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Standardized, Open-source Processing of Hyperpolarized 13C Data

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Standardized, Open-source Processing of Hyperpolarized 13C Data

by
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Dedicated to my brother, Ishan Sinha, who is always there for me.

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Abstract

Standardized, Open-source Processing of Hyperpolarized 13C Data

Avantika Sinha

Magnetic Resonance Spectroscopic Imaging (MRSI) allows us to visualize metabolites within the body without radioactive tracers, such as those used in PET scans. Hyperpolarized MRI exploits this process by using dynamic dissolution nuclear polarization to enhance the signal of and visualize previously difficult-to-detect metabolic intermediates such as pyruvate[20]. 13C is a common hyperpolarized (HP) tracer, used for pyruvate imaging, that can help with cancer detection and tracking[6]. MRSI and HP data contain varying numbers of spatial, spectral and temporal dimensions and are typically encoded using proprietary vendor-specific file formats, which presents challenges for post-processing and analysis using standard medical imaging software. The spectral data needs to be registered with the anatomical data, and temporal dimensions represented, if necessary[9]. The Hyperpolarized MRI Technology Resource Center (HMTRC) was created for the dissemination of tools to make HP MRI more accessible, one of its aims being the development of free, open-source software (FOSS). At the University of California, San Francisco, the SIVIC (Spectroscopic Imaging, Visualization, and Computing) software package was developed to aid in this process [9]. Bruker is a vendors with proprietary data files from their newer 3T small animal scanner at UCSF that cannot be directly read into SIVIC. This lack of standardization for spectral data causes problems across research, as each research group must manually pre-process the data before analysis. In this work, we aim to streamline this workflow by introducing a function that can take as input Bruker 2dseq files from an EPSI sequence and output in a standardized DICOM MRS format. Ultimately, this provides a data pipeline that enables efficient analysis of Bruker HP data, allow for greater collaboration between research groups, and lines up with the HMTRC's aim of developing additional FOSS. As of the time of this thesis submission, the pipeline can identify the 2dseq file and write metadata from parameter maps, but cannot fully handle spectral data.

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Chapter 1

Introduction

Magnetic Resonance Spectroscopic Imaging (MRSI)

Magnetic Resonance Spectroscopy (MRS) can be very useful in both clinical and pre-clinical settings, but the data must be pre-processed. Conventional Magnetic Resonance Imaging (MRI) provides imaging data, and the workflows are well established, but the same does not exist for MRSI. A combination of magnetic gradients, RF transmit and receive coils, and a variety of standard pulse sequences (T1, T2, Gradient Echo, etc) are used to provide noninvasive images of the body's tissues with standard MRI. The dimensionality of these images varies, starting with 2-dimensional slices of slabs and evolving all the way up to 3-dimensional voxels over time.

In contrast, or as a complement, MRS can use gradients, RF coils, and different pulse sequences to obtain spectral information from a sample or a section of a patient. This data can be 1D (as in signal from an entire sample) or 2D (signal coming from a slice). With an additional (third) dimension of localization using a specialized sequence, such as PRESS, STEAM, etc., the spectra can be shown for individual voxels. The spectra can be shown as a series of individual spectra with relative concentrations, or it can be visualized as a metabolite map.

This data can be used to give at-a-glance information about the underlying tissues such as heterogeneous necrotic tumors, edema, benign tumor, etc., and help inform treatments. However there is no gold standard for reliable MRS data and no vendor support for standardized DICOM MRS format, so clinical deployment is not yet feasible. The imaging community must open-source solutions to drive MRSI to the next phase in the path to the clinic.

Hyperpolarized MRI

Hyperpolarized MRI builds upon the principles of MRS by acquiring previously inaccessible spectral information, such carbon-based metabolic data, and adding a dynamic time component to measure relative metabolism, as seen in Figure 1.1 [20]. This is accomplished with a combination of customized pulse sequences, new coils, hyperpolarized (HP) substrate injections, polarizing and dissolution hardware, and specialized data processing pipelines. The information acquired from these scans shows great promise in illuminating basic science research, pathophysiology of disease, and translation to clinical research. 13C is a common HP tracer, used for pyruvate imaging, that can help with cancer detection and tracking[6]. Another area of research is co-polarization with deuterium (2H), which increases the polarization duration of 13C, as demonstrated in a murine tumor study using [U-2H,U-13C]glucose, which showed promise as an early marker for treatment response[17, 11]. For these next steps to proceed smoothly, robust and repeatable processing tools need to be made and implemented universally.

The basic principle of hyperpolarization is low temperature and high field, but brute force polarization is technologically challenging. A more elegant and practical approach is dynamic nuclear polarization, where electron spins are polarized and then transferred to nuclear spins[3]. Dynamic Dissolution Nuclear Polarization (dDNP) has successfully been carried out in various labs and is the current method of hyperpolarization in pre-clinical and clinical studies. In this process, the substrate is typically brought down to a temperature of 1K at 3.34T, mixed with a radical of concentration of 1:1000, hit with microwaves to transfer radical polarization to the 13C nucleus, and then dissolved in solution. This solution is then injected into the subject, and a specialized pulse sequence is run. This entire process results in a 10,000-fold signal increase of endogenous 13C[20].

Carbon, which is not visible under conventional MRI, can be tracked with the use of hyperpolarized 13C nuclei by dynamic nuclear polarization. Rapid sequencing allows for the capture of useful information before the magnetization decays. Common sequences include STEAM, PRESS, and FID-CSI[3]. HP MRI has been used to study prostate tumor metabolism, gliomas, and tumor response, and HP studies can take place on relatively low field strength scanners that are already available at most institutions. The equipment for dynamic nuclear polarization would be the added investment[7, 15].

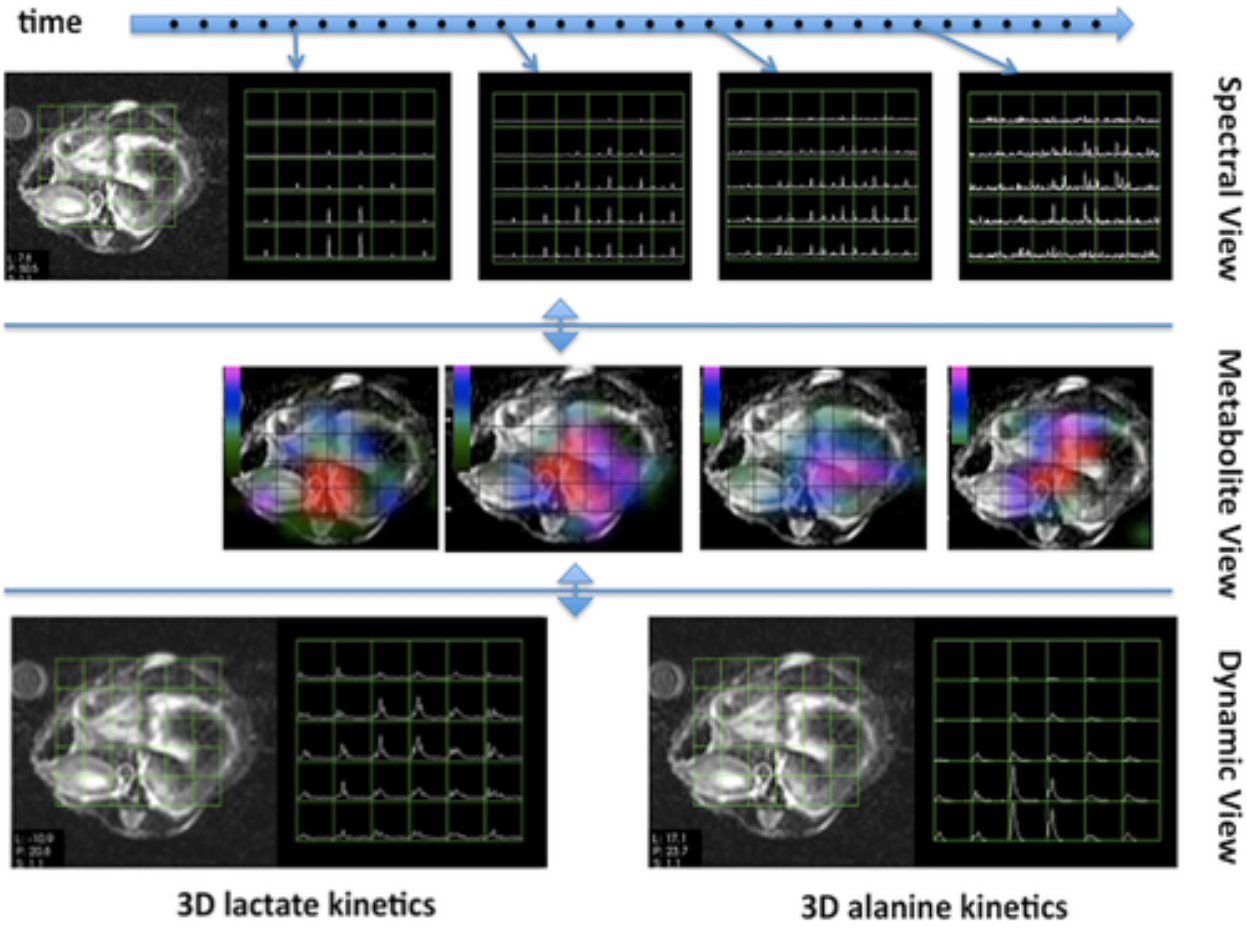


Figure 1.1: The many dimensions of hyperpolarized data: The top row of spectral view shows the dynamic time dimension of the spectrum. The middle metabolite view shows the overlaid metabolite map; different colors represent different metabolites. The dynamic view in the bottom row shows the change of single metabolites over time.[10]

Hyperpolarized MRI vs PET

Positron Emission Tomography (PET) scans, the current gold standard for cancer research, are great for assessing glucose uptake in tumor cells as a result of the Warburg effect and sequestration, but cannot be used for tracking downstream metabolite changes over time[19]. PET scans have limited viability in the brain due to the brain's overall glucose usage. PET also involves the use of radioactive probes, so there is known risk associated with repeat scans for long-term disease tracking. Currently the benefits outweigh the risks, but HP MRI offers a low risk complementary or even alternative methodology.

HP MRI vs Conventional MRI and MRS

While standard MR can image up to three spatial dimensions, HP MRI can encode these plus spectral information and a time component (see Figure 1.1[10]). Conventional MRI uses frequency for spatial encoding, while MRS and HP MRI use the frequency differences to separate metabolites and additional phase encoding gradients to localize signals. These 5D datasets, often with low SNR from a rapidly decaying signal, need to be processed differently than conventional 3D MR datasets. The tools to do so need to be made available so researchers can spend more time testing novel probes, collaborating, and analyzing results, as opposed to spending time on manipulating large sets of unformatted binary data. While many robust packages are available for visualizing standard DICOM images, these do not extend to MRS and HP MRI.

Hyperpolarized MRI predominantly focuses on 13C because it is invisible on conventional MR, there is low sensitivity in naturally abundant (1.1%) samples with MRS, and carbon is the backbone to many key metabolites. In general, higher field better resolves the peaks in MRS but can reduce the time of polarization in HP MRI. The clinically relevant field strength is 3T. T1 values of hyperpolarized probes currently investigated are 10-60 seconds, which makes them useful for tracking movement across membranes and short term metabolic reactions.

HMTRC

To further the research and progress of HP MRI, the Hyperpolarized MRI Technology Resource Center (HMTRC) was created at UCSF. The center has funding from the National Institute of Biomedical Imaging and Bioengineering to further its 3 main Technology Research & Development (TR&D) goals:

> "TR&D1 is focused on DNP polarizer and MR acquisition development and pre-clinical animal studies. TR&D2 focuses on the development of new robust and realistic pre-clinical models for HP MR studies, optimization of current HP probes & investigation of new HP probes, and the development of methods that provide appropriate correlative pathologic, biologic and other imaging data for understanding and validating HP MR findings. TR&D3 focuses on the development of a free open-source specialized data analysis platform for HP MR data reconstruction and interpretation."[14]

Standardized, Open-source Tools

The aim of this work was to develop standardized, open-source tools for processing HP MRI data. Standardized, open-source tools also support comparing data across experiments and across institutions, thus increasing the scientific power of all HP MRI experiments.

The HMTRC developed and maintains the open-source Spectroscopic Imaging Visualization and Computing (SIVIC) package[9]. This has allowed for greater internal cohesion and collaboration externally as this is a free, open source software (FOSS), and has been widely used within the HP MRI and MRSI community. It also supports the emerging DICOM MRS standards for data formats, which provides a unified format for storing spectroscopy data.

In this thesis, I specifically focused on adding functionality for standardized processing of a new acquisition method to SIVIC. The acquisition is an echo-planar spectroscopic imaging (EPSI) sequence, which provides rapid HP MRSI scanning, on a Bruker small-animal MRI scanner. For this EPSI sequence, each research group has to manually pre-process the data before analysis, so their research currently cannot scale well. I aim to streamline this workflow by introducing a function that can take as input Bruker proprietary file types from the EPSI sequence and convert them to the DICOM MRS format with SIVIC. Ultimately, this will provide a data pipeline that enables efficient analysis of Bruker HP data and expands the standardized, open-source HP MRI data processing capabilities.

Chapter 2

Related Work and Background

This work builds off prior work in developing standardized, open-source HP MRI software tools, particularly the SIVIC package. Another key requirement of this project was to conform with the DICOM standard. SIVIC, DICOM, and the Bruker EPSI acquisition are described in more detail within this chapter.

2.1 SIVIC

Spectroscopic Imaging Visualization and Computing (SIVIC) software has a user friendly Graphical User Interface (GUI) that enables simultaneous visualization of anatomical reference data alongside spectral data, so the user can select voxels or ROIs and process or quantify as necessary. Some of the tools include Fourier transforms, apodization, zero filling, kinetic modeling, and metabolite map quantification[9]. The command line tools can be used to batch process data and create pipelines. SIVIC can take as input the UCSF internal .ddf file, DICOM, and select vendor specific files, and it outputs DICOM (the gold standard in medical imaging). SIVIC can convert .ddf to the industry standard DICOM + DICOM MRS.

SIVIC has multiple classic dependencies: CMake, VTK, KWWidgets, and DCMTK. When running command line tools and building from source code, these packages need to be either manually configured, or built in a preconfigured container. Tarquin and LCModel are other popular spectroscopy quantification software packages, and can be made compatible with SIVIC. The standardized DICOM MRS output enables integration with PACS and other software packages such as Tarquin, allows for ease of use across research facilities, and

works towards the end goal of a scanner-to-PACS workflow.

One of the many attractions of SIVIC is the ability to write to the DICOM and DICOM MRS standard, which furthers the goal of "application of MRS to medical imaging studies"[9]. Most of the standard sequences and many of the spectroscopic sequences have full reading and writing support in SIVIC. The new Bruker 3T EPSI sequence is the only sequence at UCSF at the time of writing that is not fully supported. To create full internal cohesion, we are writing an adaptor function (see Fig 2.1.

Software Development

The SIVIC codebase is written in C++ and compiled using GCC Compiler on a Redhat Linux 64 system (check type -a gcc). Familiarity with these languages and MR fundamentals is a prerequisite for working with this type of project. Various implementations were explored with this project, starting with local laptop. Ultimately, I tunneled into a virtual machine (VM) and used a No VNC setup through a browser on the local machine, allowing me to use a remote Gnome desktop to run a docker container for a sub-build of svk_file_convert. I worked on a branch of the sivic Github repository, bruker_epsi. I recommend a shared code repository for collaborative debugging purposes as this may be the first time looking under the software hood for many MR researchers.

The SIVIC source code can be found on sourceforge[9], and tutorials to build can be found on the Wiki[8]. To add readers, the sub-build of interest is svk_file_convert. The first step of this application is to identify the input by passing the file through a series of readers in the ImageReaderFactory function. The ImageReaderFactory consists of several vendor-specific readers (GEPFileReader, BrukerRawMRSReader, Siemens, Philips, etc), and each reader has a CanReadFile function within it to detect the extension of the input file. Once the file is matched with its appropriate reader, it is piped to the ImageMapperFactory function. The ImageMapperFactory works the same way as the ImageReaderFactory, and is responsible for mapping out the parsed data to the DICOM Information Object Definition (IOD). The information is then passed to the appropriate writer in the ImageWriterFactory and ultimately written to a file type. The most relevant functions for the Bruker 3T EPSI sequence are the svkBrukerRawMRSReader.cc/.h, svkBrukerRawMRSMapper.cc/.h, and svkBrukerRawMRSWriter.cc/.h.

Supported File Formats*

SIVIC Supported File Formats*

Format	Read	Write
DICOM MRSpectroscopyStorage	✓	✓
DICOM MRImageStorage	✓	✓
DICOM Enhanced MRImageStorage	✓	✓
DICOM Secondary Capture		✓
DICOM Segmentation Object	✓	
DICOM Positron EmissionTomographyCurve	✓	
Bruker DICOM MRS	✓	
Bruker ser MRS	✓	
GE P-Files (9.x-26.x) **	✓	
GE .shf	✓	
GE Postage Stamp MRS	✓	
GE Signa MRI	✓	
MR Solutions MRS	In Progress	
Philips SPAR/SDAT	✓	
Siemens .rda	✓	
Siemens .IMA ****	✓	
Varian .fdf	✓	
Varian/Agilent fid ***	✓	
JPEG	✓	
TIFF	✓	
EPS+	✓	
PDF+	✓	
SVG+	✓	
Other	RequestRequest	

*Version numbers indicate future target release

**PSD specific, currently supports: probe-p, presscsi, mbrease. Please request or implement additional support.

***PSD specific, currently supports UCSF compressed sensing and 2D CSI, product CSI in development. Please request additional support.

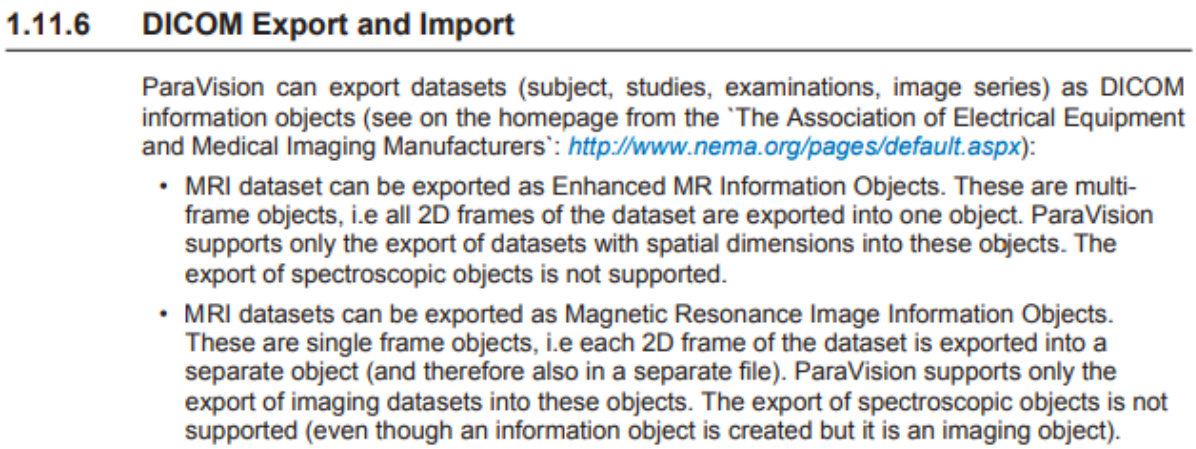
****Only supports .IMA files that represent the DICOM MRImageStorage SOP Class.

+Not distributed with binary release, but may be compiled when built from source

Figure 2.1: Current SIVIC Support includes 1) all standard DICOM medical images; 2) various GE, Philips, and Siemens proprietary file types to meet UCSF campus needs; 3) Bruker ser files[8]. The Bruker 2dseq MRS is in progress.

2.2 DICOM Standard

Digital Imaging and Communications (DICOM) is a vendor-agnostic standard used for various types of biomedical images and associated metadata, allowing for efficient communication between research centers, clinicians, picture archiving and communication system (PACS), and software packages. To accommodate the shift towards more imaging and digital records, DICOM has the options of both free-form and structured input fields to gather information in the various modules, and is designed to be extensible as diagnostic technology creates more data fields. Due to the complex nature of both medical and imaging data, a "plug and play" experience with DICOM-compliant devices and software is not feasible, though the support increases the odds of compatibility[2].



1.11.6 DICOM Export and Import

ParaVision can export datasets (subject, studies, examinations, image series) as DICOM information objects (see on the homepage from the `The Association of Electrical Equipment and Medical Imaging Manufacturers`: *http://www.nema.org/pages/default.aspx*):

- MRI dataset can be exported as Enhanced MR Information Objects. These are multi-frame objects, i.e all 2D frames of the dataset are exported into one object. ParaVision supports only the export of datasets with spatial dimensions into these objects. The export of spectroscopic objects is not supported.
- MRI datasets can be exported as Magnetic Resonance Image Information Objects. These are single frame objects, i.e each 2D frame of the dataset is exported into a separate object (and therefore also in a separate file). ParaVision supports only the export of imaging datasets into these objects. The export of spectroscopic objects is not supported (even though an information object is created but it is an imaging object).

Figure 2.2: DICOM non-Conformance. The above section is an excerpt from the Bruker ParaVision User Manual, alongside a section detailing the importance of adhering to the DICOM Medical Imaging standard. However, "the export of spectroscopic objects is not supported"[4].

DICOM MRS

DICOM has been expanded to include DICOM MRS for spectral data by including several modules. The Information Object Definition (IOD) for spectral data contains information on Pulse Sequences, Acquisition Parameters, and Volume Localization Techniques (PRESS, STEAM, etc). Specifically the modules required for a DICOM MRS are:

Mandatory MRS Modules
Multi-Frame Functional Groups Module
Multi-frame Dimension Module
Acquisition Context Module
MR Spectroscopy Module
MR Spectroscopy Pulse Sequence Module
MR Spectroscopy Data Module
SOP Common Module

The MR Spectroscopy specific modules are useful because they allow sharing of more sequence specific information across research groups and with PACS for clinicians. Currently the data is shared as screenshots or "Secondary Screen Captures" of anatomical and spectral data, so there is loss of all spectroscopy-related metadata. While an extensible DICOM standard exists, vendor support is lacking and therefore community driven solutions must be conceived.

2.3 Bruker EPSI Pulse Sequence

Fast spectral imaging and chemical shift imaging are the two main classes of pulse sequences for acquiring HP MRI data. With spectro-spatial imaging, both types of information are acquired simultaneously and quickly. With chemical shift imaging, the individual metabolites are excited and imaged, so *a priori* information on chemical shift is mandatory. Currently there is support for CSI as it is the traditional method of spectral imaging, but less support exists for EPSI and newer sequences.

The EPSI sequence used on the Bruker 3T system at UCSF is a symmetric sequence, with 2 dimensions of spatial k-space along with spectral information over time, resulting in a 4D dataset. Bruker ParaVision provides data files as well as parameter files in proprietary formats needed to interpret the data. The anatomical and spectral data are both saved as separate "2dseq" image files. These are binary files, written "sequentially, line by line, frame by frame, starting from the top left pixel of the first frame" [5]. The acquisition parameters are stored as "acqp", dataset description for visualization as "visu_pars", the reconstruction and processing parameters as "reco", and the general method information as the "method" file. These are all binary files.

The data comes in the PROCNO folder tree in a non-intuitive manner[5]. Each scan corresponds to a numbered folder. The first few scans are the localizer scans. In our example

IE/Module	DICOM Ref*	MR Image	Enhanced MR Image	MR Spectroscopy	Secondary Capture Image
Patient IE					
Patient Module	C.7.1.1	X	X	X	X
Study IE					
General Study Module	C.7.2.1	X	X	X	X
Series IE					
General Series Module	C.7.3.1	X	X	X	X
MR Series Module	C.8.13.6		X	X	
Frame of Reference IE					
Frame of Reference Module	C.7.4.1	X	X	X	
Equipment IE					
General Equipment Module	C.7.5.1	X	X	X	
Enhanced General Equipment Module	C.7.5.2		X	X	
SC Equipment Module	C.8.6.1				X
Image IE					
General Image Module	C.7.6.1	X			X
Image Plane Module	C.7.6.2	X			
Image Pixel Module	C.7.6.3	X	X		X
Multi-Frame Functional Groups Module	C.7.6.16		X		
Multi-frame Dimension Module	C.7.6.17		X		
Acquisition Context Module	C.7.6.14		X		
MR Image Module	C.8.3.1	X			
VOI LUT Module	C.11.2	X(U)			
Enhanced MR Image Module	C.8.13.1		X		
SC Image Module	C.8.6.2				X
SOP Common Module	C.12.1	X	X		X
MR Spectroscopy IE					
Multi-Frame Functional Groups Module	C.7.6.16			X	
Multi-frame Dimension Module	C.7.6.17			X	
Acquisition Context Module	C.7.6.14			X	
MR Spectroscopy Module	C.8.14.1			X	
MR Spectroscopy Pulse Sequence Module	C.8.14.2			X	
MR Spectroscopy Data Module	C.8.14.3			X	
SOP Common Module	C.12.1			X	

Figure 2.3: DICOM IOD Comparison. Each DICOM type has varied mandatory modules. The DICOM MRS modules will include both the information from a standard MR Image as well as the MR Spectroscopy information. Note that the current method of sharing, Secondary Capture Image, does not contain this information. Table from SIVIC sourceforge website[9, 8].

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dataset, the anatomical scan ends up being folder 7. Within folder 7 are the acqp, method, fid, and visu_pars files, as well as a processed data (pdata) folder. Within that enclosed pdata folder is another folder, folder 1, dedicated to magnitude data and the aforementioned image data 2dseq file. Bruker also provides reconstructed anatomical DICOMs in a separate folder. Going back up to the main PROCNO folder, we look at the other scan, folder 11, which contains the EPSI sequence. The pdata folder here contains both folders 1 and 2 – 1 for magnitude and 2 for phase. Each contains a 2dseq file. The hope is to use this phase data for phase corrections[13].

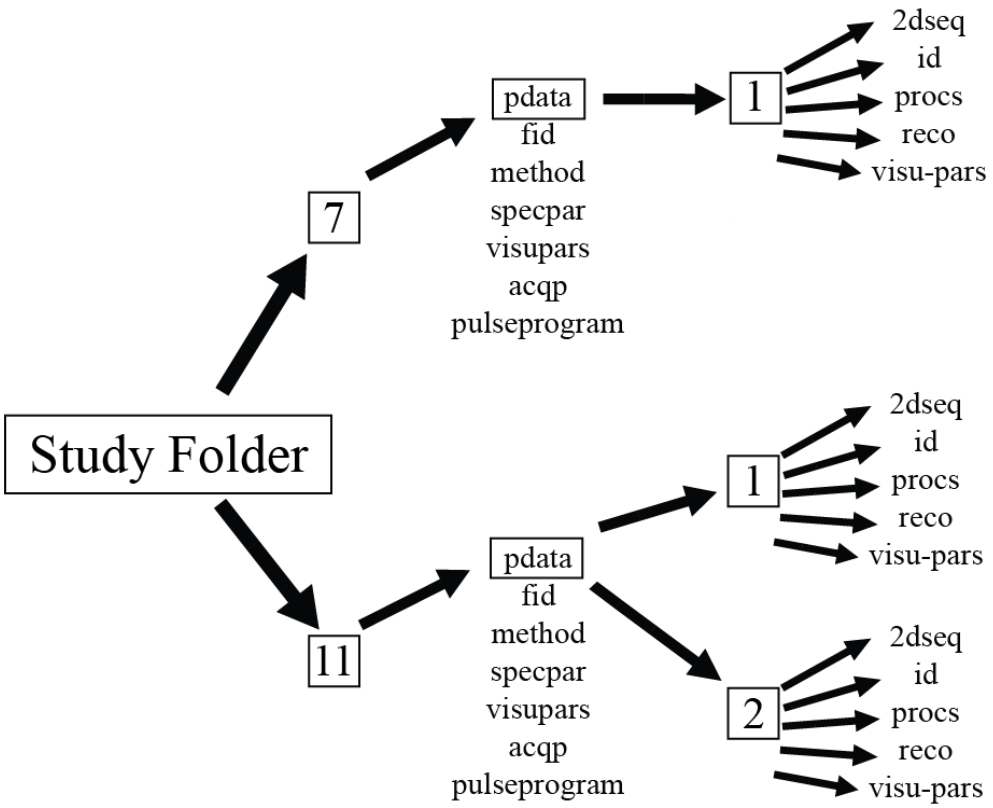

Figure 2.4: Study Folder Tree: A study from the Bruker 3T Small Animal Scanner ultimately yields an anatomical (7) folder and spectroscopic (11) folder. Each contains a processed data (pdata) folder, and the spectroscopic folder contains both phase (2) and magnitude (1) data.

The current workflow for EPSI acquisitions with 2dseq files is as follows:

- The 2dseq file is opened in MATLAB and the file is reshaped, zero-padded, and re-ordered.
- The header information is pulled and a .ddf file is created.
- This, along with the reconstructed Bruker provided anatomical DICOMs are opened in SIVIC for metabolite map creation.

Chapter 3

Open-source Software Architecture & Development

This work started with adding logic to enable SIVIC to read the 2dseq file. The method and setup are described in this chapter.

3.1 The Missing Piece

The 3T Bruker EPSI is the only sequence missing 1-click support under the SIVIC umbrella at this time. The support we are adding will be a C++ adaptor that will encompass the manual manipulation that Dr. Ronen's group has constructed, using a variety of functions in MATLAB to pre-process the data[1]. The Bruker data comes in two folders, one containing spectroscopic phase and magnitude data, and one containing reconstructed anatomical data. Bruker also provides anatomical DICOMs and these are used for this pipeline.

Briefly, magnitude and phase data must be manually brought in by running code piece-wise. The skeleton process is as follows:[1]

1. Read anatomical data: DICOM or read-one-image-ref.m
2. Read recon header
3. Read method header
4. Read 2dseq file
5. Rotate EPSI image

6. Compute ppm range
7. Create MetImages for magnitude and phase
8. Create .ddf file for SIVIC

This entire process of creating the .ddf files takes other functions that were written for this pipeline: one that opens the anatomical image, one that reads the Bruker header information, and another to write the .ddf files based on the information previously gathered[1]. This is similar to an existing process for GE postage stamp MRS, so we adapt that pipeline to include the additional phase data that Bruker scanners now capture, and then we extract complex data to create a four dimensional spectroscopic data set. Cohesion for preclinical processing pipelines will be useful for internal studies and will set the stage for later widescale dissemination.

3.2 Data Flow and Software Architecture

To enable the ImageReaderFactory to recognize the 2dseq file, an instance was added to the svkBrukerRawMRSReader. Initially a separate 2dSeqReader was created, but for the sake of simplicity it was folded into the existing Bruker reader. The CanReadFile function picks up a designated number of characters from the end of a file extension and checks it against a list of known extensions. If they match, CanReadFile identifies the input file as a known sequence and sends it downstream. Once I verified that the modified reader was able to recognize the 2dseq file, I checked that the data was being parsed. Using the svk_file_convert application, the sample Alanine 2dseq dataset as input, DICOM MRS as output, and saving the output as a .txt file, I verified that all the fields of the acqp, method, reco, and 2dseq files were being parsed correctly.

The next step was correctly mapping these parameters into the corresponding modules of the DICOM MRS file. The existing Bruker MRS Mapper had the framework, but did not have all the parameter tags to write the parsed data into the DICOM structure, because the existing Bruker set data was written into a slightly different structure than the Bruker 2dseq data. In collaboration with the sequence developer, SIVIC software developer, and the ParaVision manual, I extracted a list of parameter tags from the acqp, visu_pars, and reco files to fill out the DICOM header[5]. This process was labor-intensive because while

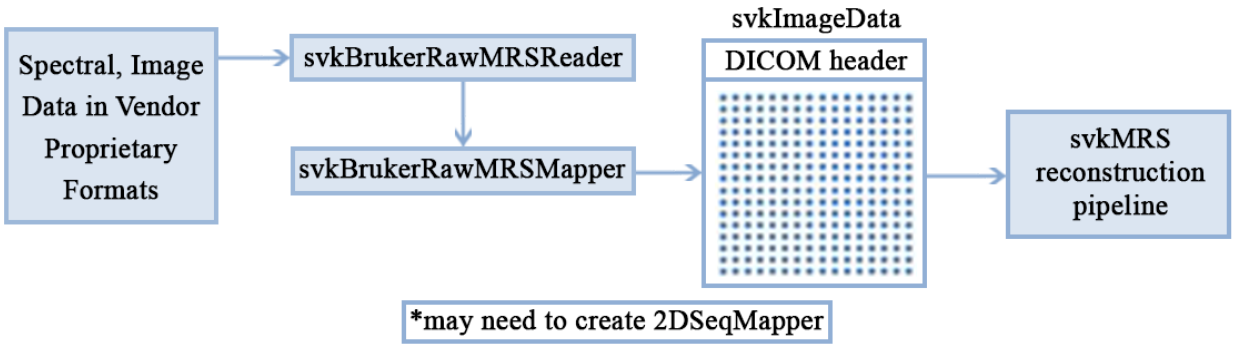

Figure 3.1: SIVIC Data Flow: The reconstructed image data (in 2dseq proprietary format, along with header files) is sent to the ImageReaderFactory where it is recognized by the svkBrukerRawMRSReader. The data is parsed and sent to the svkBrukerRawMRSMapper for mapping to the fields of the DICOM MRS structure.

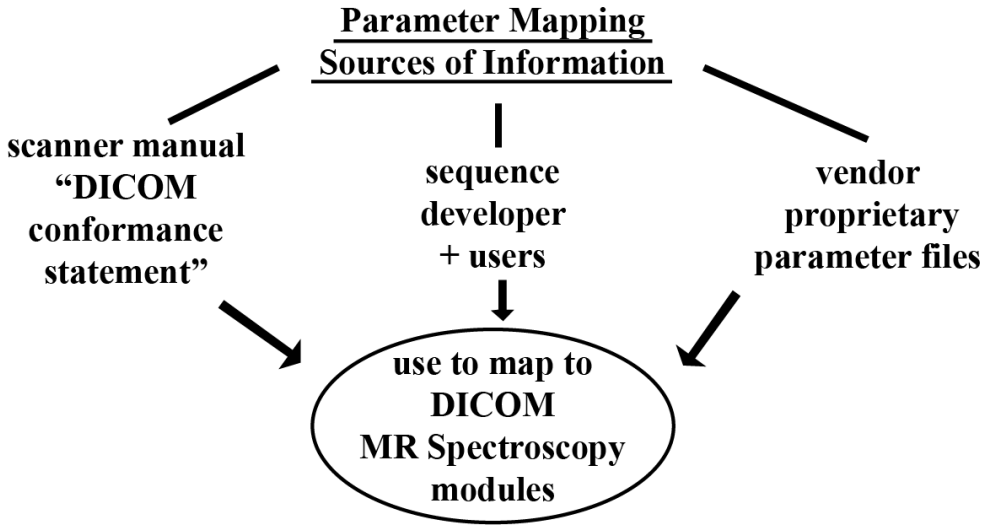

Figure 3.2: Parameter Mapping: No one source contained all the information necessary to create a DICOM MRS compliant header. Manuals, developers, and MR users had to be consulted to update the mapper.

the DICOM MRS standard exists, the support does not. The ParaVision manual contains a DICOM Conformance Statement, but it does not extend to include support for MRS. "DICOM Conformance" does not necessarily mean full conformance or compliance, just an increased likelihood[2, 4]. Additionally this did not encompass all the variables from which sequence users pull their specific information. The software developers set up the framework, but as new sequences are developed, this information needs to be inputted until vendors provide this information in a standard format. These tags were used to map our desired information to the header. As more sequences are supported, the BrukerRawMRSMapper may need to be subclassed like the GE P-File Mapper (see Fig 3.3), building upon common traits. The ImageWriterFactory may also have to be modified to complete this step[18, 16]. As of the time this thesis was submitted, the function is still in progress.

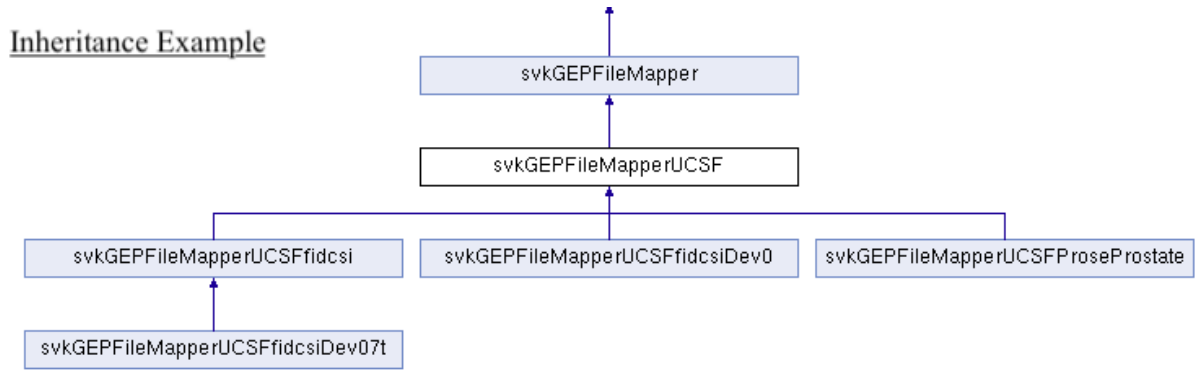

Figure 3.3: Inheritance Example: GE P-File Mapper. The GE P-File Mapper is a well-established example of inheritance that the Bruker Mapper can follow. The main BrukerRawMRSMapper is analogous to the PFileMapperUCSF and will do the heavy lifting. As additional custom sequences are created on the Bruker 3T, the mapper can be subclassed as shown here.

3.3 Development Tools

SIVIC has several dependencies and installation steps, slightly different for different operating systems. The advantage of using the SCS virtual machines is that both the dependencies and the datasets are hosted, bypassing the need to download them to a local laptop. How-

ever, more than once during development did the shared directory containing these crucial libraries move. This opened the door to trying new development approaches.

Containers

The motivation to use containers was to avoid the issues with 1) missing libraries, and 2) errors in seemingly unrelated libraries and svk_applications that prevented complete compilation and hindered progress. Containers are packaged with the code and all necessary dependencies, so they do not need to be independently sourced, and the application runs self-sufficiently and reliably. Containers are lightweight, efficient ways to work with software projects, and can usually be run on a simple laptop setup. Both Docker and Singularity containers were explored for this application, a Docker container for the sub-build of (svk_file_convert) was the final path chosen.

This was advantageous because all the dependencies (VTK, DCMTK, CMake, Tcl/Tck, KWWidgets) were reliably installed, the dataset was included in the container, and "matrix dependency hell" was sidestepped entirely. Lightweight and easy to hit the ground running, the docker container greatly sped up development because process isolation allowed me to hone in on the changes that I needed to make with the simplified UI. I was able to quickly make changes to the svkBrukerRawMRSMapper, clean rebuild the code, and debug the code to see what worked and what didn't in the command line output. The entire library of svk_file_convert can be edited and debugged this way. The docker image can be saved as a working snapshot of the application in time, and can be integrated with larger software package.

Chapter 4

Results

This work provides a solid foundation for additional pulse sequence support to be added to SIVIC. Parameter tags and mapping to DICOM IODs are explained in the chapter.

4.1 Metadata and Parameter Mapping

```
(0008,103e) LO [BRUKER EPSI Data]                    #  16, 1 SeriesDescription
(0008,1090) LO [BrukerBioSpin]                       #  14, 1 ManufacturerModelName
(0008,9206) CS [VOLUME]                              #   6, 1 VolumetricProperties
(0008,9207) CS [NONE]                                #   4, 1 VolumeBasedCalculationTechnique
(0008,9208) CS [COMPLEX]                             #   8, 1 ComplexImageComponent
(0008,9209) CS [UNKNOWN]                             #   8, 1 AcquisitionContrast
(0010,0010) PN [20190813_HP_BT142]                   #  18, 1 PatientName
(0010,0020) LO [20190813_HP_BT142]                   #  18, 1 PatientID
(0010,0030) DA [20190619]                            #   8, 1 PatientBirthDate
(0010,0040) CS [Unspecified]                         #  12, 1 PatientSex
(0018,0087) DS [3]                                   #   2, 1 MagneticFieldStrength
(0018,1000) LO [NA]                                  #   2, 1 DeviceSerialNumber
(0018,1020) LO [NA]                                  #   2, 1 SoftwareVersions
(0018,5100) CS [HeadProneP]                          #  10, 1 PatientPosition
(0018,9004) CS [RESEARCH]                            #   8, 1 ContentQualification
(0018,9052) FD 5000                                  #   8, 1 SpectralWidth
(0018,9053) FD 176.5                                 #   8, 1 ChemicalShiftReference
(0018,9054) CS [EPSI]                                #   4, 1 VolumeLocalizationTechnique
(0018,9059) CS [NO]                                  #   2, 1 Decoupling
```

Figure 4.1: In Progress Command Line Output: The DICOM MRS header output of the Alanine EPSI dataset when running the command line svk_file_convert application. Note the Patient ID, Spectral Width, Chemical Shift Reference, and Volume Localization Technique.

The updated svkBrukerRawMRSMapper is still a work in progress, but it shows great promise. The testing is done by calling the command line svk_file_convert function with the Alanine EPSI spectral 2dseq file as input, and designating a DICOM MRS (-t4) as output. Further documentation on how to call this command line will be supplied as a “cookbook”

when the function is completed, validated, and ready for internal use. I am able to bring in the basic study parameters that the sequence user accesses on a regular basis, and those relevant to the study as seen in Figure 4.1. Parameters such as spectral width, frequency offset, chemical shift reference, sequence, and manufacturer are now all stored in a DICOM MRS compliant header.

This metadata output reflects the changes made to the svkBrukerRawMRSReader and svkBrukerRawMRSMapper: recognizing the 2dseq file and mapping out the parsed parameter files to the appropriate DICOM MRS modules. Currently only the acq_p, reco, and method files are parsed into the parameter map, and the visu_pars file is needed for complete mapping of the data. When this step is completed, the metadata can be compared to the current .ddf MATLAB pipeline. I expect that this new function will result in more metadata captured than the original .ddf to DICOM pipeline, as the original MATLAB code did not contain all the parameters that will be in the final DICOM MRS.

4.2 Table of Parameters

Figure 4.2 is an example module with required parameters and corresponding tags. The first line, AcquisitionDateTime, denotes the time and date the scan was acquired. It was pulled using "VisuStudyDate", which is located in the visu_pars file (see Figure 2.4). The line item, Resonant Nucleus, gives the nucleus that is resonant at transmitter frequency[12], and was pulled using "PVM_Nucleus1Enum" from the method file. Similarly, NumberOfZeroFills was pulled using "RecoZfillFilter" from the reco file. Other fields have YES/NO options, or look for parameter tags to match pre-filled choices such as Time Domain Filtering (None, Gaussian, Lorentzian).

4.3 MRSI Data Conversion

To finish the support for the EPSI sequence, the parameter map needs to have all four parameter files parsed. Currently they can be individually parsed but not simultaneously, and the visu_pars file contains the last parameter tags to map the DICOM MRS header fields. The image data will need to be brought in from the provided Bruker anatomical DICOMs and registered with the spectral data, which may need to be flipped or rotated. These can be validated against the existing .ddf files to ensure that the spectra are in the

InitMRSpectroscopyModule();		
	AcquisitionDateTime	VisuStudyDate
	AcquisitionDuration	PVM_ScanTime
	NUC1	PVM_Nucleus1Enum
	ResonantNucleus	PVM_Nucleus1Enum
	KSpaceFiltering	NONE
	ApplicableSafetyStandardAgency	Research
	ACQ_station	ORIGIN=Bruker BioSpin MRI GmbH
	MagneticFieldStrength	Get info from TransmitFreq & Nuc
	ImageType	{ORIGINAL/PRIMARY/SPECTROSCOPY/NONE}
	VolumetricProperties	n/a
	VolumeBasedCalculationTechniqu	n/a
	ComplexImageComponent	n/a
	AcquisitionContrast	n/a
	TransmitterFrequency,	VisuAcqImagingFrequency
	SpectralWidth,	PVM_EffSWh
	SVK_FrequencyOffset,	PVM_FrqWorkOffset
	ChemicalShiftReference,	PVM_FrqWorkOffsetPpm=
	VolumeLocalizationTechnique,	EPSI {NONE, PRESS, STEAM...}
	VolumeLocalizationSequence	
	>SlabThickness	
	>SlabOrientation	
	>MidSlabPosition	
	Decoupling,	YES, NO
	TimeDomainFiltering,	NONE, GAUSSIAN, LORENTZIAN,...
	NumberOfZeroFills,	RecoZfillFilter
	BaselineCorrection,	NONE, SPLINE,..
	FrequencyCorrection,	YES, NO
	FirstOrderPhaseCorrection,	YES, NO
	WaterReferencedPhaseCorrection	YES, NO

Figure 4.2: Sample Parameters for DICOM MRS Format: A sub-sample of the collected parameter tags required for the complete DICOM MRS. The middle column is a list of the variables needed, and the right column is the corresponding parameter tag to find the value in the proprietary parameter files. These are for the MR Spectroscopy Module.

correct orientation. The final product should be able to take the Bruker 2dseq files and output a DICOM MRS.

Chapter 5

Conclusion

Starting with internal cohesion, Bruker's EPSI data is the only file type that is not supported by SIVIC or any other widely available software package. Standardization is necessary for the future of HP MRI work, and future directions are discussed in this chapter.

Summary

In summary, the MRS reader has the key shortcoming of lacking support for the Bruker 2dseq MRS file. I attempted to remediate this shortcoming by adding 2dseq reading functionality to svkBrukerRawMRSReader.cc and svkBrukerRawMRSMapper.cc. While my implementation still has not fully brought through the spectral data, it successfully wrote out the metadata of the EPSI sequence and lays the foundation for future work.

Future Work

First, in order to complete the function that I began, we need to finish bringing in the EPSI data through the svkBrukerRawMRSMapper.cc to the DICOMMRSWriter.cc, ensuring the size and orientation is correct. We will visualize with the anatomical Bruker DICOM. Then, once the pipeline is able to bring in the image data and spectral data, the test DICOM MRS output will need to be validated against the existing MATLAB pre-processing steps to ensure that the spectra correspond to the correct voxels. Additionally, the metadata will be checked to ensure the additional MR Spectroscopy specific fields are completed.

This pipeline will benefit Dr. Ronen's lab and other UCSF users of the sequence as they will be able to quickly visualize the data without spending 30 minutes per folder preprocess-

ing in MATLAB. Supporting the conversion to standard DICOM MRS with the proposed adaptor function will enable the EPSI data to be used for routine pre-clinical studies across campus.

Once we have more datapoints from UCSF usage, we can start public use to benefit the wider imaging community. The bruker_epsi branch will be merged back to the master branch and put in the next public SIVIC sourceforge release. A "cookbook" document of how to use the svk_file_convert command line function with sample data can be published for demonstration purposes.

After completion of open-sourcing the svkBrukerRawMRSReader with 2dseq reading functionality for UCSF and the public, this process can be generalized and applied to other sequences and benefit the broader community. The steps for adding support for new pulse sequences are as follows:

- Find the existing related class within the ImageReaderFactory of the svk_file_convert application.
- See if a separate reader or simply an instance needs to be created so CanReadFile can pick up your desired file type.
- Determine if the existing functions can parse your header files or if custom ones need to be written.
- Identify the appropriate file structure and header files for DICOM header creation, and map out the parameters.
- Check for an existing DICOM Conformance Statement, and with sequence developers.
- Subclass an existing mapper if possible.
- Modify DICOM Writer as necessary.
- Make sure spectra data is shaped and oriented correctly
- Move on to registering the spectral and image data

As HP MRI becomes more accessible and new sequences are pushed out, it will be important to extend processes similar to what I've described to promote uniform data processing. This will simplify and unify HP MRI research at large.

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