

Effects of tissue heterogeneity on cerebral vascular response to acetazolamide stress measured by an I-123-IMP autoradiographic method with single-photon emission computed tomography

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Objectives: Single-photon emission computed tomography (SPECT) with iodine-123 (^{123}I)-labeled *N*-isopropyl-*p*-iodoamphetamine (IMP) is widely used in measuring the cerebral blood flow (CBF) response to acetazolamide stress for assessment of cerebral vascular reserve. To quantitate CBF by means of SPECT with IMP, an autoradiographic (ARG) method has been developed and is widely used. Because the relation between the brain counts on the SPECT scan and CBF is not linear in the ARG method, a mixture of gray and white matter in a pixel causes errors in the calculation of CBF. In the present study, errors in the calculation of CBF and vascular response to acetazolamide stress by the ARG method due to tissue heterogeneity were estimated by simulation study. Correction for effects of tissue heterogeneity in SPECT data was also attempted. **Methods:** Images of gray and white matter fraction were obtained by voxel-based morphometry analysis of magnetic resonance (MR) imaging data set. Ideal CBF images, which were generated from gray and white matter fraction images with assumed blood flow values for gray and white matter, were compared to CBF images generated by the ARG method. Correction for effects of tissue heterogeneity in SPECT data was performed with gray and white matter fraction data obtained from MR images. **Results:** Systematic underestimation of CBF due to tissue heterogeneity was observed in all brain regions. In the neocortical regions, underestimation by -21% to -16% , -26% to -20% , -31% to -24% , and -35% to -27% was observed for gray and white matter blood flow of 80 and 20, 100 and 25, 120 and 30, and 140 and 35 ml/100 ml/min, respectively. Vascular response was also systematically underestimated in most brain regions. Vascular responses in the neocortical regions ranged from 17% to 20%, from 31% to 37%, and from 42% to 52% when ideal vascular responses were 25%, 50%, and 75%, respectively. After correction for the effects of tissue heterogeneity, values of vascular response to acetazolamide stress ranged from 64% to 116% in the neocortical regions, whereas values obtained by the ARG method ranged from 48% to 52%. **Conclusion:** Underestimation of the vascular response to acetazolamide stress due to tissue heterogeneity should be considered in the estimation of cerebral vascular reserve.

Key words: IMP, SPECT, acetazolamide, ARG method, tissue heterogeneity