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MR Spectroscopy in Patients with Non-Hodgkin's Lymphoma after Bone Marrow Transplant: A Comprehensive Review

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Abstract

Goal of this work is to assess importance and usefulness of Magnetic Resonance Spectroscopy (MRS) in Patients suffering from non-Hodgkin's lymphoma (NHL), submitted to bone marrow transplant (BMT) and other hematological disorders.

Keywords: Magnetic resonance spectroscopy; Non-Hodgkin's lymphoma; Bone marrow transplantation; Haematological patients

Introduction

Monitoring patients receiving bone marrow transplant (BMT) is mandatory in management and outcome, [1-5]. In fact, we may set up some invasive methods, such as bone marrow sampling, by puncture of iliac crest, not so easy to be accepted by patients already submitted to long and debilitating immunomodulation treatments, leading to the transplant [6,7]. Thus, the samplings, performed on a single region of interest, are not actually reflecting the status of the whole bone marrow of the skeletal segment examined. Magnetic Resonance Spectroscopy (MRS) is as an effective technique for the study and follow-up of transplanted patient, demonstrating that MR spectroscopy parameters of the bone marrow correlate with blood parameters variations in pre and post-transplant [6].

Although do not have yet large, multicenter studies, there are many proves that MRS is an affordable method, assessing, non-invasively, LNH hematological conditions, with a valuable ameliorant of life quality in these Patients [6,1]. Aim of this review is to point out the potentials of MR spectroscopy in patients suffering from non-Hodgkin's lymphoma (NHL) treated with autologous BMT, in assessing response to therapy.

MR Spectroscopy of Bone Marrow

MRS performed in correspondence of a vertebral body region of interest (ROI) is an effective method for a non-invasive evaluation among the different bone marrow components. In fact, signal intensity differences in T1 and T2 weighted sequences and chemical shift (i.e. the different MR frequency of hydrogen (H) atoms, related to chemical bonds in which they are taking part) allowing to qualify and quantify different metabolites included in a defined ROI.

Thus, MR spectroscopy is an effective indicator of intrinsic status of the bone marrow and its composition. The spectrum available is the graphical representation of the atom's nuclei MR signal, in function of its frequency. MRS analysis in correspondence of a vertebral body can recognize multiple peaks spectrum. Generally a first peak is located between 0.8 and 2.2 ppm, due to the signal typical of the chemical bonds of the methylene groups (- CH_2 -), at 1.2 ppm and methyl (- CH_3) at 0.8 ppm, present in the saturated fatty acids aliphatic chains (Figure 1).

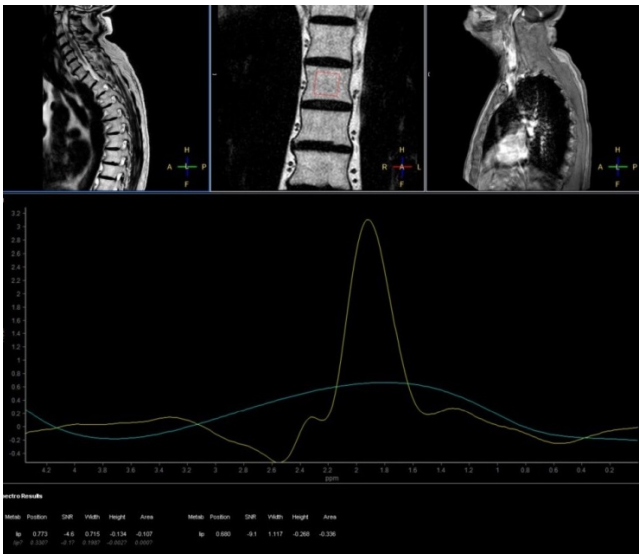

Figure 1: Voxel positioning for MRS spectra sampling, focused in D7 in a healthy control.

A second peak is present at 5.6 ppm and indicating the vinyl groups (-CH=CH) in unsaturated fatty acids. A third peak is referred to the of water signal at 4.8 ppm. The fat fraction (FF) represents the percentage between MR signal of lipids and water. It is a crucial parameter in assessing pathological bone marrow, since it allows the estimation of its composition and the calculation of the ratio between red and yellow marrow [8]. In adults, bone marrow is hypo-cellular, since mainly occupied by lipids and poorly by hematopoietic cells. In these conditions, the water content is low.

Therefore, the spectrum of yellow bone marrow shows a high FF. The red bone marrow shows on the contrary a spectrum with elevated water peak and elevated content of hematopoietic cells and water and a low FF. The rationale of the use of MR spectroscopy in these hematological patients is that the malignant bone marrow cells

displaces fat cells and lipids from the marrow, causing an increase of the water content, which corresponds to a very low FF. In successful cytotoxic chemotherapy, malignant cells are replaced by fat cells, which cause a decrease of water content and an increase of FF (Figure 2).

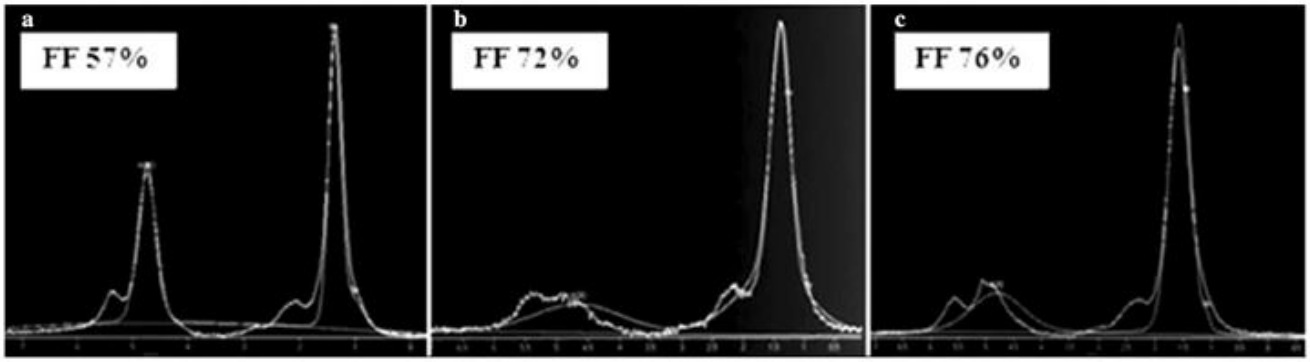

Figure 2: A 46-year-old man suffering from non-Hodgkin's lymphoma. MRS performed before **(a)** 15 days **(b)** 90 days **(c)** days after BMT shows marked increase of FF percentage associated with decrease in water peak at the second and third follow-up. This behaviour showed a bad bone marrow recovery (platelet count at the third follow-up was below $30 \times 10^3/mm^3$).

MR Spectroscopy in Monitoring Response to Therapy in Hematological Patients

The above-mentioned basic principles of MR spectroscopic study of vertebral bone marrow explain how nowadays this technique is considered a powerful diagnostic aid in monitoring marrow recovery after BMT. Several studies showed how Fat-fraction could be used for pathological condition, assessing the change in water-fat composition, for examples in fractured bone, establishing if the fracture is pathological or osteoporotic [9].

A Study [10] demonstrated MR spectroscopy of the bone marrow in hematological patients affected by NHL can be correlated with the pre and post-transplant blood parameters, resulting a viable technique for monitoring response to therapy in patients with hematological patients treated with BMT. In particular, this Research demonstrated an increase in FF value after ablative therapy in 67% of patients studied, showing a statically significant correlation between fat-fraction values and circulating platelets, predictor of bone marrow recovering.

In a more recent study Giles et al. demonstrated whole body MRI, based on Echo-planar diffusion sequences, as an effective technique in patients with multiple myeloma [11]. They found a significant correlation between two groups of Patients, responding or not to therapy, and ADC variations. Takasu et al. demonstrated, using MRS, FF values is more accurate of bone marrow plasma cell percent (BMPC %) in establishing the severity of multiple myeloma (MM), ascribing this result to the wide variability of histopathological pattern of the disease. In fact, the MM tends to form clusters with variable size and a single bone marrow samples could be not sufficient to outline the true pathological status [12].

Conclusion

MR spectroscopy can assess bone marrow's components and eventual pathophysiological changes before, during and after treatment. MR spectroscopy has been able to show an important improvement in the evaluation of bone marrow, with several advantages upon others diagnostic modalities and above all an actual determination of Fat Fraction with its different component of red and yellow marrow [13].

Whereas biopsy is able to show the bone marrow composition in the specific region where the procedure was focused, MR spectroscopy techniques provides a bone marrow structure characterization, by depicting the content of water and fat, allowing a complete and non-invasive assessment of the bone marrow [8,14-16].

Our experience also suggest the hypothesis that local biopsy is not truly representative of actual bone marrow status, perhaps because a single, small, specimen could not be representative of overall bone marrow activity. Moreover, MR could also represent the guide for conducting a biopsy towards a specific disease site or be used for monitoring response to therapy non-invasively through serial examinations [17,18].

These assumptions sustained by the literature allow us to view a future where will use MR spectroscopy not only for monitoring non-invasively BMT effectiveness, but also for directing adjustments or changes in therapeutic plans when a poor or ineffective response to therapy is detected in several hematological disorders.

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