RM IN SPREADING IN PATIENTS WITH LIVER CIRRHOSIS. VALUATION OF VALUES RELATED TO DEGREE OF FIBROSIS ADC

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[RM in diffusione in pazienti con cirrosi epatica. Valutazione dei valori di ADC correlati al grado di fibrosi]

ABSTRACT

The "technique of spreading" measures the degree of diffusion of water molecules in biological tissues and this degree is one of the flow characteristics of the MR signal.

This article will examine the other hand the technique of diffusion in the abdominal area, particularly for the assessment of fibrosis and cirrhosis in chronic patients with liver disease.

A study was conducted between September 2008 to June 2009, at the Hospital of Palermo, in patients admitted to Day Hospital in the department of gastroenterology in 25 patients.

The cirrhotic patients were admitted to day hospital, had undergone follow-up bio-humoral, liver ultrasound, liver biopsy, Fibroscan for the evaluation of liver stiffness and esophago-gastroduodenoscopy for research and possible therapy of gastroesophageal varices antiviral.

The biopsy, performed at least 2 months before the MR examination, found in all patients a grade 4 fibrosis. At Fibroscan, the value found was variable between 10.1 and 35.3 kPa. No patient had ascites or hepatic encephalopathy. In healthy patients the mean ADC value was between 2.31 x 10^{-3} and 2.67 x 10^{-3} mm. In cirrhotic patients the mean value was between 1.57 and 2.40 x 10^{-3} mm 2/sec. In cirrhotic patients the ADC value found was on average lower than in controls (2.44 x 10^{-3} compared to 1.99 x 10^{-3}), except for one patient who had a clinically and Fibroscan less advanced degree of cirrhosis (stiffness: 10.1 kPa).

This study has shown the potential for using MRI diffusion, to obtain a reliable parameter to evaluate the possible hepatic fibrosis.

Key words: Cirrhosis, fibrosis, Fibroscan, diffusion weighted magnetic resonance.

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Introduction

The "technique of spreading" measures the degree of diffusion of water molecules in biological tissues and this degree is one of the flow characteristics of the MR signal[1,2].

The technique has been used primarily in the field neuroradiological, in particular for the diagnosis of ischemic stroke in the hyperacute phase, of neoplastic lesions encephalic, of demyelinating diseases and neurodegenerative diseases, brain pathology of fetal and neonatal[3].

This article will examine the other hand the technique of diffusion in the abdominal area, particularly for the assessment of fibrosis and cirrhosis in chronic patients with liver disease.

When the liver lobule are deposited collagen fibers, it changes the content and the mobility of water molecules of which the diffusion MRI can be considered the expression[4-7].

There are several models for classification of liver damage:

• index of histological activity or KNODELL SCOREe[8];

• Index necro-inflammatory activity (grading: maximum score 18) and degree of fibrosis (staging: score maximum 6) according to ISHAK[8];

• according to SCHEUR, degree of fibrosis (from 0 to 4)[9];

• METAVIR SCORE degree of fibrosis (staging: maximum score[6] The activity varies from A0 to A3, ie from no activity to severe activity[10]. These models take into consideration the necro-inflammatory activity (depending on whether the damage is periportal, lobular and portal) and the degree of fibrosis (from 0 to 4).

Methods of assessing the fibrosis

1) *liver biopsy* (gold standard for diagnosing and staging chronic liver diseases)[11-13];

2) *the Fibroscan*, which represents a measurement system, by means of external probe, the "stiffness" of the liver tissue ("stiffness", expressed as kilopascals - kPa). The measurement takes place at the right lobe, placing the probe in the intercostal spaces with the patient in the supine position, under ultrasound control in order to avoid major vascular structures.The assessment is based on at least 10 validated measurements. The Fibroscan is useful in the diagnosis of cirrhosis, is less accurate, however, in assessing the earliest stages[21-23];

3) *the direct or indirect serum markers* [20-28.29], used in conjunction with liver biopsy;

4) T*he diffusion-weighted MRI that detects what happens in the tissues*, because the spread directly reflects the movement of water molecules in the tissue. The random motion that governs the diffusion process is called Brownian motion which can be of 2 types: "consistent" and "incoherent", governed by Fick's laws. It is estimated the spread in terms of probability with a function that indicates the probability that the particle travels a distance in a given time.

The probability function that describes this situation, for a homogeneous medium and isotropic, has a Gaussian distribution with average 0 and variance proportional to the time of observation you to the diffusion coefficient D. The diffusion coefficient is defined as the distance traveled by a molecule in his motion stochastic unit of time and is expressed in mm^2/s. From a technical point of view it is necessary to perform the examination with a high field superconducting magnet (1.5 T).

All sequences were acquired in breath. Initially a study is performed using conventional T1 and T2 weighted images, DW images are performed, with a variation of Spin-Echo sequence (Stejskal and Tanner sequence) taken with echo-planar technique of single-shot. 2 additional gradients are applied to the same amplitude and duration but opposed by line, called diffusion gradients. These gradients are the key to raising awareness of RM sequences, so as to make the diffusion phenomenon evident and measurable. The factor b (expressed in mm^2/s) expresses the degree of sensitization to the spread of the sequence, summarizing the characteristics of the gradients, according to the formula:

$$b = \gamma^2 G^2 \delta^2 (\Delta - \delta/3)$$

where γ is the constant giromagnetica, G and δ are respectively the amplitude and duration of diffusion gradients and Δ is the interval of time between their application. Is repeated for different values of b with image acquisition divers amente weighted D. With the increase of b increases the "weighting" in diffusion of the sequence. A low degree of diffusion of water corresponds to a signal slightly reduced, but a high degree of diffusion of water corresponds to a very small signal. The sequences used are based on echo-planar technique (EPI = Echo Planar Imaging.)

The diffusion produces, in each pixel, a reduction in signal intensity given by: $S = S_0 e^{-bADC}$

where S and S_0 are respectively the intensities of signal with and without the sensitization to the diffusion and the ADC apparent diffusion coefficient.

The ADC is measured, using the linear regression analysis calculated on the basis of the formula: $ADC = In (S_0/S) b$

The measurement of the ADC allows the evaluation of the space in which the molecules are moving, their transfer and disposition in the different compartments of the cell structures. We obtain the ADC maps and mean diffusivity through which you can measure the ADC values along the different axes in different tissues and compare any changes in ADC values in pathological processes.

Methods and results

A study was conducted between September 2008 to June 2009, at the Hospital of Palermo, in patients admitted to Day Hospital in the department of gastroenterology: 25 patients (16 females, 9 males) aged between 46 and 69 years (mean age 59.2 years) hospitalized for HCV-related liver cirrhosis and 8 patients (6 females, 2 males) aged between 37 and 79 years (mean age 64 years) hospitalized as a probable healthy controls. The ethics commission has given the his permission to perform this type of examination, all patients gave their informed consent before undergoing MRI examination without contrast medium.

The cirrhotic patients were admitted to day hospital for about 6 months, had undergone follow-up bio-humoral, liver ultrasound, liver biopsy, Fibroscan for the evaluation of liver stiffness and esophago-gastroduodenoscopy for research and possible therapy of gastroesophageal varices antiviral. All patients had HCV-related cirrhosis Child-

Pugh class A5. None had a known hepatocellular carcinoma. The biopsy, performed at least 2 months before the MR examination, finded in all patients a grade 4 fibrosis. At Fibroscan, the value found was variable between 10.1 and 35.3 kPa. No patient had ascites or hepatic encephalopathy. 13 of 25 patients had esophageal varices and 25/25 splenomegaly.

The MR examinations were performed with 1.5 Tesla unit (Signa, GE Medical Systems, Milwaukee, Wis.) with surface coils or "phase array" (8 channels).

The study was carried out in a diffusion single breath hold first in one direction and then apply on the 3 spatial directions through a series of single-shot spin echo planar using the following acquisition parameters: TR 1400, TE minimum, 8/mm slices, Nex 5.Sono were obtained by applying a set of 6 images 3 different b values (50,300,800 mm^2/sec). The acquisition time was for each sequence of about 30 seconds.

ADCs have been measured on the corresponding ADC maps on a workstation using the software GE Functool. Were applied 3 different ROI (50 mm^2) in correspondence of the right lobe of the liver, the hepatic lobe of the left and in the center-liver, avoiding great vessels, diaphragm and gall-bladder as to be artifacts. From these 3 ROI are obtained the different ADC values for individual patients and the mean value was used for statistical analysis.

The results of the ADC results are independent of the value of b is used.

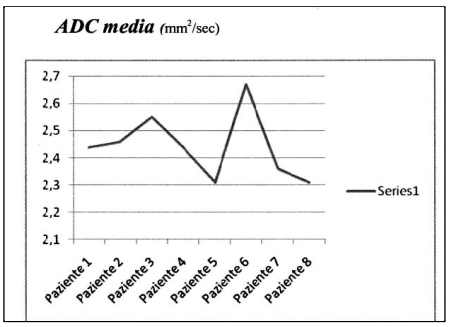
In healthy patients the mean ADC value was between 2.31 x 10^{-3} and 2.67 x 10^{-3} mm.

In cirrhotic patients the mean value was between 1.57 and 2.40 x 10 -3 mm^2/sec.

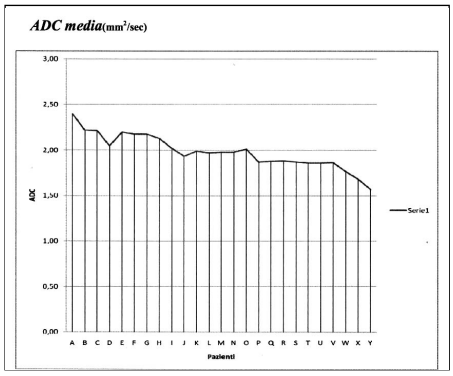
In cirrhotic patients the ADC value found was on average lower than in controls (2.44 x 10^{-3} compared to 1.99 x 10^{-3}), except for one patient who had a clinically and Fibroscan less advanced degree of cirrhosis (stiffness: 10.1 kPa).

In cirrhotic patients the value of the ADC units found in the left lobe was consistently higher than that of the right lobe, an aspect not highlighted in a constant way in healthy controls.

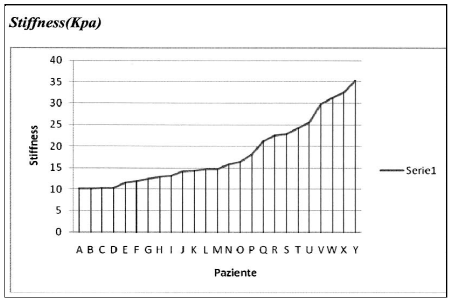
The patient with the lowest stiffness value presented the highest value of ADC, showing a lower degree of fibrosis. The results are represented in graphs 1, 2 and 3.



Graph 1:



Graph 2:



Graph 3:

Conclusions

This study has shown the potential for using MRI diffusion, to obtain a reliable parameter to evaluate the possible hepatic fibrosis.

It's necessary to continue the study, in order to evaluate more patients, also using the new technology that allows the Propeller to obtain breath-hold diffusion-weighted sequences, which are shorter and therefore not linked to breathing artifacts, therefore, also applicable uncooperative patients. With the spread opens interesting possibilities to succeed early to quantify the degree of fibrosis in patients with chronic liver disease. The search for alterative methods to liver biopsy is certainly desirable to improve the prognosis and clinical management of these patients.

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