10.1

Single photon emission computed tomography (SPECT) perfusion imaging for detection of subendocardial extent of myocardial infarction compared with contrast-enhanced magnetic resonance.

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Background: Contrast-enhanced magnetic resonance has significantly improved image quality and delayed hyperenhancement identify subendocardial infarction accurately when >50% transmural extent of the left ventricular wall is compromised.
We compared the delayed hyperenhancement cardiac resonance (DE-CR) with the visual quantification of the SPECT perfusion myocardial imaging (PMI) for the assessment of subendocardial myocardial infarction (MI).
Methods and Results: 22 patients (55±9 y/o), 18 males, with first MI and significant obstruction only in the infarct responsibly artery (IRA) were studied with DE-CR with Gd-DTPA and 99mTc-sestamibi SPECT PMI at rest (40±5 days post-MI). Both images modalities were analyzed in a 17 segment model, considering for DE-CR subendocardial infarction when >50% transmural extent of the left ventricular wall was compromised and a score=1 for 99mTc-sestamibi SPECT PMI at rest, in a 5-points, semi-quantitative nominal scoring system representing perfusion in each segment (0=normal, 1=mildly, 2=moderate, 3=severe reduction in counts and 4=absent uptake). The localization of the MI related with the IRA, 13: inferior (59%) and 9: anterior (41%). 99mTc-sestamibi SPECT PMI at rest found 121 hypoperfused segments and 18(15%) met the score=1. DE-CR found 112 delayed hyperenhancement segments and 19 (17%) had >50% transmural extent of the left ventricular wall. The sensitivity and specificity of 99mTc-sestamibi SPECT PMI to detect subendocardial infarction was 97% and 64% respectively.
Interpretation: SPECT PMI at rest using a semi-quantitative nominal scoring system may be useful to recognize segments with subendocardial infarction.

10.2

Diagnostic value of transthoracic ultrasound for assessment of distal graft anastamosis patency.

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The finding of simple tool for visualisation of bypass graft and coronary artery blood flow is in patients after coronary surgery. However there have been problems of assessment of internal thoracic artery (ITA) graft with systolic/diastolic ratio (s/dR) > 1 and of examination of vein graft to coronary artery another than the left anterior descending artery (LAD).
The aim of this study was evaluation of LAD blood flow if ITA graft s/dR was >1 and possibility of visualization of vein graft to major diagonal branch (DB) of the left main artery with combination of vascular and cardiac echo.
Methods. We compared ultrasound and angiographic images of 14 ITA grafts and 20 saphenous vein grafts to DB. Ultrasound examination of blood flow in bypass grafts and recipient coronary arteries was performed with combined two-dimensional and Doppler echocardiography (Sonos 5500, probe 2-4MHz).
Results. The ITA graft patterns before distal anasthamosis and in site of distal anasthamosis were biphasic with higher systolic velocity and were characterized with high systolic/diastolic ratio 1.4±0.2. The flow characteristics within the LAD distal to anasthamosis were diastolic with either normal (45.3± 6.5cm/s) or diminished (22.2±5.2cm/s) peak velocity. By comparing ultrasound images with angiographic data we concluded that ITA graft flow with s/dR >1 and diminished velocity in the distal to anasthamosis portion of LAD was relative to poor coronary bed run-off.
On the other hand the blood flow of the saphenous vein grafts to DB was detected in 8 patients, whereas the blood flow of the recipients DB was obtained in 18 persons. If saphenous vein grafts to DB was patent we registrated diastolic blood flow in the DB with diastolic peak velocity 60.5±10.1 cm/s.
Conclusion. Assessment of distal anasthamosis and coronary artery distal to anasthamosis may clarify the ITA graft function with systolic/diastolic ratio > 1. Modern ultrasound technology let to evaluate vein graft to major diagonal branch of the left main artery.

10.3

**Improving the image quality o
dimensions of the pinhole openi**

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Background: Pinhole collimation is typically used to improve spatial resolution required for small animal SPECT imaging. During the reconstruction process it is usually assumed that the pinhole opening is infinitesimally small. This assumption is acceptable for very small pinhole openings but may introduce artifacts when using larger pinhole openings (3mm) required to increase the sensitivity necessary for cardiac gated SPECT.
Purpose: To investigate the potential of resolution recovery (RR) in pinhole gated myocardial perfusion SPECT by modeling the finite dimensions of the pinhole opening during reconstruction.
Methods. A dynamic mathematical cardiac-torso phantom was designed to simulate circular orbit pinhole gated myocardial perfusion SPECT projections of a rat heart. The phantom included the finite dimension of the pinhole aperture (3 mm), camera blurring and Poisson noise. The projection data were reconstructed using OSEM (5 iterations; 16 subsets) incorporating the pinhole geometry and taking into account the finite dimension of the pinhole opening, for which we have implemented a forward projector, where each projection pixel is calculated as a weighted average of seven rays. The seven rays intersect the circular opening of the pinhole in a hexagonal pattern with one of the points at the center. The systematic error (SysErr) and statistical error (StatErr) were calculated on the reconstructed data. The StatErr was determined using five noise generations with a global count density of 6.75 million counts.
Results: Results are summarized in Table 1. The SysErr decreased and the StatErr increased when RR was applied during reconstruction. The StatErr could be decreased by reducing noise amplification during the reconstruction process using a median root prior (MRP) and/or using a temporal Fourier filtering (TFF) during reconstruction.
Conclusion: Modeling the pinhole opening during reconstruction decreases the SysErr but increases the StatErr. Consequently, additional spatial and/or temporal filtering is required to improve image quality.

Table 1

	No RR-No MRP-No TFF	RR-No MRP-No TFF	RR + MRP-No TFF	RR + TFF-No MRP	RR + MRP + TFF
SysErr (%)	23.6	10.6	13.8	10.6	13.9
StatErr (%)	25.3	65.1	6.7	33.9	4.1

Systematic and statistical errors

10.4

Left ventricular remodeling after coronary artery ligature demonstrated by serial pinhole gated SPECT in rats.

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Background. We have previously shown that accurate and reproducible measurements of myocardial perfusion and function can be obtained in rats using pinhole gated SPECT.
Aim. To develop a rat model of left ventricular remodeling following the ligature of the left anterior descending coronary artery (LAD).
Methods. Male Wistar rats (n= 18, body weight 360-540g) were studied 7 days, 1 month and 2 months after the ligature of the mid portion of the LAD. Imaging was performed under pentobarbital anesthesia (60 mg/kg intraperitoneal) 1 hour after intravenous administration of Tc99m sestamibi (500 MBq). ECG gated SPECT (64 projections, 20 sec per step, 360-degree rotation and 16 time bins) was acquired on a single head gamma camera equipped with a pinhole collimator (3mm opening, focal length 171 mm, radius of rotation 44mm). Data were reconstructed using PH-OSEM 4D, an iterative reconstruction algorithm adapted for pinhole geometry and incorporating a temporal filter based on Fourier series (Univ. of Brussels). Myocardial perfusion polar maps were generated from the reconstructed short axis slices and used to quantify the extent of perfusion defects defined as the area below 2 SD of a normal database obtained in 12 age matched rats. Left ventricular (LV) volumes and ejection fraction (EF) were calculated using the 4DMSPECT program (Univ. of Michigan).
Results. Perfusion defects were detected in all animals at 7 days after the ligature. Defect size ranged from 3% to 55% of the LV surface. Abnormal LVEF and volumes were only observed in animals with perfusion defects > 35% of LV surface. Two animals with the largest defects died during follow-up. Perfusion defect sizes decreased slightly between 7 days and 1 month but were unchanged thereafter. Volumes increased and EF decreased progressively at 1 month and 2 months after the ligature in rats with perfusion defects > 35% of LV area. No significant changes in LV function were observed in animals with perfusion defects >35%.
Conclusion. The ligature of the LAD results in variable perfusion defects size in rats. Changes in LV volumes and EF indicating progressive remodeling were observed only when perfusion defects exceed 35% of the LV surface. Pinhole gated SPECT can be useful to select animals with similar infarct size and to monitor both myocardial perfusion and LV function over time in the same animal.

10.5

Ischemia in women with angina and normal coronary angiograms.

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Women without angiographic coronary heart disease but with persistent angina constitute a challenge for diagnosis and treatment. Noninvasive tests that suggest myocardial ischemia have limited utility due to anatomical differences and technical artifacts specific to women.
Aim: To assess the presence of coronary microvascular disease in postmenopausal women. Methods: Twenty-five patients (mean age: 55±6 years) with typical angina and normal coronary angiograms were included. All underwent technetium-99m methoxy-isobutyl-isonitrile myocardial scintigraphy (protocol stress-rest); endothelial function measured by ultrasonography at brachial artery; 24 hours ambulatory electrocardiographic recording (Holter) and lipidogram.
Results: The mean body mass index was 28±4 (overweight) and the mean waist/hip index was 0.83±0.05. Regarding coronary risk factors, there was only one smoker (4%), but 12% were ex-smokers, 28% had diabetes, 40% dyslipidemia and 76% hypertension. Sixty percent of patients experienced stress and rest angina, 20% predominantly at stress and the other 20% at rest. Anemia was constated in only one patient. In eight cases, perfusion defects were detected in the scintigraphy, all in anteroapical and septal territories, which in half of cases coincided with the presence of endothelial dysfunction, but not with ischemia during the Holter recording. Endothelial dysfunction was founded in 40% of patients and ambulatory ischemia by Holter in 12%. Thirty-six percent had supraventricular arrythmias and 8% intermitent left bundle branch block.
Conclusion: In women with typical angina and normal coronary angiograms, the presence of ischemia due to coronary microvascular disease, with alterations of myocardial perfusion and endothelial dysfunction, should be taken into account as cause of their symptoms.

10.6

Cell proliferation and differentiation of 111In-labelled CD34- human endothelial progenitor cells.

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Aim: Endothelial progenitor cells (EPCs) from bone marrow is a promising therapy for neovascularization in patients with severe ischaemic heart disease, but data concerning the fate of the transplanted cells remain poor. Non-invasive monitoring of In-111 labelled EPCs would be a valuable tool for evaluation of the success of monitoring homing and myocardial retention of the cells within the first few days after intramyocardial transplantation.
Methods: EPCs in culture (CD45-/CD34- adherent cells) were labeled directly in the culture flask with 10 MBq In-111 tropolone for 15 min in 5 ml medium (3x105 cells/flask). The cells were then washed with PBS and new medium added to the flask. 10-20% labeling efficiency was measured. Membrane markers (FACS) and gene expression (Taqman real-time PCR) were studied following 10 days of growth in cell culture. For measuring proliferation the cells were labeled with the membrane marker PKH26-GL and grown in 24 well trays. The cells were labeled with In-111 tropolone 24 hours after the PKH labeling. PKH was measured by FACS every 24 hours on cells from 4 wells and a doubling time was calculated. Cell survival was also measured in cells grown in 24 well trays. Every 24 hours after indium labeling live cells from 3 wells were counted in a microscope using trypan-blue as an indicator of vitality.
Results: No change in common progenitor and endothelial markers (the phenotype) by FACS (CD10, CD13, CD31, CD34, CD45, CD73, CD90, CD105, CD106, CD166, VEGFR-2) was observed. However, cell survival was reduced by 30% after 3 days, compared to control cells. This difference increased during the next days: After 7 days 85% more control cells had survived compared to labeled cells. Preliminary results also indicate that the labeled cells do not proliferate as fast as unlabeled cells. The doubling time for unlabeled cells is app. 2-3days compared to 5-6 days for labeled cells.
Conclusions: Cell viability was reduced after In-111 labeling with the present technique. This harmful effect may be less with lower activity amount used for In-labeling. The unchanged phenotype indicates that In-labeling does not affect cell function. The differentiation potential of these cells will be measured after VEGF stimulation and with angiogenesis assays, which may give more information about their ability to differentiate into endothelial cells after labeling.

10.7

Myocardial perfusion SPECT in hypertensive patients with microvascular angina; predictors of false positive perfusion defect and the role of coronary flow reserve.

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Background: We sought to evaluate patients (pts) with hypertension (HT) presenting with angina (AG) and a positive stress/rest Tl-201 myocardial perfusion SPECT (MPS) in the setting of normal coronary angiogram (NCA). These patients presenting with false positive defects are a source of clinical dilemma.
Patients: our study encompassed 43 pts (age 51±8.8, 64% females) with mild to moderate HT, AG and NCA who underwent stress/rest MPS within 1 month of NCA, and a control group of 20 subjects.
Methods: Images were scored on a 5 point 20-segment scale (0=normal, 4=no uptake), MPS was considered positive when SSS was >3. Echo-Doppler study was done within 1 week of MPS for LV mass index (LVMI), diastolic function: E/A and isovolumic relaxation time (IVR). In a sub group of 11 pts and 10 controls Dipyridamole (D) trans-esophageal echo (TEE) was done within a week of MPS to evaluate coronary flow reserve (CFR) at rest (R) and after D injection (0.56mg/kg). Peak systolic and diastolic velocities and systolic, diastolic and total velocity integrals were estimated at rest (R) and after (D) injection; these were expressed as ratios of D/R (CFR).
Results: MPS was positive in 25 (58%). Discriminate function coefficient analysis showed the predictors of abnormal MPS were as follows in descending order; E/A, duration of HT, DBP, duration of AG, LVMI, IVR, SBP. SSS correlated with LVMI R=0.79, P<0.001. In the subgroup that underwent D-TEE, 7 pts had limited CFR >1.85 vs 2.8 in the controls, p=.0.001. However, none had regional wall motion abnormalities.
Conclusion: False positive perfusion defects may frequently be encountered in HT pats with AG. Diastolic dysfunction and decreased CFR are usually present in these pats and may explain the underlying pathophysiology of these defects.

10.8

Assessment of 99mTcN-NOET and thallium-201 myocardial uptake in experimental models of chronic non-reperfused and reperfused myocardial infarction.

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Background: TcN-NOET (NOET) is a pure myocardial blood flow tracer. As flow and viability are correlated in chronic non-reperfused and reperfused myocardial infarction, we hypothesized that the uptake of NOET would also reflect myocardial viability and would be similar to the uptake of the flow/viability tracer thallium-201 (Tl201) in this setting. Methods and Results: Rats were subjected to permanent coronary occlusion (OCC, n=8) or to a 45 min occlusion and reperfusion (REP, n=11). Seven days later, the tracers were co-injected and the animals were euthanized 15 min afterwards. Infarct size determination and NOET and Tl201 ex vivo imaging were performed. Regional flow and tissue oedema were quantified using radioactive microspheres and Tc-DTPA, respectively. In both groups, mean NOET and Tl201 defect extents were not significantly different from infarct size. NOET and Tl201 defect magnitudes were similar in OCC animals (0.11±0.01 vs. 0.13±0.01). In REP animals, Tl201 defect magnitude (0.25±0.02) was significantly lower than the magnitude of NOET and flow defects (0.14±0.03 and 0.17±0.01, respectively, P<0.05) (see Figure for representative examples). Tc-DTPA indicated the presence of oedema in the reperfused area. Blood distribution studies showed that, unlike NOET, Tl201 plasma activity was mostly unbound to plasma proteins. Conclusions: NOET delineated the viable area in chronic non-reperfused and reperfused myocardial infarction. The significantly decreased Tl201 defect in reperfused infarction was likely due to partial diffusion of the tracer from the plasma into the oedema present in the infarcted area. NOET might represent a valuable diagnostic tool for the clinical assessment of microvascular obstruction following reperfusion of acute myocardial infarction.

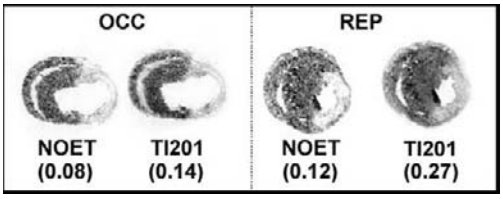

Figure (defect magnitude in parenthesis)

10.9

Arrhythmogenic right ventricular cardiomyopathy in patients with right ventricular outflow tract premature contractions.

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Background. Vertical axis premature ventricular contractions (PVCs) originating from the right ventriclar outflow tract (RVOT), in the absence of overt heart disease, are generally considered as benign. Nevertheless, they may also represent the first manifestation of arrhythmogenic right ventricular cardiomyopathy (ARVC) which is a cause of sudden death. The high diagnostic and prognostic value of equilibrium radionuclide angiocardiography (ERNA) with multiharmonic Fourier analysis has been previously validated in patients with right ventricular tachycardia. The aim of this study was to investigate the prevalence of ARVC in patients referred for frequent and complex RVOT-PVCs, without ventricular tachycardia and without known heart disease, using ERNA with Fourier analysis.
Methods. The study population included 276 consecutive patients (age: 38±15 years, males: 52%) referred as part of an investigation on frequent (more than 1000/24 hours) vertical axis PVCs (electrical axis between +60° and + 120°) without suspected or known heart disease and without documented ventricular tachycardia. Prior to ERNA, the diagnosis criteria of the Task Force on ARVC were quoted (1 minor criteria: 110 patients (40%), 2 minor: 129 (47%), 3 minor: 31 (11%), 4 minor and more: 6 (2%)). ERNA was used to detect global and/or regional dysfunction of both ventricles.
Results. The criteria of ARVC were fulfilled in 46 patients (17%), among whom the RV involvement was segmental in 44 (1 segment: 22 patients, 2 segments: 17, 3 segments: 5), and diffuse in 2. In 3 additional patients, the diagnosis of ARVC was not achieved despite demonstrable segmental dyskinesia of the RV (1 segment in 2 and 2 segments in 1). Left ventricular segmental dyskinesia occured in association with typical RV involvement in 5 patients (18%).
Conclusions. In a specific population with frequent and complex RVOT-VPCs, the diagnosis of ARVC was achieved in 17% of patients (according to Task Force criteria), including diffuse abnormalities in some of them. Consequently, ERNA with multiharmonic analysis is useful to screen noninvasively patients with RVOT-PVCs in order to identify which may require a specific management.

10.10

Biodistribution and myocardial uptake after ischemia-reperfusion of 99mTc-AnxD1, a new marker of cell apoptosis: a preliminary study.

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Objectives: 99mTc-annexinV binds selectively to phosphatidylserins (PS), and is used for non invasive measurement of cell apoptosis, especially myocardial apoptosis induced by ischemia -reperfusion (IR). 99mTc-AnxD1 is a 4 to 5 fold smaller peptide derived from the annexinV's domain 1, with high affinity and specificity for PS. We evaluated the tissue biodistribution of this new tracer in rats, and its myocardial uptake after experimental IR.
Methods: Sixteen normal male Wistar rats were injected with AnxD1 (patented by the CEA, 7.4 MBq /100g). The labelling efficiency was always superior to 97%. Blood kinetic studies (n=10), and biodistribution studies in organs (n=6) 4h post injection were performed: after killing, aliquots of tissues were taken, weighed and placed in tubes for scintillation well counting. Myocardial IR lesions were induced in 6 anaesthetized Wistar rats by tying during 20 min then opening the left coronary artery. Two hours after reperfusion, AnxD1 was injected, then planar thoracic images were obtained using a pinhole collimator on a gamma-camera (SOPHA medical), 2h post injection. After killing, quantitative autoradiography of myocardial slices (Instant Imager, Packard) was performed. The activity ratios between the lesion area and the remote myocardium (AR) were calculated on the autoradiograms.
Results: The blood kinetic of AnxD1 fitted a two component curve with a fast decreasing phase then a plateau reached at 80 min. The t1/2 was calculated at 5.8 min, the residual blood activity at 80 min was 5.7%. Biodistribution studies showed high AnxD1 uptake in the kidneys (23.6±5.5%ID) and the liver (21.5±5.5%ID), 0.87±0.06%ID in the spleen, 0.25±0.07%ID in the lungs, and only 0.03±0.02%ID in the heart myocardium. The scintiscans showed faint AnxD1 myocardial uptake in 1 case, were doubtful in 1 case and negative 4 cases. On autoradiograms, significant AnxD1 uptake was observed in all myocardial lesions, with mean AR at 3.85±0.83.
Conclusions: In rats, AnxD1 is rapidly cleared from blood, and non specific AnxD1 uptakes in the heart and the lungs are low. However it has poor sensitivity to detect IR induced myocardial lesions on scintigraphic images, because of low (despite significant) uptake in lesions.

10.11

Validation of an automatic SPECT radionuclide angiography processing software program for the measurement of right ventricular function against echocardiography.

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Aim: Recently, completely automatic software (Quantitative blood pool SPECT software developed by Cedars Sinai, QBS) was developed to process SPECT radionuclide angiography (RNA) acquisitions. It allows the automatic calculation of both left ventricular (LV) and right ventricular (RV) ejection fraction (EF) and end diastolic and end systolic volumes (EDV, ESV). However, its value for RV function evaluation is still debated. We aimed to evaluate the performance of QBS for the calculation of RVEF (%) and RV volumes (ml) as compared to the RV fractional area shortening (FAS, %) and RV end diastolic and end systolic area (cm2, EDA and ESA) echocardiography (gold-standard). In parallel, we compared its performance to the semi-automatic manual segmentation software used in our laboratory (based on maximal activity threshold method MAT-35%).
Methods: Forty-two patients with post-embolic pulmonary hypertension were studied: 18 patients before and 24 patients after pulmonary thrombo-endarterectomy. All patients had SPECT RNA and echocardiography within a 2-days period. SPECT RNA acquisitions were processed with QBS and MAT-35%: RV EDV, ESV, and EF were noted. For echocardiography, RV EDA, ESA, and FAS were noted. For the analysis, EDV and ESV measurements were combined.
Results: RV-FSA, RVEF-QBS, and RVEF-35% were respectively 28±7 %, 53±14 %, and 48±17 % (p<0.0001 between the 3 groups). Both RVEF-QBS and RVEF-35% were well correlated to RV-FSA: RV-FAS=11.28+0.31*RVEF-QBS with an r=0.64, ser=5.2, and p<0.0001 and RV-FAS=15.18+0.25*RVEF-35% with an r=0.65, ser=5.1, and p<0.0001.
RV-A, RVV-QBS, and RVV-35% were respectively 24±7 cm2, 104±49 ml, and 162±73 ml (p<0.0001 between the 3 groups). Both RVV-QBS and RVV-35% were well correlated to RV-A: RV-A=12.13+0.12*RVV-QBS with an r=0.78, ser=4.7, and p<0.0001 and RV-A=11.17+0.08*RVV-35% with an r=0.80, ser=4.5, and p<0.0001.
Conclusion: As compared to the manual segmentation semi-automatic MAT-35% method, the completely automatic QBS software provides RVEF and RV volumes that are similarly well correlated to echocardiographic RV functional parameters.

10.12

Relative impact of left ventricular (LV) dyssynchonism (D), right ventricular (RV) D, and interventricular D for the determination of LV function.

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Aim: Recently, a lot of debate has been reported as to the interaction between intra and inter ventricular (V) LV and RV mechanical D and LV function. Actually, these latter are being used as the basis for biV pacing in the treatment armamentarium of heart failure, particularly the D between LV lateral and septal walls. However, the relative importance of each of these parameters is still unclear. Planar radionuclide angiography (RNA) using Fourier phase analysis (FPA) has been used for the characterization of intra-V and inter-V LV and RV mechanical D. We aimed to evaluate in patients with ischemic hear disease the contribution of the different quantitative parameters reflecting LV and RV intra-V and inter-V D using planar-RNA FPA.
Methods: Our study included 103 consecutive patients with ischemic heart disease addressed for LV function evaluation with planar-RNA. Mean age was 61±15 years, 83% were men, 60% had previous myocardial infarction (MI) with 29% having a previous anterior MI, 35% an inferior MI, and 5% a lateral MI. Planar-RNA (best septal) were processed for FPA with XT-RNA software program (Vision, GEMS, France). Global LV and RV FPA were calculated as the first harmonic mean±SD (normalized to heart rate and expressed in degrees) of all corresponding LV and RV pixels: LV-SD was considered to reflect the heterogeneity in global LV contraction, (intra-V global LV mechanical D). Inter-V D was calculated as the difference between mean LV and mean RV FPA. Similarly, two different ROIs were manually drawn on the antero-lateral (AL) and antero-septal (AS) regions of the LV. And corresponding mean±SD FPA were calculated. AL-AS D was calculated as the difference between mean AL and AS FPA.
Results: Mean LVEF, LV-SD, and AL-AS D were respectively 40±18%, 7±17 degrees, and −4±27 degrees. LVEF was highly correlated to LV-SD: LVEF=71*exp(−0.025*LV-SD) , r=0.84, ser=7.7, P <0.0001. LVAF was mildly and linearly correlated to inter-V D (r=0.34, P <0.0001). And there was a trend for a linear correlation between LVEF and AL-AS D (r=0.18 , P=0.074). On stepwise regression analysis, the only correlated factor was LV-SD (F=228, r=0.832, ser=10, P <0.0001) while the inter-V D (F=0.001) and AL-AS D (F=1.553) were no longer significant factors.
Conclusion: In patients with ischemic heart disease, there is a high correlation between LV function and global LV D (reflected by LV-SD) which appears to be the major influencing factor. The influence of interV D and AL-AS D seem much less important. This should be considered in the work-up of patients considered for BiV pacing.

10.13

Impact of patient movement on gated myocardial perfusion SPECT (GSPECT) and radionuclide angiography SPECT (RNA SPECT) for the quantification of left ventricular (LV) function.

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Aim: Both GSPECT and SPECT RNA provide reliable estimation of LV Ejection Fraction (EF). A previous study has demonstrated the better robustness to patient movement of planar RNA as compared to GSPECT for the measurement of LVEF. What remains unclear is whether this better robustness is due to the difference in acquisition methods (planar versus SPECT) or whether it is due to different types of exams (RNA versus myocardial perfusion). We aimed to compare the robustness to patient movement of GSPECT and SPECT RNA for the measurement of LVEF.
Methods: The population included 20 patients with CAD having both rest Tl-201 GSPECT and SPECT RNA. All acquisitions were done on a DST-XL two-head gamma camera (GEMS, France) with 90 seconds/projection, 32 projections/180°. Patient movement was simulated by applying 1-pixel, 2-pixels, 3-pixels, 4-pixels, and 5-pixels deviation in the z axis (caudal to cranial axis) on each acquired study from the 9th projection to the 16th projection and from the 25th projection to the 32 projection. Eighty GSPECT studies and 80 SPECT RNA studies were generated: 0-pixel, 1-pixel, 2-pixels, 3-pixels, 4-pixels, and 5-pixels acquisitions. GSPECT was processed with the QGS software and SPECT RNA with the QBS software and corresponding LVEF were noted.
Results: For the 4-pixels and 5-pixels GSPECT studies, the LV myocardial wall presented double contour walls and it was impossible to generate acceptable LV contours and therefore calculate LV volumes with QGS. At 0-pixel, 1-pixel, 2-pixels, and 3-pixels QGS LVEF were respectively 36±12, 35±11, 32±10 °, and 27±9 * % (° : p<0.02 versus the other groups; * : p<0.0002 versus the other groups). For SPECT RNA, the aspect of the LV cavity was still acceptable for the 4-pixels and 5-pixels reconstructed studies. For QBS, the 0-pixel, 1-pixel, 2-pixels, 3-pixels, 4-pixels, and 5-pixels were respectively 47±17, 46±16, 44±14, 44±17, 43±16, and 45±19 for EF (NS).
Conclusion: Despite similar gated SPECT acquisition techniques, SPECT RNA seems to be less sensitive to patient movement than GSPECT for the quantification of LVEF.

10.14

Repeatability of two different ECG gated blood pool SPECT processing software for the quantification of left ventricular function.

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Aim: Despite some limitations inherent to its 2-dimensional nature, planar equilibrium radionuclide angiography (RNA) remains the clinical gold-standard for the measurement of left ventricular (LV) ejection fraction (EF). The 3-dimensional ECG-gated blood pool SPECT (GBPS) has been proposed to surpass the planar RNA limitations. However, its use has been limited by the unavailability of an automatic processing software. We previously validated the use of a manual maximal activity threshold (35%) method for the processing of GBPS (GBPS-35%) for LV function including its limits of repeatability. Recently, an interesting automatic processing software has been developed (QBS, Cedars-Sinai). We previously defined its value for LV function. We aimed to define its limits of repeatability for LVEF and volume (V) measurement as compared to planar equilibrium radionuclide angiography (RNA) and GBPS-35%.
Methods: Ten patients with CAD had RNA studies acquired as follows. First, planar left anterior oblique (LAO) then GBPS RNA acquisitions were realized by one technician. Then, the patients were allowed to rest in the waiting room for at least 15 min and a second set of acquisitions (LAO and GBPS) were realized by another technician. GBPS acquisitions were processed with QBS and GBPS-35%. All 4 acquired studies were processed by 2 different observers.
Results: For LVEF the intraobs, interobs, and interstudy reproducibility (absolute paired difference) of QBS, GBPS-35%, and LAO were respectively 3.1±5.1%, −1±4%, and 2.1±7.1% versus −0.6±1.9%, −0.8±3.1%, and −0.2±4.5% versus 0±0.8%, −0.7±1.1%, and −0.8±3.8%.
For LV end diastolic V the intraobs, interobs, and interstudy reproducibility (% variation) of QBS versus GBPS-35% were respectively (0±17%), (1±16%), and (−1±21%) versus (−1±1%), (−2±5%), and (1±5%).
For LV end systolic V these were respectively −8±15%, 3±17%, and −6±25% versus 0±5%, 0±10%, and 2±13%.
Conclusion: The limits of repeatability of LV function are considerably wider with QBS as compared to LAO and GBPS-35%. These limits should be considered when analyzing the temporal evolution of LV function.

10.15

Radionuclide angiography SPECT (RNA SPECT): performance of two different methods for the calculation of volumes.

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Aim: Cardiac chamber volume (V) measurement has an additive clinical value to LVEF. As compared to planar RNA, ECG-gated SPECT RNA presents the advantage of easy clinical applicability for V calculation. We have previously compared in phantom cardiac studies, 5 methods for the calculation of V with Tc-99m SPECT and we concluded that the 35% maximal activity threshold method was the most accurate method (MAT) (SNM 2000). Recently, a completely automatic software for SPECT RNA processing (QBS, Cedars-Sinai Center) based on gradient method was commercialized. We aimed to compare its performance to the MAT method for V measurement in RNA phantom studies.
Methods: Different cardiac phantom V were used (25≥V≥500ml), each with (+) and without (−) background (BKG) activity (A) and with different acquisition times (4 s and 8 s/step). SPECT acquisitions were realized on a DST-XL dual-head gamma camera (GEMS) with 32 steps/180°. Gated SPECT RNA studies were created and analyzed with the QBS software and the MAT software. Statistical analysis included linear regression analysis and % error ((calculated V-phantom V)*100 / phantom V).
Results: For the 4s BKG (−) studies, the % error, correlation coefficient, and ser were respectively −1±8, 0.9975, and 11.25 for QBS and −3±9, 0.9975, and 11.46 for MAT. For the 8s BKG (−) studies, the % error, correlation coefficient, and ser were respectively 2±10, 0.9975, and 11.32 for QBS and −1±8, 0.9946, and 16.74 for MAT. For the 4s BKG (+) studies, the % error, correlation coefficient, and ser were respectively −2±14, 0.9944, and 16.93 for QBS and −4±9, 0.9903, and 22.27 for MAT. For the 8s BKG (−) studies, the % error, correlation coefficient, and ser were respectively 4±13*, 0.9951, and 15.82 for QBS and 2±7*, 0.9863, and 26.46 for MAT.
Conclusion: Both QBS and MAT provided volumes highly correlated to phantom values over the wide range of evaluated volumes. This was verified for short and long acquisitions time (4s/step and 8s/step) and with or without BKG activity. In contrast to MAT, the performance of QBS seems to be influenced (lower) by the presence of BKG activity. This may explain in part the better reported performance of MAT as compared to QBS in patient studies.

10.16

Monitoring left-ventricular dilation in mice by high-resolution small-animal-PET: validation study using MRI.

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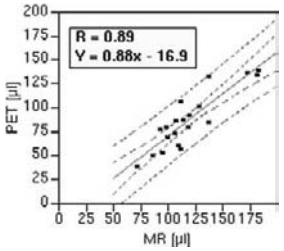
Background: Molecular imaging by small animal positron emission tomography (PET) is an important non-invasive means to phenotype transgenic mouse models in vivo. When investigating pathologies of the left ventricular (LV) myocardium (e.g. cardiomyopathies) the serial assessment of LV volumes is important. By this, the presence of left ventricular dilation as a sign of developing heart failure can be detected. Where PET imaging is usually used to derive biochemical/molecular information, the functional parameters such as ventricular volumes are generally measured by using morphological and functional imaging modalities such as echocardiography or magnetic resonance imaging. Here, a method to monitor left ventricular dilatation in mice with PET and thus obviating the need for a second imaging modality is presented and evaluated using cardiac MRI as the gold standard.

Methods: The method uses a semiautomatic 3D-algorithm to delineate the left ventricular myocardial wall on static Small-Animal-PET images depicting myocardial glucose metabolism (F-18-fluoro-2-deoxy-glucose-PET). The volume enclosed by the three-dimensional midmyocardial contour is calculated.

Data for twenty mice, ten wildtype mice and ten transgenic mice developing dilated cardiomyopathy, were obtained and compared to volumes measured by magnetic resonance imaging in the same animals.

Results: Data obtained by PET and MRI correlated well (R=0.89). Graphical analysis according to Bland and Altman did not reveal a dependency on volume.

Conclusion: Small animal PET imaging allows to monitor LV dilation in mice, thus obviating the need for a second imaging modality making serial measurements more efficient.



Correlation

10.17

Myocardial blood flow and coronary vascular resistance are dependent on thyroid function-a quantitative study using positron emission tomography and oxygen-15-labeled water.

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Introduction: Alterations of thyroid function are known to be associated with changes of the cardiovascular system. Aim of this study was to investigate the effects of an altered thyroid function on myocardial blood flow (MBF) and coronary vascular resistance (CVR).

Methods: Twenty hypothyroid patients (4m,16f,38±9 years) with a history of differentiated thyroid carcinoma, eleven patients (4m,7f,48±15 years) during clinical or subclinical hyperthyroidism and ten euthyroid controls (6m,4f,32±4 years) were enrolled in this study. Entry criteria included the absence of coronary artery disease, risk factors and cardiac medication. MBF (ml/g/min) was quantified by dynamic PET and 15O-labeled water. MBF was measured at rest, during adenosine infusion to provoke maximal hyperaemic MBF and calculate the coronary flow reserve (CFR), and during cold pressor testing (CPT) to obtain maximal perfusion stimulated by the endothelial response. In addition, CVR (mmHg/ml/g/min) in the different settings was calculated dividing mean arterial blood pressure by the respective MBF. Rate pressure product (RPP) was calculated for each group to compare hemodynamic parameters during the scans.

Results: Mean RPP at baseline were similar in the three groups excluding an effect of different cardiac work on MBF (Hypo:7660±1429,Eu:8131±2422,Hyper:8438±1101; p=ns). Baseline MBF was significantly higher in the hyperthyroid group (Hyper:1.15±0.23, Hypo:0.89±0.22, Eu:0.94±0.24; p<0.05). Absolute MBF during adenosine infusion and CFR were similar between the three groups (3.79±1.18, 3.66±1.26, 3.73±1.17; p=ns). MBF during CPT was significantly higher in the hyperthyroid group (Hyper: 1.57±0.39,Hypo:1.08±0.22, Eu:1.18±0.31; p<0.05).

Baseline CVR was significantly lower in the hyperthyroid group (Hyper:78±12.2,Hypo: 105.7±27.6, Eu:99.9±20.0; p<0.05). CVR during adenosine infusion was not significantly different between the three groups (27.4±14.4, 29.6±18.6, 27.6±11.3; p=ns). CVR during CPT was significantly lower in the hyperthyroid group (62.1±15.9) than in the hypothyroid group (91.9±24.7, p<0.05). It was also lower compared to the euthyroid group (80.4±19.6), however this difference only reached borderline significance (p=0.058).

Conclusion: Our results show an increased MBF at baseline and during CPT in patients with clinical and subclinical hyperthyroidism. Under the same conditions CVR is reduced in these patients. Adenosine infusion does not cause any significant changes, therefore our results strongly suggest an endothelium-mediated effect of clinical and subclinical hyperthyroidism on MBF and CVR.

10.18

Assessment of base-to-apex gradients of myocardial blood flow after statin therapy at different stages of coronary atherosclerosis.

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Diffuse coronary atherosclerosis is the common substrate for plaque rupture and cardiovascular events. Assessment of longitudinal, base-to-apex gradients (BAG) of myocardial perfusion abnormalities is a potential noninvasive marker for the functional integrity of the coronary endothelium. The aim of our study was the examination of reversibility of BAG after 6-month statin therapy.

Methods: 31 pts (age 62.4 ± 7.7 years; 22 males) with mild-to-moderate angina and LDL cholesterin (LDL-C) of 183 ± 40 mg/dl at baseline were included. Coronary angiography revealed minimal disease in terms of wall irregularities or stenosis < 30% in 19 pts and moderate coronary artery disease (CAD) with stenosis >50% in 11 pts. The reference group consists of 22 pts without detectable CAD. Absolute myocardial blood flow (MBF) was measured with ammonia PET under pharmacologic stress (adenosine). Basal mid (termed base) and mid-to-apex (apex) segments were analyzed. Minimal coronary resistance (MCR) was calculated as the ratio mean arterial pressure/ MBF-adenosine.

Results: Before therapy BAG-MCR was significantly lower in pts (0.91 ± 0.12) as compared to reference group (0.97 ± 0.14; p<0.05). After statin therapy BAG-MCR increased from 0.91 ± 0.12 to 0.95 ± 0.12 (p<0.05). BAG-MBF decreased from 1.12 ± 0.20 to 1.07 ± 0.13 (p<0.05). Even in segments with normal MCR (<0.40 mmHg/(ml/min/100g) BAG-MCR increased from 0.90 ± 0.10 to 0.96 ± 0.11 (p<0.05). LDL-C decreased to 104 ± 30 mg/dl at follow-up (p<0.001).

Conclusions: These PET results demonstrate a short-term reversibility of base-to-apex gradients of myocardial perfusion disturbance at early or moderate coronary atherosclerosis after 6-month statin therapy. The pathophysiologic mechanism behind probably reflects healing endothelium with improved flow-dependent dilation of epicardial vessels prone to atherosclerosis and risk factors such as LDL-C.

10.19

Effect of spinal cord stimulation on myocardial blood flow in patients with therapy refractory angina pectoris.

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Spinal cord stimulation (SCS) has proven to be a safe procedure in patients with symptomatic angina pectoris (AP) refractory to medical therapy and without any option for PCI or CABG. This technique has repeatedly demonstrated an antianginal effect by reducing AP symptoms. The mechanism, however, remains controversial. The aim of the study is the assessment of the effect of SCS on myocardial blood flow (MBF) and minimal coronary resistance (MCR).

Methods: In 6 male patients (mean age 66 years) with multi-vessel disease which were scheduled for NS, perfusion at rest and during the maximum hemodynamic effect of intravenous adenosine were studied by ammonia PET (Siemens ECAT EXACT HR+) on two different occasions: directly before SCS and 13 ± 0.5 months after SCS. The stimulator was active in all patients at 21 ± 5 hours before PET scan was done. MBF and MCR were calculated for the most impaired myocardial segments at baseline (initial MBF stress < 190 ml/min/100g). We correlated these data with clinical CCS angina score and NYHA class.

Results: Outpatients visits and hospitalization where significantly reduced in the 12 months post SCS compared to a 12 months interval before stimulation. Corresponding to the reduction in angina, the consumption of short-acting nitrates was also significantly reduced.

There was an increased hyperemic myocardial blood flow (138.8 ± 26.7 before SCS vs. 147.5 ± 0.37 ml/min/100g during SCS; p<0.05) and decreased minimal coronary resistance (0.65 ± 0.20 before SCS vs. 0.59 ± 0.18 mmHg/(ml/min/100g) during SCS; p<0.05) in the initial most impaired myocardial segments.

Conclusions: SCS has been shown to improve anginal status in patients with severe coronary artery disease. Our preliminary results suggest that the anti-anginal effect of SCS is associate with an improved regional MBF and vasodilator capacity in the most impaired myocardial segments.

10.20

Integrating cardiac PET/CT list mode acquisition in a clinical routine environment: implementation and initial experiences.

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Aim: Due to the success of PET/CT devices in oncology and the availability of high resolution CT scanners being part of it, the application in cardiac imaging offers an attractive perspective. However, cardiac imaging protocols require more flexibility as compared to whole body oncology scans: dynamic and gated acquisition modes are typically used extensively. List mode acquisition offers these advantages but is considered to be too demanding in a clinical routine environment. Thus, we investigated whether flexible yet easy to use front-end applications could be implemented and were suitable in such a setting.
Methods: List mode acquisitions were initiated from a dedicated user interface on the scanners console where essentially only the desired acquisition time was entered. Subsequently, the list mode data stream was acquired in parallel with the ECG and the respiratory signal. After the completion of the patient study, all data was transferred automatically to an offline workstation for further processing. There, the data was histogrammed into sinograms depending on the actual patient protocol. Essentially, the user only selected the type of the examination (e.g. ischemia [NH3 rest / NH3 stress] or viability [NH3 rest / FDG rest]) and the appropriate sinograms were generated automatically. In the examples above, the complete list mode stream was used to generate dynamic sinograms which were used for the calculation of e.g. myocardial blood flow. In addition, the parts of the same list mode stream where the tracer distribution reached a steady state were utilized to create gated sinograms. This saved considerable acquisition time as this study is traditionally measured in a separate step. Finally, the CT based transmission was checked for patient motion against a PET test volume and corrected if necessary.
Results: The developed programs were applied in twenty patient studies. The amount of list mode data averaged 5.3±3.2 Gigabytes. The time necessary to transfer the data was 13±8 min on a standard fast Ethernet network. Processing time including correction for photon attenuation, scatter correction and iterative reconstruction using an OSEM algorithm (8 subsets, 4 iterations) ranged between 30 and 40 min on standard PC hardware.
Conclusions: List mode data acquisition and patient protocol specific histogramming and reconstruction were implemented with an efficient and user friendly interface allowing its use in a clinical routine setting.

10.21

Peripheral arterial endothelial response to exercise in the evaluation of patients with coronary artery disease.

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Background: Endothelial dysfunction(ED) is a generalised abnormality of the vascular system and its detection in the coronary vasculature is of outmost importance for the clinical relevance and prognostication of coronary artery disease (CAD). Published data suggest that many CAD patients manifest concomitant peripheral ED. However little is known of a reverse relationship.
Aim of our study is to evaluate peripheral arterial tone (PAT) response to exercise as a marker of ED , correlating it to the magnitude of Tc-99m Tetrofosmin SPECT myocardial perfusion imaging (MPI) defects.
Methods: Twenty-one consecutive pts with suspected or known CAD, by history or angiography and a referent group of twenty-four normal volunteers with a < 5% likelihood of CAD or negative ETT and/or MPI (mean age 46±20 yrs, 18 men 75%) were enrolled in our prospective study. All underwent treadmill exercise testing (ETT) followed by MPI. Pulsatile finger pulse volume responses were assessed using a plethesmographic device (Itamar-Medical). Exercise PAT responses were compared to clinical, hemodynamic, ECG and MPI parameters.
Results: Among normal subjects, 22 (91.7%) manifested vasodilation throughout exercise and 2 (8.3%) manifested initial vasodilation followed by vasoconstriction at higher heart levels. None manifested vasoconstriction throughout exercise. In contrast, 6 CAD pts (28.6%) Group I, manifested vasoconstriction throughout exercise , 6 (28.6%) Group II, maintained a constant pulse wave amplitude (PWA) throughout exercise and other 9 (42.9%) Group III, sustained a vasodilating pattern of PAT throughout exercise ($p<0.01$ vs Group I,II). All Group I pts had exercise-induced reversible MPI defects, while Group II pts revealed predominantly persistent MPI defects compared to Group III pts who demonstrated a lesser degree of persistent perfusion abnormalities. Hemodynamic responses to exercise revealed progressive higher systolic and diastolic blood pressure and lower peak heart rates with diminishing PAT ratios.
Conclusions: Our data suggest that the progressive diminution in peripheral artery tone during exercise , measured by a plethesmographic system, can differentiate CAD pts with non-ischaemic ETT from normal individuals correlating well with the magnitude of the perfusion abnormalities. It may also represent a generalised vascular abnormality governed by altered endothelial function.

10.22

Equilibrium radionuclide angiography: 24 vs 32 frames per cardiac cycle.

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Aim: This study compares the values of systolic and diastolic parameters derived from 24 and 32 frames/R-R equilibrium radionuclide angiography (ERNA).
Method: Twenty-five consecutive patients, aged 56±9 yrs, with coronary artery disease were enrolled. Patients were submitted to ERNA (740 MBq 99mTc-RBC)in the best septal view, in two consecutive acquisitions, using 24 and 32 frames/R-R for 8 and 11 minutes, respectively. The following parameters were calculated: R-R interval, left ventricular ejection fraction (LVEF), end-diastolic and end-systolic volume (EDV and ESV, using the Massardo's technique), peak emptying rate (PER), time to PER from end-diastole (TPER), peak filling rate (PFR), time to PFR from end-systole (TPFR), and the left ventricular filling fraction during the first third of diastole (1/3FF, as % of stroke volume (SV)).
Results: These are summarized in table 1 (continuous variables are expressed as mean (SD); #, paired t-test; r, Pearson's correlation coefficient; B-A, the 95% limits of agreement from the Bland-Altman statistic; *, $p<0.005$; **p, ns). There was no significant difference in R-R between paired acquisitions (958± 190 msec vs 939± 169 msec).
Conclusion: In ERNA: 1) The 32 frames/R-R acquisition tends to overestimate both systolic and diastolic function in comparison to the 24 frames/R-R technique. 2) Despite good correlation, the values of common systolic and diastolic indices show significant differences and wide 95% limits of agreement between the 24 and 32 frames/R-R acquisitions. 3) Apparently, the selection of the number of frames/R-R may be based on the reproducibility of each technique.

Table 1

	24 frames/R-R	32 frames/R-R	p#	r	B-A
LVEF (%)	53.0(9.5)	56.1(9.1)	<0.001	0.92*	±7.4
EDV (ml)	84(29)	85(30)	ns	0.85*	± 33
ESV (ml)	40(19)	39(21)	ns	0.91*	± 18
PER (EDV/sec)	3.24(0.80)	3.72(0.86)	<0.001	0.74*	± 1.19
TPER (msec)	157(42)	130(43)	<0.05	0.29**	±101
PFR (EDV/sec)	2.44(0.84)	3.03(0.77)	<0.001	0.61*	± 1.42
TPFR (msec)	201(78)	192(78)	ns	0.70*	±121
1/3FF (%SV)	0.40(0.18)	0.41(0.20)	ns	0.82*	± 0.24

10.23

Reduced cardiac sympathetic innervation contributes to elevated proinflammatory cytokines levels in patients with congestive heart failure.

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Background: In heart failure (HF) both plasma and myocardial tissue levels of cytokines are increased. Experimental animal studies showed that cytokines production might be regulated in part, by sympathetic nervous system (SNS) stimulation of cardiac beta-adrenergic receptors. The cardiac response to sympathetic stimulation is impaired in HF and this may contribute to elevated levels of circulating cytokines. The cardiac fixation of 123-Metaiodobenzylguanidine (MIBG) a norepinephrine analogue, was developed to visualize sympathetic innervation, has the potential to mirror the whole myocardial adrenergic pathway disintegrity and has been found to be reduced in HF.
Objectives: We evaluated the relationship between MIBG cardiac uptake and circulating levels of pro-inflammatory cytokines in patients with idiopathic dilated cardiomyopathy (IDC).
Methods: Thirty-seven patients (7 women, mean age 54 ±11,3 y) with angiographically proven IDC, NYHA class II-III, with Left Ventricular ejection fraction (LVEF) 31,1 + 8,1%, underwent a planar MIBG study and early (10 min) and late (4 hour) heart to mediastinum uptake ratio and washout rate were calculated. Twenty age-matched normal (N) individuals who served as a control group underwent the same procedure. Blood sampling of all patients with IDC for circulating plasma levels of Interleukin -1(IL-1), Interleukin-6(IL-6), TNF-a and its soluble receptors sTNFr1 and sTNFr2 were measured by immunoassay. None of study pts were on beta-blockers or suffered from diabetes mellitus.
Results: The IDC group had significantly reduced MIBG uptake values at 10 min (1,6 ±1.15 vs 1,91 ±0,08, $p<0,001$) and 4 hrs (1,48 ± 0,17 vs 1,84 ±0,12, $p<0,001$) and increased WO (7 ± 4%vs 3 ±3%, $p<0,005$), compared to the control group. Univariate analysis showed that in the patients' group early and late MIBG uptake correlated significantly with NYHA class($r=-0,70$,$p<0,001$ and $r=-0,63$, $p<0,001$), LVEF ($r=-0,38$,$p=0,05$ and $r=-0,34$ $p=0,01$), IL-1 (r=-0,53, p=0,01 and r=-0,50, p=0,01) and sTNFr2 (r=-0,70, p=0,001 and p=-0,61, p=0,001) respectively.Multivariate regression analysis revealed that MIBG at 4 hours was independently associated with sTNFr2 (p=0,01).
Conclusions: The reduced cardiac sympathetic innervation in CHF is related to elevated circulating IL-1 and sTNFr2 levels. The impaired response to increased sympathetic stimulation in CHF may be accompanied by a chronic inflammation state, which further leads to a vicious cycle and cardiac function deterioration.

10.24

Attenuation and scatter correction in myocardial perfusion scintigraphy: differences between exercise and pharmacologic stress.

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Aim: To evaluate the clinical usefulness of attenuation and scatter correction in myocardial perfusion scintigraphy according to different types of stress.
Materials and methods: We studied 104 patients (64 males-40 females) who were subjected in coronary angiography (CA) prior or after the scintigraphy. The maximum time interval between scintigraphy and CA was 3 weeks. Tl-201 one day protocol (stress-4hrs delay) was used. Sixty-eight patients underwent exercise stress (group I) and 36 patients pharmacologic stress (group II). Simultaneous transmission-emission images were obtained by a dual-head ã-camera equipped with two moving collimated Gd-153 rod sources. Stress and delay reconstructed images, non-corrected for attenuation and scatter, were diagnosed by two readers blinded to CA findings. One month later, corrected images for attenuation and scatter were diagnosed by the same readers. Heart was divided in five regions (apical, anterior, lateral, inferior and septal). The results were compared using as reference the CA findings.
Results: In group I, corrected images demonstrated significant increase in specificity for the inferior wall (90% vs 41% for non-corrected images). No significant differences in specificity and sensitivity were observed for the rest walls. In group II the specificity for the corrected compared to uncorrected images was for the inferior wall 86% vs 28% and for the apex 86% vs 100%.
Conclusion: Attenuation and scatter correction in TL-201 SPECT studies may significantly decrease false positive lesions in inferior wall. This is more prominent in patients that underwent pharmacologic stress. The creation of apical artefacts is a minor disadvantage of the method.

10.25

Institutional based assessment of myocardial viability by nitrate augmented Tc99m Sestamibi gated SPECT and low dose Dobutamine stress echo - a comparative study.

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Aim: to compare Nitrate augmented Tc-99m Sestamibi gated SPECT and low dose Dobutamine stress echo a)for assessment of myocardial viability and b)for predicting functional improvement and recovery of myocardial segments post revascularisation. Present study is an ongoing study and hence we will be discussing about the first part of the study.
Materials and methods: total number of patients included were thirty (27 males and 3 females, age ranging from 30 to 72years) with angiography proven coronary artery disease and left ventricular dysfunction (Mean LVEF 26.13 % ±10.33%). All patients underwent both Dobutamine stress echo (DSE) & Nitrate augmented gated SPECT (gSPECT) using Tc99m labelled Sestamibi within 1 week. 26 patients had history of myocardial infarction (18 < 3months & 8 > 3months duration). Angiographically, 15 patients had TVD, 11 had DVD and 4 had SVD (LAD = 29, RCA = 22, LCX = 19). Rest and Nitrate augmented Gspect was performed on the same day using rest bolus dose (8 -- 10mCi) and MIBI infusion (25 -- 30mCi) following administration of 5-10mg Sorbitrate sublingually. DSE was performed at doses of 5, 7.5, 10, 15 and 20mg/kg and images were obtained and stored in digitised form for subsequent analysis. Both the studies were analysed by a blinded observer. A 16 segment model was used for analysis and wall motion score index for DSE and a matched segmental scoring was performed for gSPECT.
Results: out of 264 dysfunctional segments, both techniques showed an overall agreement for viability / non viability in 171 segments (64.77%). Disagreement was present in 93 segments (35.22%). Of the 182 segments viable by gSPECT, DSE showed absence of contractile reserve in 45.60% segments. Conversely, 9.1% of segments non viable by gSPECT exhibited contractile reserve by DSE.
Conclusion: we conclude that our study showed a good agreement between nitrate gSPECT & DSE although a substantial number of segments with preserved viability on gSPECT did not exhibit contractile reserve, indicating underestimation of viability by DSE compared to gSPECT.

10.26

Prediction of the left ventricular ejection fraction using cavity-to-myocardium count ratio and perfusion scores in myocardial perfusion SPECT.

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Aim: Good correlation was reported between left ventricular cavity to myocardial count ratio (LVCMR) and left ventricular ejection fraction (LVEF). The aim of this study was to find a model to correlate and predict LVEF from LVCMR and perfusion indices.
Methods and patients: We studied 77 patients (44 males, 33 females) aged 30-70 years, mean age 52.7 years, who underwent 99mTc-MIBI myocardial perfusion SPECT. Cardiac catheterization followed within 6 months. The LVCMR was obtained from the mid short-axis slice on both stress (with dipyridamole) and rest images using an 8 pixels circle ROI in the LV cavity and the same ROI on the hottest area of the myocardium. The 17-segment, 5-point scoring system was used as a semiquantitative global index for overall assessment of extent and severity of perfusion abnormality.
Results: Our study showed a significant correlation between angiographic LVEF and stress LVCMR ($p<0.001$, r: 0.612) or rest LVCMR ($p<0.001$, r: 0.671). There was significant correlation between LVEF or LVCMR and summed stress or rest score (SSS or SRS). Stress and rest LVCMR in patients with LVEF < 45% were significantly lower than in patients with LVEF ≥ 45% ($p<0.001$). Using regression analysis for the prediction of LVEF, the best model was achieved using SRS and rest LVCMR [$Y = 46.70 + (1.13 \times \text{Rest LVCMR}) - 0.59\ \text{SRS}$].
In conclusion, our study showed that LVEF can be easily estimated using a combination of rest LVCMR and summed rest score. This estimation may also be useful in nuclear medicine laboratories that do not have a gating option in their gamma cameras.

10.27

Right ventricular function and functional capacity in patients with primary pulmonary hypertension: correlation and outcome.

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Most patients with Primary Pulmonary Hypertension (PPH) have severe exertional limitation which ultimately lead to right heart failure and death. The clinical course and survival of these pts has been improved with the new therapeutic modalities. The purpose of the study was to reassess right ventricular (RV) profile with correlation to exercise tolerance and the predictors of adverse outcome in treated patients with PPH.
Methods: We prospectively studied 29 patients (pts), 17 with PPH and 12 with PPH due to collagen disease. All treated with anti coagulation, 17 with prostacyclines and 12 with calcium channels blocker. Pulmonary function and RV parameters assessed by echo (including Doppler RV index, Doppler Tissue Imaging, tricuspid regurgitation (TR), RV shortening fraction (SF) %, right atrial (RA) size) and RVEF by first pass RNA were correlated to functional capacity assessed by six minutes walk test and NYHA class.All ptients were followed up for death and clinical deterioratin.
Results: Mean age was 51±15 yrs, 22 (78%) women. NYHA class1 in 2 pts, class 2 in 17, class 3 in 8 and class 4 in 2 pts. Pulmonary function (DLCO) was low in 25 (86%) pts, mean 22±48%. Six min. walk distance was 358±132 meters and RVEF was 34±11% (range 16-51%). Significant correlation between RV variables and functional capacity were as in the table.
Within follow up of 2 years, there were 10 patients with adverse outcome (4 deaths and 6 deteriorated to NYHA class 3 and 4). Among all clinical and non-invasive variables, RVEF only was correlated to adverse outcome ($r = -0.4$, $p = 0.04$)
Conclusion: Although there is a significant correlation between RV variables and functional capacity, RVEF was the only variable predicting adverse outcome in pts with PPH.

TABLE

Variables	NYHA class Correlation coeficient (r)	NYHA class p value	6 min walking test Correlation coeficient (r)	6 min walking test p value
RVSF %	−0.38	0.04	0.23	0.22
RVEF %	0.45	0.019	0.50	0.0075
DLCO %	−0.46	0.013	0.53	0.033
RA area cm^2/m	0.39	0.036	−0.42	0.02
TR	0.42	.025	−0.52	0.0038

10.28

90Sr/90Y beta-radiation intracoronary brachytherapy efficacy in patients with aggressive coronary in-stent restenosis.

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Introduction: In-stent restenosis (ISR) is a clinical and financial problem after angioplasty and stenting (PCI-S), despite the introduction of drug-eluting Stent(DES). Intracoronary (IC) radiation therapy, gamma and beta- emitters brachytherapy (ICBT) has been proposed for preventing ISR.
Aim: To evaluate beta-ICBT efficacy in the outcome of patients (pts) treated for aggressive and recurrent ISR.
Methods: 27 pts (23 men; 4 female), 9 of them with previous myocardial infarction (MI), all of them with more than 2 coronary risk factors, no previous CABG and less than 1 year (3-8 m) PCI-S (DES in 2 pts), were enrolled into beta-ICBT in presence of stress related ischemia at stress-rest M-GSPECT(555/555MBq 99-Tc-Sestamibi) and ISR agreement at angiography: LDA in 11 pts; LCx in 9 pts; RCA in 2 pts; in two vessels in 4 pts and three vessels in 1 pt. We used 90Sr/90Y beta-source, delivered by the BetaCath-3.5 F System, after positioning the delivery catheter in the C artery at the site of ISR by using X-ray during a cardiac catheterization. The transfer device was connected to the delivery catheter and used to deliver the radioactive seeds to the location until the end of treatment: dose prescription for visual reference stenting vessel sizes range 2.7-3.35 mm = 18.4 Gy mm at 2 mm, in short treatment times = 3min 07sec. All pts underwent stress-rest GSPECT at 3-6m after ICBT. Pre-ICBT, 3m and 6m post-ICBT GSPECT data were analysed both visually and by evaluating in 20 M segments/each study: perfusion as Summed Stress, Rest and Difference Scores (SSS, SRS, SDS) and LV function as post-stress and rest LVEF, regional wall motion(RWM) and thickening %(RWT).
Results: No early or late angiographic complications and no angina in one year follow-up period. Comparative G-SPECT data showed in ICBT treated areas : -No differences between 3m and 6m post-ICBT;-Post-ICBT perfusion improvement (SRS, SSS and SDS: $p<0.001$);-LVEF improvement(more than 5%)in 5/9 pts with previous MI and resting mild-moderate LV dysfunction (LVEF = 45%-50%). In addition, 6m post-ICBT G-SPECT showed mild-moderate ischemia stress related in 5 pts with new stenosis in a coronary territory different from that with ISR at angiography.
Conclusions: 90Sr/90Y beta-ICBT is both safe and effective in aggressive and recurrent ISR and should be considered as a therapeutic option for preventing recurrence in this difficult pts subset. Stress-rest myocardial GSPECT is a good marker in monitoring perfusion and function outcome of treated areas and in defining functional implications in the other ischemic ones.

10.29

Incremental diagnostic value of 99m-Tc-DTPA non-gated first-pass radionuclide angiography over 201-Thallium gated-SPECT in the assessment of global left ventricular function.

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The value of perfusion defects assessed with automatic measurements on 201-Thallium gated-SPECT (Tl-G-SPECT) is well established but informations on global left ventricular (LV) function are still uncertain. We have thus compared estimates of LV ejection fraction (LVEF) , end-diastolic (EDVs) and end-systolic volumes (ESVs) assessed by Tl-G-SPECT with those obtained by 99m-Tc-DTPA non-gated first-pass radionuclide angiography (FPRNA) in 400 consecutive patients (pts) with mean age of 62±11 years ,88% (249/400) males with suspected or established ischemic heart disease.
Method 1: A stress/rest Tl-G-SPECT was thus performed in all pts on a double-head gamma camera. Rest LVEFs,EDVs,and ESVs were processed with a Cedars-QGS software.Perfusion defects were examined with a quantitative program (CEqual).Extent of abnormal defects (ADS) was thus calculated as a percentage (%)of total left ventricle pixels while reversibility was calculated as a % of the stress defect. METHOD 2:The non-gated FPRNA was acquired during an intravenous bolus injection of 99m-Tc-DTPA immediately after rest Tl-G-SPECT acquisition and analyzed with a commercially available software (RNA 2)on a SOPHA vision power station. Results: When Tl-G-SPECT and FPRNA data were compared (Student paired t-test ; correlation analysis) , mean values were similar for LVEFs and ESVs (53±11% vs 53±10%) and (33 ± 23ml vs 34 ± 18ml),p = ns for both ; r > than 0.80 for both, but not for EDVs (68±26 ml vs 72±15 ml, $p < 0.001$; r = 0.76).However , Bland-Altman plots revealed between Tl-G-SPECT and FPRNA,with limits of agreement (± two standard deviations) of 12%,26 ml and 39 ml for LVEFs,ESVs and EDVs ,respectively,clinically important shifts for the estimation of volumes.Infact,the QGS software failed to identify the LV cavity in 15% (59/400) of pts due to small heart dimensions (88% of these pts were females with LV volumes < than 30 ml, ADS of 1.4 ± 2.6% and R of 3 ± 10%).In another 1.5% (6/400) of pts , QGS did not correctly identify LV borders due to large infartions (67% of these pts were males with volumes > than 60 ml, ADS of 29 ± 6% and R of 13 ± 15%). Conclusions: These data suggest that Tl-G-SPECT and 99m-Tc-DTPA non-gated FPRNA had an excellent correlation in global LV function evaluation but 99m-Tc-DTPA non-gated FPRNA had an incremental diagnostic value over Tl-SPECT in pts with small heart dimensions or large infarctions.The use of 99m-Tc-DTPA non-gated FPRNA has thus clinical validity in such circumstances and it is a rapid and low cost procedure.

10.30

Correlation between cardiac dyssynchrony by radionuclide phase analysis and systolic and diastolic function. Implication for cardiac resynchronization therapy.

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Aim. The aim of the study was to correlate the indexes of cardiac synchronism obtained by radionuclide phase analysis (PhA) and systolic and diastolic function.
Methods. 160 consecutive pts (age 60±9) with known or suspected cardiac disease, underwent a rest radionuclide ventricolography. QRS duration (QRSd) was automatically calculated. The left (LV) and right (RV) ejection fractions (LVEF, RVEF) and the LV peak filling rate (PFR) were calculated. Phase and amplitude images were obtained by Fourier PhA; ROI were separately placed over the RV and LV phase image and from the pixel-value distribution histograms the RV and LV standard deviations (SD) were calculated, as an index of intra-ventricular synchronism. The inter-ventricular asynchrony (LV-RV delay; LV-RVd) was calculated as difference in the mean value of the RV and LV histogram. LV was considered asynchronous if SD >18° (mean±2SD of our normal limits).
Results. A significant non-linear relation was found between LVSD and LVEF (LVEF=101.2-20.1*ln(SD); r=0.79;p≥.0001) or PFR (PFR=4.4-0.9*ln(SD); r=0.64; $p<0.0001$). A significant non-linear relation was also found between RVSD and RVEF (RVEF=63.3-9.2*ln(SD);r=0.49;$p<0.001$).
A significant non-linear relation was observed between QRSd and LVEF (r=0.66, $p<0.001$) or PFR (r=0.60, $p<0.001$); however, no correlations were observed between QRS and RVEF or RVSD. A weak linear correlation was observed between QRSd and LVSD (r=0.51, $p<0.01$) or LV-RVd (r=0.37, $p<0.05$).
No significant correlation was found between LV-RVd and RVEF, LVEF or PFR.
Pts were then divided according to QRSd in normal (QRSd< 80 msec), prolonged (QRSd 80 to 120 msec) or long (QRS120 msec) QRSd. No significant differences were observed between groups in RVEF or RVSD. Significant differences were observed in the LVEF (58±5%, 37±17%, 27±7%, $p<0.001$), LVSD (9.4±3.7°, 19.6±9.8°, 29.8±18.5°, $p<0.001$) and PFR (2.9±0.6, 1.7±1.0, 1.2±0.3, $p<0.001$). A significant difference was observed in the LV-RVd of the 3 groups (11±7, 28±20, 40±26 msec, $p<0.05$). 11% and 42% of pts with prolonged QRSd had abnormal LV-RVd and LVSD, respect., and 56% and 25% of pts with long QRSd had normal LV-RVd and LVSD.
Conclusions. In a large group of patients with various degrees of cardiac function, intra-ventricular PhA better correlated with abnormal LV function than QRSd or LV-RVd; moreover, a consisted number of pts had inter- or intra-ventricular dyssynchrony by PhA despite a QRSd < 120 msec. Thus, the assessement of cardiac dyssynchrony by RNV may be proposed in all pts with heart failure, independently from QRSd.

10.31

Correlation between radionuclide phase analysis and echocardiography in the assessement of cardiac dyssynchrony.

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Background. Few data exist on the correlation between synchronism of cardiac contraction as assessed by radionuclide phase analysis (PhA) and echocardiography.
Aim. The aim of this study was to correlate the indexes of cardiac asynchrony from radionuclide PhA and echocardiography.
Methods. We evaluated 20 consecutive pts (age 60±9) with CHF (NYHA III) and LVEF < 35%. All pts underwent a radionuclide ventricolography (RNV, 32 frames) and echocardiography to assess systolic and diastolic function, as well as the synchronism of contraction. QRS duration (QRSd) was automatically calculated. The left (LV) and right (RV) ejection fractions (LVEF, RVEF) and the LV peak filling rate (PFR) were Calculated. Phase and amplitude images were obtained by Fourier PhA; ROI were separately placed over the RV and LV phase image, using the amplitude image as a guide. From the RV and LV phase-distribution histogram, the RV and LV standard deviations (SD) were obtained, as index of intra-ventricular synchronism of contraction; the inter-ventricular asynchrony (LV-RV delay; LRD) was calculated as difference in the mean value of the RV and LV histogram. By echocardiography the interventricular delay (IVD) was determined as the time between onset of aortic and pulmonary flow; the intraventricular asynchrony was assessed as the time from maximal septal to lateral wall contraction (S-Ld) by TDI
Results. The QRSd was 138±31 msec. By RNV the average LVEF was 26±7%, the RVEF 32±5%, the PFR 1.12±0.3 EDV/sec. By PhA, LVSD was 32.2°±14.0°, the RVSD was 21.1°±10.2°, the LRD was 37±18 msec. At echocardiography, the average LVEF was 24±5%, the IVD was 47±33 msec, the S-Ld was 66±53 msec. A weak correlation was observed between RNV and echocardiographic LVEF (r=0.68, $p<0.05$), and a significant relation was observed between LRD and IVD (r=0.77, $p<0.01$). No significant relation was observed between LVSD and S-Ld (r=0.28, NS); however, when the lateral-septal delay was calculated on the phase image, a significant relation was obtained (r=0.77, $p<0.01$). No correlation was observed between QRSd and LV-RVd or IVD, as well as between QRSd and LVSD or S-Ld.
Conclusions. In a group a pts with severe LV dysfunction and CHF, a significant relation was observed between RNV and echocardiography in the evaluation of inter-ventricular delay. In the assessment of intra-ventricular asynchrony, echocardiographic methods assessing only lateral and septal walls underestimate the global LV asynchrony. Finally, QRSd is not a reliable measure of inter- or intra-ventricular asynchrony.

10.32

Noninvasive assessment of coronary flow reserve by cardiac SPECT in patients with peripheral artery disease: correlation with flow mediated dilation index.

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Aim: It has been recently reported that peripheral endothelial function correlates with coronary vasodilator response. However, the relationship between peripheral endothelial function and coronary circulation has not been extensively assessed. This sudy was designed to assess the relationship between estimated coronary flow reserve (CFR) using cardiac SPECT and the degree of endothelial dysfunction in patients with documented peripheral artery disease.
Methods: Forty-four consecutive patients (40 men, mean age 62±10 years) with documented peripheral artery disease were studied. A separate group of 13 patients (7 men, mean age 59±10 years) without peripheral or coronary artery disease constituted the control group. All patients and control subjects, underwent dipyridamole (0.74 mg/Kg) sestamibi imaging. Myocardial blood flow (MBF) was estimated by measuring first transit counts in pulmonary artery and myocardial counts from SPECT images. On a separate day the same acquisitions were repeated after tracer injection under resting conditions. Estimated CFR was expressed as the ratio estimated MBF stress/MBF rest. The accuracy and reproducibility of this method has been previously assessed in our laboratory. In all patients with peripheral artery disease, flow mediated dilation index of the brachial artery was assessed by ultrasound.
Results: All patients and control subjects successfully completed the dipyridamole myocardial perfusion study without major side effects. In control group, estimated CFR was 2.2±0.5. Patients with peripheral artery disease were separated into group 1 (n=22, patients with mild-moderate impairment of arterial reactivity) and group 2 (n=22, patients with severe impairment of arterial reactivity). Estimated CFR was 1.5±0.4 in group 1 ($P<0.05$ vs control subjects) and 1.0±0.4 in group 2 ($P<0.0001$ vs control subjects and $P<0.01$ vs group 1), respectively.
Conclusion: CFR estimated by myocardial SPECT was significantly reduced in patients with peripheral artery disease as compared to control subjects and CFR reduction correlates with the degree of peripheral artery dysfunction. Thus, this noninvasive method might be useful in the early detection of coronary arteriosclerosis.

10.33

Assessment of Tc-99m MIBI washout in animals with induced heart failure.

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To validate reduced Tc-99m MIBI (MIBI) retention in myocardium with damaged mitochondria, myocardial MIBI uptakes of rats administrated with doxorubicin (DXR) were measured in a fixed interval using gamma camera, and these serial myocardial MIBI uptakes were compared with serum troponin T (TnT) level as one of indicators representing ongoing myocardial damage (OMD), as well as pathological findings. Twenty Wistar-Kyoto rats of 10 weeks of age were enrolled as induced heart failure and control model animals. Five out of the ten with induced heart failure were subcutaneously administrated with 2mg/kg/W DXR over 7 weeks, and the other five were administrated with the same dose of DXR over 9 weeks. The ten control rats were also divided into 2 clusters (5 each) subcutaneously administrated with the same dose of saline over 7 and 9 weeks, respectively. BP, HR, and BW of each rat were measured periodically. Three min. acquisition of total and myocardial activities were carried out 10, 60, and 120 min. after 3MBq MIBI injection, using two-head gamma camera (PRISM 2000) equipped with ultra-high-resolution and pinhole collimators, respectively. Myocardial to total ratios (H/T) and washout ratios from 10 min. H/T (WO) were compared between DXR and control groups. Following autopsy 120 min. after MIBI administration, %ID/g (percentage activity of injected dose) of heart, lung, and liver as well as serum TnT level were measured. Histologic scoring index by Herman and Ferrans for DXR cardiomyopathy was estimated with grading on a scale of 0-4 on the basis of the number of myocytes showing cytoplasmic vacuolization and myofibrillar loss. There were significant differences of BP, HR, and BW after 8 weeks between DXR and control groups, suggesting successful preparation for heart failure models in the former group. %ID/g of lung and liver showed no significant differences between two groups. On the other hand, %ID/g of myocardium and H/T in DXR were significant lower than those in control, and WO in DXR showed significant greater values compared with those in control. All in DXR and two in control showed positive in serum TnT level, representing histologic damage of myocardium. Serum TnT showed significant negative correlation with 10, 60, 120 min. H/T, respectively. Positive and negative correlations of histologic score were obtained significantly with 120 min. H/T and 120 min. WO, respectively. In conclusion, MIBI retention in mitochondria closely related with OMD in doxorubicin cardiomyopathy, suggesting MIBI WO might be an alternative indicator of heart failure with OMD.

10.34

New departure in Fourier analysis using gated cardiac POOL-SPECT for indication of cardiac resynchronisation therapy.

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Background: Although cardiac resynchronisation therapy(CRT) has been reported to produce clinical benefits in patients with heart failure, the exact method to estimate of cardiac asynchrony has been yet well defined.
Methods and results: Consecutive 19 patients with DCM underwent heart blood pool scintigraphy. As an evaluation for analysis of cardiac asynchrony, we attempted to apply the Fourier analysis using gated cardiac pool SPECT (POOL-SPECT). For the qualitative SPECT data analysis, we compared the phase histogram (PH) patterns of left ventricular with the right ventricular, which were obtained individually. The phase images of patients with progressive heart failure were represented visually as an inhomogeneous color pattern either right or left ventricle. This study has shown that patients with both inter- and intra-ventricular asynchrony had significant deteriorations in both the LVEF(P lower 0.05) and the New York Heart Association functional class(P lower0.01). Moreover, after CRT for patients with progressive heart failure, the phase images clearly improved. The internal of RV-LV delay in the mean phase was significantly decreased from pre- to post-CRT (75.9 vs. 57.1 degrees, p equal 0.01).
Conclusion:
These results have shown that the phase images using POOL-SPECT is useful for evaluation of cardiac asynchrony and the effect of CRT in patients with heart failure, which suggests that it may provide the information for indication of CRT.

10.35

Tc-99m-annexin V uptake depends on ischemic severity and reperfusion time.

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We study the relation between the degree of ischemia and time course of the uptake of technetium-99m labeled annexin-V (Tc-AV), a tracer selectively binding to phosphatidylserine which externalizes to the cell surface in the early phase of apoptosis, in an rat model of cardiac ischemia and reperfusion.
Methods: Ischemia and reperfusion was induced in rat hearts by ligation and release of a snare around the left coronary artery. After 10, 15, 20 min of ischemia, Tc-AV (80-150MBq) was injected intravenously at 30, 90 min, 6, 24 hr after reperfusion. After 5 min of ischemia Tc-AV was also injected at 30 and 90 min after reperfusion. To verify the area at risk, 1 hour after Tc-AV injection, Tl-201 (0.74 MBq) was injected intravenously just after the re-ligatation of the artery and the rat was euthanized 1 minute later. Dual autoradiography was performed to assess Tc-AV uptake and area at risk. TUNEL staining was also performed in 6 hr reperfusion group.
Results: After 20 min of ischemia followed by 30 and 90 min of reperfusion, strong uptake of Tc-AV was observed (uptake ratios (UR) of ischemic to non ischemic areas were 4.84 ± 2.3 and 4.35 ± 1.6 (mean ± SD), respectively). The URs decreased time dependently at 6 (3.47 ± 1.5) and 24 hours (2.57 ± 0.54) after reperfusion. After 15 min of ischemia URs in each reperfusion time were 3.14 ± 2.3, 1.96 ± 0.55, 1.91± 0.87, 1.29 ± 0.23, respectively. In 10 min ischemia in each reperfusion time, URs were 1.56 ± 0.23, 1.27 ± 0.10, 1.19 ± 0.19, 1.04 ± 0.21, respectively. In 5 min ischemia, no significant uptake was observed. % apoptotic area (% area of Tc-AV uptake to that of ischemic area) was similar among various ischemic severity, but in 24 hr reperfusion model, 10 min ischemia rats showed smaller % apoptotic area than 20 min and 15 min ischemia. 21 ± 11.2 %, 3.5 ±1.3 %, and 1.0 ± 0.40% of the myocardial cells were positive in TUNEL staining in 20 min, 15 min, 10 min ischemiac group, respectively.
Conclusion: Tc-99m-annexin-V uptake, in ischemia and reperfusion rat model, depends on the severity of ischemia and reperfusion time. Its uptake in ischemic area is high in longer ischemic time and earlier after reperfusion (30 min) and decreased gradually over 24 hours after reperfusion. On the other hand, Tc-AV uptake areas were similar among various ischemic severity. Even in 10 min ischemia and reperfusion, which showed no apparent necrosis, significant uptake was observed.

10.36

Efficacy of myocardial gated SPECT in follow-up study for coronary artery disease.

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OBJECTIVE: This study was designed to assess the prognostic value of left ventricular (LV) functional parameters as measured by quantitative gated-SPECT (QGS) and their contribution to a follow-up study in patients with coronary artery disease (CAD.

BACKGROUND: The prognostic value of QGS in a follow-up study has not been fully evaluated yet, although the high reproducibility of QGS has been well validated.

METHODS: After coronary intervention, 89 patients underwent two times of myocardial SPECT, and were followed up for a mean period of 393 ± 169 days. The segmental perfusion was analyzed visually, while the ejection fraction (EF) and end-diastolic volume (EDV) were calculated using an automatic QGS algorithm. The differences between the second and first time of the LV fuctional values were calculated as dEF (%) and dEDV (ml), respectively.

RESULTS: The 89 patients were classified into 3 groups according to their second time of myocardial perfusion imaging as follows: 65 patients with unchanged perfusion were classified into group A, 6 patients with improved perfusion into group B, and 18 patients with worsening perfusion into group C. There were no significant differences in the LV parameters in group A (dEF: 2.7 ± 8.4, dEDV: −1.1 ± 11.9%) and group B (dEF: 1.2 ± 6.7, dEDV: −10.8 ± 14.0). In group C, significantly increased LV volume was observed at the second time SPECT (dEDV: 20.9 ± 15.4, p=0.03) although there was no difference in EF (dEF: −1.5 ± 6.6).

CONCLUSION: The QGS measurements of LV functional parameters were highly reproducible over a long period of time. Furthermore, an increased LV volume was observed in patients in whom myocardial perfusion had deteriorated at the follow-up SPECT. We concluded that QGS is a clinically useful tool for follow-up of the patients with CAD.

Result in this study

Group	EF	(%)		EDV	(ml)	
	2 nd time	1 st time	Difference	2 nd time	1 st time	Difference
A	61.2 ± 12.4	58.8 ± 11.1	2.7 ± 8.4	82.3 ± 25.8	83.5 ± 26.6	−1.1 ± 11.9
B	59.6 ± 22.2	58.2 ± 20.1	1.2 ± 6.7	86.6 ± 46.9	98.0 ± 44.4	−10.8 ± 14.0
C	48.2 ± 14.9	49.8 ± 15.8	−1.5 ± 6.6	125.6 ± 46.9	102.7 ± 40.0	20.9 ± 15.4

10.37

Strategy of quantitative assessment of myocardial perfusion and coronary flow reserve using intravenous Tl-201 and micro-SPECT in rat.

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Objectives: Tl-201 has a high first-pass extraction fraction, and is known to be an ideal tracer for quantitation of myocardial blood flow (MBF) and coronary flow reserve (CFR) in vivo. Previous studies demonstrated that a single tissue compartment model is feasible to estimate MBF and CFR, as well as the potassium potential, and that regional radioactivity distribution can be determined accurately using a 3D-OSEM reconstruction for a projection data obtained with a specially designed orbit which satisfies the completeness of the Radon transform (Zeniya et al., EJNM 2004). This study was aimed at developing and validating a strategy for quantitative assessment of MBF and CFR in rat using Tl-201 and micro SPECT. In particular, accuracy and feasibility of a realistic method that determines the individual arterial input function has been evaluated.

Methods: Arterial input function was determined in 8 rats. Sixteen samples were obtained from the femoral artery following slow infusion (2 min) of 37 MBq Tl-201 into the tail vein until 60 min, and their whole blood and plasma radioactivity concentrations were measured using a well counter. The plasma separation was carried out immediately after the withdrawal (<15 sec). Both the whole blood and plasma radioactivity concentration curves were averaged, and accuracy of using this standardized curve calibrated with a single blood sample was evaluated. The optimal calibration time was then determined so as to provide the best agreement of the area under the curve (AUC) between the estimated (EIF) and the individual input functions (IIF). Monte Carlo simulation was also carried out to evaluate the accuracy of MBF determined with EIF.

Results: Plasma/whole blood ratio was >1 before 1 min of Tl-201 injection, and decreased upto 0.5 at 3 min. This ratio then increased gradually and reached to a constant level of approximately 0.8. AIC of EIF showed the best agreement with that of IIF when calibrated at 10 min (standard deviation of 9.5%). MBF values determined with a compartment model analysis using EIF also agreed with those using IIF when calibrated at 10 min, with the accuracy of 2.9 ± 11%. Using this standardized input function, a dynamic micro-SPECT study on a rat at rest provided regional MBF of 0.78 ml/min/ml without the partial volume correction, and the distribution volume of 76 ml/ml, which are within an acceptable range of a literature value.

Conclusion: Determination of IIF is feasible only with a single blood sampling, which is feasible for assessing physiological alterations of MBF with minimal invasive procedures.

10.38

Ammonia-PET perfusion scan in the assessment of the endothelial function in patients with primary antiphospholipid syndrome.

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Positron emission tomography (PET) allows a non invasive absolute quantification of the coronary blood flow. The antiphospholipid syndrome (APS) has been recognized as an endotheliopathy with thrombotic microangiopathy which results of the interaction between antibodies, endothelial cells and platelets. By the Cold Pressor Test (CPT) with PET, it is possible to evaluate the endothelial function. CPT induces release of norepinephrine by sympathetic stimulation. Norepinephrine causes vasoconstriction on smooth muscle cell, however at the same time it is opposed by the release of nitric oxide from the endothelium as a result of an alpha2-adrenoceptor-mediated-stimulation, which causes endothelium mediated vasodilatation. Therefore when endothelial function is altered vasoconstriction from smooth muscle cells predominate over the vasodilatation stimulus from the endothelium.

AIM: To evaluate endothelial function in patients with primary antiphospholipid syndrome using the cold pressor test.

METHODS: Twelve consecutive patients with diagnosis of antiphospholipid syndrome were studied. All of them underwent into a three phase (rest-CPT-stress) PET protocol using a total of 60mCi of 13NH3 (ammonia) radiotracer, 20mCi for each phase. CPT was performed immersing one hand in a 5 centigrade water for about two minutes, applying the radiotracer at the end of the first minute. The stress test was performed using adenosine (140mcg/kg/min/6min). Coronary blood flow (CBF) was calculated using the polar flow UCLA program. Coronary flow reserve (CBF at stress/CBF at rest) and the endothelial dependent vasodilatation index (CBF during CPT/CBF at rest) were determined. Results obtained in the antiphospholipid syndrome patients group (ASG) were compared with the results obtained in a healthy volunteers group (HVG).

RESULTS: A total of twelve patients (8 females and 4 males) were studied. The CBF obtained in the ASG were; 0.540 ml/kg/minute at rest, 0.626 ml/kg/minute at CPT and 1.742 ml/kg/minute at stress. Neither rest CBF nor stress CBF were statistically different among both groups, therefore, coronary flow reserve also was similar in both groups. But when the endothelial dependent vasodilatation index was obtained (1.15 for the ASG and 1.45 for the HVG), a significant difference ($p<0.05$) was found.

CONCLUSION: Patients with primary antiphospholipid syndrome develop endothelial dysfunction which could be identified using a CPT ammonia-PET scan.

10.39

MIBI uptake in myocardial volume (MIV) may help to distinguish the degree of segmental dysfunction but not the viability.

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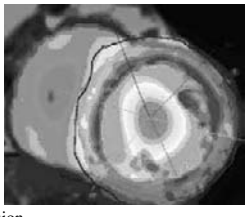
Background: There are several modalities that can diagnose myocardial viability but so far only the myocardial perfusion imaging SPET is the one widely used in clinical practice. The aim of the study was to evaluate the new index of MIBI uptake in myocardial volume calculated from the magnetic resonance imaging (MRI).

Methods: We analysed 685 myocardial segments assessed in gated SPET and MRI(6 segments in each short axis slice) obtained from 18 patients with ischemic left ventricular dysfunction. Myocardial wall function was evaluated using fused images of diastolic and systolic phases of cine MRI. MIV perfusion (counts/mm3) in each myocardial segment was evaluated by fusion of diastolic phases of cine MRI and GSPECT. PMOD and HERMES were used as the fusion software. The segmental motion was assessed in cine MRI and the delayed enhancement imaging (segmented inversion recovery gradient echo pulse sequence 10-20 min after gadolinium administration) served to exclude or confirm the viability of the dysfunctional segment.

Results: Dysfunctional segments had significantly less MIV (MIV = 4.63 SD 1,58) than normal segments (MIV = 8.86 SD 2.77) ($P<0.05$ for comparison in each wall). The Receiver-Operating-Characteristic curve showed that the MIV value of 5 (counts/mm3) discriminates between normal and dysfunctional segments with a 95 % accuracy. There was no significance difference in MIV between viable and non-viable dysfunctional segments defined by DE MR.

Conclusion: MIBI uptake in myocardial volume (MIV) may help to distinguish the degree of segmental dysfunction but not the viability.



short axis slice image fusion

10.40

Comparison of gated spect imaging and 2-D echocardiography in ischemic dilated cardiomyopathy.

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Background: In coronary artery disease (CAD), gated SPECT (GSPECT) is widely used for the assessment of left ventricular ejection fraction (LVEF) and regional wall function (motion and thickening). However a number of factors may affect the reproducibility of these measurements, namely ventricular enlargement.
We analyse the information obtained from GSPECT in patients with ischemic dilated cardiomyopathy (ICD) and correlate it to 2-D echocardiography, a technique used in daily practice to evaluate left ventricular function.
Methods: 19 patients (16 male), mean age 69.3 years, admitted in our hospital department for acute coronary syndromes, were studied. Patients had extensive CAD on catheterization (47% with three-vessel disease). 2-D echocardiography was performed 5.5 ± 3.3 days from GSPECT. All patients underwent one-day stress-adenosine Tc-99 tetrofosmin GSPECT. Summed stress (SSS) and summed difference scores (SDS) were determined using the 17 segment (0-4 perfusion scale) model. LVEF, wall motion (WM) and wall thickening (WT) scores were calculated from post-exercise gated images.
We examined the correlation between LVEF, WM and WT scores derived from GSPECT and LVEF and WM score obtained from 2-D echocardiography.
Results: GSPECT revealed reduced ejection fraction (32.8 ± 8.2%) and ventricular enlargement (EDV 170 ± 50 ml; ESV 116 ± 40 ml) in all patients. An abnormal perfusion study (SSS ≥ 4) was observed in all cases, with reversible defects (SDS ≥ 4) in 10 (53%) of patients. 2-D ecocardiography estimated ejection fraction was higher (44.1 ± 11.4%), even in patients with no ischemia (fixed defects) in GSPECT. We found no significant correlation between LVEF estimations from the two techniques (r=0.47). In WM score analysis significant correlation was present only in the lateral segments (r=o.73; p<0.01). Similar results were observed comparing WT score obtained from GSPECT to WM score in 2-D echocardiography (r=0.87; p<0.01).
Conclusion: In our sample of patients with IDC, estimations of LVEF and WM score analysis by GSPECT and 2-D echocardiography were not significantly correlated. These data are important in clinical practice and must be confirmed in future studies.

10.41

Gated SPECT-methods variability for ejection fraction determination.

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Aim: Gated SPECT is recognized as a very important additional value in the information of myocardial perfusion studies. In the last years, several packages to calculate global LVEF have been available. Our aim was to compare 3 different methods: QGS(Germano), S(Smith) and 4D-MSPECT(4D)(Hamilton).
Methods: The images were acquired in two different GE cameras (MG and VG). 46 patients were studied: MG (24): 18 normal; VG (22): 19 normal.
Processing was done in a GE Xeleris computer, using the 3 methods. EDV and ESV were also determined by QGS and 4D. According to QGS, two groups of patients were extracted: Normal(Np)(LVEF =50%) and dilated(Dp)(LVEF < 50%, EDV 130ml).
Considering QGS as a standard, we calculated the differences' average and the correlation coefficient (CC) for LVEF, EDV and ESV, for the two cameras.
Results: - About LVEF: the table shows that there are statistically significant(SS) differences(dif) between LVEF by S and QGS for Np, but not for Dp. Between 4D and QGS, SS dif may be observed for Np(VG) and for Dp(MG). The CC between the dif of LVEF by S-QGS and 4D-QGS were, for Np, 0.40 and 0.53 (MG and VG) and for Dp, 0.20(MG). About volumes: (a) For Np, one has also observed a high CC between EDV by 4D and QGS: 0.97(MG) and 0.98(VG). For ESV, CC's were still high: 0.92 and 0.95 (MG and VG). However, the dif between volume values, obtained by the two methods, were SS(pMG<0.01 and pVG<0.05 for EDV and pMG<0.1 and pVG<0.01 for ESV). (b) For Dp, the dif between EDV by 4D and QGS were not SS. The same happened for ESV. For MG, the CC between EDV by 4D and QGS was 0.68 and 0.98 between ESV.
Conclusions: Results indicate several significant dif between the proposed methods. We think that further studies are necessary in order to fully test and validate the methods proposed in the literature, in order to guarantee that software variabilities will not compromise quantitative data that is important for clinical patient management.

table

Camera	Normal	Pathological Dilated
GE MG	(n = 18) 12 ± 17 | 0 ± 9---------- (p < 0.01 | p = ns)	(n = 6) 21 ± 25 | −4 ± 2---------- (p = ns | p = < 0.05)
GE VG	(n = 19) -5 ± 4 | 5 ± 5---------- (p < 0.01 | p < 0.01)	(n = 2) -1 ± 10 | 4 ± 1---------- (p = ns | p = ns)

Averages and SD (%) of LVEF differences for (S-QGS) | (4D-QGS) and corresponding p-values.

10.42

Quantitative low dose dobutamine gated perfusion SPECT.

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Background: Quantitative assessment of regional left ventricular function (RF) by gated perfusion tomography (GSPECT) is now feasible using automated software. We hypothesized that the combination of low dose dobutamine with GSPECT would be feasible and potentially improve objectivity of assessment of RF over visual methods.
Methods: A regional specific normal range for RF (wall motion-WM and wall thickening-WT) using quantitative GSPECT was developed from 20 patients with normal RF by echocardiography. In 23 patients, GSPECT was performed at rest (2-detector camera, 20s/stop, 30 mCi rest injection of Tc-99m tetrofosmin or sestamibi) and during low dose intravenous infusion of dobutamine (5 and 10 mcg/kg/min). For acquisiton during dobutamine, acquisition was modified to 10s/stop. Automated software (QGS) was applied to the processed data sets after filtered backprojection and re-orientation.
Results: In 2 patients, the protocol was terminated after completion of acquisition at 5 mcg/kg/min, due to breathlessness. In the remaining 21 patients, the protocol was successful with no complications. Of the 21 patients, 8 had normal stress-rest perfusion and normal rest WM, while 13 had abnormal rest WM and perfusion studies due to prior infarct. GSPECT WM values were higher at rest in the 8 normal patients compared to the 13 abnormal patients (rest WM 7.2±2.3mm vs 3.8±2.7mm, p<0.001) and increased with dobutamine infusion to a higher value at 10 mcg/kg/min (WM 10.2+3.2mm in normals vs 4.0±2.9mm in abnormals, p<0.001, mean WM increase with dobutamine 2.9+2.1mm vs 0.2+1.8mm, p<0.001). GSPECT WT values were higher at rest in the 8 normal patients compared to the 13 abnormal patients (rest WT 41.9±20.1% vs 18.4±13.1%, p<0.001) and increased with dobutamine infusion to a higher value at 10 mcg/kg/min (WT 66.2+31.6% vs 20.3+15.0%, p<0.001, mean WM increase with dobutamine 24.3+16.2% vs 1.9+8.5%, p<0.001). These increases in GSPECT values from rest to peak dobutamine dose were statistically significant using a paired t-test in normal patients for both WM and WT (p<0.001), and also in abnormal patients for WT (p<0.001) but was of borderline significance for WM in abnormal patients (p = 0.055).
Conclusion. Automated quantitative GSPECT in combination with low dose dobutamine appears feasible and may have the potential to improve objectivity of RF assessment.

10.43

Causes of discrepancy between ejection fraction estimated by echocardiography and the obtained by gated-SPECT.

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Introduction. Left ventricle ejection fraction (EF) is a very important parameter in our patients. There are different techniques to calculate it. Sometimes there is disagreement between EF estimated by TTE and the obtained by Gated SPECT (GS). We sought to analise which factors could be associated with this disagreement.
Patients and Methods. We compared restrospectively the EF obtained by GS and by TTE in 268 patiens along one year. We excluded the following cases: 1) More than six months between both tests, 2) inadequate echocardiographic window and 3) significant clinical changes, such us an acute myocardial infarct, between both tests. One hundred and seventy four patients were men, mean age 63,9±10,8 years; there were 110 treadmill exercise tests and 158 pharmacological stress tests. EF by TTE was classified, subjetively, as normal or depressed (mild, moderate or severe dysfunction). Four similar groups were established depending on the Gated-SPECT EF (>50% normal, 40-49% mild dysfunction, 30-39% moderate dysfunction,>30% severe dysfunction). We studied, such us theorical causes for disagreement, the following parameters: ancient myocardial infarct, left ventricle enlargement (more than 5.8 cm telediastolic diameter), bundle branch block, sex, type of test (treadmill vs pharmacological stress) and cardiac rhythm (sinus rhythm or atrial fibrillation/flutter).
Results.
In 211 cases (79%), there was agreement between both explorations. On the other hand, there was disagreement in 57 cases (21%). One hundred and two patients had an ancient myocardial infarct (38%). There were 46 cases with left ventricle enlargement (17.1%), 46 cases with bundle branch block. There was 34.3% of cases with discrepancy between both tests in the myocardial infarct group, whereas patients without infarct had only 13.2% of cases with discrepancy. (p<0.0001). Left ventricle enlargement was associated with 34.7% of cases with discrepancy. Patients without left ventricle enlargement had 18.1% of cases with discrepancy. (p<0.01). We did not found significant association for the bundle branch block, sex, type of test and presence of atrial fibrillation/flutter.
Conclusions. 1)The presence of myocardial infarct or left ventricle enlargement is associated with more discrepancy between both explorations. 2) The bundle branch block was not associated with more discrepancy, at least in this group of patients. 3) It would be necessary more studies, to know the accuracy of this explorations in the established situations.

10.44

A new automated method for quantification of gated myocardial perfusion SPECT based on a 3-dimensional heart shaped model.

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We have developed a new automated method based on heart shaped model for quantification of left ventricular (LV) function from gated myocardial perfusion SPECT images. The method was optimised using a digital heart model.

Methods: This new method for cardiac function evaluation (CAFU) uses an active shape algorithm. The geometric approximations are based on a human heart model containing a statistical information about the LV shape variability in 50 patients. The dynamic anthropomorphic computer phantom NCAT v1.12 and the Monte-Carlo program SIMIND were used to simulate gated eight-frame myocardial perfusion SPECT studies with five different LV volumes. Enddiastolic volume (EDV) ranged between 57-186 ml and endsystolic volumes (ESV) between 22-72 ml. The ejection fraction (EF) in all studies was 61%. The CAFU algorithms were adjusted based on the results from the analysis of the phantom. Thereafter, CAFU was applied on rest gated SPECT studies from ten routine patients selected with EDV approximately in the same range (50-200 ml) as in the simulated studies. The simulated studies and patient studies were quantified using CAFU and Cedar-Sinai quantitative gated SPECT (QGS) program.

Results: The CAFU calculated EF values in the range 58-62%, for the phantom studies. The ESV by QGS was clearly overestimated in three largest phantom studies with calculated values 57, 83 and 122 ml (true values 43, 59 and 71 ml). The EF calculated by QGS was as low as 39% compared to the true EF of 61% for the largest phantom study. In the patient studies, a similar relation between CAFU and QGS was seen as in the phantom studies, i.e. much larger estimations of ESV for QGS compared to CAFU, resulting in lower estimations of EF.

Conclusion: The new automated method CAFU showed to be a promising tool for quantification of LV EF, EDV and ESV.

10.45

Relationship of transient ischemic dilation in dipyridamole myocardial perfusion imaging and ischemic stunning: evaluated by thallium-201 gated SPECT.

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Background and Purpose: Transient ischemic dilation (TID) is occasionally observed in exercise or pharmacologic stress myocardial perfusion imaging. This study assessed whether TID is related to ischemic stunning.

Methods: Ninety-two patients undergoing dipyridamole Tl-201 gated SPECT for evaluation of coronary artery disease were included. Summed gated images were processed by QPS, and LV volumes of DS and RD images were generated. TID was defined as the ratio of DS and RD LV volumes ≥ 1.22. The global wall motion was expressed by summed motion score (SMS), which was automatically generated by QGS. LV ejection fraction (LVEF), end-diastolic volume (EDV) and end-systolic volume (ESV) were also generated by QGS.

Results: Of the 92 patients, 16 patients had TID. Functional variables of patients with and without TID were shown in Table 1. Patients with TID had a significant lower mean LVEF on DS images than on RD images ($P = 0.001$). Patients without TID had a borderline higher mean LVEF on DS than on RD ($P = 0.05$). Patients with TID had a significant higher mean SMS on DS than on RD ($P < 0.001$), but patients without TID did not. In patients with TID, the EDV and ESV were both significantly larger on DS images than on RD images ($P < 0.001$). The mean rEDV (ratio of EDV between DS and RD) and rESV (ratio of ESV between DS and RD) were 1.18 ± 0.11 and 1.51 ± 0.32, respectively ($P < 0.01$). In patients without TID, the ESV was significantly smaller on DS images than on RD images ($P = 0.02$), but there was no significant difference in EDV between DS and RD.

Conclusion: TID in dipyridamole myocardial perfusion imaging was significantly correlated to the decrease of LVEF and worsening of wall motion after stress. Enlargement of ESV secondary to dipyridamole-induced systolic dysfunction (ischemic stunning) should be an important factor resulting in TID.

Table 1.

	TID(+)			TID(−)		
	DS	RD	P value	DS	RD	P value
LVEF (ml)	56.2 ± 13.7	64.4 ± 12.4	0.001	65.0 ± 11.8	63.6 ± 12.2	0.05
SMS	16.9 ± 13.9	8.8 ± 7.9	<0.01	5.5 ± 9.1	6.0 ± 8.9	NS
EDV (ml)	69.9 ± 32.3	59.1 ± 25.8	<0.001	67.4 ± 27.1	67.8 ± 30.5	NS
ESV (ml)	32.3 ± 21.7	22.7 ± 16.4	<0.001	25.6 ± 17.6	27.2 ± 20.5	0.02

Functional variables of patients with and without TID assessed by gated SPECT

10.46

Evaluation of leg muscle perfusion by 99mTc sestamibi scintigraphy in patients with unilateral chronic venous insufficiency and acute deep venous thrombosis.

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Although muscle perfusion has been evaluated with the use of 99mTc sestamibi in peripheral arterial vascular disease, there is no study in venous disease.It is known that raised venous pressure directly influes the microcirculation and may be cause tissue hypoxia.

Material and **Methods.**This study included 11 patients with unileteral chronic venous insufficiency (CVI) and 13 patients with unileteral acute deep venous thrombosis(DVT) of the lower limbs. Patients underwent Doppler studies,99mTc red blood cell and 99mTc sestamibi imaging. Arterial and metabolic diseases were excluded from study. Post-therapy images were also obtained in 11 pts. All study patients were in a fasted state and had rested for at least 15 min before the intravenous administration of 99mTc-sestamibi [555MBq]. Percent of difference of uptake (DU%) between affected extremitiy and opposite normal side was calculated by semiquantitative analysis. DU% values >10 was accepted as abnormal.

Results: There was different 99mTc sestamibi uptake patterns regarding normal, increased and decreased uptake in thighs and calves segments. Of 11 pts with CVI, six had normal perfusion in both thigh and calf region, 3 had normal perfusion in thigh and increased uptake in calf. One had increased uptake in thigh and normal uptake in calf while there was increased perfusion in both thigh and calf in one pt. Normal uptake values were seen in 2 of 4 pts after therapy. Of 13 pts with DVT, while 6 pts had normal uptake in both thigh and calf, one pt had decreased uptake in thigh and normal uptake in calf region. In 2 pts, there was normal perfusion in thigh and increased perfusion in calf. While one pt had decreased uptake in both thigh and calf, one had increased uptake in both thigh and calf. Of other 2 pts, one had increased uptake in thigh and normal uptake in calf, and other had decrease uptake thigh and increased uptake in calf. Whereas normal uptake were observed in 2 of 7 pts after therapy, there was different uptake patterns in other 5 pts. No correlations were found between durations of disease, girth measurements of extremity and DU% values. There was discordant results between Doppler and scintigraphy patterns in some pts.

Conclusion: We think that pre-and post-therapy different uptake patterns in CVI and DVT are due to abnormalities of microcirculation which are possible related with edema, hyperemia, functional shunts and tissue hypoxia

10.47

Reversibility of systolic and diastolic function abnormalities by low dose dobutamine radionuclide ventriculography.

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Background

In patients with coronary artery disease (CAD) and severe LV dysfunction, the determine the presence of metabolically active yet mechanically dysfunctional myocardium is an important distinction.Identify those patients most likely to have recovery of ventricular function, alleviation of symptoms and improvement in outcome postrevascularization. Most studies have focused on LV systolic function instead of systolic and diastolic function. It would appear likely that a more complete study of ventricular function would be useful The aim of the study was to evaluate the ability of low dose dobutamine radionuclide ventriculography (RNV) to detect contractile reserve in patients with CAD.

Methods

The study group consisted of 22 consecutive patients (5 female, 17 male, mean age 61.04 ± 3 years) with previous myocardial infarction and resting regional dyssynergy, in whom diagnostic cardiac catheterization revealed significant coronary artery stenosis suitable for angioplasty. Each patient underwent equilibrium 99m-Tc radionuclide ventriculography which was performed at rest and low dose dobutamine infusion (up to 10 mcg/kg/min). Ejection Fraction (EF), Peak Ejection Rate (PER), Time to Peak Ejection Rate (TPER), First third Ejection Fraction (1/3ER), Peak Filling Rate (PFR), Time to Peak Filling Rate (TPFR), First third Filling Rate (1/3FR) values were calculated for both right and left ventricles. Results

Nine patients had one-vessel disease, 5 had two-vessel disease and 8 had three-vessel disease. 11 patients with one and two vessel disease were responders during low-dose dobutamine (78.5%), whereas 3 patients weren't responders (21.4%). EF and 1/3ER significantly increased after low dose dobutamine compared with baseline values ($p<0.05$ and $p<0.05$, respectively)

In patients with three-vessel disease, there was an increase in EF, PER, PFR, and 1/3FR significantly increased after low dose dobutamine compared with baseline values ($p<0.05$, $p<0.05$, $p<0.001$, $p<0.05$ respectively)

Conclusion

Low dose dobutamine induced higher rate of positive responses during RNV. Evaluation of systolic and diastolic function may be useful in detecting subtle abnormalities in ventricular function in patients with CAD

10.48

Does motion correction of myocardial perfusion SPECT studies influence the clinical outcome of the study?

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Introduction: Patient motion during myocardial perfusion SPECT (MPS) acquisition can contribute to the generation of artefacts in the reconstructed images, which may decrease the accuracy of image interpretation. This study was performed to determine whether automated motion correction (MC) available with the AutoSpect Plus algorithm has a significant effect on the clinical outcome of MPS when reported by an experienced observer.
Method: 60 patients were selected retrospectively from the clinical patient population. By observing the raw data, patients were visually classified into 3 categories: 0 (n=15), 1 (n=15) and 2 (n=30) pixel motion. Each study was reconstructed with and without MC. For each reconstructed stress and rest image, automatic quantification of myocardial perfusion uptake was performed using QPS, where an uptake score (0=100-70%, 1=69-50%, 2=49-30%, 3=29-10%, 4=9-0% uptake) was assigned to each segment of a 20-segment model. In addition, MC and non-MC studies were randomised and corresponding stress and rest images presented to an experienced observer who assigned a defect classification (normal, fixed, mixed, reversible) to each segment of a 9-segment model. 30 studies were scored twice to assess intra-observer variability.
Results: Agreement of automatic uptake scores and visually scored defect classification between MC and non-MC studies were assessed by unweighted kappa statistics. Kappa values show very good agreement in automatic uptake scores and good agreement in visual defect classification between MC and non-MC studies for all motion categories.
Conclusion: The application of the MC algorithm does not significantly change the clinical outcome of MPS when reported by an experienced observer for the degree of patient motion observed routinely in the clinical patient population in our department.

Table 1. Kappa analysis

	Automatic Uptake Score MC vs non-MC	Visual Defect Classification MC vs non-MC
0 pixel motion	0.984	0.761
1 pixel motion	0.926	0.771
2 pixel motion	0.878	0.765
intra-observer		0.825

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The effect of attenuation on ejection fraction and volumes values in women calculated from gated SPECT data.

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Ejection Fraction (EF) values obtained from gated SPECT data are generally significantly greater for women compared to men and ventricular volumes lower. This necessitates different normal ranges for men and women. It has been suggested that the differences are due to breast attenuation in women as differences in defining the ventricular edges in the presence of attenuation may result in reduced volumes and thus higher EF values in women. To investigate the effect of attenuation we looked at EF and volumes obtained from rest 99mTc tetrofosmin gated SPECT in 464 female patients. EF and ventricular volume values were calculated using QGS. All patients had both a low likelihood of coronary artery disease and ventricular dysfunction, all had normal stress-rest perfusion images and normal wall motion on gated SPECT imaging. Patient weight ranged from 38 to 125 Kg, BMI from 16.9 to 61.1 and mean age was 61 ± 10 years. Mean EF was 61.4 ± 6.5, mean end diastolic volume (EDV) 90 ± 22 ml and mean end systolic volume (ESV) 36 ± 13 ml. There was no correlation between EF and BMI (r = −0.19) or between EF and body surface area (r = −0.25). To look further at any possible effects of attenuation we divided the patients into two groups, those who were obese with a BMI of more than 30 (n = 164) and those with a BMI of less than or equal to 30 (n=300). If attenuation results in lower volumes and higher EF values we would expect a significant difference in EF and volumes between these two groups. However mean EF in the obese group was 59.0 ± 6.3 which was not significantly different from the non obese group value of 60.9 ± 5.5. Similarly there was no significant difference in either EDV or ESV between the two groups. Looking at a subgroup of women with a BMI 25 (n = 108) also showed no significant difference in either mean EF (62.2 ± 7.0), mean EDV (85 ± 20 ml) or mean ES volume (33 ± 13 ml). It has been noted that QGS may result in erroneous values if the ventricular volume is small (EDV < 70ml). We found a total of 78 patients with low EDV (15 in the obese group and 63 in the non obese group). Excluding these patients did not significantly affect the mean EF or volume values. We conclude that in a large group of female patients with normal ventricular function there is no evidence that attenuation causes changes in calculated EF and volume values.

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Display of myocardial motion by projecting specific components of the 3D motion of myocardial elements on the plane of origin.

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The analysis and display of myocardial kinetics is generally based on a-priori assumptions about the direction of the myocardial displacement (centripetal-centrifugal) and about the identity of the myocardial segment moving along that direction. In addition, many displays are slice displays, in which the displacement of myocardial segments between slices is not taken into account. The purpose of this study was to devise an analytical tool in which the motion of myocardial elements in 3D space can be measured and then represented as projection on the original location plane, therefore eliminating artifacts from off-plane motion. Furthermore, components of the motion vectors can be reanalyzed a posteriori e.g. for centripetal-fugal and torsion (see figure). The data are masked gated myocardial perfusion volumes. Cumulative activities across the image are computed in x, y, and z, and image elements are defined by their percentile ranking in cumulative activity in x, y, and z. Myocardial elements whose motion in "x" will be analyzed, are identified by their percentile value in y and z. After this the motion of any voxel is defined as the vector sum of the motions in x, y, and z. The pathway is akin to that demonstrated with tagged MRI.
A posteriori analysis based on specific motion (e.g. centripetal-fugal and torsion) show a tendency for orderly motion except in myocardium regions with abnormal perfusion. Specifically, disorganization of specific motion is present in fixed defects and to a lesser degree in some profound but transient defects (even in the corresponding resting image) Analysis of the motion of individual myocardial elements is shown to be possible and to provide a more sensitive measure of myocardial health.

figure

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Measurement of right and left ventricular ejection fraction and volume with tomographic radionuclide ventriculography: validation using electron-beam computed tomography.

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Aim: a readily available, accurate and non-invasive method to measure right (R) and left (L) ventricular (V) ejection fraction (EF) and end-systolic (ES) and end-diastolic (ED) volume (V) would be clinically valuable. Tomographic radionuclide ventriculography (TRNV) may fulfill this goal.
Method: in order to establish a method that utilized TRNV to measure RV and LV EF, ESV and EDV and to validate that method, TRNV (16-frames/cardiac cycle, 180° rotation, 30 images/rotation, and 60 sec/stop, standard erythrocyte labeling) was obtained concurrently with 35 assessments of RV and LV EF, ESV and EDV measured by electron beam computed tomography (EBCT). The transaxial TRNV images were reconstructed into 2-pixel thick, horizontal long-axis and short-axis slices and ES and ED RV and LV regions of interest were traced from the former and the latter respectively and RV and LV EF, ESV and EDV were determined using pixel number and dimension.
Results: in the establishment phase of this study, 18 paired TRNV and EBCT assessments were compared: when TRNV was compared to EBCT, RVEF (0.40±0.12 vs 0.43±0.15, p=0.14) and LVEF (0.56±0.08 vs 0.61±0.07, p=0.04) were less and RVESV (168±90 vs 137±85, p=0.002), RVEDV (265±104 vs 219±99, p=0.0005), LVESV (74±24 vs 46±19, p<0.0001) and LVEDV (170±38 vs 113±40, p<0.0001) were greater. Since the observed TRNV volumes were greater than the EBCT volumes, it was hypothesized that the regression equations relating EBCT (Y) and TRNV (X) RV (Y=0.87X+10.9, r=0.94) and LV (Y=0.72X-9.60, r=0.89) volumes would correct the observed TRNV. This method was validated in the remaining 17 paired TRNV and EBCT studies: no differences were evident between corrected-TRNV and EBCT in RVEF (0.44±0.11 vs 0.43±0.11), LVEF (0.60±0.09 vs 0.59±0.07), RVESV (133±61 vs 135±61), RVEDV (231±76 vs 229±70), LVESV (49±20 vs 50±18) and LVEDV (121±29 vs 119±30).
Conclusion: the TRNV method proposed in this study was a readily available, accurate and non-invasive means to measure RV and LV EF, ESV and EDV.

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A stochastic approach for quantification of hotspot focal uptake from cardiac SPECT/CT images: a canine validation.

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Aim: To validate our approach for quantification (quant) of targeted "hotspot" (HS) images using a canine model of myocardial infarction (MI). Our method was incorporated with dual-isotope SPECT to quant targeted HS activity in the myocardium with a targeted Tc99m labeled tracer, where Tl201 was used for reference perfusion (RP). Images incorporated a Tc99m point source as a known reference. Procedure of estimating HS normal limits was considered as a stochastic process with random variables of RP and HS. Maximization of mutual information of RP and HS count profiles was adapted into the estimation. Abnormal HS uptake resulted from radiotracer accumulation in MI regions. Dogs were injected with Tc99m labeled agent targeted at avb3 integrin (n= 2) or matrix metalloproteinase (n= 2). Tc99m/Tl201 dual-isotope SPECT/CT images were acquired at multiple time points of post MI. Images (n= 6) were reconstructed via FBP and OSEM with attenuation correction (AC)and OSEM without AC (NC). Absolute HS uptake was quantified (mCi) and normalized by the injected dose (% inject dose). Dogs were sacrificed for tissue well-counting to determine true uptake. SPECT-derived indices of uptake were compared with true measured uptake. Fig.'s 1 and 2 show HS uptake and % inject dose quantified from FBP, NC and AC SPECT images. Image with AC resulted in higher quant HS uptake and % inject dose. Mean absolute errors of quant HS uptake were small (FBP: 0.031±0.042; NC: 0.027±0.04; AC: 0.015±0.017 mCi). Errors for estimated % inject dose were also small (FBP: 0.12±0.147; NC: 0.105±0.143; AC: 0.058±0.061 %). SPECT images with AC resulted in the least errors. Conclusions: Our approach provided a reliable estimate of focal myocardial uptake. AC improved the precision of HS quant from cardiac SPECT/CT.

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Predictors of differences in left ventricular ejection fraction and volumes determined by quantitative gated rest and post-stress Tc-99m sestamibi SPECT.

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Background: Quantitative gated SPECT (QGS) is useful in evaluating left ventricular ejection fraction (LVEF), end systolic volume (ESV), and end diastolic volume (EDV). Less is known regarding factors potentially associated with differences in LVEF and volumes obtained from QGS at rest and post-stress.
Methods: Using a 2-day protocol, SPECT data was obtained at rest and post-stress with high dose (25 mCi) Tc-99m sestamibi bolus. LVEF, ESV, and EDV were derived from automated Cedars-Sinai QGS software. Of 100 patients prospectively studied, 92 studies were technically adequate. Delta LVEF was defined as QGS post-stress LVEF minus QGS rest LVEF. Delta ESV and delta EDV were similarly defined.
Results: LVEF, ESV, and EDV rest and post-stress were highly correlated(Table 1). LVEF and EDV were higher at rest than post-stress for the entire study population. Summed difference score (SDS)>0 was significantly associated with negative delta LVEF (p=0.02). Mean LVEF post-stress in ischemic patients was 55.0% vs 61.1% in nonischemic patients (p<0.01). SDS>0 was associated with increased delta EDV (p<0.01). Mean post-stress EDV in ischemic patients was 94.4 cc vs 80.1 cc in nonischemic patients (p<0.01). SDS0 was associated with increased delta ESV (p<0.01). Mean post-stress ESV in ischemic patients was 43.4 cc vs 32.1 cc in nonischemic patients (p<0.01). In a multivariate linear regression model which considered gender, age, diabetes mellitus, history of myocardial infarction, and type of stress test, SDS>0 was independently predictive of negative delta LVEF.
Conclusion: QGS post-stress is highly correlated with QGS rest for LVEF, EDV, and ESV. The mean QGS rest LVEF and rest EDV are significantly higher than post-stress LVEF and post-stress EDV. Stress-induced ischemia is predictive of lower QGS post-stress LVEF which may represent post-stress ischemic LV dilatation with increased post-stress ESV and EDV.

Table 1

	Rest	Post-Stress	r	p	Mean delta	p
LVEF (%)	61.1	59.2	0.89	<0.01	−1.9	<0.01
EDV (cc)	88.1	84.8	0.88	<0.01	−3.3	<0.01
ESV (cc)	35.4	35.8	0.93	<0.01	+0.4	NS

NS=Not significant

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Differential effects of filtering and attenuation correction on assessments of left ventricular volumes and ejection fraction from ECG-gated SPECT: evaluation of four different software.

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Effects of different (diff) filtering associated with attenuation correction (AC) on left ventricular (LV) volumes and ejection fraction (EF) using diff quantification (quant) software are unknown. 36 normal volunteers (19 males, 17 females, age 39±11) had stress MIBI SPECT studies. ECG-Gated SPECT images were acquired using a hybrid SPECT/CT camera and were reconstructed by the OSEM with AC and without AC (NC). 3D Butterworth filter with 3 diff cutoff frequencies: 0.2x, 0.4x, and 0.6x Nyguist, was used to filter SPECT images. End diastolic volume (EDV), end systolic volume (ESV) and LVEF were computed using four diff software: Wackers-Liu CQ (WLCQ), Quant Gated SPECT (QGS), Emory Cardiac Toolbox (ECTB), and 4DMSPECT(4DMS). Differences of EDV, ESV and LVEF using 3 diff cutoffs were computed in-pair (n= 36 subjects x 3 cutoffs). WLCQ LVEF from NC images and 4DMS LVEF from AC images were not affected by filtering (Table 1). WLCQ resulted in least variation in LVEF (Fg. 1) and ECTB yielded smallest diff in EDV (Fg. 2) and ESV (Fg. 3).

Table 1. P-values of ANOVA for LVEF, EDV, ESV calculated from AC/NC SPECT images filtered with 3 different cutoff frequencies and using 4 software (ns: not significant)

Software	LVEF_NC	LVEF_AC	EDV_NC	EDV_AC	ESV_NC	ESV_AC
WLCQ	ns	0.03	ns	0.04	ns	ns
QGS	<0.001	0.02	0.002	0.002	<0.001	0.006
ECTB	<0.001	0.005	ns	ns	ns	ns
4DMS	0.003	ns	<0.001	<0.001	<0.001	<0.001

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Differential effects of filtering and attenuation correction on assessments of left ventricular volumes and ejection fraction from ECG-gated SPECT: evaluation of four different software.

V. Tsatkin[1], F.J.TH. Wackers[2], Y.H. Yi-Hwa Liu.[2] [1]Yale New Haven Hospital, Nuclear Cardiac Imaging Laboratory, New Haven, CT, United States, [2]Yale University, Internal Medicine (Cardiology), New Haven, CT, United States

Effects of different (diff) filtering associated with attenuation correction (AC) on left ventricular (LV) volumes and ejection fraction (EF) using diff quantification (quant) software are unknown. 36 normal pts (19 M, 17 F, age 39±11) had stress MIBI studies. Gated SPECT images were acquired using a hybrid SPECT/CT camera and were reconstructed by OSEM with AC and without AC (NC). Butterworth filter with 3 diff cutoff frequencies: 0.2x, 0.4x, and 0.6x Nyguist, was used to post-filter images. End diastolic volume (EDV), end systolic volume (ESV) and LVEF were computed using four diff software: Wackers-Liu CQ (WLCQ), Quant Gated SPECT (QGS), Emory Cardiac Toolbox (ECTB), and 4DMSPECT(4DMS). Differences of EDV, ESV and LVEF using 3 diff cutoffs were computed in-pair (n= 36 subjects × 3 cutoffs). WLCQ LVEF from NC and 4DMS LVEF from AC were not affected by filtering (Table 1). WLCQ resulted in least variation in LVEF (Fg. 1) while ECTB yielded smallest diff in EDV (Fg. 2) and ESV (Fg. 3). The quant diff were varied by the software used.

Table 1

Software	LVEF_NC	LVEF_AC	EDV_NC	EDV_AC	ESV_NC	ESV_AC
WLCQ	ns	0.03	ns	0.04	ns	ns
QGS	<0.001	0.02	0.002	0.002	<0.001	0.006
ECTB	<0.001	0.005	ns	ns	ns	ns
4DMS	0.003	ns	<0.001	<0.001	<0.001	<0.001

P-values from ANOVA test for LVEF, EDV and ESV calculated from SPECT AC/NC images filtered with 3 different cutoff frequencies and quantified by 4 different software.

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Effect of age and menopausal status on indices of coronary vasomotion in women without coronary risk factor.

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Aim: The effect of menopause on coronary vasomotion indices has not been characterized in healthy women, and may help to understand the controversial cardiovascular effects of hormone replacement therapy (HRT). This study investigated whether aging and menopause would influence myocardial blood flow (MBF) responses to cold pressor testing (CPT; mainly endothelium-dependent, a marker of future atherosclerotic events) and pharmacologic vasodilation (STR; mainly vascular smooth-muscle-dependent) as measured by PET and ^{13}N-ammonia.
Methods: Thirty women without coronary risk factor or HRT were subdivided according to menopausal status: Group 1 (n=14 premenopausal women; aged 32±6y [24-43y]) and Group 2 (n=16 postmenopausal women [menses cessation ≥1y]; aged 55±6y [46-67y]). MBF was measured at rest, during CPT (ice water) and STR (dipyridamole/adenosine). Wilcoxon ranksum tests and Spearman correlations were considered significant for p≥0.05.
Results: All laboratory and clinical variables were within normal range, but postmenopausal women presented higher total cholesterol (204±22 vs. 166±33mg/dl), LDL (124±19 vs. 102±30mg/dl), fasting glucose (87±9 vs. 78±8mg/dl) and mean arterial pressure (MAP; 89±10 vs. 74±6mmHg). During CPT, MAP and rate-pressure product (RPP; cardiac work index) were higher in Group 2, but the change in RPP from rest was similar across groups; during STR, heart rate (HR) was lower in Group 2. There was no intergroup difference in MBF at rest or in response to CPT and STR. Moreover, although some hemodynamic variables were correlated with age (MAP-RST, MAP-CPT, MAP-STR, RPP-RST, HR-STR), none of the MBFs was associated with age (all p>0.47).
Conclusions: Menopause and aging did not worsen the endothelium-dependent and -independent indices of coronary vasomotion in women with presumably healthy vasculature. Thus, in this population with low risk of cardiovascular events and normal coronary vasomotion, HRT might bring limited cardioprotective benefit.
Myocardial Blood Flows

MBF (ml/min/g)	Group 1	Group 2	P-Value
Rest	0.62±0.10	0.67±0.16	0.59
CPT	0.84±0.09*	0.91±0.20*	0.23
Deta-CPT from Rest	0.22±0.09	0.23±0.10	0.53
STR	2.08±0.34*	2.12±0.63*	0.97

*p≥0.001 vs. Rest.

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A study of changes in deformation and metabolism in the left ventricle as a function of hypertrophy in spontaneous hypertensive rats using microPET technology.

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In the case of hypertrophy caused by pressure overload there is an increase in cardiac mass and modification of cardiac metabolism.
Aim: To study the changes in glucose metabolism, ejection fraction, and deformation in the left ventricle (LV) with the progression of hypertrophy in spontaneous hypertensive rats (SHR).
Methods: Dynamic PET data were acquired using the microPET II. Normotensive Wistar Kyoto (WKY) and SHR rats were imaged at 10-week intervals. Each time a dose of 1- 2 mCi of F-18-FDG was injected and gated list mode data of 600-900 million counts were acquired over 60-80 mins. To evaluate glucose metabolism, list mode data were histogrammed into dynamic sequences (42 frames over 80 mins) including only the diastolic phase of the cardiac cycle. Dynamic sequences of 128×128×83 matrices of 0.4×0.4×0.582 mm^3 voxels in x, y, and z were reconstructed from 1203 140×210 sinograms using an iterative MAP reconstruction. Time activity curves were generated for the blood and left ventricular tissue volumes of interest and estimates of kinetic parameters were obtained by fitting a 2-compartment model to these curves. For the analysis of deformation, the list mode data were histogrammed into 8 gates of the cardiac cycle; summing the later 50 mins of the 80 min acquisition. The reconstructed images were interpolated to 256×256×83 to increase the in-plane sampling for the analyses. The end-systolic image data sets were manually segmented creating epi- and endocardial surfaces of the LV. Finite element models were created using the segmented surfaces and defining a transversely isotropic material with realistic fiber angle distributions. Hyperelastic Warping was performed on these images to obtain a fit to the end-diastolic image data sets providing an analysis of diastolic relaxation.
Results: In one study, the average first principal Green-Lagrange strain, fiber stretch, and ejection fraction were 0.22, 1.08, 80% for the WKY rat and 0.16, 1.06, 50% for the SHR rat. In another study the metabolic rate of F-18-FDG was 0.08 for a second WKY rat and 0.21 for a second SHR rat. For these same rats studied a year later the metabolic rate was 0.01 and 0.16 for the WKY and SHR, respectively. Over the first year of study average strain and ejection fraction were 0.21, 72.7% for the 2 WKY and 0.17, 69.8% for the 2 SHR rats with good correlation between strain and ejection fraction (r=0.91).
Conclusion: In the case of pressure overload there are decreases in strain and an increased reliance on carbohydrate oxidation in an attempt to maintain contractility and relaxation.

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A population pharmacokinetic/pharmacodynamic analysis of regadenoson, an A2A adenosine receptor agonist, in healthy subjects.

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Regadenoson is a novel, short-acting, and selective A2A adenosine receptor agonist under clinical investigation for use as a coronary vasodilator in pharmacological stress myocardial perfusion imaging (MPI).
Aim: To investigate the pharmacokinetics (PK), pharmacodynamics (PD), and the maximum tolerated dose of regadenoson in healthy subjects.
Methods: Thirty-six healthy, male subjects were included in the study. Subjects received single, IV bolus doses of regadenoson ranging from 0.1 to 30 μg/kg. Concentrations of regadenoson were determined in plasma samples collected at various times and urine collected over a 24-hour period after drug administration. ECG, blood pressure (BP), and heart rate (HR) were recorded for up to 24 hours post-dose. Adverse events (AE) were monitored for 24 hours post dose and via telephone 7 days later. A population approach was utilized in applying a three-compartmental PK model to the plasma concentration-time and a Michaelis-Menten model to the time-course of changes in HR. The potential influence of various covariates on PK and PD model parameters was investigated.
Results: The population value of clearance (CL) was estimated to be 40.6 L/h, with renal clearance accounting for 57% of the total clearance. The volume of distribution of regadenoson was estimated to be 83.3 L. The model estimated a baseline and a maximal increase in HR of 62 and 76 bpm. The concentration of regadenoson causing half-maximal increase in HR (potency) was estimated to be 12.4 ng/mL. Covariates such as body mass index, body weight, age, and height had no influence on the PK or PD parameters. AEs were generally mild to moderate, of rapid onset, short duration, and none required medical intervention. They included abdominal discomfort, chest pressure/tightness, dizziness, dyspnea, flushing, headache, hyperventilation, nausea, palpitations, and vomiting, and increased with dose level. The maximum tolerated dose was 20 μg/kg in the supine position and 10 μg/kg in the standing position, with dose-limiting syncope or near syncope observed in subjects in the standing position.
Conclusions: Regadenoson is well tolerated in healthy subjects. The lack of any significant influence of the covariates on the PK and PD model parameters suggests a unit-based dosing for regadenoson.

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A population pharmacokinetic/pharmacodynamic analysis of regadenoson, an A2A adenosine receptor agonist, suggests unit-based dosing in humans.

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Regadenoson is a novel, short-acting, and selective A2A adenosine receptor agonist under clinical investigation for use as a coronary vasodilator in pharmacological stress myocardial perfusion imaging (MPI).
Aim: To investigate the pharmacokinetics (PK) and pharmacodynamics (PD) of regadenoson in subjects undergoing clinically indicated cardiac catheterization
Methods: Thirty-six male and female subjects undergoing clinically indicated coronary angiography were included in the study. Subjects received single, IV bolus doses of regadenoson ranging from 10 to 500 μg. Concentrations of regadenoson were determined in plasma samples collected at various times prior to and after drug administration. ECG, average coronary peak flow velocity (APV), measured using intracoronary Doppler flow wire, blood pressure (BP), and heart rate (HR) were continuously monitored for up to 3 hours post-dose. Occurrence of adverse events (AEs) was monitored for approximately 3 hours post dosing and via telephone approximately 14 days later. A population approach was utilized in applying PK and PD models to the plasma concentration, APV, and HR data. The potential influence of various covariates on PK and PD model parameters was investigated.
Results: The PK data were best described by a three-compartment model. The population value of clearance and volume of distribution were estimated to be 29.8 L/h and 60.1 L, respectively. The PD model of the APV data included a hypothetical effect compartment. The baseline and the maximal increase in APV were estimated to be 16.5 and 77.0 cm/seconds, with a potency (concentration of regadenoson that causes half maximal effect) of 30.8 ng/mL. The model estimated a small value for the distribution rate constant (4 /min) from the plasma to the effect site, indicating a rather rapid onset of effect. A Michaelis-Menten model resulted in the best fit of the HR data, with estimates of 69 and 16 bpm for the baseline and maximum increase in the HR, and a potency of 10 ng/mL. Covariates such as body mass index, body weight, age, and height had no significant influence on the PK or PD parameters. AEs were reported for fewer than half (n=17) of the subjects; events reported for 3 or more subjects were chest discomfort (n=3), tachycardia (n=4), and bleeding at the catheter site (n=3).
Conclusions: Regadenoson is a potent and well-tolerated coronary vasodilator. The lack of any significant influence of the covariates on the PK and PD model parameters suggests a unit-based dosing for regadenoson.