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Practical tips and tricks in cardiovascular computed tomography: diagnosis of myocardial infarction.

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In addition to accurately diagnosing coronary artery disease, cardiac CT (CCT) has the potential to provide information on myocardial function, perfusion, and viability. As ongoing research continues to support the utility of such noncoronary uses of CCT, this information is increasingly being integrated into clinical practice. An emerging important use of CCT is the ability to accurately identify areas of infarcted myocardium. From a clinical perspective, detecting and quantifying infarct size has important prognostic and therapeutic implications. This article provides a brief overview on the use of CT to diagnose myocardial infarction (MI) and provide practical “tips and tricks” that can aid in the CT-based detection of MI.

Quantitative assessment of left atrial volume by electrocardiographic-gated contrast-enhanced multidetector computed tomography.

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BACKGROUND: Left atrial (LA) volume is a predictor of cardiovascular events. Information on LA volume is available on contrast-enhanced electrocardiogram (EGC)-gated multidetector computed tomography (MDCT) scans. OBJECTIVE: To assess interobserver and intraobserver reproducibility of 3-dimensional threshold-based volume (3DTV) and 2-dimensional (2D) measurements for the assessment of LA volumes with contrast-enhanced cardiac 64-slice MDCT. METHODS: Contrast-enhanced 64-slice MDCT (0.6-mm slice thickness, 120 kVp, 850 mAs effic) was performed in 96 consecutive subjects (mean age 52 years; 48% women) as a subset of the Rule Out Myocardial Infarction using Computer Assisted Tomography trial. Two observers independently measured maximal (LAV(max)) and minimal (LAV(min)) LA volumes with (1) a modified Simpson's method (3DTV) based on delineation of LA areas in axial slices and (2) estimated LA volumes typically used in 2D echocardiography (area length and prolate ellipse). Interobserver and intraobserver reproducibility for each method as well as correlations between the methods were calculated. RESULTS: Interobserver (n = 96) and intraobserver (n = 20) variability was significantly lower for 3DTV (8%) than for area length (13%; P < 0.001) or prolate ellipse (16%; P < 0.001). 2D-based measurements rendered significantly lower LA volumes than did 3DTV (area length: -17% and -22%; prolate ellipse: -43% and -46% for LAV(max) and LAV(min), respectively; P < 0.001 for all). By 3DTV, mean LA volume was 90.4 +/- 24.5 mL for LAV(max) and 52.5 +/- 17.6 mL for LAV(min). CONCLUSION: ECG-gated contrast-enhanced cardiac MDCT offers volumetric assessment of LA volume with excellent reproducibility without additional contrast administration or radiation exposure. 3D measures of LA volume are more reproducible and render larger volumes than 2D-derived estimates, typically used in echocardiography.

Nuclear cardiology in India and the developing world: opportunities...and challenges!

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Role of nuclear imaging in regenerative cardiology.

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Advances in noninvasive imaging techniques may aid in the understanding of cardiac stem cell therapy. Nuclear imaging enables in vivo evaluation of myocardial perfusion, metabolism, and function, in addition to the stem cell fate. This article summarizes recent clinical and experimental nuclear imaging studies in cardiac stem cell therapy.
In the last two decades, the field of nuclear cardiology has experienced significant progress. The introduction of positron emission tomography (PET) imaging represented a major breakthrough that has significantly contributed to a better understanding of physiology and pathophysiology of several heart diseases. Currently, PET imaging is recognized as a well-established method to assess cardiac perfusion, function, metabolism, and viability. This article summarizes the main clinical applications of state-of-the-art cardiac PET technology.

Altered sympathetic nervous activity has been linked to the development and persistence of obesity, partly relating to overfeeding. Binding of the selective, positron-emitting phosphodiesterase-4 (PDE4) inhibitor (R)-[11C]rolipram provides a direct index of the cAMP-hydrolyzing enzyme PDE4. This study examines progressive alterations in PDE4 in a high-fat-fed obese animal model. (R)-[11C]Rolipram was injected into diet-induced obese (DIO) and diet-resistant (DR) rats; the animals were killed after 45 min, tissues were extracted, and radioactivity was quantified. Responsiveness of PDE4 to acute noradrenaline (NA) stimulation was determined by 3 h pretreatment with the NA reuptake inhibitor desipramine. There was minimal variance in caloric intake, weight gain, fasting were extracted, and radioactivity was quantified. Responsiveness of PDE4 to acute noradrenaline (NA) stimulation was determined by 3 h pretreatment with the NA reuptake inhibitor desipramine. There was minimal variance in caloric intake, weight gain, fasting glucose, insulin, and energy expenditure (indirect calorimetry) measures. Basal (R)-[11C]rolipram binding was comparable between DIO and DR rats at 2 or 8 weeks of feeding. The normal increase of PDE4 levels in response to elevated NA by desipramine pretreatment was ablated in PDE4-rich tissues, including brain, heart, and skeletal muscle, of DIO animals after 8 weeks of high-fat diet. Lean DR rats maintained PDE4 responsiveness indicative of a normal NA signal transduction.

Reduced in vivo phosphodiesterase-4 response to acute noradrenaline challenge in diet-induced obese rats.


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PET-Cardiology


Cardiac positron emission tomography: current clinical practice.

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In the last two decades, the field of nuclear cardiology has experienced significant progress. The introduction of positron emission tomography (PET) imaging represented a major breakthrough that has significantly contributed to a better understanding of physiology and pathophysiology of several heart diseases. Currently, PET imaging is recognized as a well-established method to assess cardiac perfusion, function, metabolism, and viability. This article summarizes the main clinical applications of state-of-the-art cardiac PET technology.


Reduced in vivo phosphodiesterase-4 response to acute noradrenaline challenge in diet-induced obese rats.


National Cardiac PET Centre, Division of Cardiology, University of Ottawa Heart Institute, 40 Ruskin Street, Ottawa, ON K1Y4W7, Canada; and Department of Cellular and Molecular Medicine, University of Ottawa, Ottawa, Ontario, Canada.

Altered sympathetic nervous activity has been linked to the development and persistence of obesity, partly relating to overfeeding. Binding of the selective, positron-emitting phosphodiesterase-4 (PDE4) inhibitor (R)-[11C]rolipram provides a direct index of the cAMP-hydrolyzing enzyme PDE4. This study examines progressive alterations in PDE4 in a high-fat-fed obese animal model. (R)-[11C]Rolipram was injected into diet-induced obese (DIO) and diet-resistant (DR) rats; the animals were killed after 45 min, tissues were extracted, and radioactivity was quantified. Responsiveness of PDE4 to acute noradrenaline (NA) stimulation was determined by 3 h pretreatment with the NA reuptake inhibitor desipramine. There was minimal variance in caloric intake, weight gain, fasting glucose, insulin, and energy expenditure (indirect calorimetry) measures. Basal (R)-[11C]rolipram binding was comparable between DIO and DR rats at 2 or 8 weeks of feeding. The normal increase of PDE4 levels in response to elevated NA by desipramine pretreatment was ablated in PDE4-rich tissues, including brain, heart, and skeletal muscle, of DIO animals after 8 weeks of high-fat diet. Lean DR rats maintained PDE4 responsiveness indicative of a normal NA signal transduction.

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Imaging of Inflamed and Vulnerable Plaque in Coronary Arteries with 18F-FDG PET/CT in Patients with Suppression of Myocardial Uptake Using a Low-Carbohydrate, High-Fat Preparation.


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PET/CT imaging with (18)F-FDG has been used to detect inflammation in carotid and aortic plaque; its use in detecting coronary plaque has been limited by avid (18)F-FDG uptake by the myocardium. We investigated whether (18)F-FDG PET/CT could be used to image inflammation in coronary arteries as a potential noninvasive method to detect vulnerable plaque. METHODS: We retrospectively studied 32 patients treated for malignancy who underwent (18)F-FDG PET/CT and concomitant cardiac catheterization. As part of the recently described protocol, all patients were instructed to eat a low-carbohydrate, high-fat meal the night before and drink a vegetable oil drink the morning of the study. We reviewed the patients' baseline characteristics and their (18)F-FDG PET/CT scans for adequacy of myocardial uptake suppression and correlated the presence of angiographically apparent plaque with (18)F-FDG uptake in the major coronary arteries. Two independent observers assessed the angiographic images and (18)F-FDG PET scans. RESULTS: A total of 95% of patients had 2 or more coronary disease risk factors, and 25% had unstable symptoms; 30% of index catheterizations resulted in intervention. In 20 of 32 patients (63%), myocardial suppression was good (12) or adequate (8). Inadequate suppression was due to self-reported dietary nonadherence. Patients with good, adequate, and poor suppression had maximal myocardial standardized uptake values of 2.8 +/- 0.7, 5.0 +/- 1.3, and 17.0 +/- 9.7, respectively. We identified (18)F-FDG uptake in 15 patients in 1 or more coronary segments. A trend to significance in correlation between presence of angiographic disease and signal in the vessel was observed (P = 0.07; 80 vessels examined). A total of 7 patients with significant coronary artery disease had aortic (18)F-FDG uptake. CONCLUSION: In this retrospective study, we demonstrated the potential use of (18)F-FDG PET in imaging of inflammation in coronary arteries. The potential of (18)F-FDG PET is also being investigated in a prospective study.
Current methods of pharmacologic stress testing and the potential advantages of new agents.

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This article presents the exciting advances made and ongoing in the area of pharmacologic cardiac stress testing. In particular, new A(2A)-specific receptor agonists work like adenosine but promise the delivery of uncomplicated vasodilator stress testing or the diagnosis and prognosis of coronary disease. These agents, although not perfect, do likely present a level of protection against the complications of bronchospasm and heart block. Phase III studies have shown that these agents promise a reduced symptom intensity and greater patient tolerance. One of these agents, regadenoson, is now Food and Drug Administration approved and will be delivered as the same single-dose bolus in all patients, regardless of weight, greatly simplifying the method and increasing its acceptability. Most widely applied with myocardial perfusion SPECT, these agents will find application with PET myocardial perfusion studies and likely MRI studies. Because of their effect on coronary supply rather than demand, they will not be applied with stress echocardiography. Before considering these agents, we will consider the principles and methods of stress testing, and particularly pharmacologic stress testing. The learning objectives of this article are to familiarize the reader with the methods and choices in stress testing for coronary disease diagnosis and prognosis, to present the advantages and disadvantages of pharmacologic stress testing, to review current pharmacologic stress-testing methods and their specific combination with imaging methods, to present the chemistry and effects of the new A(2A)-specific receptor agonists and their advantages compared with existing nonspecific agents, and to help the reader better understand the clinical role of the A(2A)-specific receptor agonists and their application.

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BACKGROUND: Patients with pre-eclampsia and eclampsia constitute a special high risk group for future hypertension. They require a long term follow up to be able to detect and treat emerging hypertension early enough to prevent complications. Unfortunately, this is not so. This study was undertaken to find out the incidence of history of pre-eclampic toxaemia (PET) in our female hypertensive patients attending cardiac clinic and to also determine the incidence of complications of hypertension in those with previous history of PET. METHODS: Fifty consecutive female hypertensive patients seen in cardiac clinic were recruited. Detailed history including full obstetric and family history was taken. A full clinical examination was done including blood pressure and a search for complications of hypertension. Findings were then analyzed and various frequencies determined. RESULTS: Forty-nine patients were studied. The mean age was 47.29 +/- 11.46 years. The mean SBP, DBP and MAP were 143.18 +/- 25.05, 90.49 +/- 14.19 and 108.12 +/- 16.71 mmHg respectively. Between the last child birth and the time of established hypertension in those who had PET ranged from 3-25 years. Sixteen, (32.7%) of the 49 patients had history of PET and 7(43.75%) of these 16 patients had complications of hypertension. CONCLUSION: The incidence of history of PET in our female hypertensive patients attending cardiac clinic is significant (32.7%). Also the 43.8% incidence of complications of hypertension seen in those patients with history of PET in this study is high. PET patients, therefore, constitute a special risk group for future hypertension. Therefore collaboration between the Obstetricians and the Cardiologists is important for patients with PET and eclampsia.

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[Value of the assessment of myocardial viability: evaluation with positron emission tomography 18F-FDG]

Alexánderson Rosas E, Lamothe Molina PA, Iñarra Talboy F, Calleja Torres R, Martínez García A, Ochoa López JM, Meave González A.

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It used to be thought that the consequences of coronary artery disease were final, and that the prognosis of the patient was limited to the extent of the ventricular dysfunction. This paradigm changed radically when the concept of hibernating myocardium was introduced, which states the existence of tissue that can regain contractile function after being re-vascularized. This introduced a new concept in cardiology: myocardial viability. This work presents a clear example of the importance of detecting myocardial viability in selected patients, due to the impact not only in treatment but in prognosis as well. It is also emphasized that positron emission tomography (PET) is the gold standard method to detect myocardial viability.

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Atherosclerosis still represents killer number one in industrialized nations, and is starting to have increased impact in developing countries. Atherosclerotic plaques are the net result of a complex interplay between vascular cholesterol deposition, inflammatory activity and extracellular matrix formation. The result is luminal narrowing of arteries, which may ultimately lead to compromised blood flow to essential body organs, most notoriously to the heart. Most of the cardiovascular events that are caused by atherosclerosis, such as acute myocardial infarction or stroke, are the result of a transition of so-called stable atherosclerotic plaques to vulnerable plaques, that are prone to rupture. The direct consequence of atherosclerotic plaque rupture is exposure of thrombogenic plaque constituents to the blood, leading to instant local thrombus formation. The formation of this localized thrombus may ultimately result in sudden obstruction of blood flow and consequent infarction of distal tissue. Clinical risk profiling methods, such as the Framingham and Procam risk scores, are reasonable predictors of myocardial infarction over a 10-year time-span. However, the challenge remains to identify those patients with a very high risk of suffering from myocardial infarction in the coming months. Imaging may provide the necessary diagnostic information to identify such individuals. The transition of stable atherosclerotic plaques to vulnerable plaques is typically heralded by inflammation, thinning of the overlying fibrous cap, and the presence of a large necrotic core. Apoptosis is linked to all of these features of plaque vulnerability, and may, therefore, provide uniquely useful targets for the identification of plaque vulnerability. In recent years, a number of molecular imaging technologies have been developed to image apoptosis, which will be discussed in this review. Further development of apoptosis imaging technologies may aid us in the years to come to identify patients with critical cardiovascular risks, to treat myocardial infarction in its imminent, instead of its evident phase.

PET and SPECT imaging of apoptosis in vulnerable atherosclerotic plaques with radiolabeled Annexin A5.

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Atherosclerosis is the net result of a complex interplay between vascular cholesterol deposition, inflammatory activity and extracellular matrix formation. The result is luminal narrowing of arteries, which may ultimately lead to compromised blood flow to essential body organs, most notoriously to the heart. Most of the cardiovascular events that are caused by atherosclerosis, such as acute myocardial infarction or stroke, are the result of a transition of so-called stable atherosclerotic plaques to vulnerable plaques, that are prone to rupture. The direct consequence of atherosclerotic plaque rupture is exposure of thrombogenic plaque constituents to the blood, leading to instant local thrombus formation. The formation of this localized thrombus may ultimately result in sudden obstruction of blood flow and consequent infarction of distal tissue. Clinical risk profiling methods, such as the Framingham and Procam risk scores, are reasonable predictors of myocardial infarction over a 10-year time-span. However, the challenge remains to identify those patients with a very high risk of suffering from myocardial infarction in the coming months. Imaging may provide the necessary diagnostic information to identify such individuals. The transition of stable atherosclerotic plaques to vulnerable plaques is typically heralded by inflammation, thinning of the overlying fibrous cap, and the presence of a large necrotic core. Apoptosis is linked to all of these features of plaque vulnerability, and may, therefore, provide uniquely useful targets for the identification of plaque vulnerability. In recent years, a number of molecular imaging technologies have been developed to image apoptosis, which will be discussed in this review. Further development of apoptosis imaging technologies may aid us in the years to come to identify patients with critical cardiovascular risks, to treat myocardial infarction in its imminent, instead of its evident phase.

PET and SPECT imaging of apoptosis in vulnerable atherosclerotic plaques with radiolabeled Annexin A5.
Role of nuclear imaging in cardiac resynchronization therapy.

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Cardiac resynchronization therapy (CRT) has become an integrated treatment option for patients with drug-refractory heart failure. Selection of patients for CRT is based on moderate-to-severe heart failure (New York Heart Association functional class III or IV), depressed left ventricular (LV) systolic function of 35% or below and prolonged QRS interval of 120 ms or more. However, 30-40% of selected patients do not exhibit improvement in heart failure symptoms or LV systolic performance. Efforts have been made to improve patient selection criteria and several studies using echocardiography have demonstrated the significance of LV dyssynchrony for prediction of CRT response as an additional selection criteria. In addition, (location and extent of) viability and scar tissue are important for outcome following CRT. Nuclear imaging with ECG-gated myocardial perfusion single-photon emission computed tomography (GMPS) permits assessment of viability, scar tissue and LV dyssynchrony from one dataset; the potential value of GMPS in CRT patients is discussed in this review. In addition, the use of nuclear imaging (and particularly PET) for evaluation of changes in blood flow, metabolism and innervation after CRT is addressed.
Tunneled left anterior descending artery in a child with hypertrophic cardiomyopathy.

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BACKGROUND: A 10-year-old boy presented with a history of severe angina on exertion. A two-dimensional echocardiogram showed mild asymmetric left ventricular (LV) hypertrophy localized to the interventricular septum, consistent with nonobstructive hypertrophic cardiomyopathy. A maximal treadmill exercise test was terminated early owing to marked downsloping of the ST-T segment on all precordial leads, associated with mild chest discomfort. Cardiac MRI and coronary angiography showed that the left anterior descending (LAD) artery was ‘tunneled’ from its origin to the junction of the middle and lower segments, causing systolic obliteration. PET showed diffusely blunted myocardial blood flow after dipyridamole infusion. A beating-heart technique was used to perform surgical mobilization of the superficial and lateral surfaces of the LAD artery. The patient was free from angina at 6 months after surgery. A repeat exercise test showed considerable improvement in exercise tolerance, which was associated with a marked decrease in ST-T changes on exertion. INVESTIGATIONS: Physical examination, laboratory tests, 12-lead electrocardiography, two-dimensional echocardiography, exercise testing, cardiac MRI, coronary angiography, PET. Holter electrocardiographic monitoring. DIAGNOSIS: Angina caused by extensive myocardial tunneling of the LAD artery in nonobstructive hypertrophic cardiomyopathy. MANAGEMENT: Bisoprolol therapy and surgical mobilization of the tunnelled LAD artery.


Ectopic expression of the sodium-iodide symporter enables imaging of transplanted cardiac stem cells in vivo by single-photon emission computed tomography or positron emission tomography.


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OBJECTIVES: We examined the sodium-iodide symporter (NIS), which promotes in vivo cellular uptake of technetium 99m (99mTc) or iodine 124 (124I), as a reporter gene for cell tracking by single-photon emission computed tomography (SPECT) or positron emission tomography (PET) imaging. BACKGROUND: Stem cells offer the promise of cardiac repair. Stem cell labeling is a prerequisite to tracking cell fate in vivo. METHODS: The human NIS complementary deoxyribonucleic acid was transduced into rat cardiac-derived stem cells (rCDCs) using lentiviral vectors. Rats were injected intramyocardially with up to 4 million NIS(+) rCDCs immediately after left anterior descending coronary artery ligation. Dual isotope SPECT (or PET) imaging was performed, using (99mTc) or (124I) for cell detection and thallium 201 (or ammonia 13) for myocardial delineation. In a subset of animals, high resolution ex vivo SPECT scans of explanted hearts were obtained to confirm that in vivo signals were derived from the cell injection site. RESULTS: NIS expression in rCDCs did not affect cell viability and proliferation. NIS activity was verified in isolated transduced cells by measuring (99m)Tc uptake. NIS(+) rCDCs were visualized in vivo as regions of (99m)Tc or (124)I uptake within the injection site. RESULTS: NIS expression in rCDCs did not affect cell viability and proliferation. NIS activity was verified in isolated transduced cells by measuring (99m)Tc uptake. NIS(+) rCDCs were visualized in vivo as regions of (99m)Tc or (124)I uptake within the injection site. CONCLUSIONS: Ectopic NIS expression allows noninvasive in vivo stem cell tracking in the myocardium, using either SPECT or PET. The general approach shows significant promise in tracking the fate of transplanted cells participating in cardiac regeneration, given its ability to observe living cells using clinically applicable imaging modalities.


Comparison between adenoviral and retroviral vectors for the transduction of the thymidine kinase PET reporter gene in rat mesenchymal stem cells.


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Mesenchymal stem cells (MSCs) are a promising cell line for the treatment of ischemic heart disease. To evaluate the success of their transplantation into living animals, noninvasive imaging techniques that are able to track the distribution and fate of those cells would be useful. The aim of this study was to investigate the feasibility of infecting rat MSCs with adenoviruses and retroviruses carrying the herpes simplex virus type 1 thymidine kinase (HSV1-tk) gene; to compare the level of transgene expression induced by the 2 viral vectors; to evaluate the effects of viral transduction on cell phenotype, viability, proliferation rates, and differentiation capabilities; and to test the possibility of noninvasively imaging transduced MSCs using 9-(4-18F-fluoro-3-[hydroxymethyl]butyl)guanine (18F-FHBG) and small-animal PET after their transplantation into living rats. METHODS: We infected rat bone marrow MSCs with adenoviruses carrying the HSV1 mutant tk (Ad-HSV1-sr39tk) PET reporter gene (PRG) or with a retroviral construct expressing the wild-type HSV1-tk PRG. The efficacy and intensity of HSV1-sr39tk and HSV1-tk gene
expression were determined by a direct comparison of [8-3H]-penciclovir ([8-3H]-PCV) cell uptake in both infected MSC populations and noninfected control MSCs. Small-animal PET studies were performed on living rats after an intramuscular injection of infected MSCs. The MSCs either have been incubated in advance with 18F-FHBG or they were administered and 18F-FHBG was thereafter intravenously administered [corrected] RESULTS: Both adenoviral and retroviral vectors can be used to introduce the tk PRG in MSCs. Neither adenovirus nor retrovirus infections significantly modify MSC phenotype, viability, proliferation, and differentiation capabilities. No significant 3H-PCV uptake was observed in noninfected MSCs. By contrast, after both adenoviral and retroviral infections, the infected MSC populations exhibited a similar, significantly higher, 3H-PCV accumulation. Small-animal PET images showed intense activity within the transplanted regions irrespective of the infected MSC population used. CONCLUSION: Our results demonstrate the feasibility of infecting MSCs with adenoviruses and retroviruses expressing the HSV1-tk PRG and suggest that infected MSCs can be noninvasively imaged with 18F-FHBG and small-animal PET after their transplantation into living animals.


Independent and incremental prognostic value of left ventricular ejection fraction determined by stress gated rubidium 82 PET imaging in patients with known or suspected coronary artery disease.

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BACKGROUND: Whether left ventricular ejection fraction (EF) obtained by gated rubidium 82 positron emission tomography (PET) myocardial imaging can identify patients at risk for future cardiac events is unclear. METHODS AND RESULTS: Consecutive patients with known or suspected coronary artery disease who underwent dipyridamole stress gated Rb-82 PET imaging were evaluated. Scoring of perfusion was accomplished by use of a 17-segment model. EF was automatically generated. Patients were stratified based on summed stress scores (SSSs) (0-3, 4-8, or >8) and stress EF (>50%, 40%-49%, or <40%). All-cause mortality was determined by use of the Social Security Death Index. Of 1,441 patients, 132 (9.2%) died during mean follow-up of 2.7 +/- 0.8 years. Annualized mortality rates across SSS groups were 2.4% for SSS of 0 to 3, 4.1% for SSS of 4 to 8, and 6.9% for SSS greater than 8 (P < .001). Similarly, annualized mortality rates were 2.4%, 6.2%, and 9.2% for the group with EF greater than 50%, group with EF of 40% to 49%, and group with EF lower than 40%, respectively (P < .001). On multivariate analysis, the addition of EF to clinical and perfusion variables significantly increased the global chi(2) (73.3 to 107.7, P < .001). Integration of EF with SSS significantly enhanced risk stratification. CONCLUSION: EF assessed by stress gated Rb-82 PET imaging provides independent and incremental prognostic information and, hence, should be routinely incorporated in risk assessment.

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Protocol for measuring myocardial blood flow by PET/CT in cats.

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PURPOSE: The aim of this study was to establish a protocol for measuring myocardial blood flow (MBF) by PET/CT in healthy cats. The rationale was its future use in Maine Coon cats with hypertrophic cardiomyopathy (HCM) as a model for human HCM. METHODS: MBF was measured in nine anesthetized healthy cats using a PET/CT scanner and (13)NH(3) at rest and during adenosine infusion. Each cat was randomly assigned to receive vaso dilator stress with two or three adenosine infusions at the following rates (microg/kg per minute): 140 (Ado 1, standard rate for humans), 280 (Ado 2, twice the human standard rate), 560 (Ado 4), 840 (Ado 6) and 1,120 (Ado 8). RESULTS: The median MBF at rest was 1.26 ml/min per g (n = 9; range 0.88-1.72 ml/min per g). There was no significant difference at Ado 1 (n = 3; median 1.35, range 0.93-1.55 ml/min per g; ns) but MBF was significantly greater at Ado 2 (n = 6; 2.16, range 1.35-2.68 ml/min per g; p < 0.05) and Ado 4 (n = 6; 2.11, 1.92-2.45 ml/min per g; p < 0.05). Large ranges of MBF values at Ado 6 (n = 4; 2.53, 2.52-5.63 ml/min per g; ns) and Ado 8 (n = 3; 2.21, 1.92-5.70 ml/min per g; ns) were noted. Observed adverse effects, including hypotension, AV-block and ventricular premature contractions, were all mild, of short duration and immediately reversed after cessation of the adenosine infusion. CONCLUSION: MBF can be safely measured in cats using PET. An intravenous adenosine infusion at a rate of 280 microg/kg per minute seems most appropriate to induce maximal hyperaemic MBF response in healthy cats. Higher adenosine rates appear less suitable as they are associated with a large heterogeneity in flow increase and rate pressure product, most probably due to the large variability in haemodynamic and heart rate response.
Positron emission tomography for modeling pathophysiological processes in vivo.

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Positron emission tomography (PET) is a powerful tool for imaging and quantifying (patho)physiological processes in the human body. PET has been successfully used for staging diseases and evaluating response to treatment. Furthermore, PET may contribute to drug development and individualized treatment planning. This article reviews the use of several PET tracers in drug development and their clinical application in the fields of neurology, oncology and cardiology.

Clinical evaluation of iterative reconstruction (ordered-subset expectation maximization) in dynamic positron emission tomography: quantitative effects on kinetic modeling with N-13 ammonia in healthy subjects.

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BACKGROUND: The purpose of this study was to investigate the quantitative properties of ordered-subset expectation maximization (OSEM) on kinetic modeling with nitrogen 13 ammonia compared with filtered backprojection (FBP) in healthy subjects. METHODS AND RESULTS: Cardiac N-13 ammonia positron emission tomography (PET) studies from 20 normal volunteers at rest and during dipyridamole stimulation were analyzed. Image data were reconstructed with either FBP or OSEM. FBP- and OSEM-derived input functions and tissue curves were compared together with the myocardial blood flow and spillover values. The late area under the OSEM input functions during dipyridamole is overestimated by 30% (P < .0001) relative to FBP. Conversely, the area under the late part of the OSEM tissue curves is underestimated by 20% (P < .0001) compared with FBP during both rest and dipyridamole. These differences in tissue and input functions cause the resting myocardial blood flow to be underestimated by 15% (P < .0001). During dipyridamole, the OSEM flow is underestimated by 25% (P < .0001) relative to FBP, causing the myocardial flow reserve to be underestimated by 10% (P < .0001). Large inter-regional differences in FBP and OSEM flow values were observed with a flow underestimation of 45% (rest/dipyridamole) in the septum and of 5% (rest) and 15% (dipyridamole) in the lateral myocardial wall. CONCLUSIONS: OSEM reconstruction of myocardial perfusion images with N-13 ammonia and PET produces high-quality images for visual interpretation. However, compared with FBP, OSEM is associated with substantial underestimation of perfusion on quantitative imaging. Our findings indicate that OSEM should be used with precaution in clinical PET studies.

Radionuclide PET and PET/CT in coronary artery disease.

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In the present review, the basis of non invasive assessment of CAD, the most recent technical developments and results obtained by PET in cardiovascular research and clinical cardiology are described. PET has provided a wealth of new information in the field of cardiac pathophysiology and remains the gold standard for non-invasive measurements of MBF and CFR against which new techniques should be tested. The possibility to combine this relevant functional information with the anatomic details on luminal and arterial wall abnormalities, provided by multislice CT with or without the use of "hybrid" scanners, offers new opportunities for comprehensive non-invasive assessment of CAD and efficacy of new treatments.

[Myocardial perfusion scintigraphy in the diagnosis and prognostic assessment of coronary artery disease: SPET and PET]

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In this article, the role of nuclear cardiology modalities in the diagnosis and follow-up of ischemic coronary artery disease in respect of myocardial perfusion and determination of left ventricular ejection fraction are reviewed. Single photon emission tomography (SPET) and positron emission tomography (PET) techniques are applied for imaging of myocardial perfusion and evaluation of global and regional wall motion and contractility. These techniques could be applied with physiological or pharmacological stress and show different properties when compared to other imaging modalities mostly depending on anatomical details. Diagnostic value of myocardial perfusion scintigraphy and incremental value of SPET or PET/CT (computerized tomography) hybrid imaging is considered. Nuclear cardiology techniques may provide useful prognostic information besides their diagnostic use.
Evaluation of the myocardial perfusion and the structures of coronary arteries with the use of various high technologies, such as advanced echocardiography, magnetic resonance tomography, spiral computed tomography as well as large spectrum of techniques of nuclear cardiology, gains more and more important significance in the diagnosis and management of coronary artery disease. Detection of coronary atherosclerosis and evaluation of early signs of myocardial hypoperfusion provide to select effective treatment modality. Nuclear cardiac studies are being frequently used in this field. In asymptomatic and intermediate likelihood patients, assessment of myocardial perfusion by single photon emission computed tomography (SPECT) or positron emission tomography (PET) appears to be valuable even when coronary arteries are normal. Different imaging protocols and radiopharmaceuticals allow us to evaluate ventricular functions and myocardial metabolic state besides of myocardial perfusion. In this plane, definite successes are being achieved by PET and combined acquisitions by PET/CT and SPECT/CT hybrid systems. Coronary computed tomography angiography (CTA) and myocardial perfusion imaging provide complementary information on vascular structure and myocardial perfusion. However, CTA with fast 16-slice or greater scanners may emerge as the initial test of choice. Myocardial perfusion studies would then be used if the CTA is not available or to assess how a stenosis defined by CTA effects coronary supply. Spiral computed tomography which allows to reveal calcium depositions in blood vessels has an important role in the detection of the severity and extent of atherosclerotic lesions. The use of multislice computed tomography in perspective might partially replace coronary angiography especially for assessing the degree of stenosis and patency of grafts. Magnetic resonance imaging (MRI) also has provided noticeable success in this era. Cardiac MRI clearly has the potential for this application and has already emerged as a highly effective method for assessing ventricular function, myocardial mass and myocardial viability. There is an increasing use of this approach for clinical rest and stress perfusion measurements. While cardiac MRI angiography (CMRA) has great promise as a radiation-free, it currently lags behind CTA for noninvasive coronary angiography. Further perfection of equipment and methodological approaches with the use of novel contrasts is necessary. In patients with coronary artery disease, multimodality applications covering both morphological and functional assessment are helpful for diagnosing and planning of therapeutic strategy. Recent developments in the field of ultrasonography have allowed us objectively quantify global and regional ventricular function and to get real-time evaluation of coronary walls and lesions. While we achieve more knowledge about atherosclerotic lesions by using intravascular ultrasound technique, tissue Doppler imaging has given us attempt to provide a more objective assessment of myocardial function. Finally, although CTA and CMRA are likely to grow considerably in diagnostic evaluation over the next several years, myocardial perfusion studies with SPECT and PET equipment will continue to be very valuable techniques for this purpose.

**Recent advances in nuclear cardiology.**

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Nuclear cardiology is an essential part of functional, non-invasive, cardiac imaging. Significant advances have been made in nuclear cardiology since planar (201)thallium ((201)TI) scintigraphy was introduced for the evaluation of left ventricular (LV) perfusion nearly 40 years ago. The use of nuclear cardiology has been steadily increasing over the last 20 years with important steps being the introduction of (99m)technetium- ((99m)Tc)-labelled perfusion radiotracers, the change from only planar to now much more single photon emission computed tomography (SPECT) and positron emission tomography (PET), electrocardiogram gating of nuclear perfusion imaging, and finally introducing nuclear hybrid imaging using either SPECT or PET together with either computed tomography or magnetic resonance imaging. The indications have extended from nearly only coronary artery diseases to several non-coronary cardiac diseases. The advances in nuclear cardiology are discussed under the four headlines of: 1) myocardial perfusion, 2) cardiac performance including LV and right ventricular (RV) function, 3) myocardial metabolism, and 4) experimental nuclear cardiology.

Am J Cardiol. 2008 Jul 15;102(2):129-34.

**Comparison of accuracy in the prediction of left ventricular wall motion changes between invasively assessed microvascular integrity indexes and fluorine-18 fluorodeoxyglucose positron emission tomography in patients with ST-elevation myocardial infarction.**


Department of Cardiology, School of Medicine, Ajou University, Suwon, Korea. We compared the accuracy in predicting regional wall motion score index (RWMSI) changes between microvascular integrity indexes measured during primary percutaneous coronary intervention (PCI) and fluorine-18 fluorodeoxyglucose (FDG) positron emission tomography (PET) in ST-elevation myocardial infarction (STEMI). Fifty patients with STEMI were enrolled. Microvascular integrity indexes were measured using an intracoronary...
Doppler wire and a pressure wire after primary PCI. We performed FDG-PET 7 days after PCI. RWMSI on follow-up echocardiogram (5.8 +/- 1.7 months) revealed good correlations with coronary flow reserve (r = -0.442, p = 0.002), diastolic deceleration time (r = -0.511, p < 0.001), microvascular resistance index (r = 0.443, p = 0.002), coronary wedge pressure (r = 0.474, p <0.001), and FDG uptake rate (r = -0.571, p <0.001). There were no significant differences in areas under the curve for predicting RWMSI changes between microvascular integrity indexes and FDG-PET (coronary flow reserve 0.696, diastolic deceleration time 0.731, microvascular resistance index 0.748, coronary wedge pressure 0.694, Thrombolysis In Myocardial Infarction myocardial perfusion grade 0.702, and FDG-PET 0.755). In conclusion, microvascular integrity indexes assessed during primary PCI are useful and comparable to FDG-PET in predicting left ventricular functional changes in STEMI.


Present and future of clinical cardiovascular PET imaging in Europe—a position statement by the European Council of Nuclear Cardiology (ECNC).

Le Guludec D, Lautamäki R, Knuuti J, Bax JJ, Bengel FM; on behalf of the European Council of Nuclear Cardiology (ECNC).

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Introduction: This position statement was prepared by the European Council of Nuclear Cardiology (ECNC) and summarizes the current and future potential of positron emission tomography (PET) as a clinical cardiovascular diagnostic imaging tool. A first section describes how methodological developments have positively influenced the transition of PET from a research tool towards a clinical diagnostic test. In a second section, evidence in support of its superior diagnostic accuracy, its value to guide decision making and to predict outcome, and its cost-effectiveness is summarized. A third section finally outlines new PET-based approaches and concepts which will likely influence clinical cardiovascular medicine in the future. Conclusion: The notion that integration of cardiac PET into healthcare systems and disease management algorithms will advance quality of care is increasingly supported by the literature highlighted in this statement.


[Cardiac imaging: specific clinical role of newly developed non invasive techniques. Part II: functional evaluation]

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The non-invasive evaluation of myocardial ischemia is a priority in cardiology. The preferred initial non-invasive test is exercise ECG, because of its high accessibility and its low cost. Stress radionuclide myocardial perfusion imaging or stress echocardiography are now routinely performed, and new non-invasive techniques such as perfusion-MRI, dobutamine stress-MRI or 82rubidium perfusion PET have recently gained acceptance in clinical practice. In the same time, an increasing attention has been accorded to the concept of myocardial viability in the decisional processes in case of ischemic heart failure. In this indication, MRI with late enhancement after intravenous injection of gadolinium and 18F-FDG PET showed an excellent diagnostic accuracy. This article will present these new imaging modalities and their accepted indications.


Routine quality control of clinical nuclear medicine instrumentation: a brief review.

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This article reviews routine quality-control (QC) procedures for current nuclear medicine instrumentation, including the survey meter, dose calibrator, well counter, intraoperative probe, organ ("thyroid") uptake probe, gamma-camera, SPECT and SPECT/CT scanner, and PET and PET/CT scanner. It should be particularly useful for residents, fellows, and other trainees in nuclear medicine, nuclear cardiology, and radiology. The procedures described and their respective frequencies are presented only as general guidelines.
Present and future of clinical cardiovascular PET imaging in Europe--a position statement by the European Council of Nuclear Cardiology (ECNC).


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This position statement was prepared by the European Council of Nuclear Cardiology and summarises the current and future potential of PET as a clinical cardiovascular diagnostic imaging tool. The first section describes how methodological developments have positively influenced the transition of PET from a research tool towards a clinical diagnostic test. In the second section, evidence in support of its superior diagnostic accuracy, its value to guide decision making and to predict outcome and its cost effectiveness is summarised. The third section finally outlines new PET-based approaches and concepts, which will likely influence clinical cardiovascular medicine in the future. The notion that integration of cardiac PET into healthcare systems and disease management algorithms will advance quality of care is increasingly supported by the literature highlighted in this statement.


Mycotic aneurysm of the aorta as an unusual complication of coronary angiography.

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INTRODUCTION: Mycotic aneurysm of the aorta is a rare diagnosis with high mortality. REPORT: Percutaneous coronary intervention was complicated by bacteraemia with Staphylococcus aureus and a mycotic aortic aneurysm, an unusual complication of coronary angiography. Combining CT and PET scan showed a hotspot in the thoracic aorta. After six months of antibiotic treatment she fully recovered. Repeated CT/PET scanning revealed complete abolishment of the aortic abnormalities. DISCUSSION: This report suggests that diagnosing and follow-up of aortitis is feasible with combined CT/PET scan and may help in determining choice and duration of therapy.

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Abnormal sympathetic innervation of viable myocardium and the substrate of ventricular tachycardia after myocardial infarction.


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OBJECTIVES: The aim of this study was to characterize the relationship between impaired sympathetic innervation and arrhythmia with noninvasive biologic imaging in an animal model of post-infarct ventricular tachycardia (VT). BACKGROUND: Innervation might be abnormal in the normally perfused borderzone of myocardial infarction, contributing to myocardial catecholamine overexposure and arrhythmogenic risk. METHODS: Myocardial infarction was induced by mid-left anterior descending coronary artery balloon occlusion in 11 pigs. Positron emission tomography (PET) of tissue perfusion and catecholamine uptake and storage was performed with [13N]-ammonia and [11C]-epinephrine 4 to 12 weeks later. Magnetic resonance imaging and invasive electrophysiology (electroanatomic mapping, basket catheter, VT inducibility) were performed within 1 week of PET. RESULTS: When compared with a normal database of 9 healthy animals, reduced perfusion was observed in 37 +/- 7% of the left ventricle (LV). Epinephrine retention was reduced in 44 +/- 7% of LV, resulting in a perfusion/innervation mismatch of 7 +/- 4% LV. Sustained monomorphic VT was inducible in 7 of 11 animals. These animals showed a larger perfusion/innervation mismatch (10 +/- 4% vs. 4 +/- 2% LV for animals without VT; p = 0.02). Regionally, the degree of perfusion/innervation mismatch did not correlate with wall thickness or thickening but showed a significant correlation with reduced myocardial voltage (r = 0.93; p = 0.001) and with the site of earliest VT activation (chi-square 13.1; p < 0.001). CONCLUSIONS: Noninvasive mapping of cardiac sympathetic nerve terminals reveals regionally impaired catecholamine uptake and storage in the normally perfused borderzone after experimental myocardial infarction. These areas might be useful to characterize the individual risk for ventricular arrhythmia.


Evaluation of combined cardiac positron emission tomography and coronary computed tomography angiography for the detection of coronary artery disease.


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BACKGROUND: Coronary artery disease is a leading cause of morbidity and mortality. Multiple imaging modalities are used to screen for significant coronary artery disease. We report the concordance between coronary computed tomography angiography (CTA) and stress cardiac positron emission tomography (CPET) to detect significant coronary artery disease, the feasibility of combining CTA and CPET in one diagnostic test, and the ability of CTA and CPET to detect significant coronary artery disease by comparison with cardiac catheterization. METHODS: Forty patients were prospectively enrolled and imaged with a hybrid PET/CT scanner. Eighteen patients had cardiac catheterization data for comparison. Concordance of findings between diagnostic tests was assessed by examining overall percentage in agreement, area under the receiver operating characteristic curve, sensitivity, specificity, and positive and negative predictive values. RESULTS: The overall agreement between CTA and CPET for detecting significant coronary artery disease was 81.3% with a sensitivity and specificity of 81.8 and 80.0%, respectively. CONCLUSION: CTA and CPET can be performed in a single diagnostic test interval to simultaneously assess the extent of coronary artery disease and its hemodynamic significance. The sensitivity and specificity of CTA and CPET are similar to existing noninvasive screening tests.

Heart. 2008 Dec;94(12):1627-33.

Myocardial blood flow in patients with low-flow, low-gradient aortic stenosis: differences between true and pseudo-severe aortic stenosis. Results from the multicentre TOPAS (Truly or Pseudo-Severe Aortic Stenosis) study.


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BACKGROUND: Impairment of myocardial flow reserve (MFR) in aortic stenosis (AS) with normal left ventricular function relates to the haemodynamic severity. OBJECTIVES: To investigate whether myocardial blood flow (MBF) and MFR differ in low-flow, low-gradient AS depending on whether there is underlying true-severe AS (TSAS) or pseudo-severe AS (PSAS). METHODS: In 36 patients with low-flow, low-gradient AS, dynamic [13N]ammonia PET perfusion imaging was performed at rest (n = 36) and during dipyridamole stress (n = 20) to quantify MBF and MFR. Dobutamine echocardiography was used to classify patients as TSAS (n = 18) or PSAS (n = 18) based on the indexed projected effective orifice area (EOA) at a normal flow rate of 250 ml/s (EOA(proj) \leq 0.55 cm2/m2). RESULTS: Compared with healthy controls (n = 14), patients with low-flow, low-gradient AS had higher resting mean (SD) MBF (0.83 (0.21) vs 0.69 (0.09) ml/min/g, p = 0.001), reduced hyperaemic MBF (1.16 (0.31) vs 2.71 (0.50) ml/min/g, p<0.001) and impaired MFR (1.44 (0.44) vs 4.00 (0.91), p<0.001). Resting MBF and MFR correlated with indices of AS severity in low-flow, low-gradient AS with the strongest relationship observed for EOA(proj) (r(s) = -0.50, p = 0.002 and r(s) = 0.61, p = 0.004, respectively). Compared with PSAS, TSAS had a trend to a higher resting MBF (0.90 (0.19) vs 0.77 (0.21) ml/min/g, p = 0.06), similar hyperaemic MBF (1.16 (0.31) vs 1.17 (0.32) ml/min/g, p = NS), but a significantly smaller MFR (1.19 (0.26) vs 1.76 (0.41), p = 0.003). An MFR \leq 1.8 had an accuracy of 85% for distinguishing TSAS from PSAS. CONCLUSIONS: Low-flow, low-gradient AS is characterised by higher resting MBF and reduced MFR that relates to the AS severity. The degree of MFR impairment differs between TSAS and PSAS and may be of value for distinguishing these entities.


Reperfused myocardial infarction: contrast-enhanced 64-Section CT in comparison to MR imaging.

Nieman K, Shapiro MD, Ferencik M, Nomura CH, Abbara S, Hoffmann U, Gold HK, Jang IK, Brady TJ, Cury RC.

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The transmural extent of contrast enhancement in DE-CMRI is used to predict functional recovery after revascularization in delayed-enhancement (DE) technique directly visualizes non-viable myocardium due to an altered contrast-media distribution in both entities. Recent studies demonstrated the superiority of DE-CMRI compared to single photon emission tomography (SPECT) in patients with severely impaired left ventricular (LV) function. The low-dose dobutamine stimulation (LDDS) cine-CMRI analyses the contractile reserve of dysfunctional but viable myocardium in AMI and CMI with high specificity. Sensitivity of LDDS cine-CMRI is superior to LDDS echocardiography but reduced in patients with severely impaired LV function. The delayed-enhancement (DE) technique directly visualizes non-viable myocardium due to an altered contrast-media distribution in necrotic and fibrotic tissue. DE-CMRI identifies non-viable myocardium with high spatial resolution independently from LV function. The transmural extent of contrast enhancement in DE-CMRI is used to predict functional recovery after revascularization in AMI and CMI. Furthermore, the amount and pattern of contrast enhancement in DE-CMRI provide important prognostic information in both entities. Recent studies demonstrated the superiority of DE-CMRI compared to single photon emission tomography (SPECT) and positron emission tomography (PET) to assess myocardial viability. Therefore, DE-CMRI is currently recognised as the standard of reference for assessment of myocardial viability. The technical background, clinical application and accuracy of the different CMRI techniques to assess myocardial viability in AMI and CMI are discussed in this work.
Should we use more PET-CT in clinical cardiology?

Knuuti J.


Pericardial malignant mesothelioma: a latent complication of radiotherapy?

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Pericardial diseases can be difficult to differentiate from myocardial conditions. Diagnosis can be challenging and often requires the use of different imaging modalities. Here, we describe a case which presented with common cardiac symptoms which were shown to be the result of a rare condition. A 62-year-old lady presented with left femoral artery embolism. Post-embolectomy she developed cardiac failure. Three months previously an acellular, sterile pericardial effusion had been drained. In 1993 a left mastectomy and axillary node clearance was performed for breast cancer. Adjuvant chemotherapy and radiotherapy were administered. Examination revealed a raised jugular venous pressure (JVP) with rapid Y descent and Kussmaul's sign. CT chest and abdomen found no recurrence of breast carcinoma. Cardiac MRI demonstrated thickened pericardium. At cardiac catheterisation haemodynamic responses consistent with constrictive pericarditis were seen. Pericardectomy was performed. Histology revealed pericardial epithelioid malignant mesothelioma. 18-FDG-PET CT post-operatively was negative in the pericardium and pleura. Chemotherapy with pemetrexed and carboplatin was given. The patient died 9 months after presentation. Radiotherapy and asbestos exposure are both associated with pericardial mesothelioma and the aetiology in this case was not clear. The condition carries a poor prognosis and is invariable fatal although newer chemotherapeutic regimens have prolonged survival times.
Successful surgery in late onset epilepsy with tuberous sclerosis complex.


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[Case records of Epileptic Disorders. Anatomo-electro clinical correlations. Case 01-2009]. Tuberous sclerosis complex (TSC) is a multisystemic genetic disorder with variable phenotypic expression, caused by mutations in one of the two tumor suppressor genes, TSC1 or TSC2. Epilepsy is the most common neurological presentation and seizures are often medically intractable. Definition of the epileptogenic zone during presurgical evaluation is challenging given the multiple potentially epileptogenic lesions visible on MRI. However, TSC patients may nevertheless achieve seizure freedom, when preoperative evaluation yields concordant results. The strategies used in these patients vary substantially among different epilepsy surgery centres. We present a 21-year-old right-handed, intellectually not impaired woman with TSC and medically intractable seizures since the age of 15 years. Careful multi-stage presurgical evaluation, including prolonged video-EEG-monitoring, cerebral high resolution MRI, ictal and interictal [99m Tc]HMPAO-SPECT, [18 F]FDG-PET and further invasive recordings with subdural and depth electrodes led to the identification of an epileptogenic tuber with concordant seizure onset zone in the right neocortical temporal lobe. A tailored resection was performed leading to excellent surgical outcome (follow-up 12 months, Engel class I).

Neurology. 2009 Apr 1.

Effect of APOE genotype on amyloid plaque load and gray matter volume in Alzheimer disease.


OBJECTIVE: To examine the influence of the APOE genotype on levels of beta-amyloid (Abeta) plaque load and atrophy in patients with Alzheimer disease (AD) in vivo. METHODS: Thirty-two patients with moderate AD were divided into carriers and noncarriers of the epsilon4 allele. These groups were matched for age, disease duration, education, and cognitive impairment. In all subjects, [(11)C]PIB-PET was performed for measurement of cerebral Abeta plaque deposition and cranial MRI for the assessment of gray matter volume by voxel-based morphometry (VBM) and for correction of partial volume effects (PVE) in the PET data. Voxel-based comparisons (SPM5) were performed between patient groups and healthy control populations and completed with multiple regression analyses between imaging data and epsilon4 allele frequency. RESULTS: Compared to controls, AD-typical patterns of [(11)C]PIB retention and atrophy were detected in both epsilon4-positive and epsilon4-negative patient groups. In direct comparison, significantly stronger and more extended [(11)C]PIB uptake was found in epsilon4-positive patients in bilateral temporoparietal and frontal cortex, surviving PVE correction. VBM analysis demonstrated comparable levels of atrophy in both patient groups. Regression analyses revealed a linear association between higher epsilon4 allele frequency and stronger temporoparietal Abeta plaque deposition, independently of other confounds. No major correlation between epsilon4 allele frequency and gray matter decrease was observed. CONCLUSION: These results indicate that the epsilon4-positive APOE genotype not only represents a risk factor for Alzheimer disease (AD), but also results in higher levels of Abeta plaque deposition in epsilon4-positive patients with AD compared to age-matched epsilon4-negative patients with similar levels of cognitive impairment and brain atrophy. The potential role of Abeta plaque imaging for patient inclusion and follow-up in anti-amyloid therapy trials is strengthened by these findings.


Do parkinsonian patients have trouble telling lies? The neurobiological basis of deceptive behaviour.


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Parkinson's disease is a common neurodegenerative disorder with both motor symptoms and cognitive deficits such as executive dysfunction. Over the past 100 years, a growing body of literature has suggested that patients with Parkinson's disease have characteristic personality traits such as industriousness, seriousness and inflexibility. They have also been described as 'honest', indicating that they have a tendency to not deceive others. However, these personality traits may actually be associated with dysfunction of specific brain regions affected by the disease. In the present study, we show that patients with Parkinson's disease are indeed 'honest', and that this personality trait might be derived from dysfunction of the prefrontal cortex. Using a novel cognitive task, we confirmed that patients with Parkinson's disease (n = 32) had difficulty making deceptive responses relative to healthy controls (n = 20). Also, using resting-state (18)F-fluorodeoxyglucose PET, we showed that this difficulty was significantly correlated with prefrontal hypometabolism. Our results are the first to demonstrate that the ostensible honesty found in patients with Parkinson's
disease has a neurobiological basis, and they provide direct neuropsychological evidence of the brain mechanisms crucial for human deceptive behaviour.

Parkinsonism Relat Disord.

**Performance on an Alzheimer-selective odor identification test in patients with Parkinson's disease and its relationship with cerebral dopamine transporter activity.**

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**BACKGROUND:** Previous studies have shown selective deficits of odor identification in both Parkinson's disease (PD) and Alzheimer's disease (AD). Brief, selective AD smell screening tests have been developed to identify subjects at risk of AD. The disease specificity of such screening tests has not been formally evaluated. **OBJECTIVE:** To evaluate the performance of an Alzheimer-selective odor identification test in patients with PD and its relationship with cerebral dopamine transporter (DAT) activity. **METHODS:** PD patients (n=44; Hoehn and Yahr stages I-III; 13f/31m; mean age 59.3+/−10.1) and 44 controls matched for gender and age completed the University of Pennsylvania Smell Identification Test (UPSIT). All patients had PD duration>1 year and none had evidence of dementia. Using the UPSIT, we calculated performance on the 10 odors previously reported to be selective for AD risk (UPSIT-AD10). A subset of 29 PD patients also underwent brain DAT [(11)C]beta-CFT (2-beta-carbomethoxy-3beta-(4-fluorophenyl) tropane) PET imaging. DAT binding was assessed in the hippocampus, amygdala, ventral and dorsal striatum. **RESULTS:** UPSIT-AD10 scores were significantly lower in the patient (5.8+/−2.1) compared to the control group (8.6+/−2.4) (t=5.8, P<0.0001). However, UPSIT-AD10 performance in the PD patients did not correlate with striatal or mesolimbic DAT activity. **CONCLUSIONS:** Hyposmia in PD and AD overlap and supposed Alzheimer-selective smell screening tests may not be specific for AD. However, the supposed AD-selective hyposmia scores in PD did not correlate with cerebral DAT binding and may reflect a non-dopaminergic olfactory mechanism.


**NCI-Sponsored Trial for the Evaluation of Safety and Preliminary Efficacy of 3'-Deoxy-3'-(18)F]fluorothymidine (FLT) as a Marker of Proliferation in Patients with Recurrent Gliomas: Preliminary Efficacy Studies.**

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**PURPOSE:** 3'-Deoxy-3'-(18)F]fluorothymidine ([(18)F]FLT) is being developed for imaging cellular proliferation. The goals were to explore the capacity of FLT-posioton emission tomography (PET) to distinguish between recurrence and radionecrosis in gliomas and compare the results to those obtained with 2-fluoro-2-deoxy-D-glucose (FDG). **PROCEDURES:** Fifteen patients with tumor recurrence and four with radionecrosis, determined by clinical course and magnetic resonance imaging results, were studied by dynamic [(18)F]FLT-PET with arterial blood sampling. A two-tissue compartment four-rate constant model was used to determine metabolic flux (K (FLT)), blood to tissue transport (K (1)), and phosphorylation (k (3)). FDG-PET scans were obtained 75-90 min postinjection. **RESULTS:** K (FLT) and k (3), but not K (1) or k (3)/k (2) + k (3), reached significance for separating the recurrence from radionecrosis groups. Standardized uptake value and visual analyses of FLT or FDG images did not reach significance. **CONCLUSIONS:** K (FLT) (flux) appears to distinguish recurrence from radionecrosis better than other parameters, FLT and FDG semiquantitative approaches, or visual analysis of images of either tracer.


**A history of neuroimaging in epilepsy 1909-2009.**

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Profound advances in the field of clinical imaging in epilepsy occurred between 1909 and 2009, the century of the International League Against Epilepsy, and these are reviewed briefly in this paper. Initially imaging was carried out with plain x-ray, air encephalography, and angiography, and these techniques had a relatively minor role in epilepsy. Computerized tomographic (CT) scanning was introduced in 1971, and magnetic resonance imaging (MRI) a decade or so later, and both these technologies had an immediate and far-reaching impact on epilepsy. MRI techniques continued to evolve during the 1990s and profoundly influenced many aspects of epilepsy clinical practice. These structural imaging techniques revealed pathological lesions in large numbers of patients with hitherto cryptogenic epilepsy, widened the indications for surgical therapy, and improved our understanding of the pathogenesis and etiology of epilepsy. In recent years, the research focus has turned to IMRI but its impact on epilepsy currently is relatively small. Magnetic resonance spectroscopy (MRS), positron emission tomography (PET) and single photon emission computed tomography (SPECT) also have had a limited impact on clinical practice in epilepsy.
However, that does not exclude the possibility that the A11 system is involved in RLS symptoms. Changes at the cellular level in support the concept of dramatic cell loss or of a neurodegenerative process in the A11 hypothalamic region of patients with RLS. Dopaminergic metabolism or at the distal synapse with changes in receptors or transporters were not evaluated in this study.

Histological indication of any significant inflammation or concurrent ongoing pathology in these RLS cases. The findings do not control cases on any measure used: TH (+) cell volume, fractional GFAP staining, or general histological examination. Nor was there technique for kinetic modelling of tracers. At the moment there are still several issues which need further research and evaluation before we can fully employ the possibilities of PET as an in-vivo measurement of underlying molecular biology. These issues relate to improved quantification of measurements, improved image reconstruction and processing, and the use of blood plasma data in combination with kinetic models. Besides the more technical issues, there are two more issues which need further clarification: the effect of the anaesthesia, and the effect of radiation on the experiment itself. In this review, we will give an overview of how the technique can be used but we will also discuss the issues mentioned above. The focus will be on the three major parts of the imaging procedure: acquisition, reconstruction of images, and kinetic modelling of the data.

Small animal imaging with positron emission tomography has undergone a major evolution. This has been driven by technical improvements and the development of dedicated PET camera's for small animals. The focus has shifted from detection of tracer uptake and visualization of the tracer distribution towards the quantification of the physiological parameters necessary to use this technique for kinetic modelling of tracers. At the moment there are still several issues which need further research and evaluation before we can fully employ the possibilities of PET as an in-vivo measurement of underlying molecular biology. These issues relate to improved quantification of measurements, improved image reconstruction and processing, and the use of blood plasma data in combination with kinetic models. Besides the more technical issues, there are two more issues which need further clarification: the effect of the anaesthesia, and the effect of radiation on the experiment itself. In this review, we will give an overview of how the technique can be used but we will also discuss the issues mentioned above. The focus will be on the three major parts of the imaging procedure: acquisition, reconstruction of images, and kinetic modelling of the data.

Although the positive clinical benefits of levodopa have fostered the concept of an abnormality in the dopaminergic system in Restless Legs Syndrome (RLS), research into the nigro-striatal (PET/SPECT studies) or tubero-infundibular (i.e., prolactin secretion) dopaminergic pathways has shown limited positive results. Some research groups have focused on the A11 dopaminergic system in the hypothalamus as this is the primary source of descending dopaminergic input into the spinal cord, an area of the nervous system believed by some investigators to be involved in RLS symptom development. Some investigators have now proposed lesioning or toxin-inhibiting the A11 system as a model of RLS, even though there has been no clear clinical or autopsy data to suggest that RLS is a neurodegenerative disorder. In this study, the A11 cell bodies were identified in 6 RLS and 6 aged-matched control autopsy cases. Cells were stained for tyrosine hydroxylase (TH), and stereological measure of the individual TH (+) cell volume was made. Regional assessment of gliosis as assessed by immunostaining for glial fibrillary acidic protein (GFAP) was made in the surrounding tissue. General histological staining was also performed on the tissue. This study found no significant difference between RLS or control cases on any measure used: TH (+) cell volume, fractional GFAP staining, or general histological examination. Nor was there histological indication of any significant inflammation or concurrent ongoing pathology in these RLS cases. The findings do not support the concept of dramatic cell loss or of a neurodegenerative process in the A11 hypothalamic region of patients with RLS. However, that does not exclude the possibility that the A11 system is involved in RLS symptoms. Changes at the cellular level in dopaminergic metabolism or at the distal synapse with changes in receptors or transporters were not evaluated in this study.

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Anterior thalamic nucleus stimulation modulates regional cerebral metabolism: An FDG-MicroPET study in rats.


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The mechanism underlying the antiepileptic function of deep brain stimulation (DBS) of the anterior thalamic nucleus (ATN) remains unknown, presumably related to functional lesioning of target. We measured the regional normalized cerebral metabolic rate of glucose (nCMRglc) with [18F]-fluorodeoxyglucose (FDG)-MicroPET in animals receiving either ATN stimulation or lesioning. Bilateral ATN stimulation reversibly increased glucose uptake in the target region, the thalamus and hippocampus, and decreased glucose uptake in the cingulate cortex and frontal cortex. However, bilateral ATN lesioning decreased glucose uptake only in the target region. Animals with bilateral ATN lesions showed no metabolic changes after ATN stimulation. Thus, bilateral DBS of the ATN reversibly induces metabolic activation of the target area and modulates energy metabolism in remote brain regions via efferent or afferent fibers in non-epileptic rats. DBS of the ATN may work by a different mechanism than ATN lesioning.
Assessing the microlesion effect of subthalamic deep brain stimulation surgery with FDG PET.

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Object The authors investigated whether the insertion of deep brain stimulation electrodes into the subthalamic nucleus can alter regional brain metabolism in the absence of stimulation. Methods Six patients with Parkinson disease (PD) underwent preoperative FDG PET scanning, and again after STN electrode implantation with stimulation turned off. Results Compared with baseline values, glucose utilization was reduced in the postoperative off-stimulation scans in the putamen/globus pallidus and in the ventral thalamus (p < 0.01), and there was increased metabolism in the sensorimotor cortex and cerebellum (p < 0.005). The expression of a specific PD-related spatial covariance pattern measured in the FDG PET data did not change after electrode implantation (p = 0.36), nor was there a significant change in clinical motor ratings (p = 0.44). Differences in PD-related spatial covariance pattern expression among the patients after electrode implantation did, however, correlate with the number of microelectrode recording trajectories placed during surgery (r = -0.82, p < 0.05). Conclusions These findings suggest that electrode implantation can impart a microlesion effect on regional brain function. Nonetheless, these local changes did not cross the threshold of network modulation needed to achieve clinical benefit.

J Nutr Health Aging. 2009 Apr;13(4):332

Editorial: Imaging and Biomarkers Will be Used for Detection and Monitoring Progression of Early Alzheimer's Disease.

Weiner MW.

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During the early development of medicine, clinical diagnosis relied on symptoms, history, as well as the visual, auditory, tactile, and olfactory skills of the physician. More recently, advances of technology led to the development of the stethoscope, EKG machine, X-ray, etc. Another line of technology involved measurements of electrolytes and other substances in blood, urine and other body fluids. Most areas of medicine have greatly benefited from these advances especially in recent decades. In addition to the clinical diagnostic use of imaging and laboratory tests on body fluids, these same types of measurements have been used in epidemiological studies, for assessment of risk, early detection of disease, leading to the development of risk prevention trials. A prominent example is cardiovascular disease. Even as clinicians argued how much myocardial infarctions should be diagnosed (e.g. how much to rely on symptoms, EKG, serum enzymes) a half century of work demonstrated that hypertension and hyperlipidemia were risk factors for subsequent vessel disease. Treatment trials aimed at correction of biomarkers such as hyperlipidemia ultimately demonstrated the value of reducing cardiovascular risk factors. Many other examples of how medicine uses technology for early disease detection include use of the Prostatic Specific Antigen for prostate cancer and mammography to detect breast cancer. In each of these examples, there was always considerable debate concerning whether the biomarker (e.g. an imaging measurement, or laboratory test) provided a "valid" measurement of the disease process. Ultimately, validation required correlation between the biomarker and the ultimate clinical diagnosis and autopsy confirmation. Concerning treatment, validation meant that a treatment which affected the biomarker (e.g. by reducing lipid levels or blood pressure) ultimately had a beneficial clinical outcome (reduction of strokes and heart attacks). For a variety of reasons (e.g. the brain being surrounded by the skull, brain function not easily quantified by technological measurements) the assessment of brain disorders has largely relied on traditional methods of assessing behavior and cognition. Early uses of technology to detect brain disorders included EEG, measurement of cerebral spinal fluid and brain imaging with X-Ray CT and MRI. However, even today most clinicians use imaging to "rule out" other causes of dementia, and the diagnosis of Alzheimer's disease primarily uses clinical information. Fortunately, this situation is now undergoing rapid evolution. There are a number of candidate biomarkers which can be used for diagnosis, early detection, or monitoring progression of Alzheimer's disease. Structural MRI demonstrates hippocampal atrophy in demented and mildly impaired subjects. Fluorodeoxyglucose PET shows reduced glucose metabolism in the posterior cingulate gyrus and hippocampal regions. Recent studies with C-11 FIB and F18 amyloid ligands suggest that the brain amyloid load may be quantified. As expected, subjects with Alzheimer's almost all have high amyloid loads detected by such imaging techniques. A high fraction of MCI and a lower fraction of normal elderly also have high brain amyloid. Measurements of CSF obtained by lumbar puncture show that patient's with Alzheimer's disease have low CSF betaamyloid and elevated tau and phosphotau. A variety of proteins and other substances in blood also appear to change in Alzheimer's disease. For many years its been known that many elderly subjects who appear cognitively normal for age, have evidence of Alzheimer's pathology at autopsy. An important question is: do normal elderly subjects with evidence for Alzheimer's pathology (e.g. small hippocampus, reduced posterior cingulate glucose metabolism, reduced CSF betaamyloid and elevated tau etc) have a higher risk for cognitive decline and ultimate conversion to dementia? Similarly, do subjects with MCI who have biomarker/imaging evidence for Alzheimer's pathology have a higher risk for future conversion to dementia? This special (1-17) issue focuses on the use of various imaging techniques and biomarkers for Alzheimer's disease clinical trials. In this setting imaging/biomarkers have at least 4 uses: 1) As markers of progression. In this case, it is expected that a treatment which slows the rate of progression, would slow the rate of change of the biomarker. Brain atrophy, especially in the hippocampal region, is generally thought to be a good progression marker. 2) To stratify subjects into "groups" especially to identify AD pathology. There are a number of candidates for this use including: hippocampal or total brain volume, FDG PET uptake, amyloid imaging, and CSF betaamyloid and tau 3) As "predictors" of future...
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decline and conversion to AD (the same as mentioned previously). These predictors, when used as baseline covariates, can be used to improve power in trials 4) To identify Alzheimer's pathology in normal elders or those with mild complaints or cognitive impairments. The same aforementioned markers are candidates. The various papers in this special issue all deal with one or another use of such imaging/biomarkers for clinical Alzheimer's trials. Ultimately as prevention treatments are worked out, imaging/biomarkers will be used to identify people at risk and also as progression markers/ The ultimately validation will be achieved by following subjects to conversion (to MCI or dementia) and finally pathological validation with autopsy. Ultimately, early intervention trials will be performed on normal elderly subjects, or subjects with mild cognitive complaints, using imaging/biomarkers to select subjects at high risk for AD pathology, and as outcome measures to detect treatment effects. The value of the biomarkers will be validated by following such subjects long term to determine cognitive decline, conversion to dementia, and pathological confirmation at autopsy. This is the path to the prevention of Alzheimer's disease.

Curr Opin Neurol. 2009 Apr;22(2):179-84.

The current status of neuroimaging for epilepsy.

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PURPOSE OF REVIEW: Neuroimaging research continues apace and is being applied to further understanding of the epilepsies, and improve clinical management. RECENT FINDINGS: Structural imaging has become more sensitive with developments of MRI hardware, acquisition and postprocessing methods. Tractography is being used to define critical pathways prior to surgery. Functional MRI for language lateralization is now a clinical tool. PET studies with specific ligands reveal neurochemical changes associated with specific epilepsy syndromes. SUMMARY: MRI at 3T with FLAIR and multiple channel coils identifies and clarifies relevant abnormalities in 20% of patients with previously unremarkable scans. Voxel-based analysis of diffusion scans may identify abnormalities in group comparisons. Identification of relevant abnormalities using voxel-based methods in individual patients requires a careful balance of sensitivity and specificity, and has a 10-30% yield. The PROPELLER sequence improves the detail of hippocampal anatomy and correlation with histological slices shows the pathological basis of MRI signal changes. Tractography has shown the connections of the language cortex and visualizes specific tracts. Electroencephalograms with simultaneous functional MRI and perfusion have shown that perfusion changes are a major determinant of changes in blood-oxygen-level-dependent signal. Functional MRI of language and memory are becoming used as a predictor of deficits as a result of temporal lobe resection. Increased uptake of the PET tracer 11C-alpha-methyl tryptophan shows promise for localizing epileptogenic malformations of cortical development. Abnormalities of 5HT-1A receptor ligands have been reported in temporal lobe epilepsy, with controversial association with depression. Dopamine uptake abnormalities have been noted in autosomal dominant nocturnal frontal lobe epilepsy.


Delayed postanoxic encephalopathy with serial MRI and PET studies.

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PET-Neurology


Quantitative analysis of donepezil binding to acetylcholinesterase using positron emission tomography and [5-(11)C-methoxy]donepezil.


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The aim of this study was to establish kinetic analysis of [5-(11)C-methoxy]donepezil ([11C]donepezil), which was developed for the in-vivo visualization of donepezil binding to acetylcholinesterase (AChE) using positron emission tomography (PET). Donepezil is an AChE inhibitor that is widely prescribed to ameliorate the cognitive impairment of patients with dementia. Six healthy subjects took part in a dynamic study involving a 60-min PET scan after intravenous injection of ([11C]donepezil. The total distribution volume (tDV) of ([11C]donepezil was quantified by compartmental kinetic analysis and Logan graphical analysis. A one-tissue compartment model (1TCM) and a two-tissue compartment model (2TCM) were applied in the kinetic analysis. Goodness of fit was assessed with chi(2) criterion and Akaike's Information Criterion (AIC). Compared with a 1TCM, goodness of fit was significantly improved by a 2TCM. The tDVs provided by Logan graphical analysis were slightly lower than those provided by a 2TCM. The rank order of the mean tDVs in 10 regions was in line with the AChE activity reported in a previous post-mortem study. Logan graphical analysis generated voxel-wise images of tDV, revealing the overall distribution pattern of AChE in individual brains. Significant correlation was observed between tDVs calculated with and without metabolite correction for plasma time-activity curves, indicating that metabolite correction could be omitted. In conclusion, this method enables quantitative analysis of AChE and direct investigation of the pharmacokinetics of donepezil in the human brain.
Relationship between hypometabolic patterns and ictal scalp EEG patterns in patients with unilateral hippocampal sclerosis: An FDG-PET study.


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This study was to explore the relationship between scalp ictal EEG patterns and interictal hypometabolic patterns in hippocampal sclerosis-associated mesial temporal lobe epilepsy (HS-MTLE) and determine the clinical significance of interictal hypometabolic patterns. Twenty-five patients were classified into 2 groups based on initial ictal discharge (IID) frequency on scalp EEG: (a) those with a sustained regular 5- to 9-Hz rhythm with a widespread distribution (group 1, N=16); and (b) those with an irregular 2- to 5-Hz rhythm with a restricted temporal or subtemporal distribution (group 2, N=9). Using statistical parametric mapping, the PET results of each group were compared with age- and sex-matched controls to identify regions of significant hypometabolism, and the clinical characteristics were compared. Group 1 showed focal hypometabolism confined to the ipsilateral temporal lobe, whereas group 2 showed widespread hypometabolism in the ipsilateral temporal lobe, insular cortex and anterior part of the putamen. The two groups showed no significant differences in clinical characteristics. Among semiologic features, dystonic limb posturing was more frequently observed in group 2 (p=0.03). In summary, scalp EEG IID patterns in HS-MTLE can be important in determining hypometabolic patterns on interictal PET. Differences in hypometabolic patterns may reflect preferential pathways of ictal propagation rather than intrinsic epileptogenic regions.

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Olfaction in patients with suspected Parkinsonism and scans without evidence of dopaminergic deficit (SWEDDs).


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BACKGROUND: PET and SPECT scanning have 87%-94% sensitivity and 80%-100% specificity to differentiate patients with Parkinson's disease (PD) from control subjects and patients with essential (ET) or atypical tremor. More than 10% of patients diagnosed as early PD can have scans without evidence of dopaminergic deficiency (SWEDDs). We investigated whether smell tests can help identify possible cases with SWEDDs. METHODS: The 40 item University of Pennsylvania Smell Test (UPSIT) was used to evaluate the sense of smell in 21 SWEDDs patients. We also tested 26 ET patients, 16 patients with a diagnosis of idiopathic adult-onset dystonia (D), 191 non-demented PD patients and 136 control subjects. We used multiple regression analyses to compare the mean UPSIT score in the SWEDDs group with the other 4 groups (ET, D, PD and controls) after adjusting for the effects of relevant covariates. RESULTS: The mean UPSIT score for the SWEDDs group was greater than in the PD group (p<0.001) and not different from the mean UPSIT in the control (p=0.7), ET (p=0.4), or D (p=0.9) groups. Smell tests indicated a high probability of PD in only 23.8% of SWEDDs as opposed to 85.3% of PD patients. CONCLUSIONS: In a patient with suspected PD, a high PD probability on smell testing favours the diagnosis of PD, and a low PD probability strengthens the indication for dopamine transporter imaging.


Microdosing, imaging biomarkers and SPECT: a multi-sided tripod to accelerate drug development.

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The advances of nuclear medicine imaging instrumentation and radiopharmaceutical sciences allow their involvement in the developmental processes of therapeutic drugs. New chemical entities, meant as potential drugs, need to comply with the proof-of-principle. Tomographic imaging methods as PET, SPECT and CT have been used for small animal and human studies at an early stage of drug development. Using a drug candidate in a radiolabeled form in obtaining quantitative imaging data provides opportunity for a complete morphological and functional overview of targeting properties and overall pharmacokinetics. This can be helpful in go/no-go decision making. Microdosing, using e.g.1% of the proposed dose of the radiolabeled potential drug plays an important part in this early development and notably reduces the risk of serious adverse effects in human volunteers or patients. This paper primarily focuses on the way in which microdosing and SPECT imaging may contribute to the development of drugs. Furthermore, this paper illustrates how these techniques may help to eliminate weak drug candidates at early stage, making time and funds available for potential lead compounds. Eventually this approach facilitates and accelerates new drug approval. The present paper highlights how these techniques make drug development easier in the field of oncology and neurology.
Imaging of early inflammation in low-to-moderate carotid stenosis by 18-FDG-PET.

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It is not clear if 18FDG-PET can be useful for detection of inflammation in low to moderate carotid stenosis. We studied 15 patients scheduled for endarterectomy with contralateral carotids with less than 50% stenosis. 18-FDG-PET was performed prior to CEA and 3 months following surgery. FDG-uptake values were calculated based on maximum standardized uptake value (SUV) and corresponding uptake ratios. We confirmed by CD68 macrophage staining that FDG accumulation corresponds to active inflammation (R=0.8 p less than 0.005). We found significant correlation between the FDG-uptake in the carotids scheduled for CEA and contralateral carotids with low to moderate stenosis (R=0.9 p less than 0.001). The FDG uptake ratio in the contralateral arteries remained stable on the follow-up imaging (1.15+/-0.2 vs. 1.14+/-0.1, R=0.7 p=0.006). We did not find correlation between FDG uptake and symptomatic or asymptomatic patients, degree of carotid stenosis and vascular risk factors. This is a prospective, preliminary in vivo study demonstrating that low to moderate carotid atherosclerosis can be detected using 18-FDG-PET imaging and highlights the truly systemic nature of atherosclerosis.

Multitracer assessment of dopamine function after transplantation of embryonic stem cell-derived neural stem cells in a primate model of Parkinson's disease.


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The ability of primate embryonic stem (ES) cells to differentiate into dopamine (DA)-synthesizing neurons has raised hopes of creating novel cell therapies for Parkinson's disease (PD). As the primary purpose of cell transplantation in PD is restoration of dopaminergic neurotransmission in the striatum, in vivo assessment of DA function after grafting is necessary to achieve better therapeutic effects. A chronic model of PD was produced in two cynomolgus monkeys (M-1 and M-2) by systemic administration of neurotoxin. Neural stem cells (NSCs) derived from cynomolgus ES cells were implanted unilaterally in the putamen. To evaluate DA-specific functions, we used multiple [(11)C]-labeled positron emission tomography (PET) tracers, including [beta-(11)C]L-3,4-dihydroxyphenylalanine (L-[beta-(11)C]DOPA, DA precursor ligand), [(11)C]-2beta-carbomethoxy-3beta-(4-fluorophenyl)tropane ([(11)C]beta-CFT, DA transporter ligand) and [(11)C]raclopride (D(2) receptor ligand). At 12 weeks after grafting NSCs, PET demonstrated significantly increased uptake of L-[beta-(11)C]DOPA (M-1:41%, M-2:61%) and [(11)C]beta-CFT (M-1:31%, M-2:36%) uptake in the grafted putamen. In addition, methamphetamine challenge in M-2 induced reduced [(11)C]raclopride binding (16%) in the transplanted putamen, suggesting release of DA. These results show that transplantation of NSCs derived from cynomolgus monkey ES cells can restore DA function in the putamen of a primate model of PD. PET with multitracers is useful for functional studies in developing cell-based therapies against PD.
PET-Miscellaneous

Positron emission tomography in lung cancer.

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Recent advances in positron emission tomography (PET) with 2-deoxy-2-fluoro [F-18]-D-glucose (FDG) has enabled not only the diagnosis and staging of lung cancer but also the prediction of its malignancy grade. However, FDG-PET has been known to have several pitfalls for imaging of lung cancer. For the effective clinical use of FDG-PET in lung cancer, we reviewed the pitfalls of using FDG-PET in the diagnosis of pulmonary nodules, semiquantitative analysis of FDG-uptake, N-staging, prediction of tumor aggressiveness, prognostic significance, and prediction of pathological response after chemoradiotherapy.

PET without cyclotron.

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A recovery coefficient method for partial volume correction of PET images.

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OBJECTIVES: Correction of the "partial volume effect" has been an area of great interest in the recent times in quantitative PET imaging and has been mainly studied with count recovery models based upon phantoms that incorporate hot spheres in a cold background. The goal of this research study was to establish a similar model that is closer to a biological imaging environment, namely hot spheres/lesions in a warm background and to apply this model in a small cohort of patients. METHODS: A NEMA phantom with six spheres (diameters 1-3.7 cm) was filled with (18)FDG to give sphere:background activity ratios of 8:1, 6:1, and 4:1 for three different acquisitions on a Philips Allegro scanner. The hot sphere SUVmax and the background average SUV were measured for calculation of recovery coefficients (RCs). Using the RCs, the lesion diameters, and the lesion:background ratio, the SUVmax of 64 lesions from 17 patients with biopsy proven lung cancer were corrected. RESULTS: The RCs versus sphere diameters produced characteristic logarithmic curves for each phantom (RCs ranged from 80% to 11%). From a cohort of 17 patients with biopsy proven lung cancer, 64 lesions combined had a mean SUVmax of 7.0 and size of 2.5 cm. After partial volume correction of the SUVmax of each lesion, the average SUVmax increased to 15.5. CONCLUSIONS: Hot spheres in a warm background more closely resemble the actual imaging situation in a living subject when compared to hot spheres in a cold background. This method could facilitate generation of equipment specific recovery coefficients for partial volume correction. The clinical implications for the increased accuracy in SUV determination are certainly of potential value in oncologic imaging.

Introduction The identification of a ground-glass opacity on chest CT is a frequent problem because of the number of exams performed. Observation We report the case of a man of 66 years with a very slowly increasing ground-glass opacity during 5 years. Although the lesion was negative for positron emission tomography and because of its increasing size and the appearance of a solid part, our patient underwent surgery. The final diagnosis was stage I adenocarcinoma. Conclusions The management of a ground glass opacity differs from solid nodules of the lung. The rate of malignancy is high in the published studies, especially in south-east Asia. PET is not as useful as for solid nodules. Long term follow up is necessary because of the long doubling time in these neoplasms.


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We have investigated the role assignment and radiation exposure of medical workers (including receptionists) in PET (positron emission tomography) facilities in Japan using a questionnaire. The survey period was from October 1st to November 15th 2006. The response rate for the questionnaire was 60.0% (72/120 facilities). Nurses were engaged in the intravenous administration of radioactive FDG in 66.9% of PET facilities. In 89.5% of PET facilities, radiological technologists mainly performed the PET examination. The average radiation exposure to medical workers was 0.13 mSv/month (n: 709, S.D.: 0.16) as the effective dose. It was shown that radiation exposure was significantly different depending on the occupation and content of work (p<0.01). The radiation exposure of cyclotron operators and radiological technologists was higher than that of the other occupations (p<0.01). The highest radiation dose to one worker per a PET facility was 0.60 mSv month(-1)), which was 4.6 times higher than the average dose of 0.13 mSv month(-1)). We have clarified the actual conditions of radiation protection in PET facilities in Japan for the first time.


Imaging Gene Expression in Human Mesenchymal Stem Cells: From Small to Large Animals.


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Purpose: To evaluate the feasibility of reporter gene imaging in implanted human mesenchymal stem cells (MSCs) in porcine myocardium by using clinical positron emission tomography (PET)-computed tomography (CT) scanning. Materials and Methods: Animal protocols were approved by the Institutional Administrative Panel on Laboratory Animal Care. Transduction of human MSCs by using different doses of adeno virus that contained a cytomegalovirus (CMV) promoter driving the mutant herpes simplex virus type 1 thymidine kinase reporter gene (Ad-CMV-HSV1-sz399k) was characterized in a cell culture. A total of 2.25 x 10(6) transduced (n = 5) and control nontransduced (n = 5) human MSCs were injected into the myocardium of 10 rats, and reporter gene expression in human MSCs was visualized with micro-PET by using the radionuclide 9-[(4-[fluorine 18]-fluor-3-hydroxymethylbutyl)-guanine (FHBG). Different numbers of transduced human MSCs suspended in either phosphate-buffered saline (PBS) (n = 4) or matrigel (n = 5) were injected into the myocardium of nine swine, and gene expression was visualized with a clinical PET-CT. For analysis of cell culture experiments, linear regression analyses combined with a t test were performed. To test differences in radiotracer uptake between injected and remote myocardium in both rats and swine, one-sided paired Wilcoxon tests were performed. In swine experiments, a linear regression of radiotracer uptake ratio on the number of injected transduced human MSCs was performed. Results: In cell culture, there was a viral dose-dependent increase of gene expression and FHBG accumulation in human MSCs. Human MSC viability was 96.7% (multiplicity of infection, 250). Cardiac FHBG uptake in rats was significantly elevated (P < .0001) after human MSC injection (0.0054% injected dose [ID]/g +/- 0.0007 [standard deviation]) compared with that in the remote myocardium (0.0003% ID/g +/- 0.0001). In swine, myocardial radiotracer uptake was not elevated after injection of up to 100 x 10(6) human MSCs (PBS group). In the matrigel group, signal-to-background ratio increased to 1.87 after injection of 100 x 10(6) human MSCs and positively correlated (R(2) = 0.97, P < .001) with the number of administered human MSCs. Conclusion: Reporter gene imaging in human MSCs can be translated to large animals. The study highlights the importance of co-administering a “scaffold” for increasing intramyocardial retention of human MSCs.

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Quantitative Metrics of Net Proliferation and Invasion Link Biological Aggressiveness Assessed by MRI with Hypoxia Assessed by FMISO-PET in Newly Diagnosed Glioblastomas.


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Glioblastoma multiforme (GBM) are aggressive and uniformly fatal primary brain tumors characterized by their diffuse invasion of the normal-appearing parenchyma peripheral to the clinical imaging abnormality. Hypoxia, a hallmark of aggressive tumor behavior often noted in GBMs, has been associated with resistance to therapy, poorer survival, and more malignant tumor phenotypes. Based on the existence of a set of novel imaging techniques and modeling tools, our objective was to assess a hypothesized quantitative link between tumor growth kinetics [assessed via mathematical models and routine magnetic resonance imaging (MRI)] and the hypoxic burden of the tumor [assessed via positron emission tomography (PET) imaging]. Our biomathematical model for glioma kinetics describes the spatial and temporal evolution of a glioma in terms of concentration of malignant tumor cells. This model has already been proven useful as a novel tool to dynamically quantify the net rates of proliferation (rho) and invasion (D) of the glioma cells in individual patients. Estimates of these kinetic rates can be calculated from routinely available pretreatment MRI in vivo. Eleven
adults with GBM were imaged preoperatively with (18)F-fluoromisonidazole (FMISO)-PET and serial gadolinium-enhanced T1- and T2-weighted MRIs to allow the estimation of patient-specific net rates of proliferation (rho) and invasion (D). Hypoxic volumes were quantified from each FMISO-PET scan following standard techniques. To control for tumor size variability, two measures of hypoxic burden were considered: relative hypoxia (RH), defined as the ratio of the hypoxic volume to the T2-defined tumor volume, and the mean intensity on FMISO-PET scaled to the blood activity of the tracer (mean T/B). Pearson correlations between RH and the net rate of cell proliferation (rho) reached significance (P < 0.04). Moreover, highly significant positive correlations were found between biological aggressiveness ratio (rho/D) and both RH (P < 0.00003) and the mean T/B (P < 0.0007).


The maximum standardized 18F-fluorodeoxyglucose uptake on positron emission tomography predicts lymph node metastasis and invasiveness in clinical stage IA non-small cell lung cancer.


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In patients with clinical stage IA non-small cell lung cancer (NSCLC), we investigated whether the maximum standardized uptake value (SUVmax) of (18)F-fluorodeoxyglucose (FDG) by the tumor correlated with lymph node metastasis, intratumoral lymphatic and vascular invasion of tumor cells, and pleural invasion. From April 2005 to November 2008, 58 patients underwent a lobectomy with systematic hilar and mediastinal lymph node dissection for clinical stage IA NSCLC. All patients had integrated FDG-positron emission tomography (PET)/computed tomography (CT) performed in our center as part of the preoperative workup within one month of resection. The relationships between the SUVmax and pathologic results of lymph node metastasis, intratumoral lymphatic and vascular invasion of tumor cells, and pleural invasion were examined. Compared with tumors with an SUVmax</=2.0, tumors with an SUVmax>2.0 had more frequent lymph node metastasis, intratumoral lymphatic and vascular invasion of tumor cells and pleural invasion (all P<0.05). Our results suggest that in patients with clinical stage IA NSCLC, SUVmax is an important predictor of tumor invasiveness. Keywords: Non-small cell lung cancer; FDG-PET; SUV; Thoracic surgery.


The relationship between subjective well-being and dopamine D2 receptors in patients treated with a dopamine partial agonist and full antagonist antipsychotics.


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Antipsychotic drugs produce unpleasant subjective experiences, which have been associated with high levels of dopamine D2 receptor occupancy. Aripiprazole is a partial agonist antipsychotic, which is hypothesized to produce a different subjective experience profile compared to standard D2 antagonist antipsychotics. The aim of this study was to compare the effect of D2 occupancy produced by a partial agonist antipsychotic (aripiprazole) to that of antagonist antipsychotics (risperidone or olanzapine) on the subjective well-being of patients. Subjective well-being was measured using the Subjective Well-being under Neuroleptics Scale (SWN) and was related to dopamine D2 receptor occupancy using [11C]raclopride PET. Patients that were switched to aripiprazole showed improvement in their subjective well-being from 79.80 (s.d.=16.08) to 89.90 (s.d.=15.33), an effect that was sustained for 6 months. This sustained improvement was observed despite very high levels of DA D2 occupancy (82-99%), in contrast to the effects of antagonist antipsychotics on subjective well-being.


Usefulness of PET/CT scan in the early evaluation of treatment response in gastrointestinal stromal tumor.

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Psychoneuroendocrinology. 2009 Apr 9.

Stress regulation in the central nervous system: Evidence from structural and functional neuroimaging studies in human populations.


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The metabolic effects of stress are known to have significant health effects in both humans and animals. Most of these effects are mediated by the major stress hormone axis in the body, the hypothalamic-pituitary-adrenal (HPA) axis. Within the central nervous system (CNS), the hippocampus, the amygdala and the prefrontal cortex as part of the limbic system are believed to play important roles in the regulation of the HPA axis. With the advent of structural and functional neuroimaging techniques, the role of different CNS structures in the regulation of the HPA axis can be investigated more directly. In the current paper, we summarize the findings obtained in our laboratory in the context of stress and HPA axis regulation. Our laboratory has developed and contributed to the development of manual and automated segmentation protocols from structural magnetic resonance imaging (MRI) scans for assessment of hippocampus, amygdala, medial temporal lobe and frontal lobe structures. Employing these protocols, we could show significant age-related changes in HC volumes, which were different between men and women, with pre-menopausal women showing smaller age-related volume decline compared to men. We could recently extent these findings by showing how estrogen therapy after menopause leads to higher volumes in the HC. Investigating possible neurotoxicity effects of steroids, we showed effects of long-term steroid exposure on HC volumes, and investigated variability of HC volumes in relation to HPA axis regulation in young and elderly populations. Here, we were able to follow-up from non-imaging studies showing that subjects low in self-esteem have higher cortisol stress responses, and the HC emerged as the critical link between these variables. Recently, we have made two more important discoveries with regard to HC volume: we could show that HC volume is as variable in young as it is in older adults, in subjects ranging in age from 18 to 80 years. Also, we have linked birth weight and maternal care to HC volumes in young adults, demonstrating the effects of variations in maternal care on the integrity of the CNS. Besides structural assessments, there is increasing interest in functional techniques to investigate possible links between CNS activity and HPA axis regulation. These two approaches complement each other; some aspects of HPA axis regulation might be linked to the integrity of a specific CNS structure, while other aspects might be linked to the function of a specific structure with no involvement of CNS morphology. Thus, we have developed a mental arithmetic stress task that can be employed in functional neuroimaging studies, and have used it in a number of functional neuroimaging studies. Employing positron emission tomography (PET), we were able to demonstrate that stress causes dopamine release if subjects reported low maternal care early in life. Finally, employing the task in functional magnetic resonance imaging (fMRI), we could show how exposure to stress and activation of the HPA axis are associated with decreased activity in major portions of the limbic system, a result that allows to speculate on the effects of stress on cognitive and emotional regulation in the brain. Taken together, the use of neuroimaging techniques in Psychoneuroendocrinology opens exciting new possibilities for the investigation of stress effects in the central nervous system.

Neuroimage. 2009 Apr 8.

Neural correlates of affective picture processing - a depth ERP study


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Using functional neuroimaging techniques (PET and fMRI), various cortical, limbic, and paralimbic structures have been identified in the last decade as neural substrates of human emotion. In this study we used a novel approach (intracerebral recordings of event-related potentials) to add to our knowledge of specific brain regions involved in affective picture processing. Ten intractable epileptic patients undergoing pre-surgical depth electrode recording viewed pleasant, neutral, and unpleasant pictures and intracerebral event-related potentials (ERPs) were recorded. A total of 752 cortical and subcortical sites were investigated. Significant differences in ERPs to unpleasant as compared to neutral or pleasant pictures were frequently and consistently observed in recordings from various brain areas - the mesial temporal cortex (the amygdala, the hippocampus, the temporal pole), the lateral temporal cortex, the mesial prefrontal cortex (ACC and the medial frontal gyrus), and the lateral prefrontal cortex. Interestingly, the mean latencies of responses to emotional stimuli were somewhat shorter in the frontal lobe structures (with evidently earlier activation within lateral prefrontal areas when compared to mesial prefrontal cortex) and longer in the temporal lobe regions. These differences, however, were not significant. Additional clearly positive findings were observed in some rarely investigated regions - in the posterior parietal cortex, the precuneus, and the insula. An approximately equivalent number of positive findings was revealed in the left and right hemisphere structures. These results are in agreement with a multisystem model of human emotion, distributed far beyond the typical limbic system and substantially comprising lateral aspects of both frontal lobes as well.
Molecular Imaging of Prostate Cancer.

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Prostate carcinoma is the most common non-cutaneous malignancy in males. Imaging of prostatic lesions is of great importance and aids in oncologic management and monitoring of therapy response. Particularly molecular imaging based on positron emission tomography (PET) and single photon emission computerized tomography (SPECT) has great potential. Using radio-labelled molecular probes, these approaches are highly sensitive and can provide key molecular and functional information on tumours. The identification of suitable targets based on unique genetic and biochemical features of cancer lesions, is one of the core activities driving progress in molecular imaging of pathological processes. Nowadays, mainly metabolic probes are being used routinely for detection and staging of prostate cancer. The development of new specific receptor ligands and targeted probes and antibodies holds great promise to further enhance the performance of molecular imaging and to further improve the diagnosis and monitoring of prostate cancer.

Molecular imaging in neuroendocrine tumors: Molecular uptake mechanisms and clinical results.

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Neuroendocrine tumors can originate almost everywhere in the body and consist of a great variety of subtypes. This paper focuses on molecular imaging methods using nuclear medicine techniques in neuroendocrine tumors, coupling molecular uptake mechanisms of radiotracers with clinical results. A non-systematic review is presented on receptor based and metabolic imaging methods. Receptor-based imaging covers the molecular backgrounds of somatostatin, vaso-intestinal peptide (VIP), bombesin and cholecystokinin (CCK) receptors and their link with nuclear imaging. Imaging methods based on specific metabolic properties include meta-iiodobenzylguanide (MIBG) and dimercapto-sulphuric acid (DMSA-V) scintigraphy as well as more modern positron emission tomography (PET)-based methods using radio-labeled analogues of amino acids, glucose, dihydroxyphenylalanine (DOPA), dopamine and tryptophan. Diagnostic sensitivities are presented for each imaging method and for each neuroendocrine tumor subtype. Finally, a Forest plot analysis of diagnostic performance is presented for each tumor type in order to provide a comprehensive overview for clinical use.

A case of small bowel adenocarcinoma in a patient with Crohn's disease detected by PET/CT and double-balloon enteroscopy.


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Small bowel adenocarcinoma (SBA) in patients with Crohn's disease (CD) is quite rare, difficult to diagnose without surgery, and has a poor prognosis. Here, we report a 48-year-old man with SBA and a 21-year history of CD who was diagnosed by a combination of positron emission tomography/computed tomography (PET/CT) and double-balloon enteroscopy (DBE). Since the age of 27 years, the patient had been treated for ileal CD and was referred to our hospital with persistent melena. Multiple hepatic tumors were found by CT. PET/CT detected an accumulation spot in the small bowel. DBE revealed an ulcerative tumor in the ileum about 100 cm from the ileocecal valve. An endoscopic forceps biopsy specimen showed poorly differentiated adenocarcinoma. There were some longitudinal ulcer scars near the tumor, and the chronic inflammation in the small bowel appeared to be associated with the cancer development. Previous reports suggest the risk of SBA in patients with CD is higher than in the overall population. Since early diagnosis is extremely difficult in these cases, novel techniques, such as PET/CT and DBE, may be expected to help in making a preoperative diagnosis of the development of SBA in CD.
Dopaminergic activity in depressed smokers: A positron emission tomography study.

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Tobacco dependence is highly prevalent in depressed patients. We assessed changes in [(11)C]-raclopride binding potential (BP) using positron emission tomography (PET) before and after the oral administration of d-amphetamine in healthy controls and unmedicated patients with current depression with and without current tobacco dependence. Over a single study day 2 [(11)C]-raclopride positron emission tomography scans were taken in 38 subjects: at baseline and 2 h following oral d-amphetamine 30 mg. Twenty controls (9 smokers, 11 non-smokers) and 18 subjects with current major depressive episode (8 smokers, 10 non-smokers). Striatal [(11)C]-raclopride binding potential was measured before and after d-amphetamine administration. Depressed smokers had a lower baseline [(11)C]-raclopride binding potential compared with both control non-smokers (P < 0.007) and depressed non-smokers (P < 0.001). There was a main effect of smoking status on amphetamine-induced change in [(11)C]-raclopride binding potential (P < 0.02), but no main effect of depression. This may be due to a floor effect because of the low BP at baseline. Depressed subjects reported significant increase of positive mood after d-amphetamine administration compared with controls (depressed smokers vs. control smokers: P < 0.05; depressed non-smokers vs. controls: P < 0.055). Tobacco dependence appears to decrease d-amphetamine-induced changes in [(11)C]-raclopride binding potential as measured by positron emission tomography. Comorbid major depression and tobacco dependence exacerbates this effect, suggesting an altered dopamine system in comorbid patients.


Influence of residual oxygen-15-labeled carbon monoxide radioactivity on cerebral blood flow and oxygen extraction fraction in a dual-tracer autoradiographic method.

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OBJECTIVE: Cerebral blood flow (CBF), cerebral metabolic rate of oxygen (CMRO(2)), oxygen extraction fraction (OEF), and cerebral blood volume (CBV) are quantitatively measured with PET with (15)O gases. Kudomi et al. developed a dual tracer autoradiographic (DARG) protocol that enables the duration of a PET study to be shortened by sequentially administrating (15)O(2) and C(15)O(2) gases. In this protocol, before the sequential PET scan with (15)O(2) and C(15)O(2) gases, a PET scan with C(15)O should be preceded to obtain CBV image. C(15)O has a high affinity for red blood cells and a very slow washout rate, and residual radioactivity from C(15)O might exist during a (15)O(2)-C(15)O(2) PET scan. As the current DARG method assumes no residual C(15)O radioactivity before scanning, we performed computer simulations to evaluate the influence of the residual C(15)O radioactivity on the accuracy of measured CBF and OEF values with DARG method and also proposed a subtraction technique to minimize the error due to the residual C(15)O radioactivity. METHODS: In the simulation, normal and ischemic conditions were considered. The (15)O(2) and C(15)O(2) PET count curves with the residual C(15)O PET counts were generated by the arterial input function with the residual C(15)O radioactivity. The amounts of residual C(15)O radioactivity were varied by changing the interval between the C(15)O PET scan and the absolute inhaled radioactivity of the C(15)O gas. Using the simulated input functions and the PET counts, the CBF and OEF were computed by the DARG method. Furthermore, we evaluated a subtraction method that subtracts the influence of the C(15)O gas in the input function and PET counts. RESULTS: Our simulations revealed that the CBF and OEF values were underestimated by the residual C(15)O radioactivity. The magnitude of this underestimation depended on the amount of C(15)O radioactivity and the physiological conditions. This underestimation was corrected by the subtraction method. CONCLUSIONS: This study showed the influence of C(15)O radioactivity in DARG protocol, and the magnitude of the influence was affected by several factors, such as the radioactivity of C(15)O, and the physiological condition.


Cardiac hybrid imaging: state-of-the-art.

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The field of noninvasive cardiac imaging has experienced enormous advances including computerized tomography coronary angiography (CTCA). Invasive angiography remains the anatomic standard of reference but it is associated with a non-negligible peri-procedural morbidity and mortality which suggests confining its use to patients who will benefit from a revascularization procedure. Many factors that are beyond the simple quantification of diameter narrowing and therefore cannot be fully assessed with lumino logic will eventually determine whether or not a given lesion produces stress-induced ischemia. Myocardial perfusion scintigraphy by single photon emission computerized tomography (SPECT) is one of the most widely used and well established methods.
noninvasive tools for the diagnosis of ischemic heart disease. Although positron emission tomography (PET) offers a higher accuracy than SPECT its use is often limited to large centers. This article explains the great potential of cardiac hybrid imaging which allows a comprehensive evaluation of coronary artery disease as it combines both morphological and functional information by fusing either SPECT or PET with CTCA. SPECT/CT and PET/CT hybrid imaging can provide entirely noninvasively unique information which helps improving diagnostic assessment and risk stratification and also impacts decision making with regard to revascularization in patients with coronary artery disease.


P-glycoprotein expression affects 18F-fluorodeoxyglucose accumulation in hepatocellular carcinoma in vivo and in vitro.


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18F-fluorodeoxyglucose (FDG) uptake in hepatocellular carcinoma (HCC) is associated with tumor differentiation and expression of P-glycoprotein (P-gp), a drug efflux pump that plays an important role in chemoresistance. The aim of the study was to clarify the factors that affects FDG uptake in HCC in vivo and in vitro. The standardized uptake value (SUV) and the tumor to non-tumor SUV ratio (TNR) for FDG uptake in HCC in vivo was determined by FDG-PET in 28 patients. Expression levels of glucose transporter-1 (GLUT-1), GLUT-2 and type II hexokinase (HK-II) were examined immunohistochemically in resected specimens. The glucose-6-phosphatase (G-6-Pase) activity was determined in tissue homogenates. In vitro, PLC/PRF/5 cells and doxorubicin-resistant PLC/DOR cells were used to examine the effect of P-gp on FDG uptake. The effects of two P-gp inhibitors, verapamil and cepharanthine, on accumulation of FDG were also examined in vivo; GLUT-1 expression was low in HCCs, but was significantly higher in poorly differentiated HCCs than in moderately differentiated HCCs (P=0.043) and was positively correlated with SUV (r=0.75, P<0.0001) and TNR (r=0.7, P<0.0001). GLUT-2 and HK-II expression and G-6-Pase activity were not correlated with tumor differentiation, SUV or TNR. P-gp was over-expressed in PLC/DOR cells, and accumulation of FDG was significantly higher in PLC/PRF/5 cells than in PLC/DOR cells (P=0.04). Verapamil and cepharanthine restored FDG uptake in PLC/DOR cells, but not in PLC/PRF/5 cells. Collectively, our results show that FDG uptake in HCC is weakly correlated with GLUT-1 expression, and that FDG could be a substrate of P-gp, which may act as an efflux pump to reduce FDG accumulation.


Survival in Malignant Peripheral Nerve Sheath Tumours: A Comparison between Sporadic and Neurofibromatosis Type 1-Associated Tumours.

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We studied 123 patients with malignant peripheral nerve sheath tumours (MPNSTs) between 1979 and 2002. However, 90 occurred sporadically whereas 33 were associated with neurofibromatosis type 1 (NF1). Survival was calculated using Kaplan-Meier survival curves and we used Cox's proportional hazards model to identify independent prognostic factors. A 5-year survival for 110 nonmetastatic patients was 54% (33% NF1 and 63% sporadic P = .015). Tumour stage and site were significant prognostic indicators after univariate analysis. When multivariate analysis, however, only NF1 (P = .007) and tumour volume more than 200 m(P = .015) remained independent predictors of poor outcome. We recommend that NF1 be taken into account during MPNST staging. As the survival rate in the NF group was dependent on tumour volume, routine screening of these patients with FDG PET and/or MRI may be warranted, thereby staging and controlling them at the earliest possible opportunity.


The maximum standardized uptake values on positron emission tomography to predict the Noguchi classification


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This study investigated whether the standardized uptake value (SUV) of the tumor correlated with the Noguchi classification and tumor invasiveness in patients with clinical stage IA adenocarcinoma </=2 cm in size. Fifty-four patients that underwent a curative surgical resection for clinical stage IA adenocarcinoma </=2 cm from April 2005 through December 2008 had integrated positron emission tomography (PET) - computed tomography (CT) with (18)F-fluorodeoxyglucose (FDG) as part of the preoperative workup. The relationships between the maximum SUV (SUVmax) and Noguchi classification, pathological results of intratumoral lymphatic or vascular invasion of tumor cells, and pleural invasion were examined. In comparison to tumors with an SUVmax>1.0, tumors with an SUVmax</=1.0 were more frequently classified as Noguchi type A or B (p<0.0001). Tumors with an SUVmax>1.0 had more intratumoral lymphatic or vascular invasion of tumor cells and pleural invasion (P=0.0005 and P=0.0002). These results suggest that an SUVmax is an important predictor for the Noguchi classification and tumor invasiveness in patients with clinical stage IA adenocarcinoma </=2 cm in size.
Integrated PET/CT and cancer imaging.

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Integrated Positron Emission Tomography/Computed Tomography (PET/CT) is an imaging technique that was introduced in clinical practice in 1998. PET/CT is the combination of two different examination techniques in one machine: Computed Tomography (CT) giving anatomic information and Positron Emission Tomography (PET) giving metabolic information. PET/CT has two major advantages: CT can be used for attenuation correction and PET/CT improves diagnostic accuracy when compared to CT and PET alone. The quality of PET/CT images depends on different parameters such as CT dose, patient respiration, and the use of intravenous (i.v.) and per oral (PO) contrast. A rapidly expanding amount of literature demonstrates the additional value of PET/CT in the diagnosis, staging, prognosis, treatment planning, assessment of treatment response and diagnosis of recurrence of many tumor types. CT increases the sensitivity of the PET/CT examination, but the most beneficial effect of having the CT data is the increase of the specificity of the PET data. PET data also helps to specify CT information. The utility of PET/CT for tumor staging, which is one of the major imaging study indication, seems to be very high, and therefore PET/CT may become the scanner of the future. Till this moment there are no many published studies about the cost-effectiveness of PET/CT. The integration of PET/CT in clinical practice will result in higher equipment running costs, but these costs are likely not to be prohibitive to the diffusion of this combined technology.
PET-Miscellaneous

Laryngoscope. 2009 Apr 8.

Positron emission tomography-computed tomography surveillance for the node-positive neck after chemoradiotherapy.


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OBJECTIVES/HYPOTHESIS: To review our results with positron emission tomography and computed tomography fusion imaging (PET-CT) surveillance of the postchemoradiotherapy neck in patients with advanced head and neck squamous cell carcinoma.

STUDY DESIGN: Retrospective.

METHODS: Four hundred twenty-eight patients with advanced head and neck squamous cell carcinoma were treated with nonsurgical therapy from September 2002 to March 2007 and followed with post-treatment PET-CT surveillance of the neck. Fifty-two patients meeting inclusion criteria were analyzed. Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and accuracy of PET-CT were determined. RESULTS: Ten patients had a positive post-treatment PET-CT for residual neck disease, and 42 patients had negative scans. The NPV and PPV were 100% and 40%, respectively. The sensitivity, specificity, and accuracy were 100%, 87.5%, and 88%, respectively. CONCLUSIONS: Planned neck dissection can be deferred with a negative post-treatment PET-CT. Assuming a complete response at the primary site and a negative PET-CT scan, there may be a role for serial PET-CT surveillance in patients with residual palpable cervical lymphadenopathy.


[Noninvasive diagnostic of coronary artery disease.]

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Noninvasive imaging of coronary artery disease has extensively evolved during the last decade. Today, at least four imaging techniques with excellent image quality such as echocardiography, myocardial perfusion scintigraphy and PET, cardiac magnetic resonance and cardiac CT are widely available in order to estimate the risk for future ischemic events, to corroborate the suspected diagnosis of coronary artery disease, to demonstrate the extent and localisation of myocardial ischemia, to diagnose myocardial infarction and measure its size, to identify the myocardium at risk during acute ischemia, to differentiate between viable and non-viable myocardium and thereby the basis for indications of revascularisation, to follow revascularized patients over long time, to assess the risk for sudden cardiac death and the development of heart failure after myocardial infarction and to depict atheromatosis and atherosclerosis of the coronary artery tree. Echocardiography is the most widely used imaging method in cardiology. It provides excellent information on morphology and function of nearly all cardiac structures. Stress echocardiography has been proven to be a reliable tool for the demonstration of myocardial ischemia and for the acquisition of prognostic data. Newer ultrasound techniques may further improve investigator dependence and thereby reproducibility. The completeness of echocardiography will always depend on acoustic windows, which are given in a specific patient. Myocardial perfusion scintigraphy provides the largest database especially on prognosis in coronary artery disease. It has been the “work horse” for the depictions of ischemic and infarcted myocardium. Radiation exposure will always be an issue. Newer hybrid techniques combining nuclear methods with cardiac CT may add arguments, which will be needed for clinical decision-making. Cardiac magnetic resonance has evolved as an important tool in the diagnosis of cardiovascular diseases. It is investigator independent, does not apply any biologically hazardous energy and has the largest potential for tissue characterization due to its high contrast resolution. It therefore is an excellent technique to investigate all the aspects of coronary artery disease. Its availability is increasing, however in order to fully utilize its large potential an optimal collaboration among specialists (cardiologists, radiologists, physicists) is mandatory. Cardiac CT has evolved as an excellent method for the depiction of the coronary arteries. Due to its high spatial and time resolution it provides high quality luminography of the coronaries and newer technique are also investigating plaque composition of diseased coronary arteries. Overestimation of coronary artery stenosis in calcified vessels is an inherent problem of the technique and the risk of radiation exposure has to be weighted against the benefit of non-invasively depicting the coronary arteries. It will be the future task of all specialists in this field to define the most efficient and cost-effective way to apply these excellent techniques for the investigation of all the different aspects of patients with coronary artery disease.