MR ONCO-TREAT: A New Tool for Volumetric and Functional Analysis of Hepatic Tumors Monitored with Multi-Modal MRI

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Introduction: The RECIST criteria have been the gold standard for determining therapeutic response of a tumor, defining partial response as ≥ 30% decrease in diameter in a single dimension [1]. Recent data strongly suggest that the RECIST criteria are a poor indicator of therapeutic response for hepatic tumors (either primary or metastatic) which have been treated with intra-arterial therapy. In contrast, multi-parametric MRI, including diffusion weighted imaging (DWI) and T1-weighted dynamic contrast-enhancement (DCE), has been shown to be a sensitive indicator of tumor response [2]. Typically, measurements of liver tumor size, Apparent Diffusion Coefficient (ADC) characteristics and perfusion are performed manually, and visual comparisons are made across serial examinations. This process is time consuming, is inherently subjective, and may inaccurately assess liver tumor response to intra-arterial therapy. The automation of this task would allow for objective evaluation, decreased inter-observer variability, and increased accuracy of evaluation of liver tumor response to therapy. In this abstract we present our design of MR ONCO-TREAT, a highly flexible, semi-automated software package for three dimensional intra- and inter-study image registration, segmentation, volumetric analysis and functional analysis. We present early data showing that this software package can provide objective evaluation of liver tumor response to intra-arterial therapy on either a global or voxel-by-voxel basis.

Materials and Methods: The images in pre- and post-treatment studies are registered in two steps, in order to work in a fixed frame of reference (Fig. 1a-c). In the first step, *intra*-study registration, images within each study are registered using the venous phase post-contrast DCE volume as the reference image set. Motion is corrected in the dynamic contrast-enhanced images and diffusion weighted images are registered to the reference DCE volume by a deformable registration technique [3]. In the second step, *inter*-study registration, venous phase DCE images from both studies are co-registered, and the resulting deformation field is applied to all images in the post-treatment study. The deformable registration technique first aligns the images with a rigid method to improve the capture range and accuracy, and then works with a multi-resolution strategy focusing on global and local image features at different resolution levels.

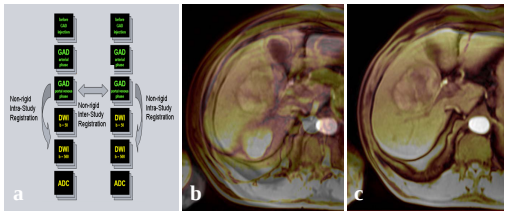

Figure 1: Registration process (a). Color blended display of pre- and post-treatment venous phase DCE images before (b) and after registration (c)

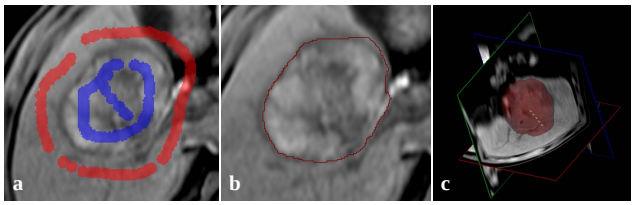

Figure 2: Segmentation process. Seeds placed in tumor and surrounding tissue (a), segmentation results in 2D (b) and 3D (c).

A "Random-Walker" 3D segmentation technique is then used to define tumor borders [4]. This semi-automated method requires manual placement of seed points which correspond to tumor and surrounding tissue (Fig. 2a). This technique produces a unique solution without any assumptions or adaptive knowledge, and is capable of accurately localizing weak boundaries despite missing boundary information. After automatically segmenting the target tumor volume from any DCE or diffusion weighted image, the results can be corrected by either giving additional seed points or editing manually with a paint feature.

Segmentation results can be displayed either in 2D on multiplanar reformatted images as intersection boundaries or in 3D as a surface mesh (Fig. 2b-c).

Once the images are registered and the tumor is segmented, the MR ONCO-TREAT software package can automatically evaluate: a) volumetric data (including tumor volume, surface area and longest diameter), b) ADC values, and c) DCE in multiple vascular phases. The software can automatically compare two studies either using percent volume or on a voxel-by-voxel basis. In voxel-by-voxel comparison, the voxels are classified in three different groups based on threshold criteria; red for increased values, blue for decreased values and green for intermediate values, and the corresponding scatter plot is generated to better assess overall changes in ADC/DCE values (Fig. 3) [5]. Data presentation with this tool is highly flexible: histograms as well as more conventional mean, standard deviation and median values can be produced for each parameter measured. Color maps of ADC and DCE analysis can be overlaid on any image from both studies, and direct comparison becomes possible between ADC and DCE analysis (Figs. 3a & 4a,b). With this software package, it is also possible to evaluate more than one segmented region at the same time to compare tumor to healthy tissue. The application also includes tools for 3D visualization, including Maximum Intensity Projection, Volume Rendering Techniques and 3D Multi-Planar Reformat rendering modes for visualizing the entire volume, and tools for measurement, including distance and pixel lens tools.

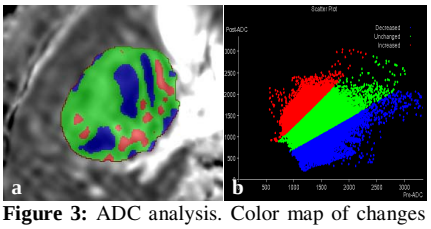

Figure 3: ADC analysis. Color map of changes in ADC overlaid on ADC image (a), and scatter plot (b). Red = increased ADC, Blue = decreased ADC (Green = intermediate)

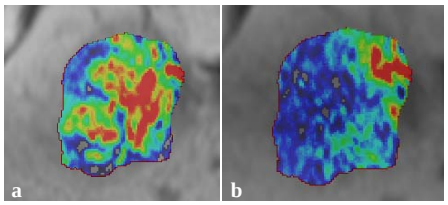

Figure 4: Pre- (a) and post-treatment (b) arterial enhancement color maps overlaid on arterial phase DCE images. Enhancement increases from blue to red (Green = intermediate)

Results: In order to test the software package, standard clinical MR studies from 6 patients with hepatocellular carcinoma were evaluated both before and 4-6 weeks after trans-arterial chemoembolization. In all 6 patients, the software was able to register the MR studies and to segment the tumors from the surrounding liver. For each patient, the software was then used to calculate changes in tumor volume, DCE and ADC values, between the pre- and post-treatment studies. In one patient the tumor volume did not change and voxel-by-voxel analysis of the tumors could be performed. In the remaining 5 patients, the pre- and post-treatment studies were segmented separately, and global analysis (% volume) was performed. On average, tumor size increased by 24%, ADC increased by 9.5%, and percent enhancement decreased by 35.7 (arterial) and 14.5 (venous), these last two being absolute changes between percent values.

Discussion: The MR ONCO-TREAT software represents a flexible, semi-automated framework for the registration, segmentation, and analysis of MR images both within single studies and, more importantly, between serial studies on the same patient. This initial technical evaluation demonstrates the ability of this software package to provide comprehensive, three dimensional analysis of liver tumors, including both volumetric and functional data. Future work will focus on testing of this software package in the clinical setting, in order to correlate data acquired from this software with current evaluation techniques and with clinical outcomes in patients who have undergone intra-arterial therapy of hepatic tumors. This software package can be applied to cancers elsewhere in the body as well, and testing of this software on brain tumors is currently underway.

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