Canon

Detection of carotid plaque neovascularization with Superb Micro-vascular Imaging

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Background

Conventional color Doppler ultrasound imaging is a radiation free, non-invasive technique for visualizing carotid arterial structures and hemodynamics, therefore it is regarded as one of the preferred tools for diagnosing carotid artery disease. A motion wall filter is applied when using Doppler imaging techniques to remove artefacts and clutter, however, during this process, the low-velocity blood flow signal may also be removed, causing a loss of the low blood flow signal. Therefore the limitation for conventional Doppler imaging to detect micro vascularity e.g. in the evaluation of intra-plaque neovascularization is highly challenging.

Superb Micro-vascular Imaging (SMI) is an innovative, unique Doppler technology created by Toshiba to overcome limitations of the conventional Doppler technique. SMI employs an exclusive algorithm to distinguish true low-velocity flow from clutter. As a result, SMI allows the visualization of minute vessels with low velocity flow signals without the use of contrast agents. There are two modes in SMI: monochrome (mSMI) and color (cSMI).

Monochrome SMI provides unparalleled sensitivity, by subtracting background information, allowing users to focus on the vasculature and as a result is useful for detecting minute vessels originating in intra-plaque neovascularization. Early detection of neovascularization within atherosclerotic plaque as an indicator in assessing the stability of vulnerable plaque, will assist in the planning of interventional treatment[1-3].

The advantage of SMI in carotid plaque neovascularization

Approximately 30% of strokes are caused by atherosclerotic plaque[4]. The main reason for stroke in this clinical situation is not the stenosis caused as a result of the size of the atheromatous plaque, but its rupture due to instability. Plaque instability can be caused by neovascularization through the intussusceptive angiogenesis from adventitial vasa vasorum[1-3].

Neovascularization originates from vascular tunnels formed by endothelial cells. As they lack the support from connective tissue and basement membrane, the blood vessels becomes fragile and have a high tendency for vessel rupture and hemorrhage. Neovascularization may promote rapid growth of plaque, and even induce intra-plaque hemorrhage and plaque rupture, causing ischemic strokes.

Histopathological evidence shows that vulnerable plaque has twice the neovascularization of stable plaque. With the neovacsularization density in ruptured plaque being four times that of stable plaque. Neovascularization is frequently located in the fibrous cap, lipid rich regions or areas of active inflammation[4].

Previous studies have shown that conventional color Doppler and power Doppler imaging techniques have limitations in visualizing plaque neovascularization. Contrast-enhanced ultrasound imaging (CEUS) is recognized as the gold standard in the detection of carotid plaque neovascularization. CEUS couples contrast specific imaging techniques with ultrasound microbubble contrast agents to better differentiate contrast signals within vessels and the surrounding tissue. CEUS visualization of intra-plaque neovascularization in carotid arteries has good correlation with histological scores. However, there are drawbacks with CEUS, in particular there are restrictions to access in some areas of the world and it places an additional cost burden on the patient.

Without the use of contrast media and utilizing SMI technology we could detect micro vessel flow from 39 plaques in 32 patients with symptomatic carotid artery stenosis (percent diameter stenosis <50%) with mSMI. The plaque included 25 hypoechoic plaque and 14 were mixed. Table 1 shows the distribution of neovascularization inside the plaque. In this study, the neovacsularization location and vasculature detected by SMI correlates well with the CEUS Kappa value of 0.72. The result shows that SMI is a highly reliable method for observing carotid plaque neovascularization.

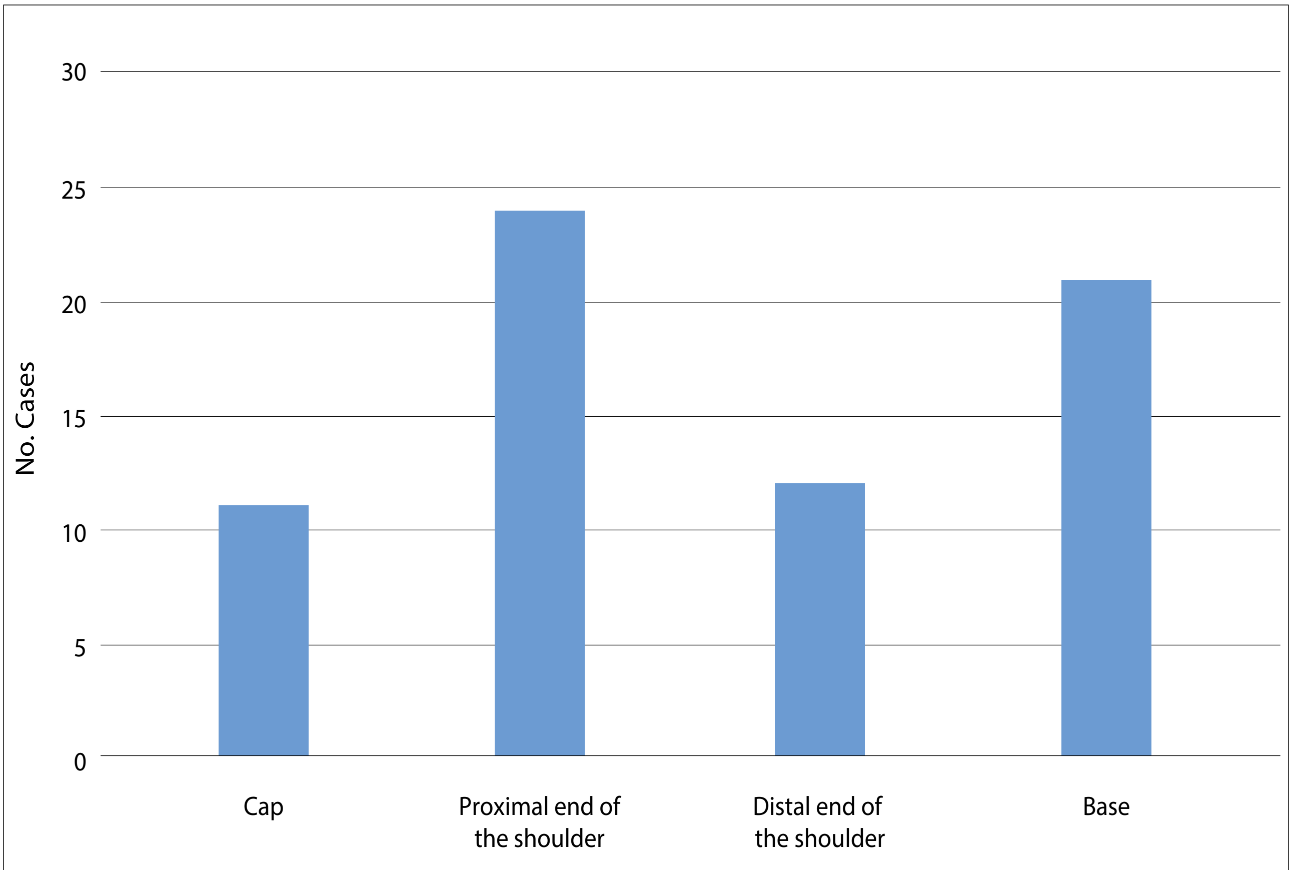


Table 1. SMI imaging for distribution of neovascularization inside the plaque

Case studies

Case 1 : 67 years old male

The patient presented with high blood pressure and vertigo. B-mode demonstrated a predominantly hypoechoic mixed plaque measuring 0.5 cm × 2.8 cm and situated on the anterior wall of the left common carotid artery bifurcation.

Intra-plaque neovascularization was detected with SMI. A microvessel located between the cap and the center of plaque can be visualized.

Using carotid CEUS, contrast agent perfused into the plaque through the cap proving conclusive correlation between SMI and CEUS.

Figure 1. B-mode image of plaque located at LCCA
A predominantly hypoechoic mixed plaque is detected along the anterior wall at the left common carotid artery bifurcation.

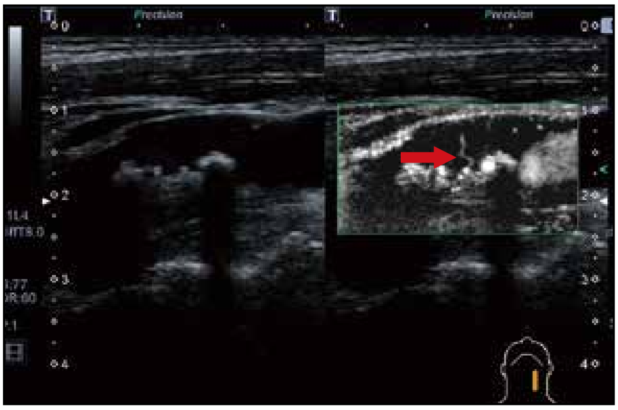
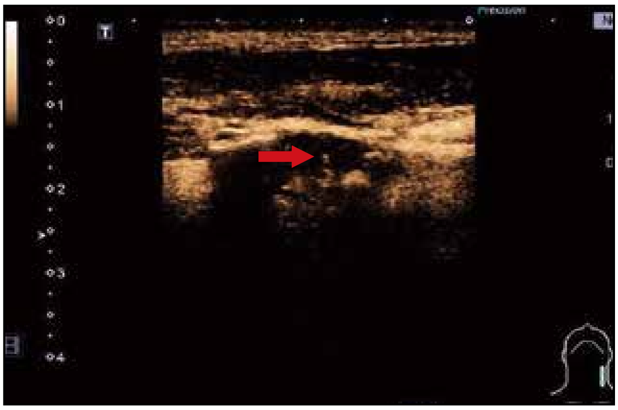


Figure 2. SMI image of plaque located at LCCA
SMI clearly detected micro vessels located between the cap and the center of the plaque.



3a. CEUS

3b. MFI

Figure 3. CEUS image of plaque located at LCCA
Enhancement can be seen within the plaque. Contrast agents perfused into the plaque through the cap. Micro Flow Imaging (MFI) increased the consistency of detection.

Case 2 : 54 years old male

This patient presented with bilateral leg edema. B-mode images detected a hypoechoic plaque along the anterior wall in the middle right common carotid artery, measuring 0.23 cm × 3.0 cm.

SMI demonstrated micro vascularity situated at the distal shoulder of the plaque and extending from the adventitia.

CEUS confirmed these results with enhancement demonstrated at the distal shoulder of the plaque extending from the adventitia into the plaque.

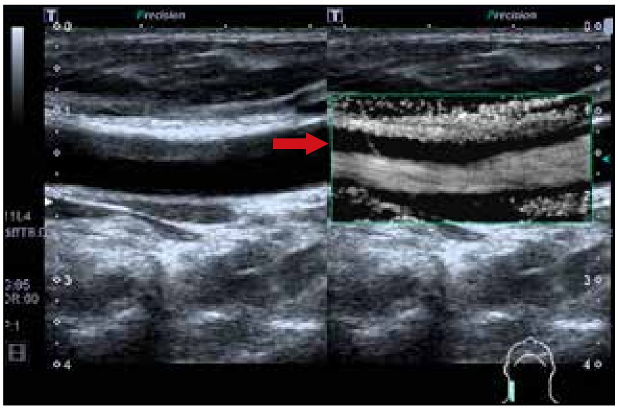


Figure 4. SMI image of hypoechoic plaque situated at the anterior wall of the right common carotid artery
SMI clearly detected micro flow inside the hypoechoic plaque.

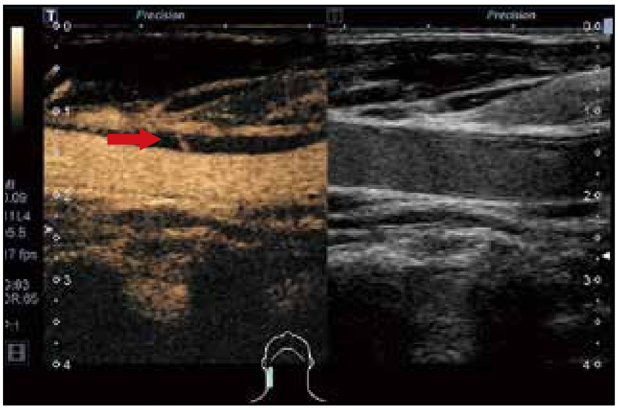


Figure 5. CEUS image of hypoechoic plaque situated at the anterior wall of the right common carotid artery
Contrast enhancement was demonstrated within the hypoechoic plaque, with microflow at the distal shoulder of the plaque extending from the adventitia into the plaque.

Case 3 : 58 years old male

A patient with Ischemic Cerebrovascular disease and type 2 diabetes was diagnosed with a hypoechoic plaque measuring 0.37 cm × 3.1 cm, situated at the anterior wall of the right carotid bifurcation. SMI detected irregular perfusion within the plaque (Figure 6). This finding was confirmed with CEUS, demonstrating intra-plaque neovascularization.

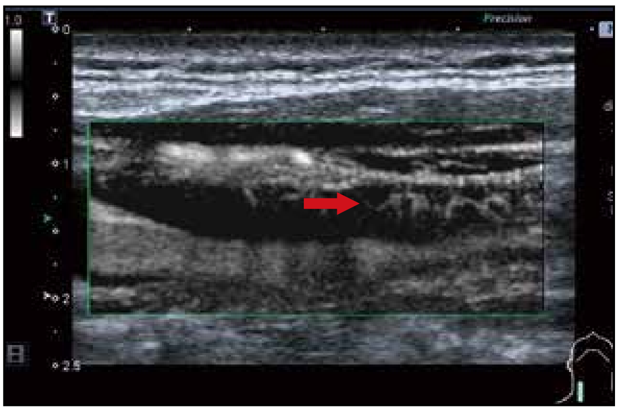


Figure 6. SMI image of hypoechoic plaque situated at the anterior wall of the right common carotid bifurcation
SMI detected irregular perfusion within the hypoechoic plaque situated on the anterior wall of the right common carotid artery

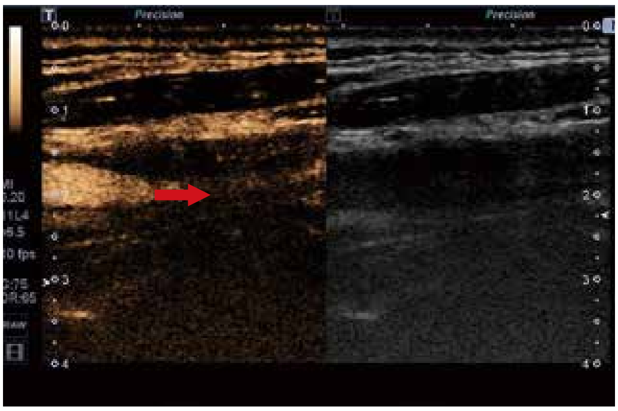


Figure 7. CEUS image of hypoechoic plaque situated at the anterior wall of the right carotid bifurcation
CEUS demonstrated irregular perfusion from within the hypoechoic plaque at the anterior wall of right carotid bifurcation

Case 4 : 59 years old female

Routine ultrasound screening of a patient suffering from vertigo demonstrated hypoechoic plaque measuring 0.4 cm × 3.5 cm situated on the posterior wall of the left carotid bifurcation. SMI demonstrated neovascularization with multiple branches within the plaque (Figure 8). Carotid CEUS confirmed the above findings.

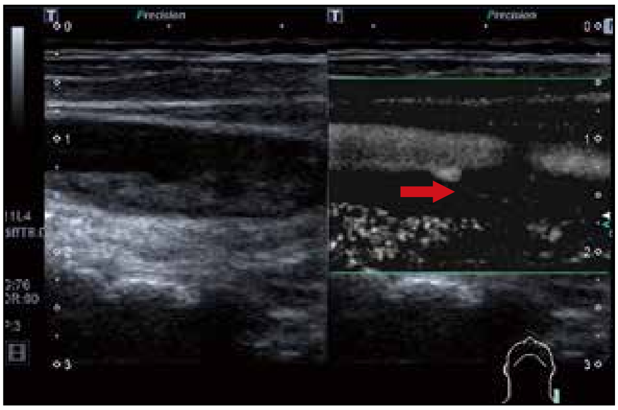


Figure 8. SMI image of hypoechoic plaque situated at the posterior wall of the left carotid bifurcation
SMI detected a branch like pattern within the hypoechoic plaque at the posterior wall of the left carotid bifurcation.

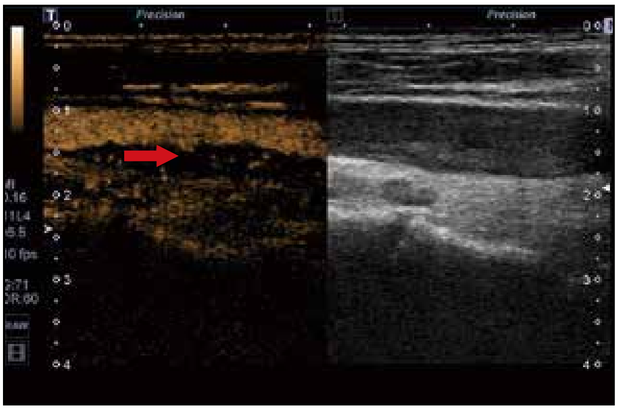


Figure 9. CEUS image of hypoechoic plaque situated at the posterior wall of the left carotid bifurcation
CEUS detected a branch like pattern within the hypoechoic plaque situated at the posterior wall of the left carotid bifurcation.

Future work

In majority of the cases, SMI demonstrated neovascularization that was confirmed by CEUS. In a small percentage for hypoechoic or predominantly mixed plaque where no neovacsularization was detected by SMI, CEUS examinations will be conducted. SMI and CEUS outcomes will be analyzed within the criteria of statistical calculation of sensitivity, specificity and accuracy to enable causes for significant variations between SMI and CEUS results to be investigated.

Quantitative analysis for carotid plaque neovacsularization is required to enable appropriate drug therapy to be given. Further development of SMI and its uses, to facilitate a quantitative measurement, has great potential for the future.

Conclusion

SMI offers the ability to detect carotid plaque neovascularization without the use of CEUS. As a result, SMI may become a powerful tool for evaluating vulnerable carotid plaque.

Reference

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Additional reading

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Comment from reviewer

The existence of blood flow in plaque is known to be important for evaluating the characteristics of the plaque.

With the introduction of SMI, observation of blood flow in plaque could be observedwithout the use of CEUS. It is clear that SMI is a method that is free of contrast medium, easy-to-use and inexpensive for observing blood flow in plaque.

Henceforth, the study of relationship between characteristics and blood flow in plaque that has been difficult to observe is expected to have an additional contrast free process.

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