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Software development for assessing cellular heterogeneity and its clinical application in gadoxetic acid-enhanced MRI of hepatocellular carcinoma

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요 약

In this paper, we developed the quantification software for evaluating the voxel-based cellular heterogeneity of gadoxetic acid-enhanced magnetic resonance imaging (MRI) in the liver. Our software is clinically applied to accurately quantify and interpret the alterations of liver functions in patients with hepatocellular carcinoma.

1. Introduction: Quantification of cellular heterogeneity is very important for evaluating disease progression in the lesional tissue because inter- and intra-disease specific differences have limited the development of targeted therapies for patients. At the cellular level, lesional heterogeneity can consider influenced by the cell's difference such as genes and origin. From this point of view, a recent study, demonstrated that the heterogeneity of tumor cells is highly influenced by the cell's genetic background and origin as well as the environment where it establishes. Therefore, this has direct implications on the clinical outcome as well as the development of adequate diagnosis and therapies; however intra-disease specific cellular heterogeneity prevents an adequate clinical diagnosis and is involved in disease's resistance.

This study was to develop the quantification software for evaluating the voxel-based cellular heterogeneity of gadoxetic acid-enhanced MRI in the liver, and to determine the heterogeneity difference between normal controls and patients with hepatocellular carcinoma (HCC).

2. Materials and Methods: Quantification program was coded by MATLAB (R2012a) and its algorithm can be summarized as follows: bias correction of intensity inhomogeneity; liver segmentation with the active contour; followed by calculation of coefficient of variation (CV) map as CV value at each pixel.

This study were performed a retrospective study of gadoxetic acid (Gd-EOB-DTPA, Primovist®, Bayer)–enhanced MRI performed in a total of 20 subjects consisting of 10 HCC patients (age 65.2±11.2 years) and 10 normal controls (age 51.1±18.1 years), which were pathologically proven. The subjects were studied using a 3T MRI scanner (Achieva; Philips) with a 32-channel body coil. The abdominal MR images were obtained the images at 20 minutes after intravenous administration (0.025 mmol/kg dosage) of gadoxetic acid. The gadoxetic acid–enhanced MRI was performed using T1 high-resolution isotropic volume excitation (ETHIRVE) pulse sequence with following parameters: TR/TE= 3.18/1.57 ms, flip angle 10°, matrix size 315×350 and slice thickness 5 mm. Statistical analysis was performed with two sample *t*-test.

3. Result & Discussion: Liver MRI data are essential to reduce unexpected un-uniformity field bias (Fig. 1). Figure 2 demonstrated the representative CV maps in a normal control and a patient with hepatocellular carcinoma. Hepatic cellular heterogeneity of HCC patients was significantly higher than that of normal controls (normal control 7.55 ± 1.06 vs. HCC 8.85 ± 0.96; $p<0.01$). Using developed software, the cellular heterogeneity in the HCC patients was well differentiated from that in normal controls.

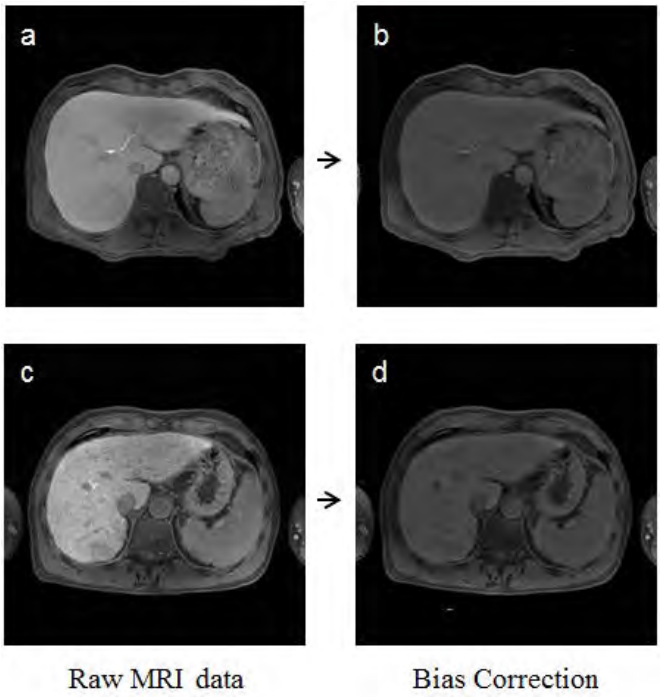

Figure 1. The examples of bias correction in a normal control (before correction (a) and after correction (b)) and a patient with hepatocellular carcinoma (before (c) and after (d))

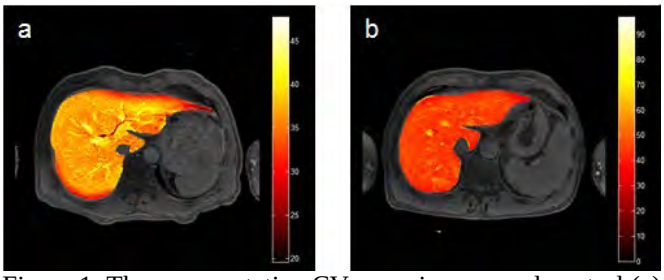

Figure 1. The representative CV maps in a normal control (a) and a patient with hepatocellular carcinoma (b)

4. Conclusion: The developed program is capable of providing quantitative cellular heterogeneity results of gadoxetic acid–enhanced MRI data. Clinical application of this software to the analysis of liver MRI data would be helpful to accurately quantify and interpret the liver functions.

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