Correlation Between Ultrasound B-mode Images of Carotid Plaque and Histological Examination

S. K. Jespersen[1,2], M.-L. M. Grønholdt[3], J. E. Wilhjelm[2], B. Wiebe[4], L. K. Hansen[5] & H. Sillesen[3]

Center for Arteriosclerosis Detection with Ultrasound (CADUS), http://www.it.dtu.dk/~wilhjelm/cadus.html.
[1]B&K Medical, Sandtoften 9, 2820 Gentofte, Danmark. [2]Dept. of Information Technology, Bldg. 344, [5]Dept. of Mathematical Modeling, Bldg. 321, Techn. Univ. of Denmark, DK-2800 Lyngby, Denmark. [3]Dept. of Vascular Surgery, [4]Dept. of Neuropathology, Rigshospitalet, University of Copenhagen, Blegdamsvej 9, DK-2100 Copenhagen Ø, Denmark.

Abstract

This paper reports on a study on 69 patients where image features extracted from B-mode ultrasound images of atherosclerotic plaque in the carotid arteries were compared to histological results obtained from the same plaque after carotid endarterectomy. The study also investigated the correlation between image features and visual classification of the plaque appearance as revealed by ultrasound scanning. The study found that a few texture features are found to be significantly correlated to the histological findings within the training set (p = 0.002 - 0.04). However, the correlation found may not be reliable for clinical determination of plaque composition. The correlation between image texture features and the visual classification of the B-mode images was, not surprisingly, found to be much better. Thus, numerical analysis is likely to be useful in future investigations as many problems with intra- and inter-observer variations that inherently exist in the subjective visual classification can be eliminated.

1 Introduction

Investigation of the carotid arteries with ultrasound has become a predominant tool during the last decades. The parameter most used in the clinical diagnosis today is the degree of stenosis, determined by ultrasound duplex examination, assisted by color flow mapping (CFM). It has been proven that plaques causing significant stenosis can be diagnosed with high specificity and reproducibility and that a high degree of narrowing leads to a high risk of stroke [1]. When it comes to patients with smaller degrees of stenosis results are less clear, but according to recent research certain types of arteriosclerotic plaque might have a significantly higher risk of causing stroke than other types of plaque. The plaques that are considered most likely to cause stroke are those that reflect ultrasound poorly and plaques that have a very inhomogenous structure, [2, 3]. It would be desirable if these plaques could be classified into more or less dangerous types as this would be a valuable tool in the selection of patients to undergo carotid endarterectomy, which is both a costly procedure and constitutes a notable risk for the patient.

With the exception of a few studies [4, 5], plaque classification has been made by visual inspection. A typical classification could be three classes for echogenicity (weak, intermediate, strong). However, the subjective classification suffers from inter- and intra-observer variation that particularly makes multi-center studies difficult; further a simple visual interpretation might not extract all information available in the B-mode image data.

This study investigates whether image features extracted from B-mode images of carotid artery plaques can be used to predict the histology of the plaque and how well image texture features correlate with the subjective visual classification of B-mode ultrasound images.

2 Materials and Methods

An overview of the experimental procedure is given in Figure 1.

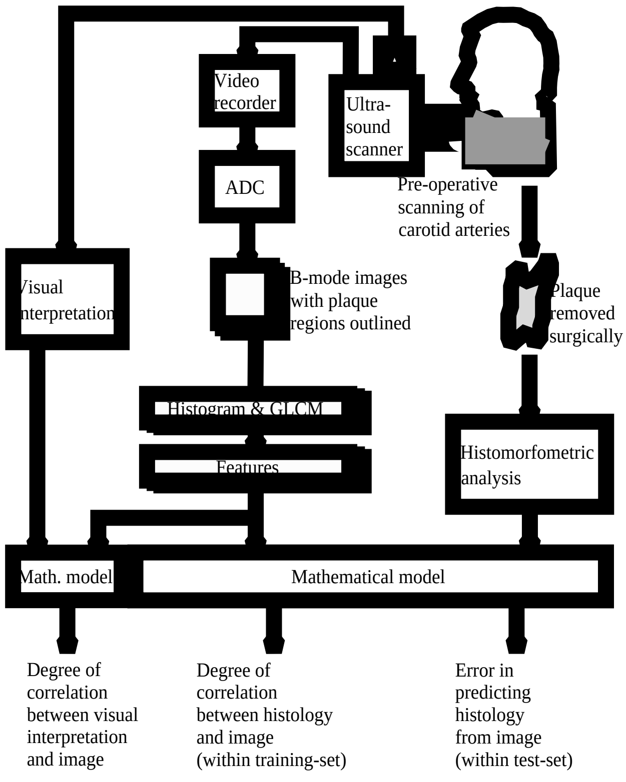

Figure 1. Overview of the experimental procedure.

2.1 Patients and Clinical Procedure

From December 1994 to April 1996 69 patients (51 men and 18 women, median age 63 years) with carotid disease were scanned after experiencing neurological symptoms. Ultrasound scanning was performed using a 7.5 MHz linear array transducer and scanning sequences were recorded from three different scan planes (lateral, anterior and cross-sectional) and stored on super VHS video tape. All scannings were made at the Department of Vascular Surgery, Rigshospitalet, Copenhagen. The scannings were stored a on super VHS video tape in preparation for the subsequent image analysis. The plaques were classified during scanning by a single experienced ultrasonographer using the following characteristics, [6]:

1. Plaque echogenicity: weak, intermediate, strong.
2. Plaque structure: homogeneous or heterogeneous.

Following prophylactic carotid endarterectomy the removed plaques were analyzed histologically as follows: The plaques were fixed in formalin and transverse blocks were cut at ~3 mm distance. After embedding in paraffin microtome sections were cut from each block. Sections were stained with haematoxylin and eosin as well as Van Gieson for determining connective tissue content. Histological analysis was performed by a single experienced pathologist using a microscope and transferred to an image analysis computer for calculation of the areas of each component. The analysis concerned the following constituents: lipid, hemorrhage, thrombus, calcification and fibrous tissue. The mean and standard deviation of all histological results are given in Table 1.

Constituents	Mean	Standard dev.
Lipid	37.3	12.6
Blood	0.4	0.5
Calcification	1.5	1.8
Thrombus	0	0
Fibrous	60.9	12.9

Table 1. The relative estimated volume (%) of plaque constituents in the 69 plaques analyzed histologically.

2.2 Image Features and Mathematical Model

By reviewing the videotapes of the scannings the best B-mode images from the three different scan planes of each carotid artery were selected and digitized by a frame grabber (with G = 256 gray levels) and stored on a PC. Using image processing software the plaques were outlined by the ultrasonographer. An example of a B-mode image and outlined plaque is seen in Figure 2. The outlining was determined from the video recorded scannings so that both B-mode images and combined CFM/B-mode images could be used in order to fully utilize both the structural and the flow information.

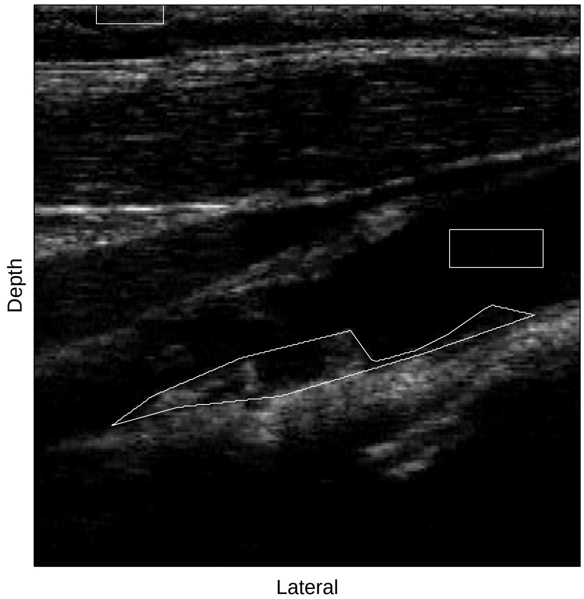

Figure 2. Longitudinal B-mode image of atherosclerotic carotid artery with the plaque region outlined. The other outlined regions are intended for calibration purposes.

This outlining procedure can be advantageous when investigating echolucent plaques as these are difficult to outline from the B-mode image only, as blood and plaque can be very hard to distinguish.

Seventeen first-order image features were calculated from the normalized gray level histogram. The first order features were: mean, variance, coefficient of variation, skewness, kurtosis, energy, entropy and percentiles for 10%, 20%, ..., 100%.

In order to further describe the image texture information the gray level cooccurence matrix (GLCM), [7], was calculated for the plaque regions. The GLCM describes the number of gray-level changes between pairs of pixels, separated by a displacement vector, $\vec{h}$, specifying an offset in column and row indices. When the number of gray levels is G = 256 and $\vec{h} = (8,0)$ the GLCM will be a 256 x 256 matrix and the content of *e.g.* element (i, j) = (17, 130) indicates the number of pixels with value 16 (= i - 1) that has a pixel with value 129 (= j - 1) 8 rows further down and 0 columns further right in the image. By varying $\vec{h}$ and testing which direction and distance gave the most significant features a displacement vector $\vec{h} = (8,0)$ was found to perform best. All subsequent second order features are extracted from GLCM's calculated with this displacement vector. This displacement vector corresponds to a displacement of 0.8 mm (corresponding to ~4 wavelengths) in the direction of the ultrasound beam. Ten second-order image texture features were calculated from the GLCM: energy, entropy, maximum, correlation, diagonal moment, contrast, mean in *i*-direction, mean in *j*-direction, standard deviation in *i*-direction and standard deviation in *j*-direction, [7].

The mathematical model used to analyze the correlation between texture features and visual classification or histological results is the general linear model:

$$\underline{Y} = \underline{\underline{X}}\beta \qquad (1)$$

The least squares error solution is used to find the estimated regression parameters, $\hat{\beta}$. The residuals are found as $\underline{\varepsilon} = \underline{Y} - \underline{\underline{X}}\hat{\beta}$. Assuming that $\underline{\varepsilon}$ follows a normal distribution, the *p*-value is found as well.

In order to facilitate comparisons between the performance of different features each feature vector was normalized so it ranged from 0 to 1. All features were tested to evaluate their performance in predicting the visual classification and the histological results, respectively. The following two step procedure was used:

1. First and second order features were calculated and the mean residual, $\bar{\varepsilon} = E\{\underline{\varepsilon}\}$, was found. Only features for which $\bar{\varepsilon} < 0.1$ and $p < 0.05$ were selected for further processing.
2. The hypothesis that the remaining features could be used for prediction was tested by splitting the data set into a training set (80%) and test set (20%). The training set was used to obtain $\hat{\beta}$ and the test set used to find test residuals. Different training and test sets were extracted 50 times from the entire data set by means of resampling.

For the correlation between image features and histology it was decided to combine lipid, blood and thrombus into a group denoted soft materials as these materials are all echolucent and can probably not be differentiated by ultrasound. Consequently three groups of materials were present: Soft materials, fibrous tissue and calcification.

3 Results

The result of the analysis for the visual classification showed that images from the anterior scan plane gave the best correlation and the smallest test error. A result for the relationship between echogenicity class estimated from image features and echogenicity class found by visual inspection is shown in Figure 3. Agreement between classifications from the test set and from the visual inspection was found in 76% (average) of the cases and a kappa analysis showed $\kappa = 0.62$, which indicates good agreement.

For the correlation between image features and histology the following results were found:

1. No significant features (with a cutoff at $p = 0.05$) for the content of calcification were found for any of the scan planes.
2. For the content of fibrous tissues three significant features were found for the lateral scan plane, namely: coefficient of variation from the histogram, diagonal moment from the GLCM and standard deviation in the j-direction from the GLCM. One significant feature for the cross-sectional plane, the contrast from the GLCM, was found.

In Figure 4 an example of the relationship between normalized contrast from the GLCM for the cross-sectional scan plane and fibrous tissue content is shown. The estimated regression line is also plotted in Figure 4. It is obvious from the plot that the relationship between image feature and histology is not very strong. Expressed numerically the data showed a correlation coefficient of $r = 0.44$ and a significance level of $p = 0.002$. The results for the other significant features can not be presented here due to the limited space.

4 Discussion

The results of the correlation between image features and visual inspection illustrated in Figure 3 showed a 76% (average) agreement in the test set between classifications of echogenicity and a kappa value of $\kappa = 0.62$. This agreement is so good that it could be possible in the future to substitute the visual classification by image feature extraction.

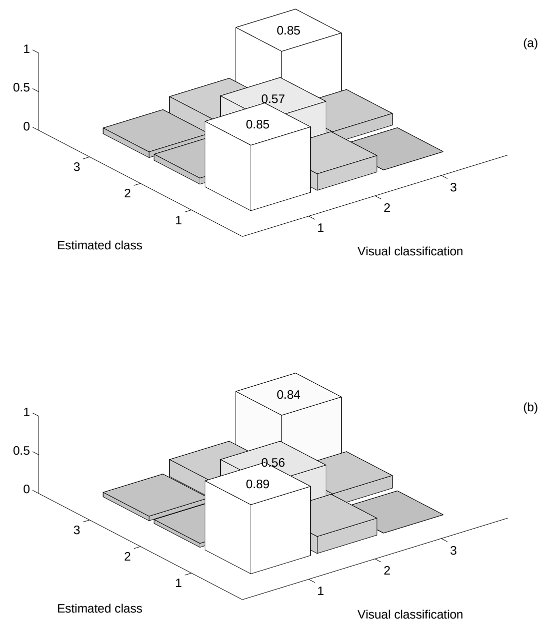

Figure 3. Relationship between echogenicity class estimated from image features and echogenicity class found by visual inspection. Images are from the anterior scan plane. (a) shows correlation within the training set and (b) shows correlation within the test set.

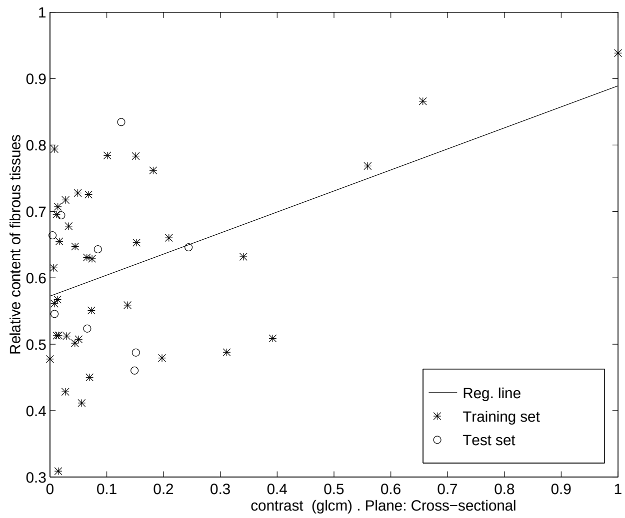

Figure 4. Fibrous tissue content versus normalized contrast from the GLCM for the cross-sectional scan plane.

The main advantage of this approach is that most of the inter- and intra-observer variation that inherently exists in the subjective visual classification can be eliminated, leaving only the outlining of plaque regions to the operator.

The results of the correlation between image features and histological results presented in section 3 are not very encouraging. The correlation found is, as is evident from the example illustrated in Figure 4, quite low and consequently a prediction of plaque histology from B-mode ultrasound image features will, at the present state, probably be too unreliable for clinical application.

We believe that a significant limiting factor in the present study is the outlining procedure. Including the CFM information while creating the outlines clearly constitutes an advantage with respect to outlining echolucent plaques. However, there is also a risk of marking areas of blood as part of the plaque region since regions of no or low blood flow typically exist near the artery walls “downstream” from the plaque and the CFM image will show no flow information in these regions. Further, due to the thresholding used in the CFM system a small region near the plaque surface might be shown as having no flow. Consequently the plaque region size might be slightly overestimated. Another source of error is plaques containing calcifications or other strongly attenuating material. In these plaques dark regions exist due to the shadowing effects of the attenuating materials. Both the above-mentioned effects will generally bias the classifications towards more echolucent plaque types.

5 Conclusion

It was found that classification of echogenicity from B-mode image texture features correlated well to visual classification of echogenicity. When using three classes for the echogenicity agreement between classes were found in 76% (average) of the classifications and a kappa analysis showed $\kappa = 0.62$, indicating good agreement.

The correlation between image texture features and histological results obtained from the same plaque after carotid endarterectomy was investigated and a few image features were found to correlate significantly to the content of fibrous tissue. A correlation coefficient of $r = 0.44$ was found for the cross-sectional plane ($p = 0.002$). However, the correlations may be too low to be used for reliable clinical determination of the plaque composition.

6 Acknowledgments

Center for Arteriosclerosis Detection with Ultrasound (CADUS) is supported by the Danish Technical and Medical Research Councils.

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