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A new method based on MTANNs for cutting down false-positives:An evaluation on different versions of commercial pulmonary nodule detection CAD software [1]

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Abstract. One of the major problems for computer-aided pulmonary nodule detection in chest radiographs is that a high false-positive (FP) rate exists. In an effort to overcome this problem, a new method based on the MTANN (Massive Training Artificial Neural Network) is proposed in this paper. An MTANN comprises a multi-layer neural network where a linear function rather than a sigmoid function is used as its activity function in the output layer. In this work, a mixture of multiple MTANNs were employed rather than only a single MTANN. 50 MTANNs for 50 different types of FPs were prepared firstly. Then, several effective MTANNs that had higher performances were selected to construct the MTANNs mixture. Finally, the outputs of the multiple MTANNs were combined with a mixing neural network to reduce various different types of FPs. The performance of this MTANNs mixture in FPs reduction is validated on three different versions of commercial CAD software with a validation database consisting of 52 chest radiographs. Experimental results demonstrate that the proposed MTANN approach is useful in cutting down FPs in different CAD software for detecting pulmonary nodules in chest radiographs.

Keywords: False Positive, cutting down, Mixture of MTANNs, Commercial CAD

1. Introduction

Computer-aided diagnosis (CAD) has been proven to be a very effective in assisting radiologists and improving the diagnostic accuracy [1,2,3,4]. However, one of the main difficulties of applying the CAD for nodule detection on chest radiographs in clinical is the relatively great amount of false positives

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(FPs). Because of too many FPs, the performance of detecting true-positive regions may potentially be degraded, and there may also be a subsequent increase in "unnecessary" follow-up examinations.

For the aforementioned reasons, various past methods have been proposed to cut down FPs number [5,6,7,8], most of them have used a two-step pattern-recognition approach: i.e., feature extraction firstly and then classification with features. However, one main limitation associated with such methods is that classification performances directly depends on the discriminatory power of features, but to specify a suitable feature set is one of the most difficult tasks in classification.

Recently, Suzuki et al. showed that this limitation could be overcome by using a MTANN[9,10,11, 12,13,14]. The MTANN comprises a modified linear output multi-layer neural network with a linear function rather than a sigma function serving as its output layer activation function. Compared with the conventional pattern classification model, the MTANN has three major advantages: namely, (1) it can directly operate on pixel data; thus, no feature extraction is required; (2) it has a high generalization performance; and (3) it can be trained with a very small amount of cases [14]. Although the MTANN approach had demonstrated promise in its applications to chest radiography, thoracic CT, and CT colonography, it was not clear whether the MTANNs were capable of cutting down false-positives in different CAD schemes, especially, when it is applied to commercial CAD software.

Motivated by above mentioned problems, in this paper, a new method termed as a mixture of MTANNs was developed for cutting down FPs in a chest radiographs pulmonary nodule detection CAD scheme, which is an extension of Suzuki's works in [15] and [16]. We evaluate the performance of this MTANNs mixture on FPs produced by three different versions of commercial CAD software. Experimental results index that the approach is useful in cutting down FPs in different CAD software for determining the existence of pulmonary nodules in chest radiographs.

2. Materials and method

2.1. Materials

The database employed in our study comprised three validation test sets that produced by applying three different versions of commercial CAD software on a chest radiographs set which consisted of 29 posterior-anterior (PA) chest radiographs of nodule free cases and 23 PA chest radiographs with nodules acquired with a computed radiography system, Of the three validation test sets, 281 FPs and 29 nodules (produced by CAD software 1 (Riverain CAD Ver.1.0)) are included in set I, 143 FPs and 33 nodules (produced by CAD software 2 (Riverain CAD Ver.3.0)) are included in set II,and 108 FPs and 31 nodules (produced by CAD software 3 (Riverain CAD Ver.3.0)) are included in set III. The nodule locations were confirmed by a physician and were used as "gold standard" locations in the evaluation of our scheme.

2.2. Mixture of MTANNs

The key principle underlying this method is the conclusion that cutting down false-positives in computer-aided pulmonary nodule detection is a multi-classification problem in essence. To deal with such a multi-classification problem, multiple classifiers and their combination are needed. First, 50 M-TANNs for 50 different types of false positives were prepared, where an MTANN is a modified three layer artificial neural network (ANN) in which a linear, a sigmoid, and a linear function are employed as the activation function of the unit in the input, hidden, and output layers, respectively. Then, several effective MTANNs that had higher performances were selected to construct a MTANNs mixture. A M-

TANNs mixture is an ensemble of multiple MTANNs that comprises several parallel arranged MTANNs that are trained for the same task [15,16,17], as shown in Figure 1.

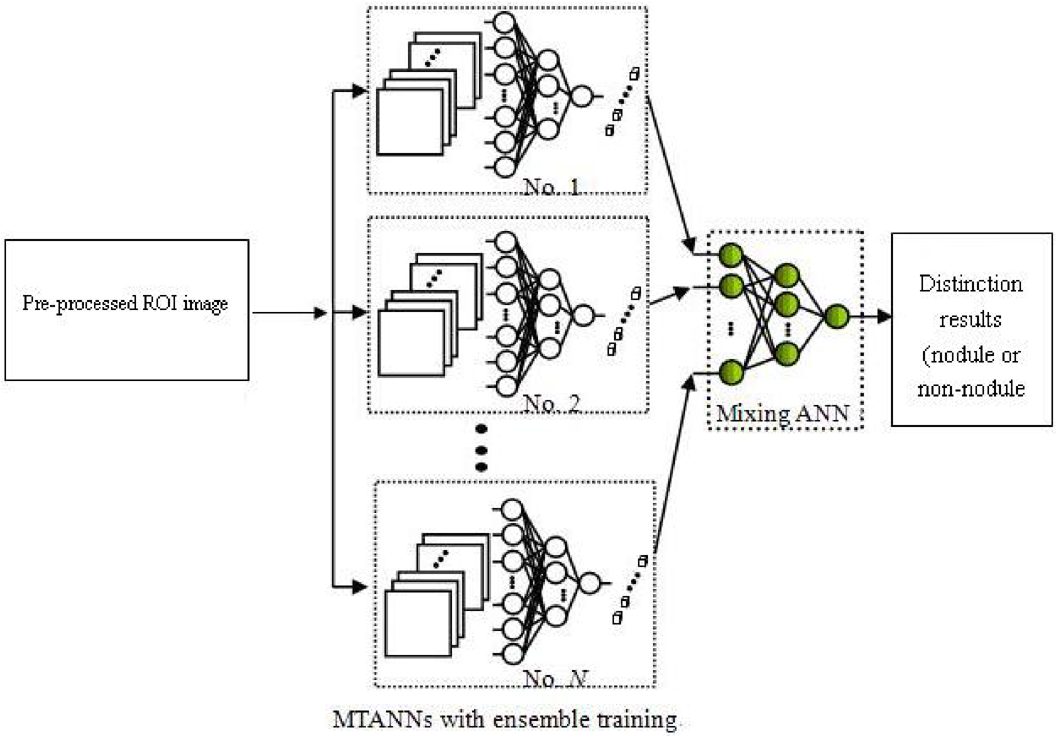

Fig. 1. Mixture of MTANNs.Each expert MTANN can distinguish a specific type of non-nodule from nodules. The outputs of these MTANNs are combined for removing various types of non-nodules (FPs).

In order to remove all major FPs sources, the outputs of multiple MTANNs were combined with a modified three layer BP neural net work, where an identity, a sigmoid, and a linear function are employed as the activation functions of the units in the input, hidden, and output layers, respectively. Each selected MTANN's outputs are used as the input of the combining neural network; the amount of the combining network's input units is determined by the amount of MTANNs. The output of each MTANN is used for discriminating nodules from a particular kind of non-nodule, as represented in Eq.(1):

$$O_m = NN[S_{n,c}], 1 \leq n \leq N \tag{1}$$

where $NN\{\bullet\}$ is the output of the modified three layer BP ANN. The referential values for nodules are decided as the value "1", and those for non-nodules are "0".

In order to cut down the effects caused by background on the MTANNs performance, an image pre-processing step [12] was utilized for input ROIs.

2.3. Training the mixture of MTANNs

A method termed as ensemble training [15] was employed for training the MTANNs mixture in this work. The cases for training the multiple MTANNs are systematically selected. A seed MTANN trained

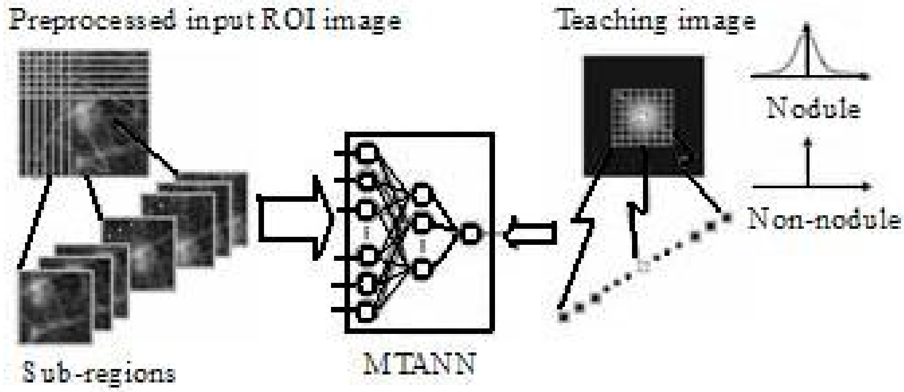

Fig. 2. Training of MTANN. The input image is divided into many overlapping sub-regions pixel by pixel, and then these sub-regions are preprocessed. All pixel values of each sub-regions are used as input to the MTANN, whereas a sigle pixel value from the teaching image is used as a teaching value.

with typical nodules and non-nodules of a seed type is selected firstly. Then, the seed MTANN was applied to nodules and various non-nodules.

The training for a single MTANN of the MTANNs mixture was implemented by using a large number ($361 = 19 \times 19$ pixels) of image blocks obtained by scanning the training region (27×27 pixels) in an input image pixel by pixel, also with the teaching images that contained the distribution for a "likelihood of being a nodule, as shown in Figure 2.

In order to ensure that each of the multiple MTANNs was the most effective for a particular kind of non-nodule, parameters for the multiple MTANNs were optimized. We started from a seed set of training parameters. Each MTANN was trained based on the seed parameter set, and each MTANN's performance was valuated by using the receiver-operating-characteristic (ROC) analysis. Based on the valuation results of the ROC ,better parameters for each MTANN was determined.

All MTANNs with optimized parameters were applied for identifying nodules and non-nodules. Each selected MTANN's outputs were used as an input to the combination ANN with an input, a hidden, and an output layer,where the numbers of units in the three layers were determined based on experiments to be 8, 7, and 1 , respectively. The training of the combination ANN was performed by using a leave-one-nodule-out cross-validation scheme. After trained, the ANN could be used to classify a nodule and a non-nodule.

2.4. Distinct nodules from non-nodules

The identification of a nodule and a non-nodule is obtained by using a score defined from the output images of the n^{th} trained MTANN and a 2D Gaussian weighting function [12], as shown in the following equation:

$$S_{ns} = \sum_{x,y \in R_E} f_G(\sigma_n, x, y) \times f_{ns}(x, y) \tag{2}$$

where S_{ns} is the score of the n^th trained MTANN for the s^th nodule candidate, R_E is the region for evaluation, $f_{ns}(x, y)$ is the output image of the n^th trained MTANN for the s^th nodule candidate where its center corresponds to the center of R_E, $f_G(\sigma_n, x, y)$ is a 2D Gaussian function with deviation σ_n, and n is the MTANN number in the multiple MTANNs. This score represents the weighted sum of the

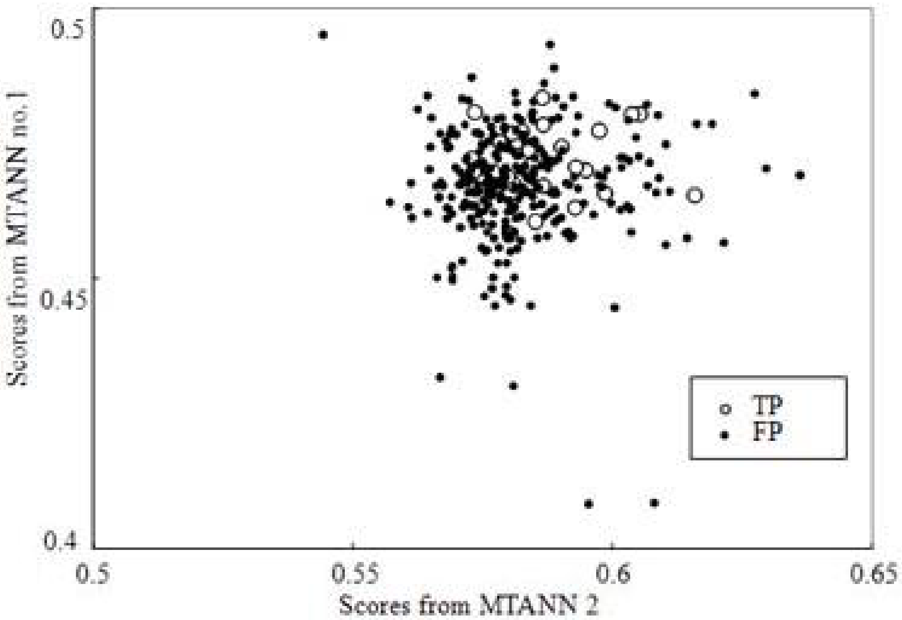

Fig. 3. Distributions of scores from MTANN No.1 and MTANN No.2 for nodules and non-nodules in validation set 1.

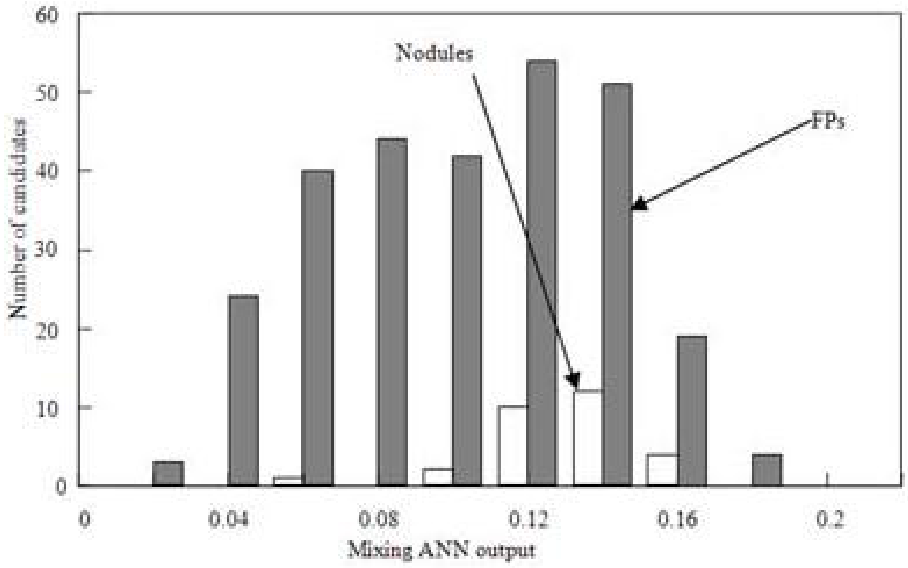

Fig. 4. Distribution of outputs from the trained mixing neural network for validation set 1.

estimate of how likely a nodule is. Then, the abilities of these MTANNs to cut down false-positives were arranged in an ascending order.

As an example, the score distributions of the output images of validation test set 1 from MTANN No.1 and MTANN No.2 are shown in Figure. 3. As can be seen from Figure.3 that each expert MTANN re-

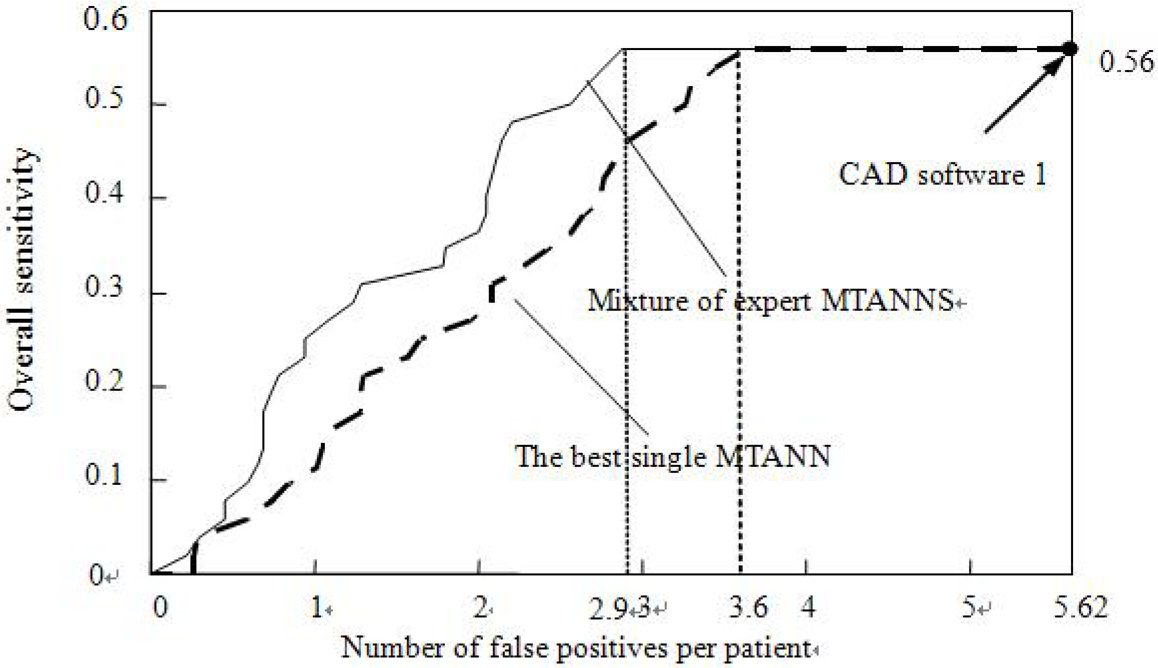

Fig. 5. The FROC curve of the MTANNs mixture of(thick solid curve) and that of the best single MTANN (dashed curve) for 281 FPs and 29 nodules by CAD software 1

moved different FPs. Accordingly, using the MTANNs mixture removes a substantial fraction of various FPs.

In order to distinguish nodules from various FPs, several effective MTANNs for non-nodules at certain difficulty levels were selected. In this study, four most effective MTANNs were selected and merged with a mixing ANN. An example for validation test set 1 was shown in Figure 4. As it can be seen that all nodules can be discriminated from the majority of FPs, though the distributions overlap.

3. Experimental results

The overall performance of the MTANNs mixture for FPs reduction was valuated on three different versions of commercial CAD software using the free-response ROC (FROC) analysis. Figure 5-7 show the experimental results on different CAD software,respectively.As can be seen from Figure 5,Figure6, and Figure 7 that with the MTANNs mixture, the false-positive rate of CAD software 1 was cut down by 48% (from 5.62 to 2.93 FPs per image) while maintaining an original sensitivity of 60%; that of CAD software 2 was cut down by 44% (from 2.86 to 1.6 positives per image) while maintaining an original sensitivity of 60%; and that of CAD software 3 was cut down by 49% (from 2.16 to 1.1 FPs per image) while maintaining an original sensitivity of 60%. In contrast, at a same sensitivity level,with the best single MTANN, the FP rate of CAD software 1 was cut down by 36% (from 5.62 to 3.6 FPs per image),the FP rate of CAD software 2 was cut down by 23% (from 2.86 to 2.2 FPs per image), and CAD software 3 was cut down by 12% (from 2.16 to 1.9 FPs per image). These results suggest that the capability of a MTANNs mixture is superior to that of a single MTANN.

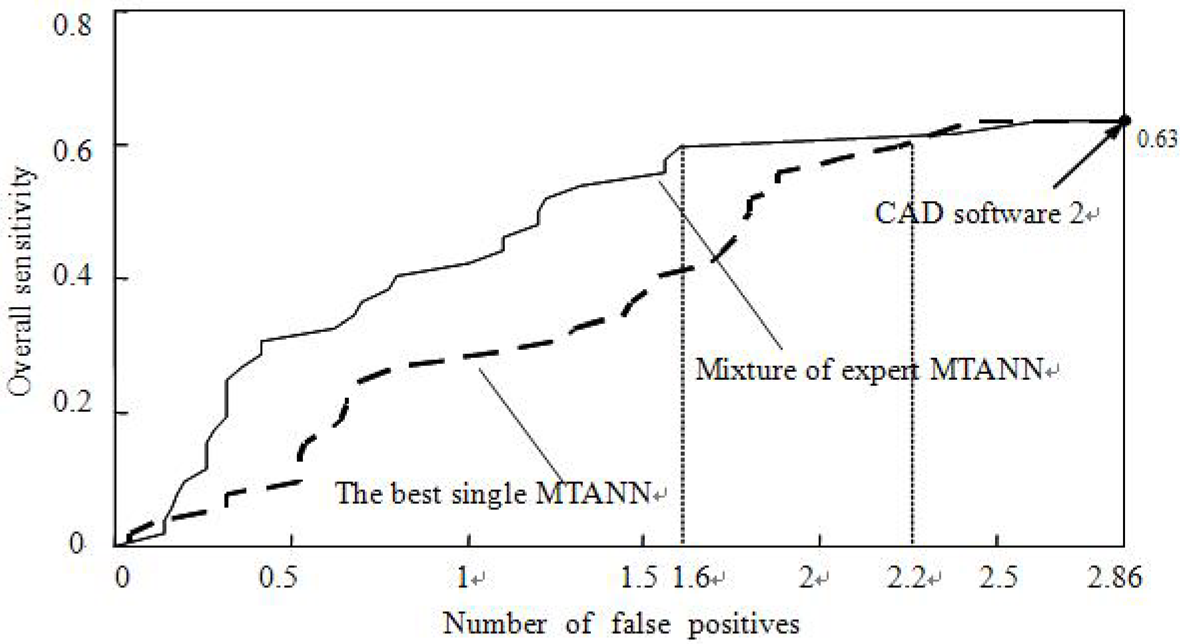

Fig. 6. The FROC curve of the MTANNs mixture(thick solid curve) and that of the best single MTANN (dashed curve) for 143 FPs and 33 nodules by CAD software 2.

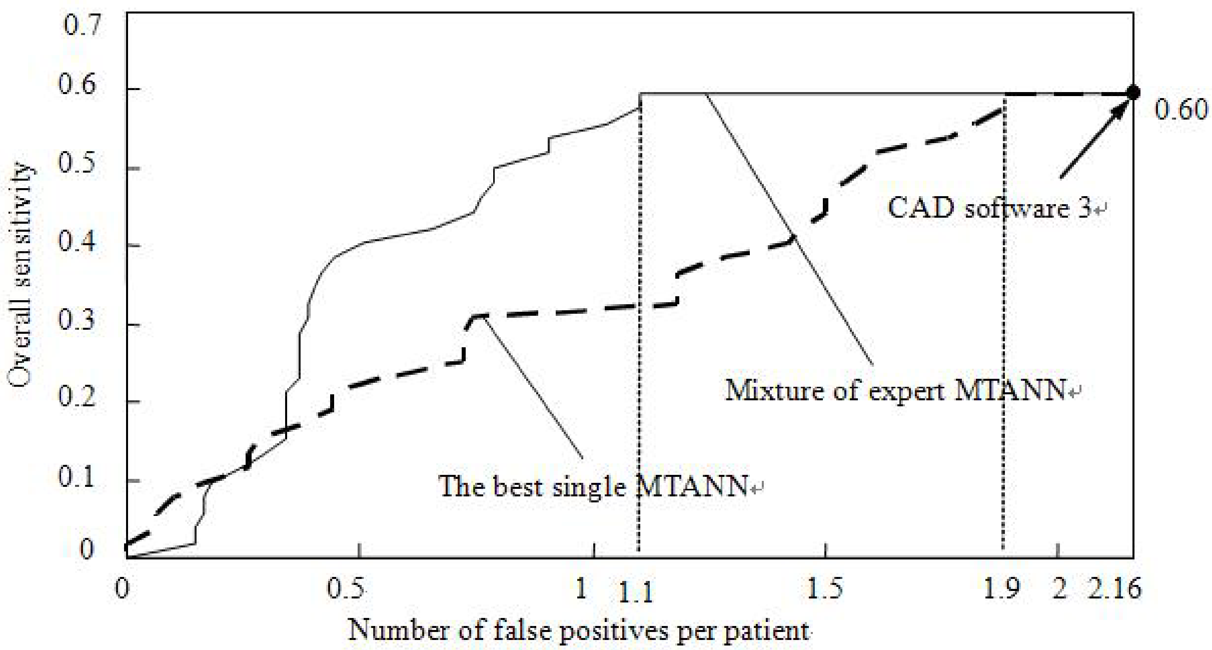

Fig. 7. The FROC curve of the MTANNs mixture(thick solid curve) and that of the best single MTANN (dashed curve) for 108 FPs and 31 nodules by CAD software 3.

4. Conclusion

An MTANNs mixture based method for FPs reduction was developed in this paper. Experiments on datum produced by three different versions of commercial CAD software for detecting pulmonary nodules in chest radiographs show the MTANNs mixture could substantially cut down the false-positive rate of each of the three CAD softwares, while still preserving a high sensitivity level.

However,it should be noted that the number of test cases in this work is limited, and more test cases should be employed for valuating the performance of the MTANNs mixture. This is a step that will be taken in future studies.

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