Review

J Lipid Atheroscler 2017 June;6(1):15-21
https://doi.org/10.12997/jla.2017.6.1.15
pISSN 2287-2892 • eISSN 2288-2561

Diagnostic and Therapeutic Approach of Carotid and Cerebrovascular Plaque on the Basis of Vessel Imaging

Dong Hyun Lee, Jong-Ho Park

Department of Stroke Neurology, Seonam University Myongji Hospital, Goyang-si, Korea

Atherosclerosis, characterized by chronic systemic inflammation with plaque formation, is one of the major causes of cerebrovascular disease. Recent advances in imaging technologies can help further understand the overall process and biology of plaque formation and rupture. Thus, these imaging techniques could aid clinicians to make better decision for risk stratification, therapeutic planning, and prediction of future cerebrovascular event. Ultrasonography, magnetic resonance imaging, and positron emission tomography are the rapidly-evolving imaging modalities dealing with assessment of atherosclerotic plaque. By advances in imaging technology for evaluating plaque, we can characterize the vulnerability of plaque in-vivo, understand the composition and activity of plaque, assess therapeutic response to treatment, and ultimately predict the overall risk of future cerebrovascular episodes. In this review, we will introduce current understanding of various advanced imaging modalities and clinical application of these imaging technologies. **(J Lipid Atheroscler 2017 June;6(1):15-21)**

Key Words: Atherosclerosis, Plaque, Imaging, Carotid artery disease, Cerebrovascular disease

INTRODUCTION

Atherosclerosis is a chronic systemic inflammatory disease with an insidious process caused by multiple pathological changes triggering lipoprotein dysregulation and immunocyte activation within the arterial system.[1] As clinical vascular events happen to patients abruptly without any warning sign following the rupture of plaque and the formation of thrombus, various risk stratification and prediction systems had been developed. Despite of improved treatment and prevention strategies based on these systems, cardiovascular and cerebrovascular disease are still the major causes of death and disability in the global population. Therefore, it is a great challenge to accurately identify the patients with high risk of future vascular episodes, and reliably monitor the therapeutic response to medication.

Recent advances in imaging technologies can help further understand the overall process in atherosclerosis including molecular biology of plaque formation and rupture. These imaging techniques can aid clinicians to make more accurate decision for risk stratification, therapeutic planning, and prediction of future risk of clinical vascular events. Three-dimensional ultrasonography, high-resolution magnetic resonance imaging (MRI), and positron emission tomography (PET) with specific molecular tracers are the main imaging modalities dealing with assessment of atherosclerotic plaque. In this review, we will introduce current understanding of various advanced imaging modalities and clinical application of

Received: May 31, 2017
Revised: June 8, 2017
Accepted: June 7, 2017

Corresponding Author: Jong-Ho Park, Department of Stroke Neurology, Seonam University Myongji Hospital, 55 Hwasu-ro 14beon-gil, Deogyang-gu, Goyang-si, Gyeonggi-do 10475, Korea
Tel: +82-31-810-5417, Fax: +82-31-969-0500, E-mail: neurotector.jhp@gmail.com

these imaging technologies.

PLAQUE IMAGING IN THE CAROTID ARTERY

Carotid artery, superficially located and easily palpated, has a bifurcating region, which bears significant amount of shear stress, and is susceptible to early atherosclerotic changes. Therefore, carotid bifurcation is suitable for imaging evaluation and generally a good surrogate for other systemic vascular beds.

1. Assessment of carotid plaque burden using ultrasonography

Measurement of the plaque severity to accurately quantify the plaque burden in the carotid arteries have been tried before, because the predictive power for clinical outcome is limited in the assessment of the luminal stenosis in the carotid arteries. The assessment of plaque burden in the carotid arteries using ultrasonography had begun from measuring carotid intima-media thickness (IMT) around 1985. Since then, unfortunately IMT did accurately reflect neither atherosclerosis nor prediction of clinical events.[2,3] To improve the predictive power of plaque screening for cardio-cerebrovascular events beyond IMT, quantifying the carotid plaque burden has been developed as a good alternative to IMT measurement. Carotid plaques grow along the artery 2.4 times faster than they thicken, thus we can easily deduce that two-dimensional measurement of total plaque area reflects the actual plaque burden more accurately. Actually, measurement of total plaque area had more predictive power in future risk of stroke, death, or myocardial infarction than measurement of carotid IMT, and also improved the accuracy of risk scoring system.[4-6] Carotid plaques also progress circumferentially, thus quantification of plaque volume instead of plaque area can reflect the actual plaque burden more sensitively.[3,4,7,8] Recent study[8] compared progression of IMT, total plaque area, and total plaque volume in the same patients. The study demonstrated that progression of total plaque volume strongly predicted stroke, death or transient ischemic attack (Kaplan-Meier log rank p=0.001), stroke/death/myocardial infarction (p=0.008). Annual changes in total plaque area and total plaque volume reach around 10 mm^2/year and 50 to 100 mm^3/year respectively.[9] It is thus more advantageous and sensitive to monitor treatment effect on carotid arteries during statin therapy in patients with vascular risk factors for measuring total plaque volume than total plaque area. The previous methodology of measuring the plaque volume goes beyond the scope of this review, and summarized well elsewhere.[4] Among semi- or fully automated methods, mechanical sweep using Philips system recently has shown the excellent reproducibility and feasibility in the plaque volume quantification.[10,11]

Atherosclerotic stenosis in the carotid arteries is one of the major risk factor of ischemic cerebrovascular diseases. Besides degree of the luminal narrowing or quantification of plaque volume, both the composition and the morphological characteristics of the plaques are related to future cerebrovascular ischemic episodes.[12] Histopathologically, it is known that a vulnerable plaque is covered with a thin fibrous cap, and contains a large necrotic lipid core.[13,14] A recent meta-analysis demonstrated that plaques with complex features such as intra-plaque echolucency, neovascularization, ulceration, and intra-plaque motion were significantly associated with cerebral ischemic symptoms.[12] Intra-plaque echolucency represents intra-plaque hemorrhage and lipid-rich necrotic core histologically. Ultrasonography is more sensitive to detect the size and location of echolucency within the plaque than computed tomography (CT) or magnetic resonance imaging (MRI). Large-sized echolucency adjacent to lumen, especially, is associated with increased risk of stroke episodes.[3] Although ultrasonography is generally inferior to CT or MRI for detecting ulceration, three dimensional ultrasonography can reliably

Table 1. Typical MRI signal characteristics of carotid plaque composition

	T1W	T2W	PDW	3D TOF	T1GD
Fibrous cap	Isointensity	Mixed intensity	Mixed intensity	Hypointensity	Isointensity
Lipid-rich necrotic core	Iso/hyperintensity	Mixed intensity	Hypointensity	Hypointensity	Hypointensity
Intra-plaque hemorrhage	Hyperintensity	Mixed intensity	Mixed intensity	Hyperintensity	Hyperintensity
Calcification	Hypointensity	Hypointensity	Hypointensity	Hypointensity	Hypointensity

T1W; T1-weighted image, T2W; T2-weighted image, PDW; proton density weighted image, 3D TOF; three dimensional time-of-flight image, T1GD; T1 gadolinium enhancement image

detect the ulceration, and characterize the surface morphology of plaques.[15]

• Intravascular Ultrasound (IVUS)

As IVUS gets a three dimensional image from inner vascular lumen, the characteristics of vessel wall and atherosclerotic plaques can be analyzed with excellent resolution compared to routine ultrasonographic study.[16] IVUS has gained clinical usefulness from several studies dealing with coronary artery diseases. In carotid artery diseases, IVUS is used as a complementary tool during carotid artery stenting. IVUS can accurately detect plaque characteristics such as calcification, necrosis, lipid-rich core, and measure a degree of stenosis in eccentric lesion the digital subtraction angiography cannot detect.[17]

2. Intravascular near-infrared spectroscopy

Intravascular near-infrared spectroscopy (NIRS) is an emerging imaging modality, which can detect a lipid core inside the unstable atherosclerotic plaque.[18,19] Briefly, NIRS emits near-infrared light to specified tissue of interest, and measures the proportion of reflected light determined by scattering and absorption according to different biochemical compositions of the specified tissue. Thus, NIRS easily distinguish cholesterol from other constituents.[18] A small experimental study tried to show safety and feasibility of application of NIRS to detect and analyze the lipid-rich plaque into patients with carotid stenosis combined with IVUS.[19]

3. Assessment of carotid plaque burden using MRI

High resolution carotid MRI has a good spatial, temporal, contrast resolution, and can evaluate accurately both the carotid stenosis and plaque characterization.[20,21] MRI can visualize the carotid wall, and quantify the vascular burden by three dimensional volumetric measurement.[22,23] Detailed advanced technique of high resolution MRI sequence is well described in recent article.[24] Changes of plaque burden after therapeutic interventions can be monitored by MRI. A small study comparing high resolution MRI with ultrasonography, however, showed inferiority of MRI in detecting small-size plaque (<2.5 mm).[22] Several key features of vulnerable plaque can also be visualized by high resolution MRI. These features include positive remodeling in the vessel wall, lipid-rich necrotic core, intra-plaque hemorrhage, and presence of thin/ruptured fibrous cap.[20,23,25-27] Typical characteristic features of plaque in the variable MRI sequence were shown in the Table 1. Recent cross sectional study in the stroke-free population from Rotterdam study investigated determining factors of carotid plaque burden in about 1500 subjects. This study measured vessel wall volume and lumen volume as a plaque burden by using high resolution MRI. The study showed that intra-plaque hemorrhage is strongly associated with luminal stenosis independent of plaque burden.[28] In the substudy of Atherothrombosis Intervention in Metabolic Syndrome with Low HDL/High Triglycerides: Impact on Global Health

Outcomes (AIM-HIGH) trial, 214 patients receiving intensive medical therapy with established atherosclerotic diseases underwent high resolution MRI and ultrasonography in the carotid arteries, and was prospectively followed for about 3 years. The study demonstrated that plaque characteristics suggestive of vulnerability rather than clinical vascular risk factor and plaque burden was strongly associated with clinical outcomes such as myocardial infarction, ischemic stroke, etc.[23] In the study, subjects with thin/ruptured fibrous cap and lipid-rich necrotic core volume had a 4-fold and 1.5-fold risk of future vascular events respectively. None of the plaque burden measurement (maximum wall thickness, maximum percent wall area, and percent wall volume) were significantly associated with clinical outcomes describe above. Therefore, markers of carotid plaque vulnerability may serve as novel surrogate markers for systemic atherothrombotic risk, and overcome the limited predictive power of plaque burden and luminal stenosis.

4. Assessment of carotid plaque burden using molecular imaging

Progression of atherosclerosis and plaque rupture are mostly determined by extent of the inflammatory reaction within the vessel wall triggered by vascular risk factors. Macrophage among immune cells is a key player in the pro-inflammatory signaling cascade within vulnerable plaques. Thus, macrophage is an attractive molecular imaging target to track vascular inflammation.[26]

- **^{18}F-fluorodeoxyglucose (FDG) PET**

FDG is a radio-labeled glucose analogue used commonly in PET imaging. In atherosclerosis, vascular ^{18}F-FDG uptake seems to be highest during early foam cell formation, and at late time points (>2 hours) reflects increased activity of macrophages.[26] Several studies in vascular inflammation by using ^{18}F-FDG PET demonstrated good correlation to macrophage density within carotid plaque and high-risk plaque morphology.[27,29] However, as ^{18}F-FDG is taken up by all cells with active glucose metabolism, it provides a nonspecific marker of inflammation in atherosclerosis. Vascular ^{18}F-FDG uptake is also influenced by plaque hypoxia and the efficiency of tracer delivery by the microcirculation.[26] Due to these limitations, specialized molecular PET tracers are actively investigated for atherosclerotic imaging including ^{64}Cu-DOTATATE (macrophages), ^{18}F-galacto-RGD (angiogenesis), ^{18}F-sodium fluoride (calcification), and ^{64}Cu-ATSM (hypoxia).[27,30] As previously mentioned, high resolution MRI well visualizes vessel wall and plaque, whereas PET has poor resolution with high sensitivity for visualizing specific molecular targets. Recently, hybrid PET/MR imaging for carotid plaque can provide morphological (plaque characteristics) and functional (macrophage activity) information of atherosclerotic plaques simultaneously. One study reported high frequency of active unstable plaques found by the hybrid PET/MR imaging in patients with cryptogenic ischemic stroke. The study showed high prevalence of vulnerable plaques in the ipsilateral carotid artery in patients with ischemic stroke.[31] Therefore, hybrid PET/MR imaging may have a potential benefit of early detection of carotid atherosclerosis.

PLAQUE IMAGING IN THE INTRACRANIAL ATHEROSCLEROTIC DISEASE

1. Intracranial atherosclerotic plaque

Intracranial atherosclerotic disease is the main cause of ischemic stroke in Asian population including South Korea.[32] Like atherosclerosis in other vascular beds, those in the intracranial vessels also start to grow outward direction from the center of lumen then enlarge the size of vessel (positive remodeling) before reaching up to detectable stenosis.[33,34] Traditional vascular imaging mainly focuses on the lumen, thus frequently misses non-stenotic lesions or underestimates the atherosclerotic

burden caused by positive remodeling.[35] Recent autopsy studies from ischemic stroke show that the degree of stenosis cannot fully be responsible for intracranial atherosclerotic burden.[36,37] The burden, characteristics, and morphology of atherosclerotic plaques in the intracranial vessels are essential in assessing the vulnerability of the plaque similar to those in the extracranial arteries. In this regard, it is an important field of research to investigate the intracranial vascular burden by using vessel wall imaging.

2. Assessment of plaque burden in the intracranial atherosclerotic disease vessel wall MRI

High resolution, black-blood MRI with fast spin echo sequence is the typical imaging modality to directly evaluate and visualize intracranial vascular morphology. This imaging modality can acquire the accurate structure of the arterial wall by selective signal suppression from the arterial lumen.[38,39] Compared to extracranial vessel wall imaging, intracranial vessel wall imaging is technically limited due to sensitivity to motion artifact, small caliber and tortuous course of the intracranial arteries, and requires high-resolution and superior signal-to-noise ratio.[35] Notwithstanding this limitation, advanced MR imaging techniques make us improve in understanding the pathomechanism of intracranial atherosclerosis.

The frequent locations of atherosclerotic plaques are distal internal carotid artery (ICA), intracranial ICA bifurcation, and the M1 segment of the middle cerebral artery (MCA).[40] The plaque characteristics shown in the vessel wall imaging may be one of important predictors of future stroke episodes, and correlate well with pathological findings.[41,42] Positive remodeling,[34,43,44] the degree of stenosis, and ratio of wall thickening to lumen[44] is associated with symptomatic plaque. Size of the lipid-rich necrotic core, which is isointense on T1 and hypointense on T2, correlates with risk of plaque rupture.[43,44] Presence of plaque eccentricity can help differentiate intracranial atherosclerosis from other etiologies. Eccentric wall thickening seems to be associated with frequent cerebrovascular episodes. Histology-verified *in vitro* study on intracranial atherosclerotic diseases showed the trend that eccentric plaques were associated with higher risk of cerebrovascular episodes compared with concentric plaques (30.77% vs. 17.39%, p=0.241).[42] Retrospective high resolution MR study including non-significant stenosis in the intracranial vessel demonstrated that eccentricity was more higher in the symptomatic plaque than in the asymptomatic plaque (p=0.028).[45] Another study including symptomatic significant MCA stenosis showed that plaques with non-significant luminal narrowing was associated with eccentricity (p<0.05).[40] Therefore, the analysis of the plaque component and characteristics as well as the wall remodeling pattern in the vessel wall imaging can further reinforce the current therapeutic strategy toward ischemic cerebrovascular diseases primarily limited to the steno-occlusion in the luminal imaging.

CONCLUSION

With remarkable advances in imaging technologies during last decades, we can evaluate not only the presence or burden of atherosclerosis but the composition, activity, and vulnerability of the plaques *in vivo*. As we have further understood the molecular biological process of atherosclerosis by the help of multimodal imaging, we are narrowing the gap little by little between the area of basic research and the routine clinical practice. By these advanced imaging modalities, we can assess more accurately the therapeutic response to anti-atherosclerosis treatment. In the future, we will reach up to the extent which we precisely tailor and predict the risk of forthcoming clinical vascular episodes individually.

REFERENCES

1. Libby P. Inflammation in atherosclerosis. Arterioscler Thromb Vasc Biol 2012;32:2045-2051.
2. Lorenz MW, Polak JF, Kavousi M, Mathiesen EB, Völzke H, Tuomainen TP, et al. Carotid intima-media thickness progression to predict cardiovascular events in the general population (the PROG-IMT collaborative project): a meta-analysis of individual participant data. Lancet 2012;379:2053-2062.
3. Ho SS. Current status of carotid ultrasound in atherosclerosis. Quant Imaging Med Surg 2016;6:285-296.
4. Spence JD, Parraga G. Three-dimensional ultrasound of carotid plaque. Neuroimaging Clin N Am 2016;26:69-80.
5. Spence JD, Eliasziw M, DiCicco M, Hackam DG, Galil R, Lohmann T. Carotid plaque area: a tool for targeting and evaluating vascular preventive therapy. Stroke 2002;33:2916-2922.
6. Mathiesen EB, Johnsen SH, Wilsgaard T, Bønaa KH, Løchen ML, Njølstad I. Carotid plaque area and intima-media thickness in prediction of first-ever ischemic stroke: a 10-year follow-up of 6584 men and women: the Tromsø Study. Stroke 2011;42:972-978.
7. Spence JD. Time course of atherosclerosis regression. Atherosclerosis 2014;235:347-348.
8. Wannarong T, Parraga G, Buchanan D, Fenster A, House AA, Hackam DG, et al. Progression of carotid plaque volume predicts cardiovascular events. Stroke 2013;44:1859-1865.
9. Spence JD. Carotid ultrasound phenotypes are biologically distinct. Arterioscler Thromb Vasc Biol 2015;35:1910-1913.
10. Græbe M, Entrekin R, Collet-Billon A, Harrison G, Sillesen H. Reproducibility of two 3-D ultrasound carotid plaque quantification methods. Ultrasound Med Biol 2014;40:1641-1649.
11. Kalashyan H, Shuaib A, Gibson PH, Romanchuk H, Saqqur M, Khan K, et al. Single sweep three-dimensional carotid ultrasound: reproducibility in plaque and artery volume measurements. Atherosclerosis 2014;232:397-402.
12. Brinjikji W, Rabinstein AA, Lanzino G, Murad MH, Williamson EE, DeMarco JK, et al. Ultrasound characteristics of symptomatic carotid plaques: a systematic review and meta-analysis. Cerebrovasc Dis 2015;40:165-174.
13. Stone GW. In search of vulnerable plaque. Circ Cardiovasc Imaging 2012;5:428-430.
14. Brinjikji W, Huston J 3rd, Rabinstein AA, Kim GM, Lerman A, Lanzino G. Contemporary carotid imaging: from degree of stenosis to plaque vulnerability. J Neurosurg 2016;124:27-42
15. Rafailidis V, Chryssogonidis I, Tegos T, Kouskouras K, Charitanti-Kouridou A. Imaging of the ulcerated carotid atherosclerotic plaque: a review of the literature. Insights Imaging 2017;8:213-225.
16. Hitchner E, Zhou W. Utilization of intravascular ultrasound during carotid artery stenting. Int J Angiol 2015;24:185-188.
17. Umemoto T, Pacchioni A, Nikas D, Reimers B. Recent developments of imaging modalities of carotid artery stenting. J Cardiovasc Surg (Torino) 2017;58:25-34.
18. Kilic ID, Caiazzo G, Fabris E, Serdoz R, Abou-Sherif S, Madden S, et al. Near-infrared spectroscopy-intravascular ultrasound: scientific basis and clinical applications. Eur Heart J Cardiovasc Imaging 2015;16: 1299-1306.
19. Štěchovský C, Hájek P, Horváth M, Špaček M, Veselka J. Near-infrared spectroscopy combined with intravascular ultrasound in carotid arteries. Int J Cardiovasc Imaging 2016;32:181-188.
20. Singh N, Moody AR, Roifman I, Bluemke DA, Zavodni AE. Advanced MRI for carotid plaque imaging. Int J Cardiovasc Imaging 2016;32:83-89.
21. Mossa-Basha M, Wasserman BA. Low-grade carotid stenosis: implications of MR imaging. Neuroimaging Clin N Am 2016;26:129-145.
22. Hjelmgren O, Schmidt C, Johansson L, Bergström GM. Comparison between magnetic resonance imaging and B-mode ultrasound in detecting and estimating the extent of human carotid atherosclerosis. Clin Physiol Funct Imaging. Forthcoming 2017.
23. Sun J, Zhao XQ, Balu N, Neradilek MB, Isquith DA, Yamada K, et al. Carotid plaque lipid content and fibrous cap status predict systemic CV outcomes: the MRI substudy in aim-high. JACC Cardiovasc Imaging 2017;10:241-249.
24. Yuan C, Parker DL. Three-dimensional carotid plaque

MR imaging. Neuroimaging Clin N Am 2016;26:1-12.
25. Virani SS, Ballantyne CM. From plaque burden to plaque composition: toward personalized risk assessment. JACC Cardiovasc Imaging 2017;10:250-252.
26. Tarkin JM, Dweck MR, Evans NR, Takx RA, Brown AJ, Tawakol A, et al. Imaging atherosclerosis. Circ Res 2016;118:750-769.
27. Ripa RS, Pedersen SF, Kjær A. PET/MR imaging in vascular disease: atherosclerosis and inflammation. PET Clin 2016;11:479-488.
28. Selwaness M, Hameeteman R, Van 't Klooster R, Van den Bouwhuijsen Q, Hofman A, Franco OH, et al. Determinants of carotid atherosclerotic plaque burden in a stroke-free population. Atherosclerosis 2016;255: 186-192.
29. Tarkin JM, Joshi FR, Rudd JH. PET imaging of inflammation in atherosclerosis. Nat Rev Cardiol 2014; 11:443-457.
30. Lau JM, Laforest R, Nensa F, Zheng J, Gropler RJ, Woodard PK. Cardiac applications of PET/MR imaging. Magn Reson Imaging Clin N Am 2017;25:325-333.
31. Hyafil F, Schindler A, Sepp D, Obenhuber T, Bayer-Karpinska A, Boeckh-Behrens T, et al. High-risk plaque features can be detected in non-stenotic carotid plaques of patients with ischaemic stroke classified as cryptogenic using combined (18)F-FDG PET/MR imaging. Eur J Nucl Med Mol Imaging 2016;43:270-279.
32. Banerjee C, Chimowitz MI. Stroke caused by atherosclerosis of the major intracranial arteries. Circ Res 2017;120:502-513.
33. Qiao Y, Anwar Z, Intrapiromkul J, Liu L, Zeiler SR, Leigh R, et al. Patterns and implications of intracranial arterial remodeling in stroke patients. Stroke 2016;47:434-440.
34. Shi MC, Wang SC, Zhou HW, Xing YQ, Cheng YH, Feng JC, et al. Compensatory remodeling in symptomatic middle cerebral artery atherosclerotic stenosis: a high-resolution MRI and microemboli monitoring study. Neurol Res 2012;34:153-158.
35. Alexander MD, Yuan C, Rutman A, Tirschwell DL, Palagallo G, Gandhi D, et al. High-resolution intracranial vessel wall imaging: imaging beyond the lumen. J Neurol Neurosurg Psychiatry 2016;87:589-597.
36. Gutierrez J, Elkind MS, Virmani R, Goldman J, Honig L, Morgello S, et al. A pathological perspective on the natural history of cerebral atherosclerosis. Int J Stroke 2015;10:1074-1080.
37. Mazighi M, Labreuche J, Gongora-Rivera F, Duyckaerts C, Hauw JJ, Amarenco P. Autopsy prevalence of intracranial atherosclerosis in patients with fatal stroke. Stroke 2008;39:1142-1147.
38. Cao Y, Sun Y, Zhou B, Zhao H, Zhu Y, Xu J, et al. Atherosclerotic plaque burden of middle cerebral artery and extracranial carotid artery characterized by MRI in patients with acute ischemic stroke in China: association and clinical relevance. Neurol Res 2017;39:344-350.
39. Zhu XJ, Du B, Lou X, Hui FK, Ma L, Zheng BW, et al. Morphologic characteristics of atherosclerotic middle cerebral arteries on 3T high-resolution MRI. AJNR Am J Neuroradiol 2013;34:1717-1722.
40. Dieleman N, Yang W, Abrigo JM, Chu WC, van der Kolk AG, Siero JC, et al. Magnetic resonance imaging of plaque morphology, burden, and distribution in patients with symptomatic middle cerebral artery stenosis. Stroke 2016;47:1797-1802.
41. Turan TN, Rumboldt Z, Granholm AC, Columbo L, Welsh CT, Lopes-Virella MF, et al. Intracranial atherosclerosis: correlation between in-vivo 3T high resolution MRI and pathology. Atherosclerosis 2014;237:460-463.
42. Yang WJ, Chen XY, Zhao HL, Niu CB, Xu Y, Wong KS, et al. In vitro assessment of histology verified intracranial atherosclerotic disease by 1.5t magnetic resonance imaging: concentric or eccentric? Stroke 2016;47:527-530.
43. Xu WH, Li ML, Gao S, Ni J, Zhou LX, Yao M, et al. In vivo high-resolution MR imaging of symptomatic and asymptomatic middle cerebral artery atherosclerotic stenosis. Atherosclerosis 2010;212:507-511.
44. Chung GH, Kwak HS, Hwang SB, Jin GY. High resolution MR imaging in patients with symptomatic middle cerebral artery stenosis. Eur J Radiol 2012;81:4069-4074.
45. Niu PP, Yu Y, Zhou HW, Liu Y, Luo Y, Guo ZN, et al. Vessel wall differences between middle cerebral artery and basilar artery plaques on magnetic resonance imaging. Sci Rep 2016;6:38534.