Computer Vision and Image Understanding 151 (2016) 3–13

Contents lists available at ScienceDirect

Computer Vision and Image Understanding

journal homepage: www.elsevier.com/locate/cviu

Modeling 4D pathological changes by leveraging normative models

Bo Wang [a,b,*], Marcel Prastawa [c], Andrei Irimia [d], Avishek Saha [e], Wei Liu [a,b], S.Y. Matthew Goh [d], Paul M. Vespa [f], John D. Van Horn [d], Guido Gerig [g]

[a] Scientific Computing and Imaging Institute, University of Utah, 72 Central Campus Drive, Salt Lake City, UT 84112 USA
[b] School of Computing, University of Utah, 50 S., Central Campus Drive, Salt Lake City, UT 84112 USA
[c] Icahn School of Medicine at Mount Sinai, 1468 Madison Avenue, New York, NY 10029 USA
[d] The Institute for Neuroimaging and Informatics, Keck School of Medicine, University of Southern California, 2001 North Soto Street, Los Angeles CA 90089 USA
[e] Yahoo Labs, 701 1st Ave, Sunnyvale, CA 94089 USA
[f] Brain Injury Research Center, Department of Neurosurgery, David Geffen School of Medicine, University of California, Los Angeles, CA 90095 USA
[g] Tandon School of Engineering, Department of Computer Science and Engineering, NYU, USA

ARTICLE INFO

Article history:
Received 16 February 2015
Accepted 18 January 2016

Keywords:
Image segmentation
Brain parcellation
Medical imaging

ABSTRACT

With the increasing use of efficient multimodal 3D imaging, clinicians are able to access longitudinal imaging to stage pathological diseases, to monitor the efficacy of therapeutic interventions, or to assess and quantify rehabilitation efforts. Analysis of such four-dimensional (4D) image data presenting pathologies, including disappearing and newly appearing lesions, represents a significant challenge due to the presence of complex spatio-temporal changes. Image analysis methods for such 4D image data have to include not only a concept for joint segmentation of 3D datasets to account for inherent correlations of subject-specific repeated scans but also a mechanism to account for large deformations and the destruction and formation of lesions (e.g., edema, bleeding) due to underlying physiological processes associated with damage, intervention, and recovery.

In this paper, we propose a novel framework that provides a joint segmentation-registration framework to tackle the inherent problem of image registration in the presence of objects not present in all images of the time series. Our methodology models 4D changes in pathological anatomy across time and also provides an explicit mapping of a healthy normative template to a subject's image data with pathologies. Since atlas-moderated segmentation methods cannot explain appearance and locality pathological structures that are not represented in the template atlas, the new framework provides different options for initialization via a supervised learning approach, iterative semisupervised active learning, and also transfer learning, which results in a fully automatic 4D segmentation method.

We demonstrate the effectiveness of our novel approach with synthetic experiments and a 4D multimodal MRI dataset of severe traumatic brain injury (TBI), including validation via comparison to expert segmentations. However, the proposed methodology is generic in regard to different clinical applications requiring quantitative analysis of 4D imaging representing spatio-temporal changes of pathologies.

1. Introduction

Quantitative studies in longitudinal image data from traumatic brain injury (TBI), autism, and Huntington's disease, for example, are important for assessment of treatment efficacy, monitoring disease progression, or making predictions on outcome. In this paper, we will use the term '*pathological anatomy* to indicate image data that represent pathologies and lesions and therefore differ from normative anatomical templates that encode healthy anatomy. The modeling of four-dimensional (4D) pathological anatomy is essential to understand the complex dynamics of pathologies and enables other analyses such as structural pathology [1] and brain connectivity [2]. Modeling pathological changes is a challenging task because of the difficulties in localizing multiple lesions at specific time points and estimating deformations across time points with changing lesion patterns. Such modeling involves solving interdependent segmentation and image registration since registration needs to know about areas of pathology but 4D segmentation requires an intrasubject mapping across time points.

* Corresponding author was at: School of Computing, University of Utah, 50 S., Central Campus Drive, Salt Lake City, UT 84112 USA. Bo Wang is with the GE Global Research Center, Niskayuna, NY 12309 USA

E-mail address: bowang@cs.utah.edu (B. Wang).

http://dx.doi.org/10.1016/j.cviu.2016.01.007
1077-3142/

Furthermore, subject-specific registration across time points is not sufficient to segment pathological anatomy if we follow the well-established concept of atlas-driven segmentation, which includes probabilistic tissue priors for a Bayesian maximum posterior classification. Such a scheme requires an explicit registration from a normative template atlas to each subject's image time point, with the additional advantage of using anatomical labeling of subregions as used in brain connectivity analysis, for example.

The main goal of this paper therefore is the development of a new 4D pathological anatomy modeling framework that simultaneously solves segmentation of each time point and also estimates nonlinear deformations to a normative atlas space and across time points. We will use severe TBI as our clinical driving problem to demonstrate the different components of the novel method and to validate results in comparison to human expert segmentations. TBI is not only a critical problem in healthcare that impacts approximately 1.7 million people in the United States every year [3], but also one of the most challenging tasks for quantitative image-based interpretation and analysis. The varying causes (falls, car accidents, etc.) and degrees of TBI present highly heterogeneous multifocal patterns of lesions with largely variable morphometry. Spatio-temporal analysis of serial TBI imaging is motivated by the clinical need for improved insight and quantitative data from therapeutic intervention and rehabilitation that change brain neuroanatomy and function with a reduction/cessation of symptoms.

2. Related work/previous work

4D pathological anatomy modeling is closely related to longitudinal image analysis, a research area of increasing interest to the scientific community due to the availability and use of longitudinal imaging in medical research and clinical practice.

Researchers have proposed different methods for longitudinal image/shape analysis [4–8]. These image regression methods were developed for image data resembling normal anatomy with small-scale temporal deformations. However, these methods are not designed for pathological anatomy presenting nondiffeomorphic deformations and topological changes due to spatio-temporal lesion evolution. In the following sections, we discuss previous work related to pathological brain MR image analysis, organized by the type of problem to be solved.

2.1. 3D/4D segmentation

One class of work focuses on 3D volume data segmentation [9–13]. Menze et al. [9] presented a generative model for brain tumor segmentation using multimodal MR images. Geremia et al. [10] proposed to use random forests for automatic segmentation of multiple sclerosis (MS) lesions in multimodal MR images. Bauer et al. [11] presented an automatic segmentation method based on support vector machine classification with smoothness constraints. Gao et al. [12] developed a robust statistics-based interactive multiobject segmentation tool. Ledig et al. [13] proposed a method based on the Gaussian mixture modeling (GMM) with patch-based spatially and temporally varying constraints to enforce temporal coupling. All these methods use different classifiers with different image-derived features as input or even incorporate temporal information for pixel classification, but they are not designed for longitudinal pathological anatomy studies due to the lack of intra- and intersubject registration.

Atlas-based segmentation has been demonstrated to be a powerful solution in the case of segmenting healthy or normal-looking brain MR images [14]. In scenarios where pathological structures are present in the subject image but not in the atlas, this method could be extended to a GMM-based approach where an affine-registered atlas and user initialization are combined [15].

2.2. Intrasubject registration

A second class of methods is concerned with registration across time points [16–19]. Chitphakdithai and Duncan [16] proposed a registration method accommodating the missing correspondences for preoperative and post-resection brain images. Niethammer et al. [17] presented a registration framework for TBI images using geometric metamorphosis that maps TBI over time using known, presegmented lesion boundaries defined manually. Ou et al. [18] proposed a generic deformable registration method using attribute matching and mutual-saliency weighting. Lou et al. [19] presented a deformable registration method for intra-time point multimodal image registration. However, these image-registration methods describe deformations but do not provide segmentation of anatomical structures.

2.3. Pathological anatomy growth model

A third class of methods focuses on modeling the growth of pathological anatomy such as tumor or glioma [20–24]. Kyriacou et al. [20] proposed a finite element-based biomechanical model for registering a normal atlas to a patient image. Cuadra et al. [21] developed an atlas-based segmentation method using a lesion growth model. Zacharaki et al. [22] proposed a multiresolution method that utilized a principal component analysis (PCA)-based model of tumor growth for deformable registration of brain tumor images. Gooya et al. [24] presented a segmentation and registration method for MR images of glioma patients using a tumor growth model. Menze et al. [23] proposed a generative model of tumor growth and image appearance that relies on modeling the pathophysiological process and data likelihood. These methods provide a segmentation of pathological anatomy or mapping from an atlas to the pathological data but do not include intrasubject registration for a full 4D modeling of healthy and pathological structures.

2.4. Joint segmentation and registration

A fourth class of methods is joint segmentation and registration [25–28]. Pohl et al. [25] proposed a Bayesian framework for joint segmentation and registration for normal brain MR images. Parisot et al. [26] proposed a tumor segmentation and registration method to solve brain tumor segmentation and atlas to patient image registration simultaneously by using a Markov random field model with a sparse grid. Kwon et al. [27] developed a deformable tumor registration tool for preoperative and postrecurrence brain MR scans. Liu et al. [28] proposed a low-rank image decomposition-based atlas registration method to map a healthy brain atlas to a patient image. These methods approach problems similar to those discussed in this paper but focus on one subproblem such as atlas registration [28], intrasubject registration [27], and tumor segmentation with atlas registration [26] rather than a combined, joint framework.

2.5. Novel methodological framework

Although significant progress has been demonstrated in various aspects of methods for longitudinal pathological image analysis, we propose a solution that includes the remaining open issues related to multimodal image analysis and longitudinal modeling. The processing framework includes explicit mapping from a normative probabilistic template representing healthy anatomy to each image of the subject's image time series and multimodal segmentation and extends early work [29] in which we focused on a pathological anatomy modeling framework with transfer learning-based image appearance model estimation by adding user initialization and user