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ORIGINAL REPORT

Dynamic magnetic resonance imaging of the breast: Comparison of gadobutrol vs. Gd-DTPA☆

F. Escribano[a,*], M. Sentís[a], J.C. Oliva[b], L. Tortajada[a], M. Villajos[a], A. Martín[a], S. Ganau[a]

[a] *Área de Radiología Mamaria y Ginecológica, Hospital Universitari Parc Taulí, UDIAT, Institut Universitari Parc Taulí-UAB, Sabadell, Barcelona, Spain*
[b] *MPharm, MStat, Institut d'Investigació i Innovació Parc Taulí (I3PT), Sabadell, Barcelona, Spain*

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KEYWORDS
Breast cancer;
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Abstract
Objective: To compare the pharmacokinetic profile of gadobutrol versus Gd-DTPA in dynamic contrast-enhanced MRI (DCE-MRI) in patients with breast cancer. Secondary objectives included comparing the safety profiles and diagnostic efficacy of the two contrast agents for detecting additional malignant lesions.
Material and methods: This retrospective observational study included 400 patients with histologically confirmed breast cancer; 200 underwent DCE-MRI with Gd-DTPA (Magnevist®) and 200 underwent DCE-MRI with gadobutrol (Gadovist®). Pharmacokinetic parameters and signal intensity were analyzed in a region of interest placed in the area within the lesion that had greatest signal intensity in postcontrast sequences. We compared the two groups on pharmacokinetic variables (K^{trans}, K_{ep}, and V_e), time-signal intensity curves, and the number of additional malignant lesions detected.
Results: The relative signal intensity (enhancement) was higher with gadobutrol than with Gd-DTPA. Washout was lower with gadobutrol than with Gd-DTPA (46% vs. 58.29%, respectively; $p = 0.0323$). Values for K^{trans} and K_{ep} were higher for gadobutrol ($p = 0.001$). There were no differences in the number of histologically confirmed additional malignant lesions detected ($p = 0.387$).
Conclusions: Relative enhancement is greater with gadobutrol, but washout is more pronounced with Gd-DTPA. The number of additional malignant lesions detected did not differ between the two contrast agents. Both contrasts are safe.

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* Corresponding author.
E-mail address: ferescri@gmail.com (F. Escribano).

PALABRAS CLAVE
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Resonancia magnética dinámica de mama: estudio comparativo de gadobutrol y Gd-DTPA

Resumen
Objetivo: Evaluar el perfil farmacocinético del gadobutrol en comparación con el Gd-DTPA, en resonancia magnética de mama con contraste (RM-DC). El objetivo secundario es valorar la eficacia diagnóstica en la detección de lesiones adicionales tumorales en RM-DC, y el perfil de seguridad de ambos contrastes.
Material y métodos: Estudio retrospectivo y observacional que incluyó 400 pacientes con diagnóstico histológico de cáncer mamario. A 200 pacientes se les realizó RM-DC con contraste Gd-DTPA (Magnevist®) y a las otras 200 con gadobutrol (Gadovist®). Se analizaron los parámetros farmacocinéticos y la intensidad de señal mediante una ROI *(region of interest)* en el área intralesional con mayor intensidad de señal en las secuencias poscontraste. Se compararon las variables farmacocinéticas (K^{trans}, K_{ep} y V_e) y las curvas de intensidad de señal-tiempo de ambos grupos, así como el número de lesiones adicionales tumorales detectadas con ambos contrastes.
Resultados: El realce relativo de intensidad de señal es más alto con gadobutrol que con Gd-DTPA. El gadobutrol muestra significativamente menos lavado (46%) que el Gd-DTPA (58,29%) (p = 0,0323). Se observan valores más altos de K^{trans}, K_{ep} y V_e para el gadobutrol, siendo la diferencia estadísticamente significativa para los dos primeros parámetros (p = 0,001). No se encuentran diferencias en el número de lesiones adicionales malignas confirmadas histológicamente (p = 0,387).
Conclusiones: El gadobutrol tiene valores más altos de realce, mientras que el Gd-DTPA muestra un lavado más marcado. El gadobutrol no es inferior en cuanto a número de lesiones adicionales malignas detectadas. Ambos contrastes son seguros.

Introduction

The IV dynamic contrast-enhanced MRI (DCE-MRI) of the breast is an imaging modality more and more widely accepted as a diagnostic tool for the detection and staging of breast cancer.[1]

Since it is based on neoangiogenesis, the DCE-MRI allows us to make functional assessments of tumors, unlike conventional modalities (mammograms and ultrasound scans) that are just morphological.

The DCE-MRI is conducted using a T-1 weighted sequence acquired previously and several times after the IV injection of a gadolinium-based contrast agent of low-molecular weight. Each acquisition lasts for approximately 1 min and one (1) pre-contrast acquisition and, at least, two (2) post-contrast acquisitions are conducted, one after 2 min and the other one later.[2] However, normally five (5) post-contrast acquisitions are usually conducted up to 5–8 min.[3–5]

The DCE-MRI has a high sensitivity and lower specificity for the identification and characterization of breast focal lesions.[6–10] The time-resolved imaging of contrast kinetics includes one time-signal intensity curve from the manual ROI (region of interest). One early and one late phase can be distinguished, being the early phase rapid or slow based on the signal enhancement during the 2 min that follow the contrast injection; based on how the washout curve looks like, it is categorized as persistent enhancing (type 1), plateau (type 2), and washout (type 3). The categorization of the kinetics curve contributes to distinguish benign from malignant lesions.

The pharmacokinetics model provides one quantitative approach in the analysis of IV contrast distribution based on the vascularization of breast lesions.[11–13] The simplest model describes two (2) different behaviors: the tissue of interest and the plasma. In the pharmacokinetics model of the DCE-MRI of the breast three (3) pharmacokinetics parameters are normally used: the endothelial transfer constant (K^{trans}, expressed in min^{-1}), the reverse volume transfer constant (K_{ep}, expressed in min^{-1}) and the fraction of tumor volume occupied by the extravascular space (V_e).[12,14,15]

The pharmacokinetics parameters can help us characterize breast lesions as benign or malignant, since high patency and low extravascular fractions are signs of malignancy.[16–20]

The first gadolinium-based contrast agent for MRI-based diagnoses was gadopentetate dimeglumine (Gd-DTPA; Magnevist, Bayer Healthcare, Berlin, Germany).[3] Since then, other contrast agents have been studied with different physical and chemical properties. The T1-relaxivity[21,22] is one important physical property, meaning that a higher T1-relaxivity will imply greater enhancement and better visualization of brain and breast lesions.[23–26] Another property that may have something to say when it comes to spreading among biological tissues is the electric charge of the molecules from the contrast agent. Gadolinium-based contrast agents can be ionic or non-ionic; ionic agents have a negative charge, whereas non-ionic agents have a neutral charge. These differences in the electric charge may alter the contrast uptake in tissues with negatively charged components such as mucopolysaccharides.[27,28] It is widely known that malignant breast lesions have a high content of mucopolysaccharide acids.[29–31]