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LEARNING GLOBAL BRAIN MICROSTRUCTURE MAPS USING TRAINABLE SPARSE ENCODERS

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ABSTRACT

Diffusion-Weighted Magnetic Resonance Imaging is the only non-invasive technique available to infer the underlying brain tissue microstructure. Currently, one of the promising methods for microstructure imaging is signal modelling using convex formulation, e.g. using the COMMIT framework. Despite the benefits introduced with such framework, an important limitation is the long convergence time, making the method unappealing for clinical applications. In order to address this limitation, we propose to use a neural network to learn the sparse representation of the data and perform an end-to-end reconstruction of the microstructure estimates directly from the diffusion-weighted data. Our results show that the neural network can accurately estimate the microstructure maps, 4 orders of magnitude faster than the convex formulation.

Index Terms— Diffusion MRI, Neural Networks, Sparse Encoding, Convex Optimization, Microstructure Imaging, Tractography.

1. INTRODUCTION

Diffusion-Weighted Magnetic Resonance Imaging (DW-MRI) has become the method of choice to probe the human brain's white matter *in-vivo* [1]. DW-MRI has been used for the reconstruction of the white matter pathways of the brain using so-called tractography algorithms [2]. However, tractography has been shown to be not a truly quantitative method [3, 4, 5, 6]. To overcome such limitation, the Convex Optimization Modeling for Microstructure Informed Tractography [7, 8] (COMMIT) framework was introduced by Daducci et al. in 2013. In previous studies, this framework was successfully used to recover Axon Diameter Indices [9] (ADI) from whole-brain tractography on ex-vivo monkey data [10] and on in-vivo human data [11]. However, even if the convex optimization formulation brings fast estimations for simple biophysical forward models, with the increase in complexity of the forward models, the optimization procedure can reach several hours/days of computation time. In the following sections, we propose the use of a deep neural network to learn the sparse representation of the data and perform an end-to-end reconstruction of the microstructure estimates directly from the DW-MRI data.

2. METHODS

2.1. COMMIT

The COMMIT framework associates whole-brain tractography streamlines—estimating the white matter pathways—and microstructure imaging in a joint formulation. The framework is expressed as a linear equation:

$$y = Ax + \mu, \tag{1}$$

where y contains the acquired DW-MRI voxels of the brain, A is a matrix generated applying multi-compartmental biophysical modeling, and μ is the acquisition noise. The contributions x of the compartments are estimated by solving a non-negative least-square problem:

$$\underset{x \geq 0}{argmin} ||Ax - y||_2^2. \tag{2}$$

The estimated coefficients x, which are associated to each streamline, are commonly projected back to the voxel space. This procedure generates biophysical maps allowing comparison to stat-of-art voxel-based methods [9, 12].

2.2. Learned Sparse Encoding

The goal of sparse encoding is to reconstruct an input signal using a linear combination of basis functions with a sparse set of coefficients. In the work of Gregor and LeCun (2010) [13], a learned method that computes approximations of optimal sparse codes in a fixed amount of times was proposed. The

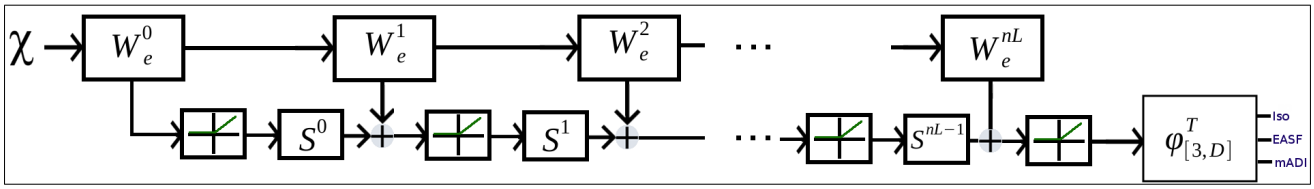

Fig. 1. Network architecture of LISTA, truncated to the number of layers nL. Matrices W_e and S are learned and correspond to the learned auto-encoder. The matrix ϕ^T is learned as part of the microstructure estimation rendered as a supervised learning classification.

method uses a time-unfolded neural network architecture where back-propagation through time can be applied. This method was coined Learned ISTA (LISTA) since it unfolds the popular ISTA algorithm [14], which solves the most common form of sparse encoding. This is summarized in equation 3,

$$E_{W_e}(X,Y) = \frac{1}{2}||X - W_e Y||_2^2 + \alpha||Y||_1, \qquad (3)$$

where W_e is a $N_{signals} \times N_{atoms}$ dictionary matrix of which the columns are the basis vectors, α is a coefficient controlling the sparsity penalty, and the vector Y is the signal data. ISTA finds the sparse coefficients X by iterating until convergence the following equation:

$$Y_{k+1} = h_\theta(W_e X + S Y_k), Y(0) = 0, \qquad (4)$$

where $W_e = \theta W_d^T$ is the filter matrix, $S = (I - \theta W_d^T W_d)$ is the mutual inhibition matrix θ-weighted, and $h_\theta(\cdot)$ is the shrinkage function [13]. The idea of LISTA is to unfold the iterative process in Equation 4 and map it into a sequential neural network as shown in Figure 1.

Sparse Encoding for Microstructure Estimation. In a previously proposed framework, Daducci et al. used sparse encoding to infer microstructure information using dictionaries of microstructure compartmentalized signals, coined as AMICO [12]. More recently [15] used the LISTA architecture to learn microstructure properties by mimicking the computation of the Neurite Orientation Dispersion and Density Imaging (NODDI) estimates as proposed in AMICO.

Inspired by Ye et al. (2017) [15], we propose to learn the sparse representation of the voxel-wise mean Axon Diameter Index (mADI) computed with the aforementioned COMMIT framework. Differently from local microstructure frameworks like AMICO, where the estimations are computed voxel-by-voxel independently, COMMIT computes the microstructure properties jointly for the whole-brain, using the geometry of the streamlines to create voxel connections. We use the LISTA Network architecture to map the voxel-wise DW-MRI signal to the estimated mADI by adding a full connected layer that maps directly into the learned coefficients.

2.3. In-Vivo Dataset and Processing

We used 34 subjects of the MGH-USC Human Connectome Project (HCP) Adult Diffusion Dataset [16, 17]. The DW-MRI acquisition scheme consists of 552 q-space samples over 4 shells with $b = 1, 3, 5, 10\ ms/\mu m^2$ and 40 $b = 0$ images. The DW-MRI images were acquired at $1.5mm$ isotropic voxel size (Spin-echo EPI sequence, $TR/TE = 8800/57ms$, $\delta = 12.9ms$, $\Delta = 21.8ms$). DW-MRI images were corrected for motion and EDDY currents [16]. The fibre Orientation Distribution Functions (ODFs) were computed using a single averaged fibre response (white matter voxels with fractional anisotropy above 0.7) as input for the spherical deconvolution [18, 19] on single-shell DW-MRI images ($b = 3ms/\mu m^2$ and a maximum spherical harmonic order 8). Partial Volume Estimates (PVEs) for the white matter, gray matter and cerebrospinal fluid were obtained from the provided T1-weighted using FSL/FAST [20]. We used the PVEs as input for the probabilistic Particle Filtering Tractography (PFT) algorithm [21, 22], and ten streamlines were initiated per voxel of the white matter volume, the resulting streamlines are shown in Figure 2a.

We used the COMMIT framework to estimate the ADI coefficients [9] for each streamline, Figure 2b, and the Extra Axonal Signal Fraction (EASF) for each voxel, as previously done in [10, 11]. We used the *Cylinder-Zeppelin-Ball* multi-compartment model [9, 23] with extra-axonal perpendicular diffusivity $d_\perp = \{0.51,\ 0.68,\ 0.85,\ 1.02\} * 10^{-3} mm^2/s$, isotropic diffusivity $d_\circ = 3.0 * 10^{-3} mm^2/s$, and intra-axonal longitudinal diffusivity $d_\parallel = 1.7 * 10^{-3} mm^2/s$ with 9 cylinders with diameters ranging from $2\mu m$ to $10\mu m$ [10, 11]. The mean Axon Diameter Index (mADI), Figure 2c, is reported voxel-wise as:

$$mADI = \frac{\sum_s^S w_s \cdot l_s \cdot ADI_s}{\sum_s^S w_s \cdot l_s}, \qquad (5)$$

where S is the set of all streamlines crossing the voxel, ADI_s is the ADI of the streamline s, l_s is the length of the segment intersecting the voxel, and w_s is the intra-axonal contribution of the streamlines.

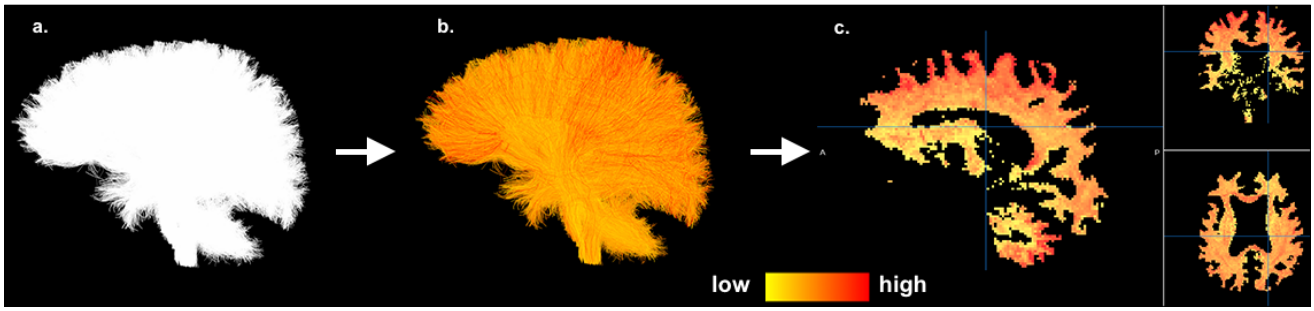

Fig. 2. a) Whole-brain tractography of one of the subjects of the HCP dataset; the white colour of the streamlines means that no quantitative information is associated to the tractography; b) Whole-brain tractography with streamlines colored according to the Axon Diameter Index (ADI) estimated using the COMMIT framework; c) Voxel-wise map of the mean Axon Diameter Index (mADI); left: sagittal view, top right: coronal view; bottom right: axial view.

2.4. Neural Network Parameters

Training data. We used a total of 20 subjects for training and 14 for testing. The input data consisted of all 552 q-space samples over the 4 shells for all the DW-MRI voxels inside a predefined white matter mask. The total number of input voxels counted in all training subjects was 3066226 voxels, and 2178620 voxels for the testing set. In this study, no validation set was employed.

Network Hyperparameter Tuning. We performed a selective tuning of the network parameters by discretely varying the following parameters and re-training the network: a) the number of hidden layers from 5 to 10 layers, which relates to the number of ISTA iterations to achieve convergence, b) The number of epochs from 200 to 500 epochs, c) The column-dimensionalty of the matrix W_e from 200 to 500, which is related to the number of dictionary atoms to learn in the encoder, and the dimension of the last layer for microstructure estimation denoted as D. Each network was generated by varying one parameter at the time and fixing all others to the median value in the compared range. In the following results we used the set of parameters which resulted in the lowest mean squared error over the training set, 8 layers, 300 columns, and 200 epochs.

3. RESULTS

Figure 3 shows the mADI and the EASF maps obtained for a single volume in the test dataset from both the Neural Network (NN) and COMMIT. The bottom row shows the difference map between both estimations. The overall mean (μ) and standard deviation (σ) of the mADI and ECSF error, calculated as the difference between the estimations of COMMIT and the NN over 14 training subjects, were $\mu = 0.627$ and $\sigma = 0.083$, and $\mu = 0.028$ and $\sigma = 0.003$, respectively. In addition, a regular trend of high mADI estimations near the Corpus Callosum (CC) can be observed in both COMMIT and NN methods, as well as a decrease of the EASF in both maps in the same CC regions. The average computation time for COMMIT was approximately 15 hours per subject on a machine with 12 cores, while with NN, the computation time went down to a few seconds per subject using a NVIDIA Titan Xp GPU.

Limitation and future work: The presented work is exploratory in nature, and further experiments will be carried out in order to address some limitations, such as the quality of the microstructure maps. This can be done by using data with higher diffusion gradients strength to improve the sensitivity to smaller axon diameters' indices. Finally a thorough comparison of the network's architecture and convergence, for instance, against more robust architectures as the one proposed in [25] will be considered in future work.

4. CONCLUSIONS

In this work, we present a preliminary exploration of the use of learned sparse encoders in order to estimate tissue microstructure properties derived from a whole-brain tractography informed microstructure framework, i.e. COMMIT. The first advantage of the proposed method is the speed up in computation time of the microstructure maps from several hours for COMMIT to a few seconds. The second advantage is that the learned network can compute the microstructure maps directly from the raw DW-MRI data, and thus it doesn't require the use of tractography methods. The results presented in this work shows the feasibility of this approach to replicate such maps accurately.

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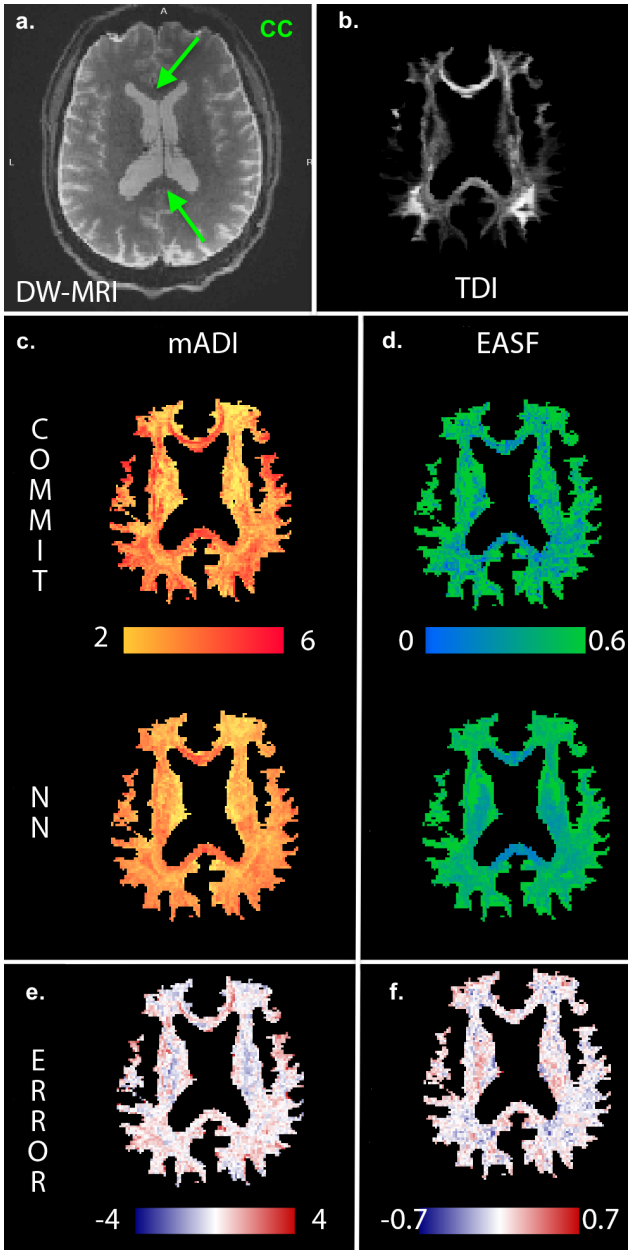

Fig. 3. a) axial view of the b0 image. b) Track Density Imaging [24] (TDI) counting the number of tractography streamlines passing through each voxel. c) Top: mADI map estimated with COMMIT; bottom: mADI map estimated with the neural network (NN). d) Top: EASF map estimated with COMMIT; bottom: EASF estimated with the NN. e) Map of the difference between the mADI estimated with COMMIT and with the NN. f) Map of the difference between EASF estimated with COMMIT and with the NN.

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5. REFERENCES

[1] D.K. Jones, *Diffusion MRI: Theory, Methods, and Application*, Oxford University Press, 2010.

[2] B. Jeurissen, M. Descoteaux, S. Mori, and Leemans A., "Diffusion MRI fiber tractography of the brain," *NMR in Biomedicine*, 2017.

[3] S. Jbabdi and H. Johansen-Berg, "Tractography: where do we go from here?," *Brain connectivity*, 2011.

[4] K. H. Maier-Hein, P. F. Neher, J.-C. Houde, M.-A. Ct, E. Garyfallidis, J. Zhong, M. Chamberland, F.-C. Yeh, Y.-C. Lin, Q. Ji, W. E. Reddick, J. O. Glass, D. Q. Chen, Y. Feng, C. Gao, Y. Wu, J. Ma, H. Renjie, Q. Li, C.-F. Westin, S. Deslauriers-Gauthier, J. O. O. Gonzlez, M. Paquette, S. St-Jean, G. Girard, F. Rheault, J. Sidhu, C. M. W. Tax, F. Guo, H. Y. Mesri, S. Dvid, M. Froeling, A. M. Heemskerk, A. Leemans, A. Bor, B. Pinsard, C. Bedetti, M. Desrosiers, S. Brambati, J. Doyon, A. Sarica, R. Vasta, A. Cerasa, A. Quattrone, J. Yeatman, A. R. Khan, W. Hodges, S. Alexander, D. Romascano, M. Barakovic, A. Aura, O. Esteban, A. Lemkaddem, J.-P. Thiran, H. E. Cetingul, B. L. Odry, B. Mailhe, M. S. Nadar, F. Pizzagalli, G. Prasad, J. E. Villalon-Reina, J. Galvis, P. M. Thompson, F. D. S. Requejo, P. L. Laguna, L. M. Lacerda, R. Barrett, F. DellAcqua, M. Catani, L. Petit, E. Caruyer, A. Daducci, T. B. Dyrby, T. Holland-Letz, C. C. Hilgetag, B. Stieltjes, and M. Descoteaux, "The challenge of mapping the human connectome based on diffusion tractography," *Nature Communications*, vol. 8, no. 1, pp. 13, 2017.

[5] G. M. Innocenti, T. B. Dyrby, G. Girard, E. St-Onge, J.-P. Thiran, A. Daducci, and M. Descoteaux, "Topological principles and developmental algorithms might refine diffusion tractography," *Brain Structure and Function*, Sep 2018.

[6] K. G. Schilling, V. Nath, C. Hansen, P. Parvathaneni, J. Blaber, Y. Gao, P. Neher, D. B. Aydogan, Y. Shi, M. Ocampo-Pineda, S. Schiavi, A. Daducci, G. Girard, M. Barakovic, J. Rafael-Patino, D. Romascano, G. Rensonnet, M. Pizzolato, A. Bates, E. Fischi, J.-P. Thiran, E. J. Canales-Rodrguez, C. Huang, H. Zhu, L. Zhong, R. Cabeen, A. W. Toga, F. Rheault, G. Theaud, J.-C. Houde, J. Sidhu, M. Chamberland, C.-F. Westin, T. B. Dyrby, R. Verma, Y. Rathi, M. O. Irfanoglu, C. Thomas,

C. Pierpaoli, M. Descoteaux, A. W. Anderson, and B. A. Landman, "Limits to anatomical accuracy of diffusion tractography using modern approaches," *NeuroImage*, vol. 185, pp. 1 – 11, 2019.

[7] A. Daducci, A. Dal Palù, A. Lemkaddem, and J. Thiran, "A convex optimization framework for global tractography," in *IEEE 10th International Symposium on Biomedical Imaging (ISBI)*, 2013.

[8] A. Daducci, A. Dal Palù, A. Lemkaddem, and J. Thiran, "Commit: Convex optimization modeling for microstructure informed tractography," *IEEE Transactions on Medical Imaging*, 2015.

[9] D.C. Alexander, P.L. Hubbard, M.G. Hall, E.A. Moore, M. Ptito, G.J.M. Parker, and T.B. Dyrby, "Orientationally invariant indices of axon diameter and density from diffusion MRI," *NeuroImage*, 2010.

[10] M. Barakovic, D. Romascano, T.B. Dyrby, D.C. Alexander, M. Descoteaux, J.-P. Thiran, and A. Daducci, "Assessment of bundlespecific axon diameter distributions using diffusion mri tractography," in *Proc. 22nd Annual Meeting of the Organization for Human Brain Mapping (OHBM)*, 2016.

[11] M. Barakovic, D. Romascano, G. Girard, M. Descoteaux, J.-P. Thiran, and A. Daducci, "In-vivo bundlespecific axon diameter distributions estimation across the corpus callosum," in *Proc. 25nd Annual Meeting of the International Society for Magnetic Resonance in Medicine (ISMRM)*, 2017.

[12] A. Daducci, E.J. Canales-Rodrguez, H. Zhang, T.B. Dyrby, D.C. Alexander, and J.-P. Thiran, "Accelerated microstructure imaging via convex optimization (amico) from diffusion mri data," *NeuroImage*, 2015.

[13] K. Gregor and Y. LeCun, "Learning fast approximations of sparse coding," in *Proc. of the 27th International Conference on Machine Learning (ICML)*, 2010.

[14] I. Daubechies, M. Defrise, and C. De Mol, "An iterative thresholding algorithm for linear inverse problems with a sparsity constraint," *Communications on Pure and Applied Mathematics*, 2004.

[15] C. Ye, "Tissue microstructure estimation using a deep network inspired by a dictionary-based framework," *Medical Image Analysis*, 2017.

[16] Q. Fan, T. Witzel, A. Nummenmaa, K. Van Dijk, J. Van Horn, M. Drews, L. Somerville, M. Sheridan, R. Santillana, J. Snyder, T. Hedden, E. Shaw, M. Hollinshead, V. Renvall, R. Zanzonico, B. Keil, S. Cauley, J. Polimeni, D. Tisdall, R. Buckner, J. Van Wedeen, L. Wald, A. Toga, and B. Rosen, "MGHUSC Human Connectome Project datasets with ultra-high b-value diffusion MRI," *NeuroImage*, 2016.

[17] K. Setsompop, R. Kimmlingen, E. Eberlein, T. Witzel, J. Cohen-Adad, J.A. McNab, B. Keil, M.D. Tisdall, P. Hoecht, P. Dietz, S.F. Cauley, V. Tountcheva, V. Matschl, V.H. Lenz, K. Heberlein, A. Potthast, H. Thein, J. Van Horn, A. Toga, F. Schmitt, D. Lehne, B.R. Rosen, V. Wedeen, and L.L. Wald, "Pushing the limits of in vivo diffusion mri for the human connectome project," *NeuroImage*, 2013.

[18] J.-D. Tournier, F. Calamante, and A. Connelly, "Robust determination of the fibre orientation distribution in diffusion MRI: non-negativity constrained super-resolved spherical deconvolution.," *NeuroImage*, 2007.

[19] E. J. Canales-Rodrguez, J. H. Legarreta, M. Pizzolato, G. Rensonnet, G. Girard, J. Rafael-Patino, M. Barakovic, D. Romascano, Y. Alemn-Gmez, J. Radua, E. Pomarol-Clotet, R. Salvador, J.-P. Thiran, and A. Daducci, "Sparse wars: A survey and comparative study of spherical deconvolution algorithms for diffusion mri," *NeuroImage*, vol. 184, pp. 140 – 160, 2019.

[20] Y. Zhang, M. Brady, and S. Smith, "Segmentation of brain MR images through a hidden Markov random field model and the expectation-maximization algorithm.," *IEEE Transactions on Medical Imaging*, 2001.

[21] G. Girard, K. Whittingstall, R. Deriche, and M. Descoteaux, "Towards quantitative connectivity analysis: reducing tractography biases," *NeuroImage*, 2014.

[22] E. Garyfallidis, M. Brett, B. Amirbekian, A. Rokem, S. Van Der Walt, M. Descoteaux, and I. Nimmo-Smith, "Dipy, a library for the analysis of diffusion MRI data," *Frontiers in Neuroinformatics*, 2014.

[23] E. Panagiotaki, T. Schneider, B. Siow, M. G. Hall, M. F. Lythgoe, and D. C. Alexander, "Compartment models of the diffusion MR signal in brain white matter: A taxonomy and comparison," *NeuroImage*, vol. 59, no. 3, 2012.

[24] F. Calamante, J.-D. Tournier, G. D Jackson, and A. Connelly, "Track-density imaging (TDI): Super-resolution white matter imaging using whole-brain track-density mapping.," *NeuroImage*, vol. 53, no. 4, pp. 1233–1243, jul 2010.

[25] D. Perdios, A. Besson, P. Rossinelli, and J. Thiran, "Learning the weight matrix for sparsity averaging in compressive imaging," in *2017 IEEE International Conference on Image Processing (ICIP)*, Sept 2017.