Combined PET-FDG and USPIO-enhanced MR Imaging in Patients with Symptomatic Moderate Carotid Artery Stenosis


Cambridge Vascular Unit, University Department of Radiology, Department of Clinical Neurosciences, Cambridge University Hospitals NHS Foundation Trust, Cambridge, UK

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Abstract

Introduction: PET-FDG and USPIO-enhanced MRI are increasingly being used in depicting carotid atheroma inflammation — a risk factor for the high risk plaque. Their combined use has not been previously reported.

Report: Two patients presenting with stroke and identified with 50% carotid stenosis on duplex ultrasonography, underwent PET FDG and USPIO-enhanced MR imaging. Results were concordant and complementary suggesting that both techniques reflect similar metabolic processes.

Discussion: The selection of patients for carotid revascularisation has largely been based on the severity of luminal stenosis alone. The two imaging modalities, which identify inflammatory activity, may be potential surrogate risk markers in the selection of patients eligible for carotid surgery, if plaque inflammation can be correlated with risk of developing clinical symptoms.


Introduction

Appreciation of the inflammatory nature of the atherosclerotic process has prompted the need for non-invasive characterization of the metabolic and functional state of atherosclerotic plaques in vivo. Positron emission tomography with 18F-Fluorodeoxyglucose (PET FDG) and high-resolution magnetic resonance imaging (MRI) using ultrasmall superparamagnetic iron oxide (USPIO) particles
(Sinerem™, Guerbet, France) have both emerged as promising techniques to address this in the carotid circulation. We report, for the first time, on using both modalities in two symptomatic patients with moderate carotid artery disease.

**Case Report 1**

A 76-year-old man experienced several brief episodes of right upper limb weakness, visual disturbance and speech difficulty over two weeks, consistent with a transient ischaemic attack. The only known vascular risk factor was essential hypertension. Duplex ultrasonography revealed a left 55% carotid stenosis. Brain MRI revealed a recent left frontal infarction. He was started on aspirin and atorvastatin. The dysphasia resolved completely over the subsequent two weeks but the patient suffered a further right-sided hemiparesis just prior to his planned left carotid endarterectomy.

An initial high-resolution MRI of the neck (imaging parameters on request), performed 2 weeks after presentation, showed an eccentric plaque in the left ICA (Fig. 1). PET FDG performed on the same day (acquired in 3D-mode for 75 minutes after injection of 185 MBq FDG; GE PET Advance scanner) showed increased uptake of the tracer into the plaque (SUVmax 3.6). USPIO enhanced MR imaging was also acquired using a quadruple inversion recovery spiral 2D T2*W sequence, pre and 36 hours post intravenous administration of Sinerem, and showed a drop in signal intensity within the plaque indicating uptake of USPIO and likely inflammatory activity. MR images were manually co-registered according to plaque morphology and distance from the carotid bifurcation at the time of imaging.

**Case Report 2**

A 59-year-old man presented with a right amaurosis fugax. He had been a heavy smoker for 25 years. MRI of the brain showed some evidence of small vessel disease. He was found to have a right 50% ICA stenosis on duplex ultrasonography. He was started on aspirin and atorvastatin and remains symptom free.

Three weeks after the onset of symptoms, high-resolution MRI of the neck showed a concentric plaque in the right ICA (Fig. 1). Sinerem-enhanced MRI and PET FDG performed within a week of the initial MRI showed no change in signal intensity between pre and post USPIO imaging and no significant uptake of the tracer respectively into the plaque.

Both patients did not experience any side effects from either the tracer or USPIO infusion.

**Discussion**

In both of these cases, moderate carotid disease was identified on ultrasonography and assumed to be the culprit lesions. Current evidence from large clinical trials (based solely on luminal narrowing) suggests that a stenosis of 50% represents a rather grey area in terms of the decision of

![Figure 1](image_url)
carotid endarterectomy with wide variation in clinical practice. The detailed structural and functional information provided by MRI and PET may aid in making this decision. In patient 1, remodelling of the ICA had accommodated the large plaque, which might have otherwise warranted surgical intervention. Functionally, both PET FDG and MRI USPIO suggest high inflammatory activity within the plaque in patient 1, but not in patient 2. It is interesting to note that patient 1 developed recurrent symptoms as well. The agreement in defining the metabolic status of the plaque is very encouraging and gives further strength to the evidence that both modalities reflect similar aspects of the atherosclerotic process, namely, macrophage recruitment and activation. The apparent quiescence of the plaque in the second patient may be attributed to (i) the lag between symptoms and imaging and the use of a statin, both possibly allowing stabilization of the inflammatory process (although the sequence of events is similar to patient 1) or (ii) that indeed the plaque was not the culprit in this case.

USPIO-enhanced MRI has been used to demonstrate macrophage activity in symptomatic human carotid plaques and whilst the tool appears useful, imaging relies on areas of signal loss making quantification difficult. Moreover imaging has to be repeated within 36 hours, thus adding impracticability. PET FDG with its associated radiation burden limits the number of PET scans that patients can undertake. Accurate quantification, however, is possible when used in conjunction with MRI or computed tomography, despite being time- and labour-intensive and having limited spatial resolution.

There is an increasing desire to formulate surrogate endpoints for clinical trials with imaging being a possible biomarker for assessing vulnerable plaque and evaluating new therapeutic approaches in atheromatous disease. The feasibility of combining PET and contrast enhanced MRI opens the way to studies where these techniques can be complementary and their utility in clinical practice compared and cross-validated. However it needs to be appreciated that the sample size used in this study is too small and the results need to be validated with a larger cohort of patients.

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Competing Interests

JHG is a consultant to GSK.

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References