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Multivariate image regression and analysis

Useful techniques for the evaluation of clinical magnetic resonance images

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Abstract

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Multivariate image analysis (MIA) and multivariate image regression (MIR) techniques are useful tools in the extraction of information from magnetic resonance images. They aid the characterization of different tissues and can be used to describe their size and distribution. The obtained new information can be used to monitor growth, progression and effects of a treatment. The methodology is illustrated by a clinical example. The ongoing development of MIA and MIR, combining parameters from different imaging modalities, is commented on.

INTRODUCTION

Imaging and spectroscopic NMR techniques, magnetic resonance imaging (MRI) and magnetic resonance spectroscopy (MRS), are undergoing rapid development [1,2]. The potential applications in medical and biological research are immense [3]. The techniques that create new unique possibilities to characterize and describe tissue in normal and infirm states also permit pathological courses and effects of a treatment to be monitored. A major advantage is that the imaging procedure can be performed in vivo/in situ and that a series of measurements can be repeated over a longer period of time.

MRI is today a well-established clinical diagnostic technique and has been found to be a valuable tool in many different areas of medical research. There are a number of different MR imagers, from whole-body to micro-imagers. New developments in the field of electronics and pulse-sequences can combine MR spectroscopy and imaging in a technique called volume-selective spectroscopy, which enables extraction of information both about chemical and spatial composition in tissue from images [4].

Among all the methods that generate images, MRI has a special place because the signal recorded is not the image itself, but rather an indirect signal that has to be transformed into an image. MRI techniques are also able to show the inside of a solid or tissue, whereas most other imaging techniques are based on projection of a surface.

Furthermore, an improved resolution (in animal studies sometimes even better than 10 μm) and the possibility to chemically quantify tissue properties have increased the usefulness of the MR technique.

MR images can also be combined with other forms of imaging techniques such as EEG, PET and SPECT. In this way, new mixed images may be obtained which result in information both about anatomy and function.

The wealth of information that the MR technique produces is usually presented in the form of images. These images can experimentally be weighted differently, relating different chemical, physical and physiological parameters. Examples of such parameters are macromolecular distribution, ion concentration, diffusion, flow, pH and temperature.

Quite often the complexity of the images create difficulties in visual interpretation. By using advanced image analysis tools it is now possible to extract more information than is traditional in radiology. Modern image analysis comprises several new techniques, amongst others multivariate image analysis (MIA) [5–9] and multivariate image regression (MIR) [10,11]. By calculating a regression model between several images (acquired under different experimental conditions but on the same anatomical site) and related dependent images (typically binary), estimations can be made showing tissue with the same MR characteristics. In this way a rational and effective analysis and classification of tissue can be performed. Furthermore, the operator of the MR instrument can interactively use the scope of the technique for the design and optimization of the experiment.

The purpose of this presentation is to introduce some practical principles of multivariate image regression on MR images and to show how these can be used and envisioned in clinical and pharmaceutical research using a clinical case report.

MAGNETIC RESONANCE IMAGING

The technique of observing the behaviour of nuclear magnetic spins, when placed in a magnetic field, was first utilized for structure determination in organic chemistry.

MR imaging can be considered as an extension of the MRS technique. A sample (liquid, tissue or solid) is introduced in a spatially inhomogeneous magnetic field. The lineshape in the MR spectrum reveals the spatial distribution of nuclear magnetic spins. Nuclei in different magnetic fields will resonate at different frequencies and the spectral lineshape thus obtained comprises the total number of resonant frequencies weighted by the number of nuclei resonating at each frequency. Using methods similar to two-dimensional recording and processing techniques an image can be constructed.

The volume-selective imaging technique, where chemical information is combined with the spatial information from imaging, has received enormous attention in the past two years. This form of localized spectroscopy is applied to research as well as clinical imaging systems. Basically, the region of interest is selected from an image. In the context of multivariate image analysis, volume-selected imaging means simply adding a new variable that will strengthen the statistical significance.

MULTIVARIATE IMAGE ANALYSIS

The result from an MRI study is highly dependent on the extent to which the images can be physically interpreted. By varying one instrumental parameter in an experiment, one can obtain a totally different image. Usually these images are weighted using changes in some physical environment of the nuclei in the tissue. The contrast between different tissues in a sample can be changed through spin interactions like the relaxation rates and chemical shift. In this way, it is possible to distinguish between tissue like fat and water, making the MRI method very useful in the separation of soft tissues. However, there are cases where the MRI experimental method fails to discriminate between unrelated materials. The eye cannot discover any differences, although one knows there are discrete dissimilarities. Efforts to overcome these problems have resulted in the development of various texture-analysis techniques in MRI where odd behaviour in for example damaged tissue can successfully be discriminated [12–13].

Another way of analyzing images for separation and classification is to use a multivariate technique for analysis of several congruent images. A typical MRI experiment can easily produce five to ten images, each experiment weighted to enhance physical features in the tissue. Image analysis tools for handling this massive amount of data have been developed in accordance with modern multivariate statistical analysis.

CLINICAL STUDY, CASE REPORT

A 44-year old female patient with a long-standing history (ten years) of a cystic astrocytoma in the left fronto-temporal region of the brain. The pathology was first established by X-ray computed tomography (CT). At the beginning of her illness, the patient first showed only moderate psychiatric aberrations, mainly depression, but after the onset of a more rapid tumour progression she also developed substantial neurological symptoms. At this time she was examined using MRI, a technique with known superiority in the detection of white matter diseases as compared to CT. The patient was undergoing treatment with cytostatic pharmaceutics. The drug was injected directly into the cyst in order to achieve a high concentration locally in the tumour tissue. The effect of the treatment was followed by repeated examinations with MRI. One of the aims with these examinations was to distinguish between healthy and pathological tissue as well as the different components of the tumour. Another goal was to describe and visualize the distribution of the different tissues.

TISSUE CHARACTERIZATION FROM MR IMAGES

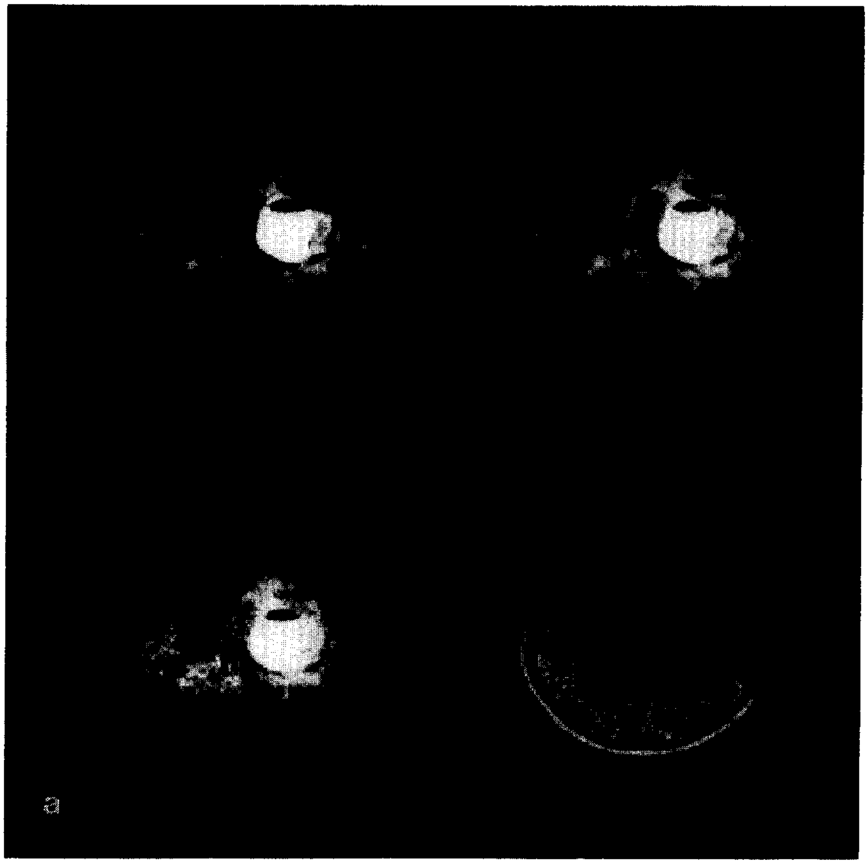
In order to achieve these goals, the abovementioned classification technique (MIR) was applied to a set of five MR images (Fig. 1a). The images were taken from the same slice of the brain, but with different pulse sequences. The MIR approach is discussed further in an accompanying contribution in this issue [14].

In the MIR analysis we used three disjoint classification variables defining the Y block. Pixels describing healthy brain tissue, solid tumour tissue and cystic tumour component were selected from the original grey-scale MR images and characterized by binary (1, 0) class belongings by the three Y variables. Fig. 1b shows the distribution of normal healthy brain tissue. High intensities (bright areas) have been selected in order to visualize the modelled tissue. Fig. 1c shows an estimation of the solid tumour parts of the pathological tissue. Finally in Fig. 1d the cystic components of the tumour are outlined.

DISCUSSION AND SUMMARY

The complexity of the images provided by recently developed imaging techniques, i.e., MRI, CT, SPECT and PET, call for new and more powerful analytical tools in order to extract the vast amount of information hidden in this type of images. Possibilities to tackle this task are the use of MIA and MIR.

These multivariate techniques have the qualifications to be valuable tools to characterize tissue in MR imaging. Tissue can be separated and individually modelled and used to predict the occurrence of the same tissue in another sample, animal or individual. In this basic form, the technique provides a visualization of the distribution of different tissues. This is especially important for tissues having a diffuse appearance where the outlining is usually almost impossible in the origi-



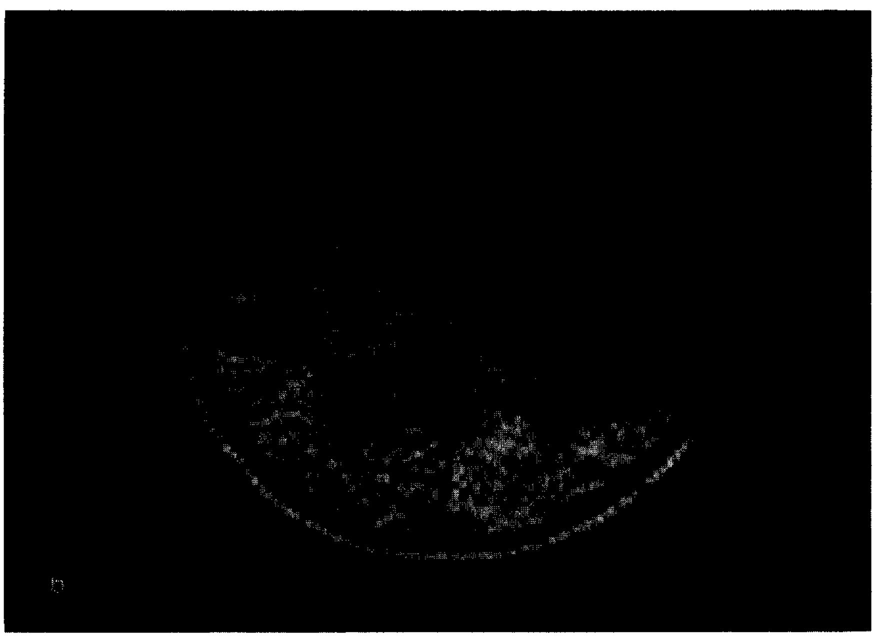


Fig. 1. (a) MR images of a patient with a cystic astrocytoma in the left hemisphere of the brain (to the right in the image; patients are observed from underneath). The images were obtained at 0.8 MHz. The pulse sequences used were spin-echo (upper) and inversion-recovery (lower). The images shown constitute four in a set of a total of five used in the statistical evaluation (MIR). Using MIR, tumour tissue could be separated from normal brain and the tumour could be differentiated into two different components. The result is visualized in (b) healthy brain tissue; (c) solid tumour; and (d) cystic tumour component.

Fig. 1 (continued).

nal MR images. From the resulting classification images, the area and/or the volume of a structure or tissue can easily be estimated simply by counting the number of voxels belonging to the predicted class. By repeated examinations the technique can now be used to follow the progression (e.g. growth) or the effect of a treatment.

In a future perspective, additional variables such as information from MRS, or other imaging modalities (CT, PET and SPECT) can be added to the model. This opens the possibility to study the relation between form and function. From a practical point, it would be possible to differentiate between tissues with similar MR appearance but with different metabolic functions, such as pituitary tumours.

Other important features for a successful tissue characterization are texture (local spatial frequency), form and spatial relation to other tissue. Such features can easily be included in the model, thus increasing the reliability of the characterization.

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