

Automated Prescription and Reconstruction of Brain MR Spectroscopy Data for Rapid Integration into the Clinical Workflow

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ABSTRACT

Objectives: To implement and evaluate a fast, automated, end-to-end brain MR Spectroscopy workflow for rapid integration of metabolic parameters into clinical care.

Materials and methods: An automated and reproducible atlas-based prescription for single and multi-voxel MR spectroscopy (MRS) data has been developed and combined with an online reconstruction that enables DICOM MRS results to be generated and sent to clinical PACS in real-time by the end of the MRI exam with the rest of the imaging data. The prescription method has been generalized for arbitrary classes of neurological exams through a library of templates that provide localization to specific anatomical locations. This enables rapid and consistent localization from serial follow-up studies, which is important for streamlining longitudinal comparisons.

Results: When implemented in conjunction with spectroscopy sequences that are able to provide echo planar spatial encoding, the scan preparation time is reduced to approximately 1 minute, with a typical scan time of as little as 6 minutes for volumetric MRSI. Integration with automated online reconstruction methods that are able to utilize parallel computing strategies for analyzing large datasets permits delivery of the results in DICOM format to clinical PACS in real-time, and is critical for incorporating them into the radiological workflow. Total active console time for such studies including prescription, shimming, acquisition and report generation is 9.5 minutes. These methods have been implemented at UCSF, with 139 volumetric MRSI exams having been obtained from patients with brain tumors in the past year 18 months. 16 subjects scanned serially with the same prescription template had an average Dice overlap ratio of prescribed MRSI volumes of 0.979 ± 0.016 .

Conclusions: Robust, fast and automated MRS workflows, capable of delivering results to the reading room are feasible in clinically acceptable time frames. These workflows facilitate the integration of metabolic parameters into patient care.

Introduction

Recent studies have shown that proton MR Spectroscopy (MRS) and spectroscopic imaging (MRSI) of the brain is important for characterizing metabolic changes associated with neurological and psychiatric diseases, as well as monitoring response to therapeutic interventions. The widespread adoption of this technology has been hindered by workflow challenges that make it difficult to reliably deliver high quality metabolic parameters to the clinic in real-time. Challenges to implementing a fast and robust solution include complex and time consuming prescriptions that impact data quality and reproducibility and long scan times that are difficult to accommodate during an exam. The lack of flexible, commercially available tools that are capable of rapidly processing and exporting DICOM [1] MRS results to clinical PACS (Picture Archiving and Communication Systems) is another factor that prevents real-time delivery to the radiology reading room. The four high-level elements of a workflow needed to overcome these current limitations are represented in (Figure 1) and include prescription, acquisition, processing, and data transfer.

Prescribing MRS scans of the brain requires specialized training to place the selected volume and lipid saturation bands in the appropriate locations and can be time consuming, even for an experienced user. The process is prone to error and variability between serial scans that often results in signal contamination artifacts and limits the quality of the data [2,3]. Several groups have previously reported on methods to automate various aspects of the prescription of MRS acquisitions [2-9]. The method presented here achieves this via an automated atlas-based approach to integrate the pre-defined definition of PRESS or slice selected volumes with multiple pre-defined saturation bands. This provides advantages in terms of reproducible coverage, artifact-free placement, reduced prescription time and improved data quality [3,5,8]. Incorporating multi-voxel MRSI into a 30-60 minute clinical MR examination that can be interpreted in conjunction with the corresponding imaging data also necessitates the use of rapid

acquisition and post-processing tools. Although numerous fast MRS techniques have been demonstrated in the literature [10], many of the current product sequences take 20 minutes or more to obtain volumetric coverage. Acquisition of MR spectroscopic imaging (MRSI) data in a clinically feasible time means that alternative k-space sampling strategies such as flyback echo planar spectroscopic imaging must be implemented [11,12]. Reconstruction and analysis of data obtained using such novel sequences requires specialized software packages to be made available at the console for rapid quantification of clinically relevant parameters with minimal user interaction.

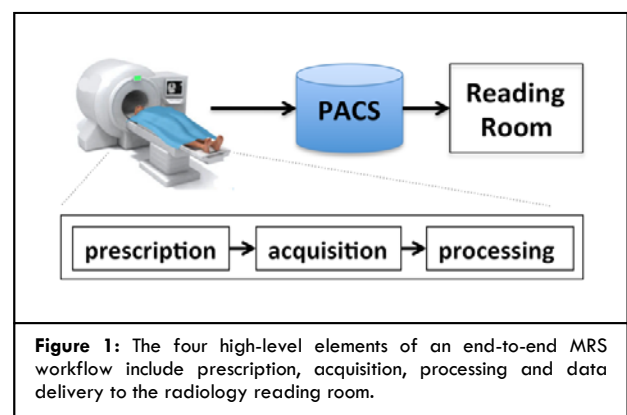


Figure 1: The four high-level elements of an end-to-end MRS workflow include prescription, acquisition, processing and data delivery to the radiology reading room.

The other critical component of the workflow is the delivery of the MRS results and quantitative metabolite maps to the radiologist and referring physician. To be transferred to PACS and transmitted to both the radiology reading room and the patient's electronic record, the outputs must be in standard DICOM format and be available for transfer by the end of the exam with the rest of the MR images. This is essential for streamlining the incorporation of metabolic imaging findings into the assessment of the patient's condition. The current study presents the strategies that have been developed at UCSF to overcome these challenges and demonstrates how they have been applied to provide rapid evaluation of patient data. This work focuses specifically on describing the implementation for a multi-voxel, multi-channel MRSI workflow for brain tumor studies. The implementation and integration of

individual modules are described in the methods section and applied to implement a fast, end-to-end workflow that provides routine, real-time delivery of quantitative metabolic data to the clinic.

Materials and Methods

1. MRS workflow implementation

The MRS workflow (Figure 2) comprises multiple software modules. The key elements are described here at a high level with further details being presented as supplementary digital content.

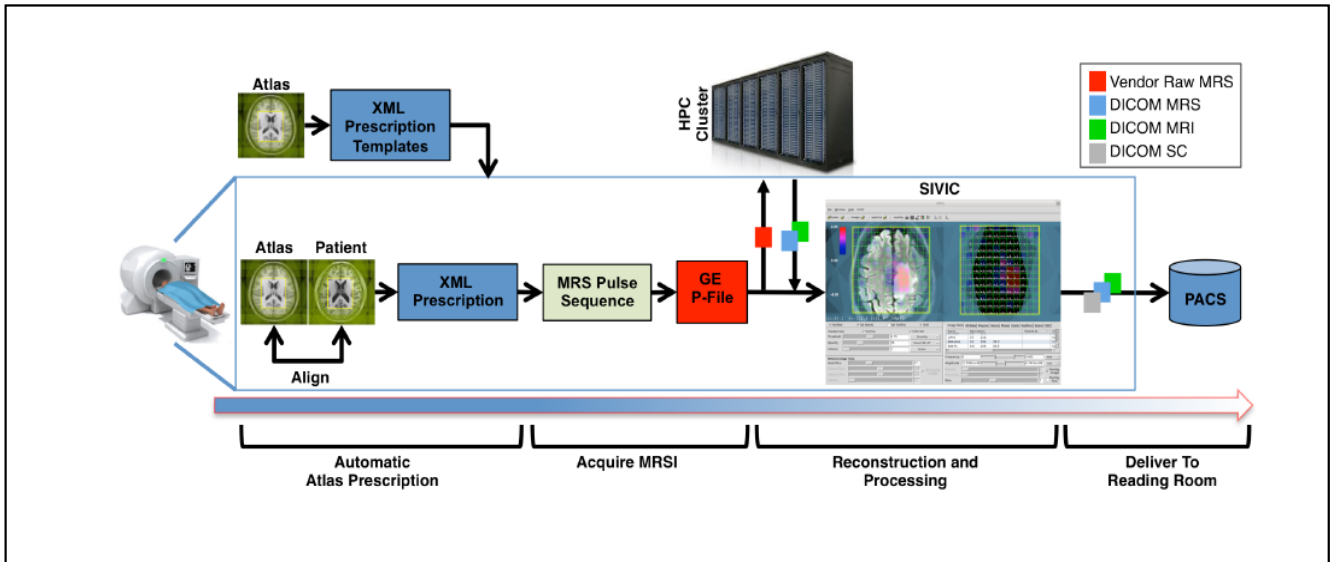


Figure 2: Schematic diagram of a real-time automated MRS workflow. Atlas templates are generated offline prior to the exam. External HPC resources can be utilized for computationally expensive analysis. MRS results are encoded in DICOM format (MR Spectroscopy (MRS), Secondary Capture (SC), Enhanced MR Image (MRI) metabolite maps) and sent to PACS at the end of the exam with the other imaging series.

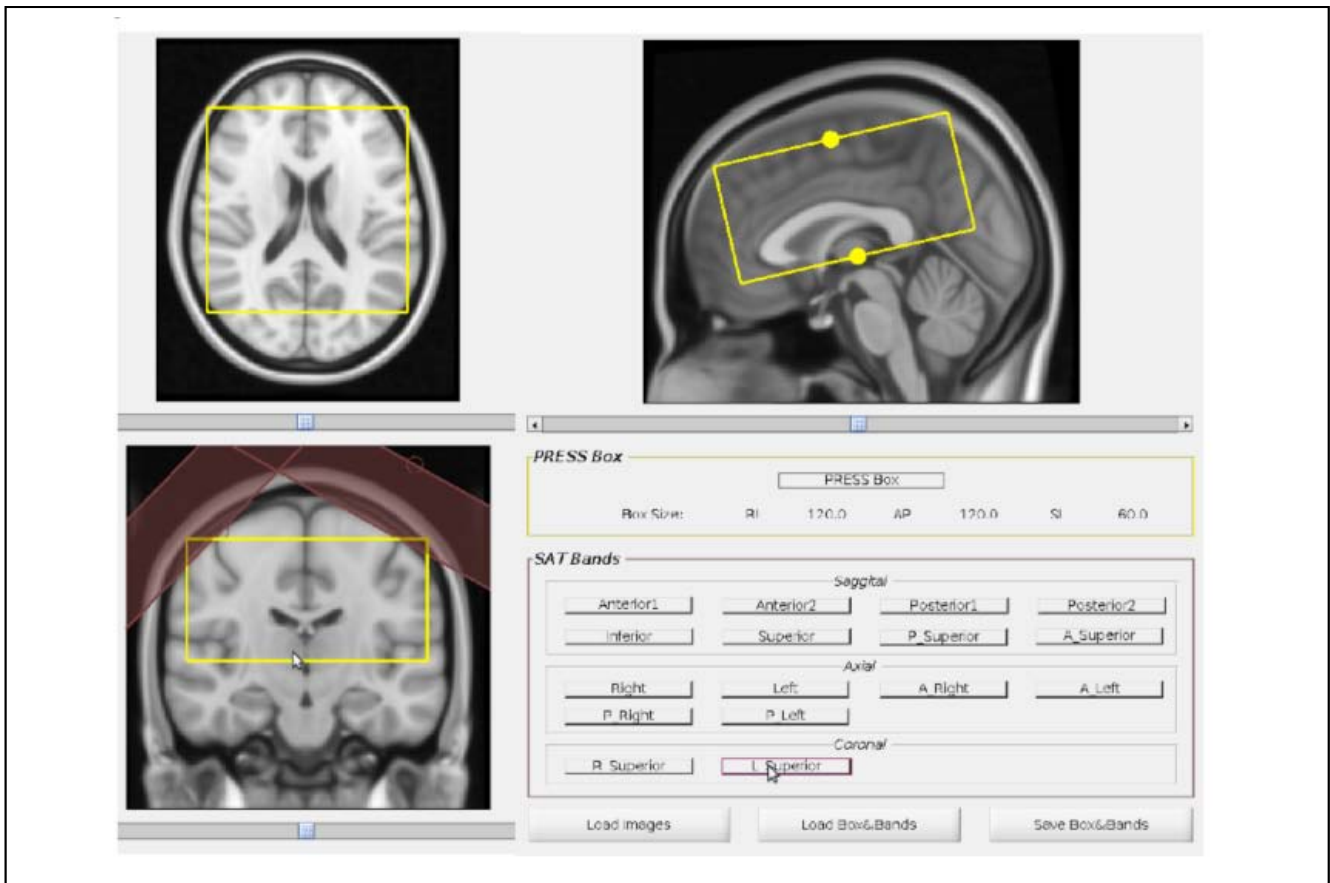


Figure 3: Graphical offline prescription software showing the initial steps in defining a prescription template. The MNI152 atlas is displayed in all three planes with a PRESS box and two sat bands placed in the coronal view.

The majority of the underlying source code and binaries are freely available through the SIVIC project open-source software portal [13,14]. The workflow has been implemented on a GE MR750 3T scanner, but the underlying software packages were designed to run on multiple platforms including Linux, Windows and OSX and could be adapted to work with other vendor's scanner platforms and pulse sequences [15].

2. Console job staging software

The application pipeline was configured through the SIVIC GE console job staging software package. This permits user-friendly push-button execution of the software pipeline and manages data selection from the scanner's database, staging computation on an external high-performance cluster and import of DICOM results back into the scanner console. The online MRS prescription application and the online reconstruction application described below were configured to run on the console via this framework.

3. MRS prescription

The automatic atlas-based prescription method has been described previously [5,8] and only a brief overview is provided here in order to appreciate how it is integrated into the current MRSI workflow. A GUI called "Draw_Box_SATBands" [16] was developed in MATLAB [17] and used to prescribe the MRS acquisitions on an atlas image prior to the exam on an offline workstation. A library of templates was developed to account for the variations in anatomic locations that are required for different applications. For the present work all of the templates were drawn on an MNI152 atlas [18,19]. The GUI permits the user to adjust the size, orientation and position of the PRESS volume and a set of sat bands (Figure 3) on the specified atlas. Once graphically prescribed in the Draw_Box_SAT Bands application the prescription is exported in XML format [20].

Further details about this software together with links to example prescription templates are provided separately (see supplemental digital content that contains a tutorial demonstrating the use of the Draw_Box_SATBands program [16]). Once created, XML prescription templates are copied to a directory on the scanner console for use at exam time as described

below. The radiologist can thus simply request an MRS acquisition type to be prescribed from one of the predefined templates.

The online prescription software that transforms the prescription into the patient frame is configured to run on the scanner console. The package is initiated at scan time by selecting the "3T MRS SAT Placement" application button that is configured on the scanner console. Pressing this button loads the MRS auto prescription GUI called "Atlas_Based_Auto_MRS_Prescription" [21] (Figure 4), also written in-house in MATLAB. This application permits the user to select an application specific prescription template and a T1 weighted image from the current exam to align the atlas to. Once selected the application uses FSL flirt [22] to apply an affine registration (Scaling, Translation, Rotation, Shearing) of the MNI atlas to the selected T1 volume from the current exam. The resulting transformation parameters are applied to the elements in the selected prescription template to bring them into the patient frame [5] and the patient aligned prescription is displayed in the GUI (Figure 4). The patient aligned prescription parameters are then written to a new XML file that can then be read by the pulse sequence.

4. Acquisition of MRS data

The auto-prescription method was integrated into a pulse sequence which is able to obtain both single voxel MRS and multi-voxel EPSI flyback data [11,12]. Acquisition times for volumetric MRSI from the brain using an 18x18x16 matrix with flyback readout in the SI direction were ~5.5 minutes for single cycle and ~11 minutes for two-cycle lactate edited data. The current study used a commercially available 8 channel head coil, but the software is capable of working with single and other multi-channel coils. The pulse sequence was customized to read in the prescription parameters from the patient aligned data from the new XML file using methods from the SIVIC library svkSatBandsXML class [23]. The svk function calls for reading the prescription file from within the pulse sequence code are provided (see supplemental digital content that contains relevant code snippets from the pulse sequence [24]). The

prescription information is used together with the MRS raw file on the scanner for reconstruction and quantification since the parameters describing the custom saturation bands are not natively encoded in the raw file. Shimming is performed using the standard package available on the scanner.

5. Data processing

The reconstruction and analysis software were developed at UCSF in SIVIC [15] and with other in-house routines [25,26] that read the custom prescription parameters, reconstruct and quantify the raw MRS data via the job-staging interface on the console.

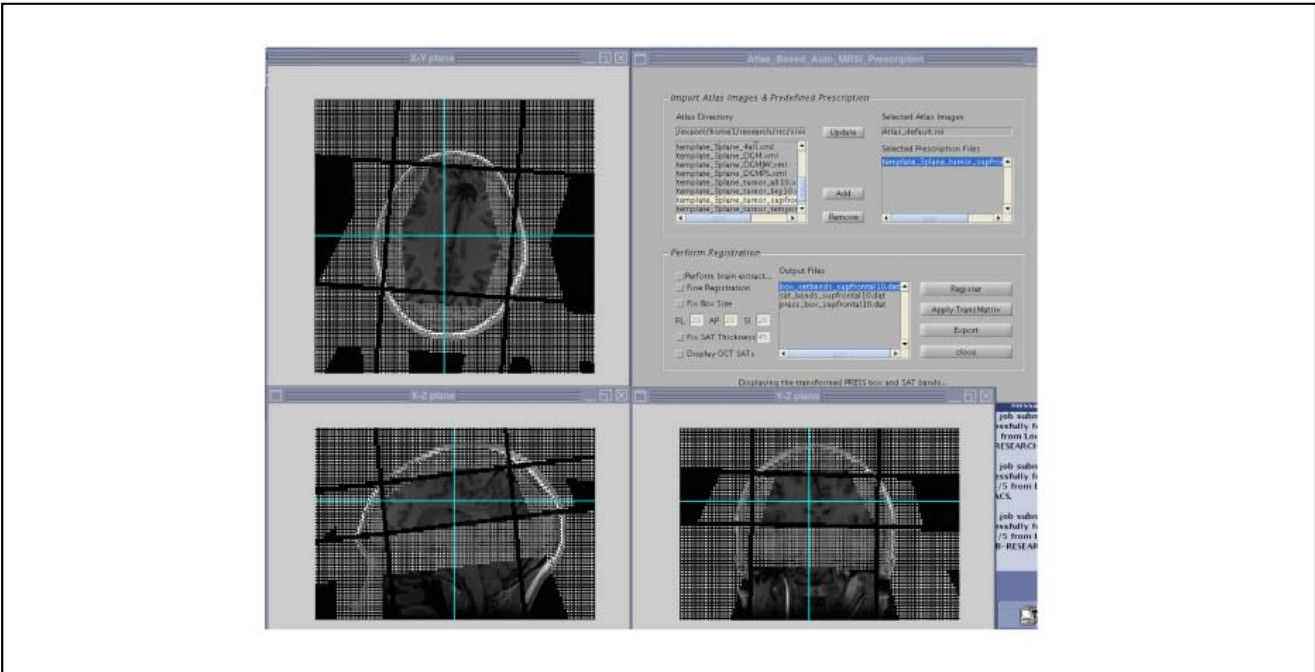


Figure 4: Starting MRS Automatic Prescription GUI on the GE console from a push button. The GUI permits selection of an MRS prescription template and atlas as well as a T1 series from the current exam to align the prescription template to. The patient aligned prescription is displayed in the GUI on the T1 volume (intersecting black lines represent the PRESS box and hatched areas represent sat bands).

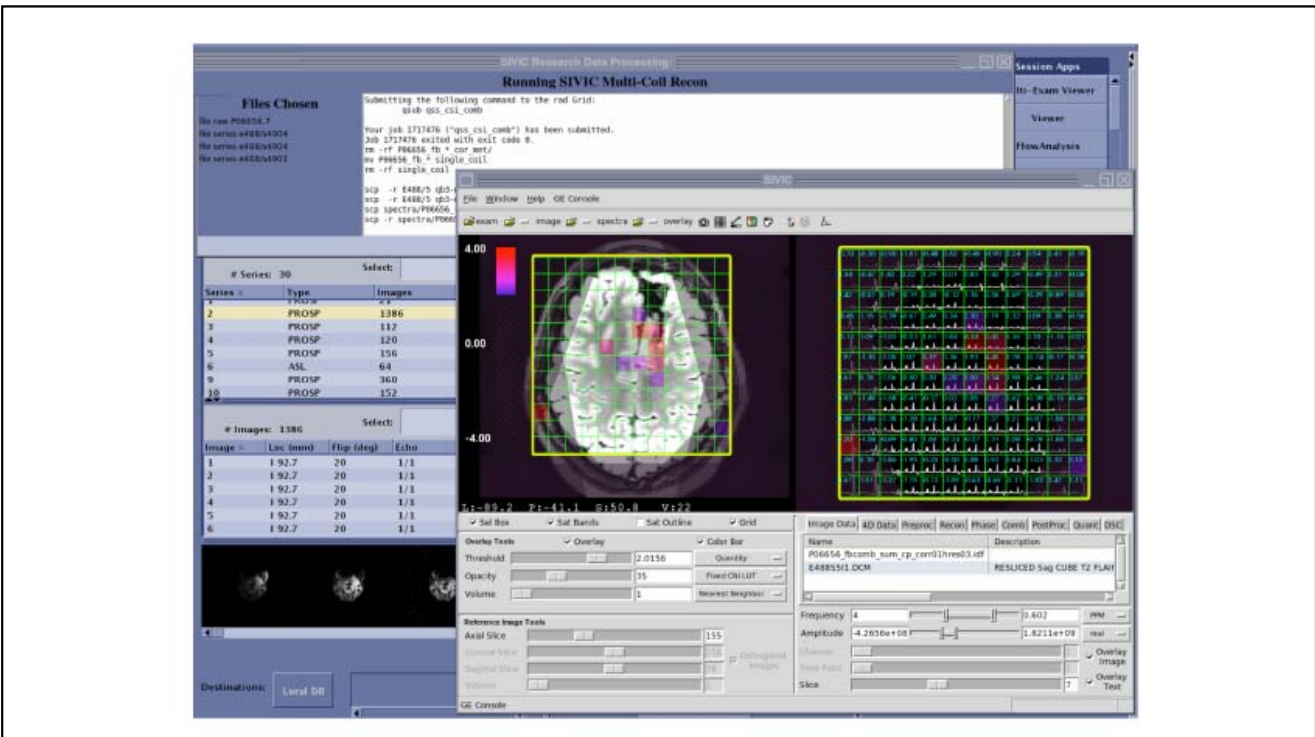


Figure 5: Reconstructed spectra and CN1 metabolite maps are automatically loaded into the SIVIC GUI for viewing on the scanner at the completion of processing. Note the display and correspondence of the PRESS box and sat bands with the auto-prescription from Figure 4. The ROI of interest is defined in the SIVIC GUI and a DICOM secondary capture report is generated and imported into the scanner's DICOM DB at the click of a button.

This automated pipeline utilizes a priori knowledge of peak locations for analysis and returns reconstructed spectra, as well as maps of quantitative parameters such as the Choline-to-NAA z-score Index (CNI) [27] to the scanner in real-time and in DICOM format with no user input. Because reconstruction and analysis of multi-channel MRSI data is computationally expensive, the job-staging interface was configured to execute this analysis externally on a high-performance computing cluster. For this application, namely the reconstruction and quantification of multi-channel, multi-voxel data, the user is asked to select the MRS raw file, an ASSET Calibration series for coil weighting during reconstruction as well as T1 and T2 series as reference images for generating visual DICOM Secondary Capture reports for PACS. Once the input data fields have been selected, the data are copied via SCP [28] to a secure LINUX computational cluster at UCSF and the automatic reconstruction and quantification is executed. Results comprise DICOM MRS files and DICOM metabolite maps that are returned to the scanner via SCP and automatically loaded into the SIVIC GUI (Figure 5), where they can be reviewed and secondary capture DICOM reports generated for PACS (Figure 6). The SOP (Standard Operating Procedures) contains additional details (see supplemental digital content) [29].

The reproducibility of the prescription was assessed for subjects who were scanned serially with the same prescription template by computing the Dice ratio for the PRESS volumes from the two exams as described previously [5].

Results and Discussion

The individual steps in the pipeline and their duration are represented in the timing diagram show in (Figure 7). Two operators reported on typical times for individual steps in the workflow. For volumetric MRSI data, the overall time from the start of the workflow to delivery of an MRSI report was 15.5 minutes (21 minutes for lactate editing), but approximately 6 minutes was background processing time during which the anatomical T1 + contrast data are acquired. Active console time used for volumetric MRSI is therefore only 9.5 minutes for single cycle data and 13.5 minutes for lactate edited data. The atlas-based auto-prescription took approximately 1 minute and shimming approximately 30 seconds. Reconstruction setup and report generation also took approximately 1 minute each.

The full pipeline has been used to acquire 139 exams from patients with brain tumors during the past 18 months. 16 subjects were scanned serially with the same prescription template. The average Dice overlap ratio of MRSI PRESS volumes for these serial cases was 0.979 ± 0.016 and was comparable to results obtained from reproducibility measurements on normal volunteers [5].

The average difference in prescribed centers was 0.42 ± 0.40 (RL), 0.91 ± 0.94 (AP) and 0.48 ± 0.62 (SI) mm. (Figure 8) shows a representative prescription for a patient with a low grade brain tumor scanned 3 times over a 3 year period. The first scan was manually prescribed, whereas the subsequent two scans were acquired using the current atlas prescription.



Figure 6: Portion of a DICOM Secondary Capture report generated on the scanner showing the placement of the PRESS box, sat bands, reconstructed spectra in an ROI and CNI map color overlay for a single slice. The reference image is the T1 contrast enhanced image from the exam.

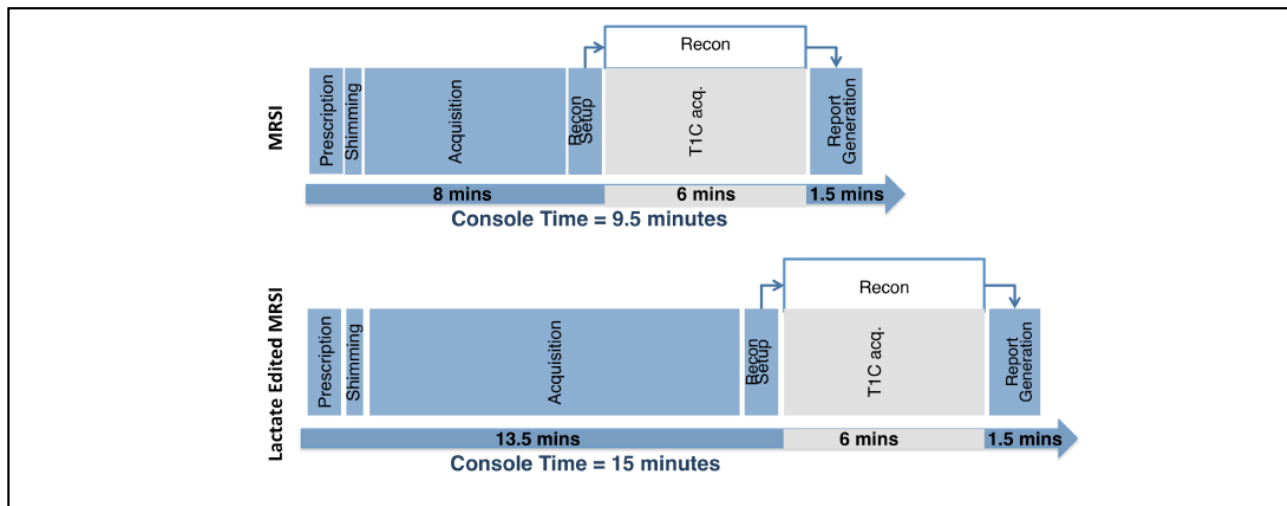


Figure 7: MRSI workflow timing diagram (lactate editing timing is shown in the lower diagram). Blue elements represent console time dedicated to the MRS workflow. Grey blocks represent times when other data is being acquired and MRS analysis is being done simultaneously in the background. The active time for the complete MRS workflow is 9.5 minutes (15 minutes for lactate editing).

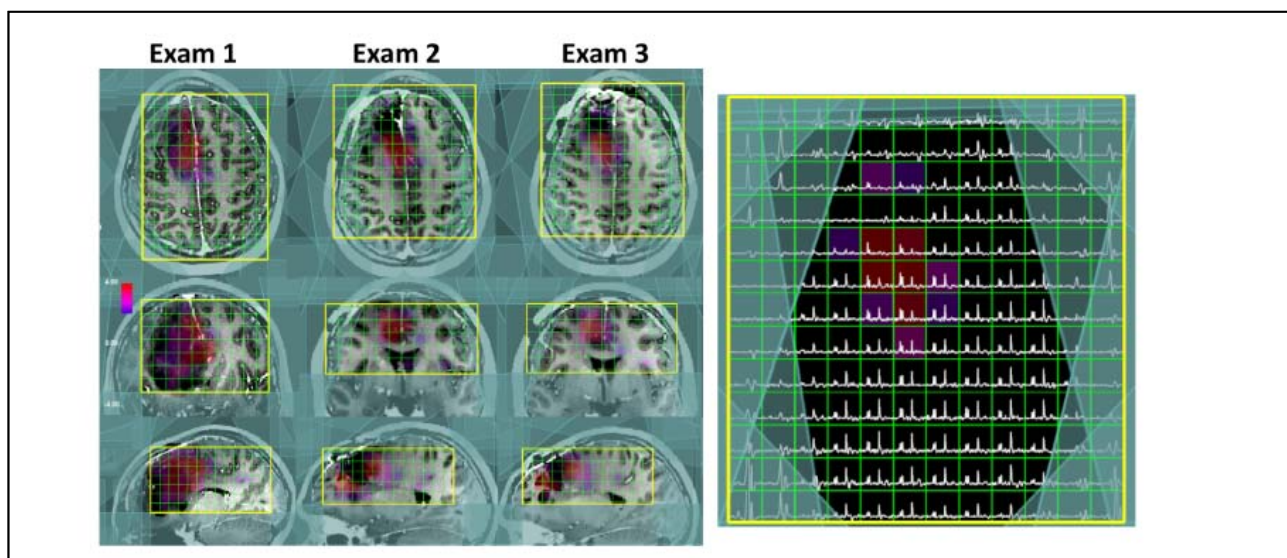


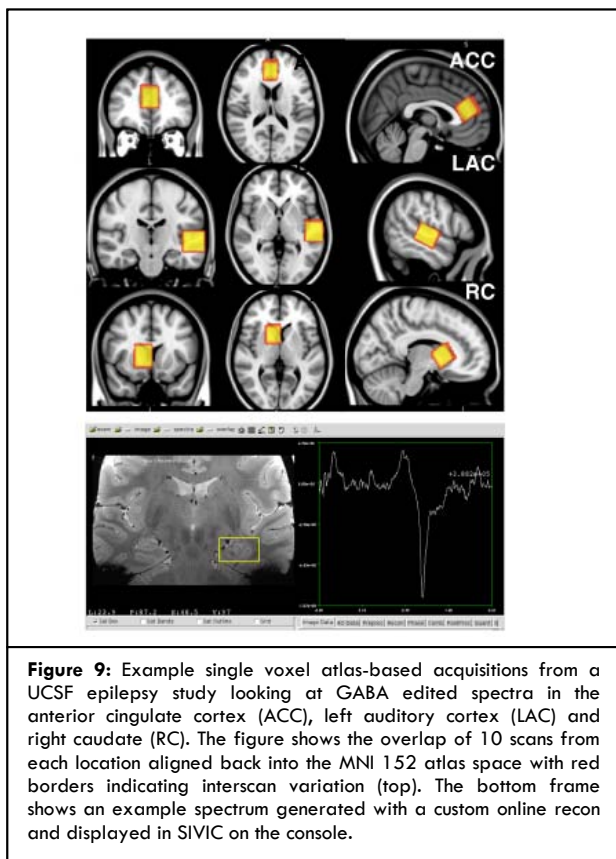
Figure 8: Serial MRSI exams (T1 post Gad and CNI metabolite map color overlay). Exam 1 was manually prescribed. The two subsequent exams were auto-prescribed from an atlas. The PRESS box is shown in yellow, voxel grid in green and sat bands in teal. Spectra from the axial slice of exam 3 is shown on the right.

MRSI Secondary Capture reports were sent to the clinical reading room in real-time for the majority of exams. Networking failures between the scanner and the computing infrastructure occurred for 3 out of 139 examinations, and required spectra to be transferred manually and processed offline. The atlas-based prescription was ineffective in a small number of cases due to head shape or because tumor locations extended outside the prescribed volume. These could be resolved in the future by increasing the number of predefined prescriptions available on the scanner. In these cases, manual MRSI prescription was used, and data were still

processed on the console in real-time using the methods described above.

Making the processed MRS results available for review at the console affords an opportunity for additional scans to be acquired, time permitting, while the patient is still in the scanner. Prescription and sat band misplacement are common reasons for poor data quality requiring rescanning, but artifacts from these causes are reduced through use of the automated prescription strategy. However, findings from real-time analysis may indicate when additional data would yield diagnostic insight and can also be used to direct prescription of

single voxel acquisitions for regions of interest within the preliminary MRSI scan.



Multiple users were trained to perform the acquisition and analysis at the console. Compared with the offline reconstruction workflow, not only was the MRS data delivery faster, but the workflow was significantly simplified and did not require extra communication between technical staff and clinical staff to coordinate specialized interpretation of the MRS data.

Radiologists reported that the workflow resulted in improved clinical efficiency and rapid report turn-around, by (1) enabling rigorous longitudinal comparison of MRSI voxels across exams, (2) permitting 3D MRSI acquisition within standard clinical time slots for exams, and (3) facilitating their review of processed spectra together with anatomic images immediately after the exam and within the clinical workflow, which requires that interpretations are issued shortly after completion of the examination.

Conclusion

A rapid, automated MRS workflow was implemented for acquiring and delivering data to PACS in a clinically

acceptable time frame and was demonstrated to be robust for supporting routine clinical requirements.

The auto-prescription strategy was successful in speeding up the data acquisition, simplifying the workflow and increasing the robustness of the scan. While the main focus for the current study was the use of multi-voxel MRSI for pre-surgery and serial studies of patients with brain tumors, there are many other applications and the methods are not limited to a particular acquisition sequence. Strategies other than OVS based lipid suppression have been presented [30,31] in the literature and though these don't require fat placement they would still benefit from an atlas based approach in terms of serial reproducibility, real-time data review at the console and a DICOM based data flow to the reading room. Reproducibility and accuracy of positioning is also critical for single voxel MRS studies of the brain and the atlas-prescription has been used at UCSF to acquire GABA-edited single voxel MRS data as part of a smaller temporal lobe epilepsy study [32] (Figure 9). This could easily be expanded to support other neurological studies by extending the prescription library. As well as streamlining the prescription workflow, the atlas-based method is critical for obtaining consistent coverage in longitudinal MRS exams that are essential for evaluating serial changes associated with response to therapy or disease progression.

In addition to the prescription, other aspects of an MRS pipeline will vary by application and with the pulse sequence and reconstruction strategy. In some cases, product reconstruction software is sufficiently fast for single voxel analysis to be performed online, however these tools are, in many cases, still limited by their lack of support for outputting results in standard DICOM format. Additionally, not all DICOM devices (scanners, PACS) currently support the full range of DICOM SOP classes [33] required for the analysis. There is a growing body of evidence indicating that metabolic imaging augments the diagnostic value of an MR exam. This work and referenced studies demonstrate the feasibility of applying spectroscopic imaging methods in a robust and automated clinically integrated pipeline. Broader

adoption of MRS will be facilitated by the availability of multi-vendor products capable of reliably generating high-quality, quantified spectroscopic data in DICOM format for transmission to the clinical PACS in conjunction with the other imaging data from the exam so they can be easily incorporated into the clinical workflow. Future work will be aimed at improving the robustness of the workflow components, installing the packages on additional scanners and porting modules to other vendor platforms.

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