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Comparison between magnetic resonance spectroscopy and diffusion weighted imaging in the evaluation of gliomas response after treatment

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ABSTRACT

Purpose: To compare magnetic resonance spectroscopy (MRS) and diffusion weighted imaging (DWI) in the assessment of progression and regression of brain tumors in order to assess whether there is correlation between MRS and DWI in the monitoring of patients with primary tumors after therapy.
Methods: Magnetic resonance imaging (MRI) has been performed in 80 patients, 48 affected by high grade gliomas (HGG) and 32 affected by low grade gliomas (LGG). The variation of apparent diffusion coefficient (ADC) value and metabolite ratios before and after treatment has been used to test DWI sequences and MRS as predictor to response to therapy. Comparison between post contrast-enhancement sequences, MRS and DWI has been done in terms of accuracy, sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV). Moreover statistical correlation of ADC deviations with MRS metabolites variations before and after therapy have been studied.
Results: In the case of HGG, MRS shows better sensitivity, specificity, PPV, NPV and accuracy compared to DWI, especially when considering the Choline/N-acetylaspartate (Cho/NAA) ratio. Regarding the LGG, the technique that better evaluates the response to treatment appears to be the DWI. A moderate correlation between ADC deviations and Cho, Lipide (Lip) and Lactate (Lac) has been found in LGG; while NAA revealed to be weakly correlated to ADC variation. Considering HGG, a weak correlation has been found between ADC deviations and MRS metabolites.
Conclusion: Combination of DWI and MRS can help to characterize different changes related to treatment and to evaluate brain tumor response to treatment.

1. Introduction

Brain tumors are the most frequent primitive tumors in the adult population and originate from cells of the brain and the neuroglia [1]. These tumors are classified on the basis of malignancy and aggressiveness in tumors of I, II, III and IV grade [2]. An accurate assessment of the degree of cancer is important for a proper treatment of these patients also because the prognosis of these patients is related to the degree of disease [3–6].

Magnetic resonance imaging (MRI), is the most commonly used method in the evaluation of brain tissue [7]. However, conventional MRI can be non-specific and not a direct measurement of tumor activity [8]. In patients with brain tumor, for example, conventional MRI sequences have several limitations in differentiating recurrent or residual tumor tissue from reactive post-therapeutic [9], in fact the assessment of and the effects of radiation therapy and chemotherapy, are assessed on the basis of the morphology of the lesion with very limited specificity [10]. Traditionally, in fact, T1-weighted MRI, with or without gadolinium, is the gold standard method [8]. It contributes to accurately define margins but it shows some limitations in defining tumor size and activity, due to vascular

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damage, for LGG that in 90% of cases don't show contrast enhancement and are better evaluable in T2 and FLAIR sequences [8]. Today MRI benefits from the use of functional imaging techniques, such as diffusion weighted imaging (DWI) [11] and magnetic resonance spectroscopy (MRS) [12], that may allow early detection of treatment induced changes in tumor biology and physiology.

The DWI and the derived apparent diffusion coefficient (ADC) can be used to evaluate the radiation damage or disease recurrence after radiotherapy in brain tumors, lower values of ADC are related to a reduced diffusivity of water molecules in the extracellular compartment for greater cellularity, so in tumor recurrence, than in areas of radio necrosis, there is a higher ADC value [13]. Even MRS is able to assess the degree of brain tumors [14],differentiate the type of cancer [15] and to distinguish tumor recurrence and progression of disease, this last can be done on the basis of changes in the ratio of various metabolites and lipid-lactate, particularly an increased level of Choline (Cho) indicates a non-response to therapy and suggests disease progression [16].

Recent studies [10,17,18] have assessed the role of MRS and DWI separately in the evaluation of brain tumor response to treatment. To our knowledge there are no studies comparing MRS and DWI as techniques to assess the gliomas response to therapy. The aim of our study is to compareMRS and DWI in the assessment of progression and regression of brain tumors in order to assess whether there is correlation between MRS and DWI in the monitoring of patients with primary tumors after therapy.

2. Materials and methods

2.1. Patients

In our study we included 80 patients in the period between 2012 and 2014 with suspected brain tumor whose diagnosis was performed at our institution with 3T MRI and confirmed by histological examination. Patients had a mean age 56.7, range 31–83 year. Histological examination revealed 48HGG (III-IV) and 32 LGG (II) according to the WHO [2]. The interval time between the end of RT and/or CHT and MRI follow-up was at least three months, in order to ensure that the effects of acute post-RT did not affect our observation. The mean interval of MRI examinations was 2–3 months for HGG and 4–6 months for LGG. Our study was approved by the ethics committee of our Institution. All patients signed an informed consent.

2.2. Therapy

All patients with LGG (32) were subjected to RT alone (total dose of 40–60 Gy, 2 Gy/fx). 46 patients with HGG were subjected to surgical treatment, radiation therapy (mean total dose of 60 Gy, 2 Gy/fx) and adjuvant chemotherapy with temozolomide (75 mg/m^2 per area of body weight);2 patient with HGG was not surgically treated for advanced age. 34 patients of which 32 with LGG and 2 with HGG were subjected to stereotactic biopsy only because in such cases the surgery was not indicated.

2.3. Definition of progression and regression of disease

Definition and evaluation of progression and regression of disease in LGG and HGG has been done using RANO criteria [19–20] (Table 1).

A lesion is considered in progression of disease if, in addition to responding to the RANO criteria, it presents metabolic activity with metabolic ratios cho/cr> = 2 and cho/NAA> = 2.5 [21] and a lower mean ADC value compared to the previous MRI check, on the basis of studies in the literature [22].

A lesion is considered in regression of disease if, in addition to the RANO criteria, it presents reduction of cho/cr <2 and cho/ NAA <2.5 and ADC value higher than starting values [22].

Lesions with morphological, spectroscopic and diffusion aspect suspicious for radiation damage and patients with partial response or stable disease were revalued at distance and classified as responders or non-responders, based on the evolution / involution of the disease.

2.4. MRI methods

The examinations were performed on a 3T MRI unit (Achieva, Philips Medical Systems, Best, The Netherlands) equipped with gradients of amplitude and maximum slew rate respectively of 80 mT/m and 200 mT/m/ms, using a 8 channel receiver head coil. The MRI protocol consisted of T2-weighted turbo spin echo axial sequences (TSE) (Echo Time, TE = 82 ms; Repetition Time, TR = 3000 ms; FOV = 23 cm AP, 18.5 cm RL, 12.4 cm FH; 25 slices of 4 mm of thickness; gap = 1 mm), T1 weighted inversion recovery (IR) sagittal sequences (TE = 20 ms; TR = 2000 ms; FOV = 23 cm AP, 22 cm RL, 11.9 cm FH; 24 slices of 4 mm of thickness; gap = 1 mm), fluid-attenuated inversion recovery (FLAIR) coronal sequences (TE = 125 ms; TR = 11000 ms, IR delay 2800 ms, FOV = 23 cm AP, 18.3 cm RL, 14.9 cm FH; 30 slices of 4 mm of thickness; gap = 1 mm), and diffusion weighted image (DWI) sequences (TE = 46 ms; TR = 2719 ms; FOV = 25 cm AP, 25 cm RL, 12.4 cm FH; 25 slices of 4 mm of thickness; gap = 1 mm) and finally T1 weighted Spin-Echo (SE) after medium injection (Magnevist; Bayer Schering Pharma, Berlin, Germany) (TE = 10 ms; TR = 600–700 ms; FOV = 23 cm AP, 18.3 cm RL, 12.4 cm FH; 25 slices of 4 mm of thickness; gap = 1 mm). For MRS imaging, multivoxel two-dimensional 1H MRS was performed after contrast injection on a volume of interest (VOI) positioning (Fig. 1) on three reference images was

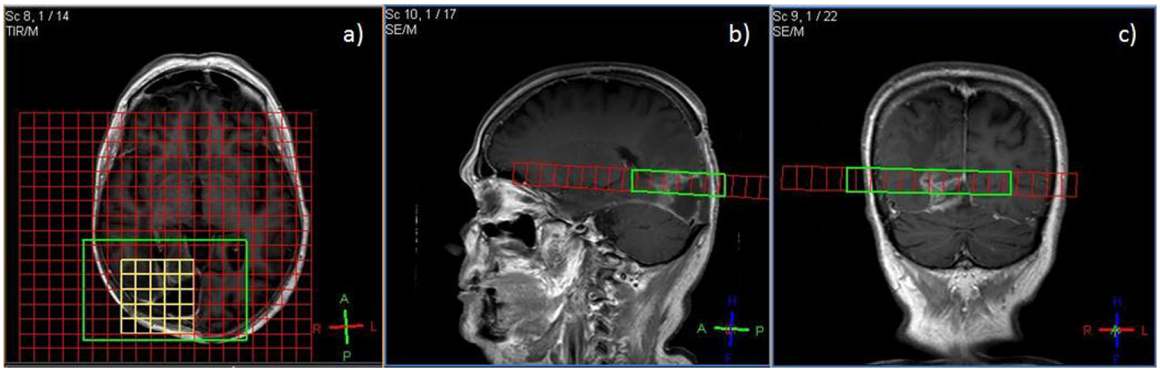

Fig. 1. Multivoxel two-dimensional 1H MRS performed on a volume of interest (VOI) positioned on three reference images: axial (a), sagittal (b) and coronal (c).