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ORIGINAL REPORT

Evaluation of the reproducibility of a protocol for the pharmacokinetic study of breast tumors by dynamic magnetic resonance imaging☆

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KEYWORDS
Breast cancer;
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Abstract
Objective: To evaluate the reproducibility of a protocol for dynamic contrast-enhanced magnetic resonance imaging (DCE-MRI) for the pharmacokinetic study of breast tumors.
Materials and methods: We carried out this prospective study from October 2009 through December 2009. We studied 12 patients with stages II-III invasive breast cancer without prior treatment. Our center's research ethics committee approved the study. The 12 patients underwent on two consecutive days DCE-MRI with a high temporal resolution protocol (21 acquisitions/minute). The data obtained in an ROI traced around the largest diameter of the tumor (ROI 1) and in another ROI traced around the area of the lesion's highest K^{trans} intensity (ROI 2) were analyzed separately. We used parametric and nonparametric statistical tests to study the reproducibility and concordance of the principal pharmacokinetic variables (K^{trans}, K_{ep}, V_e and AUC_{90}).
Results: The correlations were very high ($r > .80$; $P < .01$) for all the variables for ROI 1 and high ($r = .70–.80$; $P < .01$) for all the variables for ROI 2, with the exception of V_e both in ROI 1 ($r = .44$; $P = .07$) and in ROI 2 ($r = .13$; $P = .235$). There were no statistically significant differences between the two studies in the values obtained for K^{trans}, K_{ep} and AUC_{90} ($P > .05$ for each), but there was a statistically significant difference between the two studies in the values obtained for V_e in ROI 2 ($P = .008$).
Conclusions: The high temporal resolution protocol for DCE-MRI used at our center is highly reproducible for the principal pharmacokinetic constants of breast.

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PALABRAS CLAVE
Cáncer de mama;
Imagen por resonancia magnética;
Farmacocinética

Evaluación de la reproducibilidad de un protocolo de resonancia magnética dinámica para el estudio farmacocinético de los tumores de mama

Resumen
Objetivo: Evaluar la reproducibilidad de un protocolo de resonancia magnética dinámica (RM-DC) con contraste para el estudio farmacocinético de los tumores de mama.
Material y métodos: Estudio prospectivo realizado entre octubre y diciembre de 2009, que incluyó 12 pacientes con cáncer de mama infiltrante en estadios II-III sin tratamiento previo. Este trabajo fue aprobado por el Comité de Ética de Investigación de nuestro centro. A las 12 pacientes se les realizó 2 RM-DC en 2 días consecutivos con un protocolo de alta resolución temporal (21 adquisiciones/minuto). Se analizaron por separado los datos obtenidos en un ROI trazado alrededor del diámetro tumoral mayor (ROI 1) y otro que abarcaba la zona de mayor intensidad de K^{trans} de la lesión (ROI 2). Se emplearon pruebas estadísticas paramétricas y no paramétricas para estudiar la reproducibilidad y concordancia de las principales variables farmacocinéticas (K^{trans}, K_{ep}, V_e y AUC_{90}).
Resultados: Las correlaciones fueron muy altas ($r > 0,80$; $p < 0,01$) en todas las variables del ROI 1, y altas ($r = 0,70–0,80$; $p < 0,01$) en todas las del ROI 2, excepto en V_e tanto en el ROI 1 ($r = 0,44$; $p = 0,07$) como en el ROI 2 ($r = 0,13$; $p = 0,235$). No hubo diferencias estadísticamente significativas entre los 2 estudios para los valores obtenidos de K^{trans}, K_{ep} y AUC_{90} ($p > 0,05$ para todas ellas), pero sí que las hubo para V_e en el ROI 2 ($p = 0,008$).
Conclusión: El protocolo de alta resolución temporal de RM-DC de nuestro centro es muy reproducible para las principales constantes farmacocinéticas de los tumores de mama.

Introduction

The dynamic magnetic resonance imaging (DMR) with IV contrast is one image modality more and more widely used in daily practice. Its indication in high risk patients, the preoperative staging of breast cancer, the hidden breast cancer, the detection of relapses and for the evaluation of the neoadjuvant chemotherapy[1–3] are very well known. Because it is based on neoangiogenesis DMR allows the functional assessment of tumors different than conventional modalities–mammography and ultrasound that are only morphological.

The actual protocols have a high spatial (with cutting thickness close to 1 mm) and temporal resolution (acquisition in approximately 60 s) that allow us to do semiquantitative dynamic studies based on the curves of signal/time intensity. However if temporal resolution is increased the vascular patency can be determined by quantifying pharmacokinetic parameters that describe the passing of contrast from vascular space to the tumor interstitial compartment.[4] To that end it is also necessary to have a specific software capable of estimating these pharmacokinetic parameters.

There are many protocols of pharmacokinetic study with DMR reported in the reference (Table 1).[5–12] Some of them have even been modified along the study.[10] This technical variability can also make the value of pharmacokinetic parameters change–something necessary to study the reproducibility of different protocols.

The goal of this study is to evaluate the reproducibility and concordance of data obtained through a DMR protocol optimized for the pharmacokinetic study of stages II-III-breast tumors after the administration of neoadjuvant chemotherapy.

Materials and methods

Patients

Between October and December 2009 we performed one prospective study in our center including 12 treatment naive patients with confirmed histological diagnosis of infiltrating stages II-III breast cancer. These 12 patients were part of a phase 2 multicenter clinical trial including 12 hospitals (clinical trial code ML22197/2009-01) sponsored by F. Hoffman–La Roche. This trial enrolled 76 patients and assessed the predictive markers to treatment response with the antiangiogenic drug bevacizumab (Avastin®, F. Hoffman–La Roche, Basel, Switzerland) and neoadjuvant chemotherapy (docetaxel plus adriamicine) in patients with locally advanced breast cancer. In Table 2 the criteria for the inclusion of patients in the study can be seen. The study protocol was approved by the ethical committee of our hospital and all patients gave their informed written consent.

Technique

To validate the DMR protocol two daily examinations were performed in two consecutive days with identical technical parameters and the patients did not follow any therapies between both examinations. The MRI protocol can be seen in Table 3.

The DMR was performed in one 1.5 T resonance (Magnetom Symphony®, Siemens Healthcare, Erlangen, Germany). T1-weighed standard fl3D echo-spin gradient-enhanced images were modified in an attempt to improve its spatial resolution (150 measurements instead of 6 in a total of 7 min per test with approximately 21 acquisitions per