Scan (Sequence 5)

Patient position	Prone
Scan type	T_1-weighted 2-D gradient echo
Imaging plane (orientation)	Transverse
Central slice or volume center	Middle of the breast
Echo time (T_E)	5 msec
Repeat time (T_R)	100 msec
Flip angle (FA)	80°
Fields of view (FOV_x, FOV_y)	315 mm, 350 mm
Resolution (Δx, Δy)	1.23 mm, 1.37 mm
Number of data points collected (N_x, N_y)	256, 256
Slice thickness (Δz)	3–5 mm
Number of slices	24
Slice gap	0.1–1.0 mm
Number of acquisitions (N_{acq})	1
Number of repetitions	7
Scan time	1 min, 0 sec (after 7 repetitions the scan time adds to 7 min)

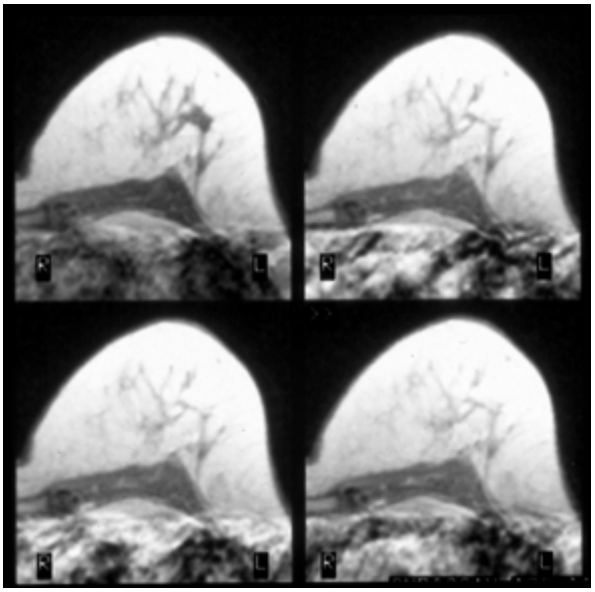

Figure A21.1.2 Four images of the same slice before injection of contrast medium (upper left) and 1 min (upper right), 2 min (lower left) and 7 min (lower right) after injection of contrast medium. Strong initial signal increases in a focal lesion (ductal invasive cancer) as well as segmental, dotted increases in the left segmental area oriented towards the nipple (neighbored DCIS). Signal decreases (washout) in the focal lesion in the late scan. These signal changes can be better detected in the corresponding subtractions in Figure A21.1.3.

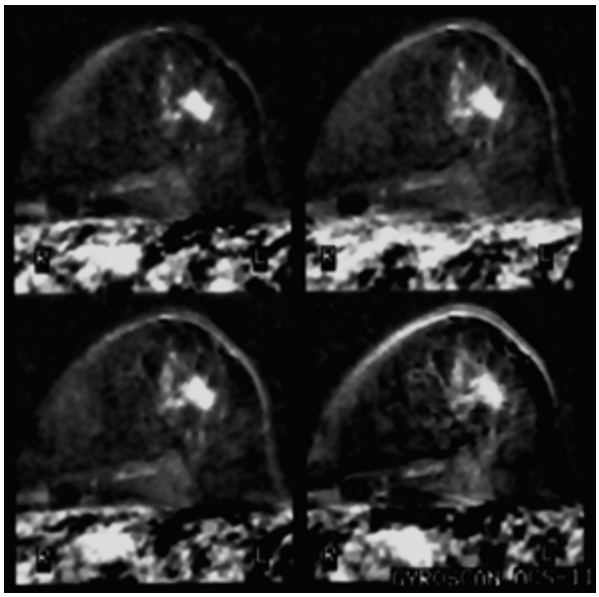

Figure A21.1.3 Here the image subtractions (post-minus pre-contrast scan) are seen after 1 min (upper left), 2 min (upper right), 3 min (lower left), and 7 min (lower right) post-contrast injection. The focal lesion including the washout effect as well as the corresponding segmental enhancement in the DCIS are documented.

matic data evaluation enables a real time navigation through all slices in four dimensions (three spatial dimensions and one time dimension).

25. However, pitfalls concerning automatic data evaluation should not be overlooked (see Critical Parameters and Troubleshooting). Some examples are an inadequate or wrong injection technique; an inappropriate receiver/transmitter adjustment; a misinterpretation of inflow phenomena; hormone effects, and vessels as lesions.

Sequence 6: coronal T_1-weighted gradient echo (post-contrast scan)

The final examination is a repetition of the T_1-weighted gradient echo sequence in the coronal orientation.

26. Run sequence 6 according to Table A21.1.4.
27. After the last post-contrast scan at checkpoint III (see Fig. A21.1.1), the contrast uptake is tested according to enhancement in breast parenchyma, vessels, muscles, etc.

The constancy of tuning parameters during the complete time of the dynamic scan has to be checked by a constant time-intensity curve in the fatty tissue, because that does not enhance. If the fat signal is inhomogeneous and/or varying over time, the signal-intensity versus time curve is not helpful or will be misleading (see Critical Parameters and Troubleshooting).

ALTERNATE PROTOCOL 1

MR IMAGING BY CONTRAST-ENHANCED DYNAMIC 3-D TECHNIQUE

In the past years, different dynamic techniques have been evaluated, including multi-slice 2-D (see Basic Protocol) or 3-D techniques. 3-D scans allow a better spatial resolution with thinner slices. However, the homogeneity of 3-D sequences on some machines has been limited, so that inhomogeneity artifacts deteriorated the kinetic data evaluation. Today both multi-slice 2-D and 3-D sequences can be applied with equal results in most machines, and therefore this alternate protocol is given in detail here.

Table A21.1.8 Primary Clinical Imaging Parameters for Scout Scan (Sequence 7)

Patient position	Prone
Scan type	3-D gradient echo
Imaging plane (orientation)	Transverse or coronal (but not sagittal)
Central slice or volume center	Centered at the nipple level
Echo time (T_E)	As short as possible (but in a "in-phase" echo time, i.e., multiple of 4.8 msec)
Repeat time (T_R)	As short as possible (e.g., 10 msec)
Flip angle (FA)	10° to 15°
Fields of view (FOV_x, FOV_y)	350 mm, 350 mm
Resolution (Δx, Δy)	1.37 mm, 1.37 mm
Number of data points collected (N_x, N_y)	256, 256
Slice thickness (Δz)	1–2 mm (depending on breast size)
Number of slices	48
Slice gap	No gap
Number of acquisitions (N_{acq})	1
Scan time	<90 sec (depending on T_R)

Table A21.1.9 Primary Clinical Imaging Parameters for Dynamic 3D MR Mammography at 1.5 T (Sequence 8)

Patient position	Prone
Scan type	3-D short T_R gradient echo
Imaging plane (orientation)	Transverse
Central slice or volume center	Middle of the breast
Echo time (T_E)	4 msec
Repeat time (T_R)	8.1 msec
Flip angle (FA)	20°
Fields of view (FOV_x, FOV_y)	320 mm, 240 mm
Resolution (Δx, Δy)	1.25 mm, 1.25 mm
Number of data points collected (N_x, N_y)	256, 192
Slice thickness (Δz)	1–2 mm
Number of slices	48
Slice gap	0
Number of acquisitions (N_{acq})	1
Fat suppression	Temporal subtraction
Scan time	75 sec

Set up equipment and patient

1. Use the same equipment and perform patient set-up as for the previous method (see Basic Protocol, steps 1 to 13). This is also valid for the establishment of an intervenous line as well as the information and informed consent obtained from the patient.

Sequence 7: Scout scan

2. Run a rapid 3-D pilot scan to demonstrate the position of the breast in the coil (Table A21.1.8).

   One can also run sequence 1 (Table A21.1.3) instead.

Sequence 8: 3-D short T_R gradient echo scans

3. Run a 3-D short T_R gradient echo sequence according to Table A21.1.9.
4. Repeat steps 20 and 21 of the Basic Protocol (to inject the contrast agent).
5. After a 20 sec wait time, run the 3-D gradient echo sequence 5 times according to Table A21.1.9 to get 6 data points for a signal-intensity time curve.

   This is not the same as setting the number of acquisitions to be 5.

FAT-SATURATED 3-D SCAN: HIGH SPATIAL RESOLUTION

ALTERNATE PROTOCOL 2

In the United States fat saturation techniques have been evaluated which focus especially on the high spatial resolution used to describe morphological features of lesions. These techniques are also mentioned in this unit.

Set up equipment and patient

1. Use the same equipment and perform the same patient set up as in the Basic Protocol (steps 1 to 14).

Sequence 9: 3-D short T_R gradient echo scans: fat suppression

2. Run a 3-D short T_R gradient echo sequence according to Table A21.1.10.
3. Repeat steps 20 and 21 of the Basic Protocol (to inject the contrast agent).

Table A21.1.10 Primary Clinical Imaging Parameters for Focusing High Spatial Resolution at the Cost of High Temporal Resolution (Sequence 9)

Patient position	Prone
Scan type	3-D short T_R gradient echo
Imaging plane (orientation)	Sagittal (dual volume) with lateral compression
Central slice or volume center	Middle of the breast
Echo time (T_E)	2.2 msec
Repeat time (T_R)	22 msec
Flip angle (FA)	30°
Fields of view (FOV_x, FOV_y)	160 mm, 160 mm
Resolution (Δx, Δy)	0.31 mm, 0.625 mm
Number of data points collected (N_x, N_y)	512, 256
Slice thickness (Δz)	1.875 mm
Number of slices	32
Slice gap	0
Number of acquisitions (N_{acq})	1
Fat suppression	Yes
Scan time	180 sec

4. After a 20-sec wait time, run the 3-D gradient echo sequence twice according to Table A21.1.10.

   This is not the same as setting the number of acquisitions to be 2.

ALTERNATE PROTOCOL 3

FAT-SATURATED 3-D SCAN: RODEO (ROTATING DELIVERY OF EXCITATION OFF-RESONANCE)

As mentioned in Alternate Protocol 2, this is another alternate protocol to describe morphological features of lesions.

Set up equipment and patient

1. Use the same equipment and perform the same patient setup as in the Basic Protocol (steps 1 to 14).

Table A21.1.11 Primary Clinical Imaging Parameters for RODEO (see Harms et al., 1993; Sequence 10)

Patient position	Prone
Scan type	3-D short T_R gradient echo
Imaging plane (orientation)	Sagittal
Central slice or volume center	Middle of the breast
Echo time (T_E)	5 msec
Repeat time (T_R)	20 msec
Flip angle (FA)	45°
Fields of view (FOV_x, FOV_y)	120 mm, 120 mm
Resolution (Δx, Δy)	0.47 mm, 0.94 mm
Number of data points collected (N_x, N_y)	256, 128
Slice thickness (Δz)	1.2 mm
Number of slices	128
Slice gap	0
Number of acquisitions (N_{acq})	1
Fat suppression	Yes
Scan time	320 sec

Sequence 10: 3-D short T_R gradient echo scans: fat suppression

2. Run a 3-D short T_R gradient echo sequence according to Table A21.1.11.
3. Repeat steps 20 and 21 of the Basic Protocol (to inject the contrast agent).
4. After a 20-sec wait time, run the 3-D gradient echo sequence according to Table A21.1.11.

COMMENTARY

Background Information

The development of MR Mammography has included several phases up to now. At first MR tomography in general had to be developed, then special breast coils (single breast coils, followed by double breast coils and later combined imaging/interventional coils) had to be built and optimized. Contrast media were used at first in spin-echo sequences and later in sophisticated so-called "dynamic" techniques using gradient echo sequences for a better differential diagnosis. The main topics today are technological optimization, evaluation of diagnostic criteria, and development of interventional procedures.

Already in 1971 different relaxation times in tumor tissue as compared with normal tissue were measured using in vitro experiments (Damadian, 1971). However, MR imaging of the human body was possible only after the application of local gradient fields (Lauterbur, 1973). The first tissue samples of the breast were published by Mansfield (1979). These tissue samples were taken ~90 min after operation. The first in vivo images of whole-body MR machines from 128 breasts of 65 patients including 7 cancers were taken in 1982 (Ross et al., 1982). In these reports a whole-body scanner in a field strength of 0.045 T was used and each patient was imaged in a supine position, providing 2 proton density–weighted images and 6 T_1 relaxation time measurements. In 1983, El-Yousef published results of 2 patients using an experimental surface coil in a field strength of 0.03 T and reported a reduced signal intensity of both cancers. In a following publication, El-Yousef (1984) reported images of 10 volunteers and 45 patients describing a reduced signal intensity of breast lesions in spin echo and inversion-recovery sequences.

Starting in 1983, special breast coils were developed which were used only for breast imaging and later sold commercially. Until 1986 only single breast coils were available (Fritschy et al., 1984; Kaiser, 1985; Stelling et al., 1985). After first disappointing trials in a supine position, the examinations were performed in a prone position to minimize movement and artifacts caused by breathing. However, at that time the available spin-echo and inversion-recovery sequences did not allow a definite detection and differentiation of small lesions in all cases, yet the advantage of imaging in thin slices in any orientation in a variable soft tissue contrast without X-rays was already clear (Heywang et al., 1985; Kaiser and Zeitler, 1986a,b). Further progress was the development and introduction of the MR contrast medium Gadolinium-DTPA (Weinmann et al., 1984), because experiments were possible in analogy to computer tomographic results using ionized X-ray contrast medium and radioactive iodine uptake from the mid 1970s (Eskin et al., 1974; Chang et al., 1978). The first group, which got and used contrast medium, was Heywang et al. (1986). Initially spin-echo sequences in relatively long examination times and high contrast dosages were applied and reported; however, the uptake of contrast medium of cancers, normal tissue, and proliferative changes could not be differentiated sufficiently. After the introduction of fast gradient echo sequences (Haase et al., 1986), the first dynamic examinations were established that used repetitive measurements of the same slices before and in short- time intervals after contrast medium injection (Kaiser and Oppelt, 1987; Kaiser and Zeitler, 1989). However how to better differentiate between benign and malignant lesions was the subject of scientific discussion for a long time (see subsection in Literature Cited listing References on Differentiating Benign and Malignant Breast Lesions). The following development of a double breast coil (Kaiser and Kess, 1989) allowed routine measurements of both breasts of a patient in a single examination with a good signal-to-noise ratio.

After these initial steps, a period of evaluation of dynamic techniques using different measurement sequences and dosages followed, mainly in Europe. Since 1991 American groups reported contrast-enhanced MR Mammography, too, using mainly fat saturation sequences

(Harms et al., 1993; Orel et al., 1995) in single breast coils. The results of the enormous variety of measurement techniques were confusing and resulted in a wide variation of opinion about the usefulness of MR Mammography (Kaiser, 1996).

By using MR Mammography, doctors could detect small lesions on the size of a few millimeters. These lesions were often not seen by X-ray or ultrasound. Therefore, the need for the development of interventional MR procedures increased, at first for positioning of markers, later for biopsy and therapeutic removal (Hussman et al., 1993; de Souza et al., 1995; Silverman et al., 1995; Doler et al., 1996; Mahfouz et al., 1996; Sittek et al., 1996; Kuhl et al., 1997; Wurdinger et al., 1997; Thiele et al., 1998). Up to now these techniques required additional MR imaging on another day, i.e., a second measurement in a repetitive use of the MR device and contrast medium injection. At present, single breast biopsy coils in so-called "closed" as well as in "open" MR machines are tested. A bilateral coil for combined imaging and simultaneous intervention has been clinically tested since 1997 (Wurdinger et al., 1997).

Today modern high-field MR machines (above 1.0 T) do not allow direct access to the breasts during data acquisition. The patient has to be in the isocenter of the main magnetic field during imaging and must be moved outside the machine for the following intervention. The position of a wire marking, a core biopsy, or a laser fiber has to be checked after the positioning of the interventional device with further imaging in the MR machine, therefore increasing measurement time, artifacts and pitfalls. An MR compatible robotic system for simultaneous imaging and immediate biopsy/intervention at high field strength is in clinical testing (Kaiser et al., 2000).

Critical Parameters and Troubleshooting

MR Mammography has to be performed in pre- and post-contrast scans to detect the tumor-specific vessel structure which is called tumorangiogenesis. Up to now a non-contrast scan alone is insufficient in detecting very small lesions. In addition to morphological evaluations, the time intensity curve is very important in making the diagnosis. The signal intensity in the first post-contrast images is absolutely crucial for a correct interpretation of the data. This first contrast signal intensity image depends critically on exact measurement parameters. Injection time, injection site, sodium chloride bolus, length of plastic tube, arm position, and tuning parameters are major factors of this critical image signal intensity.

According to our experience, an increase of >90% of signal intensity in the first 90 sec after the start of contrast medium injection ("90-90 rule") is a threshold for a malignant enhancement using 2-D dynamic imaging at 1.5 T (Fig. A21.1.4 and Fig. A21.1.5). To reach this critical threshold, the measurement using a region of interest (ROI) procedure has to be performed carefully. Only the "vital" tumor areas (Fig. A21.1.5 and Fig. A.21.1.6) show a critical initial enhancement followed by a plateau phenomenon or a washout effect. An inclusion of necrotic areas of the tumor or surrounding normal glandular or fatty tissue will deteriorate and

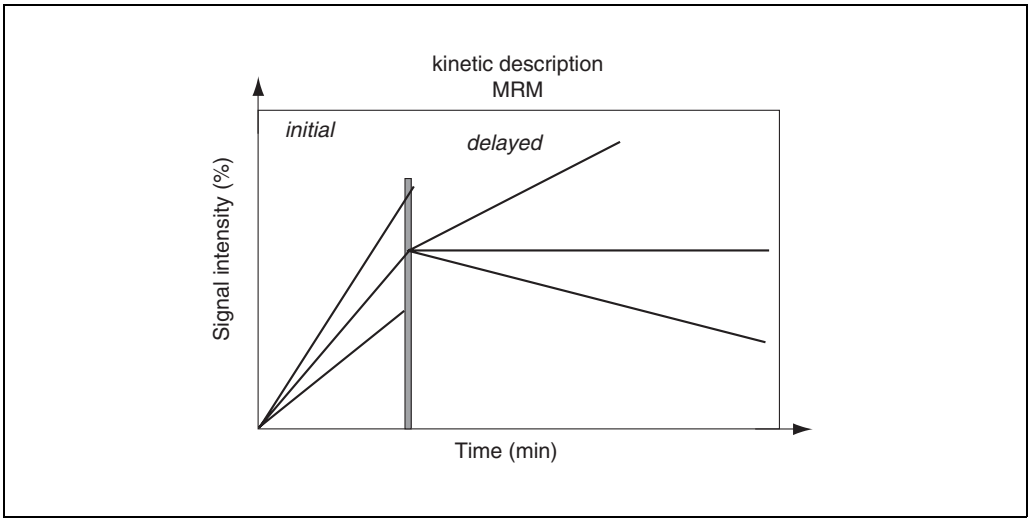

Figure A21.1.4 Signal intensity versus time curve showing relative (percentage) changes of signal after injection of contrast agent: the early ("initial") and later ("delayed") phases are described separately.

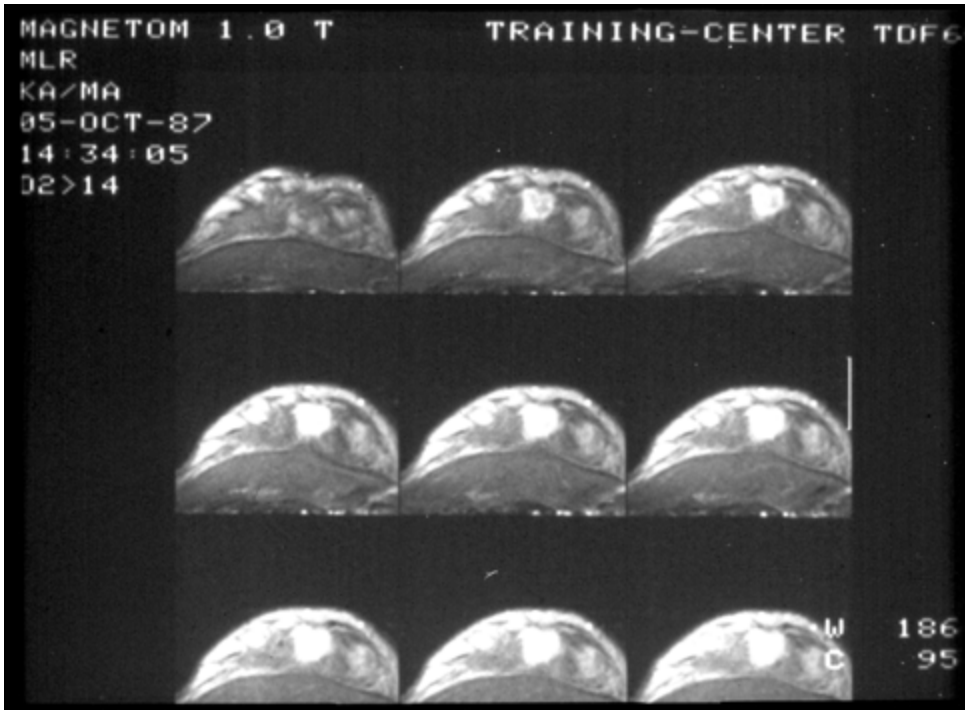

Figure A21.1.5 Nine images of the same slice before (upper left) and every minute after injection of contrast medium: a malignant lesion shows a striking initial signal increase especially in the tumor periphery and a constancy of signal intensity during the following dynamic examination. Note the slower signal change of the normal breast parenchyma.

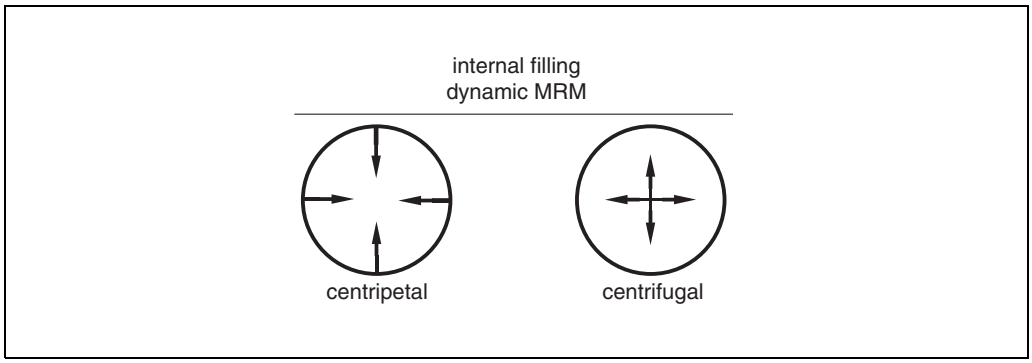

Figure A21.1.6 Different types of enhancement after injection of contrast medium: centrifugal (from inside to outside) and centripetal (from outside to inside).

falsify the effect of kinetic data evaluation. It is necessary to look for the fastest enhancing portion of the lesion.

It is also important not to include just any enhancing spot and describe it as malignant. Vessels are cut in different orientations in the slice and are therefore displayed in a round, oval or comet shaped manner. The observance of inflow phenomena, the delineation of vessels in other slices or other orientations or, if you have still any doubts, an additional MR angiography sequence (see Chapter A1 for MRA sequence) all help clarify whether the tiny enhancing area is a vessel or not.

Fat saturation techniques are in a relatively widespread use in the United States. They allow a pretty high spatial resolution, but have a limited value in the kinetic data evaluation. Since a pre-pulse in a low bandwidth is necessary, the adjustment parameters in pre- and post-contrast scans are not identical. Present fat saturation techniques usually have a relatively high signal inhomogeneity, so that a quantitative evaluation is difficult and subtractions are difficult, nevertheless often necessary. The measurement time in most cases is longer than in non fat saturation techniques and the "diagnostic window" for the detection of differences between benign and malignant enhancement criteria is restricted.

Fat suppression methods may either be by temporal subtraction (which is ideal for fat

suppression, since only enhancing structures are delineated as high signal intensity lesions), or by pre-pulses with the above-mentioned limitations present.

The injection of contrast medium is made in a bolus (3 ml/sec) either manually or by an automatic injector followed by a post-contrast bolus of physiological sodium chloride of 20 ml (cubital vein) or 30 ml (lower arm/hand). It is preferable not to move or talk to the patient during injection, but rather to explain the procedure before positioning the patient in the machine. According to our experience, the dose of contrast medium should not be higher than 0.1 mmol/kg. A higher dose shortens the already short "diagnostic window", i.e., the time difference of only 1 to 2 min where the contrast uptake between malignant and benign lesions is sufficiently different in order to enable a differential diagnosis.

The data evaluation begins by looking at fatty tissue on both breasts and to control if the signal intensity of fatty tissue is constant everywhere in the breast. If this signal intensity of fatty tissue as an "internal standard" varies, consider that it might be due to a changing receiver adjustment or field inhomogeneity effects or artifacts. In these cases a quantitative evaluation is difficult or impossible, since the technical problems overlap any morphological information.

Dynamic MRM should be performed using transverse scans (sequence 5), because in this orientation the identification of vessels, nipples, posterior borders of implants, fatty layer between parenchyma and muscle, signal homogeneity of the coil and signal correlation with the aorta is much easier. However, if the lateral border of the parenchyma towards the axillary region and/or lymph nodes is especially important, a dynamic MRM in coronal scans is advantageous. A sagittal orientation should be avoided because of doubled measurement time and the lack of correlation with the other breast. Furthermore, it is difficult to detect inflow phenomena and hormone effects, etc., in this orientation

If only the axillary region is important, the rotation of phase encoding direction towards a dorsoventral orientation is recommended to keep the lateral axillary region free of phase encoding artifacts.

It is of crucial importance to use echo times where fat and water protons are in "in-phase" conditions, because only in these echo times will Gd have a signal-*increasing* effect on the water protons in the voxel. Especially tiny reticular structures like DCIS or lobular cancers can be examined only in this "in-phase" image. "In-phase" situations for 1.5 T are even multiple numbers of 2.4 msec, i.e., 4.8 msec, 9.6 msec, etc. Odd multiple numbers of 2.4 msec, for example, 7.2 msec, are "forbidden" because of the "opposed effect" of water and fat protons. This effect is field strength dependent and should be adjusted according to the field strength used.

During the dynamic examination it is essential not to change tuning parameters between scans in order to guarantee identical pulses in pre- and post-contrast scans. Only under these conditions is a correct signal intensity versus time evaluation possible.

The pre-contrast signal intensity of parenchyma should be in a typical range for this sequence. If it is too low, look for an inappropriate receiver adjustment or inappropriate coil as the problem and try to change the receiver adjustment. If this pre-contrast signal intensity is too high, it could also suggest an inappropriate receiver adjustment or some other medical/biological reason for the problem, such as bleeding after puncture/biopsy, hormone effect, pregnancy, previous operation and/or radiation.

Anticipated Results

Morphological and kinetic information

Diagnosis of breast lesions in MR Mammography is always made by a combined morphological and kinetic analysis. It is the main feature of MRM that tumortypic "tumorangiogenesis" can be detected by signal intensity versus time curves. Various curves are listed in Figure A21.1.4. A typical malignant lesion shows the striking initial increase (wash-in phenomenon) within the first 1 to 2 min after the injection of contrast medium followed by either a constant signal (plateau phenomenon) or—more specifically—a decrease in signal intensity (washout effect). The sudden increase and the following constancy or washout effect make the so-called "cancer-corner" of the signal-time curve. Benign lesions normally show a slower initial increase which is continuouly rising over the complete dynamic examination. Morphological analysis describes the type of enhancement as shown schematically in Figure A21.1.6. The distribution of a lesion is described as either regional or patchy or diffuse or symmetric, and the morphology of the lesion itself is described as a focal mass with sharp or non-sharp margins, linear, linear-branched, or

Table A21.1.12 Morphological Analysis of Breast Lesions

Shape	Margin	In the mass
Round	Smooth	Homogeneous
Oval	Scalloped	Heterogeneous
Lobulated	Irregular	Rim
Irregular	Spiculated	Septations
Stellate		Enhancing
		Non-enhancing

segmental aspects (Harms, 1999). The initial and late enhancement is described as being homogeneous, heterogeneous, rim enhancement, bright or dark septations after contrast medium injection and centripetal or centrifugal filling effect over time. A centrifugal filling (from inside to outside) directs mainly towards a benign lesion, a centripetal filling (from outside to inside) towards a malignant lesion (Fig. A21.1.6). An overview of the morphological analysis according to shape, margins and enhancement is listed in Table A21.1.12.

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I would like to thank my secretary Dorit Dirlam for typing this unit.

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Internet Resources

http://www.mediteach.de

List of detailed courses in MR Mammography, history of MR Mammography, MRM publications of the author.

http://www.mrisafety.com

List of possible safe or unsafe materials for a quick overview.

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