Evaluation of Carotid Artery Plaque Using IVUS Virtual Histology

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Summary

Currently carotid artery stenting (CAS) as well as carotid endarterectomy (CEA) have become widely accepted forms of treatment for carotid artery stenosis, although complications associated with distal embolism remain problematic. Therefore it is important to have an accurate understanding of the properties of carotid plaque before undertaking CAS in order to ensure the safety of such a therapeutic treatment. This study was undertaken to determine the efficacy of using IVUS Virtual Histology TM (VH-IVUS) to evaluate the pathological properties of plaque contained within carotid artery stenosis.

VH-IVUS was performed for six cases undergoing CAS during the period of July to December, 2005. VH-IVUS displays plaque composition under four color mappings of fibrous, fibro-fatty, calcification and necrotic core, being able to offer detailed tissue characterization of soft to hard plaque components. Plaque evaluation by VH-IVUS is both reproducible and objective, and is considered to be an effective method for evaluating the risk complications associated with CAS.

Introduction

Recently, carotid artery stenting (CAS) has become one choice of treatment for cases involving carotid artery stenosis. Although the development of various devices in recent years

has brought about a reduction in the complication rates associated with CAS, distal embolism remains a serious problem. Therefore it is important to have an accurate understanding of the properties of carotid plaque before undertaking CAS in order to ensure the safety of such a therapeutic treatment. Within current investigative methods available, Ultrasonography (US) is non-invasive and highly efficacious in evaluating plaque composition, with diagnostic accuracy improving yearly. However, diagnosis of plaque composition by the operator when using US is subjective, and along with resolution, accurate diagnosis of plaque composition cannot be guaranteed.

An investigation was undertaken to evaluate VH-IVUS (having been developed for the purpose of evaluating coronary artery plaque) in determining composition of carotid artery plaque, with a comparative study performed with other investigative examinations such as US, CT, and MRI.

Methods

The study population consisted of six lesions [six cases (four male, two female)] that underwent CAS from July to December, 2005 at our institution. Age ranged from 63 to 75 years old (mean 70.3 years old). Analysis was performed using Volcano Therapeutics® EagleEye Gold catheter and Volcano Therapeutics® IVG3 Oracle Imaging System.

Figure 1 (Case 4). A) Rt. carotid angiography revealed 80% stenosis of the Rt proximal ICA. B,C) Black blood MRI of plaque. T1 black blood (B) shows iso- and T2 black blood; C) shows high intensity. Diagnosis of black blood MRI is soft plaque (hemorrhage). Arrow indicates plaque of the Rt proximal ICA. D) VH-IVUS of the plaque. Fibro-lipidic lesion is evident.

In VH-IVUS, the RF signal from IVUS is obtained and a power spectrum is calculated after averaging across all scan lines in the region. The average spectrum from region of interest (ROI) is normalized and then used to compute eight spectral parameters (maximum power, corresponding frequency, minimum power, corresponding frequency, slope, y-intercept, mid-

band fit and integrated backscatter) for each ROI. A classification tree then determines the type of plaque component using these parameters. The plaque component values are assigned color codes and tissue maps are reconstructed: fibrous (green), fibro-lipidic (light green), necrotic core (red), calcification (white).

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Figure 2 (Case 3) A) Rt. carotid angiography revealed 80% stenosis of the Rt proximal ICA. B,C) 3DCT analysis of carotid plaques. Severe calcification is evident in the plaque. D) Ultrasonography shows severe calcification and shadowing. Adequate information of the plaque cannot be obtained due to shadowing. E) IVUS VH of the plaque. 270 flarc of calcified lesion is evident on the surface of plaque. The plaque is not only calcified as fibro-lipidic component was confirmed at the opposite side to the calcified lesion (arrowheads).

VH-IVUS is reported as fibrous 79.7% fibro-fatty 81.2% necrotic core 85.5% dense calcium 92.8%². Plaque evaluation was performed by VH-IVUS in all cases immediately before CAS. Each plaque was then classified into four patterns of 1) fibrous rich 2) lipid rich 3) calcified rich and 4) mixed, according to the VH-IVUS analysis.

In all cases distal protection was performed using Percutaneous GuardWire plus (Medtronic) and blood containing debris was collected by Thrombuster-2 with a 30 ml syringe two times after post-dilatation.

This was then filtered by a Cell Strainer 2340 (Falcon) for cell separation. Debris that remained in the filter was observed, and was clas-

sified into a large, middle and small amount. Before CAS, evaluation of the carotid artery plaque was undertaken by US, CT (3DCT) and MRI (black blood method) with a comparative study against VH-IVUS performed.

Results (table 1)

Results from VH-IVUS for the plaque of the six cases were 1) fibrous rich one case 2) lipid rich one case 3) calcified rich one case and 4) mixed three cases. In the one case of fibrous rich plaque the amount of debris was small. The lipid rich case also contained a small amount of debris.

The calcified rich case contained a large amount of debris. The mixed cases contained one middle amount and two small amount of debris respectively. For the comparison among US, CT, and MRI, VH-IVUS was well correlated with CT for calcified lesions, with diagnosis of calcification difficult by MRI. On the other hand, a good correlation with MRI was obtained for fibro-lipidic lesions (excluding case 5). Though ultrasonography achieved a proximate correlation with VH-IVUS, an accurate comparison was not possible due to a lack of information being obtained because of issues relating to resolution and shadowing caused by calcification.

Two cases (lipid rich: case 4 and calcified rich: case 3) are presented (figures 1 and 2).

Cases

Case 4. A 68-year-old male having developed left hemiparesis. Right internal carotid artery stenosis was diagnosed by screening MRA, and cerebral infarction was determined in the right frontal and parietal lobe with MRI.

Carotid angiography showed 80% stenosis in the right internal carotid artery (figure 1A). Plaque composition by VH-IVUS determined a large amount of fibro-fatty tissue of the stenosis, classified as lipid rich (figure 1D). Black blood MRI revealed soft plaque (hemorrhage involved) (figure 1B,C). The debris obtained during the procedure was a small amount.

Case 3. A 65-year-old female diagnosed with right internal carotid stenosis by screening MRA preceding CABG for angina pectoris. Angiography and 3D-CT showed severe calcification of the plaque (figure 2A,B,C).

Plaque composition by VH-IVUS determined severe calcification on the surface of the plaque (figure 2E), and was classified as calcified rich. Fibro-fatty plaque was confirmed at the opposite side and just under the calcified lesion.

Table 1 Summary of the patients with VH-IVUS analysis.

case	age	sex	symptom	ultrasonography	3DCT	Black blood MRI	VH-IVUS	debris
1	74	male	asymptomatic	low echoic (homogenous)	n.e.	Soft plaque (hemorrhage)	mixed	(++)
2	75	male	asymptomatic	n.e.	n.e.	Soft plaque (hemorrhage)	mixed	(+)
3	67	female	asymptomatic	High echoic (acoustic shadow)	Calcification (+++)	n.e.	calcified rich	(+++)
4	68	male	symptomatic	n.e.	n.e.	Soft plaque (hemorrhage)	lipid rich	(+)
5	75	male	symptomatic	high & low echoic (heterogeneous)	Calcification	Soft plaque (Lipid+ hemorrhage)	fibrous rich	± (+)
6	63	female	asymptomatic	high echoic	Calcification (+)	Fibrous plaque	mixed	±

Note. n.e.= not examined

Although severe calcification was similarly determined by 3D-CT, diagnosis of the position of the calcification was impossible. The debris obtained during the procedure was a large amount.

Discussion

Although until now the first selection for treatment of carotid artery stenosis has been CEA, recently the number of cases involving treatment by CAS has increased, with results being obtained that are not inferior to CEA⁵. Vasodilatation obtained by PTA can incur intimal dissection and overexpansion of the intima due to balloon expansion⁷.

As a result, fat and thrombus from within the plaque are exposed and enter the blood flow⁴ causing micro embolism leading to a cerebral embolism, the worst complication that can occur^{1,3,6}. Although various protection devices have been developed and used as a method of preventing distal embolism, no system has yet been established that can ensure complete protection. Therefore, to improve the safety of CAS, pre-operative diagnosis of plaque composition is important.

Plaque composition is classified as homogeneous or heterogeneous by the luminance distribution of the echo signal and often divided according by the echo brightness to low or hypo -, iso - and hyper. As diagnostic evaluation of US by the operator is subjective, accurate plaque assessment can not be guaranteed. VH-IVUS was used to objectively evaluate carotid artery plaque for six cases. Plaque composition for all cases was heterogeneous.

From the acquired data of VH-IVUS, plaque composition was classified into four patterns of 1) fibrous rich 2) lipid rich 3) calcified rich and 4) mixed.

Moreover, results from a comparison of the amounts of debris aspirated during the procedure showed a tendency for lipid rich plaque. However, in calcified rich and mixed plaques aspirated volume was much larger than expected. When the data of VH-IVUS was examined closely for calcified rich lesions, plaque was not homogeneous and fibro-lipid tissue was confirmed on the opposite side and just under the calcification.

Therefore, the tendency to use higher infla-

tion pressures in order to achieve adequate expansion for heavily calcified lesions with PTA, does not only impact on calcification but also fibro-lipid components, considered to result in the flow of large amounts of fat and thrombotic material. Besides VH-IVUS, comprehensive evaluation is currently being performed by US, 3DCT and black blood MRI for the diagnosis of plaque composition.

Although US is performed at a low price and generally widespread, disadvantages include tortuous vessels and heavy calcification, as well as operator skill level producing varying analysis and subjective evaluations by operator. Although 3D-CT is easy to operate, the spatial resolution is high, and calcified lesions can be easily evaluated, limitations remain due to contrast, plaque other than calcification being difficult to evaluate, and the location of calcification with the plaque unable to be determined. Although black blood method MRI is simple to operate and portrays plaque in high contrast, limitations remain in that artifact occurs due to the motion of the heartbeat, evaluating fibrous caps is not possible and calcified lesions are difficult to determine.

Results of the evaluation performed by VH-IVUS have proven to be efficacious, and that while invasive, is able to obtain adequate information on plaque composition (accurately diagnosing calcified and fibro-lipidic tissue) by color mapping, as well as excelling in reproducibility and objectivity. At present VH-IVUS is used before CAS is performed, and although it does not directly reflect the selection of treatment method, when compared to US, 3D-CT and black blood MRI, it is considered that VH-IVUS analysis may offer the ability to select devices for CAS as well as treatment selection for CEA and CAS.

Conclusions

1. Because VH-IVUS shows plaque property as color-mappings corresponding to pathological composition, IVUS data can be evaluated objectively without being an IVUS expert.

2. When determining plaque composition, VH-IVUS offers an objective evaluation.

3. There is a possibility that the amount of debris during procedure can be forecast by VH-IVUS.

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