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Classification of *small* lesions on dynamic breast MRI: Integrating dimension reduction and out-of-sample extension into CADx methodology

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ABSTRACT

Objective: While dimension reduction has been previously explored in computer aided diagnosis (CADx) as an alternative to feature selection, previous implementations of its integration into CADx do not ensure strict separation between training and test data required for the machine learning task. This compromises the integrity of the independent test set, which serves as the basis for evaluating classifier performance.
Methods and materials: We propose, implement and evaluate an improved CADx methodology where strict separation is maintained. This is achieved by subjecting the training data alone to dimension reduction; the test data is subsequently processed with out-of-sample extension methods. Our approach is demonstrated in the research context of classifying small diagnostically challenging lesions annotated on dynamic breast magnetic resonance imaging (MRI) studies. The lesions were dynamically characterized through topological feature vectors derived from Minkowski functionals. These feature vectors were then subject to dimension reduction with different linear and non-linear algorithms applied in conjunction with out-of-sample extension techniques. This was followed by classification through supervised learning with support vector regression. Area under the receiver-operating characteristic curve (AUC) was evaluated as the metric of classifier performance.
Results: Of the feature vectors investigated, the best performance was observed with Minkowski functional 'perimeter' while comparable performance was observed with 'area'. Of the dimension reduction algorithms tested with 'perimeter', the best performance was observed with Sammon's mapping (0.84 ± 0.10) while comparable performance was achieved with exploratory observation machine (0.82 ± 0.09) and principal component analysis (0.80 ± 0.10).
Conclusions: The results reported in this study with the proposed CADx methodology present a significant improvement over previous results reported with such small lesions on dynamic breast MRI. In particular, non-linear algorithms for dimension reduction exhibited better classification performance than linear approaches, when integrated into our CADx methodology. We also note that while dimension reduction techniques may not necessarily provide an improvement in classification performance over feature selection, they do allow for a higher degree of feature compaction.

1. Introduction

Computer aided diagnosis (CADx) aims to assist in the characterization of a previously annotated pattern in terms of its morphological or functional attributes, and in the estimation of its probability of pathological (or healthy) state [1]. Approaches to CADx typically involve three steps: (1) an extraction step where features characterizing the healthy or pathological patterns are computed, (2) a feature reduction step where the initial set of computed features are reduced to a smaller subset of features most relevant to the classification task, and (3) a supervised learning step where the classification performance of the pattern characterizing features is evaluated. This has been widely demonstrated in the current literature in several contexts such as chest CT [2,3], dynamic breast MRI [4–6], digital mammography [7,8], etc.

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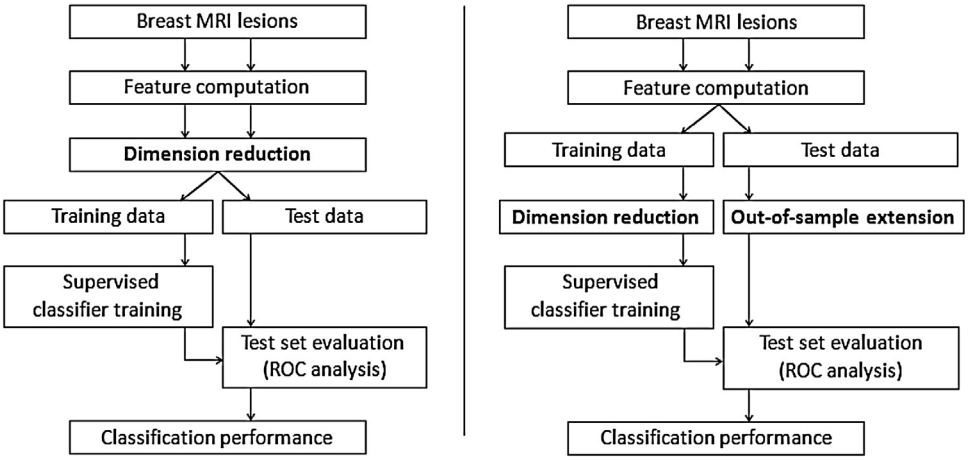

Fig. 1. A comparison of the CADx approach previously used in the literature (A) and our CADx methodology proposed in this study (B). Note the splitting of the data into training and test sets at different stages in each approach. Our proposed methodology limits the application of dimension reduction to the training data alone, thus preserving the integrity (independence) of the test set.

Of particular interest in this study is feature reduction, which aims to efficiently represent the originally extracted high-dimension pattern characterizing feature vectors in a low-dimension space; this has been previously accomplished through feature selection in CADx [5,6,9]. Feature selection involves reducing the size of the originally extracted feature set through exclusion of features that are either irrelevant to the feature task, or are redundant in information content. Recently, dimension reduction was proposed as an alternative to feature selection in breast CADx [7,10]. Rather than explicit inclusion or exclusion of specific features, such techniques allowed for algorithmic-dependent weighting of all features while computing a new feature set in the low-dimension space. While integration of dimension reduction into CADx presents an interesting innovation, the implementation is not without complications.

The supervised learning step, where features are evaluated in their ability to distinguish between healthy and pathological classes of patterns, is an important step in currently established CADx methodology. Here, a strict separation of training and test data is mandatory for proper execution of this step, especially since the performance of the features are evaluated on the test data. Feature selection can be easily integrated into CADx while maintaining this strict separation because it yields explicit selection of features that are best suited for the task. This allows simple selection of the *best* features from the training set alone for subsequent application to the test set. However, dimension reduction yields a new set of features in a different feature space; the mapping between the high-dimension feature set and the corresponding low-dimension representation is not as easy to interpret and subsequently replicate in the test set. Thus, the ideal approach to integrating dimension reduction in CADx while also maintaining strict training–test separation is not immediately clear. Previous approaches to integrating dimension reduction in CADx have taken to applying such algorithms to the entire dataset [7,10] which unfortunately violates the requirement of strict separation between training and test sets. This is attributed to the fact that dimension reduction imposes no such restriction regarding training–test data separation; data points from both sets are free to interact and influence the computation of their low-dimension representations. A direct consequence of such interaction between the training and test data, prior to the supervised learning step, is the *contamination* of the independent test set. Evaluating the performance of the classifier on such a test set is not representative of the real world application of CADx where all information about the test set would be completely hidden from the classifier until its training is complete.

To address this shortcoming, we propose an improved CADx methodology where the required strict separation between training and test data is maintained while concurrently integrating dimension reduction. This involves restricting the application of dimension reduction techniques to the training data alone. The low-dimension representation of data points in the test set are computed through out-of-sample extensions. A comparison of the CADx methodology proposed in this study and the one previously used is shown in Fig. 1. As shown here, the use of such out-of-sample extension techniques allows for integration of dimension reduction in CADx while maintaining the integrity of the independent test set.

We demonstrate our CADx methodology in the research context of classifying small diagnostically challenging lesions on dynamic breast magnetic resonance imaging (MRI). Breast cancer is among the leading causes of mortality for women in North America [11]. In this regard, dynamic contrast-enhanced MRI (DCE-MRI) has emerged as a promising diagnostic modality for detection and evaluation of suspicious mammographic lesions. However, while breast cancer diagnosis on DCE-MRI has been the subject of research in the area of CADx [4,5,12–21], not many studies have focused on evaluating the value of DCE-MRI in *small* lesions. Accurate diagnosis of such *small* lesions is clinically important for improving disease management in patients, where evaluating the dignity of breast lesions is specifically challenging as typical benign and malignant characteristics are harder to discern. In this regard, Leinsinger et al. reported a diagnostic accuracy of 75% in detecting breast cancer through cluster analysis of signal intensity time curves [22]. More recently, Schlossbauer et al., attempting to classify a dataset of small lesions (mean size 1.1 cm), reported an AUC value of 0.76 when using dynamic criteria [23].

Our work falls in the general research context of improving the classification performance of such *small* lesions on breast DCE-MRI. Here, we specifically focus on the evaluation of different feature reduction approaches through dimension reduction and feature selection using previously proposed topological feature sets derived from Minkowski functionals [24]. Our goals in this work are to evaluate the ability of such feature reduction algorithms in terms of the classification performance of the reduced feature sets as well as the degree of feature compaction achieved by both approaches, as discussed in the following sections.