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CA 2468777 (カナダ)
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- 3) 入力関数持続モニター
特許第4375978号
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- 4) 単一光子エミッションコンピュータ断層撮影のための装置と方法
特許第4424911号
登録日：平成21年12月18日
- 5) 磁気共鳴撮像法によるデータ収集方法及びプログラム
出願日：2003年12月2日
公開番号：2005-185296
- 6) 放射性薬剤のための放射線重量測定装置と濃度モニター統合装置
特許第4399588号
登録日：2009年11月6日
- 7) 粒子線加速器
特許第4714884号
登録日：2011年4月8日
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- 8) PET撮像による画像定量化装置、方法、プログラム及び該画像定量化プログラムを記録したコンピュータ読み出し可能な記録媒体
特許第4701406号
登録日：2011年3月18日
- 9) 動脈閉塞性疾病モデル動物の作製
特許第4779122号
登録日：2011年7月15日
- 10) 断層撮影画像の重ね合わせ方法及び断層撮影画像を重ね合わせて表示するためのコンピュータプログラム
出願日：2006年9月28日
出願番号：2007-537664
- 11) 心筋血流量の定量法、血流量定量プログラム及び血流量定量システム
特許第4895080号
登録日：2012年1月6日
- 12) 断層撮影装置
特許第4929448号
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- 13) 実験動物固定装置
出願日：2007年4月24日
公開番号：2009-213373
- 14) 脳画像化装置用頭部模型及びその製造技術
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- 15) 標識化合物供給システム
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II. 研究成果の刊行に関する一覧表

研究成果の刊行に関する一覧表

雑誌

発表者氏名	論文タイトル名	発表誌名	巻号	ページ	出版年
Nezu T, Yokota C, Uehara T, Yamauchi M, Fukushima K, Toyoda K, Matsumoto M, <u>Iida H</u> , Minematsu K	Preserved acetazolamide reactivity in lacunar patients with severe white-matter lesions: ^{15}O -labeled gas and H_2O positron emission tomography studies.	<i>J Cereb Blood Flow Metab</i>	—	Epub ahead of print	2012
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III. 研究成果の刊行物・別刷

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Preserved acetazolamide reactivity in lacunar patients with severe white-matter lesions: ¹⁵O-labeled gas and H₂O positron emission tomography studies

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Limited evidence exists on the relationships between severity of white-matter lesions (WMLs) and cerebral hemodynamics in patients without major cerebral artery disease. To examine changes of cerebral blood flow (CBF), oxygen metabolism, and vascular reserve capacity associated with severity of WML in patients with lacunar stroke, we used a positron emission tomography (PET). Eighteen lacunar patients were divided into two groups according to the severity of WMLs, assessed by Fazekas classification; grades 0 to 1 as mild WML group and grades 2 to 3 as severe WML group. Rapid dual autoradiography was performed with ¹⁵O-labeled gas-PET followed by ¹⁵O-labeled water-PET with acetazolamide (ACZ) challenge. Compared with the mild WML group, the severe WML group showed lower CBF (20.6 ± 4.4 versus 29.9 ± 8.2 mL/100 g per minute, $P=0.008$), higher oxygen extraction fraction (OEF) (55.2 ± 7.4 versus $46.7 \pm 5.3\%$, $P=0.013$), and lower cerebral metabolic rate of oxygen (CMRO₂) (1.95 ± 0.41 versus 2.44 ± 0.42 mL/100 g per minute, $P=0.025$) in the centrum semiovale. There were no significant differences in the ACZ reactivity between the two groups ($48.6 \pm 22.6\%$ versus $42.5 \pm 17.2\%$, $P=0.524$). Lacunar patients with severe WMLs exhibited reduced CBF and CMRO₂, and increased OEF in the centrum semiovale. The ACZ reactivity was preserved in both patients with severe and mild WMLs in each site of the brain.

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Keywords: acetazolamide challenge; centrum semiovale; cerebrovascular reactivity; ischemic stroke; leukoaraiosis

Introduction

White-matter lesions (WMLs), observed as white-matter hyperintensity in T2-weighted magnetic reso-

nance imaging or fluid-attenuated inversion recovery (FLAIR) image, are commonly observed among elderly people (Hachinski *et al*, 1987). However, they are also associated with hypertension, diabetes, and other vascular risk factors (Murray *et al*, 2005; Pantoni and Garcia, 1997). Development of WMLs is known to be a cause of cognitive impairment, dementia, and disability (Prins *et al*, 2005). Recent studies showed that WMLs are not only a stroke risk factor (Streifler *et al*, 2002) but also a predictor of unfavorable stroke outcome (Koton *et al*, 2009). Despite accumulating evidence of the clinical significance of WMLs, the pathogenesis of WMLs has not been fully clarified.

Healthy elderly subjects with severe WMLs were reported to have reduced cerebral blood flow (CBF) and preservation of oxygen metabolism

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(Meguro *et al*, 1990). Patients with dementia of the Binswanger type have marked decrease of both CBF and oxygen metabolism in the white matter; however, patients without dementia have a lesser decrease in CBF with preservation of almost-normal oxygen metabolism (Yao *et al*, 1992). These findings indicated that chronic hypoperfusion due to the progression of small artery disease is associated with the development of WMLs. In addition, hemodynamic disturbance induced by internal carotid artery occlusive disease was suggested to contribute to the development of extensive WMLs (Yamauchi *et al*, 1999).

Limited evidence exists on the relationships between severity of WMLs and hemodynamic disturbance in patients without major cerebral artery occlusive disease. Some studies showed that vascular reactivity was not related to severity of WMLs (Birns *et al*, 2009; Turc *et al*, 1994). Other studies reported that vascular reactivity in patients with severe WMLs is impaired (Bakker *et al*, 1999; Chabriat *et al*, 2000; Fu *et al*, 2006; Isaka *et al*, 1994; Kozera *et al*, 2010; Mochizuki *et al*, 1997). These inconsistencies may be due to differences in modalities for evaluation of vascular reserve capacity; i.e., transcranial Doppler ultrasound (Bakker *et al*, 1999; Birns *et al*, 2009; Fu *et al*, 2006; Kozera *et al*, 2010), perfusion MRI (Chabriat *et al*, 2000), xenon inhalation computed tomography (Isaka *et al*, 1994; Mochizuki *et al*, 1997), and single photon emission computed tomography (Turc *et al*, 1994). There are also differences in the vasodilatory stimulus used; i.e., CO₂ inhalation (Bakker *et al*, 1999), breath holding, hyperventilation tests (Birns *et al*, 2009; Kozera *et al*, 2010), and acetazolamide (ACZ) challenge test (Chabriat *et al*, 2000; Fu *et al*, 2006; Isaka *et al*, 1994; Mochizuki *et al*, 1997; Turc *et al*, 1994). Although single photon emission computed tomography study with ACZ challenge can detect stage II hemodynamic failure (Powers, 1991) by positron emission tomography (PET) in patients with major cerebral artery occlusive disease (Hirano *et al*, 1994), the relationship between ACZ reactivity and oxygen metabolism in patients with WMLs without major artery disease has not been elucidated. We hypothesized that either impairment of vascular reserve capacity or chronic hypoperfusion in the white matter contributes to the development of WMLs without major artery disease.

The aim of this study was to examine the changes of CBF, oxygen metabolism, and vascular reserve capacity associated with the severity of WMLs in patients with lacunar stroke.

Materials and methods

Patients

This study was a single-center hospital-based prospective study. The study protocol was governed by the guidelines

of national government based on the Helsinki Declaration revised in 1983, and it was approved by the Institutional Research and Ethics Committee of our hospital. All patients gave written informed consent to participate in the study. Patients with lacunar stroke, at least 3 weeks after the onset, were enrolled between April 2009 and April 2010. All patients underwent PET studies with ¹⁵O-labeled gas (C¹⁵O₂, ¹⁵O₂, C¹⁵O) inhalation and ¹⁵O-water with ACZ challenge autoradiography as described previously (Kudomi *et al*, 2005, 2007), as well as MRI studies. Lacunar stroke was defined as a typical clinical syndrome associated with a small infarct, <15 mm in diameter on MRI, restricted to the territory of a perforating artery without adjacent major artery occlusive lesions. Patients with stenosis (>50% in diameter) or occlusion of the internal carotid artery or the trunk of the middle cerebral artery on magnetic resonance angiography or ultrasonography were excluded from the study. The median time interval between the onset of stroke and PET studies was 1,017 days (interquartile range 519 to 1,856).

Baseline clinical characteristics including age, sex, hypertension, diabetes mellitus, dyslipidemia, and current smoking were recorded. Information of risk factors and medical history was collected from a self-reported medical history or inferred from prescribed medication by the primary physicians. Criteria for hypertension, diabetes mellitus, and dyslipidemia were as previously defined (Yokota *et al*, 2009). Cognitive function was evaluated in all patients by the minimal state examination (Folstein *et al*, 1975) and clinical dementia rating (Hughes *et al*, 1982). Dementia was defined as clinical dementia rating ≥ 1 , and patients with dementia met the criteria proposed by National Institute of Neurological and Communicative Disorders and Stroke and the Alzheimer's Disease and Related Disorders Association (NINCDS-ADRDA Alzheimer's Criteria) (Roman *et al*, 1993).

Magnetic Resonance Imaging

Magnetic resonance imaging was performed on a 1.5-T scanner (Magnetom Vision or Magnetom Sonata; Siemens Medical Systems, Erlangen, Germany). The imaging protocol consisted of a T1-weighted spin-echo, a T2-weighted spin-echo, and FLAIR image. Severity of WMLs was assessed using the FLAIR (repetition time 900 ms, echo time 119 ms, field-of-view 230 × 201 mm², matrix 256 × 210, 4 mm slice thickness, and 2 mm gap between slices).

Two investigators (CY and TN), who were unaware of all clinical data, graded the degree of severity of WMLs by visual inspection using the Fazekas classification of WMLs as follows: none (grade 0), punctate (grade 1), early confluent (grade 2), and confluent lesions (grade 3) (Fazekas *et al*, 1987). The patients with grades 0 to 1 were defined as the mild WMLs group and those with grades 2 to 3 were defined as the severe WMLs group. Additionally, WMLs volume was measured manually based on FLAIR imaging (20 slices) using Dr View/LINUX software (AJS, Ver R2.5, Tokyo, Japan).

Positron Emission Tomography Imaging

We used an ECAT47 PET scanner (Siemens Medical Systems), which provided an intrinsic spatial resolution of 4.5 mm full-width at half-maximum at the center of the field-of-view. Data were acquired in 2D mode, and corrected for scatter compensation. A catheter was placed in the brachial artery for continuous monitoring of the arterial blood radioactivity concentration and arterial input function using a scintillator block detector system (BeCON; Molecular Imaging Labo, Suita, Japan) (Kudomi *et al*, 2003).

Quantitative images of CBF and oxygen extraction fraction (OEF) were obtained from a series of PET scans with ^{15}O -labeled gas (C^{15}O_2 , $^{15}\text{O}_2$, and C^{15}O) inhalation after a rapid dual autoradiography protocol as reported in a series of publications by Kudomi *et al* (2005, 2007). Briefly, after a 10-minute transmission scan for the attenuation correction and an ^{15}O -labeled carbon monoxide (C^{15}O) scan for the blood volume assessment, a single dynamic scan was performed for 8 minutes, during which 4,000 MBq of oxygen ($^{15}\text{O}_2$) and 5,000 MBq of ^{15}O -labeled carbon dioxide (C^{15}O_2) gases were inhaled each > 1 minute, sequentially at an interval of 5 minutes. Time to complete the whole dual autoradiography protocol was ~40 minutes. Cerebral metabolic rate of oxygen (CMRO_2) was calculated by multiplying the arterial oxygen content to the product images of OEF times CBF.

Additionally, two sets of PET scans were performed, each followed with ^{15}O -labeled water injection to assess regional CBF images using ^{15}O -water autoradiography (Kanno *et al*, 1987). The first scan was initiated without any pharmacological or physiological stress (at rest) and the second scan was performed at 10 minutes after an intravenous injection of ACZ titrated to 17 mg/kg. Physiological and laboratory data such as blood pressure, heart rate, and blood gas analysis (Siemens RAPIDLab 1265; Siemens Medical Systems) were obtained during the PET study.

Data Analysis

The small circular regions of interest (ROIs) (10 mm in diameter) were placed in the frontal cortex, parietal cortex,

occipital cortex, basal ganglia, and centrum semiovale based on automatic registration of MRI to PET by using PVElab (the PVEOut Consortium) (Quarantelli *et al*, 2004; Svarer *et al*, 2005). The program is followed by automatic segmentation (running with Statistical Parametric Mapping 5 (SPM5) Software (Institute of Neurology, University College of London, London, UK) and correction of PET counts for fractional volume as determined from the segmentation. The ROIs were manually placed on the FLAIR images and transferred to the CBF images for analysis (Figure 1). We defined the ACZ reactivity as the percentage increase in CBF after ACZ administration relative to baseline CBF. In each subject, the mean measures were obtained by averaging the values for both hemispheres.

Statistical Analysis

Statistical analysis was performed using JMP 7.0 software (SAS Institute, Cary, NC, USA). The statistical significance of intergroup differences was assessed by χ^2 tests, unpaired *t*-tests, and the Mann-Whitney *U*-test, as appropriate. Logarithmic transformation was performed on WMLs volumes, which was a skewed variable. The relationship between each parameter of PET and log-WML was examined by Pearson's correlation. A value of $P < 0.05$ was considered statistically significant.

Results

Patients were divided into two groups of severe WMLs ($n = 9$) and mild WMLs ($n = 9$) on the basis of MRI findings. There were no significant differences in age, sex, and vascular risk factors between the two groups (Table 1). Three patients with dementia defined as clinical dementia rating ≥ 1 were enrolled in the severe WMLs group; however, the rating of mini-mental state examination was not significantly different between the two groups. There were no significant differences in baseline CBF values between the gas-PET and H_2O -PET results. Compared with patients in the mild WMLs group, the patients

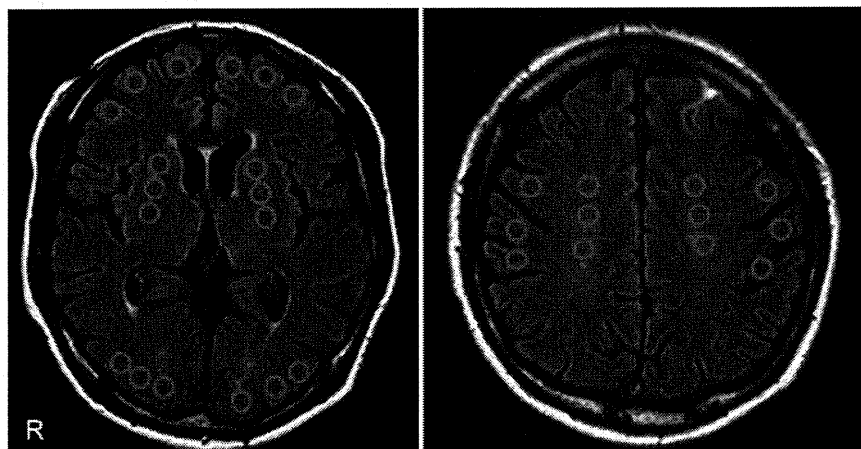


Figure 1 Regions of interest (ROIs) on fluid-attenuated inversion recovery (FLAIR). The small circular ROIs (10 mm in diameter) were placed on the frontal cortex, parietal cortex, occipital cortex, basal ganglia, and the centrum semiovale based on FLAIR image.

Table 1 Baseline characteristics

	Severe WMLs group (n = 9)	Mild WMLs group (n = 9)	P
Age (years)	76 (73–78)	74 (70–77)	0.329
Male	6 (67)	8 (89)	0.577
Current smoker	7 (78)	7 (78)	0.999
Hypertension	9 (100)	8 (88)	0.999
Diabetes mellitus	3 (33)	3 (33)	0.999
Dyslipidemia	6 (67)	6 (67)	0.999
WMLs (cm ³)	33.3 (21.5–90.9)	3.1 (1.3–4.4)	0.003
History of stroke	3 (33)	2 (22)	0.999
Time interval between stroke onset and PET study (days)	953 (445–1,958)	1,017 (519–1,623)	0.847
MMSE	24.0 (20.5–28.5)	28.0 (24.5–29.5)	0.140
CDR	0.5 (0–1)	0 (0–0.5)	0.185
Dementia	3 (33)	0 (0)	0.206

WMLs, white-matter lesions; PET, positron emission tomography; MMSE, mini-mental state examination; CDR, clinical dementia rating.

Data are number of patients (%), median (interquartile range) for discontinuous variables.

in the severe WMLs group had lower CBF (20.6 ± 4.4 versus 29.9 ± 8.2 mL/100 g per minute, $P=0.008$), higher OEF (55.2 ± 7.4 versus $46.7 \pm 5.3\%$, $P=0.013$), and lower CMRO₂ (1.95 ± 0.41 versus 2.44 ± 0.42 mL/100 g per minute, $P=0.025$) in the centrum semiovale, by gas-PET study (Table 2). There were no significant differences in any other parameters of the gas-PET in other ROIs between the two groups. Cerebral blood flow and CMRO₂ had a negative correlation with the severity of WMLs, and OEF had a positive correlation with the severity of WMLs (Figure 2). There were no significant differences in ACZ reactivity between the severe and mild WMLs groups in each site of the brain by H₂O-PET examination (Table 3). The results of physiological data and blood gas analysis during ACZ challenge were comparable between the two groups (data not shown). The ACZ reactivity was not correlated with the OEF or with the severity of WMLs ($P=0.422$ and $P=0.316$, respectively) (Figure 3).

Discussion

This study showed reduced CBF, reduced CMRO₂, and increased OEF in patients with severe WMLs compared with those with mild WMLs in the centrum semiovale. All patients in this study had lacunar stroke without major cerebral artery disease. The study also showed that ACZ reactivity was not impaired in either the cortex or the white matter of the patients of both groups.

Hatazawa *et al* (1997) found asymptomatic WMLs subjects exhibited reduction of CBF in the white matter and basal ganglia without decrease in CMRO₂. They also observed an increase in OEF in these areas, suggesting a chronic hypoperfusion in these territories. The present study provided additional information of reduction of both CBF and CMRO₂ with an increase in OEF in the WML in the patient groups with severe WMLs. Centrum semiovale is

Table 2 Comparison of each parameter of the gas-PET study between patients with severe or mild WMLs in the brain

	Severe WMLs group (n = 9)	Mild WMLs group (n = 9)	P
<i>Frontal cortex</i>			
CBF (mL/100 g per minute)	35.7 ± 9.0	37.8 ± 8.5	0.630
CBV (mL/100 g)	3.0 ± 0.9	3.0 ± 0.6	0.969
OEF (%)	54.1 ± 14.7	48.3 ± 5.2	0.275
CMRO ₂ (mL/100 g per minute)	3.24 ± 0.49	3.26 ± 0.73	0.946
<i>Parietal cortex</i>			
CBF	40.2 ± 6.9	44.1 ± 11.6	0.403
CBV	2.8 ± 0.7	3.1 ± 0.5	0.284
OEF	50.6 ± 6.9	46.3 ± 4.9	0.146
CMRO ₂	3.53 ± 0.35	3.62 ± 0.80	0.743
<i>Occipital cortex</i>			
CBF	40.4 ± 8.6	47.4 ± 16.1	0.266
CBV	3.5 ± 0.9	3.7 ± 1.5	0.745
OEF	55.8 ± 8.8	50.4 ± 4.5	0.116
CMRO ₂	3.88 ± 0.63	4.22 ± 1.16	0.442
<i>Basal ganglia</i>			
CBF	45.1 ± 9.4	49.5 ± 13.1	0.426
CBV	2.3 ± 0.7	2.5 ± 0.5	0.521
OEF	52.8 ± 7.9	50.5 ± 6.3	0.505
CMRO ₂	4.14 ± 0.66	4.43 ± 0.90	0.441
<i>Centrum semiovale</i>			
CBF	20.6 ± 4.4	29.9 ± 8.2	0.008
CBV	1.2 ± 0.4	1.4 ± 0.3	0.217
OEF	55.2 ± 7.4	46.7 ± 5.3	0.013
CMRO ₂	1.95 ± 0.41	2.44 ± 0.42	0.025

CBF, cerebral blood flow; CBV, cerebral blood volume; CMRO₂, cerebral metabolic rate of oxygen; OEF, oxygen extraction fraction; PET, positron emission tomography; WMLs, white-matter lesions.

P value by Mann–Whitney U-test.

located at the border of an area supplied by deep perforating arteries and the terminal branches of the middle cerebral artery. A decrease in CBF with reduction of CMRO₂ in the centrum semiovale in the present study should indicate a consequence of a reduced tissue metabolism in this terminal zone.

In the present study, patients with severe WMLs without major artery disease had increased OEF showed by gas-PET; however, their ACZ reactivity by H₂O-PET was preserved. The vascular reserve capacity evaluated by ACZ reactivity was preserved in both patients with severe and mild WMLs. Reduction of both CBF and CMRO₂ in the white matter was previously shown in patients with the Binswanger type dementia (Yao *et al*, 1990), being consistent with our results. Postmortem neuropathologic studies have shown decreased neuronal connectivity in the white matter in progressive subcortical vascular encephalopathy of Binswanger type (Yamanouchi *et al*, 1989, 1990). Functional reduction in cortical neuronal activity due to disruption of connections between the cortex and subcortex, as indicated previously (Pozzilli *et al*, 1987; Sette *et al*, 1989), is likely to be associated with a reduction of CMRO₂ in the centrum semiovale

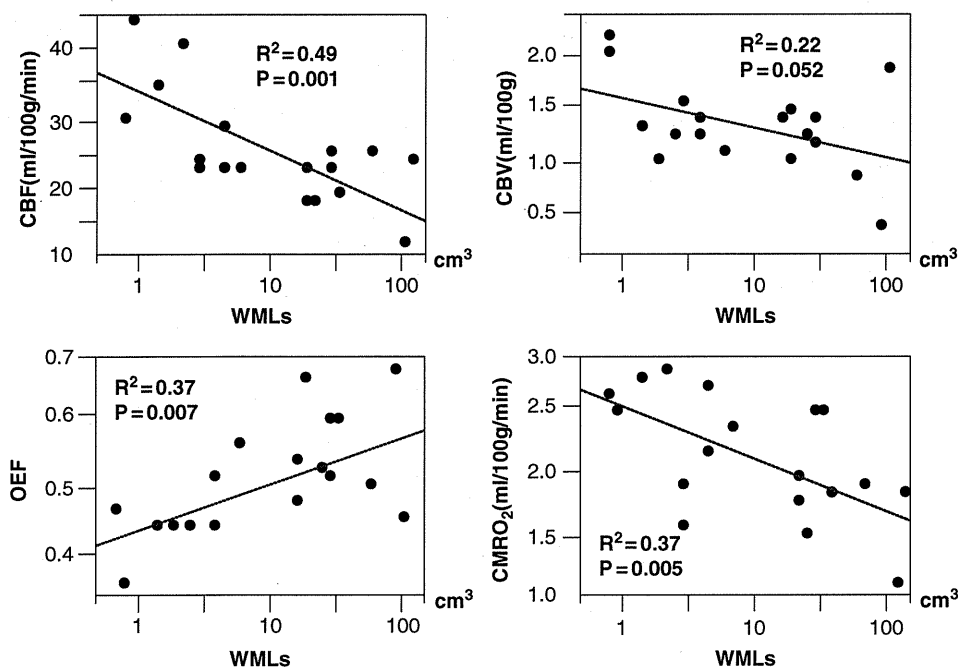


Figure 2 Correlation between WML volume and each gas-PET parameter in the centrum semiovale. CBF and CMRO₂ had a negative correlation with the severity of WMLs, while OEF was positively correlated with the severity of WMLs. CBF, cerebral blood flow; CBV, cerebral blood volume; OEF, oxygen extraction fraction; CMRO₂, cerebral metabolic rate of oxygen; WMLs, white-matter lesions; PET, positron emission tomography.

Table 3 Comparison of CBF between patients with severe or mild WMLs in the brain by H₂O-PET

	Severe WMLs group (n = 9)	Mild WMLs group (n = 9)	P
<i>Frontal cortex</i>			
CBF baseline	36.1 ± 7.2	40.2 ± 7.3	0.244
CBF ACZ	58.5 ± 10.2	59.9 ± 10.3	0.770
ACZ reactivity (%)	64.6 ± 28.5	49.7 ± 14.9	0.183
<i>Parietal cortex</i>			
CBF baseline	39.7 ± 4.8	45.7 ± 10.5	0.136
CBF ACZ	62.0 ± 7.1	66.9 ± 14.6	0.387
ACZ reactivity (%)	57.2 ± 17.1	47.1 ± 13.5	0.181
<i>Occipital cortex</i>			
CBF baseline	38.1 ± 7.1	45.7 ± 11.5	0.109
CBF ACZ	61.7 ± 13.3	70.1 ± 17.0	0.259
ACZ reactivity (%)	62.2 ± 21.5	54.2 ± 16.6	0.392
<i>Basal ganglia</i>			
CBF baseline	47.1 ± 9.8	54.6 ± 11.3	0.148
CBF ACZ	73.7 ± 10.5	85.7 ± 24.6	0.200
ACZ reactivity (%)	60.9 ± 31.0	55.7 ± 22.9	0.694
<i>Centrum semiovale</i>			
CBF baseline	19.0 ± 4.1	29.8 ± 9.2	0.005
CBF ACZ	28.5 ± 5.9	41.8 ± 10.9	0.005
ACZ reactivity (%)	48.6 ± 22.6	42.5 ± 17.2	0.524

ACZ, acetazolamide; CBF, cerebral blood flow; PET, positron emission tomography; WMLs, white-matter lesions.
P value by Mann-Whitney U-test.

in the patients with severe WMLs. Furthermore, the cerebral vessels would not dilate during fluctuations in systemic arterial pressure in daily life in these conditions of disruption of connections. Chronic hypoperfusion with a reduction of CMRO₂ in accordance with a disconnection between the cortex and subcortex may be the cause of development of WMLs without major artery disease.

To our knowledge, this is the first report of alterations in CBF, CMRO₂, and OEF, with preservation of ACZ reactivity in patients with mild or severe WMLs, with careful consideration of possible methodological errors. Indeed, quantitation of physiological parameters using PET is still a challenging issue, particularly in the white-matter area. As shown in earlier studies (Herscovitch and Raichle, 1983; Huang et al, 1987), the absolute values of both CBF and CMRO₂ could be biased because the spatial resolution of PET devices is limited compared with the physical size of the brain tissue component, or the partial volume effects. Oxygen extraction fraction is relatively stable and is less affected by partial volume effects. Our observation of increased OEF could not be explained by partial volume effects alone. Scatter is smaller in 2D mode in PET as compared with 3D acquisition. In this study, scatter correction was applied to minimize the contribution of radioactivity from the surrounding tissue components due to scatter. The ROIs were placed carefully with a guide of anatomical MRI to

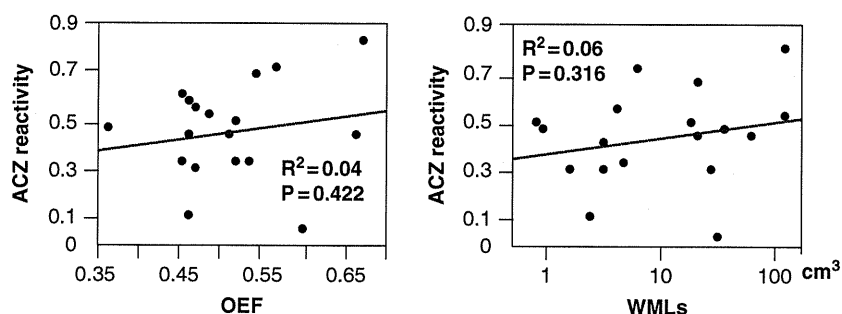


Figure 3 The correlation between ACZ reactivity and OEF or WML volume in the centrum semiovale. Neither OEF nor WML volume was correlated with ACZ reactivity. ACZ, acetazolamide; OEF, oxygen extraction fraction; WMLs, white-matter lesions.

minimize the errors arising from radioactivity counts of surrounding tissues. These factors remain concerns to be dealt with in future investigations.

There are several issues that need to be addressed, as follows. First, we intended to avoid possible bias in the patient selection, but a relatively small number of subjects could cause selection bias despite our efforts. Second, three patients with dementia were enrolled in the severe WMLs group. Because oxygen metabolism in demented patients was reported to be different from that in non-demented patients (Yao *et al*, 1992), a reduced CMRO₂ with reduced CBF in the severe WMLs group could be attributed to secondary effects arising from decreased cognitive function. Third, we examined the vascular reserve capacity by ACZ challenge. Recently, ACZ-induced vasodilation was reported not to inhibit the visually evoked flow response (Yonai *et al*, 2010), which indicates that the vasodilatory mechanism during neurovascular coupling may be different from the mechanism of ACZ-induced vasodilation. Acetazolamide at a dose of 17 mg/kg would not cause maximal cerebral vasodilatation. However, there were no significant differences in ACZ reactivity between the two groups, and ACZ reactivity was preserved in all patients in the present study. Fourth, PET imaging in the present study was a single scatter subtraction technique based on the Klein–Nishina formulation which was implemented in the reconstruction software (Watson, 2000). This technique was shown to provide reasonable accuracy in several phantom experiments. It should also be noted that the data were acquired in 2D mode, which has much smaller amount of scatter as compared with recently available 3D mode. Further, the filtered-back projection technique was applied for the image reconstruction. In this procedure, the scatter contribution is likely reduced in the reconstructed images. However, limited spatial resolution of PET devices is a significant source of errors that causes possible contamination of radioactivity counts of cortical grey matter tissue. Exact magnitude of errors in the calculated parameters in the WML cannot be well defined. In addition, PET scanning in the present study has not been applied to age-matched normal subjects. Further systematic study is needed.

In conclusion, we showed that there is reduced CBF and CMRO₂, and increased OEF in the centrum semiovale of patients with severe WMLs compared with patients with mild WMLs. The ACZ reactivity was preserved in both patients with severe and mild WMLs. Further studies will be needed to clarify the pathogenesis of WMLs.

Disclosure/conflict of interest

The authors declare no conflict of interest.

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Effects of patient movement on measurements of myocardial blood flow and viability in resting ^{15}O -water PET studies

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Background. Patient movement has been considered an important source of errors in cardiac PET. This study was aimed at evaluating the effects of such movement on myocardial blood flow (MBF) and perfusable tissue fraction (PTF) measurements in intravenous ^{15}O -water PET.

Methods. Nineteen ^{15}O -water scans were performed on ten healthy volunteers and three patients with severe cardiac dysfunction under resting conditions. Motions of subjects during scans were estimated by monitoring locations of markers on their chests using an optical motion-tracking device. Each sinogram of the dynamic emission frames was corrected for subject motion. Variation of regional MBF and PTF with and without the motion corrections was evaluated.

Results. In nine scans, motions during ^{15}O -water scan (inter-frame (IF) motion) and misalignments relative to the transmission scan (inter-scan (IS) motion) larger than the spatial resolution of the PET scanner (4.0 mm) were both detected by the optical motion-tracking device. After correction for IF motions, MBF values changed from 0.845 ± 0.366 to 0.780 ± 0.360 mL/minute/g ($P < .05$). In four scans with only IS motion detected, PTF values changed significantly from 0.465 ± 0.118 to 0.504 ± 0.087 g/mL ($P < .05$), but no significant change was found in MBF values.

Conclusions. This study demonstrates that IF motion during ^{15}O -water scan at rest can be source of error in MBF measurement. Furthermore, estimated MBF is less sensitive than PTF values to misalignment between transmission and ^{15}O -water emission scans. (J Nucl Cardiol 2012)

Key Words: Myocardial blood flow • water-perfusible tissue fraction • PET • myocardial perfusion imaging • motion correction • ^{15}O -labeled water

INTRODUCTION

Positron emission tomography (PET) has been extensively utilized for a wide range of non-invasive

functional imaging of the myocardium in vivo. When using this method, the global body movements of patients could be a source of quantitative errors. Such

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