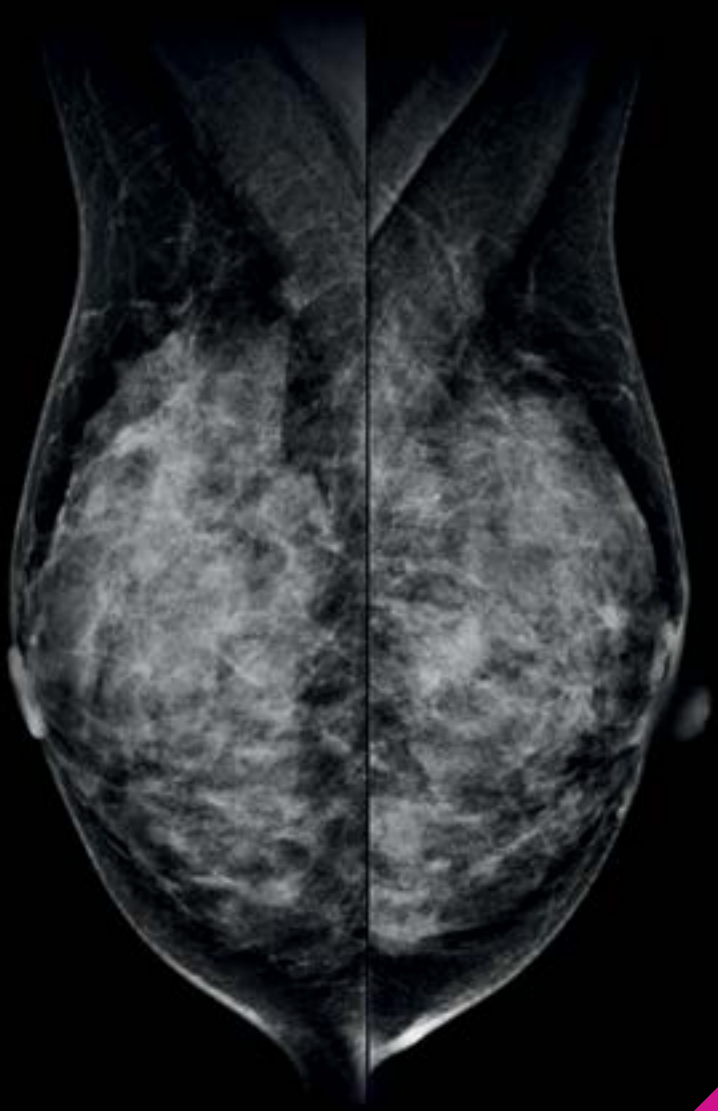
The Power of MRI in DENSE Breasts

The DENSE Tissue and Early Breast Neoplasm Screening Trial



Clear Direction. From Diagnosis to Care.

Gadovist® 1.0
Gadobutrol

DENSE: Largest MRI Screening Trial

- About 10 % of women starting screening have extremely dense breasts[1]
- Women with extremely dense breasts have an increased risk of breast cancer and lower mammographic sensitivity[2]
- Gadovist® contrast-enhanced MRI can improve breast cancer detection because of higher sensitivity compared to mammography[2]

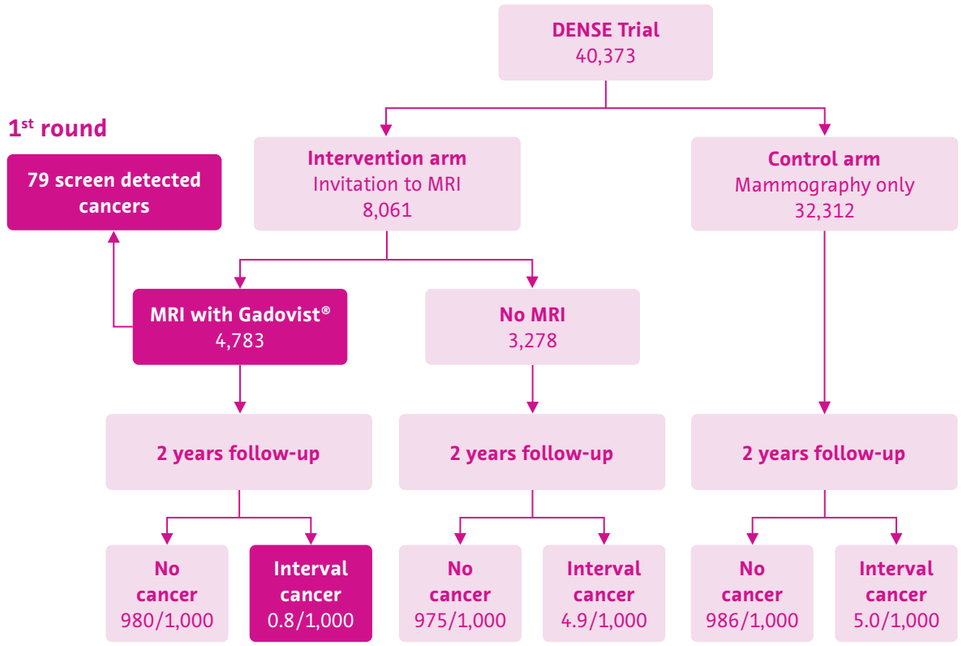


Figure 1 Flowchart. DENSE investigated the effectiveness of screening with mammography plus MRI compared to mammography alone (1:4 ratio) in women age 50–75 with extremely dense breasts (ACR 4) in a prospective, parallel-group, randomized, controlled, multicenter trial in the Dutch biennial screening program. Three consecutive screening rounds are performed (1st round prevalence, 2nd and 3rd round incidence)[1]

Gadovist® Contrast-Enhanced MRI Cuts Interval Cancers in Half

Results of 1st screening round

MRI screening participants	No./Total	Rate (95 % CI)
Breast cancers detected	79/4,783	16.5/1,000 (13.1–20.5)
Recall rate	454/4,783	94.9/1,000 (86.9–103.6)

Table 1 Secondary endpoint screening-detected cancer. Recall rate: Women with MRI for which follow-up diagnostic procedures were necessary (imaging or biopsy)

- Supplemental MRI in first screening round detected 16.5/1,000 additional cancers after negative mammography[3]

Primary endpoint Interval cancer rate per 1,000	Control arm Mammography only	Intervention arm Invitation to MRI with Gadovist®
ITT population	5.0	2.5
MRI participants	–	0.8
MRI non-participants	–	4.9

Table 2 Primary endpoint interval cancer rate assessed during 2-year follow-up after 1st MRI, ITT: Intention to treat (all woman invited for MRI) MRI participants: 59% who accepted invitation to MRI

- Supplemental MRI screening with Gadovist® in women with extremely dense breasts results in 50 % less interval cancers[2]

GADOVIST® 1.0 mmol/mL solution for injection. **Composition:** GADOVIST 1.0 is a clear, sterile, aqueous solution. Each mL of GADOVIST 1.0 contains 604.72 mg (1.0 mmol) of gadobutrol, 1.211 mg trometamol, 0.013 mg sodium (0.00056 mmol), and 0.513 mg calcium sodium butrol in water for injection. The pH of GADOVIST 1.0 is adjusted to between 6.6 and 8.0 with hydrochloric acid. **Indications:** GADOVIST 1.0 (gadobutrol) is a medicinal product for diagnostic use only. GADOVIST 1.0 (gadobutrol) is indicated in adults and children of all ages including term newborns for: contrast enhancement during cranial and spinal MRI investigations and for contrast-enhanced magnetic resonance angiography (CE-MRA); contrast enhanced MRI of the breast to assess the presence and extent of malignant breast disease, and MRI of the kidney. GADOVIST 1.0 is particularly suited for cases where the exclusion or demonstration of additional pathology may influence the choice of therapy or patient management, for detection of very small lesions and for visualization of tumors that do not readily take up contrast media. GADOVIST 1.0 is also suited for perfusion studies for the diagnosis of stroke, detection of focal cerebral ischemia and tumor perfusion. **Contraindications:** GADOVIST 1.0 should not be administered to patients who have experienced a life-threatening reaction to GADOVIST 1.0 previously. **Serious warnings and precautions for use:** Gadolinium-based contrast agents (GBCAs) increase the risk for Nephrogenic Systemic Fibrosis (NSF) in patients with: chronic severe renal insufficiency (glomerular filtration rate <30 mL/min/1.73m2), or acute renal failure / acute kidney injury. In these patients, avoid use of GBCAs unless the diagnostic information is essential and not available with noncontrast-enhanced magnetic resonance imaging (MRI). NSF may result in fatal or debilitating systemic fibrosis affecting the skin, muscle, and internal organs. Screen all patients for renal dysfunction by obtaining a history and/or laboratory tests. When administering a GBCA, do not exceed the recommended dose and allow a sufficient period of time for elimination of the agent from the body prior to any readministration. **Adverse reactions:** Patients with a history of previous reaction to contrast media, allergic disorders or bronchial asthma suffer more frequently from hypersensitivity reactions than others. As with other contrast media, delayed allergoid reactions occurring hours or days after administration have been observed, though rarely. Anaphylactoid reactions may occur. Transient sensations of taste or smell perversion may occur during or immediately after injection of GADOVIST 1.0.

1 **Sprague BL, Gangnon RE, Burt V, et al.** Prevalence of mammographically dense breasts in the United States. J Natl Cancer Inst. 2014:12;106(10).

2 **Emaus MJ, Bakker MF, Peeters PH, et al.** MR Imaging as an Additional Screening Modality for the Detection of Breast Cancer in Women Aged 50-75 Years with Extremely Dense Breasts: The DENSE Trial Study Design. Radiology. 2015;277(2):527–537.

3 **Bakker MF, de Lange SV, Pijnappel RM, et al.** Supplemental MRI Screening for Women with Extremely Dense Breast Tissue. N Engl J Med. 2019; 381(22):2091–2102.

The patient data that appears in this document is actual health information but all personal identifiers have been removed or otherwise anonymized. No personally identifiable information is shown.

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