Upper abdominal and cardiac mri protocol for the study of iron accumulation in the Thalassemic patients

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Abstract

Thalassemia is a highly prevalent inherited disorder in the Mediterranean region. Italy has a significant number of individuals affected by this condition, which, in its most severe form, requires periodic blood transfusion sessions. This leads to pathological iron accumulation in organs, particularly the heart, liver, and pancreas. The purpose of this study is to describe the imaging acquisition procedures using specific MRI techniques for the quantification of iron in these sensitive organs. Using a dedicated T2 sequence it is possible to quantify the iron overload in heart, liver and pancreas. The value of T2* equal to 20msec is considered a threshold below which accumulation is not considered pathological. In post-processing, the images obtained with the T2* sequences are analyzed by a dedicated software.*

INTRODUCTION

Thalassemia is the term used to identify a group of inherited disorders affecting hemoglobin. Thalassemia primarily affects populations in the Mediterranean region, South Asia, Southeast Asia, and the Middle East. In Italy, there are approximately three million carriers of the disease, mainly concentrated in Sardinia, Sicily, the southern regions, as well as the Po River Delta and Veneto. It is estimated that around 7,000 individuals are affected by the severe form of the disease. Thalassemias can be divided into two main groups: alpha-thalassemia and betathalassemia. In Italy and the Mediterranean region, the most common form is betathalassemia. The most severe form of the disease is known as beta-thalassemia major, also referred to as Mediterranean anemia or Cooley's anemia. Thalassemia is characterized by congenital anemia that requires regular and continuous blood transfusions starting from early infancy to prevent complications associated with low hemoglobin levels. Additionally, chelation therapy is necessary to remove the excess iron that inevitably accumulates from transfusions, as high levels of iron can be extremely toxic. Magnetic Resonance Imaging (MRI) is the preferred method for accurate, reliable, and non-invasive quantitative assessment of multiorgan iron accumulation. Target organs for studying thalassemia using MRI are the liver, pancreas, and heart.

MATERIALS AND METHODS

Superconductive MRI with field intensity equal to 1.5 TESLA, used in research mode in order to have a slew rate equal to 200T/m/s and a peak amplitude of 45mT/m.

MR-compatible ECG electrodes for cardiac monitoring, respiratory gating, prospective and/or retrospective were used with a 16-channel flex coil (55.6cm length, 67.4cm width, 3.3cm height, 2.8kg weight) in synergy with another 32-channel coil integrated in patient table usually used for spine exams. Possible antecubital venous access to complete the cardiac vitality study.

Before every MRI examination, patient is interviewed by the Radiologist to assess their suitability for the exam. Recording the patient's weight and height is important both for making calculations with the dedicated software after image acquisition and for accurately calculating the specific absorption rate (SAR). Patient clothing should be removed and a disposable gown provided. If necessary, trichotomy is performed in the chest area where the compatible RM electrodes will be positioned. The patient will be positioned supine on the table, with a preference for a "feet-first" entry into the gantry. With the arms adducted alongside the body, a respiratory gating belt is securely fastened around the patient's chest, and the positioning and verification of the coils are performed. Additionally, the patient will be provided with headphones, which serve to both attenuate the noises present in the room and facilitate communication between the operator and the patient.

Liver basic protocol consist of Coronal and Axial T2 SSFSE. These images are acquired during breath-holding, but in non-cooperative patients, they can be obtained during free-breathing with the option of navigator or respiratory trigger. The purpose is to obtain a morphological study of the organs in the upper abdomen. While Cardiac basic

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protocol consist of 2 chambers long axis, in which we have a good visualization of the atrium, the left ventricle and the mitral valve; 2 chambers short axis, positioned perpendicular to the interventricular septum and perpendicular to the plane passing from the apex to the mitral valve; 4 Chambers with plane positioned perpendicular to the center of the left ventricle and the apex of the right ventricle (Figure 1).

For iron quantification in liver and pancreas a single echo and a multi echo sequences can be acquired:

- T2*(2260) LIVER: Acquisition of single-breath Gradient Echo Multi-echo images. The sequence consists of a single slice positioned at the mid-hepatic level, creating 10 distinct images for increasing echo times (TE), while keeping the repetition time (TR) constant, with an echo spacing value of 2,260 ms. The acquisition is performed during breath-holding. The specific constant value of echo spacing needs to be manually set by the operator before starting the sequence. From the acquired images, the amount of iron content in the liver can be evaluated using dedicated post-processing software.
- T2* LIVER Single Echo Single Breath-hold: If the previous sequence already shows saturated liver images at the second echo, it is necessary to proceed with the single echo technique. In this case as well, the sequence involves positioning a single slice at the mid-hepatic level with single echo acquisitions. The acquisition is performed during breath-holding. Thirteen single echo acquisitions will be obtained with a TE ranging from 10 to 40 ms, incremented by 2.5 ms for each acquisition. This option also needs to be manually set by the radiographer (Figure 2).
- T2* (2260) PANCREAS: Acquisition of Gradient Echo Multi-echo images in a single breath-hold. The sequence consists of 10 slices, each defined by a constant and increasing TE, covering the head, body, and tail of the pancreas for accurate post-procedural evaluation. The acquisition is performed during breath-holding. Similar to the previous acquisition, 10 images of the same slice will be obtained, keeping the TR constant, increasing the TE, and using an echo spacing value of 2,260 ms for each acquisition.
- T2* (2260) PANCREAS fat saturation: The previous sequence is repeated with "fat suppression." The acquisition of this sequence is crucial, especially for patients who exhibit severe iron accumulation, as tissue degeneration in the organ may hide an optimal evaluation with the T2* GRE multi-echo single breath-hold sequence alone.

For iron quantification in heart a short axis Multi echo T2* sequence will be acquired at the basal, middle and apical level of the ventricle. Care must be taken not to position the basal plane in correspondence with the mitral valve since, also in physiological conditions there is a greater quantity of iron than the rest of the myocardium. 10 images per slice, for a total of 30 images were acquired. The TE is variable and increasing by a fixed constant The echo spacing instead is set to 2.26 msec. Thalassemia patients carry out periodic checks so

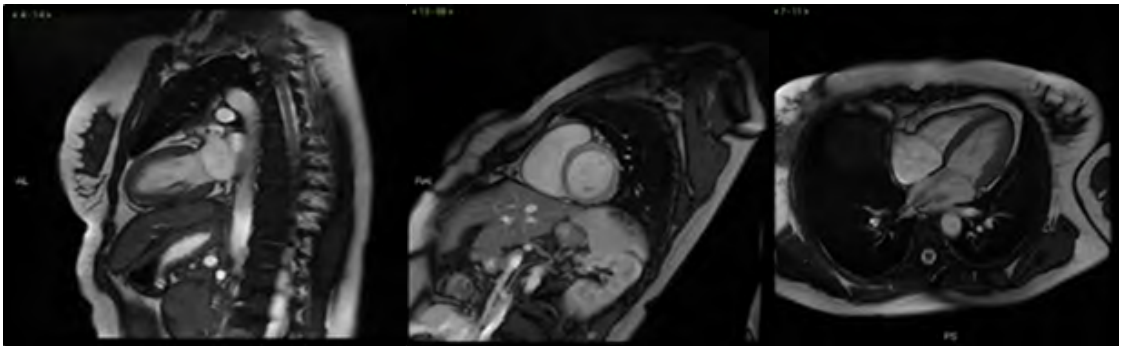

***Figure 1**. Long axis 2 Chambers; Short axis 2 Chambers; 4 Chambers*

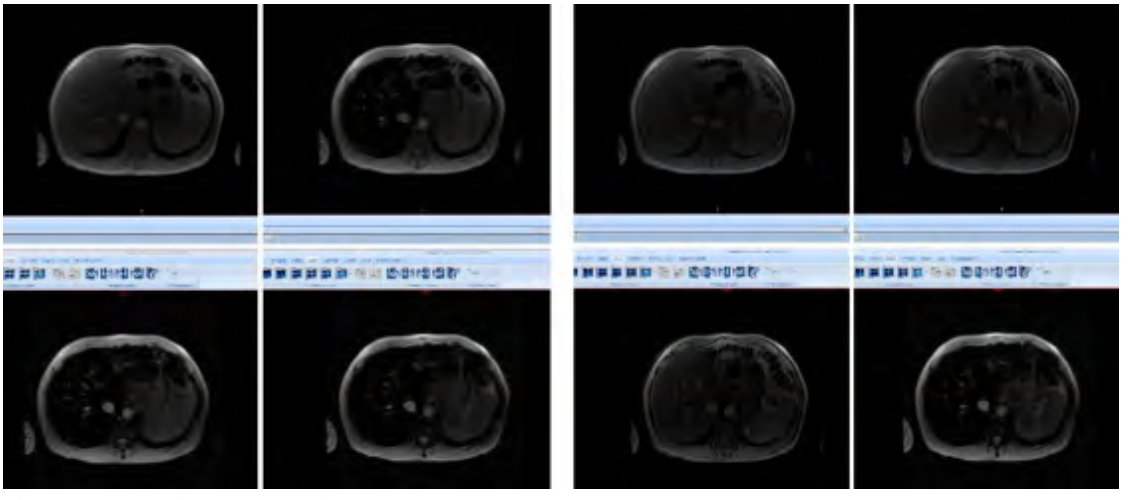

***Figure 2**. T2* Multi-echo on the left side and T2* Single-echo on the right side*

it is essential to standardize the exam. To ensure that this is carried out under the same conditions, it is important not to modify the data in any way, and above all it is necessary that the acquisition plans are always the same. The technique used is to add two planes, the first passing through the valve plane and one on the true apex. To cover the entire heart, in case it is larger, we will absolutely not modify the slice thickness value, set at 8 mm, but the spacing between the acquisition slices: this value can vary between 7-12mm (see fig. 8). The apical and basal slices are then eliminated to obtain the correct plane. After completing the exam, the 30-images dataset is used for T2* analysis with a dedicated software.

RESULTS AND DISCUSSION

T2* is a parameter that can be evaluated in addition to T1 and T2. It is linked to the loss of phase coherence of the MT determined both by the spin-spin effect and by the inhomogeneity of the magnetic field. It derives from differences in magnetic susceptibility (different magnetization capacity after the application of a magnetic field) between the various tissues which are generally canceled with the classic spin echo sequences with the 180° pulses. The T2* time can only be evaluated with Gradient-Echo sequences, which do not contain this refocusing impulse, but the application of gradients and therefore do not eliminate these dephasing effects. The presence of tissues or materials that create inhomogeneity, cause a more rapid T2* relaxation thus leading to a loss of signal in the GRE which translates iconographically into hypointense images.

Echo spacing must necessarily be set to 2.26 msec. In the multiecho images there is an oscillation of the signal which adds up to the decay of the signal, caused by the phenomenon of the 'chemical shift' between tissues with different relaxation times. The prevailing oscillation is induced by the fat-water interface and is characterized at 1.5T by a period of about 4.6 ms. It is therefore advisable to have a time interval between the various consecutive TEs equal to half of this time, therefore 2.26msec.

Currently, patients undergoing regular transfusion therapy, maintain an adequate pre-transfusion hemoglobin level, and receive appropriate iron chelation therapy with good control of body iron levels, with a high expectancy and quality of life. This highlights the importance of assessing iron accumulation in critical organs such as the liver, pancreas, and heart. We can assess that T2*-weighted Gradient Echo sequences are much more sensitive to the presence and distribution of hepatic iron overload compared to T2-weighted Spin Echo (SSFSE) sequences. As the TE increases in thalassemic patients, we observe a low intensity of liver signal due to the presence of iron. Additionally, the single-echo technique allows us to perform evaluations even in patients with severe thalassemia (Figure 3).

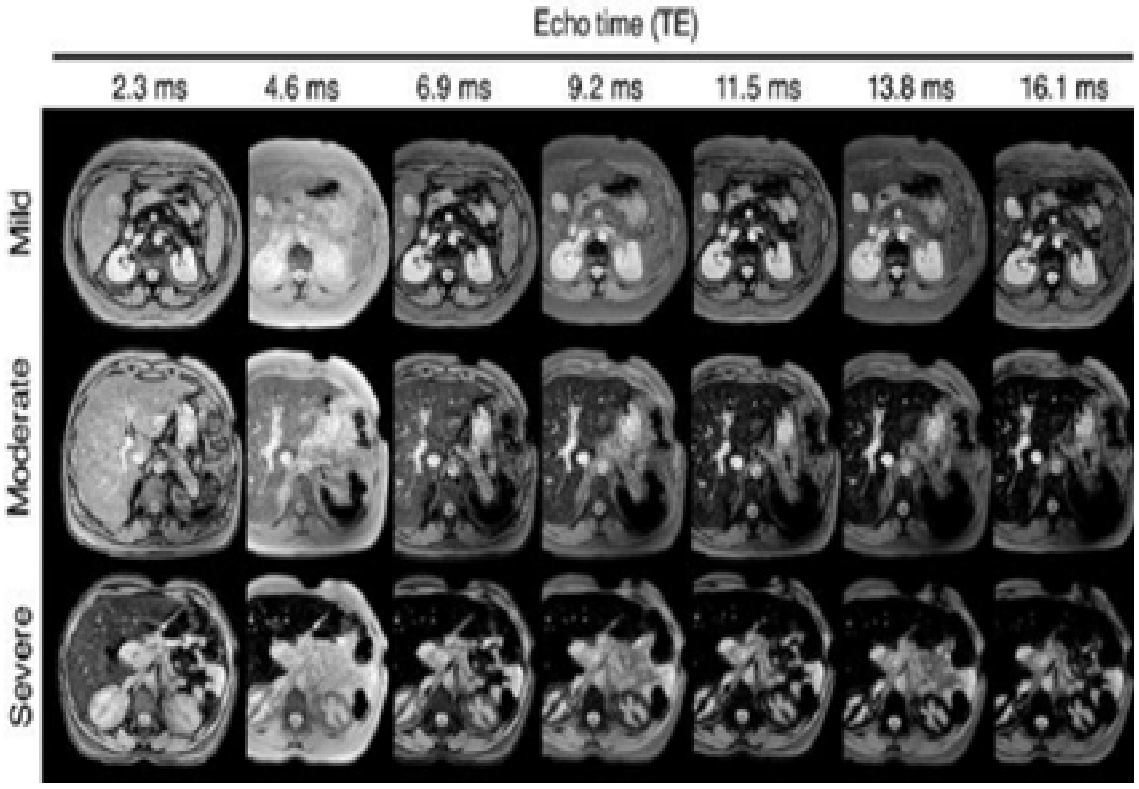

***Figure 3**. Increasing Echo Time with mild, moderate and severe iron overload in liver.*

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For the cardiac iron overload bull's eye scheme is used, which is nothing more than the schematic representation in 16 portions of the cardiac segments in the basal, medial and apical acquisitions. Each segment is scored to establish the level of iron overload in each heart portion (Figure 4).

Figure 4. *Bull's eye scheme with the* 16 *cardiac portions.*

- T2* < 10 ms: severe cardiac iron overload;
- 10ms ≤ T2* < 15ms: moderate cardiac iron overload;
- 15ms ≤ T2* < 20 ms: mild cardiac iron overload.

The value T2*=20 ms is considered as a threshold for non-iron accumulation.

CONCLUSIONS

In conclusion, MRI is currently the only technique capable of carrying out an accurate, reliable and non-invasive quantitative assessment of liver, pancreas and cardiac iron accumulation which, if left untreated, can lead to a series of serious complications such as dilated cardiomyopathy, arrhythmias, decreased contractile function up to heart failure. It is therefore necessary to institute appropriate chelating therapies in time and periodically adapt them to the conditions of all those transfusion-dependent patients who cannot undergo bone marrow transplantation.

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