Prediction of the Exact Degree of Internal Carotid Artery Stenosis Using an Artificial Neural Network Based on Duplex Velocity Measurements

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Duplex ultrasound criteria use a combination of velocity measurements to evaluate internal carotid artery (ICA) stenosis. These evaluations divide ICA stenosis into broad categories. The aim of this study was to design an artificial neural network (ANN) capable of predicting the exact degree of ICA stenosis based on duplex velocity measurements. Consecutive patients with significant carotid atherosclerosis underwent carotid duplex ultrasound and angiography. Peak systolic and end-diastolic velocities in the ICA and common carotid artery were measured. Multilayered perceptron ANNs were constructed and trained to predict the degree of ICA stenosis and band the degree of ICA stenosis into 10% intervals based on these measurements. The accuracy of the ANN models in predicting the degree of ICA stenosis and classifying the ICA stenosis was compared with the angiographic degree of ICA stenosis and duplex velocity criteria. A total of 208 carotid bifurcations were studied. ANNs were able to accurately predict the degree of angiographic ICA stenosis ($R^2 = 0.9374$, $p < 0.0001$) and band the ICA stenosis into the predefined 10% intervals [sensitivity 97.3% (95% CI 90.7-99.3), specificity 97.7 % (95% CI 93.6-99.2), accuracy 97.5%]. The ANN model was more accurate [discriminant power (DP) = 4.11] in banding the degree of ICA stenosis than duplex velocity criteria (DP = 1.67) ($p < 0.05$). The accuracy of the ANN in correctly identifying >70% ICA stenosis was 98.4% [sensitivity 96.4% (95% CI 93.8-99.3), specificity 98.7% (95% CI 93.4-99.8), DP = 4.21]. ANNs can accurately predict the degree of ICA stenosis. With further refinement, ANNs could replace velocity criteria in the assessment of ICA stenosis using duplex ultrasound.

INTRODUCTION

Randomised trials have confirmed the value of carotid endarterectomy compared with the best medical treatment for patients with significant extracranial internal carotid artery (ICA) stenosis.[1,2] These trials have required confirmation of the degree of stenosis with contrast angiography, which has been used as the gold standard for the measurement of ICA stenosis and to confirm the presence of ICA occlusion. However, angiography has a significant morbidity and a low but significant mortality rate.[3] As the technology has improved and experience has broadened, duplex ultrasound

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scanning has been found to provide sufficient information for clinical decision making in patients with ICA stenosis.[4] This is performed by obtaining peak systolic (PSV) and end-diastolic velocities (EDV) at the stenosing lesion, ICA/common carotid artery (CCA) velocity ratios, and subjective assessment of the Doppler waveform at the site of maximal stenosis and the B-mode appearance of the atherosclerotic plaque.[5-8] Cut-off values for these measurements are used to define the degree of ICA stenosis. Whilst these cut-off values are calculated using receiver operator characteristic curves, the combination of these measurements is based on empirical selection, with not enough statistical data to support which values best represent the degree of ICA stenosis,[9] especially in the presence of confounding variables such as contralateral ICA occlusion. With the increase in use of duplex ultrasound, there has been a proliferation in the number of duplex velocity criteria for measurement of the degree of ICA stenosis. These classifications vary between laboratories both in their method of calculation and in the range of degrees of stenosis used to describe each stratification or band.[10,11]

Banding of the degree of ICA stenosis using duplex criteria usually involves classification of the degree of ICA stenosis into 20% bands. Earlier broad categories did not allow an adequate estimation of the degree of ICA stenosis to provide all the information needed for clinical decision making in accordance with the Asymptomatic Carotid Atherosclerosis Study (ACAS) and the North American Symptomatic Carotid Endarterectomy Trial (NASCET).[12] A recent paper by Filis et al.[12] suggested that it is possible to accurately band the degree of ICA stenosis into 10% intervals for stratifying 50-100% carotid stenosis. Although this duplex velocity criterion does not estimate the exact degree of ICA stenosis, it provides the closest clinical method with which other models attempting to achieve a similar degree of accuracy can be compared.

The aim of this study was to examine the hypothesis that an artificial neural network (ANN) based on the most commonly used duplex velocity measurements is capable of measuring the degree of ICA stenosis and to evaluate its performance in correctly classifying the degree of ICA stenosis with a comparable, clinically used method.[12]

ANNs are a family of computational algorithms which are modeled on the capabilities of the human nervous system.[13-15] They permit recognition of patterns in data that cannot be detected with linear statistical analysis.

The neuron (node) is the basic computational unit of an ANN. It receives a variety of inputs from other neurons through connections that resemble synaptic structure and has a binary (all or nothing) output.[13] This output is determined by the sum of the inputs as well as the weight (synaptic strength) attached to these input variables.[15] The weight attached to each node is altered through a period of familiarization "training" until an optimal weight which best describes the influence of the data set, represented by the node, is reached. Each of the input nodes corresponds to a single input variable. Initial values are set for the "weights" associated with each link in the network. Input data for which an output is known are presented to the network. If the predicted output from the model does not equal the known output, the weights within the network are changed so as to narrow this difference. This process continues until the prediction errors are minimised. Once the network is trained and validated, it may be used on unseen data for prediction or classification purposes.[15]

A wide variety of neural network designs with varying degrees of complexity have been described.[15] The simplest and most commonly used form is the multilayered perceptron (MLP). The structure of this neural network model is illustrated in Figure 1.[15]

METHODS

Between April 1998 and April 2000, consecutive patients who were admitted for assessment of ICA stenosis were assessed. All patients underwent carotid duplex ultrasound scanning as well as intra-arterial digital subtraction angiography (IADSA) for assessment of the degree of extracranial carotid artery stenosis during the same hospital stay (within 3 days). At the time, angiography was routine practice in our department for patients with severe ICA stenosis (prior to carotid endarterectomy) or who had recent ocular or hemispheric symptoms together with a suspected ICA occlusion on previous duplex scanning.

Carotid Duplex Scanning

Duplex ultrasound imaging was performed using an Acuson 128 XP duplex ultrasound system with a 7.5 MHz linear array probe (Acuson, Mountain View, CA) and a 60-degree angle of insonation. PSV and EDV were measured through spectral analysis at the stenotic portion of the ICA. Representative recordings of PSV and EDV were also

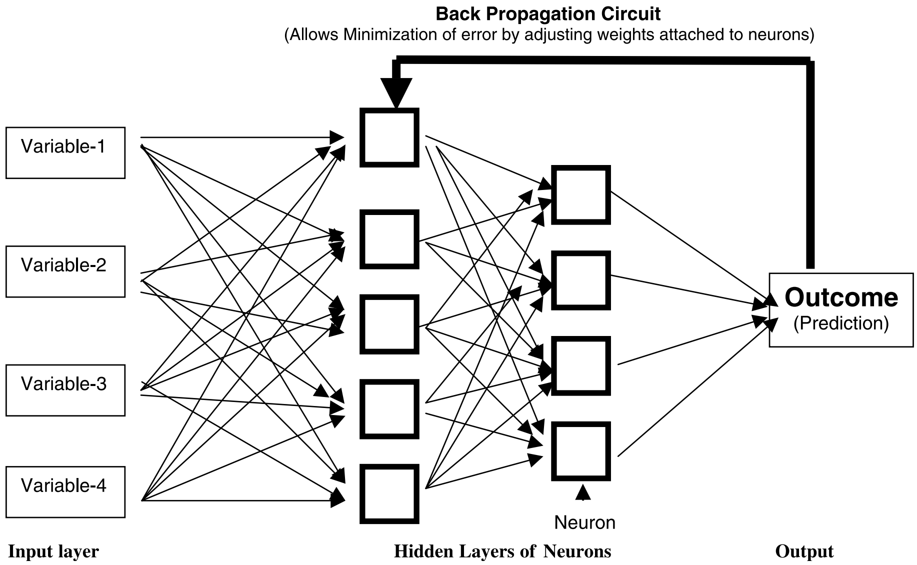

Fig. 1. A simplified diagram depicting MLP structure (for simplicity, weights associated with connections are not shown).

performed in a nonstenotic portion of the distal CCA. ICA stenosis severity was graded using haemodynamic evaluation of index stenotic vessels based on standard grading criteria.[12] These evaluations were performed retrospectively by two experienced observers, who at the time of evaluation were unaware of the identity of the patient, clinical findings, and the angiographic measurement of the degree of ICA stenosis.

Angiography

Standard IADSA was performed by retrograde catheterization via the femoral arteries. Two projections of carotid bifurcation were obtained routinely. Digitally magnified views were used to obtain the angiographic measurements.

Blinded angiographic evaluation was performed by two observers (R.M. and T.P.). The diameter of the ICA at the site of maximal stenosis and the diameter of the poststenotic ICA were measured using precision Vernier calipers to the nearest 0.1 mm. The degree of stenosis was obtained by comparing the residual angiographic lumen with the diameter of the normal distal ICA.[1]

Interobserver agreement in the measurement of ICA stenosis was assessed using linear regression and Bland-Altman analysis.[16]

Neural Network Design

MLP ANN models with a back-propagation circuit were constructed using Neuro-Solutions™ version 4 software (NeuroDimension, Gainesville, FL). This neural network design was selected because of its good analytical power and relative simplicity of design. The MLP models which were developed had six input nodes, consisting of entries corresponding to PSV and EDV in the ICA and prestenotic CCA, presence of contralateral ICA occlusion, and a bias node. The bias node performed a function similar to that of a regression constant in a standard linear regression model. The neurons in the hidden layer of these ANNs used a sigmoid activation function, which ensures that node output will lie in the range 0-1. The input data did not undergo any preprocessing steps prior to input into the neural network apart from randomisation of data sets. Two sets of ANN models were created (one of which had as its output the actual degree of ICA stenosis, whilst the other had an output which corresponded to the degree of ICA stenosis stratified to bands of predefined 10% intervals).

The available data were randomly divided into two mutually exclusive data sets. One of these was used to train the model; the other was used to validate the model by testing the out-of-sample performance of the constructed MLP (assessment of the accuracy of predictions of the trained ANN). The data sets were organised into eight different randomly selected re-cuts (reruns) of input data, each used to train eight identical MLP models (four identical MLPs for prediction of actual ICA stenosis and four to stratify the stenosis according to 10 bands).

Training. The input variables used were PSV and EDV in ICA as well as CCA and presence of contralateral ICA occlusion. All of the input variables apart from the presence of contralateral ICA occlusion were continuous. Contralateral occlusion was a categorical variable. Sixty percent of the data set was used to train the neural network. The

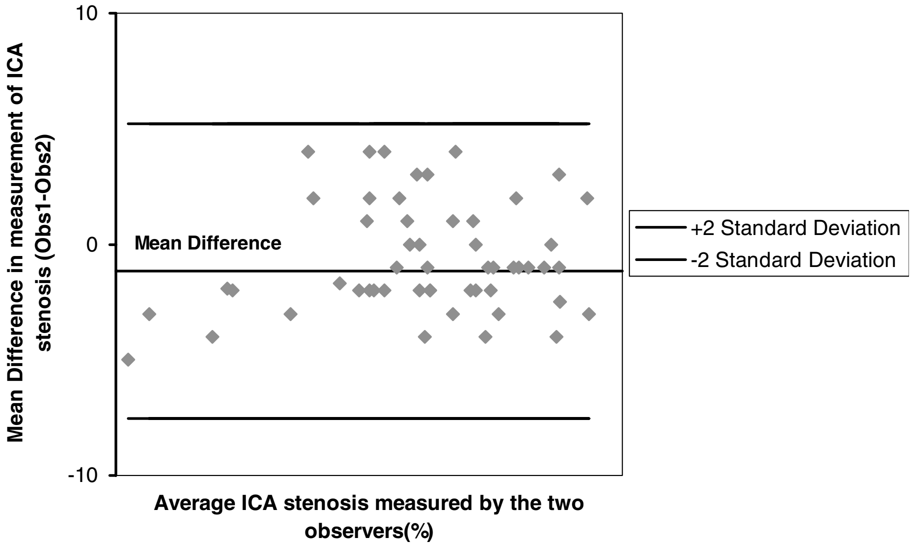

Fig. 2. Bland-Altman analysis applied to the comparison between the angiographic degrees of ICA stenosis measured by the two different observers.

training rule was back-propagation of error.[15] This adjusts the weights associated with each node during the training process until the mean squared error was reduced to a minimum.

Validation. Forty percent of the available data set was held out and not used for training of the neural network model. These data were used to evaluate the ability of the fully trained neural network to predict the degree of angiographic stenosis from which the neural network had been blinded. The mean squared error was used to express the variation of the degree of predicted ICA stenosis compared to the angiographic measurement of ICA stenosis. A classification matrix was used to assess the predictive ability of the neural network. The accuracy of the neural network in correctly classifying the degree of ICA stenosis was compared with duplex velocity criteria alone.

Statistical Analysis

The degree of ICA stenosis predicted by the ANN was compared with the angiographic measurements using linear regression and Bland-Altman analysis.

The accuracy, sensitivity (Sen), specificity (Spec), and likelihood ratios for positive and negative tests were calculated for duplex velocity criteria and the ANN. To compare the duplex velocity criteria with the ANN in correct banding of the degree of ICA stenosis, a measure of the discriminant power (DP) of a test was used:[17]

$$DP = (\sqrt{3})/\pi\{\ln[Sen/(1 - Spec)] + \ln[Spec/(1 - Sen)]\}$$

McNemar's test was used to compare the relative accuracy of the ANN model and duplex velocity criteria in correctly stratifying the degree of ICA stenosis to 10% intervals.

RESULTS

Two hundred and eight carotid bifurcations in 104 patients were studied. Eighty-three patients had ipsilateral symptoms prior to presentation (hemispheric, 51; ocular, 27; both symptoms, 5), and 21 patients were asymptomatic. The mean age of subjects was 70.1 years (standard deviation = 10.11); 38 were female and 66 were male. No patient was excluded due to inadequate angiography or duplex ultrasound.

Seventeen carotid arteries were occluded. Carotid duplex examination was able to identify occluded ICA in all patients. In the remaining ICA bifurcations, the median degree of ICA stenosis was 64% (range 0-99%). One hundred and forty-one carotid bifurcations (68%) studied possessed ≥50% degree of ICA stenosis and 114 (55%) had ≥70% stenosis, as measured by angiography.

Interobserver Agreement

There was good agreement between the two observers in the angiographic measurement of degree of ICA stenosis ($R^2 = 0.95$). Bland-Altman analysis confirmed the high degree of interobserver reproducibility of the angiographic measurement of the degrees of ICA stenosis (Fig. 2).

Interobserver variability in determining the correct banding for the degree of ICA stenosis was acceptable ($\kappa = 0.79$).

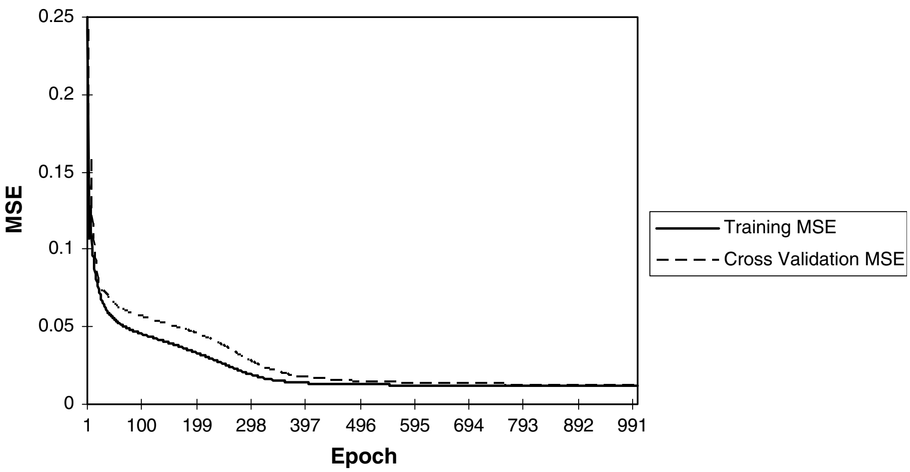

Fig. 3. The training curve of the ANN used for banding the degree of ICA stenosis showing the minimization of mean squared error (MSE, *y* axis) during the training process (*x* axis = number of epochs). The *solid line* represents the training process and the *broken line*, cross-validation.

Duplex Velocity Criteria and the Degree of ICA Stenosis

The overall agreement between the results of duplex ultrasound velocity measurement and angiography in determining the correct banding for the degree of ICA stenosis was 91.8% (191/208), with a sensitivity of 89.7% [95% confidence interval (CI) 82.8-94] and specificity of 93.5% (95% CI 86.5-97) (DP = 1.67).

The accuracy of duplex ultrasound criteria at correctly identifying >70% ICA stenosis was 95.2%, with sensitivity of 96.3% (95% CI 90.9-98.6), specificity of 94% (95% CI 87.5-97.3), and DP of 3.3. Carotid duplex examination was also able to identify over 50% ICA stenosis with reasonable accuracy [sensitivity 96.38% (95% CI 89.9-97.5), specificity 91.6% (95% CI 82.8-96.1), and accuracy 94.7% (DP = 3.09)].

Neural Network Analysis

Two hundred and eight data vectors were randomly divided as follows: 124 (59.6%) were used to train the neural network model, and 84 (40.4%) were used for model validation and out-of-sample testing.

Following completion of training, the ANN model was able to predict the degree of ICA stenosis with a high degree of accuracy (mean squared error 0.012); cross-validation confirmed the validity of the ANN model at predicting the degree of ICA stenosis (Fig. 3). Good correlation was observed between the degree of ICA stenosis predicted by the ANN and that measured angiographically ($R^2 = 0.9374$, $p < 0.0001$) (Fig. 4). Bland-Altman analysis revealed a high degree of agreement between the results of ANN and angiographic measurements (Fig. 5). Furthermore, the ANN model was able to accurately band the ICA stenosis according to the predefined 10% intervals with a sensitivity of 97.3% (95% CI 90.7-99.3), a specificity of 97.7% (95% CI 93.6-99.2), and an overall accuracy of 97.5%. The ANN model was significantly more accurate at correctly banding the degree of ICA stenosis. The DP of ANN was 4.11, while that of duplex velocity criteria alone was 1.67 (McNemar's test, $p < 0.05$).

The accuracy of the ANN at correctly identifying >70% ICA stenosis was 98.4%, with sensitivity of 96.4% (95% CI 93.8-99.3), specificity of 98.7% (95% CI 93.4-99.8), and DP of 4.21. This was comparable to duplex velocity criteria (*p* = nonsignificant). The accuracy of the ANN at correctly identifying >50% ICA stenosis was 97.4%, with a sensitivity of 97.8% (95% CI 93.8-99.3 and) specificity of 98.2% (95% CI 90.4-99.7), which was not significantly better than the duplex velocity criteria (*p* = nonsignificant). Table I illustrates the comparison between duplex velocity criteria and ANN at identification of >50% and >70% stenosis as well as correct banding of ICA stenosis for >50% ICA stenosis.

The use of ANN was associated with altered clinical decision in 2.9% of cases (5/208) compared with angiographic findings. This was not significantly different from the duplex velocity criteria, use of which was associated with altered clinical decision in eight carotid bifurcations (3.8%) compared with angiography (*p* = NS).

DISCUSSION

Duplex scanning is the principal method of imaging carotid bifurcation disease,[18] owing to its noninvasive nature and widespread availability. It has been shown that carotid endarterectomy can be

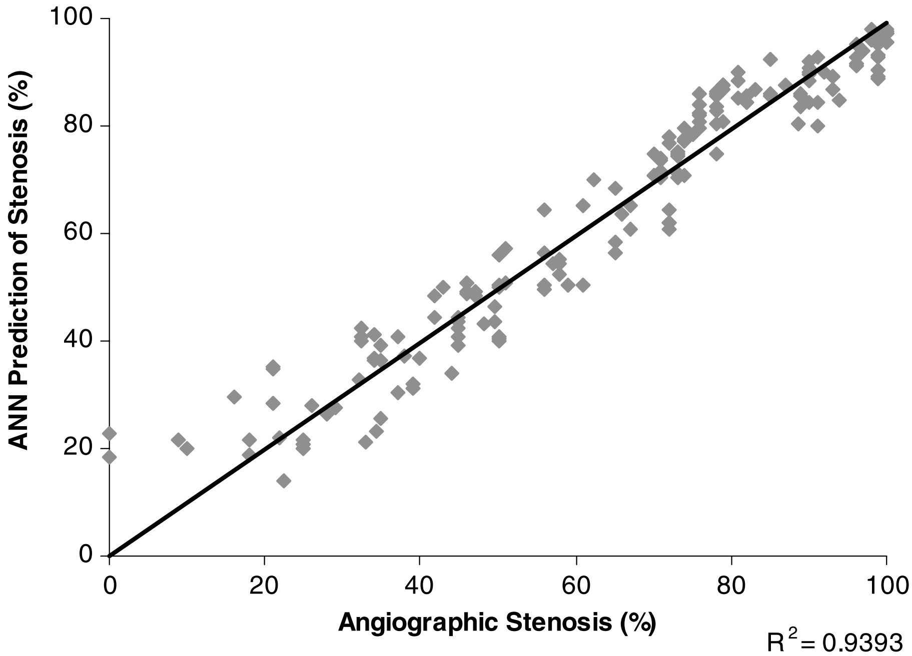

Fig. 4. A plot of the angiographic degree of ICA stenosis (*x* axis) and ANN prediction of ICA stenosis in the validation sample (*y* axis).

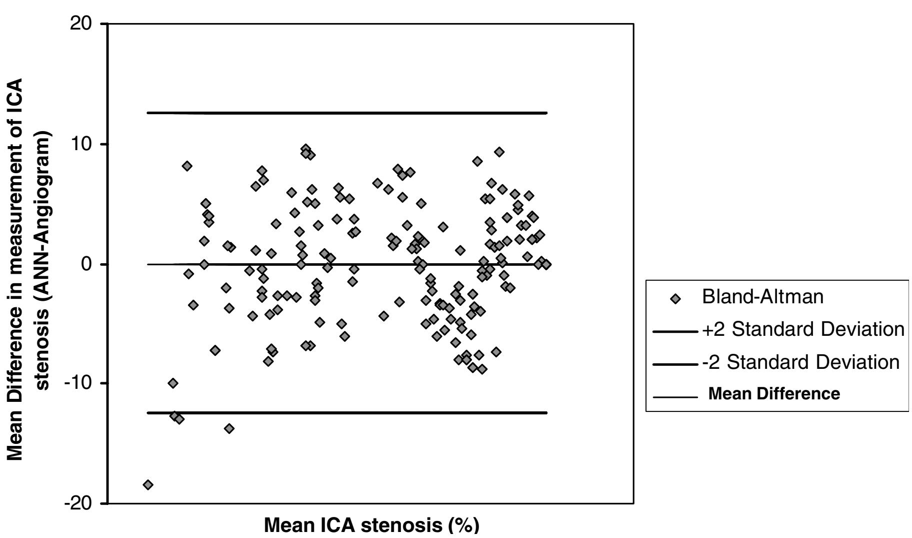

Fig. 5. Bland-Altman analysis applied to the comparison of predicted degree of ICA stenosis by ANN and the angiographic degrees of ICA stenosis.

safely performed without preoperative angiography.[4,19]

Proliferation of duplex velocity criteria has resulted in lack of uniformity in the measurement of ICA stenosis using duplex imaging, in contrast to the standardized nature of angiographic assessment of ICA stenosis during randomised controlled trials, upon which the efficacy of carotid endarterectomy is based.[1,2] The randomised controlled trials which form the evidence base for the management of symptomatic and asymptomatic carotid atherosclerosis have identified different threshold values for ICA stenosis as representing the indication to perform carotid endarterectomy.[20-22] Several previous authors have changed their velocity criteria in order to comply with these studies.[23,24]

With respect to symptomatic patients, both NASCET and the European Carotid Surgery Trial (ECST) have demonstrated a gradient effect of benefit with increasing degree of stenosis.[20,22] Therefore, in patients with moderate degrees of stenosis (50-70%), knowing the exact degree of stenosis in conjunction with preoperative clinical risk factors may influence decision making with regard to surgery.[12] Such information is of value in follow-up of patients who are treated conservatively and do not undergo carotid endarterectomy.

Table I. Comparison between accuracy, sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of duplex velocity criteria and ANN at identification of >50% and >70% stenosis as well as correct banding of ICA stenosis

	Identification of >70% stenosis (p = NS)				
Modality	**Accuracy**	**Sensitivity**	**Specificity**	**PPV**	**NPV**
Duplex velocity criteria	95.2	96.3 (90.9-98.6)	94 (87.5-97.3)	96.4	93.5
ANN	98.4	96.4 (93.8-99.3)	98.7 (93.4-99.8)	99.2	94
	Identification of >50% stenosis (p = NS)				
Modality	**Accuracy**	**Sensitivity**	**Specificity**	**PPV**	**NPV**
Duplex velocity criteria	94.7	96.4 (89.9-97.5)	91.6 (82.8-96.1)	96.5	91.2
ANN	97.8	97.4 (93.8-99.3)	98.2 (90.4-99.7)	98.2	93.9
	Correct 10% banding for stratifying 50-100% stenosis ($p < 0.05$)				
Modality	**Accuracy**	**Sensitivity**	**Specificity**	**DP**	**DOR**
Duplex velocity criteria	91.8	89.7 (82.8-94)	93.5 (86.5-97)	1.67	125 (48-323)
ANN	97.5	97.3 (90.7-99.3)	97.7 (93.6-99.2)	4.11	1,872 (306-11,431)

NS, nonsignificant; DOR, diagnostic odds ratio (95% CI in parentheses).

In order to better stratify the degree of ICA stenosis measured with duplex ultrasound, Filis et al.[12] developed velocity criteria with 10% interval categories for >50% ICA stenosis. They reported that such criteria have similar accuracy to the old 20% intervals. Using the duplex velocity criteria described by Filis et al., we found good degree of accuracy and interobserver agreement for the stratification of 50-100% ICA stenosis (into 10% bands); therefore, it was adapted retrospectively by us for comparison against the ANN model.

The use of ANNs represents a novel approach in the assessment of degree of ICA stenosis. Neural network algorithms have been applied to a variety of clinical conditions where complex relationships within the data set preclude the use of conventional linear statistical analysis.[25] Accurate measurement of the degree of ICA stenosis using velocity of blood flow contains an inherent degree of variability. This variability increases with progressively lower degrees of stenosis in the ICA.[26,27] It would be impossible to account for this variability through conventional statistical models. ANNs can be used to separate background noise (variability) from information embedded in the data set. ANN algorithms can be built into new duplex devices. In this way, after selection of the appropriate sample volume by the operator, the machine could automatically calculate the duplex parameters for predicting the probability of threshold ICA stenosis or measure the exact degree of ICA stenosis.

Our results suggest that ANNs have an acceptable degree of accuracy in predicting the exact degree of ICA stenosis and represent a modest but significant improvement in classification of ICA stenosis into 10% bands. Carotid duplex criteria have been proven to be excellent tools in identification of threshold ICA stenosis at the clinically significant 70% level used for identification of surgical candidates amongst patients with symptomatic disease[5-8] and 60% stenosis screening for asymptomatic carotid artery stenosis.[23,24] In this study, we did not find a significant difference in the accuracy of ANN in the identification of patients with clinically significant ICA stenosis compared with carotid duplex criteria.

Other approaches have been adapted as alternatives to duplex velocity criteria. Zbornikova and Johansson[28] found that multivariate regression based on PSV, EDV, and pulse pressure was more accurate than univariate analysis based on each variable at identifying >50% ICA stenosis and suggested that this could replace duplex velocity criteria in the identification of candidates for carotid endarterectomy.[28] More recently, Hwang et al.[9] used a multiple regression model to predict the exact degree of ICA stenosis using duplex velocity measurements as independent input variables. They found a reasonable correlation between the predicted and actual degrees of ICA stenosis. Apart from the current study, the publication by Hwang et al.[9] is the only study in the literature which attempts to measure the exact degree of ICA stenosis using duplex variables. Their work suggests that a linear regression model based on the equation ICA stenosis = 20.2PSV −7.4EDV + 0.4SCR + 8.5SCR [where SCR is (peak) systolic carotid ratio] can be used to predict the exact degree of ICA stenosis, albeit with a moderate degree of correlation with angiographic controls (correlation coefficient = 0.75). Such a model, whilst novel, does not offer an improvement over duplex velocity criteria[12] or an ANN.

Direct measurement of the residual lumen using a combination of B-mode ultrasound and colour flow imaging components of duplex investigation has been used to measure ICA stenosis.[29,30] These measurements have been found to correlate well with angiographic measurments[29] and examination of endarterectomy specimens.[30] However, it is important to point out that B-mode ultrasound and angiography measure the degree of vessel stenosis in different ways: duplex ultrasound assesses stenosis by percentage area reduction, whereas angiography measures the percentage reduction in luminal diameter. Therefore, despite close correlation, the two values are not interchangeable.

In our study, data analysis was performed using a neural network with a simple design and five input variables (PSV and EDV measurements in the ICA, CCA, and the presence of contralateral ICA occlusion). The reason for limiting the number of input variables and using simple neural network topography was to avoid complexity in the design of the neural network and the resultant data analysis. Nonetheless, it was able to predict the degree of ICA stenosis with a high level of accuracy.

We did not analyse the influence of factors such as heart rate, presence of cardiac arrhythmias, and systemic blood pressure, which are known to be responsible for alteration of haemodynamic findings in the carotid bulb region. These findings are hard to characterise in the linear assessment of the degree of ICA stenosis but would be ideally suited to ANN analysis. Their addition would significantly increase the complexity of the neural network model, which would require a larger pool of subjects to train and validate. However, it is likely that the future introduction of these data into the ANN model would improve its predictive ability in the assessment of ICA stenosis.

Previous authors have suggested that duplex velocity profiles may overestimate the degree of ICA stenosis in the presence of contralateral occlusion.[31,32] This is difficult to adjust for when duplex velocity criteria are used alone. However, such an adjustment is possible in an ANN model in the form of another input variable (node).

This study suggests that using ANN analysis it is possible to predict the exact degree of ICA stenosis using Doppler velocity parameters. We believe that with further refinement and the addition of new input variables ANNs can be used to perform this task in a standardized manner.

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