CARDIAC 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 9.062 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 results 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 metastasis or the detection of leptomeningeal tumours, a second injection of 0.2 mmol/kg may improve tumor characterization 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 intraorgonal 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. close 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, ecchymosis, 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 oedema, 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, 40 & 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. Tél: 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.

Guerbet

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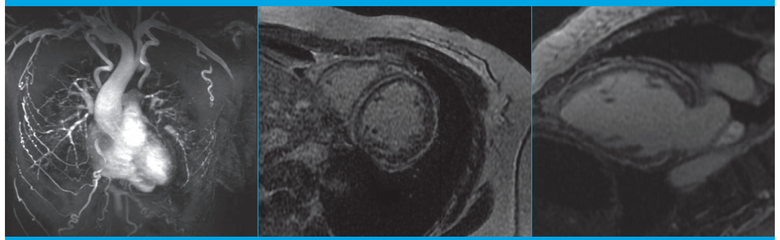
DOTAREM®

Gadoteric acid

CARDIAC MAGNETIC RESONANCE IMAGING

#1
MRI PROTOCOLS

PROF. GRAEME HOUSTON
Ninewells Hospital, Dundee, Scotland



Guerbet
Contrast for Life

DOTAREM®
Gadoteric acid

GENERAL PROTOCOL FOR ALL PATIENTS

CARDIAC MAGNETIC RESONANCE IMAGING (MRI)

is a non-ionising, non-invasive technique that can provide the referring physician with a full cardiac assessment of morphology, function, perfusion and viability in a single imaging session. The imaging protocols for cardiac MRI using intravenous Dotarem® contrast agent comprise part of the whole cardiac MRI assessment and must be tailored according to the clinical questions being asked, the patient tolerance of the MRI and the desire for quantitative data analysis. The cardiac imaging protocol is best selected prior to the start of the examination and may consist of separate components with the option of extending the protocol on reviewing the images. It is normal for the whole examination to be expected to be completed within 45 minutes.

Patients may be unsuitable for imaging if they have certain medical devices (e.g. cardiac pacemaker) or ferromagnetic fragments (e.g. shrapnel) in their bodies. Devices considered 'MR safe' at 1.5T may not be safe at 3.0T. Where doubts exist regarding MRI compatibility, the MRI physicist can refer to www.mrisafety.com. In addition, prior to cardiac MRI, the patient's renal function needs to be checked before administering gadolinium chelate according to guidance in the EU (http://www.ema.europa.eu/ema/).
The patient is prepared after exclusion of contraindications to MRI, iv cannula inserted and ECG electrodes applied with careful attention to achieving an optimal R wave trace suitable for ECG gating. After patient positioning, the cardiac coil is applied and attention to their comfort ensured before connection of the iv cannula to the pump injector.

Depending on the indication for the cardiac MRI examination, the imaging protocol is tailored according to the following assessments:

LOCALISERS

Depending on the MRI unit, single slice localisers or semi-automated localisers may be used (Figure 1 and 2).

MORPHOLOGY AND FUNCTION

The overall cardiac morphology in terms of cardiac chamber orientation, pericardial and aortic and pulmonary arterial anatomy is examined using coronal and axial T2-weighted sequences such as axial (8-10 mm) set of steady state free precession (SSFP) or half Fourier single shot turbo spin echo (HASTE) through chest. The 2, 4 chamber CINE sequences are planned from the localisers and performed using cardiac gating.

THIS IS FOLLOWED BY SHORT AXIS T2 CARDIAC

gated sequences to examine both left ventricular (LV) and right ventricular (RV) movement and to allow quantitative LV (and RV) analysis of LV mass, systolic and diastolic volumes, stroke volumes and ejection fraction. The common parameters are interleaved 5-7 mm slices, with 5-7 mm interslice gap from base of heart to apex, temporal resolution balanced against use of parallel imaging (Figure 3).

OPTIONAL PROCEDURES

IF THERE IS A NEED FOR CLINICAL VALVULAR ASSESSMENT,

then LV or RV outflow tract, or basal mitral or tricuspid valvular CINEs with phase contrast assessment of trans-valvular flow abnormality may be performed. These are usually single slice gradient recalled echo (GRE) CINE with orientations either through valve to assess turbulence or transverse phase contrast across the valve for flow quantitation with an appropriate velocity encoding to avoid aliasing.

IF LV TISSUE ASSESSMENT IS NEEDED,

short axis fat suppressed T2 (STIR) or Black Blood sequences may be acquired e.g. to assess evidence of myocarditis. T2* mapping may also be used to detect iron overload. This should be performed prior to contrast administration (Figure 4).

IF A PERFUSION ABNORMALITY IS SUSPECTED,

then dynamic contrast-enhanced first pass perfusion at rest or after stress (e.g. iv adenosine) then rest is performed. Consideration of splitting the contrast dose may be useful to better delineate the perfusion abnormality in multiple planes. Perfusion imaging is performed using a heavily T1-weighted saturation-recovery GRE, GRE-EPI hybrid, or SSFP sequence. Three short-axis images should be obtained for every heartbeat, with slice thickness 8 mm, in plane resolution 2x2 mm. Contrast is given, through an antecubital vein at a rate of 4 ml/sec followed by 20 ml saline flush at the same rate. The total dose of contrast is 0.05-0.1 mmol/kg. Images are obtained for 40 cardiac cycles to allow the contrast to have perfused the LV myocardium.

IF A STRESS THEN REST PERFUSION STUDY IS PERFORMED,

then 2 iv lines are commenced, one with contrast agent, the other with stressor. A pre-contrast perfusion acquisition is performed to check position followed by the infusion of Adenosine at a dose of 140 µg/kg/min for 2 minutes. Gadolinium contrast agent is given during the last minute of adenosine. The total adenosine infusion time is 3-4 minutes. Rest perfusion follows after 10 minutes rest (Figure 5).

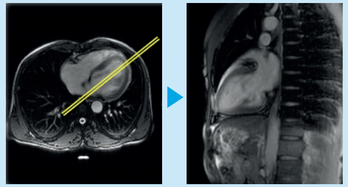
IF ASSESSMENT OF MYOCARDIAL VIABILITY IS INDICATED,

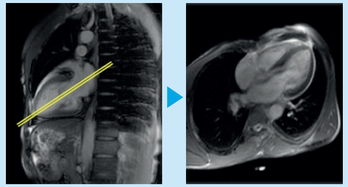
then delayed Dotarem® inversion recovery sequences after 10 minutes post-injection is undertaken (Figure 6). However, single-shot inversion recovery SSFP images with a long inversion time (~ 600 ms) can be obtained earlier, at 2-5 minutes post contrast for thrombus detection. The high-resolution inversion recovery GRE images are obtained with a segmented acquisition during mid-diastole at the same slice positions and with the same slice thickness as the short axis, 2 and 4 chamber CINE images. The in-plane resolution should be ~ 1.2-1.8 mm. The inversion time should be adjusted to null the signal from normal myocardium. An inversion time scout series may be helpful in estimating the appropriate inversion time, but a few trial images only, are usually necessary to optimize image quality. If there is inappropriate nulling, then the myocardial enhancement may not be so easily visualised.

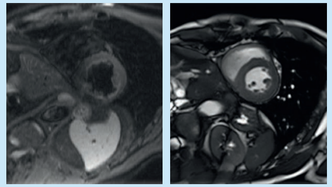
THE IMAGE POST-PROCESSING AND QUANTITATIVE

analysis is performed after the examination (Figure 7). This should be undertaken by experienced image analysis operators. The quantitative results should be viewed with knowledge of the normal ranges of the parameters. If longitudinal assessment of the quantitative parameters is undertaken, then the reproducibility of the assessment in the hands of the observer(s) should be considered before conclusions are made about a significant change in the measurements made over time.

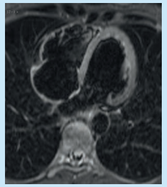
The images should be reviewed along with the quantitative results taking into account all available clinical information and previous imaging findings.

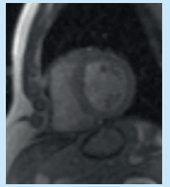
1

Axial scan used to plan 2-chamber image

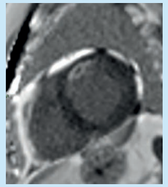
2

2-chamber localiser used to plan 4-chamber

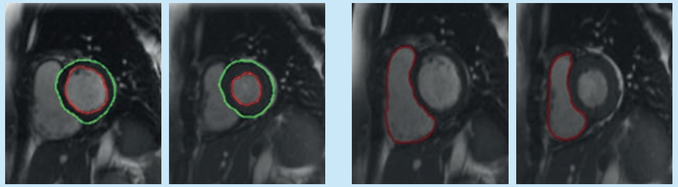
3

Black blood image of heart

Short axis T2-weighted image of heart

4

AXIAL stir image of R and L ventricles

5

Fast GRE perfusion of the heart

6

Late DOTAREM® enhancement showing infarcted lesion

7

Short-axis images are post-processed to provide important parameters of cardiac function