A Survey on Visualizing Magnetic Resonance Spectroscopy Data

M. Nunes[1] and A. Laruelo[2] and S. Ken[2] and A. Laprie[2] and K. Bühler[1]

[1]VRVis Zentrum für Virtual Reality und Visualisierung Forschungs-GmbH, Vienna, Austria
[2] Institut Claudius Regaud, Toulouse, France

Abstract
Data from Magnetic Resonance Spectroscopy Imaging (MRSI) contains signals about biomarkers concentrations, which are used to achieve new knowledge about biochemical processes. These support doctors in identifying and treat diseases as well as better defining regions of interest. In clinical environment, the lack of appropriate methods and tools to visualize MRSI has made this imaging technique information hard to interpret and include in treatment planning workflows. This paper is doing a review on how MRSI data is analysed in a medical environment as well as new approaches from the rendering and visual analytics areas. We conclude that this topic will be under the spotlight in the coming years, as current research is still facing many challenges on which the visualization community can actively contribute to.

Categories and Subject Descriptors (according to ACM CCS): J.3 [Computer Applications]: Life and Medical Sciences—Medical information systems

1. Introduction

Magnetic Resonance Spectroscopy Imaging (MRSI) is a non-invasive imaging technique that provides a spectral range of active biomarkers per sample. Each biomarker indicates a certain concentration of a specific molecule present in a sub-volume of the tissue being analysed. In medicine, this information can be used as an indicator for the presence of cancerous activity as well as other metabolic functions of *in-vivo* tissue. This technique has been primarily used to study brain and prostate cancers [VDMCW94, PTP*12].

MRSI data is usually acquired together with other imaging types, which doctors and physicians use to evaluate their patients. The combination of different images has been proved to enhance the quality of medical understanding of certain diseases and respective treatment. This helps in locating anomalous functional regions in anatomical images for better delineation of radiation target volumes and dose boosting [LCC*08].

There is a widespread interest in combining as much medical data together as possible with the purpose of achieving personalized treatments for patients [KHL12]. These range from anatomical images such as Computed Tomography (CT), Magnetic Resonance (MR) T1- and T2-weighted,

Fluid Attenuated Inversion Recovery (FLAIR), to functional images such as Positron Emission Tomography (PET), Diffusion Weighted Imaging (DWI) and functional Magnetic Resonance Imaging (fMRI). Each of these images show a fraction of the whole reality, and the combination of these different sources of information has been shown to enhance results in comparison to using each imaging technique by itself [NNW*13, JD14, MJB*14]. Alongside these imaging techniques, other types of information can support medical workflows, namely dose irradiation planning data, segmentation information of tissues and organs represented as binary masks or geometrical meshes.

MRSI brings into play highly complex information that has to be managed in a way that gives doctors enough trust to make diagnostic and treatment decisions based on it. For lack of literature gathering works on this topic for the visualization community, this paper aims to investigate current tools and methods to support the analysis and visualization of MRSI data. We include the challenges present in spectroscopy data itself, its potential advantages, existing methodologies employed in clinical settings and recent advances where the fusion and extraction of information from different types of images adds insights to medical decision making. We also give focus on works from other areas of re-
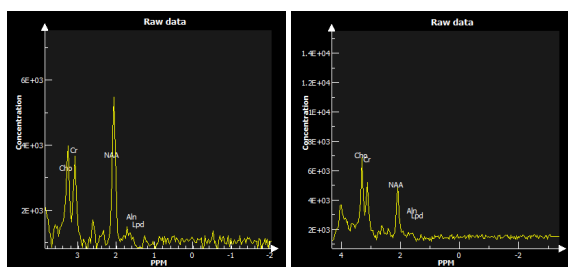
Figure 1: *Examples of MRSI spectra showing (left) healthy tissue with high NAA, intermediate choline and creatine and low lactate, compared to (right) tumour tissue with enhanced choline and lactate signals and reduced NAA.*
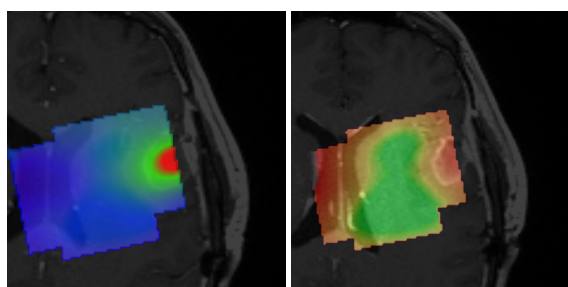
Figure 2: *Rendered images of a tumour in brain. MRI-T1 linearly fused with an interpolated coloured choline/NAA ratio map (left) and the same MRI-T1 linearly fused with an interpolated NAA biomarker coloured map (right).*

search dealing with highly complex data that can contribute to solve current challenges for better understanding and integration of MRSI data into clinical workflows.

This work is structured as follows: we introduce the specificities of MRSI data, its acquisition and pre-processing challenges, and respective technical considerations in Section 2. Here, we also discuss current use of MRSI in medical environment. In Section 3, we discuss current open challenges in the medical community to study MRSI data, and in Section 4 we list approaches from the visualization community to interpret spectroscopy data. We then proceed to Section 5 where we introduce methods and tools from other areas of research dealing with similar data that, we believe, should be taken in considerations to help solve current MRSI challenges. We finalise this work with a thorough discussion of current spectroscopy analysis and visualization together with possibilities for future research in Section 6 and concluding remarks in Section 7.

2. Magnetic Resonance Spectroscopy Workflow

MRSI is a non-invasive molecular imaging technique which provides the concentrations of multiple metabolites per spectroscopy voxel. It is used as an effective tool to find and grade malignant gliomas, assessment of treatment response and therapy monitoring [PSB*12, BJV*13]. Typically in clinical environment, its analysis and visualization is done in a voxel-by-voxel basis, limiting its use in medicine (Figure 1). This has been restricting its introduction in clinical practice, for current available tools do not provide flexibility nor speed in analysing it. The necessity of giving an in depth description of MRSI data is justified by the need of different research communities having to contribute with their own knowledge so, by joining forces, a meaningful visualization is achieved.

2.1. Raw MR Spectroscopy Data

MRSI data resolution is very low, usually having a $10mm \times 10mm \times 8mm$ voxel size. Each voxel contains a spectrum normally containing 512 or 1024 points. Each spectrum contains signals from the visible chemical compounds which depends on the nuclei, the location, the echo time and other acquisition variables. These signals are not standardized and cannot be studied by themselves [MNVN01]. Efforts have been made to significantly raise MRSI data resolution by making use of 7–Tesla scanners, but this kind of scanners are rarely found in clinical practice [SHK08]. MRSI suffers from acquisition and pre-processing challenges, which are explained in detail in section 2.2.

2.2. MRSI Data Pre-Processing

In the previous section we referred some of the technical aspects influencing the quality of MRSI data. Here, we go through the steps of MRSI data pre-processing until it reaches its final result. These steps are water subtraction, low-pass filtering, frequency-shift correction, baseline and phase correction, curve fitting in the frequency domain. The following paragraphs depict important challenges found while pre-processing this kind of data.

Voxel Quality Assurance

Between data acquisition and users being able to access MRSI metabolite information, data voxels have to be selected or discarded according to several quality parameters in order to be clinically interpretable [ÖAB*14]. These parameters include the minimum levels for signal-to-noise ratio (SNR), minimum value for spectral resolution, line shape, minimum water suppression level, absence of artifacts and lipid contamination. Also, due to bone signals interference, voxels in its vicinity are usually discarded from the final image. Furthermore, motion correction is especially relevant for the correct location and visualization/comparison of metabolic maps. Discarded voxels may contribute to an incomplete picture of the tissue under study and originate other problems such as interpolation of missing voxels, affecting treatment planning decisions.

Water Removal

After obtaining a valid spectrum from the raw data, it is then necessary to remove the water molecule signal from the raw spectrum. Water signal is the prevailing signal in the spectrum being many orders of magnitude larger comparing to the resonances of other molecules [MST*10]. Removal of the water signal is essential to access signals from other sources. Until the beginning of the decade, the majority of approaches introduced distortions to the weaker signals found in the spectrum and were not automatic. Recent works on producing automatic water signal removal that are able to correct spectral distortions in MRSI have been achieved [MST*10, SMK*11].

Data Denoising

Another key step in pre-processing MRSI data is to evaluate its SNR and improve it. SNR is very low in MRSI data for the reason that typical MR images focus on protons contained in water and fat molecules (which are highly abundant in *in-vivo* tissues), while MRSI detects all molecules signals, including the ones which exist in very low concentrations. This makes correct quantification of metabolite concentration very challenging. Several techniques have been introduced to improve the quality of SNR, but often compromising the spectral data or introducing constraints which bias MRSI data interpretation. Recent studies seem to overcome this issue by being able to maintain spatial-spectral dimensions [NHDL10, LCB*13] by exploiting the spectral-spatial properties of the MRSI signals in a less constrained way. Increasing the SNR of MRSI data is still an open challenge which greatly influences spectral concentration values and respective understanding of this data.

Quantification

Correct quantification of metabolites is a major step in obtaining meaningful values from MRSI data, as without it, it becomes impossible to construct classification images from its multivariate analysis [PSS*07]. In order to obtain accurate estimates of metabolic concentrations from spectra peaks, quantification has to be done over it. Independently from quantification methods, results are always influenced by the quality of the MRSI signals obtained from acquisition and previous pre-processing steps.

Quantification presents several challenges including lineshape distortion estimation, baseline estimation and inclusion of spatial constraints. A wide range of methods and supporting software tools were developed to minimize these issues, namely, AQSES [PSS*07], AMARES [VvdBVH97], LCModel [Pro93], MIDAS [MDA*06], TARQUIN [RWPA06] and VAPRO [GP03].

Classification

Non-invasive techniques for diagnostic such as MRSI can contribute to better discrimination between healthy and tumour tissues, and between different types of tumours [BJV*13]. Having an understanding of the relations existing among metabolites concentrations and its ratios is imperative to improve diagnostic and treatment of patients. Due to issues related from acquisition and pre-processing of its data, correct classification becomes an hazardous task. Classifying voxels can be subdivided into two cases: extracting information from MRSI data alone and the fusion of different images with spectroscopy data.

In the first case, the objective of fusing and comparing biomarkers can give origin to more interesting information than the original data. A broad range of methods has been investigated to better support decision making for MRSI [VJSRA08, AVR09, AVR12, LSC*13] and attain better classifications through analysis of concentrations of metabolites and its ratios. After classification, tissues or areas of interest can be visually depicted, improving the accuracy of diagnosis [LPDL*05]. Colour maps of ratios or concentration values of metabolites as seen in Figure 2 are an example of this.

For the second case, by combining spectral data with multimodal data from other images, such as CT, MR and PET images, it is possible to boost the meaningfulness of the final classification. This results in better voxel and tissue signatures from where more information can be extracted, for example, to find patterns; ultimately culminating in the long desired individualization of diagnostic and treatment of patients [AAB*14].

2.3. Clinical Use of MR Spectroscopy Pre-Processed Data

Combining MRSI spectral data is already a fact and grants doctors the opportunity to classify MRSI voxels according to these values. Depending on the case, different relationships between metabolites are taken into account to evaluate characteristics of tissue and differentiate tissue types. These characteristics can be more or less complicated, depending on the quantity and quality of available information, as stated in Section 2.2.

A recent clinical trial gathering CT, MRI and MRSI data [KVF*13] was performed with the objective of integrating MRSI data into the radiotherapy treatment planning system. By using the threshold equal or higher than 2 of the choline/NAA ratio, it was possible to better segment high activity tumour tissue. Several software tools and scripts were used to extract segmentations depicting this ratio value per slice. These segmentations were then fused with MR images and included in the treatment plan. The new biological volume was later targeted with a radiation boost. This work successfully confirms that fusing information from various sources has the power to enhance treatment results, despite the complexity of integrating MRSI.

Meanwhile in prostate cancer, the (choline + crea-

tine)/citrate and (choline + creatine + polyamine)/citrate ratios were used [WWG*10, CPL*11] to study the correlation between these values and cell proliferative activity for prostate cancer obtained through biopsy. In general, ratios were found to correlate, indicating the existence of several different relationships among metabolites that can be put together to better classify voxels. The inflexibility of used tools to generate any kind of desired ratio limits the range of variables to study. While advances in understanding certain relationships are being done, this limitation makes the discovery of other relationships a long process because of the time and effort needed for extraction and fusion of metabolic maps. Also, tools for running statistics in these studies are not specially designed for this kind of multivariate data.

Comparison and combination of FDG-PET and MRSI data from pediatric brain tumours [HSSP*12] showed low agreement when detecting tumour location. In this paper, FLAIR was used as common anatomical reference for both FDG-PET and MRSI datasets. Only the maximum choline/NAA ratio value was used, limiting the quality of the voxel-wise signatures. A neuroradiologist was asked to select the brightest abnormal voxel from the FDG-PET dataset. This location was then compared to the location of the maximum choline/NAA ratio value to look for agreement. One remarkable difference was that MRSI was able to show activity in tumours that appeared inactive in FDG-PET data. Through a different approach to this data, and by using new methods of visualization, it could be possible to bring more understanding about the behaviour of FDG-PET by comparing its concentrations to MRSI data, thus bringing more awareness about tumour tissue behaviour. The addition of other ratios could have shown more interesting relations between FDG-PET and MRSI.

DWI, MRSI and PET imaging were used to monitor tumour response in mice to a drug [KMK*13]. By comparing results from the different images before and after treatment, changes were detected in some cases and were in line indicating anti-proliferation of tumour cells when combining the drug with radiotherapy. In this study, there was no fusion of values from separate images, but assessment of distinct features helped creating a better picture of the underlying behaviour of the tumour. Fusing such information could support the creation of accurate voxel signatures to be used by machine learning algorithms for automatic cancer detection.

Scatter plots were used to compare NAA/creatine, choline/creatine and choline/NAA ratios to better understand relapsing of patients with gliomas [RDK*13]. After ratios were calculated and registered, they were plotted and then coloured by region membership (Figure 3). This work showed that incorporating new ratio relationships helped better defining regions of high tumour activity and consequent relapse, indicating the clear need of the visualization community to contribute to this clinical matter.

Approaches to integrate MRSI in clinical workflow have
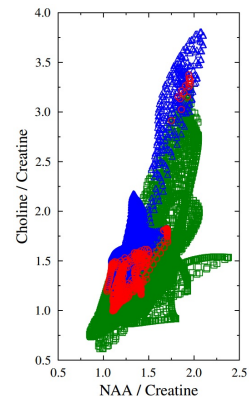
Figure 3: *Scatter plot relating two metabolite ratios. Coloured data points represent different tissue regions [RDK*13].*
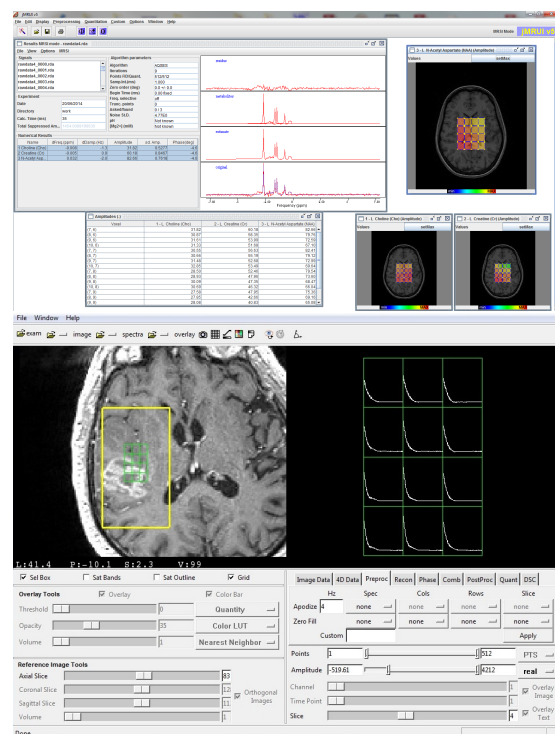
Figure 4: *Top: Screen shot of jMRUI software depicting voxels histograms, three windows displaying an anatomical image overlaid by a colour maps of metabolites' concentrations. Bottom: Screen shot of SIVIC software depicting a slice view containing MR T1-Gadolinium and MRSI data on the left window. On the right window, histograms from selected MRSI voxels are shown. Bottom half shows the controls to pre-process the raw MRSI data.*

been recently made through the development of software tools. One of these tools is MIDAS [MDA*06] which pre-processes, analyses and visualizes MRSI data. It is composed of a number of modules that can be executed without any user intervention, in a predefined sequence. Visualization options of MIDAS include visualization of metabolite maps, anatomic images such as MR-T1 or -T2 and histograms of voxels. Visualization options are rather limited, as no relation between metabolites can be viewed nor generated, and no colour map can be generated.

Another tool used in medical practice is jMRUI [SCA*09]. This tool offers a list of pre-processing and quantification algorithms, together with conversion routines fro data files, estimation of spectral parameters and signal simulators for metabolites. jMRUI is a plugin based software that allows users to add their own algorithms and methods. The java-based GUI allows multiple slice-view windows with one anatomical image with an overlaid metabolic, error or ratio maps. It is also possible to visualize multiple histograms from MRSI voxels (Figure 4 Top). However, different visualizations of data such as scatter plots or bar charts to analyse values in a statistical perspective are not included.

More recently, SIVIC [CON13] was introduced in medical practice in order to pre-process MRSI raw data into DICOM format of 3D metabolite maps so other software tools could use these maps. It also provides visualization of MRSI data together with anatomical images. SIVIC fits in different workflows, depending on the needs of the hospital, to allow MRSI data to be managed by conventional PACS solutions. Metabolites ratio maps can only be calculated in a separate software that is able to load metabolite maps and fuse them in a meaningful way. No numerical or statistical information can be assessed through SIVIC. Figure 4 Bottom depicts how medical staff visualizes MRSI data through SIVIC. Other tools used in hospitals and clinics present similar ways for visualizing MRSI.

3. Open Challenges in Clinical Environment

Nowadays, the analysis and visualization of MRSI data is inflexible and limited. Data is visualized directly through histograms for each voxel per slice depicting concentrations of metabolites, or through the rendering of slices containing colour maps of ratios or concentrations of selected metabolites. Furthermore, the rendering of colour maps is fixed and information is not correctly delivered as maximum values are calculated per slice and not per total values present in the 3D image. Adding to this, the extraction of any kind of relationship between metabolites is practically nonexistent and fusion with other datasets is limited to accompanying MR or CT images, through a rendering of overlaid images. Existing challenges in clinical environment include:

- Acquisition and pre-processing of MRSI highly influ-

ences the quality and quantity of information available to doctors.
- MRSI is not yet a DICOM format image, limiting its use by current software tools.
- Metabolic data is not easily accessed or visualized.
- Selecting and relating any given number of metabolites is missing from commercial software tools.
- The derivation of new values from acquired images and metabolites requires users to go through long and complex workflows.
- Extraction of segmentations of tissues or regions of interests is still accomplished by a tiresome slice-by-slice process of interpolation of MRSI data followed by manual segmentation and validation.
- Support for efficient multimodal and personalized analysis of data has never been delivered to clinical practice.

The current challenges doctors face limit the understanding of individual patient diagnosis and the respective best treatment approach. Lastly, MRSI data analysis is far from being integrated in a fast workflow for medical planning treatments, despite the tools and cases depicted in this section.

4. Advanced Tools for Visualization of MR Spectroscopy

The classification step, reported in Section 2.2, can also be approached using other paradigms than voxel-by-voxel analysis of histograms or overlaying colour maps of metabolites. Visual analytic tools have the power to boost the understanding of high dimensional data. Also, alternate visualisations and fusion of more images can give better support for medical decision making by enhancing the signatures of voxels and tissues. Studies have been done relating concentrations of MRSI metabolites findings with other medical data, broadening the understanding between anatomical and functional information. In this section, we decided to bring in knowledge from the visualization community which approaches to MRSI data visualization from a technical point of view, which is usually not made available to the medical community.

Presently, analysing multivariate scientific data can be done via visualization systems that can easily "show" the relation between its values. Visual Analytics (VA) tools [MFGH08, AA13] depict values and variables in different kinds of linked views which allow analysing data by decomposing the complexity of datasets into charts, parallel coordinates (PC), histograms and scatter. Another popular way to visualize data is to produce a multitude of coloured images, granting the opportunity for visual inspection of data. Many rendering and fusion algorithms have been studied and combined to deliver the best possible meaningful image to users.

Three studies by Feng et al. on visualization of MRSI data
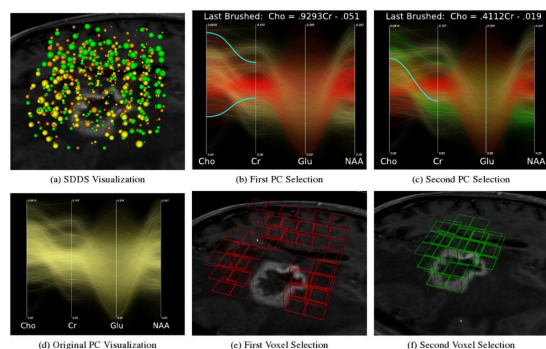
Figure 5: *Left: a 3D glyph visualization of plotted data in PC. Center: A linear brushing that selects MRSI voxels outside the tumour region. Right: A second brushing selecting MRSI voxels inside the tumour region (Image courtesy of Lester Kwock).*

allowed an approach to this data which combined rendering of anatomical slices and statistical inspection of metabolite values. Firstly, rendered glyphs depicting concentrations of metabolites through Scaled Data-Driven Spheres (SDDS) technique allowed visual value estimation and the identification of metabolites relationships and raw values [FLKT09]. Later, plotting metabolite concentration values into PC views and using a linear function brushing helped identifying linear relationships between pairs of variables. The addition of a slice rendering system to visualize cubes of selected MRSI voxels together with anatomical images and glyph rendering brought light to correlations between certain metabolites [FKLI10a]. Figure 5 depicts the visualization options of this work: 3D rendering of multivariate dataset, PC and slice rendering. All views are connected and brushing the PC results in updates in the rendered images. In a more recent work by the same authors [FKLI10b], scatter plots were included to enhance the analysis of MRSI data. In these three works, only raw values of metabolite concentration were used, however, these values are not standardized and can only be meaningfully used as ratios. Furthermore, the creation of complex voxel signatures or generation of new values for better understanding of tissue characteristics were not addressed.

Fusion of MR T2-weighted, DTI and MRSI resulted in a visualization of prostate cancer data [TVKM11]. In this work, difference maps generated from these multi-parametric datasets supported the visualization and creation of segmentations for treatment related changes. This approach demonstrated that fusing different imaging data is more efficient in detecting changes in tissues between pre- and post-radiotherapy comparing to taking each image individually. Choline and creatine biomarkers were used from MRSI spectral data ignoring other metabolites concentrations. This work only contributed with a visual multiplanar

reconstruction, leaving out other approaches to data exploration, like 3D rendering or VA tools, showing inadequacy in contributing to the discovery of new relations between MRSI data and other images.

A pure rendering work of MRI images for prostate cancer was able to deliver fusion of three imaging techniques [MK11]. MR T1, T2 and MRSI were used in this work. Through thresholds of these images, a score volume containing three values per voxel was built. Ratios of choline, creatine and citrate from MRSI data were used. Generated images could be seen in 3D rendering and 2D orthogonal views depicting prostate, its surrounding anatomy and indications for tumour and haemorrhage location within the gland.

This section clearly points in the direction of the necessity of developing complete tools for better analysing MRSI and include it in clinical workflows. The need for including all other accompanying datasets has also to be taken into account as rendering of so much information into 2D or 3D images may result in clutter of information, slow rendering speeds and the need for hardware that is not usually available in common hospitals or clinics. With this in mind, and taking recent works stated in this section, important challenges for MRSI visualization comprise:

- Limited knowledge of MRSI data.
- Lack of on-the-fly generation of complex relationships out of metabolic values.
- Visualization of data in statistical views and rendering of images has been proven useful but is rarely found together.
- Rendering of MRSI data is still an open challenge with some approaches returning reasonable information.
- The combination and fusion of MRSI and other image data is still in need research.

5. Studies on Multivariate and Multimodal Images

Datasets containing more than one element per sample have been a reality for many years, however, many challenges are yet to be addressed. The understanding of the data itself is one of these challenges, but also its analysis and visualization. Approaches to these challenges resulted in methods that allow data to be seen in numerical and statistical views [ODH*07, MFGH08] and rendering of multivariate images [KKSS13, ZH13] supporting further investigation over the data.

The work by Glaßer et al. [GPTP10] proposes a VA approach to characterize and correctly localize malignant tissues in breast cancer with Dynamic Contrast-Enhanced MRI. This type of data, similarly to MRSI, needs several pre-processing steps of analysis as, for each voxel, a time-intensity curve depicts the absorption and washout times for contrast agents. By finding similarities among voxels via 4D feature vectors, tumour regions get subdivided. Linked

views and rendering of the MR image with generated glyphs and maps support the analysis of the data. The objective of this work was to avoid manual segmentations and grant a faster way to evaluate suspicious tumour. No other medical data was used in this work and only one dataset was used per case, limiting the classification of voxels.

In another work [AFK*14], tasks for global material composition analysis, local material composition analysis, and analysis of unknown and foreign materials were formulated. A tool for analysis and visualization of CT and spectral data allowed interactive exploration of data through a multitude of linked views and volume rendering, allowing the execution of those tasks. Evaluation feedback from users pointed out the general usefulness of such a system and, more specifically, the use of glyphs pie–charts for a faster understanding of the composition of each voxel. Combination of spectral values was not present in this work, however such an extension would present itself highly useful for the analysis of MRSI data.

Model-based image segmentation supported by VA [VLBK*13] gave more detailed information regarding correspondence between data and model results. In order to segment organs in medical images, an interactive VA tool with linked views was implemented, incorporating rendering of 3D meshes obtained from expert segmentations. Model-based image segmentation stages were adapted from automatic algorithms and standardized methods into interactive steps allowing flexible change of parameters for each of the steps, giving the opportunity to evaluate and adapt parameters as needed according to visual or statistical inspection of obtained results.

Qualitative analysis of multivariate datasets using 3D visualizations by applying noise-based volume rendering assessed the capacity of users to estimate the values of two variables within a voxel [KKSS13]. 3D datasets of weather containing daily mean air temperature and specific humidity fields were used to test this method and compare it to other three well known rendering techniques: rendering of single variables with switching, mixture of values through alpha-blending and isosurfaces rendering. Results showed a significantly lower error for reading data values from generated images through this new technique comparing to the other ones.

A survey on visualization of multivariate data for medical applications gathered interesting approaches to the problem of perception via glyph rendering [ROP11]. Although MRSI was not referred, similar data was used in this study and a guideline for future applications on visualizing multivariate data was achieved.

To predict treatment response and patient outcome, a quantitative fusion of multi-scale and multi-modal data was made [MAB*11] including mass spectrometry data, which is relatively similar to MRSI data. Image features, mass spectrometry spectral data and graph-based features were combined to classify tumour grades in Gleason scale. Results show that classification is correctly achieved and that the combination of VA tools and rendering techniques highly influence such results.

Visual Analytics tools allow a change of paradigm in evaluating multivariate information. Plotting data in connected views and the ability to select specific values or patterns enhance the understanding of relations between a great number of variables. MRSI metabolite concentrations values can be easily plotted as long as the pre-processed data can be read into these tools. Calculating ratios of metabolites such as the choline/NAA or any other necessary value should be easily achieved and later plotted in such views. Also, new rendering and fusion algorithms could enhance the visualization of MRSI data in a more meaningful way, which doctors can easily assess its location in relation to anatomical images. As it has been shown in mentioned works, the combination of these two methods (rendering of images and VA) can greatly enhance medical decision making resulting in better prospects for the treatment of patients.

6. Discussion

MRSI utilization in medical fields has positively impacted patients diagnosis and follow-up studies, representing a meaningful modality to consider for treatment. However, the individualization of treatment with MRSI data is still far from being a reality since many challenges are yet to be addressed. Acquisition and pre-processing of MRSI do not yield total certainty of metabolic concentrations due to low SNR, low image resolution and fitting algorithms. Furthermore, tools for classifying MRSI metabolites are far from being flexible both in analysis and visualization of this data. Recent works stated in the previous sections pushed the integration of VA tools into clinical research to help integrate MRSI in treatment workflows.

Paper	IR	MVIR	VG	SP	PC	H
[MK11]	✓	✓				
[KKSS13]	✓	✓				
[RDK*13]	✓		✓	✓		✓
[CON13]	✓					✓
[MFGH08]				✓	✓	✓
[FKLI10b]	✓			✓	✓	
[AFK*14]	✓	✓		✓	✓	✓
[VLBK*13]	✓			✓	✓	✓

Table 1: *Summary of most important works in respect to visualization options: image rendering (IR), multivariate image rendering (MVIR), value generation (VG), scatter plots (SP), parallel coordinates (PC) and histograms (H).*

Challenges presented in Section 3 clearly show how much is missing to allow the integration of MRSI in common medical practice. The lack of powerful software tools enabling

fast and easy access to metabolite data and generation of any combination of metabolites values narrows the extraction of knowledge about relations of metabolites ratios. In some clinical situations, datasets from different modalities are still separately compared leaving doctors to achieve decisions by mentally fusing or extracting information. In addition to this, studies performed over MRSI rarely take in consideration more than one or two ratios. On the other hand, the visualization community has been active in the field of analysis and visualization of multivariate datasets. As reported in Section 4, some challenges addressed in different areas than spectroscopy have many similarities to the challenges found in the medical area. Linked views, the addition or combination of other types of views over the data, or new rendering algorithms can bring novelty to the general understanding and application of MRSI in medical environment. Table 1 summarizes the works mentioned by this survey, which the authors consider that should be taken in consideration for future development of analysis and visualization tools for MRSI data.

Allowing a flexible fusion of any given MRSI metabolite may contribute to a better understanding of both healthy and tumour tissues properties. Furthermore, fusing this knowledge to other medical images should greatly enhance the study of anatomy and functionality of tissues [PSB*12]. Doctors expect that, as more knowledge is gathered from different imaging techniques, the more personalized treatment can be achieved and automatic cancer detection algorithms can become a reality. For possible automatic cancer detection, which can be deeply influenced by better knowledge on tissue and tumour signatures, it would be ideal to have the maximum information possible per patient. Alas, gathering all imaging types and other medical data together in the same software package has not been achieved yet. Up to now, different software solutions try to solve the challenges which contain only a sub-set of all data. Even the fusion and visualization of medical data for a low number of datasets is still under research [CTHN08, JD14]. Clearly, there is room for development of frameworks that are able to support multimodal fusion and visualization of scalar, temporal and multivariate medical datasets, as it has been desired by the medical community [ZS11, PSB*12]. With this in mind, we list here open challenges that will improve the analysis, visualization and integration of MRSI data in clinical workflows:

- Development of a tool gathering multiple linked views, generation of ratios, selection of values and rendering of multimodal images.
- Immediate visualization of selected values both in rendering windows as in linked views.
- Interactive creation of segmentations representing selected voxels or signatures.
- Extraction of complex voxel signatures by adding other types of images.
- Pattern analysis and automatic cancer detection algorithms designed from newly obtained signatures.

Finally, another issue detected during this research work is that there is a range of words used for describing the type of imaging containing spectral data. Depending on the scientific area in question, a dataset containing spectral information per data point was labelled as "multivariate", "high dimensional","multi dimensional array", among others. The authors believe a normalization of these synonyms would facilitate the communication of similar issues and respective research across different fields of study.

7. Conclusion

In this article, we call for the attention that MRSI data, which is used in clinical environment, is starting to be included in studies with tools from the visualization community. The combination of MRSI with other medical data such as anatomical or functional information already contribute for better treatment personalization and better understanding of tumour behaviour. However such combination of data gives origins to challenges that have not been addressed yet. MRSI data presents itself as a complex modality since its acquisition and pre-processing steps are still shrouded by many challenges. Also, MRSI metabolites information is still under study, slowly contributing for better understanding of metabolites relationships and tissue functional characteristics. Lastly, the lack of proper tools is setting up barriers to MRSI inclusion in general clinical treatment workflows.

We presented a series of recent works focusing in analysing and visualizing MRSI data and combing it with information from other sources through rendering and VA tools. Current tools and methods already solve some of the presented issues, and have contributed to expand the understanding of voxel and tissue signatures, however, there are many open challenges to be solved in order to properly access the full potential that MRSI has to offer. Moreover, new spectral modalities are being developed, which will make spectroscopy data available in other scientific settings. On the grounds that MRSI and multimodal fusion are fundamental in several scientific research areas, new developments will only come about by close and committed interactions between visualization scientist, imaging technicians and clinicians.

Acknowledgments

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