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Medical Image Processing: A Challenging Analysis

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Abstract

Medical image processing is an multifaceted field at the intersection of computer science, electrical engineering, physics, mathematics and medicine. Medical Image processing has developed versatile computational and mathematical methods for solving problems pertaining to medical images and their use for biomedical research and clinical care. The prominent and important motive of Medical Image Processing is to extract clinically relevant information or knowledge from medical images. MIP focuses on the computational analysis of the images, not their acquisition. The methods can be grouped categorized as: image segmentation, image registration, image-based physiological modeling, Research in Medical Image Processing (MIP) is mainly driven by a technology oriented point of view. MIP research should always be able to give an answer to the question of what is the potential benefit of a solved MIP problem or a newly developed MIP-based system supporting a diagnostic or therapeutic process, in terms of outcome criteria like, e.g., Quality Adjusted Life Years (QALYs) for the patient or cost savings in health care. This paper presents the concept and the strategy of how the Most Relevant MIP problems (MRMIP) shall be identified and assessed in the context of improving evaluation of MIP solutions.

Keywords*: MIP, CAD, MRMP*

1. Introduction

The field of Medical Image Processing (MIP) and the applications in Computer Assisted Diagnoses (CAD) and therapy (*e.g.*, Computer Assisted Surgery – CAS) which strongly depend on MIP methods are of increasing importance in modern medicine. Nevertheless, due to its proximity to medical imaging devices, the field is widely considered as an engineering discipline with a methodological progress that is somehow independent from medical problems and the clinical practice. Even if this might be correct for basic research on domain independent image processing methodology, it is surely wrong if one emphasizes on system research and development meant for support of diagnostics and therapy.

While there is an ongoing broad discussion about evidence-based medicine, in which decisions are made on the basis of reliable knowledge about efficacy and – not less important on the background of the big problems in financing the healthcare systems – also about efficiency, the MIP field seems to be more or less resistant against the question about the impact of produced progress on medicine and healthcare in general. But what are the most relevant MIP problems to be solved in terms of their impact on support of major problems in medicine and modern healthcare? So far, no comprehensive attempts have been undertaken to clarify this important question. As one subtask of establishing a Reference Image Database for MIP R&D Groups, the Working Group on Medical Image Processing of the European Federation for Medical Informatics (EFMI WG MIP) has decided to work on an answer. This paper describes the concept and strategy of how such relevant MIP problems shall be identified and assessed in the framework of the working group.

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2. Definitions, Material and Methods

2.1 Review Stage

Some essential notions have to be defined for usage in the context of this paper.

A ***challenge*** is exact descriptions of a work objective for which no real ideas and methods are present how to find a solution, whereas a *task* is an exact description of a work objective for which paths to build solutions already exist. Both kinds of descriptions shall be called *problem*.

A medical problem shall be called a *Most **Relevant Medical Problem*** (MRMP), if its solution would have a high impact on the overall health status of people and/or on the efficiency of producing/sustaining health at a certain quality level.

In the context of imaging, the important notion of *Medical Image Interpretation* (MII) is introduced as denoting the process of deriving medically relevant information from analyzing a medical image or a set of images. MII can be performed either by the physician (visual assessment) or by a MIP application (computer assessment), or in a combination of both (usually as computer-supported assessment by the physician).

As material for the process planning, all kinds of actual statistics and literature have been used. The Unified Modeling Language (UML) has served as method for working out the concepts and depicting the different aspects of the assessment task.

Data Forms: Medical image computing typically operates on uniformly sampled data with regular x-y-z spatial spacing (images in 2D and volumes in 3D, generically referred to as images). At each sample point, data is commonly represented in integral form such as signed and unsigned short (16-bit), although forms from unsigned char (8-bit) to 32-bit float are not uncommon. The particular meaning of the data at the sample point depends on modality: for example a CT acquisition collects radio density values, while a MRI acquisition may collect T1 or T2-weighted images. Longitudinal, time-varying acquisitions may or may not acquire images with regular time steps. Fan-like images due to modalities such as curved-array ultrasound are also common and require different representational and algorithmic techniques to process. Other data forms include sheared images due to gantry tilt during acquisition; and unstructured meshes, such as hexahedral and tetrahedral forms, which are used in advanced biomechanical analysis (*e.g.*, tissue deformation, vascular transport, bone implants).

Segmentation: Segmentation is the process of partitioning an image into different segments. In medical imaging, these segments often correspond to different tissue classes, organs, pathologies, or other biologically relevant structures. Medical image segmentation is made difficult by low contrast, noise, and other imaging ambiguities. Although there are many computer vision techniques for image segmentation, some have been adapted specifically for medical image computing. Below is a sampling of techniques within this field; the implementation relies on the expertise that clinicians can provide.

a. **Atlas-Based Segmentation**: For many applications, a clinical expert can manually label several images; segmenting unseen images is a matter of extrapolating from these manually labeled training images. Methods of this style are typically referred to as atlas-based segmentation methods. Parametric atlas methods typically combine these training images into a single atlas image, while nonparametric atlas methods typically use all of the training images separately. Atlas-based methods usually require the use of image registration in order to align the atlas image or images to a new, unseen image.

b. **Shape-Based Segmentation**: Many methods parameterize a template shape for a given structure, often relying on control points along the boundary. The entire shape is then deformed to match a new image. Two of the most common shape-based techniques are Active Shape Models and Active Appearance Models. These methods have been very influential, and have given rise to similar models.

c. **Interactive Segmentation**: Interactive methods are useful when clinicians can provide some information, such as a seed region or rough outline of the region to segment. An algorithm can then iteratively refine such segmentation, with or without guidance from the clinician. Manual segmentation, using tools such as a paint brush to explicitly define the tissue class of each pixel, remains the gold standard for many imaging applications. Recently, principles from feedback control theory have been incorporated into segmentation, which give the user much greater flexibility and allow for the automatic correction of errors.

3. Image Based Physiological Modeling

Traditionally, medical image computing has seen to address the quantification and fusion of structural or functional information available at the point and time of image acquisition. In this regard, it can be seen as quantitative sensing of the underlying anatomical, physical or physiological processes. However, over the last few years, there has been a growing interest in the predictive assessment of disease or therapy course. Image-based modeling, be it of biomechanical or physiological nature, can therefore extend the possibilities of image computing from a descriptive to a predictive angle. Figure 1 represents the Digital Image based modeling of Left hand.

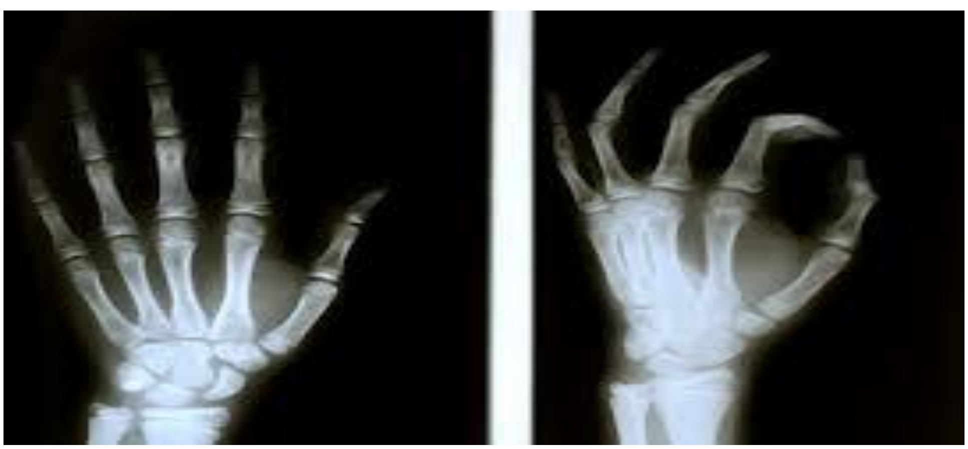

Figure 1

According to the STEP research roadmap the Virtual Physiological Human (VPH) is a methodological and technological framework that, once established, will enable the investigation of the human body as a single complex system. Underlying the VPH concept, the International Union for Physiological Sciences (IUPS) has been sponsoring the IUPS Physiome Project for more than a decade; this is a worldwide public domain effort to provide a computational framework for understanding human physiology. It aims at developing integrative models at all levels of biological organization, from genes to the whole organisms via gene regulatory networks, protein pathways, integrative cell functions, and tissue and whole organ structure/function relations. Such an approach aims at transforming current practice in medicine and underpins a new era of computational medicine.

In this context, medical imaging and image computing play, and will continue to play, an increasingly important role as they provide systems and methods to image, quantify and fuse both structural and functional information about the human being in vivo. These two broad research areas include the transformation of generic computational models to represent specific subjects, thus paving the way for personalized computational models. Individualization of generic computational models through imaging can be realized in three complementary directions:

- definition of the subject-specific computational domain (anatomy) and related sub domains (tissue types);
- definition of boundary and initial conditions from (dynamic and/or functional) imaging; and
- Characterization of structural and functional tissue properties.

In addition, imaging also plays a pivotal role in the evaluation and validation of such models both in humans and in animal models, and in the translation of models to the clinical setting with both diagnostic and therapeutic applications. In this specific context, molecular, biological, and pre-clinical imaging render additional data and understanding of basic structure and function in molecules, cells, tissues and animal models that may be transferred to human physiology where appropriate.

The applications of image-based VPH/Physiome models in basic and clinical domains are vast. Broadly speaking, they promise to become new *virtual imaging techniques*. Effectively more, often non-observable, parameters will be imaged *in silico* based on the integration of observable but sometimes sparse and inconsistent multimodal images and physiological measurements. Computational models will serve to engender interpretation of the measurements in a way compliant with the underlying biophysical, biochemical or biological laws of the physiological or path physiological processes under investigation. Ultimately, such investigative tools and systems will help our understanding of disease processes, the natural history of disease evolution, and the influence on the course of a disease of pharmacological and/or interventional therapeutic procedures.

Cross-fertilization between imaging and modeling goes beyond interpretation of measurements in a way consistent with physiology. Image-based patient-specific modeling, combined with models of medical devices and pharmacological therapies, opens the way to predictive imaging whereby one will be able to understand, plan and optimize such interventions *in silico*.

4. Mathematical Methods in Medical Imaging [5]

A number of sophisticated mathematical methods have entered medical imaging, and have already been implemented in various software packages. These include approaches based on partial differential equations (PDEs) and curvature driven flows for enhancement, segmentation, and registration. Since they employ PDEs, the methods are amenable to parallelization and implementation on GPGPUs. A number of these techniques have been inspired from ideas in optimal control. Accordingly, very recently ideas from control have recently made their way into interactive methods, especially segmentation. Moreover, because of noise and the need for statistical estimation techniques for more dynamically changing imagery, the Kalman filter and particle filter have come into use.

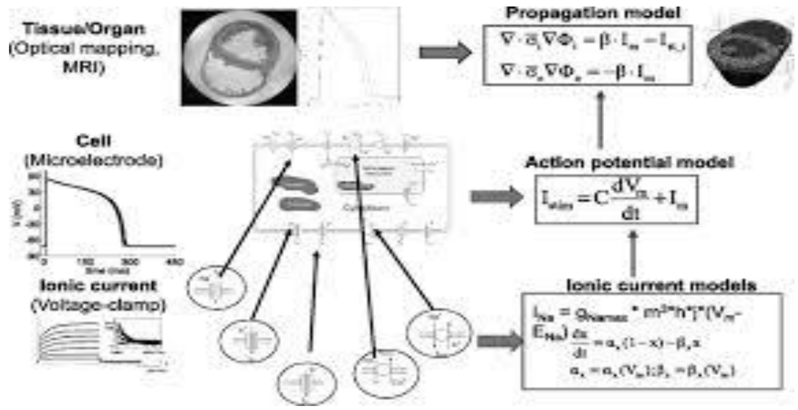

Figure 2. Mathematical Model [7]

5. Modality Specific Computing

Some imaging modalities provide very specialized information. The resulting images cannot be treated as regular scalar images and give rise to new sub-areas of Medical Image Computing. Examples include diffusion MRI, functional MRI and others.

Diffusion MRI: A mid-axial slice of the ICBM diffusion tensor image template. Each voxel's value is a tensor represented here by an ellipsoid. Color denotes principal orientation: red = left-right, blue=inferior-superior, green = posterior-anterior

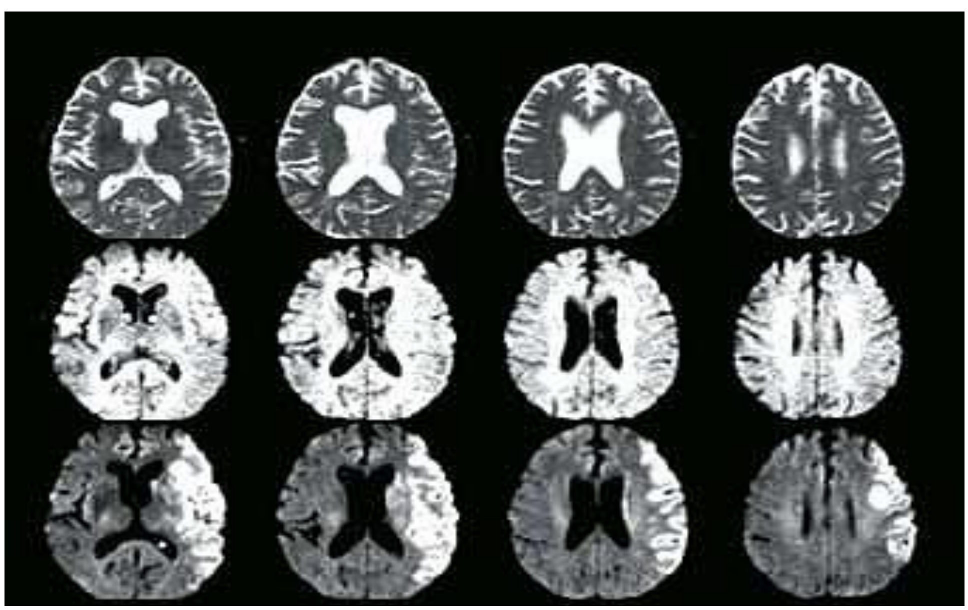

Figure 3. Diffusion-weighted MRI [8] Color-coded white matter fibers reveal the corpus callosum. Appearing as a central band of horizontal blue fibers, the structure connects the brain's hemispheres

Diffusion MRI is a structural magnetic resonance imaging modality that allows measurement of the diffusion process of molecules. Diffusion is measured by applying a gradient

pulse to a magnetic field along a particular direction. In a typical acquisition, a set of uniformly distributed gradient directions is used to create a set of diffusion weighted volumes. In addition, an unweighted volume is acquired under the same magnetic field without application of a gradient pulse. As each acquisition is associated with multiple volumes, diffusion MRI has created a variety of unique challenges in medical image computing.
In medicine, there are two major computational goals in diffusion MRI:

- Estimation of local tissue properties, such as diffusivity;
- Estimation of local directions and global pathways of diffusion.

Functional MRI: Functional magnetic resonance imaging (FMRI) is a medical imaging modality that indirectly measures neural activity by observing the local hemodynamic, or blood oxygen level dependent signal (BOLD). FMRI data offers a range of insights, and can be roughly divided into two categories:

a. **Task related FMRI** is acquired as the subject is performing a sequence of timed experimental conditions. In block-design experiments, the conditions are present for short periods of time (*e.g.*, 10 seconds) and are alternated with periods of rest. Event-related experiments rely on a random sequence of stimuli and use a single time point to denote each condition. The standard approach to analyze task related FMRI is the general linear model (GLM)

b. **Resting state FMRI** is acquired in the absence of any experimental task. Typically, the objective is to study the intrinsic network structure of the brain. Observations made during rest have also been linked to specific cognitive processes such as encoding or reflection. Most studies of resting state FMRI focus on low frequency fluctuations of the FMRI signal (LF-BOLD). Seminal discoveries include the default network, a comprehensive cortical parcellation, and the linking of network characteristics to behavioral parameters

6. Software Used In MIP

Software for medical image computing is a complex combination of systems providing IO, visualization and interaction, user interface, data management and computation. Typically system architectures are layered to serve algorithm developers, application developers, and users. The bottom layers are often libraries and/or toolkits which provide base computational capabilities; while the top layers are specialized applications which address specific medical problems, diseases, or body systems.

Toolkits, Libraries and Enabling Technologies: Visualization Toolkit (VTK), Insight Segmentation and Registration Toolkit (ITK), the Common Toolkit (CTK), Teem, DCMTK

Integration Software: Python, Qt, Midas, XNAT, C-Make.

General-Purpose Applications[4]: 3D Slicer, ITK-SNAP, GIMIAS, ImageJ, medInria, Para View.

Brain Imaging: *Free surfer, FMRIB Software Library (FSL), Statistical Parametric Mapping.*

Shape Analysis: *SPHARM-PDM.*

7. Conclusion

Even if the practical carrying-out of the assessment process will not always be possible without a certain portion of uncertainty due to missing information, it can be hoped that it will nevertheless help in setting the right priorities where to put the main efforts within the RID-MIP initiative of EFMI WG MIP and foster awareness of MIP professionals for the important question of relevance.

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