CLARET: A Tool for Fully Automated Evaluation of MRSI with Pattern Recognition Methods

B. M. Kelm[1], B. H. Menze[1], T. Neff[2],
C. M. Zechmann[2] and F. A. Hamprecht[1]

[1]Interdisciplinary Center for Scientific Computing (IWR),
University of Heidelberg, 69120 Heidelberg
[2]German Cancer Research Center (dkfz), 69120 Heidelberg
Email: fred.hamprecht@iwr.uni-heidelberg.de

Abstract. Magnetic Resonance Spectroscopic Imaging (MRSI) measures relative concentrations of metabolites *in vivo* and can thus be used for the diagnosis of certain tumors.
We introduce the program CLARET that makes MRSI accessible for clinical routine use. Instead of embarking on an error-prone quantification of metabolites that requires manual checking of the results in many voxels, the program uses pattern recognition methods to directly compute tumor probability maps. Furthermore, non-evaluable signals are identified and masked out. The user can thus save time and concentrate on suspicious regions only.

1 Introduction

With magnetic resonance spectroscopic imaging (MRSI), specific metabolites can be detected and spectrally resolved *in vivo*. Since the concentration ratios of certain metabolites change characteristically in pathologic tissue, MRSI is in principle very well suited for the detection and localization of tumors. A major challenge in MRSI, however, lies in the postprocessing and evaluation of the acquired spectral volumes.

In general, two approaches to the evaluation of MRSI have been considered in the literature. The first approach initially performs a quantification based on physical signal models [1]. Algortihms such as HLSVD, VARPRO, AMARES, LCModel, QUEST, etc. allow to incorporate different kinds of prior knowledge in order to obtain robustness towards noise. Such or similar algorithms are often provided by commerical vendors (e.g. Siemens – PRISMA, Philips – LCModel) and are also available in the popular Java solution jMRUI. However, in order to avoid wrong diagnoses because of erroneous quantification results, one has to manually verify the line fit in every single voxel. Merely because of time constraints, this approach is not viable in clinical routine, in particular at higher spatial resolutions. Furthermore, manual evaluation of MRSI data requires tissue specific domain knowledge not shared by all radiologists. Finally, such a manual evaluation lacks objectivity and reproducibility.

The second approach to the evaluation of MRSI data applies methods from machine learning and pattern recognition [2]. From this point of view, quantification is only one way of feature extraction and dimension reduction. Instead of using error-prone quantification, pattern recognition methods can as well use any other, possibly more robust, representation of the spectral information. Several techniques have been proposed in the literature among which are e.g. artificial neural networks, support vector machines, subspace methods, generalized linear models, etc. Recent results [3, 4] show that pattern recognition methods which do not rely on an explicit quantification step can be superior for a given diagnostic problem. Furthermore, pattern recognition also allows to identify spectra which are dominated by artifacts or which are just too noisy to be processed reliably [5].

Despite their considerable potential, pattern recognition methods for the evaluation of MRSI are not applied in clinical routine. One important reason is that commercial vendors do not offer or support such evaluation strategies yet. Another reason is that no software tools are available which offer pattern recognition methods for the evaluation of MRSI in a user-friendly way.

In this paper we introduce the CLARET tool (*C*SI-based *L*ocalization *A*nd *R*obust *E*stimation of *T*umor probability) for the diagnostic evaluation of MRSI data. CLARET implements powerful pattern recognition methods for an automatic evaluation of MRSI volumes. Furthermore, it provides convenient tools and a user-friendly interface for time-efficient analyses.

2 Design Principles and Use Cases

The evaluation of MRSI volumes with CLARET is designed for utmost user friendliness. After selecting an MRSI volume and a suitable MR image volume (usually T_2-weighted) from the DICOM data set, CLARET can be initiated to evaluate either individual slices or the whole loaded volume at once. The results are displayed in transparent probability maps superposed onto slices through the MRI volume (Fig. 1). One can easily switch between tumor probability estimates and their 2σ confidence intervals. In addition, voxels which cannot be evaluated are masked out. In the subsequent diagnosis the user can therefore concentrate only on regions marked suspicious in the probability map. In case of doubt, the original spectral signal is easily accessible and conspicuities in the T_2-image can also be scrutinized. Finally the extracted probability map can be stored in a file together with the analyzed MRI/MRSI volumes for later reference or it can be exported for use in the radiation planning software VIRTUOS [6].

CLARET has explicitly been designed for the application of pattern recognition methods. Therefore, it can also be used for the construction of training data sets. The automatic display of the respective spectral signals together with fitted model spectra and quantification results upon selection of an MRSI voxel allow for a semi-manual evaluation of the spectral data. The results from such a voxel-wise evaluation can easily be entered per mouse click in the probability map and stored as training data set. Since manual labels can also be entered

Table 1. Distribution of labels in the prostate data set (76 slices from 24 patients).

quality \ class	healthy	undecided	tumor	total
non-evaluable	–	–	–	15268
poor	721	437	284	1442
good	1665	629	452	2746
total	2386	1066	736	19456

after an automatic evaluation CLARET is also suitable for the correction of classification errors and is ready for active learning.

3 Experimental Results

Spectral recordings from an ongoing clinical prostate MRSI study (IMAPS, [7]) from 24 patients with $16 \times 16 \times 16$ voxels and 512 spectral channels have been included in the assessment. The data has been acquired on a common MR scanner (MAGNETOM Symphony, SIEMENS Medical Systems, Erlangen) with endorectal coil. Altogether 76 MRSI slices have been labeled with CLARET with respect to signal quality and diagnostic classification (cf. Table 1). In this way it was possible to label about 20,000 voxels in a relatively short amount of time and to store them as training data set in a machine-readable format.

The analysis of the obtained data has shown that pattern recognition methods which do not employ an explicit quantification step for feature extraction can yield better performance. For the discrimination between tumorous and healthy tissue all considered pattern recognition methods reached a median cross-validated area under ROC (receiver operator characteristic) of at least .995 and therefore performed at least as good as the best quantification approaches (cf. Fig. 2, left). The right part of Figure 2 illustrates the class separation that can be obtained for the example of a binomial PLS (partial least squares, "binom PLS (m)").

The noise classifier discriminates evaluable from non-evaluable spectra with an estimated out-of-bag error of 4.9%. With the current choice of pulse sequence and field of view, approximately three quarters of the MRSI voxels have to be discarded by the noise classifier as they are either heavily distorted by artifacts or contain noise only.

4 Discussion

For the first time a software tool is available which generates pathophysiologic probability maps from MRSI data fully automatically. CLARET is currently employed in a prostate study at the German cancer research center Heidelberg (dkfz). The graphical user interface and integrated workflow allow for an efficient evaluation of MRSI. Direct import of DICOM data from the MR scanner and the subsequent fully automatic evaluation by means of powerful pattern recognition

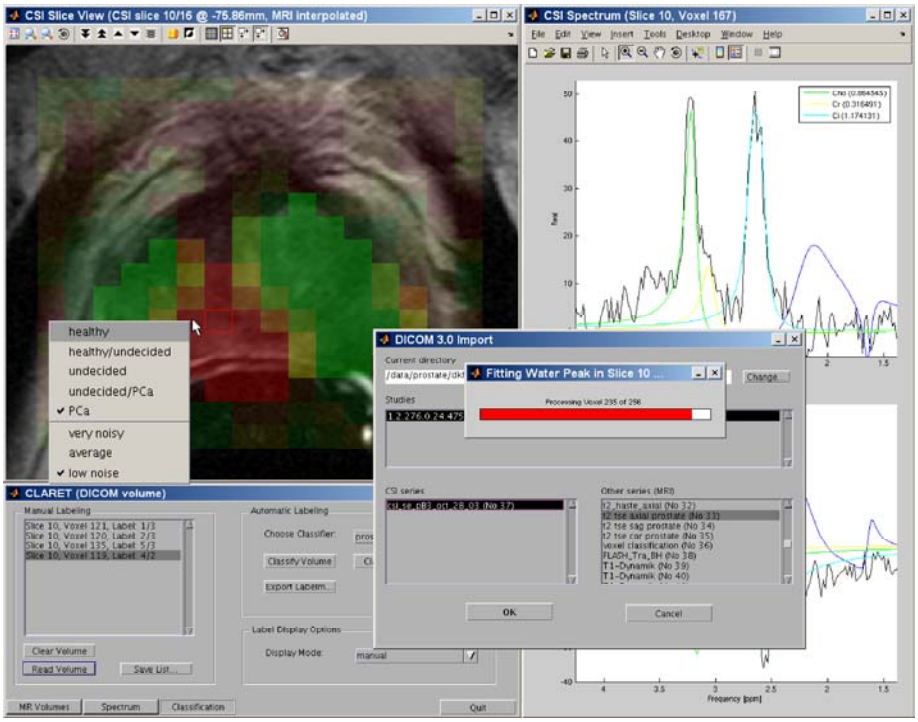

Fig. 1. The CLARET GUI can be used to evaluate MRSI efficiently. In routine use, the program automatically computes and displays tumor probability maps and confidence intervalls on top of morphologic MR images. The program also allows for a point-and-click display of spectral raw data, it can perform quantification, and it may be used for the manual labeling or the semi-manual refinement of training data sets.

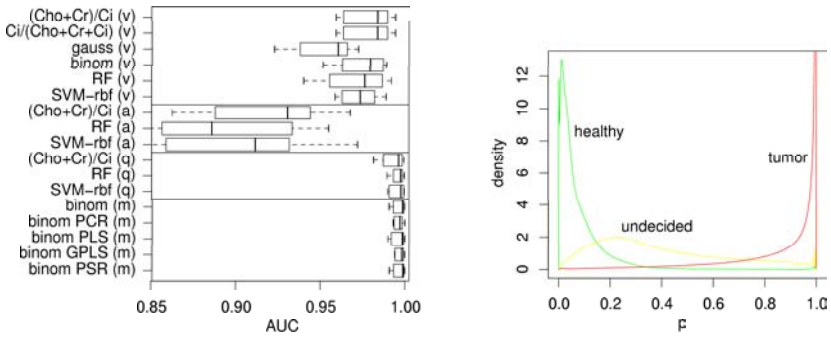

Fig. 2. Left: Comparison of the tumor prediction capability of various approaches: (v)-VARPRO, (a)-AMARES(jMRUI), (q)-QUEST(jMRUI) quantification versus spectral (m)agnitude pattern recognition approaches. The area under curve (AUC) of the receiver operator characteristic has been 8-fold cross-validated. **Right:** Density estimates of the cross-validated tumor probability estimates.

algorithms make its use simple. An application of CLARET for radiation therapy planning is projected and enabled by the integration into the software platform VIRTUOS [6].

The mentioned IMAPS prostate tumor study shows the potential of pattern recognition methods for the diagnostic evaluation of MRSI and highlights the necessity to provide suitable software. CLARET prototypically demonstrates the possibilities of a pattern recognition based MRSI evaluation. Here CLARET clearly contrasts with other MRSI evaluation tools such as jMRUI, LCModel or PRISMA which concentrate on the quantification of spectral data. Although these programs can also be used to compute and visualize color maps, only relative metabolite concentrations or ratios thereof are displayed. In contrast, CLARET is tailored towards the generation and visualization of pathophysiologic maps that report an explicit estimate for tumor probability in every voxel.

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