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CORRELATION BETWEEN CAROTID PLAQUE PARAMETERS AND FREQUENCY OF MICROEMBOLIC SIGNALS

KORELACIJA IZMEDJU PARAMETARA KAROTIDNOG PLAKA I FREKVENCIJE MIKROEMBOLIJSKOG SIGNALA

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Ključne reči
ultrazvucna slika, mikroembolijski signal, karotidni plak, korelacija

Abstract

In this study we applied image processing techiques on the B-mode ultrasound image of carotid plaque in order to isolate plaque parameters that have high correlation with the frequency of microembolic signals (MES) measured in cranial arteries. Nineteen parameters were measured on each of the seventeen plaques used in this study and results were correlated with MES. The results have shown that five parameters have a statisticaly significant correlation with MES.

INTRODUCTION

The detection of microemboli in cranial arteries can be an indication of unstable carotid plaque and can therefore imply high risk of cerebral embolic events like trasient ishemic attack and stroke or complication during endarterectomy or artery stenting procedures(1-3). Since the introduction of transcranial Doppler (TCD) for the detection of microemboli in cranial arteries there has been much effort to pinpoint the main differential characteristics of plaque with high embolic potential. Research in that field will help us to better understand the stability of plaque and allow us to make better prediction of ishemic neurological outcome based on sonographic examination of plaque.

Currently, in clinical practice, the most widely used method for the differentiation of instable plaque is duplex ultrasound scaner.(4) Past research mainly focused on few characteristics of plaque as candidates for root cause of high embolic potential. Low echogenicities of plaque that imply the presence of lipid component and hemorrhage are traditionally considered to be the characteristics of unstable plaques that can be the embolic source (4). In addition to that, irregular surface and presence of ulcers in plaque are found to have a positive correlation with embolic potential.(6-8) Also, some researches have found a correlation between other parameters like the degree of stenosis or heterogeneous structure of plaque and the frequency of MES(9).

Beside global characteristics of plaque, like the mean value of echogenicity of plaque or degree of stenosis, some researches analyzed the structure of plaque in greater details in order to correlate the tissue structure of plaque with MES. In one study(10), a stratified gray-scale median (GSM) analysis of the carotid plaque combined with the color mapping of plaque tissue was used. The results showed greater sensitivity and specificity in detecting plaques with embolic potential by looking only on surface plaque tissue rather than all plaque characteristics. A similar color analysis that reveals the structure of plaque was applied to image recorder by intravascular ultrasound (11) and it was concluded that the degree of cerebral embolization during carotid stenting procedure measured with TCD correlated with plaque burden, necrotic core, fibrofatty, and fibrous volumes of plaque.

However, at present, there is no consensus about the features of the plaque sonographic image on which we can base objective measure of the plaque embolic potential or predict the ishemic neurological outcome. Therefore, in this study we measured 19 different plaque parameters extracted from the B-mode ultrasound image and calculated their correlation with the frequency of MES in order to isolate promising candidate-features for future algorithms for the automatic objective measuring of plaque stability.

METHOD

Patients

Five patients from 61 to 80 years of age participated in this study (4 male, 1 female). Each patient went through the ultrasonic examination of left and right common (CC) and internal carotid (IC) arteries with 5 Mhz linear B-mode probe. With this examination we obtained 17 images of carotid plaques (for some arteries we made more than one image to cover the full extent of plaque). Immediately after the carotid examination of the patients, the transcranial ultrasound monitoring was applied for 30 minutes to left and right middle cerebral artery during which we recorded MES events.

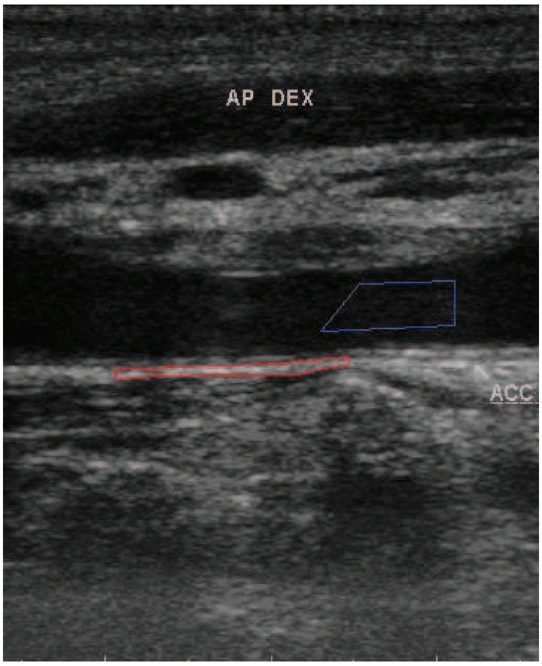

Figure 1. Selection of blood and adventitia region on B-mode ultrasound carotid image.

Image normalization

Every B-mode image was exported from ultrasound system in gray level format with the dimension of 360 by 440px. The image was then normalized and 19 parameters of extracted plaque were measured with custom made software written in MATLAB for the purpose of this study (see Figure 3.).

Before the extraction of plaque, every B-mode image was normalized in order to compensate for the influence of use of a different probe or different value of gain parameter during the recording. For the purpose of normalization, we first manually extracted one uniform area of blood tissue and one area of adventitia of artery and calculated their median pixel value M_{blood} and M_{adven} (see Figure 1). After that we linearly scaled all pixel values in the image based on these two values as

$$P_{new} = \frac{190(P_{old} - M_{blood})}{M_{adven} - M_{blood}}$$

where P_{new} and P_{old} are the new normalized and old pixel values respectively. After applying normalization to all the images, the median value of blood tissue would always be close to zero and the median value of tissue area of adventitia would be around 190. It is proven that this kind of normalization decreases variability between recordings and helps in achieving reproducibility in plaque analysis.(12)

Plaque tissue classification

Plaque can be composed of five different kinds of tissues: blood, fat, muscle, fibrous and calcified tissue. On the B-mode image, all tissues have a slightly different echogenicity and texture so we chose to form the input vector of pixel classifier out of three values that can represent these characteristics: mean value in the 3-by-3 neighborhood area of pixel, local standard deviation (3-by-3 neighborhood), and local entropy (9-by-9 neighborhood).

For the classification, we used feed-forward neural network (NN) that has two hidden layers with 5 and 3 neurons with a sigmoid transfer function and 4 output neurons with a linear transfer function. We applied the winner-take-all rule on the output neurons so that at the end of the classification only one neuron was left activated.

Even though there were five types of tissue to be classified, we made a decision to merge fat tissue and muscle tissue class into one class so that in the end our classification could discriminate only four classes. We decided to do that firstly because fat and muscle tissues have a very similar echogenicity so it is very difficult to discriminate them on a B-mode image. Secondly, muscle tissue is rarely present in plaque and has a similar influence on plaque stability to that of fat tissue.

To create the training and test set of input and output vectors we made one reference B-mode ultrasound image for every type of tissue we wanted to classify. Images were taken on a characteristic anatomical position on which we could get an extensive uniform area of tissue of interest with certainty. For fat tissue we used a B-mode image of abdominal subcutaneous fat. For fibrous tissue we used an image of Achilles tendon, for muscle biceps brahii muscle, for blood tissue image of blood in carotid artery and for calcified tissue we used parts of the image of heavily calcified plaque.

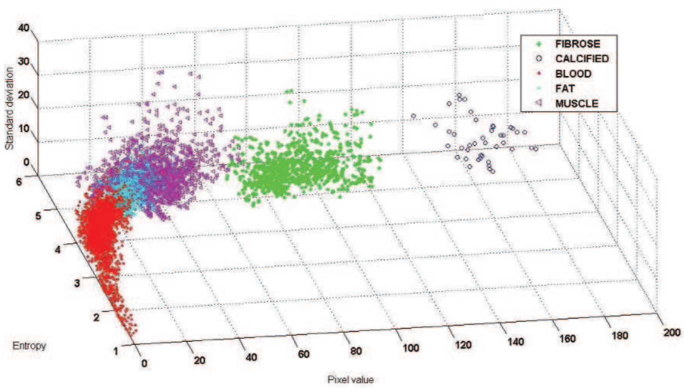

Figure 2. Vectors of neural network training set. Vectors belonging to different classes are shown in different color. On figure can be seen partial overlap of muscle and fat tissue classes.

All reference images were recorded with the same probe and gain parameters and were normalized with the previously explained procedure using median values calculated on carotid artery from the blood reference image. After normalization, we extracted one area that contains tissue of interest from every reference image, and we calculated input vector for classifier for every pixel (see Figure 2.). These input vectors, along with appropriate output vectors, were randomly divided on training (80%), validation (10%) and test (10%) subset and used for the training of NN.

The neural network was trained 25 epoches with the Levenberg-Marquardt backpropagation algorithm and it reached mean squared error of 0.0211 on the test data set. This trained NN was used during the plaque analisis to classify every pixel of extracted plaque in one of four tissue classes.

Plaque parameters

A trained specialist manually contoured plaque using mouse cursor on every B-mode image of the patients' carotid. Using digital image processing techniques, for every extracted plaque we measured 19 parameters listed below:

Average - mean average value of pixels calculated on the whole plaque.

Area of plaque - plaque size expressed as a number of pixels inside plaque contour.

Average of surface - mean value of pixels in the narrow (4-pixels-wide) area at the surface of plaque.

Plaque entropy - mean value of local entropy calculated on the whole area of plaque.

Surface entropy - mean value of local entropy in the narrow area at the surface of plaque.

Std. plaque - mean value of local standard deviation calculated on the whole area of plaque.

Std. surface - mean value of local standard deviation calculated on the narrow area at surface of plaque.

Solidity - scalar value that is calculated as the area of plaque divided by the area of the smallest convex region that contains the whole region of plaque.

Connection strength - scalar value that is calculated as the number of pixels on the surface contour of plaque divided by the number of "connective" pixels, i.e. boundary pixels that are in the vicinity of hiperechoeic tissue (adventitia).

Softest tissue - the average pixel value of the most hipoechoic 13-by-13 pixels area on the surface of plaque.

Percentage soft tissue - total percentage of blood, fat and muscle tissue in the whole plaque.

In addition to these values, we also measured the percentage of every individual tissue class in the narrow area of plaque surface and the whole plaque which gives us eight more parameters.

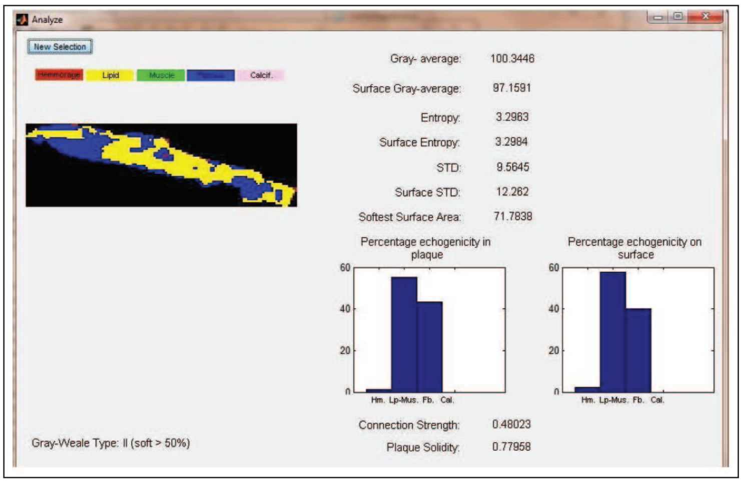

Figure 3. Layout of custom maid MATLAB GUI. On the left hand side is displayed extracted plaque with different tissue colored in different colors. On the right hand side are displayed calculated parameters.

RESULTS

After the measurement of plaque parameters listed above on all 17 images of patients' carotid, we calculated the correlation between parameters and frequency of MES. The correlation result and corresponding p-values are given in Table 1. and graphically shown on Figure 4.

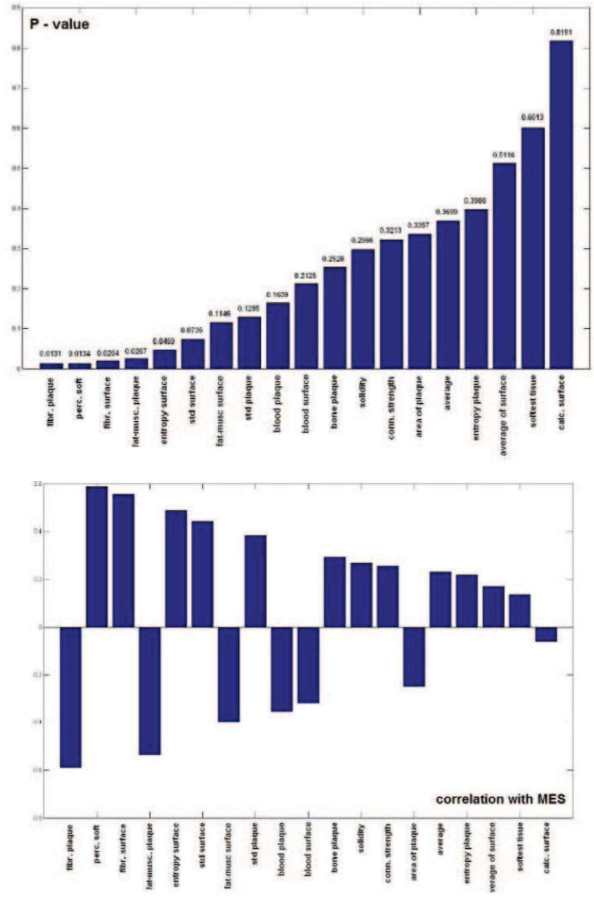

Figure 4. Correlation between parameters of plaque and MES (b) and corresponding p-values (a) sorted by statistical significance.

It can be seen from the results that there are five parameters that have a statistically significant correlation ($p<0.05$) with the frequency of MES. These parameters are: the percentage of fibrous tissue in the whole plaque ($p=0.0131$), the percentage of soft tissue in plaque ($p=0.0134$), the percentage of fibrous tissue on the surface of plaque ($p=0.0204$), the percentage of fat-muscle tissue in the whole plaque ($p=0.0267$) and the average value of local entropy on the surface of plaque ($p=0.0469$).

The high negative correlation of MES and the percentage of fibrous tissue of plaque is the expected result since it goes well in line with the traditional notion that the echogenic (calcified and fibrous) plaques are more stable than the plaques composed of softer tissues.[13] A similar argument can be applied to the high positive correlation between the percentage of soft tissue found in plaque and MES. The high statistical significance of the percentage of fibrous tissue in the surface area of plaque can be associated with the argument above and can be also attributed to the fact that the stability of plaque and the likelihood of plaque rupture is correlated with the thickness of the fibrous cap of plaque.[14]

Table 1. Correlation between parameters of plaque and MES

Parameter	p-value	Correlation
Average	0.3699	0.2322
Area of plaque	0.3357	-0.2488
Average of surface	0.5116	0.1710
Surface entropy	0.0469	0.4879
Plaque entropy	0.3986	0.2189
Std. surface	0.0735	0.4450
Std. plaque	0.1285	0.3836
Solidity	0.2966	0.2689
Conn. strength	0.3213	0.2560
Softest tisue	0.6013	0.1365
Blood surface	0.2125	-0.3187
Fat-Musc. surface	0.1146	-0.3970
Fibr. surface	0.0204	0.5561
Bone surface	0.8191	-0.0600
Bood plaque	0.1639	-0.3535
Fat-Musc plaque	0.0267	-0.5355
Fibr. plaque	0.0134	0.5861
Bone plaque	0.2528	0.2936
Perc. soft tissue	0.0131	-0.5878

Local entropy on the surface of plaque may be interpreted as the measure of irregularity of plaque surface. From that viewpoint, the higher significance of this parameter is in accordance with the findings that irregular surface correlates with cerebral embolism and overall plaque instability as it is shown in several studies.[6,15,16]

The other measured parameters did not show a significant correlation with microembolic signals. This negative result for some parameters should not eliminate those parameters from further research because sample size is not large enough to imply high statistical confidence. Therefore, further research should be conducted with greater sample size that could provide results that are more reliable and may possibly reveal more parameters with a statistically significant correlation with MES.

CONCLUSION

By applying image processing techniques on 17 B-mode ultrasound images of carotid plaque we measured 19 parameters of plaque and correlated them with the frequency of MES. The analysis showed that there are five parameters that have a statistically significant correlation with MES and that can present a solid ground for future algorithm for the objective measuring of plaque stability. Further research should be conducted with greater sample size in order to increase the statistical confidence of results.

Apstrakt

U ovoj studiji primenili smo tehnike procesiranja slike na ultrazvučnu sliku dobijenu u B-režimu pri snimanju karotidnog plaka da bismo izolovali parametre plaka koji su u korelaciji sa frekvencijom mikroemboličkih signala (MES) merenog u kranijalnim arterijama. Za svaki od 17 plakova korišćenih u ovoj studiji izmereno je 19 parametara, a rezultati su korelisani sa MES. Rezultati pokazuju da je pet parametara statistički značajno korelisano sa MES.

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