Metabolic imaging of the heart by PET

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Abstract. Metabolic imaging using positron emission tomography has provided insights into patho-physiological conditions in ischemic myocardium. FDG-PET proved to be a gold standard for asses-sing tissue viability in patients with coronary artery disease. In addition, it enables the identification of the high-risk subgroup of patients with myocardial infarction based on the presence of ischemic myocardium. Thus, the areas showing reduced perfusion and enhanced glucose metabolism, so-called perfusion metabolism mismatch, are good candidates for revascularization therapy predicated on the concept to improve regional cardiac function and to reduce future cardiac events. Recently, oxidative metabolism can be analyzed with PET and C-11 acetate. This new technique has potentials for identifying reversible ischemia. Moreover, the combined PET study using FDG and C-11 acetate may identify the areas of aerobic and anaerobic glucose utilization in vivo.

Using ^{15}O water and PET for quantitative assessment of regional myocardial per fusion and myocardial viability

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Abstract. ^{15}O-water is a freely diffusible tracer and its myocardial kinetics are not dependent on metabolism. A kinetic analysis based on a simple, one-compartment approach can provide quantitative assessment of regional myocardial blood flow (MBF). A multicenter project involving seven independent institutions in Japan demonstrated good inter- and intra-institute consistency of normal MBF values in man (MBF: 0.93± 0.34 ml/min/g at rest and 3.40 ± 1.73 after dipyridamole infusion). Relatively large interindividual variation of resting MBF in normals attributed to variation of the workload in individuals. The resting MBF significantly correlated with a rate-pressure product (RPP): $y = 0.38+5.33e-5x$, $P < 0.010$, and RPP significantly correlated with age: $y = 74 + 199x$, $p < 0.001$. These data suggest that this technique is reliable and accurate for MBF quantitation in human studies, and therefore suitable as a clinical investigative tool. Another utility of ^{15}O-water has recently been proposed for assessing myocardial viability. As an equilibrium distribution of ^{15}O-water after infinite time, the kinetic analysis for ^{15}O-water provides a proportion of water-perfusable myocardium within a volume element. An experimental study on dogs with chronic myocardial infarction demonstrated a good correlation of the water-perfusable tissue against the histochemical TTC staining, suggesting that the water-perfusable tissue provides an indirect measure of the extent of histochemically defined noninfarcted (viable) tissue. Clinical studies in both acute and chronic infarction settings demonstrated that the proportion of water-perfusable tissue > 70% for a dysfunctional segment augurs an improvement in the contractility of that region following intervention. These studies suggest that the ability to exchange water rapidly across the sarcolemma is a property of viable myocardium, and that > 70% of the tissue within a hypocontractile zone should be viable in order to enable improvement in contractile function. Thus, ^{15}O-water not only provides quantitate myocardial perfusion but also an alternative approach for assessing myocardial viability without using metabolic tracers.

Assessment of coronary flow using magnetic resonance imaging

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Abstract. The purpose of the current study was to measure the response of coronary flow velocity to dipyridamole administration as a reflection of coronary flow reserve (CFR) in healthy subjects and patients with significant coronary artery stenosis by using MR imaging.

Ten healthy volunteers and 19 patients with coronary artery diseases in the left anterior descending (LAD) artery on X-ray angiography were studied. Fast cine PC-MR images were acquired within 25s on double-oblique imaging planes perpendicular to the LAD artery, with FOV of 20 x 10 cm, velocity window of ± 1 m/s and segmented k-space data acquisition. CFR ratio was calculated as a ratio of hyperemic to baseline flow velocity in the LAD. Blood flow velocity in the LAD artery was directly measured by Doppler flow wire before and after intravenous dipyridamole administration in all patients.

MR measurement of the baseline diastolic peak velocity (DPV) in patients was not significantly different from the baseline DPV in healthy subjects (13.5 ± 3.3 vs. 13.6 cm/s ± 5.9, mean±SD). However, the DPV after dipyridamole injection (20.7 cm/s ± 8.5) and the CFR ratio (l.62 ± 0.50) in patients were significantly lower than those measured in healthy subjects (41.9 cm/s ± 13.2 and 3.14±0.59, $p < 0.01$). MR assessments of CFR ratios demonstrated a good linear correlation with those directly measured by Doppler flow wire during X-ray angiography ($r = 0.91$, $n = 19$).

In conclusion, fast cine PC MR imaging can provide noninvasive assessment offhnctional significance of coronary artery stenosis in patients with coronary artery diseases.

Relationship between myocardial flow reserve and energy metabolism in hypertrophic cardiomyopathy

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Abstract. To assess whether reduced coronary flow reserve (CFR) affects myocardial energy metabolism in hypertrophic cardiomyopathy (HCM), we evaluated regional CFR by dipyridamole (DP)-stress and resting ^{13}N-ammonia ($^{13}NH_3$) PET, and studied the relationship between CFR and myocardial metabolic abnormalities in 18 HCM patients with asymmetric septal hypertrophy and without regional ^{201}Tl defects. Myocardial free fatty acid and glucose metabolism were evaluated by fasting ^{123}I-BMIPP (α-methyl-iodophenylpentadecanoic acid) SPECT and by fasting ^{18}FDG (fluorodeoxyglucose) PET, respectively. In the midventricular transaxial tomogram, we determined the tracer distribution ratio between septal and lateral regions (S/L) after correcting the partial volume effect. $^{13}NH_3$ S/L was 1.02 ± 0.17 at rest indicating homogeneous flow distributions between both regions, but was 0.87 ± 0.23 during DP ($p < 0.01$ vs. at rest) indicating relatively reduced CFR in septal regions. The reduction in ^{123}I-BMIPP S/L did not correlate with ^{13}NH3 S/L at rest but correlated well with the extent of change in $^{13}NH_3$ S/L from rest to DP ($r = 0.740$, $p < 0.001$). On the other hand, FDG S/L did not correlate with $^{13}NH_3$ S/L at rest and during DP and ^{123}I-BMIPP S/L

These results suggest that the abnormality in myocardial free fatty acid metabolism occurs under the limited CFR due to regional hypertrophy and may play an important role in progressing myocardial failure in HCM patients. However, the response of myocardial glucose metabolism to the impairment of CFR is variable and requires further investigation.

Keywords: ^{123}I- α -methyl-iodophenylpentadecanoic acid (BMIPP), ^{18}F-fluorodeoxyglucose, ^{13}N-ammonia, positron emission tomography (PET).

Mapping human cognition with functional imaging

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Abstract. Major advances in computing and mathematics, especially the back-projection algorithms introduced for reconstructing tomographic data obtained by noninvasive imaging, have led to new opportunities for the study of the structure, function and structure-function relationships of the human brain. Until recently the methods available for studying the functional organisation of the human brain were restricted in scope. Hence, much of our understanding was inferred from studies in nonhuman primates. The only alternative approach was to draw conclusions from observations in patients with specifically distributed brain lesions. The development of noninvasive neuroimaging techniques has resulted in the emergence of new data that can now be used to test biological theories of functional brain organisation.

Keywords: fMRI, memory, pet, SPM.

The cognitive architecture of the human prefrontal cortex: PET as a tool to test and generate hypotheses

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Abstract. The human prefrontal cortex occupies approximately one-third of the total cortical space in the brain. Yet assignment of specific cognitive operations or representations to that area of cortex has lagged behind our investigation and understanding of the functions of posterior brain areas. We have developed an alternative framework for the investigation of the functions of the prefrontal cortex which argues that a unique aspect of semantic knowledge is stored in the prefrontal cortex. We have coined this aspect of semantic knowledge the structured event processing complex (SEC). One approach to testing the validity of the SEC framework is to design neuroimaging studies with an intent to map a predicted component of the SEC to a sector within the prefrontal cortex. We have used the PET as a tool to test the hypotheses that aspects of planning, sequencing, thematic knowledge, social understanding, and reasoning are stored as memories/representational knowledge in prefrontal cortex. Taken together, our PET studies support the existence of the SEC and indicate that different features of the SEC are processed by topographically restricted brain sectors in the prefrontal cortex with different sectors concerned with sequencing events, processing certain kinds of semantic information across and within events, and representing emotional and nonemotional categories of knowledge.

Keywords: cognition, cognitive neuroscience, frontal lobes, neuropsychology, positron emission tomography, prefrontal cortex.

Pain-induced cerebral blood flow changes following CO_2 laser stimulation of hand and foot in man

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Abstract. To elucidate the functional localization and somatotopic organization of pain perception in the human cerebral cortex, we studied the regional cerebral blood flow using position emission tomography during selective pain stimulation in six normal subjects. Pain perception was elicited by applying a special CO_2 laser, which selectively activates nociceptive receptors, to the hand and foot. We found that multiple brain areas, including bilateral secondary somatosensory cortices (SII) and insula, and the frontal lobe and thalamus contralateral to the stimulus side, are involved in pain perception. While our data indicate that the bilateral SII play an important role in pain perception, they also indicate that there is no pain-related somatotopic organization in the human SII or insula.

Keywords: cerebral blood flow, pain perception, positron emission tomography, somatotopic organization.

Magnetic resonance imaging of per fusion with arterial spin labeling

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Abstract. Recently, new magnetic resonance imaging techniques based on arterial spin labeling (ASL) have been developed that allow quantitative measurements of perfusion in the human brain. In ASL, the longitudinal magnetization of arterial blood is magnetically tagged. Subtraction of brain images with and without the tag yield quantitative measurements of local perfusion (i.e., the rate of delivery of blood to tissue). Several image acquisition schemes based on this idea have been developed. This paper reviews the basic principles of ASL, summarizes recent developments in pulse sequence design, and discusses various sources of error in perfusion measurements with ASL. These new arterial spin labeling techniques can provide accurate perfusion measurements in the human brain with higher spatial and temporal resolution than any previous technique.

Keywords: cerebral blood flow.

Diffusion-weighted imaging of cerebral Ischemia

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Abstract. Novel MR methods sensitive to water protonT2, diffusion, and perfusion mechanisms provide prognostic value for the detection of acute ischemic stroke and discrimination from chronic infarction. CSF-suppressed T2-weighted (FLAIR) images further improve the diagnostic utility of T2 MRI by nulling the relative hyperintense CSF protons. Diffusion-weighted imaging (DWI) is able to detect the pronounced slowing of brain water that occurs in hyperacute cerebral ischemia. Diffusional slowing provides information about the state of cellular injury and the parenchymal tissue metabolic state, at a time when the effectiveness of therapy is greatest. Perfusion imaging utilizes rapidly acquired images following a bolus injection of a magnetic-susceptibility contrast agent to assess changes in tissue perfusion by inducing a T2* shortening demonstrated as a signal loss in perfused tissue. The passage of the contrast agent can then give information on the hemodynamic status of the tissue, useful in stroke and cerebrovascular diseases.

Keywords: cerebral ischemia, diffusion, infarction, magnetic resonance, perfusion.

Diagnostic applications of PET in dementia

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Abstract. The diagnosis and differentiation of various dementing disorders using ^{18}F-fluorodeoxyglucose (FDG) positron emission tomography (PET) are discussed. The knowledge of metabolic patterns of various dementing disorders, such as Alzheimer's disease, Parkinson's disease with dementia, diffuse Lewy body disease, and frontal lobe-type dementia has been increased. The metabolic patterns of the very early stages of these diseases are now under investigation. Image analysis techniques have also improved significantly in the past several years. A combination of a priori knowledge of disease pathophysiology, metabolic features, and advanced image analysis techniques enhances the diagnostic efficacy of PET imaging in dementing disorders.

Keywords: computer-assisted diagnosis, dementia, deoxyglucose, emission computed tomography.

Synaptic potentiation visualized by positron emission tomography

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Abstract. Phosphoinositide turnover is thought to regulate synaptic function. We employed positron emission tomography to examine the phosphoinositide turnover in the human brain using carbon-11-labeled diacylglycerol. Each of the normal subjects showed intense localized accumulation of carbon-11-radioactivity in the cortex, Particularly in the regions of the association areas. These potentiated areas were different in each subject and they tended to show lateralization. The role of the metabotropic PI turnover is well established in postsynaptic mechanism of long-term potentiation. These potentiated areas probably include information about the postsynaptic response.

Keywords: diacylglycerol, long-term potentiation, phosphoinositide turnover, positron emission tomography, synaptic function.

Stratification of severity by cerebral blood flow, oxygen metabolism and acetazolamide reactivity in patients with cerebrovascular disease

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Abstract. If cerebral perfusion pressure drops, autoregulatory vasodilatation initially increases the cerebral blood volume (CBV) (stage I), then secondary metabolic compensation increases the oxygen extraction fraction (OEF) (stage II). Patients with cerebrovascular disease could be stratified with PET parameters; cerebral blood flow (CBF), CBV and OEF using steady state ^{15}O gas inhalation. In the present study, we correlated PET parameters with vasoreactivity by injecting ^{15}O water before and after administrating 1 g of acetazolamide in 17 patients with cerebrovascular disease (mean age = 61years), to stratify patients using brain SPECT. ⊿CBF and the percent ⊿CBF was also obtained by the rate of increase in CBF after acetazolamide compared with the baseline level. Sixteen regions of interest were placed in five cortical areas, two deep areas and one cerebellar area, bilaterally. ROI areas were classified by severity into normal (CBF/CBV (1/min) > 10.75 and OEF < 0.52), stage I (CBF/CBV < 10.75 and OEF <0.52)and stage II(CBF/CBV < 10.75 and OEF > 0.52) groups. One hundred and ninety-four ROI areas were stratified as 61, 113 and 20 normal, stage I and stage II, respectively. There was a significant decrease in CBF and cerebral metabolic rate of oxygen ($CMRO_2$) between normal and stage I, and in the percent ⊿CBF between stages I and II. There was an inverse correlation between the percent ⊿CBF and OEF (r = 0.680) in stage II. We estimated the severity in patients with cerebrovascular disease by measuring CBF and the percent ⊿CBF by means of brain SPECT

Keywords : acetazolamide reactivity, cerebral blood flow, cerebrovascular disease, PET, severity.

Synthesis of ^{11}C-choline: PET imaging of brain tumors, lung cancers and intrapelvic cancers

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Abstract. Background. Choline is incorporated into membrane phospholipid in tumors. Methods. [Methyl-^{11}C]choline was synthesized by reacting ^{11}C-methyl iodide with "neat" dimethylaminoethanol at 120°C for 5 min. Purification was achieved by evaporation of unreacted substrates and treatment of the residue with cation-exchange resin (-COO- form). The final product was ready to be injected for PET study. Results. In animals and humans, after the intravenous injection, ^{11}C-choline was incorporated selectively in liver, kidney, pancreas, and tumor. The radioactivity in brain, lung, heart, intrapelvic organs and blood was very low. The radioactivity distribution was unchanged for the period of 5-40 min. PET produced highly positive images of tumors in patients with malignant brain tumors (24 cases), pituitary adenomas (two cases), lung cancers (12 cases), and intrapelvic cancers (three cases).
Conclusions. PET imaging with ^{11}C-choline was very effective in detecting brain tumors, lung cancers, and intrapelvic cancers in patients.

Keywords : clinical, diagnosis, phospholipid, positron.

Breast tumor detection by means of near infrared light scanning

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Abstract. Background. The near infra-red light scanning (NIRLS) technique was invented and used for the breast tumor detection in 170 patients. Methods. NIR lights consisted of 630- and 830-nm lasers, and 1-mm diameter beams were used. Transmitted lights through the breast tissue were measured by the facing detectors. A combination of both the light source and the detector were moved over and behind the breast vertically and laterally in the range of 160 x 120 mm to cover the breast. The signals obtained by the detector were digitized and the input into the computer and the NIRLS image of the breast are constructed on the display. Results. Abnormal findings of NIRLS were determined by: 1) an isolated abnormal translucency area, 2) an abnormal difference between both breasts, and 3) an abnormal feature or inhomogeneity of the breast images. X-ray mammography (XMG) was also performed in the same group and the results were compared between the two examinations. The detection rates of breast tumor seemed nearly the same in both examinations.

Conclusions. NIRLS is suitable for repeated precise examination of the breast with the advantage of no irradiation hazard.

Keywords: breast image, no irradiation hazard, X-ray mammography.

SPECT imaging of dopaminergic function: presynaptic transporter, postsynaptic receptor, and "intrasynaptic" transmitter

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No Abstract Available

In vivo-in vitro biochemistry interface by use of positron emission tracers

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Abstract. For farther progress of the PET method the development of a variety of usefull positron-emitting radionuclide-labelled tracers is of importance. Although the synthetic methods for labeling with ^{11}C, ^{18}F, and ^{13}N have been well developed, the evaluation of the labelled compounds is still limited because of their short half lives and our inexperience with their use both in vitro and in vivo biochemistry. The experimental set-up for this purpose is especially important. Here, the examples of experimental systems and set-up including all-round in vitro laboratory and a novel in vitro PET method with living brain slices are presented.

Keywords: evaluation of labelled compounds, experimental set-up, in vitro PET, injection route, PET tracers.

Enhancement of ^{18}F-fluorodeoxyglucose uptake by successfully reperfused myocardium: role of glucose transporter 4

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Abstract. The myocardial uptake of ^{18}F-fluorodeoxyglucose (FDG) has been shown to indicate ischemia. To elucidate whether this is applicable to reperfused myocardium, ^{18}F-FDG PET study was performed in 10 patients with successfully recanalized myocardial infarction. During the chronic phase, FDG accumulated only in the region of ^{201}Tl redistribution, indicating ischemia. However, during the subacute phase, FDG accumulated mainly in the peri-infarct area. To elucidate whether reperfused myocardium, per se, shows accelerated glucose uptake, glucose uptake rate was quantified from the time course of the sugar phosphate resonance in rat myocardium (d[SP]/dt) using ^{31}P-NMR. d[SP]/dt in reperfused myocardium increased significantly compared with control, reaching the maximal stimulable uptake rate measured under nonischemic conditions during exposure to insulin.

To investigate the mechanism of augmented glucose uptake, N6-(L-2-phenylisopropyl) adenosine (PIA), a potent blocker of glucose transporter 4 (GLUT 4), was administered to these hearts and, as a control, to insulin-stimulated hearts. PIA significantly and comparably inhibited the increase in d[SP] /dt in reperfused myocardium and in insulin-stimulated myocardium. In conclusion, our results indicate that the augmented glucose uptake in reperfused myocardium is maintained by GLUT 4 and the translocated GLUT 4 remains in the sarcolemma after reperfusion. This mechanism may be responsible for the increase in FDG uptake of reperfused myocardium observed clinically.

Keywords: ^{31}P-NMR, insulin, ischemia.

In vivo visualization of abnormal brain aging by PET and SPECT

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Abstract. For the design of PET/SPECT radiopharmaceutical for abnormal brain aging as radical related disease, senescence accelerated model mouse (SAM) was used as a model of oxidative stress, a cause of radical production. When mitochondrial DNA (mtDNA) deletion was used as a marker of oxidative damage, it was cleared that SAMP8, showing accelerated senescence, received higher oxidative stress from a young age, when compared with controls (SAMRl and ddY). Using this animal model, radiolabeled radical trapping agent I- 125-p-iodopheny1-tert-butylnitrone (IPBN) and hypoxia imaging agent Cu-62-diacety1-bis(N4-methylthiosemicarbazone) (Cu-ATSM) were examined as possible diagnostic agents for abnormal brain aging. Both agents showed plausible brain accumulation in SAMP8 of presymptomatic age, indicating the possibility of early diagnosis of abnormal brain aging as radical related disease.

Keywords: brain aging, oxidative stress, PET, radical, senescence accelerated model mouse, SPECT.