Multimodal Medical Image Analysis: from Visualization to Disease Modeling

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Multimodal imagery is increasingly used in clinical practice. In the diagnosis of brain tumors, for example, multi-parametric imaging sequences are routinely used in the evaluation of high-grade glioma patients prior to and post therapy, or in the monitoring of disease progression for low-grade glioma patients. Multi-parametric sequences may reveal disease-specific differences in tissue water (T2, FLAIR-MRI), enhancement of contrast agents (post-Gadolinium T1-MRI), diffusion (DTI, DCE-MRI), or relative concentrations of selected metabolites (MRSI). This leads to large multimodal, often multi-temporal, image data sets providing multiple physical measurements in every voxel – but also raising the question of how to sensibly evaluate the information of such high-dimensional data sets.

Different strategies have been developed to help radiologists navigate such data sets and make optimally informed decisions. They differ in the amount of prior knowledge they introduce into the analysis, and in how specifically they are tailored to a given problem.

Analysis without specific prior knowledge. So-called unsupervised methods use the least amount of prior knowledge and make little assumptions about the data to be analyzed. They include multi-purpose visualization tools and clustering methods. Here, voxels which share similar physical properties -- i.e. which have similar image intensities in all modalities -- are grouped, or "clustered", and these clusters can be visualized as connected regions. This type of display allows for a high-level visualization of multimodal image information. Unfortunately, natural variability in the data, e.g. from noise, may lead to misleading groupings. Recent approaches use spatial context to enforce spatial connectivity and better repeatability of the clustering [1], or rely on "semi-supervised" strategies trained by user interaction.

Analysis with prior knowledge in image features. Pre-processed and validated image data sets from large medical studies allow for more sophisticated, "supervised" methods. These make it possible to use specific knowledge on physiological features in an automated machine-based analysis. Such prior knowledge may refer to either the spatial or spectral properties of pathologies. The expected spatial distribution of different tissue types can be summarized in "population atlases" which are then used in the segmentation of new image volumes. Alternatively, characteristic multi-parametric "fingerprints" can be used to train a classifier which, for example, identifies different pathologies and highlights them automatically in further data sets. Such "machine learning" approaches encapsulating prior knowledge now achieve highly repeatable results [2] which is of crucial importance for their use in clinical diagnostics.

Analysis with bio-physical process models. The most recent development is to go beyond statistical black-box modeling and to rely on physically grounded modeling of disease and disease progression in the analysis of complex multimodal data sets. This approach benefits from the increasing standardization of imaging protocols providing large data sets with very specific image information. It extends the idea of using prior knowledge on spatial patterns or tissue characteristics by formalizing prior assumptions on the underlying process of the evolution of a disease. Assimilating observations into a bio-physical model of disease progression, for example for glioma growth, makes it possible to characterize the disease by few model parameters which can then be used in diagnostics, or to predict the further evolution. At the same time, a disease model provides a common framework for integrating information from different image volumes [3] and can help to understand the underlying process when testing different model options. The front cover shows an example for such a biological modeling

approach: it illustrates the different tumor shapes obtained when synthetically growing a tumor with different parameterizations of a reaction-diffusion model describing glioma growth [4]. A modeling strategy crucially depends on the availability of very specific image modalities and the accuracy and validity of the chosen model. If applicable, however, disease models may provide a novel, abstract level for analyzing image information and may provide new means for image-based diagnostics and personalized therapy.

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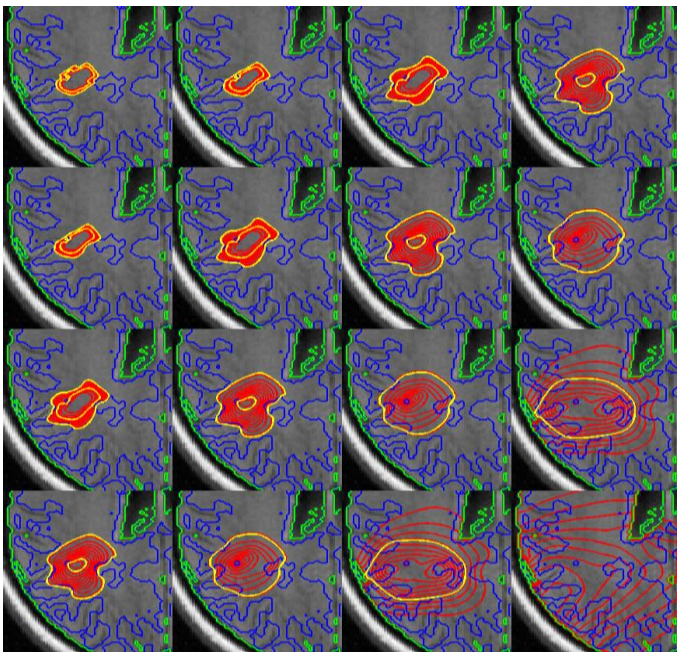
[2] Prastawa M, Bullitt E, Moon N, Van Leemput K, Gerig G. Automatic brain tumor segmentation by subject specific modification of atlas priors. Academic Radiology. 2003 10:1341-1348.

[3] Atuegwu NC, Gore JC and Yankeelov TE. The integration of quantitative multi-modality imaging data into mathematical models of tumors. Physics in Medicine and Biology. 2010. 55:2429-2449

[4] Menze BH, Strettin E, Konukoglu E, Ayache N. Image-based modeling of tumor growth in patients with glioma. In: CS Garbe, R Rannacher, U Platt, T Wagner (eds.), Optimal control in image processing. Springer, Heidelberg, Germany. 2011.



Bio-physical models of tumor growth (glioma). Red lines represent iso-concentration contours of tumor cell distributions, yellow lines indicate the outlines of 5% and 60% tumor cell infiltration. All tumors shown here have the same total mass. They differ in growth rate (increasing along the vertical axis, max.

in the top row) and their aggressiveness in tissue invasion (increasing along the horizontal axis, max. in the right column), the two parameters of the growth model.