Title:
3D Modeling for Multimodal Visualization of Medical Data

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Introduction:
Magnetic resonance imaging (MRI) is a non-invasive medical imaging technique used in radiology in most medical centers around the world. This technique very quickly imposed itself for anatomical explorations of the head and the whole body. It brings many types of advanced acquisition always based on the principle of magnetic resonance. The variety of quantitative information derived from these types of acquisition provides important structural and functional information at the cellular level, highlighting aspects of pathophysiology. It is therefore necessary to propose systems which ensure the multimodal visualization of all this complex information resulting from the different types of acquisitions, and to combine and synthesize them, in order to help the medical profession in its work: diagnosis, study of treatments [1]. In the brain analysis context, this technique provides additional information which can be represented by the molecule concentrations in a well localized volume in the cortex [2]. Several studies have shown the important role of these concentrations in combination with anatomical imaging to improve the diagnosis of certain diseases [3].
In order to visualize this data, physicians use the concentrations estimated after acquisition in a grid composed of large subdivision volumes (called macrovoxels in this article), each with a concentration value over its entire 3D space. Basic interpolation algorithms can be applied to this acquisition grid in order to improve the spatial resolution. However none of these algorithms takes into consideration the acquisition volume composition which is a mixture of three brain-forming substances: white matter, gray matter and cerebrospinal fluid, in which molecules are not uniformly distributed. Then the multimodal visualization of the anatomical data represented by the three substances with the concentrations of the molecules in a single rendering, remains a challenge.
In this article, we present a multimodal process allowing to model the molecular concentration which takes into consideration the heterogeneity of tissues in an acquisition volume. This new method makes it possible to have a 3D modeling and a visualization of the appearance of molecular concentrations taking into account the tissue composition. We expose their results, advantages and limitations. All of our

developments, tests and comparisons are done in the open-source software package 3D Slicer [4].

Standard Modeling Method:

In this section, we present the existing method to visualize the concentration of a molecule in each voxel of a regular grid well localized in the brain, representing the region where the acquisition was made (Fig 1). In order to visualize the data, two grids are considered. The first is the acquisition grid formed of the large voxels whose molecule concentration was estimated after the acquisition. This lower spatial resolution grid is obtained with a large volume of voxels, typically 7*7*20 mm3, each of them contains a concentration value uniformly distributed over its entire 3D space (Fig 1.a). The second is the segmentation grid obtained after the decomposition of the acquisition voxels into much finer voxels. This higher spatial resolution grid is obtained with a much smaller voxel volume, typically 1*1*1 mm3, each of them belongs to one of the substances that make up the brain and has been previously obtained by another process of acquisition and segmentation (Fig 1.c).

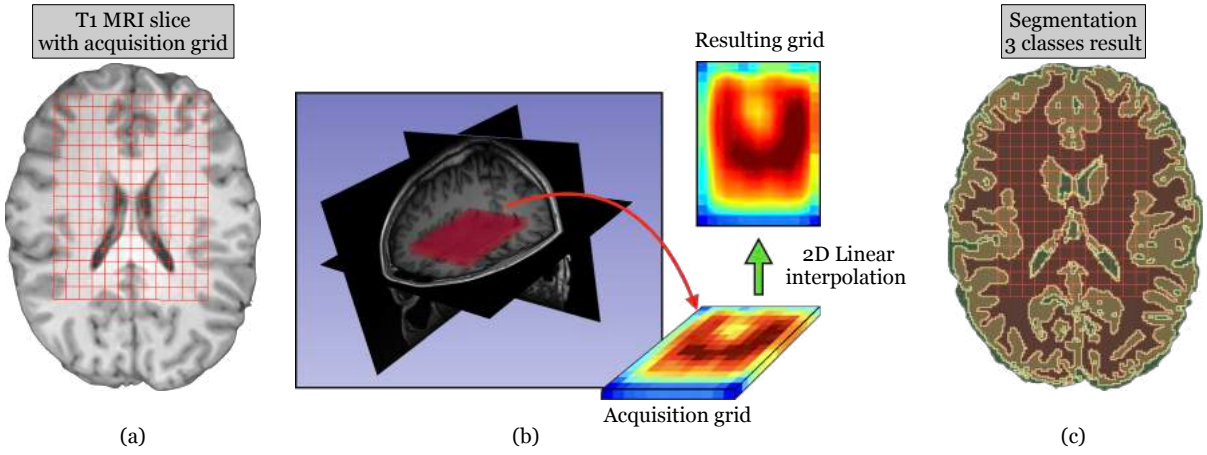

Fig. 1: Basic Visualization Method: (a) acquisition grid [red colored] on a T1 MRI slice; (b) 3D view of the acquisition grid into the brain [red colored] and the concentration distribution inside it, the concentration distribution in the segmentation grid after applying the linear interpolation on the estimated concentration values: from the higher concentration [dark red colored] to the lower concentration [dark blue colored]; (c) acquisition grid [red colored] on a MRI slice segmented into three brain substances: cerebrospinal fluid mask [green colored], white matter mask [brown colored] and gray matter mask [yellow colored].

Practical limitations of available scan time place major constraints on this type of data in terms of image resolution. An acquisition of molecule concentrations with a large voxel size allows a reasonable acquisition time for the patient but degrades the analysis of tissue microstructural features. A super resolution (SR) approach is used to refine the details of the originally acquired data. The main idea behind SR is to initialize the segmentation grid from the acquisition grid by applying a standard bilinear interpolation operation on the estimated concentration values (Fig 1.b). Moreover, the thickness of the acquisition grid being a single macrovoxel, the interpolation is finally only performed in 2D.
Conventional interpolation methods available in most processing tools apply interpolation algorithms directly to images, regardless of brain composition. These algorithms do not take into account the heterogeneity in a volume represented by a mixture of tissue compartments constituting it (Fig 1.c). This can lead to inaccuracies when quantizing the concentration of molecules in smaller voxels.

Our new Modeling Method:

Studies based on the adjustment of acquisition parameters in the clinical setting show that the molecules are not uniformly distributed among the three brain substances. The doctors succeeded to determine the distribution rates of the molecules in each brain substance [5]. Our modeling algorithm aims to estimate the concentration of a molecule in the microvoxels resolution according to their tissue nature, the overall concentration of the acquisition voxel where they are included and the distribution rates assessed in the clinical setting. This is achieved by computing, for each acquisition voxel, the concentration in each of the volumes of the substances that form it. In the following, we explain how the algorithm is applied to each voxel of the acquisition grid.

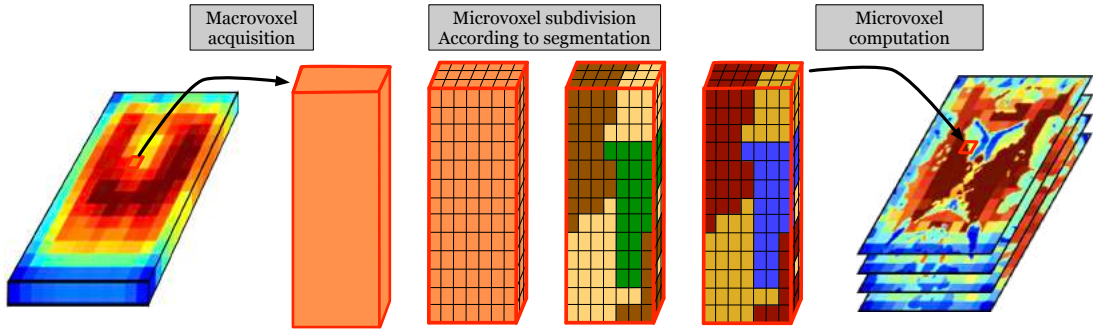

Fig. 2: Our new Modeling Method: macrovoxel acquisition estimates concentration values of a molecule in a very thick 12x16 resolution grid; microvoxel subdivision cuts each macrovoxel in order to obtain a grid as refined as the acquired MRI T1 slices. The segmentation method is used to classify each microvoxel according to its substance (white matter, gray matter or cerebrospinal fluid); The new concentration, according to anatomy is evaluated during the microvoxel computation by using the distribution rates of the literature.

For each macrovoxel, the process gives : its volume V (unit of volume) and the concentration C of a molecule X (unit of quantity/volume) inside. Those macrovoxels have been divided into microvoxels marked gray matter, white matter or cerebrospinal fluid by a segmentation process on T1 MRI. Obviously, in each macrovoxel, we cannot consider that we have the same concentration C in the three substances. The concentration of X in each substance depends on the concentration C, the volume of each substance, but also the tissular distribution rates. The computation of the volumes of these substances in a macrovoxel is done by counting the number of segmentation voxels of each substance and then multiplying by the volume of a segmentation voxel. The volumes of three substances in the acquisition voxel are respectively denoted V_1, V_2, and V_3 for the substances 1, 2 and 3. The purpose is to evaluate the concentration of X in these three substances that we note respectively C_1, C_2 and C_3 (see Fig 3 for an overview of the process). Doctors have provided us the distribution rate of X in the three brain substances that we note respectively a_1, a_2 and a_3(constant values).
The mass of molecule X in each macrovoxel is equal to $C * V$. This mass is well distributed among the three substances and is always preserved (Equ. 2.1).

$$C * V = C_1 * V_1 + C_2 * V_2 + C_3 * V_3 \tag{2.1}$$

The concentrations of molecule X in each substance are related to the distribution rates by the following equations:

$$a_2 * C_1 = a_1 * C_2 \quad ; \quad a_3 * C_2 = a_2 * C_3 \quad ; \quad a_1 * C_3 = a_3 * C_1 \tag{2.2}$$

By replacing the concentration C_2 and C_3 by their value as a function of C_1 in Equ. 2.1, we obtain the concentration C_1 in a volume V_1 as follows:

$$C_1 = \frac{C * V}{V_1 + \frac{a_2}{a_1} * V_2 + \frac{a_3}{a_1} * V_3} \Rightarrow C_1 = \frac{a_1 * C * V}{a_1 * V_1 + a_2 * V_2 + a_3 * V_3} \tag{2.3}$$

C_2 and C_3 are deduced from C_1 using Equ. 2.2. After estimating the concentration of a molecule X in each volume V_i, it is assumed that X is uniformly distributed in each volume and the concentration of X in each microvoxel is initialized in terms of the concentration values C_i estimated according to the nature of the tissue to which it belongs. Fig 3 and 4 show the results of our modeling method.

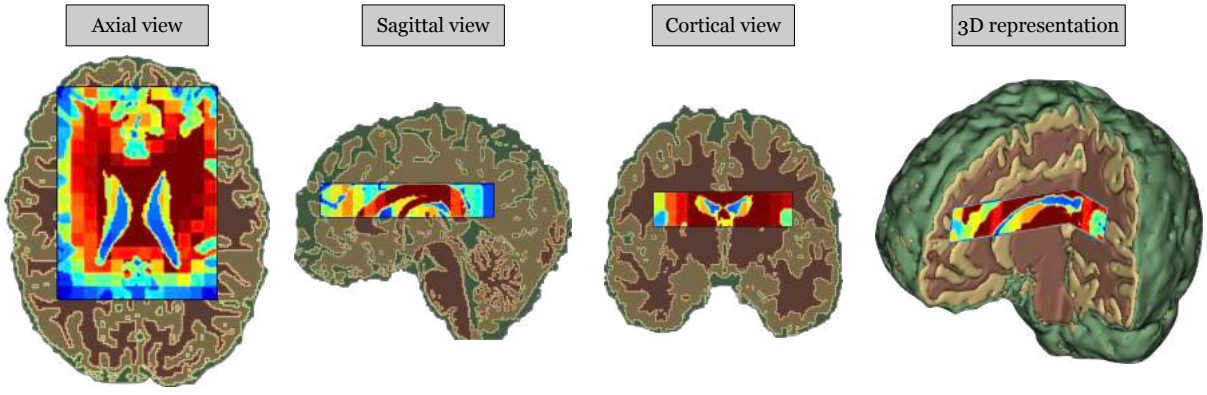

Fig. 3: Three views of the molecular concentration slices in the segmentation grid with the corresponding brain substance masks after applying our method. A multimodal 3D visualization is obtained (on right): concentration values merged with brain substances.

Comparison and Discussion

Existing methods of visualizing concentration values of molecules in the brain do not take into account the effects of partial volumes of brain substances on their distribution in the acquisition volume. The accuracy of the representation model is limited to the coarse sampling of the acquisition grid which leads to inaccuracies in the quantization process of the molecules. We have developed a concentration computation process allowing a 3D modeling of the data taking into account the spatial distribution of the tissues (Fig. 3). The results show that there is a variation of the concentrations according to the depth of the voxel depending on the nature of the tissues, whereas with the conventional methods, we have the same concentration value on all the depth of a voxel of acquisition for a 2D position (Fig. 4).

Studies have been carried out to study the variation in the concentration of a molecule in each substance on healthy patients. The results show that the molecule is distributed in each substance in a well-defined interval. This small variation, in the same substance, was obtained because the concentration value estimated does not only depend on its nature but also on its position in the brain [5]. We study the variation of the concentration of a molecule in each substance after the application of our algorithm, the results show that the concentration in each substance is well compatible with the studies in the literature.

Despite these improvements, it should be noted that there are limitations in terms of spatial resolution. One cannot refine acquisition volumes in voxels smaller than segmentation voxels. Therefore, our ability to improve the spatial resolution is limited by the spatial resolution of the segmentation grid. Although the segmentation grid represented by voxels of 1*1*1 mm3 may seem limited, it is generally adequate for

most purposes. This level of resolution allows for highly detailed visualization, providing clinicians with the information needed to effectively diagnose and treat brain diseases.

Conclusion:

In this work, we have proposed a new method for 3D modeling and visualization of medical data (Fig. 3-on right). This method allows a better modeling and distribution of the molecular concentration taking into account the real nature of the underlying tissues based on distribution rates evaluated in clinical studies. In this context, our method offers a new tool to dynamically model in 3D the distribution rates of the data.

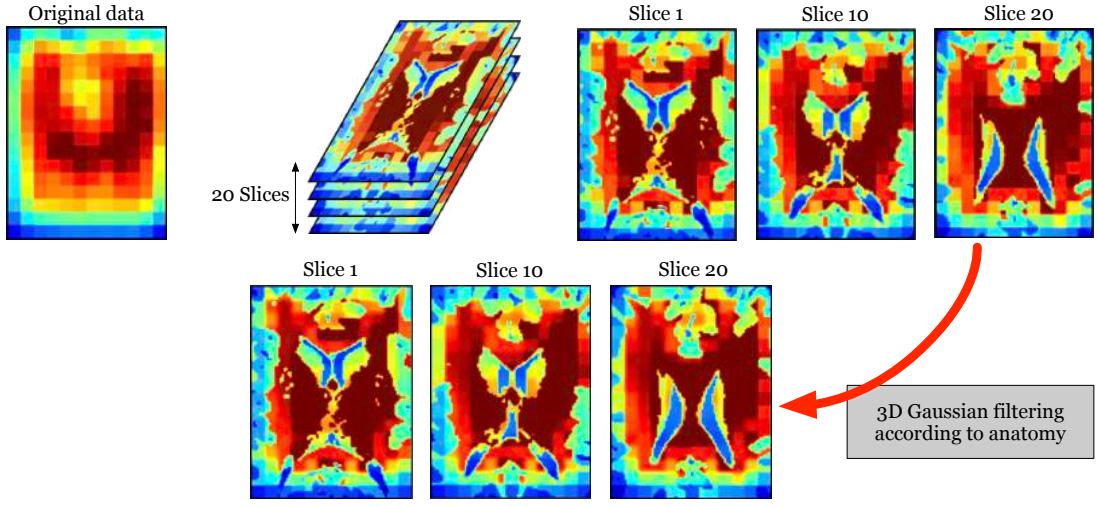

Fig. 4: Results of our process: molecular concentration distribution in the segmentation grid taking into account the nature of the underlying tissues. A slight 3D gaussian filtering is applied to improve the final visualization.

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