BREAST MAGNETIC RESONANCE IMAGING

DOTAREM 0.5 mmol/mL, solution for injection. **Composition:** For 100 mL of solution: active ingredient: Gadoteric Acid 27.932 g corresponding to: DOTA 20.246 g corresponding to gadolinium oxide 9.063 g. **Indications (*):** Medicinal product for diagnostic use only: Magnetic Resonance Imaging for cerebral and spinal disease, diseases of the vertebral column, and other whole-body pathologies (including angiography). **Posology and method of administration:** The recommended dose is 0.1 mmol/kg, i.e. 0.2 mL/kg in adults and children. In angiography, depending on the result of the examination being performed, a second injection may be administered during the same session if necessary. Angiography with Gadoteric acid is not recommended in children (0-18 years). In Encephalic and spinal MRI, in some exceptional cases, as in the confirmation of isolated metastases or the detection of leptomeningeal tumours, a second injection of 0.2 mmol/kg may improve tumor characterisation and facilitate therapeutic decision making. For patients with impaired renal function and paediatric population (0-18 years) more than one dose should not be used during a scan, injections should not be repeated unless the interval between injections is at least 7 days. The product must be administered by strict intravenous injection. Depending on the amount of gadoteric acid to be given to the child, it is preferable to use gadoteric acid vials with a single use syringe of a volume adapted to this amount in order to have a better precision of the injected volume. In neonates and infants the required dose should be administered by hand. **Contraindications:** Hypersensitivity to gadoteric acid, to meglumine or to any medicinal products containing gadolinium. **Special warnings and precautions for use:** Dotarem must not be administered by subarachnoid (or epidural) injection. The usual precaution measures for MRI examination should be taken such as exclusion of patients with pacemakers, ferromagnetic vascular clips, infusion pumps, nerve stimulators, cochlear implants or suspected intraorganal metallic foreign bodies, particularly in the eye. **General particulars corresponding to all gadolinium contrast agents:** All gadolinium based contrast media can cause minor or major hypersensitivity reactions that can be life-threatening. These can occur immediately (within 60 minutes) or be delayed (within 7 days) and are often unpredictable. Because of the risk of major reactions, emergency resuscitation equipment should be available for immediate use. Hypersensitivity reactions can be aggravated in patients on betablockers and particularly in the presence of bronchial asthma. These patients may be refractory to standard treatment of hypersensitivity reactions with beta agonists. Impaired renal function: Prior to administration of gadoteric acid, it is recommended that all patients are screened for renal dysfunction by obtaining laboratory tests. There have been reports of Nephrogenic Systemic Fibrosis (NSF) associated with use of some gadolinium-containing contrast agents in patients with severe renal impairment (GFR < 30 ml/min/1.73 m²). As there is a possibility that NSF may occur with Dotarem, it should only be used in these patients after careful consideration. CNS disorders: As with other contrast agents containing gadolinium, special precautions should be taken in patients with a low seizure threshold. Precautionary measures, e.g. dose monitoring, should be taken. All equipment and drugs necessary to counter any convulsions which may occur must be made ready for use beforehand. **Interactions with other medicinal products and other forms of interaction:** No interactions with other medicinal products have been observed. Formal drug interaction studies have not been carried out. **Fertility, pregnancy and lactation:** Gadoteric acid should not be used during pregnancy unless the clinical condition of the woman requires use of gadoteric acid. Continuing or discontinuing breast feeding for a period of 24 hours after administration of gadoteric acid, should be at the discretion of the doctor and lactating mother. **Effects on ability to drive and use machines:** No studies on the effects on the ability to drive and use machines have been performed. Ambulant patients while driving vehicles or operating machinery should take into account that nausea may incidentally occur. **Undesirable effects:** Uncommon (≥1/1000 to <1/100): hypersensitivity, headache, dysgeusia, dizziness, somnolence, paraesthesia (including burning sensation), hypotension, hypertension, nausea, abdominal pain, rash, feeling hot, feeling cold, asthenia, injection site reactions (extravasation, pain, discomfort, oedema, inflammation, coldness). Rare (≥1/10 000 to <1/1 000): anxiety, presyncope, eyelid edema, palpitations, sneezing, throat tightness, vomiting, diarrhea, salivary hypersecretion, Urticaria, pruritus, hyperhidrosis, chest pain, chills. Very rare (<1/10 000): anaphylactic reaction, anaphylactoid reaction, agitation, coma, convulsion, syncope, tremor, parosmia, conjunctivitis, ocular hyperaemia, vision blurred, lacrimation increased, tachycardia, cardiac arrest, arrhythmia, bradycardia, flushing, pallor, vasodilatation, hot flush, cough, dyspnoea, nasal congestion, respiratory arrest, bronchospasm, throat irritation, laryngospasm, pharyngeal oedema, dry throat, pulmonary oedema, erythema, angioedema, eczema, muscle cramps, muscular weakness, back pain, arthralgia, malaise, chest discomfort, pyrexia, face oedema, injection site necrosis (in case of extravasation), phlebitis superficial, decreased oxygen saturation, Not known : nephrogenic systemic fibrosis. **Overdose:** Gadoteric acid can be removed by haemodialysis. However there is no evidence that haemodialysis is suitable for prevention of nephrogenic systemic fibrosis. **Please note:** The peel-off tracking label on the vials or syringes should be stuck onto the patient record to enable accurate recording of the gadolinium contrast agent used. The dose used should also be recorded. If electronic patient records are used, the name of the product, the batch number and the dose should be entered into the patient record. **Pharmacological properties:** Pharmacotherapeutic group: paramagnetic contrast media for MRI, ATC code: V08CA02. **Presentation (*):** 5, 10, 15, 20, 60 & 100 mL in vial (glass) and 10, 15 & 20 mL in a prefilled syringe (glass). **Marketing authorization holder: (*) Information:** Guerbet - BP 57400 - F-95943 Roissy CdG cedex – FRANCE. Tel: 33 (0) 1 45 91 50 00. **Date of revision of this document:** September 2016.
For current and complete prescribing information refer to the package insert and / or contact your local Guerbet organization.
(*) Indications, presentations and marketing authorization holder may differ from country to country.
Reporting of suspected adverse reactions is important as it helps to continuously assess the benefit-risk balance. Therefore, Guerbet encourages you to report any adverse reactions to your health authorities or to our local Guerbet representative.

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DOTAREM®

Gadoteric acid

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#2
MRI PROTOCOLS

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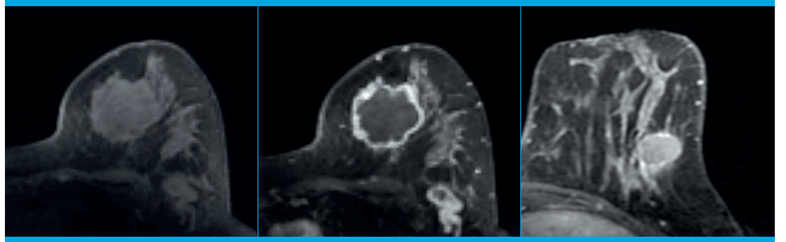


Guerbet
Contrast for Life

DOTAREM®
Gadoteric acid

WHY BREAST MRI?

Dynamic contrast-enhanced magnetic resonance imaging (DCE-MRI) of the breast has become an essential step of breast diagnosis. It is a non-ionising technique that can provide high spatial resolution, and multiplanar images with excellent contrast. Compared with conventional diagnostic methods, such as X-ray mammography and ultrasound, dynamic breast imaging offers significantly higher sensitivity and more precise insight into lesion morphology and functional features.

Indications

Currently, the most important indications are:

- Inconclusive findings on conventional imaging.
- Staging of a breast cancer.
- Evaluation of the breasts in case of metastases of an unknown primary carcinoma.
- Evaluation of therapy response in patients treated with neoadjuvant chemotherapy.
- Exclusion of local recurrence after breast-conserving therapy.
- Screening of women with a lifetime risk of 20% or more to develop breast cancer, including mutation carriers.
- Evaluation of implants integrity.
- Guiding biopsy when lesions are not visible in classic techniques.

HOW TO PERFORM A BREAST MRI?

PATIENT POSITIONING AND COILS

Because she will be required to remain still for a relatively long duration, it is advisable to **make the patient as comfortable as possible** before the start of the examination. It is better to spend a few extra minutes at the beginning of the examination to make sure that the patient is comfortable.

Breast MRI scans are performed with the patient lying on the prone position with both breasts freely hanging. The arms may be positioned along the body or above the head depending on the comfort of the patient. It is important to always scan the patient in the same position in case that image comparison between two scans is needed.
Placement of an intravenous catheter for contrast agent administration or access to an injection site in the arm or on the hand for manual injection may require that at least one arm be positioned above the head.

CONTRAST AGENT

Breast MRI that is performed to evaluate a patient for breast cancer requires the use of a contrast agent.
Posology of gadolinium-based contrast agent to apply:
A single dose of 0.1 mmol/kg body weight is enough when a sequence with fat suppression is used. Since the concentration of Dotarem® is 0.5 mmol per millliliter, the corresponding volume that needs to be injected is 0.2 ml/kg of body weight.
Injection time must be less than 10 seconds and the injection speed of 2-3 ml/sec. As the mode of injection has implications for pharmacokinetic modelling of signal intensity changes, the consistency of contrast agent injection method is most important and the use of a power injector is recommended.
An injection of saline solution (15-20 ml) should follow in order to flush the contrast agent from the tubing.

TECHNICAL ASPECTS: FIELD STRENGTH, SEQUENCES AND IMAGING PLANES

Sequences used for breast tumor detection and characterization

1 3-planes localizer. This is a quick localizer sequence obtained in three planes. It is used to confirm the optimal patient positioning within the breast coil. The sagittal views are most helpful. Bright signal from the inferior aspect of the coil should end at the inframammary fold. This will allow a maximum coil signal yield.

2 Pre-contrast sagittal T1-weighted non-fat saturated pulse sequences such as spin echo (SE) or fast spin echo (FSE) sequences were historically used to delineate fat and blood lesions like hematoma, hamartoma and fat necrosis.
They may be applied on an axial slice that is centred between the axilla and the inframammary fold, but not on the centre of the breasts. This will allow a better visualization of the axillary nodes.

Scan direction should be from left edge to right edge of the breasts with a field of view large enough to include the axilla and assess the lymph nodes.

3 Pre-contrast T2-weighted axial FSE sequences are useful to separate cysts from solid masses and mixoid fibroadenoma or coloid cancer.

4 Axial diffusion-weighted sequences. MRI can be used to measure the diffusion of water in-vivo and obtain apparent diffusion coefficient (ADC) maps. This method is used for providing additional information that might help discriminate benign from malignant contrast-enhancing lesions.
Diffusion-weighted imaging (DWI) works with pulse sequences that are sensitive to very small motion of water protons at the microscopic level.

5 A set of dynamic contrast-enhanced sequences. 3D T1-weighted gradient echo sequences may be used to acquire both pre-contrast and multiple post-contrast views in order to separate enhancing lesions from other breast tissues. The slice thickness should be < 3 mm and the acquisition time 1-2 minutes. Homogeneous and efficient fat suppression is necessary.
The field of view (FOV) should be kept as small as possible (28-32 cm) but it should include both breasts. This helps to ensure homogeneous fat saturation and optimal spatial resolution.
Peak enhancement in the case of breast cancer occurs within the first 2 min after the injection of a contrast agent. Therefore, relatively short data acquisition times, in the order of 60-120 seconds per volume acquisition, are necessary. This allows sampling of the time course of signal enhancement after contrast agent injection, which is useful because highly vascularised breast tumours usually show a faster contrast uptake than the surrounding tissue.
Parallel imaging (PI) is a simultaneous bilateral acquisition method allowing to visualize any acquisition plane:

- Sagittal plane acquisition requires the minimum FOV and generates images similar to X-ray mammography imaging. It is the best anatomical plane to study ductal infiltration.
- Axial plane acquisition is good to compare both breasts but needs a larger FOV. A larger matrix can compensate for it.
- Coronal plane acquisition can be used with rectangular FOV but needs more slices.

All acquisitions performed before, during and after contrast agent injection should be done in the same series to allow for optimal subtraction when the images are analyzed. It is important to turn on the multiphase option to ensure that the scanner memory can accommodate the number of post-contrast sequences planned. At least three phases are necessary to analyze the enhancement curve. A pre-scan image should be acquired manually to ensure the best possible fat saturation (the frequency direction should be A/P).

Use of PI increases temporal resolution. The final spatial resolution of the images depends on different factors, especially the size of the imaging volume, defined by the FOV, the slice thickness and the acquisition matrix. Breast MRI should be capable of detecting all lesions larger than or equal to 5 mm.

POST-PROCESSING, ANALYSIS AND INTERPRETATION

SUBTRACTION

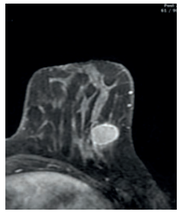
Image subtraction means subtracting pre-contrast images from each post-contrast image, pixel by pixel. A subtracted image set consisting of series of subtracted images for each time point is built. The most important subtraction series are the ones acquired at 2 minutes post-injection and the last series, representing early phase and delayed phase of the intake of contrast agent respectively.

TIME CURVES OF ENHANCEMENT

Time curves of signal enhancement can be constructed manually or automatically using breast MRI post-acquisition analysis or CAD software.
Time curves of enhancement should be constructed from the raw images which have been acquired, not from the subtracted images. The use of these raw images allows the software to determine the percent signal increase relative to pre-contrast signal.
Time curves of enhancement should be based on the most strongly and rapidly enhancing pixels in a lesion. It is recommended to use images from the early phase (1-2 min post-contrast) to determine the placement of the region of interest (ROI). It is important to confirm that the pixels showing the most suspicious curves actually represent a lesion rather than a vessel.

INTERPRETATION

The physician interpreting breast MRI scans must have the knowledge and expertise in breast disease and breast imaging diagnosis. Reporting should be performed using the American College of Radiology (ACR) BI-RADS MRI Lexicon.
It is important to follow a standardized order for the correct interpretation of the images so that all remaining findings are included in a report.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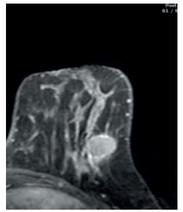
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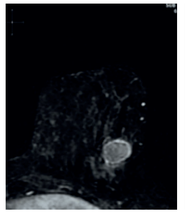
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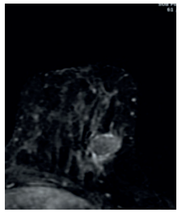
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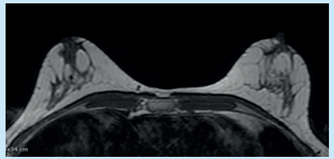

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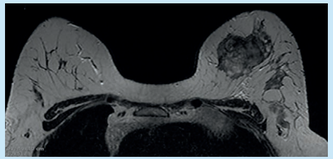

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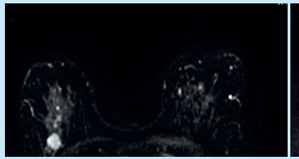
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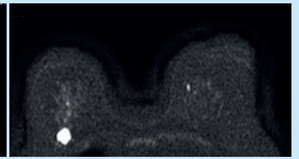
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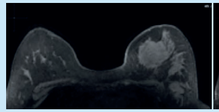
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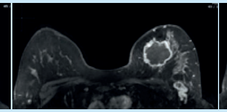
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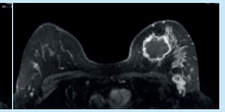
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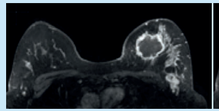
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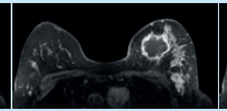
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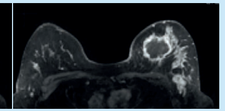
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