



Published in final edited form as:

Conf Proc IEEE Eng Med Biol Soc. 2018 July ; 2018: 1267–1270. doi:10.1109/EMBC.2018.8512556.

A Deep Unsupervised Learning Approach Toward MTBI Identification Using Diffusion MRI

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Abstract

Mild traumatic brain injury (mTBI) is a growing public health problem with an estimated incidence of one million people annually in US. Neurocognitive tests have been used to both assess the patient condition and to monitor the patient progress. This work aims to directly use diffusion MR images taken shortly after injury to detect whether a patient suffers from mTBI, by incorporating deep learning techniques. To overcome the challenge due to limited training data, we describe each brain region using the bag of word representation, which specifies the distribution of representative patch patterns. We apply a convolutional auto-encoder to learn the patch-level features, from overlapping image patches extracted from the MR images. to learn features from diffusion MR images of brain using an unsupervised approach. Our experimental results show that the bag of word representation using patch level features learnt by the auto encoder provides similar performance as that using the raw patch patterns, both significantly outperform earlier work relying on the mean values of MR metrics in selected brain regions.

I. Introduction

Mild traumatic brain injury (mTBI) is a growing public health problem, which can cause loss of consciousness, headache, difficulty thinking, memory problems, attention deficits, mood swings and frustration. Recent work using MRI revealed that there are areas of subtle brain injury after mTBI; however, no single imaging metric has been shown to be sufficient as an independent biomarker [1]-[3].

While diffusion MRI has been extremely promising in the study of mTBI, identifying patients with recent mTBI remains a challenge. The gray matter such as the thalamus and white matter including the corpus callosum and frontal deep white matter have been repeatedly implicated as areas at high risk for injury in the literature. There have been some previous studies using machine learning techniques for mTBI identification from MR images [4]-[7], however the features used in those works are mainly hand-crafted features and may not be the most discriminative feature for this task.

In this work, we develop a machine learning framework to classify mTBI patients and controls using features extracted from diffusion MRI in the thalamus and corpus callosum.

The main challenge is that we only have limited samples (only 114), and each sample has a very high dimensional raw representation (multiple 3D MR volumes). Therefore, it is not possible to directly train a classification network using the raw MRI volume data as the input. We have proposed a new approach for feature extraction from MR images, where we first learn the feature representation of patches using a deep unsupervised learning approach [8], and then aggregate the features from different patches through a bag of word representation, and use them along with demographic and neuro-cognitive test features as the overall feature vector. We then use feature selection followed by a classification algorithm to identify mTBI patients. The block diagram of the overall algorithm is shown in Fig. 1. Through experimental study, we show that by learning patch level deep features and aggregating them through a bag of word representation for each brain region, we get much higher accuracy compared to using mean values of the various MR metrics in each region.

The rest of the paper is organized as follows. Section II provides the description of the proposed framework. Section III provides the experimental studies and comparison to other works. And finally the paper is concluded in Section IV.

II. The Proposed Framework

There have been some previous studies on mTBI classification using different sets of features, from demographic (such as age and gender) and neurocognitive to hand-crafted features from medical images. In this work we propose a framework for mTBI identification based on imaging, demographic, and neuro-cognitive features. We derive the imaging features from the specialized MR imaging protocols and related image metrics that are developed and shown to be promising for distinguishing mTBI patients from controls [1]-[3]. These metrics are summarized in Table I.

Because of the limitation of the number of samples, it is not possible to train a deep convolutional network to directly classify the brain images. To tackle this problem, and also based on the intuition that mTBI would only impact some local regions in the brain, we propose to represent each brain region by a bag of words (BoW) representation, which is the histogram of different clustered patch patterns among all patches in the region.

A main challenge in using such a representation is how to describe each local patch. Because mTBI does not necessarily impact all patches, we cannot infer the patch-level labels from subject-level labels. Therefore we cannot learn patch-level features through supervised learning. To overcome this problem, we apply an unsupervised learning approach at the patch level, and train an auto-encoder to learn features that can be used to reconstruct patches. In the following, we first explain how do we learn patch level features through training an auto-encoder, and then describe how do we aggregate the patch-level features using a bag of words representation for each region, and finally how to combine the region representations and other information for patient-level classification.

A. Patch Feature Learning Using an Auto-Encoder

In order to learn patch-level features without having labels, we use a convolutional auto-encoder [10]-[11], which is an unsupervised feature learning approach. Convolutional auto-

encoder gets an image patch as the input and performs multiple convolution plus downsampling layers to encode the image into some latent representation, and then uses these features to reconstruct the original patch through deconvolution. By doing so, the network is forced to learn some representative information that is sufficient to recover the image. The overall architecture of a convolutional auto-encoder is shown in Figure 2. Here, each layer of the network performs three operations: convolution, nonlinear transformation, and pooling (downsampling). After training this model, the latent representation in the mid-layer is used as patch feature representation.

In our study we consider two scenarios when training the convolutional auto-encoder. In one scenario, we train one model for each metric (such as FA, MK, RK, etc.). In the other scenario, we concatenate all metrics together (treat them as different channels) to form a 3D patch and train one convolutional auto-encoder. We use the same model for all regions (Thalamus and CC).

B. Bag of Visual Words

Once the features are extracted from each patch, we use the bag of words (BoW) representation [9] to describe each brain region, which calculates the histogram of representative patterns (or visual words) over all patches in this region. To find the visual words, we apply the K-means clustering algorithm to the patch features obtained for all training patches. Given the MR images of a subject, we extract overlapping patches from each of two brain regions (Thalamus and CC) Each patch is quantized to its closest visual words, and each metric in each region is described by a histogram of different visual words among all patches in this region. In the case where we trained a single auto-encoder to generate a single feature representation for all metrics together, each region is represented by a single histogram. The block diagram of the BoW approach is shown in Figure 3.

C. Feature Selection and Classification

After deriving deep-bag-of-words features from diffusion MR images, we will get two feature vectors, one for Thalamus region and the other for Corpus Callosum. We concatenate the features from both regions, with demographic and neuro-cognitive test features, to form the final feature vector. We then perform feature selection [12]-[13] to minimize the risk of over-fitting before classification. We tried multiple feature selection approaches such as max-relevance and min-redundancy (MRMR) [14], maximum correlation, greedy forward selection, and it turns out that the greedy forward feature selection works best for our problem. This approach selects the best features one at a time with a given classifier, through a cross-validation approach. For classification, we tried different classifiers (such as SVM, neural network, and random forest) and SVM was chosen because it generally gave better performance.

III. Experimental Results

We evaluate the performance of the proposed approach on our dataset of 114 subjects. This dataset contains 69 mTBI subjects between 18 and 64 years old, within 1 month of mTBI as

defined by the American College of Rehabilitation Medicine (ACRM) criteria for head injury and 40 healthy age and sex-matched controls.

To evaluate the model performance, we use a cross validation approach, where each time we randomly take 20% of the samples for validation, and the rest for training. We repeat this procedure 50 times (to decrease sampling bias), and report the average validation error as the model performance.

For the convolutional auto-encoder, we learn features on patches of 16×16 pixels in each image slice. The encoder and decoder each have 4 layers, and the kernel size is always set to (3,3). The latent feature dimension is 32 for the networks which are trained on each metric, and 64 for the network which is trained on the stack of all metrics. To train the model, the batch size is set to 500, and the model is trained for 10 epochs. The learning rate for the stochastic gradient descent is set to 0.0003. The learnt auto-encoder is used to generate latent features on each overlapping patch in the training images. The resulting features are further clustered to N words using K-means clustering. N was varied among 20, 30, and 40. Each MR metric in each region is represented by a histogram of N dimension. For SVM, we use radial basis function (RBF) kernel. The hyper-parameters of SVM model (kernel width gamma, and the mis-classification penalty weight, C) are tuned based on the validation set.

In the first experiment, we compare the proposed approach with some previous works. For the proposed approach, the initial image feature representation is 260 dimensional, with 20 words for each of 8 MR metrics (AWF, DA, De par, FA, MD, AK, MK, RK) in Corpus Callosum, and 5 MR metrics in Thalamus (FA, MD, AK, MK, RK). Together with additional 2 demographic and clinical features, the total feature dimension is 266. We compare our approach with previous works that only used mean values of each MR metric in each region [6], and also the work in [4], as well as BoW approach on raw patches [6] (that is, we find the visual words by applying the K-means clustering algorithm on the raw image patches directly). It is worth to mention that the work in [4] was using a different dataset, and set of metrics.

With forward feature selection using the SVM classifier, the optimal feature subset contains 10 features FA in Thal, DA in CC, AWF in CC, AWF in CC, AWF in CC, FA in CC, RK in Thal, MK in Thal, RK in CC, FA in Thal. The comparison with previous works is provided in Table II. As we can see, Deep-BoW approach achieves reasonable improvement over previously used features, except for BoW on raw patches where it performs slightly worse than using the raw pixel values. We believe the performance of Deep-BoW could be further improved by better tuning the deep network hyper-parameters.

We have also evaluated the classification performance for feature subset of different size. Besides classification accuracy, we also report the sensitivity and specificity, which are important in the study of medical data analysis. The sensitivity and specificity are defined as in Eq. (1), where TP, FP, TN, and FN denote true positive, false positive, true negative, and false negative respectively. In our evaluation, we treat the mTBI subjects as positive.

$$\text{Sensitivity} = \frac{TP}{TP+FN}, \quad \text{Specificity} = \frac{TN}{TN+FP} \quad (1)$$

Figure 4 denotes the classification accuracies, sensitivities and specificities achieved by optimum subset of feature of dimension 1 to 10.

In Table III, we provide the comparison between the two scenarios, where in one of them one network is trained per metrics, and in the other one a single network is trained over the stack of multiple metrics (for different number of words).

To have a better generalization accuracy analysis, we also provide the comparison in terms of the accuracy on a heldout set. In each run, we randomly pick 20 samples as the heldout set. We then run cross validations 50 times within the remaining data, to generate 50 models, and use the ensemble of 50 models to make prediction on the held-out set and calculate the classification accuracy. We repeat this 6 times, each time with a different set of 20 heldout samples chosen randomly and report the average accuracy. For this evaluation, we only compare two BoW based approaches, one derived by applying K-means on the raw patch images, and another by applying K-means on the patch level deep features. The average accuracy for the heldout sets for these two approaches are given in Table III. It is interesting that, although BoW using deep patch level features had lower cross validation accuracy in Table I, it had slightly higher heldout set accuracy. For BoW on raw patches, the selected subset of features includes: Age, MK in Thal, RK in Thal, Depar in CC, AWF in CC, Depar in CC, Depar in CC, RK in Thal, MK in Thal, FA in CC. For BoW using the deep features, the selected features include: FA in Thal, DA in CC, AWF in CC, AWF in CC, AWF in CC, FA in CC, RK in Thal, MK in Thal, RK in CC, FA in Thal. This comparison is provided on Table IV.

Finally, we present the the average histogram representation of patients, and compare it with the average histogram representation of control subjects. These histograms and their difference are shown in Fig. 5. As we can see mTBI and control subjects have clear differences in some part of these representations.

IV. Conclusion

In this work, we propose a machine learning framework for mTBI identification from diffusion MR images. First, deep unsupervised learning approach is used to learn feature representation for image patches, and then patch level features are aggregated in the form of the bag of word representation to form the overall image feature. These features are used along with demographic and neuro-cognitive features for patient identification. Then greedy forward feature selection and support vector machine are used to perform classification. Through experimental studies, we show that by learning deep visual features, we obtain significant gain over using mean values of various MR metrics in each brain region.

Acknowledgment

Research reported in this publication was supported by National Institute of Neurological Disorders and Stroke of National Institutes of Health under award number R21NS090349. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

References

- [1]. Raz E, Jensen JH, Ge Y, et al. "Brain iron quantification in mild traumatic brain injury: a magnetic field correlation study", *American journal of neuroradiology*, pp.1851–1856, 2011. [PubMed: 21885717]
- [2]. Tang L, Ge Y, Sodickson DK, Miles L, et al. "Thalamic resting-state functional networks: disruption in patients with mild traumatic brain injury", *Radiology*, 260(3), pp.831–840, 2011. [PubMed: 21775670]
- [3]. Zhou Y, Kierans A, Kenul D, Ge Y, Rath J, Reaume J, Grossman RI, Lui YW, "Longitudinal Regional Brain Volume Changes in Mild Traumatic Brain Injury Patients", *Radiology*, in press 2013.
- [4]. Lui YW, Xue Y, Kenul D, Ge Y, Grossman RI, Wang Y, "Classification algorithms using multiple MRI features in mild traumatic brain injury", *Neurology* 8314: 1235–1240, 2014. [PubMed: 25171930]
- [5]. Vergara VM, Mayer AR, Damaraju E, Kiehl KA, Calhoun V, "Detection of mild traumatic brain injury by machine learning classification using resting state functional network connectivity and fractional anisotropy", *Journal of neurotrauma*, 2017.
- [6]. Minaee S, Wang S, Wang Y, et al. "Identifying Mild Traumatic Brain Injury Patients From MR Images Using Bag of Visual Words", *Signal Processing in Medicine and Biology Symposium, IEEE*, 2017.
- [7]. Minaee S, Wang Y, Chung S, et al. "A Machine Learning Approach For Identifying Patients with Mild Traumatic Brain Injury Using Diffusion MRI Modeling", *ASFN 12th Annual Meeting*, 2017.
- [8]. Goodfellow I, Bengio Y, Courville A, "Deep learning", Cambridge: MIT press, 2016.
- [9]. Yang J, Jiang YG, Hauptmann AG, Ngo CW, "Evaluating bag-of-visual-words representations in scene classification", *Proceedings of the international workshop on multimedia information retrieval, ACM*, 2007.
- [10]. Masci J, Meier U, Ciresan D, Schmidhuber J, "Stacked convolutional auto-encoders for hierarchical feature extraction", *International Conference on Artificial Neural Networks*, 2011.
- [11]. Leng B, Guo S, Zhang X, Xiong Z, "3D object retrieval with stacked local convolutional auto-encoder", *Signal Processing* 112, 2015.
- [12]. Guyon I, Elisseeff A, "An introduction to variable and feature selection", *Journal of machine learning research*, 3(Mar), 1157–1182, 2003.
- [13]. Chandrashekar G, Sahin F, "A survey on feature selection methods", *Computers and Electrical Engineering*, Elsevier, 2014.
- [14]. Peng H, Long F, Ding C, "Feature selection based on mutual information criteria of max-dependency, max-relevance, and min-redundancy", *IEEE Transactions on pattern analysis and machine intelligence*, 2005.

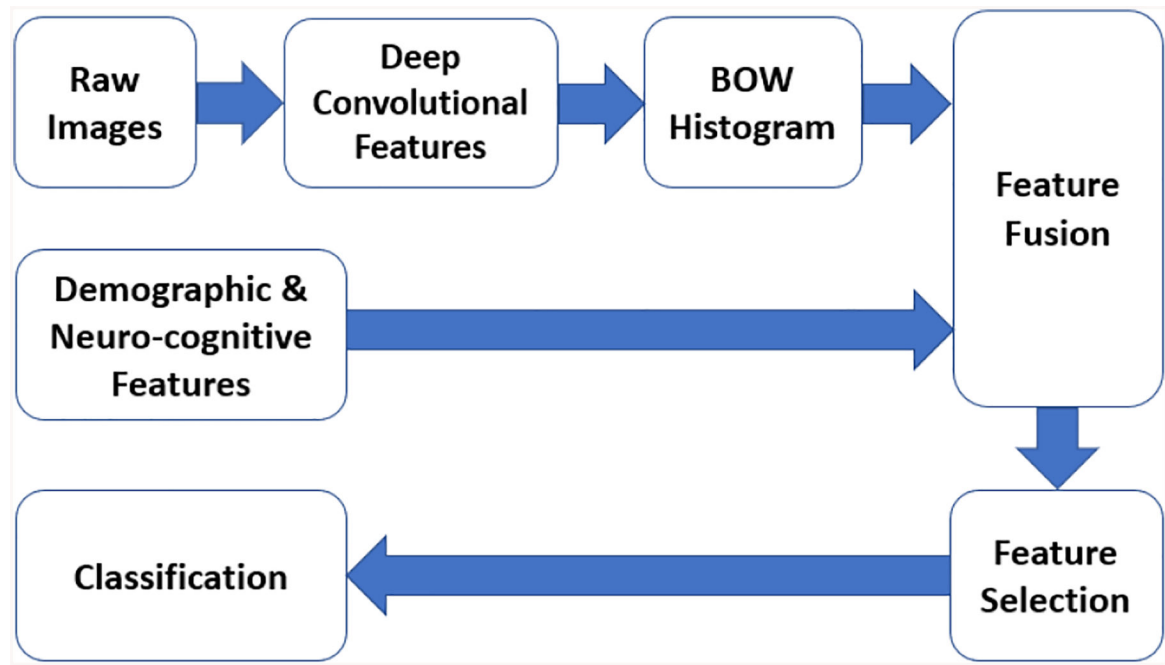


Fig. 1.

The block-diagram of the proposed mTBI identification algorithm

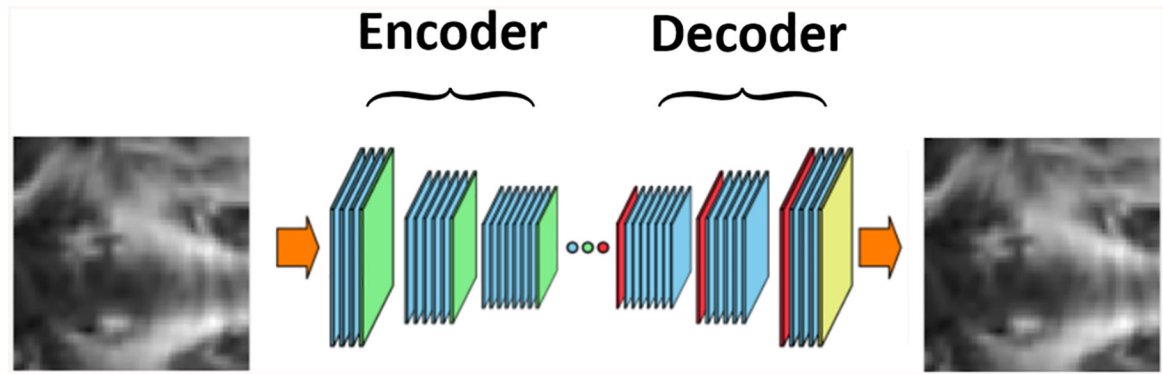


Fig. 2.
The block-diagram of the proposed convolutional auto-encoder

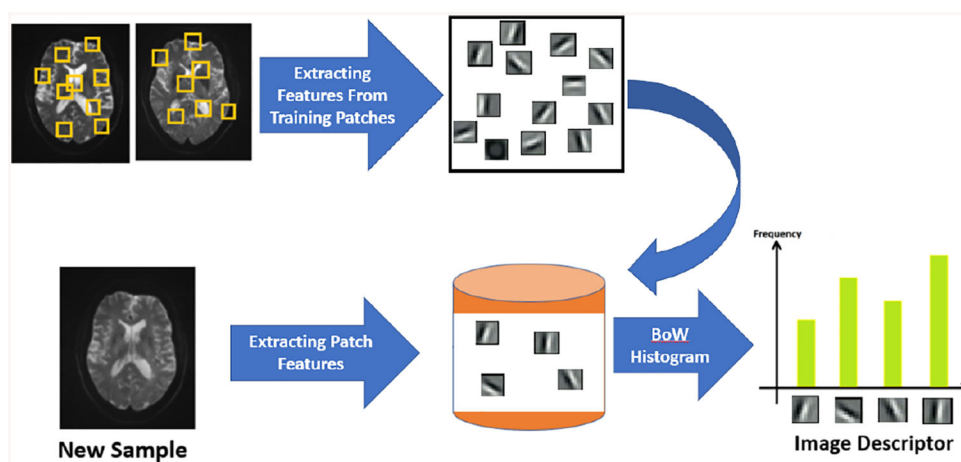


Fig. 3.
The block-diagram of the proposed BoW approach

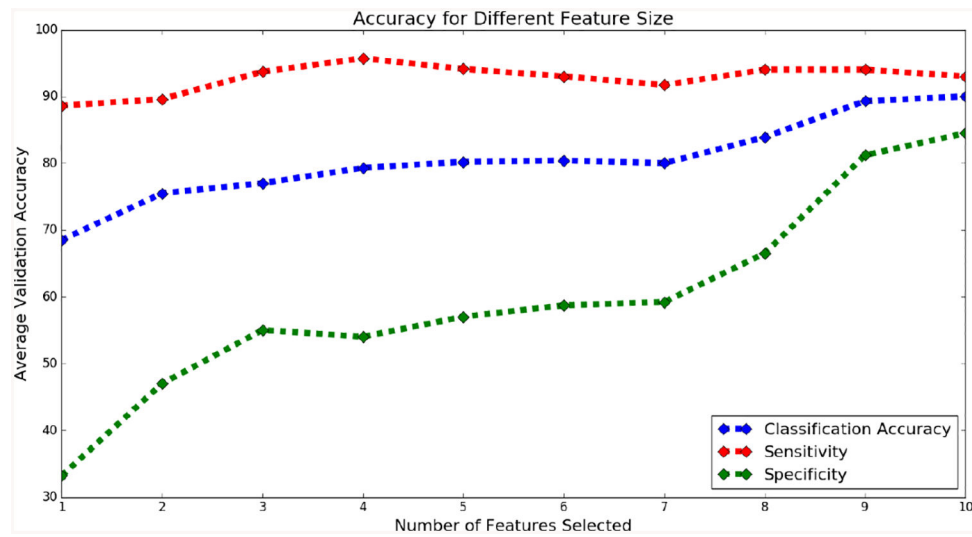


Fig. 4.
The model performance for feature set of different size

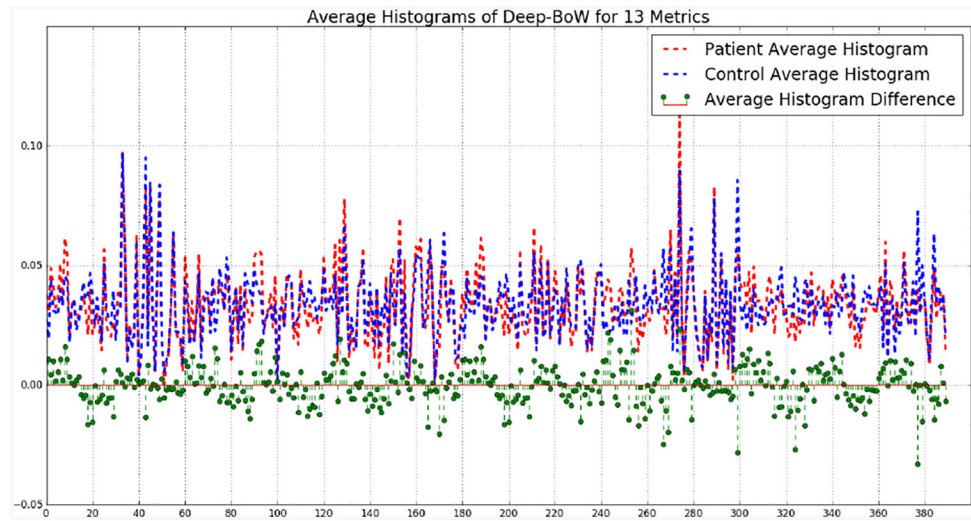


Fig. 5.
Deep-BoW histograms of patients and controls

TABLE I

MRI metrics description

MRI Metric	Metric Description
AWF	Axonal Water Fraction
DA	Diffusivity within Axons
De-par	Diffusion parallel to the axonal tracts in the extra-axonal
De-perp	Diffusion perpendicular to the axonal tracts in the extra-axonal
FA	Fractional Anisotropy
MD	Mean Diffusion
AK, MK, RK	Axial Kurtosis, Mean Kurtosis, Radial Kurtosis

TABLE II

Performance comparison of different approaches

The Algorithm	Classification Accuracy on Validation Set
Single best feature [6]	72%
The selected subset with 8 features [6]	80%
The algorithm in [4] using selected features with MRMR, and Bayesian Network	82%
BoW on raw patches and 10 metrics [7]	85.5%
The algorithm in [4] using selected features with MRMR, and Neural Network	86%
BoW on raw patches with 20D histograms [6]	92%
The proposed Deep-BoW with 20D histograms	87.8%
The proposed Deep-BoW with 30D histograms	90.1%

TABLE III

Performance comparison for different approaches

Auto-Encoder Scenario	Bow-Hist Dimension	Image Feature Dimension	Cross-Validation Accuracy
Multiple Network	20	260	87.8%
Multiple Network	30	390	90.1%
Single Network	130	260	89.4%
Single Network	190	380	90%

TABLE IV

Performance comparison of different approaches

The Algorithm	Heldout Set Accuracy
BoW on raw patches [6] using 20 words for each metric and region	86.2%
The proposed Deep-BoW	86.4%

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