Editorial: Introduction to the Issue on Domain Enriched Learning for Medical Imaging

IN RECENT years, learning based methods have emerged to complement traditional model and feature based methods for a variety of medical imaging problems such as image formation, classification and segmentation, quality enhancement etc. In the case of deep neural networks, many solutions have achieved unprecedented performance gains and have defined a new state of the art. Despite the progress, compelling open challenges remain. One such key challenge is that many learning frameworks (notably deep learning) are purely data-driven approaches and their performance depends strongly on the quantity and quality of training image data available. When training is limited or noisy, the performance drops sharply. Deep neural networks based approaches additionally face the challenge of often not being straightforward to interpret. Fortunately, exciting recent progress has emerged in enriching learning frameworks with domain knowledge and signal structure. As a couple of representative examples: in image reconstruction problems, this may involve using statistical/structural image priors; for image segmentation, shape and anatomical knowledge (conveyed by an expert) may be leveraged, etc. This special issue brings together contributions that combine signal, image priors and other flavors of domain knowledge with machine learning methods for solving many diverse medical imaging problems.

Following an open call for papers, we received a total number of 42 submissions for this special issue. After an extensive and competitive review process, 19 papers were selected for final publication. The papers cover the following themes: a.) prior information guided image formation, inversion and reconstruction, b.) exploitation of geometric and structural information for training robust medical image segmentation and classification, c.) domain enriched medical image analysis and understanding, and d.) design of interpretable and/or expressible deep networks for medical imaging.

The issue opens with the article, “Prior-Guided Image Reconstruction for Accelerated Multi-Contrast MRI via Generative Adversarial Networks” by Cukur *et al.* In this paper, the authors propose an approach for synergistic recovery of undersampled multi-contrast acquisitions based on conditional generative adversarial networks. The proposed method utilizes three priors: shared high-frequency prior available in the source contrast to preserve high-spatial-frequency details, low-frequency prior, and perceptual prior. The next article is: “RARE: Image Reconstruction using Deep Priors Learned without Ground Truth”. In this work, the authors proposed regularization by artifact-removal (RARE) by extending the regularization by denoising (RED) with the consideration of priors corresponding to networks trained for more general artifact-removal. The key benefit of the proposed family of algorithms is that it can be applicable to problems where it is practically impossible to have fully-sampled groundtruth data for training such as accelerated MRI. The reconstruction theme continues with: “PET Image Reconstruction Using a Cascading Back-Projection Neural Network”. This paper develops a deep learning PET reconstruction method using a cascading back-projection neural network (bpNet). This network consists of a domain translation operation, which acts as prior knowledge, cascaded with a modified encoder-decoder network so that the image reconstruction can be performed from the sinogram to the back-projection image and then to the PET image. Unsupervised learning for reconstruction is explored in: “Unsupervised Training Of Denoisers For Low-Dose CT Reconstruction Without Full-Dose Ground Truth”. The novelty of this work resides in unsupervised training of the DNNs using denoised measurements or sinograms and subsequent reconstruction using the classical filtered back-projection (FBP) reconstruction algorithm. The proposed method outperforms state-of-the-art low-dose CT reconstruction methods without ground truth. Subject-specific brain image priors are exploited for MR reconstruction in: “Enhanced Deep-learning-based Magnetic Resonance Image Reconstruction by Leveraging Prior Subject-specific Brain Imaging: Proof-of-concept using a Cohort of Presumed Normal Subjects”. In particular, the authors propose a methodology that integrates subject-specific prior fully sampled MR imaging information to enhance reconstruction of the patient’s following MR examinations using a deep learning model. They report an improvement in quantitative performance metrics that could potentially enable faster MR examinations while still resulting in high quality and clinically relevant images. Statistical priors are used in the next article: “StatNet: Statistical Image Restoration for Low-Dose CT using Deep Learning”. In this paper, the authors proposed an approach to statistical image restoration for LDCT using deep learning by introducing a loss function to incorporate the noise property in image domain derived from the noise statistics in sinogram domain. Sensor aware algorithm design is pursued in: “J-MoDL: Joint Model-Based Deep Learning for Optimized Sampling and Reconstruction”. The authors introduce a continuous strategy to jointly optimize the sampling pattern and deep network parameters for deep learning based MRI reconstruction. The next article considers

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noise characteristics: "SIMBA: Scalable Inversion in Optical Tomography using Deep Denoising Priors". Specifically, the authors present a new scalable iterative minibach algorithm named SIMBA for online optical tomographic image reconstruction. This algorithm enables fast and high quality image regularized inversion by combining the physical information available through the forward model and the imaging prior obtained via a convolutional neural network denoiser. The reconstruction theme wraps up with a multimodal image synthesis approach. In "Multimodal MR Image Synthesis Using Gradient Prior and Adversarial Learning," the authors explore the multimodal magnetic resonance image synthesis problem with an end-to-end generative adversarial network solution.

The segmentation and classification theme begins with: "BB-UNet: U-Net with Bounding Box Prior". El Jurdi *et al* introduce the BB-UNet (Bounding Box U-Net), a deep learning model that integrates localization as well as shape prior onto model training. Promising results are shown for challenging CT image segmentation problem. Unsupervised learning for segmentation is presented in: "Unsupervised Mitochondria Segmentation in EM Images via Domain Adaptive Multi-Task Learning". The authors proposed to use a multi-task adaptation network to address the problem of cross-domain semantic unsupervised segmentation of Electron Microscopy images. It is shown that integrating label space information (i.e., high-level geometrical information), decoding feature information (i.e., low level cues) and image visual cues improve the discriminative ability of the cross-domain predictor on an unlabeled target domain. The method has been validated on a mitochondria segmentation task in the presence of severe domain shift. Classification of ultrasound images is pursued in: "A Domain Enriched Deep Learning Approach to Classify Atherosclerosis using Intravascular Ultrasound Imaging". Intravascular ultrasound imaging (IVUS) is widely used for diagnostic imaging in interventional cardiology. The image-based tissue characterization method proposed for the detection and quantification of atherosclerosis departs from the manual expert annotation or the widely extended virtual histology IVUS (VH-IVUS), with high software and hardware requirements. The pixel-based method imposes physically relevant spatial constraints driven by domain knowledge of arterial pathology and physiology and leverages technological advances of convolutional neural networks to segment diseased vessel walls into the same tissue classes as virtual histology. It uses only grayscale IVUS images eliminating the need of analyzing backscattered radio frequency signals as VH-IVUS does, what results in more widespread applicability. The issue of limited training in segmentation is addressed in: "Learning to Segment Brain Anatomy from 2D Ultrasound with Less Data". One major problem in developing an automatic segmentation method for brain ultrasound (US) is the limited availability of annotated data. To tackle this issue, the authors propose a novel image synthesis method using multi-scale self attention generator to synthesize US images from various segmentation masks. They show that our method can synthesize high-quality US images for every manipulated segmentation label with qualitative and quantitative improvements over the recent state-of-the- art synthesis methods. Cardiac MRI specific constraints are exploited in: "Cardiac MRI Segmentation with a Dilated CNN Incorporating Domain-specific Constraints". Simantiris *et al.* present a dilated convolutional neural network and accompanying customized augmentation scheme.

"Data-Adaptive Similarity Measures for B-mode Ultrasound Images Using Robust Noise Models" appears as the first article in the theme of medical image understanding. Ouzir *et al.* design similarity measures from a maximum likelihood (ML) perspective, which allows them to take the US specificities into account. As opposed to the classical Rayleigh modelling, their proposed similarity measures incorporate more realistic scattering conditions, such as, varying speckle densities and shadowing. The theme continues with: "Adaptive constrained independent vector analysis: An effective solution for analysis of large-scale medical imaging data". In this paper, Suchita, Long, Calhoun and Adali introduce adaptive constrained independent vector analysis and demonstrate how it can be used effectively to extract meaningful functional networks from fMRI data. Dictionary learning for analysis is explored in: "Dictionary Learning-Based fMRI Data Analysis for Capturing Common and Individual Neural Activation Maps". Rui *et al.* develop a dictionary learning (DL) method to estimate sparse neural activations from multi-subject fMRI data sets. By exploiting the label information such as the patient and the normal healthy groups, the activation maps that are commonly shared across the groups as well as those that can explain the group differences are both captured.

The special issue concludes with two articles on interpretable or expressible deep networks. Algorithm unrolling for interpretable deep learning is pursued in: "Dense Recurrent Neural Networks for Accelerated MRI: History-Cognizant Unrolling of Optimization Algorithms". Hosseini *et al.* unroll the well-known proximal gradient method in a history cognizant manner with dense connections across iterations for improved performance. Their proposed history-cognizant approach reduces residual aliasing artifacts compared to its conventional unrolled counterpart without requiring extra computational power or increasing reconstruction time. The final article of the special issue is: "Geometric Approaches to Increase the Expressivity of Deep Neural Networks for MR Reconstruction". In this exciting paper, the authors apply bootstrapping and subnetwork aggregation to design more expressive deep networks for improving MR reconstruction without undue increases in computational expense.

The aforementioned articles confirm that *domain enriched learning for medical imaging* is a thriving research area. Yet, they represent only a small portion of the signal processing wisdom that has been garnered over decades and combined successfully with learning frameworks. We hope this special issue will prove timely and inspire greater interest in the area and for its potential to be fully realized.

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