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1.

EFFECTS OF TRANSJUGULAR INTRAHEPATIC PORTOSYSTEMIC SHUNT (TIPS) ON BLOOD VOLUME DISTRIBUTION IN PATIENTS WITH CIRRHOSIS

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Background and aims: Advanced liver cirrhosis is accompanied by portal hypertension and a hyperdynamic circulation with splanchnic and peripheral arterial vasodilation. Total blood volume (TBV) and plasma volume (PV) are increased, whereas the central and arterial blood volume (CBV) volume is decreased causing central hypovolaemia. Insertion of a transjugular intrahepatic portosystemic shunt (TIPS) alleviates portal hypertension, but also causes major haemodynamic changes and possibly restores central hypovolaemia. The aim of this study was to investigate (a) changes in the regional blood volume distribution, and (b) to relate these changes to haemodynamic variables after TIPS insertion.

Methods: Thirteen cirrhotic patients treated with TIPS had their regional blood volume distribution determined with a dual-head gamma-camera technique before and after TIPS. In addition we measured systemic haemodynamics during a liver vein catheterization.

Results: After TIPS, the blood volume in the thorax region increased (+12.2% of TBV, $P < 0.001$), the non-thoracic blood volume decreased (-4.0% of TBV, $P < 0.001$), whereas the blood volume in the splanchnic and liver regions did not change significantly.

Cardiac output (CO) increased significantly (+21.5%, $P < 0.0001$), mainly because of an increase in stroke volume (SV) (+12.8%, $P = 0.03$), although heart rate also increased significantly (+6.0%, $P = 0.03$). Systemic vascular resistance (SVR), and mean arterial pressure (MAP) decreased significantly ($P < 0.005$, and $P < 0.05$, respectively), whereas CBV, TBV, and PV did not change. Finally, right atrial pressure increased after TIPS (+40.0%, $P = 0.02$).

Conclusions: TIPS restores central hypovolaemia, primarily by an increase in thoracic blood volume, which represents the blood volume in the heart and the lungs, but also in the large central veins. In contrast, CBV, which besides the arterial blood volume in the heart and lungs also represents the blood volume in the large central arteries, was unaltered. Thus, the restored central hypovolaemia is predominantly based on an increase in central *venous* blood volume and not in central *arterial* blood volume. This is supported by the findings of an increase in right atrial pressure and CO, i.e. increased preload, combined with a decrease in SVR and MAP, i.e. decreased afterload.

2.

Comparison of Methods for Estimating Glomerular Filtration Rate in Head and Neck Cancer Patients Treated with Cisplatin

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Introduction Cisplatin is a chemotherapeutic agent widely used in the treatment of various solid tumours. Cisplatin induces nephrotoxicity in a dose-dependent manner and may lead to long-term reduction of kidney function. Subsequently, determination of glomerular filtration rate (GFR) is used to monitor potential kidney damage during treatment. ^{51}Cr-EDTA clearance (CrCl) is the clinical gold standard for determination of GFR. However, estimation of GFR from plasma creatinine applying different equations is widely used owing to the simplicity of the method. This study aimed to compare CrCl with two commonly used algorithms for estimating GFR (eGFR) from plasma creatinine.

Materials and Methods Retrospective single center study of 94 head and neck cancer patients treated with cisplatin at a maximum cumulated dose of 420 mg. CrCl was performed once before, during, and after treatment. CrCl was performed according to the principles of one sample clearance a.m. Broechner-Mortensen. Plasma creatinine was measured six times, concurrently. eGFR was assessed from plasma creatinine applying the Cockcroft-Gault (CG) equation that includes weight, and the Chronic Kidney Disease-Epidemiology Collaboration (CKD-EPI) equation. Agreement between the methods was assessed applying the statistical methods of Bland and Altman. A predefined limit of variation between CrCl and eGFR of 14% was applied in order to decide whether eGFR derived from the two equations would be useful in a clinical setting.

Results Comparison of CrCl and $eGFR_{CKD}$ revealed a positive slope of the linear regression line, suggesting proportional bias ($p < 0.001$). No systematic bias was found between CrCl and $eGFR_{CG}$. Concerning the precision of each equation, 49 (54%) and 43 (47%) observations exceeded the clinically acceptable limit of variation for $eGFR_{CKD}$ and $eGFR_{CG}$, respectively.

Weight changes ranged from -17.0 kg to 4.7 kg. Median weight change was -0.6 kg/week, significantly different from zero ($p < 0.001$).

Conclusion Estimated GFR_{CKD} cannot sufficiently replace CrCl in the assessment of GFR in head and neck cancer patients during treatment with cisplatin. If CrCl is unavailable, then weight-corrected $eGFR_{CG}$ is the better choice (probably due to its ability to compensate for changes in bodyweight during treatment) provided proper attention to the large variation between methods.

3.

Dosage optimization in cadmium-zinc-telluride SPECT gamma camera gated tomographic radionuclide angiography
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Purpose: To determine the influence of age, height, and weight on count rate during cadmium-zinc-telluride (CZT) SPECT gamma camera gated tomographic radionuclide angiography.

Methods: From August to December 2015 a total of 549 patients referred for routine assessment of left ventricular ejection fraction (LVEF) were registered regarding age, height, weight, and count rate in addition to the standard variables: Left ventricular end systolic and end diastolic volumes (LVESV and LVEDV respectively) and LVEF. Assessment of standard variables was performed on a dedicated cardiac CZT SPECT gamma camera, GE Discovery 530c (16 frames per R-R interval, 600 accepted beats). A dose of 550MBq 99mTc-labeled human serum albumin was administered intravenously to each patient. Each acquisition was analysed by two experienced technologists. Four patients (0.7%) were excluded from the study. Three patients because it was impossible to focus their heart within the field of view due to a high thoracic circumference and one patient because of partial paravenous administration of tracer.

Results: Count rate varied from 1.25 to 8.39 kcounts per second. Registered test variables, except age, were significantly correlated with count rate: age (adjusted R^2: 0.003, P = 0.282) height (adjusted R^2: 0.046, P < 0.0001) weight (adjusted R^2: 0.628, P < 0.0001). A log-transformation was performed on count rate and weight to increase the linear relation. Since the influence of age in a linear multivariable regression model was negligible this variable was excluded from the final model:

$log(CountRate) = \beta_0 + \beta_1 \cdot Height + \beta_2 \cdot log(Weight)$

This model explains just below 70% of the variance (adjusted R^2: 0.69) in log(count rate) with coefficients β_0 = 6.075, β_1 = 0.012 and β_2 = -1.558.

Conclusion: Patient height and weight can be used to predict count rate when performing CZT radionuclide angiography and these variables can be used for planning of tracer dosage. This provides the possibility to give a more patient specific dosage in radionuclide angiography.

4.

Left and right ventricular peak emptying and filling rates measured by gated tomographic radionuclide angiography using a cadmium-zinc-telluride SPECT gamma camera in chemotherapy-naïve cancer patients

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Aim: To establish normative data of left and right ventricular peak emptying and filling rates assessed with 99mTc-Human Serum Albumin equilibrium radionuclide angiography using a cadmium-zinc-telluride (CZT) SPECT gamma camera.

Materials and Methods: We included 718 newly diagnosed cancer patients (393 females) without diabetes mellitus or known cardiovascular diseases referred for routine baseline assessment of cardiac function prior to potential cardiotoxic chemotherapy. Each acquisition was analysed twice and mean values of left ventricular emptying (LPER), left ventricular filling (LPFR), right ventricular emptying (RPER), and right ventricular emptying (RPFR) peak rates were obtained.

Results: LPER and RPER did not differ between genders; LPFR and RPFR were higher in women (t test, $p < 0.03$).Mean and SD were: LPER (women -3.41 ± 0.9 ml/s, men -3.53 ± 0.8 ml/s), RPER (women -2.26 ± 0.6 ml/s , men -2.28 ± 0.56) LPFR (women 3.03 ± 0.86 ml/s, men 2.7 ± 0.83 ml/s), RPFR (women 1.82 ± 0.62 ml/s, men 1.73 ± 0.7). An index defined as peak filling rate/peak emptying rate (PFR/PER) less dependent of heart rate was introduced. Left ventricle PFR/PER was -0.91 ± 0.23 (women), and -0.78 ± 0.23 (men). Right ventricle PER/PFR was -0.82 ± 0.24 (women), and -0.77 ± 0.27 (men).

LPER increased numerically with age in women ($p < 0.0001$), RPER increased numerically with age in both genders ($p = 0.01$). LPFR decreased with age in both genders ($p < 0.004$), RPFR decreased with age in women ($p = 0.005$). Left and right PFR/PER decreased numerically with age for both genders ($p < 0.004$). When rates for early filling and atrial filling could be obtained separately (in 516 patients), we calculated right and left E/A ratio (early/atrial filling rate), which decreased with age in both genders ($p < 0.00001$).

Conclusion: Reference values for ventricular peak filling and emptying rates in chemotherapy-naïve cancer patients without cardiopulmonary disease are presented. Filling rates tended to be higher in women and decrease with age, the latter in accordance with age-related increasing fibrosis. Emptying rates generally increased numerically with age, which could be related to age-related changes in heart rate and size.

5.

Interstudy repeatability of left and right ventricular peak emptying and filling rates using a cadmium-zinc-telluride SPECT gamma camera for radionuclide angiography.

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Aim: To assess interstudy repeatability of left and right ventricular peak emptying and filling rates assessed with 99mTc-Human Serum Albumin equilibrium radionuclide angiography using a cadmium-zinc-telluride (CZT) SPECT gamma camera.

Materials and Methods: The study included 46 cancer patients (35 females) referred for routine assessment of left ventricular function while undergoing potentially cardiotoxic chemotherapy. A dose of 550-600 MBq 99mTc-labeled human serum albumin (HSA) was administered intravenously to each patient. Two acquisitions were performed on a CZT cardiac SPECT gamma camera, GE Discovery 530c (GE Healthcare, Milwaukee, WI, USA), between which the patient was repositioned. Each acquisition was analysed twice by two experienced technologists using a Xeleris 3 Imaging workstation reorientation software (version no. 3.0562) and Cedars-Sinai QBS processing software (revision 2009.0), and mean values of left ventricular emptying (LPER), left ventricular filling (LPFR), right ventricular emptying (RPER), and right ventricular filling (RPFR) peak rates were obtained. Interstudy repeatability was assessed by calculating the

intraclass correlation coefficient (ICC) with 95% confidence intervals for the two acquisitions. Furthermore, Bland-Altman analysis was carried out in order to assess proportional bias.

Results: One patient had an extremely high influence on the simple linear regression analysis carried out for identification of proportional bias (Cook's distance > 1). A review of the raw data revealed a high intra-observer variation for both acquisitions. This patient was excluded from the analysis.

ICC and 95% confidence intervals for LPER, RPER, LPFR, and RPFR were 0.99 (0.99-1.00), 0.94 (0.89-0.97), 0.99 (0.98-0.99), and 0.84 (0.72-0.91) respectively. There was no significant proportional bias for any of the variables.

Conclusion: The CZT camera provides reproducible estimates of left and right ventricular peak emptying and filling rates, which might be useful for monitoring cardiac function in cancer patients receiving potentially cardiotoxic chemotherapy. However, in cases where a high intra-observer variation is found, outcome should be interpreted with caution.

6.

Ny oscillometrisk metode til screening af ankelblodtryk

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Introduktion: Distal blodtryksmåling foretages oftest med standardmetoden Strain-gauge- pletysmografi. Dette er en tidskrævende undersøgelse, der typisk tager mellem ½ og 1 time. Hvis patienterne er relativt raske, kan man med fordel lave en simplere screening, for at udelukke og hjemsende de raske. Efterfølgende kan man undersøge de resterende med en mere rescoucekrævende undersøgelse. Kravene til en sådan undersøgelse er at den skal være simpel, hurtig og med sikkerhed finde de raske individer. D.v.s. den prædiktive værdi af negativ test (PNT) skal være 100%.
I denne undersøgelse har vi sammenlignet referencemetoden med et fuldautomatisk udstyr med 4 manchetter anbragt på arme og ben.

Materiale og metode: Undersøgelsen er et pilotprojekt udført over 14 dage og består af resultater opsamlet fra 22 personer henvist til distal BT måling.
Udstyret er et Automatic **A**nkle **B**rachial **I**ndex System, fra Huntleigh (ABI-metoden), og vores standard pletysmografiske udstyr fra Medimatic (SG-metoden).
Der blev først undersøgt med den traditionelle metode med SG efter afdelingens instruks og umiddelbart derefter med ABI-metoden. Et ankeltryk <0,9 blev betragtet som nedsat.
Der deltog 11 kvinder og 11 mænd med alder 42,8 (17,2) år, BMI på 28,6 (6,6) Kg/m^2. Systolisk arm BT på 126,1 (11,4) mmHg og ankeltryk på 142,7 (32,4) mmHg

Resultater*:* Resultatet er vist som et differensplot med middelværdi +/- 2 sd samt en linje skillende syge fra raske ved ABI på 0,9. Der blev målt på i alt 43 ben og heraf var de 3 lave ved begge undersøgelser. De resterende 40 var normale ved begge. Det betyder at PNT er 100%.Undersøgelsestiden var ca 15 minutter for hver deltager fsv. angår ABI-metoden.

Konklusion Ud fra de målte resultater kan vi konkludere at denne simple metode er i stand til at finde alle de raske, og at ingen af de raske blev målt som syge, samt at undersøgelsen kan udføres hurtigt og let.
Forbehold: Dette pilotprojekt har desværre en altovervejende del patienter med "normale" ankeltryk, men projektet fortsætter og vil koncentrere sig om patienter med nedsatte ankeltryk.

7.

Observer agreement of treatment responses on planar bone scintigraphy in prostate cancer patients: Importance of the lesion assessment method

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Aim: The aim of this study was to assess observer agreement in the evaluation of treatment responses of bone metastases using three different scoring methods in prostate cancer patients.

Materials and methods: Sixty-three paired bone scans were selected from prostate cancer patients with two or more bone scans (BS) within twelve month at Aalborg University Hospital from January 2009 to November 2014. BS was performed before initiation of therapy and minimum 12 weeks within treatment. Experienced nuclear medicine physicians, blinded to clinical and laboratory data, evaluated BS by three different methods, A) standard clinical assessment (improved, stable, or worse), B) MD Anderson criteria (complete response, partial response, stable disease, or progression), and C) Prostate Cancer Working Group 2 criteria (non-progression versus progression, defined as two or more new lesions). BS were evaluated for presence (M1) or absence (M0) of bone metastases, superscan (absent/present), and number of lesions per region. Observer agreement was assessed by Cohen's kappa and reported by Landis & Koch terminology.

Results: There was substantial agreement on bone response when using Prostate Cancer Working Group 2 criteria (Cohen's kappa at 0.84, 95% CI 0.69-0.99). Cohen's kappa for standard clinical assessment and MD Anderson criteria were 0.52 (95% CI 0.36-0.69) and 0.56 (95% CI 0.40-0.71), respectively, corresponding to moderate agreement. The latter methods have more response categories which is known to affect agreement negatively. Excellent agreement was demonstrated for M0/M1 (Cohen's kappa 0.94, 95% CI 0.82-1.00), and substantial agreement was found in assessment of superscan (Cohen's kappa 0.78, 95% CI 0.49-1.00). Bland-Altman analysis showed large variation in assessment of number of lesions per region, e.g. in columna, which showed the largest variation, limits of agreement (Bland Altman analysis) ranged from -14 to 15, with median number of lesions of 7 (range 0 to >20). No reader assessed the number of lesions systematically higher or lower than another.

Conclusion: Variations in BS response assessment strongly depended on the assessment method. Separate counting of lesions on repeated BSs without access to prior scans cannot be recommended. Variation in classification of progression versus non-progression might have significant impact on clinical decision-making, emphasizing the need for a uniform approach in bone response monitoring.

8.

Idiopathic inflammatory myopathy: Quantification of ^{99m}Tc-pyrophosphate uptake by SPECT/CT

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Aim: Diagnosing idiopathic inflammatory myopathy (IIM) is challenging and is currently based on clinical examinations, blood analyses and muscle biopsies. Imaging is not routine. Due to the patchy distribution of pathological muscle changes in IIM, biopsies may be falsely negative, which calls for accurate tests to detect inflammation. We present how technetium-99m-pyrophosphate (^{99m}Tc-PYP) SPECT/CT, increased uptake indicating inflammation, can distinguish between IIM patients and healthy controls.

Materials and methods: We compared ^{99m}Tc-PYP SPECT/CT scans of 77 patients with scans of 48 healthy controls. We performed semi-quantitative assessment by calculating mean standard uptake values (SUVmean) in volumes of interest (VOIs) in selected muscles, qualitative assessment scoring the amount of tracer uptake by scores of 1 to 4 with 4 indicating highest uptake, and visual assessment to determine the uptake pattern (patchy or not).

Results: Patients had significantly higher SUVmean in all VOIs compared with controls (right m. triceps brachii 46.0 $g \cdot mL^{-1}$ vs. 30.1 $g \cdot mL^{-1}$, $p < 0.0004$, left 45.3 $g \cdot mL^{-1}$ vs. 30.1 $g \cdot mL^{-1}$, right m. biceps brachii 48.6 $g \cdot mL^{-1}$ vs. 37.7 $g \cdot mL^{-1}$, left 50.0 $g \cdot mL^{-1}$ vs 36.1 $g \cdot mL^{-1}$, right m. quadriceps proximally 39.0 $g \cdot mL^{-1}$ vs. 28.7 $g \cdot mL^{-1}$, left 39.9 $g \cdot mL^{-1}$ vs. 28.6 $g \cdot mL^{-1}$, right m. quadriceps mid-thigh 39.8 $g \cdot mL^{-1}$ vs. 29.1 $g \cdot mL^{-1}$, left 38.4 $g \cdot mL^{-1}$ vs. 28.1 $g \cdot mL^{-1}$, right m. quadriceps distally 33.2 $g \cdot mL^{-1}$ vs. 24.1 $g \cdot mL^{-1}$, left 31.5 $g \cdot mL^{-1}$ vs. 23.0 $g \cdot mL^{-1}$, p for all <0.00001). Qualitative scores were distributed significantly different between groups with a larger

fraction of patients being scored as "patchy" compared to controls (24% vs. 6% for the upper limbs, 21% vs. 6% for the lower limbs, *p* for both <0.02). Compared with controls, patients had a higher median visual score (2 vs. 1, *p*<0.0001) for upper limbs but the same median visual score of 2 for lower limbs.

Conclusions: Quantitative assessment by ^{99m}Tc-PYP SPECT/CT consistently showed 30%-50% higher muscular uptake in IIM patients than in controls. A patchy pattern, typical of IIM, was more often seen in patients who also had higher visual uptake in the upper limbs compared with controls. Hence, ^{99m}Tc-PYP SPECT/CT might have a role in the diagnosis and monitoring of IIM.

9.
Characterisation & implementation of pinhole collimator for thyroid scintigraphy

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Aim The clinical value of thyroid and parathyroid scintigraphy can be improved by using a pinhole collimator rather than a high-resolution parallel hole collimator. The purpose of this study was, firstly, to characterise a newly installed gamma camera (Mediso Nucline TH45) equipped with pinhole collimator. Secondly, to implement a procedure for thyroid scintigraphy based on this characterisation.

Materials and Methods Magnification and spatial resolution were determined by imaging of ^{99m}Tc in two parallel capillary tubes 3 cm apart and subsequent determination of their imaged distance and full-width-at-half-maximum (FWHM). Sensitivity was measured for ^{99m}Tc as a point-source and in a Petri dish. Pinhole-aperture diameters of 3, 4 and 6 mm and object-aperture distances between 5 and 13 cm were applied. All measured parameters were compared to theoretical models.

The most suitable object-aperture distance in thyroid scintigraphy was judged from a series of thyroid phantom images. For a direct comparison of pinhole and parallel hole collimator, comparative images of a thyroid phantom and selected patients were recorded.

Results For the employed range of distances the magnification was 1-3. FWHM was reduced with about 1/3 from the largest to the smallest applied distance. FWHM was approximately proportional to the pinhole aperture diameter. The sensitivity was higher for the point source than the distributed source due to reduced sensitivity for activity located off-centre. The point-source sensitivity dropped by a factor of about 8, when the distance increased from 5 cm to 13 cm, while the drop was less for the distributed source.

A pinhole-aperture diameter of 4 mm yields a good compromise between spatial resolution and sensitivity, while an imaging distance of 7-10 cm is most appropriate with respect to magnification and spatial resolution. For the chosen parameters the magnification was 1.4-1.9, the spatial resolution 5.3-4.6 mm and the point-source sensitivity 87-185 cps/MBq.

Conclusion The gamma camera with pinhole collimator was characterized, and a suitable pinhole size and imaging distance was determined for thyroid scintigraphy. Judged from the determined parameters and visual evaluation of comparative images, the pinhole images represent an improvement compared to parallel hole collimator images in particular with respect to spatial resolution.

10.
The effect of dose reduction on left ventricular volumes and ejection fraction assessed by cadmium-zinc-telluride SPECT gamma camera gated tomographic radionuclide angiography

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Purpose: To examine the effect of reducing tracer dose when measuring left ventricular ejection fraction (LVEF) and left ventricular volumes by cadmium-zinc-telluride (CZT) SPECT gamma camera gated tomographic radionuclide angiography (MUGA).

Method: From September 2015 to March 2016, two consecutive MUGAs were performed on 46 patients who were injected first with a quarter of a full dose and subsequently adding up to a full dose of 550 MBq 99m Tc-HSA. All acquisitions were performed on a dedicated cardiac CZT SPECT gamma camera, GE Discovery 530c, and each acquisition was then analyzed twice by two experienced technologists. Heart

rate, left ventricular end diastolic volume (LVEDV), left ventricular end systolic volume (LVESV), LVEF, and count rate were registered. Intra-observer variation was assessed in terms of interclass correlation coefficient (ICC) for each dose level and comparisons were done with paired Student's t-test.

Results: The quarter dose series of acquisitions had a median count rate of 1.30 kcounts/sec (range: 0.58 – 2.78) while the median count rate for full dose was 4.40 kcounts/sec (range: 2.02 – 8.39).

Dose reduction gave rise to significantly lower LVEDV (mean: 91.4 mL vs. 96.0 mL; p = 0.001) and LVESV (mean: 34.2 mL vs. 38.4 mL; p < 0.001). Subsequently this gave rise to a significantly higher LVEF (mean: 63.4 % vs. 60.5 %; p < 0.001).

Reducing dose did not significantly change the intra-observer variation as the ICC between the two observers remained above 0.99 for all test variables with overlapping 95% confidence intervals.

Conclusion: Reduction of dose in CZT detector based MUGA causes a decrease in ventricular volumes and a higher LVEF which can be explained by a partial volume effect. Reproducibility in terms of intra-observer variation is not compromised by dose reduction. Subsequently, it is possible to adjust CZT-detector based MUGA outcome to a reference method without compromising reproducibility within the dose range mentioned above.

11.

Breast cancer-related lymphedema: quantification by transit-time Tc-99m-HSA lymphoscintigraphy

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Aims Lymphedema is a common and serious complication to breast cancer treatment. There is an increased focus on surgical treatment but the evidence level is still low. There is a need for standardized measurement techniques to quantify the lymphatic dysfunction so that treatments can be evaluated properly. Lymphoscintigraphy is a suitable choice for this, but hitherto, this technique was merely semi-quantitative. The aim of this study was to produce a quantifiable measure that reflects the lymphatic dysfunction.

Method and Materials Ten patients, aged 34-68 years, with unilateral arm lymphedema following breast cancer treatment were included. All patients underwent a bilateral lymphoscintigraphy using intradermal injection of Tc-99m-labelled HSA, 20 MBq in 0.1 mL. Imaging was done up to five hours after injection, and the transit-time of the tracer through the arm was calculated using time activity curves from the injection site and arm region. Arm volume was calculated using DXA scans.

Results The transit-time for the lymphedema arm was significantly higher than for the healthy arm (mean±SD, 81.8±60.9 vs. 11.3±4.5 minutes, p<0.01). The total number of removed axillary lymph nodes was positively correlated with transit-time on the lymphedema affected arm (r=0.83, p<0.01). The transit-time on the healthy arm seems to be shorter the longer the duration of the lymphedema (r=-0.63, p=0.05). There was no correlation between transit-time and excess arm volume.

Conclusion We have established a quantitative measure for the severity of lymphatic dysfunction after breast cancer treatment, which is strongly correlated with total number of removed lymph nodes. The strong trend seen between duration of lymphedema and transit-time on the healthy arm suggests that over time a systemic response occurs after breast cancer treatment. We propose that this quantification method be used for therapeutic studies on lymphedema to evaluate change in the lymphatic function.

12.

A Qualitative and Quantitative Comparison of Step-and-shoot, Acquire-during-step and Continuous SPECT Acquisition Modes

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INTRODUCTION: Time savings of >3 minutes/acquisition or dose reduction for equivalent time can be made with continuous or acquire-during-step (ADS) acquisitions, compared with step-and-shoot (SS).

Comparisons made ≥20 years ago favoured continuous acquisition mode, yet clinically SS is most common. However, given the improved image quality with modern SPECT reconstructions, an up-to-date comparison is necessary. This study provides qualitative and quantitative comparisons of images acquired with continuous, ADS and SS modes under clinically realistic conditions.

METHODS: SPECT-CT studies of a Tc-99m-filled NEMA-IEC image quality phantom were acquired on a Siemens Symbia Intevo 6, with a variety of settings used clinically, under four tracer conditions (high contrast (8:1) hot spheres with high and low activities; low contrast (7:2) hot spheres with low activity; medium contrast (1:6) cold spheres with high activity). Flash3D reconstructions were made with CT attenuation correction. Five experienced observers blind-scored confidence in uptake from 0 (no uptake) to 5 (certain significant uptake) for each sphere (10-37mm) in 90 datasets. Contrast-to-noise ratios (CNR) were also measured. Results were plotted on a curve (sphere size (mm) vs confidence; sphere size (mm) vs CNR) and AUC compared by acquisition mode.

RESULTS: High contrast hot spheres: ADS gave highest CNR at high activities (AUC: ADS 366; cont 320, SS 270) but confidence scores were comparable (AUC: ADS 109.9; SS 109.2; cont 107.2). Yet, at low activities ADS gave lowest CNR whilst SS and continuous were comparable (AUC: SS 260; cont 259; ADS 179), and continuous gave greatest confidence in lesion detectability (AUC: cont 94.5; ADS 88.0; SS 85.7). Low contrast hot spheres: CNR and confidence scores were greatest for SS (CNR AUC: SS 91; ADS 83; cont 63; confidence AUC: SS 62.0; cont 52.7; ADS 51.4). Cold spheres: CNR and confidence scores were most favourable for continuous mode (CNR AUC: cont -121; ADS -92; SS-82; confidence AUC: cont 70.8; SS 68.6; ADS 67.5).

CONCLUSIONS: For equivalent counts and reduced time to SS, continuous mode acquisitions showed favourable qualitative and quantitative results in assessing high contrast hot lesions and cold defects, although it was considered inferior to SS for low contrast hot lesions.

13.

Interpretation of SPECT images reconstructed in 256 versus 128 matrices

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INTRODUCTION: 256 matrix SPECT reconstructions provide scope for improved resolution through reduced partial volume effect. However, increasing matrix size from 128 to 256 reduces mean voxel counts by a factor of 8, thereby increasing noise. The aim was to assess how this increase in matrix size impacts on image interpretation.

METHODS: SPECT-CT studies of a Tc-99m-filled NEMA-IEC image quality phantom were acquired on a Siemens Symbia Intevo 6, with a variety of settings used clinically under four tracer conditions (high contrast (8:1) hot spheres with high and low activities; low contrast (7:2) hot spheres with low activity; medium contrast (1:6) cold spheres with high activity). Flash3D reconstructions were made in 128 and 256 matrices with CT attenuation correction. Five experienced observers blind-scored confidence in uptake from 0 (no uptake) to 5 (certain significant uptake) for each sphere (10-37mm) in each of the datasets. Results were plotted on a curve (sphere size (mm) vs mean confidence score) and AUC compared by matrix size. Observers were also blind-presented with 15 corresponding side-by-side 128 and 256 matrix reconstructions and asked to state their dataset preference.

RESULTS: Differences in AUC between 128 and 256 matrices were not considered clinically significant for high contrast hot lesions with high activity (128 matrix AUC: 108.6; 256 matrix AUC: 109.7) and low activity (128 matrix: 87.3; 256 matrix: 84.3), and for cold defects (128 matrix: 70.2; 256 matrix: 67.8), but a greater difference in AUC was seen for low contrast hot lesions with low activity, where a 128 matrix was favoured (128 matrix: 64.7; 256 matrix: 59.4). Of the 15 paired (128 matrix and 256 matrix) datasets presented to the 5 observers, 256 matrix was preferred in 40 cases, and 128 matrix preferred in 35 cases, but was observer-dependent.

CONCLUSIONS: Confidence scores in a variety of clinically realistic conditions suggested that data reconstructed in 128 and 256 matrices gave clinically comparable results for high contrast hot lesions with

high and low activity, and cold defects, although 128 matrices may be favourable for low contrast hot lesions with low activity. Preference scores were considered comparable.

14.
Continuous acquisition mode gives comparable images to step-and-shoot in lung perfusion SPECT

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AIM: EANM guidelines recommend a 5 minute lung perfusion SPECT. Step-and-shoot mode (SS) acquisitions increase scan time by >3 minutes compared with continuous mode (CONT) where data is acquired during detector motion. If image quality is comparable it would give the possibility to reduce camera time or acquire longer and improve image quality with 60 %. We have previously made a thorough phantom study and found CONT equivalent to SS in cold lesions, but should be evaluated in the patient setting prior to clinical implementation.

MATERIALS AND METHODS: Twenty two consecutive patients suspected for lung embolism were scanned first with SS and immediately after with CONT. Both SPECTs were acquired with 5 minutes sampling time (60 projections of 10 seconds), dual-head, LEAP collimator and 128 matrix, and OSEM reconstructions (30 iterations and 2 subsets) made with resolution recovery and scatter correction. Prior to the perfusion study, all patients had a Technegas® ventilation study. The two SPECT modes were compared side by side for each patient by a nuclear medicine physician. Number of perfusion defects, localisation and difference between the two modes were recorded.

RESULTS: There were 7 patients with lobar and/or several segmental perfusions defects, 7 with one subsegmental or non-segmental defects and 8 with normal perfusion. All defects seen in SS were also seen in CONT and no new defects were introduced. It was visually observed that CONT acquisitions were slightly less homogenous, but had slightly greater contrast between defects and normal perfused areas compared with SS. The minor visual difference was considered negligible in a clinical setting, especially compared with the lower count ventilation studies.

CONCLUSION: The distribution of defects is the same in CONT and SS acquisitions in lung perfusion SPECT. This gives the possibility to reduce scan time or improve image quality with CONT. If ventilation is also acquired with CONT, a total of 6-7 minutes can be saved. It is also possible to reduce doses if the perfusion/ventilation count ratio is still adequate.

15.
Bone scintigraphy of feet: Considerations when moving from planar imaging to SPECT/CT alone.

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AIM: Our standard imaging of feet was previously planar in 2-5 projections. We have experienced an increased use of supplementary SPECT/CT. Static images of feet require a long acquisition time and an additional SPECT/CT increases the time. We wanted to examine if the same information and conclusions could be obtained by a SPECT/CT alone, eliminating the need for planars.

METHODS AND MATERIALS: Thirteen consecutive patients were scanned with both planar of feet in 5 projections and SPECT/CT with and without X-SPECT® reconstruction. Eleven of the thirteen also had a whole-body acquisition. All data were blinded and planar and SPECT/CT were first evaluated separately. All lesions were marked on an anatomical bone image and scored (1-5) for localisation certainty, intensity and pathological degree. Also a conclusion was given and overall score (1-5) for the reporters diagnostic certainty, difficulty to interpret and time usage. Finally the exams were unblinded and the results were compared side by side for each patient. X-SPECT® reconstruction was qualitatively compared with the SPECT/CT

RESULTS: SPECT/CT scored better for localisation (p<0,01), a tendency to score lesions more intense (p=0,07), a little higher pathological degree on lesion basis (p=0,01) same number of lesions

(p=0,23). Overall conclusion on patient basis: the planar scored higher on diagnostic certainty (p=0,02), felt easier to interpret (p=0,01) and were faster to interpret (p<0,01). Overall X-SPECT® reconstructions showed the same lesions as SPECT/CT but with reduced intensity, consistent with planar findings. General learning points were: Characterisation of lesions on CT can help the aid diagnosis. Appropriate thresholding of SPECT images is difficult in minor lesions. Absolute quantification would be helpful. CT volume rendering was useful for localisation in the small bones where cross sectional imaging is difficult. In future acquired planar images could be substituted with reprojections from the SPECT.

CONCLUSION: The SPECT/CT alone images in all the patients gave the same information as planars and as expected, improved localisation and reduced the total acquisition time when done without planars. Awareness of interpretation should be given to small weak lesions that look more pathologic on SPECT/CT compared with reporting practice for planars.

16.

FDG-PET/CT in early stage uterine cervical cancer: can SUVmax discriminate between malignant and benign lymph nodes?

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Aim: The frequency of lymph node metastasis in early stage cervical cancer is low. If up-front FDG-PET/CT-scan detects positive lymph nodes, further staging by lymph node dissection is performed before radical hysterectomy is initiated. This set-up often drags out the staging process. We retrospectively examined whether the distinction between true positive, false positive, and merely reactive true negative lymph nodes could be assessed by SUVmax alone.

Materials and methods: A total of 134 patients (median 42 years) with early stage cervical uterine cancer, FIGO stage 1A or 1B, with preoperative FDG-PET/CT during the period 2009-2015 were retrospectively included. The scan result was compared to histopathology obtained by lymph node dissection. SUVmax was measured in PET-avid pelvic lymph nodes, and each assigned a separate SUVmax-value. The differences between the true positive, false positive and the true negative reactive lymph nodes were assessed by one-way analysis of variance, using Bonferroni's adjustment for multiple testing.

Results: Thirty women had 44 lymph nodes with increased PET activity. Eight (18%) lymph nodes were true positive, twenty-five (57%) false positive, and eleven (25%) true negative nodes. The corresponding mean SUVmax values ± SD were 3.1±0.89, 3.4±0.78 and 2.1±0.84, respectively. We found a statistically insignificant difference of 0.3 (p=0.96) in SUVmax between the true positive and false positive group, but significant differences of 1 (p=0.034) between true positive and true negative nodes and of 1.3 (p<0.0001) between true negative and false positive nodes.

Conclusion: SUVmax in preoperative FDG-PET/CT of early stage uterine cervical cancers cannot discriminate PET-positive metastatic from non-metastatic lymph nodes. Diagnostic lymph node dissection should be performed in all lymph node PET-positive patients. The SUVmax of reactive lymph nodes was significantly lower than that of both true and false PET-positive lymph nodes. Nevertheless, correct PET/CT lymph node diagnostics in early stage cervical cancer remain a complex combination of several parameters, and the SUVmax value cannot stand alone.

17.

Detection of extrahepatic metastases in patients with hepatocellular carcinoma: Comparison of PET/CT findings using ^{18}F-labeled glucose tracer (^{18}F-FDG) vs ^{18}F-labeled galactose tracer (^{18}F-FDGal)

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Introduction: The liver specific PET tracer [18F]fluoro-2-deoxy-*D*-galactose (^{18}F-FDGal) seems to be a promising supplement to contrast-enhanced CT (ceCT) and MRI for the detection of hepatocellular

carcinoma (HCC), especially extrahepatic metastases. Currently we examine patients with HCC with ^{18}F-FDGal and ^{18}F-FDG PET/CT as we wish to clarify the respective roles of the two PET-tracers in the assessment of patients with HCC. Here we present some of our preliminary results.

Method: From December 2014 to March 2016, 16 patients with HCC diagnosed according to the EASL guidelines without known dissemination of HCC outside the liver were examined with both PET tracers on two separate days (median interval 9 days, range 1-50 days). PET scans were performed with 5-7 bed positions of three minutes each from the top of the scull to mid-thigh one hour after injection of 100 MBq ^{18}F-FDGal or 5 MB/kg ^{18}F-FDG, respectively.

Results: In six of the 16 patients extrahepatic lesions with high uptake of ^{18}F-FDGal were detected. Four of these lesions (bone =3 and lung =1) were confirmed to be HCC metastases by either histology (n=2) or reexamination with ceCT/MRI. One of these patients had received a liver transplantation due to HCC and hepatic recurrence was suspected. The remaining two findings was examined with biopsy and turned out to be benign: Warthin tumor of the parotic gland and oncocytic metaplasia in the nasopharynx. Only one of the four HCC metastases was detected by ^{18}F-FDG PET/CT.

^{18}F-FDG PET/CT lead to six additional extrahepatic findings (lymph nodes in porta hepatis = 2, lymph node in relation to the ear =1, colon polyp with low grade neoplasia =1, fat necrosis =1 and poor dental status =1). One of the two patients with ^{18}F-FDG positive lymph nodes in porta hepatis had a needle biopsy performed which did not show HCC.

Conclusion: These preliminary results indicate that ^{18}F-FDGal PET/CT have a markedly better sensitivity than ^{18}F-FDG PET/CT for detection of extrahepatic metastases from HCC. Furthermore the number of non-HCC extrahepatic findings by ^{18}F-FDGal PET/CT seems to be fairly limited compared to ^{18}F-FDG.

18.

Safety evaluation and cardiovascular responses of the ^{68}Ga-PSMA ligand used for PET/CT imaging in patients with prostate cancer in a prospective, multicenter trial

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Aim: Safety reviews of non-marketed drugs are mandatory for obtaining regulatory approval for clinical or experimental use in many countries. The aim of this study was to evaluate the safety profile and cardiovascular response of the ^{68}Ga-PSMA ligand used for PET/CT imaging in prospective clinical trials.

Materials and Methods: A total of 77 patients with newly-diagnosed or recurrent prostate cancer participated in two prospective trials. Safety reporting was identical in the two trials. Patients were actively asked to report any AE during the ^{68}Ga-PSMA administration and until the end of the day of the PET/CT scan. Any AE was classified as mild, moderate or severe by the patients and categorized by Common Terminology Criteria for Adverse Events (CTCEA) v4.0 by the physician. Blood pressure (BP) and heart rate (HR) were measured prior to injection (baseline), immediately after the tracer injection, and at 1, 10 and 60 min post-injection (p.i.). A final assessment was made after the PET/CT scan. The definitions of hemodynamic adverse events were as defined: Brachycardia (HR < 50 beats per minute), tachycardia (HR > 100 beats per minute), hypertension (systolic BP > 180 mmHg) or hypotension (systolic BP < 100 mmHg).

Results: There was no reported AE. Mean systolic BP was 149 mmHg at baseline, and 145, 145, 139, 147 and 150 mmHg at injection, 1, 10, 60 minutes p.i. and after the PET/CT scan, respectively. There was no significant change in BP (p=0.74, ANOVA). Additionally, mean HR was 67 beats per minute at baseline, and 65, 62, 64, 62 and 62 beats per minute at injection, 1, 10, 60 minutes p.i. and after the PET/CT scan, respectively. There was no significant changes in mean heart rate (p=0.78). No patients developed de novo hypertension, hypotension, bradycardia, or tachycardia. Five patients presented with hypertension at baseline, but did not increase their systolic BP during/after the scan. Six patients showed brachycardia at baseline, none of these patients showed further decrease in HR p.i.

Conclusion: ^{68}Ga-PSMA PET/CT is very well tolerated. None of the patients experienced any AE and there were no changes in blood pressure or heart rate. We conclude that ^{68}Ga-PSMA is safe for human application.

19.

IMAGING OF CHRONIC RECURRENT MULTIFOCAL OSTEOMYELITIS USING ^{18}F-NaF PET/MRI

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Introduction Chronic recurrent multifocal osteomyelitis (CRMO) is a rare inflammatory disorder in children and adolescents. Reliable imaging modalities are important to support diagnosis of CRMO and detect subclinical lesions. Aim of this study was to investigate the value of ^{18}F-NaF PET/MRI in detecting CRMO lesions compared to standard ^{99m}Tc-diphosphonate bone scintigraphy with supplemental SPECT/low dose CT.

Methods ^{18}F-NaF PET/MRI was performed in four patients (all females, age range 9-12 years) with CRMO verified by histopathology. PET/MRI was performed using a Siemens Biograph mMR 3 Tesla scanner 45 minutes after administration of ^{18}F-NaF (2.2 MBq/kg, max 100 MBq). MR imaging: DIXON sequences for attenuation correction, coronal STIR and coronal T1 weighted sequences from scull base to toes for diagnostic imaging. Images were interpreted by experienced pediatric nuclear medicine physician and - radiologist. Lesions with increased tracer uptake and/or pathology identified on MRI were classified as symptomatic CRMO foci, subclinical CRMO foci, equivocal foci or classified as pathology not related to CRMO. PET/MRI results were compared to planar whole-body bone scintigraphy with supplemental SPECT/ldCT. Study was approved by the local ethical committee.

Results 21 lesions were identified (9 symptomatic CRMO foci, 8 subclinical CRMO foci, 1 equivocal focus and 3 foci not related to CRMO). The CRMO lesions were localized in the long bones (n=11), pelvis (n=3), calcaneus (n=2) and talus (n=1). All CRMO lesions had increased uptake of ^{18}F-NaF, although one histopathological verified lesion presented as lower uptake in an epiphyseal plate with adjacent diffuse increased uptake. One symptomatic CRMO focus had no corresponding pathology on MRI. Bone scintigraphy identified 8 (89%) of the symptomatic foci and two (25 %) subclinical foci.

Conclusion Preliminary results suggest that ^{18}F-NaF PET/MRI can be valuable in CRMO patients by increasing detection rate of foci compared to MRI and bone scintigraphy with supplemental SPECT/ldCT.

20.

Hepatobiliary secretion of conjugated bile acids in healthy humans quantified by ^{11}C-cholylsarcosine PET

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Background and Aims: Bile acids are the main organic constituents in bile and their hepatic transport is of prime importance for a normal bile formation. The aim was to quantify the kinetics of hepatic transport of bile acids in healthy humans. This was made possible by use of a dynamic emission tomography (PET), with a radiolabelled conjugated bile acid analogue [*N*-methyl-^{11}C]cholylsarcosine (^{11}C-CSar).

Methods: Nine healthy subjects were examined with 60-min dynamic PET recording of liver and bile ducts using injection of the conjugated bile acid tracer ^{11}C-CSar and concentration measurements of ^{11}C-CSar in a peripheral artery and a hepatic vein. Data analyses included kinetic modelling with estimation of rate constants of the hepatic transport of ^{11}C-CSar.

Results: Analysis demonstrated a first pass extraction fraction of 0.94 (95% confidence interval, 0.92 – 0.97), a hepatocyte sinusoidal membrane permeability area product of 2.06 (1.50– 2.62) mL blood/min/mL

liver tissue, a hepatic intrinsic clearance of 1.46 (1.31 – 1.61) mL blood/min/mL liver tissue, and a flow-determined systemic clearance. The rate constant for transport of ^{11}C-CSar from hepatocytes to bile was 0.39 (0.27 – 0.51) min^{-1}, which was much higher than the rate constant for backflux to blood 0.025 (0.009 – 0.041) min^{-1}. Assuming 0.32% of the liver volume to be bile ducts, the rate constant for bile flowing out of the liver 0.09 (0.049-0.174) min^{-1} could be translated into a mean bile flow rate of 0.42 mL/min. Mean hepatic residence time was 3.1 min. The average concentration ratios of ^{11}C-CSar between blood, hepatocyte, and intrahepatic bile were ≈ 1:3:6,000.

Conclusions: This PET study provided a detailed description of the transport of ^{11}C-CSar from blood to bile. The hepatic uptake step was shown to be highly efficient and followed by transport through the hepatocyte and into the bile with a high degree of polarity even though a small backflux was demonstrated.

21.

Hepatobiliary secretion of conjugated bile acids in patients with cholestasis quantified by ^{11}C-cholylsarcosine PET

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Background and Aims: Impairment of the hepatic bile formation or flow results in cholestasis with accumulation of bile acids potentially leading to liver injury. Cholestasis includes both the primary disturbance of bile acid transport and an adaptive response protecting the hepatocytes from injury. However, kinetic details of this situation have never been described *in vivo*. The aim of this study was to quantify the kinetics of the hepatic transport of bile acids in patients with cholestasis.

Methods: Twelve patients with cholestasis were examined with positron emission tomography (PET) with the conjugated bile acid tracer [*N*-methyl-^{11}C]cholylsarcosine (^{11}C-CSar) and concentration measurements of ^{11}C-CSar in a peripheral artery and a hepatic vein. Data analyses included kinetic modelling with rate constants for the unidirectional influx clearance K_1 (mL/min/mL liver tissue), backflux from hepatocyte to blood k_2 (min^{-1}), the secretion from hepatocyte to bile k_3 (min^{-1}), and flow from intrahepatic to extrahepatic bile k_5 (min^{-1}). The degree of cholestasis was estimated by the fasting plasma concentration of total bile acids and the observations were compared to those from healthy subjects.

Results: Cholestasis affected all steps of the hepatic transport of ^{11}C-CSar. In general, increasing degree of cholestasis was associated with a reduction of the uptake of ^{11}C-CSar from blood to hepatocytes and reduced intrinsic and systemic clearances. Also, k_3 decreased at cholestatic conditions while the hepatic residence time increased. We interpret increased k_2 as an adaptive response to the cholestatic condition. When the patients were grouped according to aetiology, different patterns of kinetic disturbances emerged.

Conclusions: Cholestasis reduced hepatic uptake and secretion, and increased backflux to blood of the conjugated bile acid ^{11}C-CSar, which is likely to be representative for conjugated bile acids in general. Furthermore, the findings suggest that different kinetic abnormalities may characterize cholestatic conditions according to their aetiology, but larger studies are needed to substantiate this hypothesis.

22.

18F-Fluorodeoxymannose (FDM) is a Potential New Tracer for Inflammatory Bowel Disease

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AIM: Invasive endoscopies are the current gold standard in inflammatory bowel disease (IBD). PET/CT may be a viable alternative, but controversies remain regarding FDG for imaging bowel disease. Macrophages are predominant in chronic inflammation and 18F-Fluorodeoxymannose (FDM) has been suggested instead

of FDG for macrophage imaging. We present preliminary results from a feasibility study comparing FDG and FDM uptake *in vitro* in macrophages and *in vivo* in an IBD-mouse model.

MATERIAL AND METHODS: THP-1 monocytes were differentiated into naïve M0 macrophages with PMA (phorbol 12-myristate 13-acetate). The macrophages were incubated with FDG and FDM and the uptake quantified and compared. Male C57BL/6 mice were subjected to different concentrations (2% and 4%) of Dextran Sulphate Sodium (DSS) in a predetermined schedule over a period of 37 days, a well-established rodent model for IBD. The schedule ended with FDG and FDM-scans. Afterwards, the mice were sacrificed and used for biodistribution analysis. Tracer uptake in the bowel was assessed and quantified.

RESULTS: *In vitro* there was no significant difference in macrophage uptake between FDM and FDG. The uptake for both tracers increased over time and after 180 minutes reached 0.52%±0.02% of added FDM vs 0.50%±0.03% of added FDG. Biodistribution in two control mice and one 2% IBD-mouse showed an increased uptake in the colon of the colitis mouse compared to the two controls (28.0% of IA/g (injected activity per gram) compared to 12.75%±2.95). Analysis of FDG and FDM scans at days 36 and 37 of a colitis mouse showed an increased uptake in absolute values of FDM compared to FDG. The ratios of organ specific values were similar in FDM compared to FDG, although the intestine/heart ratio was 61.8% larger in FDM compared to FDG.

CONCLUSION: *In vitro,* macrophages showed similar uptake of FDM and FDG. *In vivo,* both FDM and FDG were able to visualize IBD. Preliminary biodistribution results showed higher overall FDM uptake including in the bowel of an IBD mouse compared to controls and, thus, potentially better target-to-background delineation for FDM. Overall, our results suggest FDM as a potential tracer for macrophage imaging in IBD, but further studies are needed.

23.

CHANGES IN HUMAN RENAL CORTICAL AND MEDULLARY PERFUSION AND BLOOD OXYGENATION (BOLD) LEVELS DURING SYMPATHETIC ACTIVATION, MEASURED WITH CONTRAST-FREE, MR-BASED METHODS

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Background and aim: The hypoxic environment of the renal medulla is considered to be essential in the renal urine concentrating mechanism. Given that fluctuations in medullary hypoxia can induce renal damage, mechanisms regulating renal perfusion, including blood pressure, are believed to regulate medullary oxygen concentrations. Medullary flow abnormalities have been implicated in the pathogenesis of primary and perhaps secondary hypertension. Renal sympathetic nerve activity is involved in the regulation of medullary perfusion, and ablation of efferent sympathetic nerve activity by renal denervation drastically lowers the blood pressure in some hypertension patients. Using MRI, we have measured changes in renal flow, medullary and cortical perfusion and oxygenation in healthy humans during activation of the sympathetic nerve system.

Methods: 10 healthy subjects were examined on two occasions in a 3Tesla MR-scanner. On each occasion subjects performed 5 minutes hand-grip tests in the scanner to obtain continuous measurements of BOLD, perfusion and interleaved measurements of T2* and renal artery flow. The 5 min hand-grip test was repeated for each of the three acquisitions (in randomised order) with rest periods in between. Flow measurements were obtained from phase-encoding imaging, perfusion using arterial spin labeling (ASL) and both BOLD and T2* using gradient echo images.

Results: During hand-grip test, we observed a decrease of flow in the renal artery by 18± 10 %. BOLD signal decreased significantly by 6 % in the cortex, but increased slightly (2.7%) in the medulla. Likewise T2* values decreased by 3.8% in the cortex and did not change significantly in the medulla. Perfusion in both the cortex and the medulla was unchanged.

Conclusion: Measurements of renal artery flow, BOLD and perfusion in renal cortex and medulla, acquired for the first time in healthy subjects during hand grip testing, were consistent with a decrease in artery flow and cortical oxygenation, while medullary perfusion and oxygenation were unchanged. This is in line with

counter regulatory mechanisms protecting against medullary hypoperfusion. Cortical perfusion was expected to decrease based on findings in animal studies and given the measured flow decrease in the renal artery. Possible changes in blood volume and glomular filtration rates may have a confounding effect on ASL measurements. These techniques may be useful to asses patients having primary hypertension and renal artery stenosis and in the evaluation of the effect of renal denervation.

24.

MEASUREMENTS IN HUMANS OF RENAL ARTERY FLOW AND RENAL CORTICAL AND MEDULLARY PERFUSION AND BLOOD OXYGENATION LEVEL (BOLD) WITH MR-BASED, CONTRAST-FREE METHODS.

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Background and aim: The renal medulla plays a central role in urine concentration and blood pressure regulation. Medullary hypoxia due can induce renal damage. Flow abnormalities have been implicated in the pathogenesis of primary and perhaps secondary hypertension via animal studies. A more precise understanding of how flow within the human kidney is necessary to isolate the mechanisms involved. Renal perfusion and oxygenation has proven to be difficult to measure, especially in the medullary region. Increasingly studies use MR-T2* as an indicator of oxygenation. A decrease of deoxyhemoglobin concentration in the renal medulla can be measured by MR-T2* values but can represent either change of flow or oxygen tension. Thus, renal flow and regional perfusion has to be concurrently measured with T2* in order to interpret changes in oxygenation level.

Methods: 10 healthy subjects were examined on two occasions in a 3Tesla MR-scanner before and after injection of 20 mg of furosemide. We performed interleaved measurements of renal flow, T2* and perfusion in the renal cortex and medulla. Renal flow and regional perfusion were compared with regional changes in T2*. Coefficients of variation between the two scanning days were analysed

Results: After furosemide injection, T2* values in the renal medulla increased by 25%, while T2* values in the cortex did not. Measurements of flow in the renal artery and perfusion in the cortex and medulla did not change significantly. Reproducibility was best for flow in the renal artery and T2* values in cortex with coefficients of variation of 3.8, and 2.6% respectively. Coefficients of variation of T2* values in the medulla, and ASL measurements in cortex and medulla were 4.7, 6.2 and 6.8%, respectively.

Conclusion: Using a contrast- and radiation free method without, we have collectively measured changes in flow, perfusion and deoxyhemoglobin concentrations in renal cortex and medulla for the first time in humans. We could demonstrate the acknowledged decrease in deoxyhemoglobin content in the medulla after injection of furosemide, as measured by T2* values, that is usually ascribed to higher oxygen tension due to decreased metabolism, and we confirm that it is not the result of changes in perfusion. The combined method may be useful in future research on the pathogenesis of primary and secondary hypertension and kidney disease.

25.

Blod-perfusion i osteomyelitiske og bløddelslæsioner studeret med [^{15}O]vand i en grisemodel

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Introduktion: Knoglemarvsinfektion (osteomyelitis) er en alvorlig sygdom, som kan resultere i deforme knogler og i nogle tilfælde nødvendiggøre amputation. Osteomyelitis er svær at behandle med antibiotika. For de fleste typer akut infektion og inflammation forøges blodgennemstrømningen (perfusion), men specifikt for osteomyelitis er der kun sparsom viden om dette. I nærværende studie er følgende hypotese undersøgt: Blod-perfusionen forøges ikke eller kun i ringe grad ved akutte osteomyelitiske læsioner. Dette

kan være en mulig forklaring på den langsomt indsættende effekt af antibiotika. For at undersøge hypotesen, blev perfusionen målt ved dynamisk PET-skanning af radioaktivt vand i grise med osteomyelitis i højre bagben.

Materiale og metode: Det overordnede osteomyelitis-studie (beskrevet i Nielsen *et al* 2015, www.ajnmmi.us/files/ajnmmi0002237.pdf, samt Afzelius *et al* 2016, www.ajnmmi.us/files/ajnmmi0016443.pdf) anvender en model, hvor grise får induceret *Staphylococcus aureus* osteomyelitis i højre bagben og dynamisk PET-skannes med bl.a. [^{15}O]vand. Vand ekstraheres effektivt fra kapillærerne, og modellering af vand-optaget kan tages som mål for perfusionen af blod i vævet. Volumes-of-interest (VOIs) blev anlagt i raske dele af begge ben, samt i osteomyelitis-læsioner og i tilsvarende anatomiske positioner i det raske ben. Kinetisk modellering for hvert VOI gav et mål for perfusionen.

Resultater: 11 grise indgik i studiet, heraf 10 med osteomyelitis, i alt 25 osteomyelitiske læsioner; hertil et mindre antal bløddelslæsioner. Der fandtes kun ubetydelig forskel på højre og venstre bagben i de raske områder. I både osteomyelitiske læsioner og bløddels-læsioner var perfusionen højere end i de tilsvarende raske positioner, men stigningen i bløddelslæsionerne var dobbelt så kraftig som de osteomyelitiske læsioner.

Diskussion og konklusion: Perfusionen i osteomyelitiske læsioner kan måles med dynamisk PET-skanning med [^{15}O]vand. Hypotesen blev delvist bekræftet: Perfusionen *var* forøget i de osteomyelitiske læsioner, men ikke så meget som i bløddelslæsioner. Perfusion er en mulig forklaring på den langsomt indsættende effekt af antibiotika, men næppe hele forklaringen.

26.

The Impact of Contamination with Long-Lived Radionuclides on PET Kinetics Modeling in Multi-Tracer Studies

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Background: Kinetic modeling of sequential dynamic PET scans in the same subject enhances comparability but introduces the problem of contamination from remains of the first tracer in blood samples, thereby adding a background signal to the input function. This is a problem especially when the first tracer has to be chosen with much longer half-life than the second tracer.

Aim: We present a correction based on late re-counting of the blood samples and investigate the effect on kinetic modeling in a two-tissue compartment model with irreversible uptake (3k model).

Methods: Our study used dynamic PET scans and blood samples from the recent study by Nielsen et al (2015, www.ajnmmi.us/files/ajnmmi0002237.pdf), involving both ^{111}In and PET tracers. The radionuclide ^{111}In emits two photons in rapid cascade with a combined energy that may be detected within the PET energy window during gamma counting. Samples were re-counted 2 days (~48 hours) later when only ^{111}In ($T_{1/2}$ = 2.8 days) was left. We used these data for correction of the original (early) count rates. We performed kinetic modeling using both non-corrected and corrected input functions.

Results: The K_1 parameter was almost unaffected, in most cases k_2 was only slightly affected, while k_3 was underestimated by up to 22% if non-corrected plasma data were used. Naturally, the correction had the largest impact on the part of the input function with the weakest foreground signal.

Conclusions: The use of sequential dynamic PET scans in the same research animal or subject facilitates comparison, but care must be taken when a background signal from a previous tracer remains, especially in determining a correct input function for kinetic modeling. The more a model parameter depends on the late input function, the more it will be susceptible to background signals. The presented method is general for the situation where the first applied radiotracer has a far longer physical half-life than the following tracer(s).

27.

Parametric imaging of metabolic liver function in humans by non-invasive dynamic 18F-FDGal PET/CT

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Introduction: Parametric images of the hepatic metabolic function can be made by 20-min dynamic PET/CT with the radio-labelled galactose-analogue 2-[18F]fluoro-2-deoxy-D-galactose (18F-FDGal) in terms of hepatic systemic clearance of 18F-FDGal (K, ml blood/ml liver tissue/min). Until now, the method has required arterial blood sampling from a radial artery (arterial input function). In the present study we developed a method for extracting an image-derived, non-invasive input function.

Methods: Dynamic 18F-FDGal PET/CT data from 16 healthy subjects and 16 patients with liver cirrhosis were included in the study. Five different input volumes of interests (VOIs) were tested: four in the abdominal aorta and one in the left ventricle of the heart. Arterial input function from manual blood sampling was available for all subjects. K^*-values were calculated using time-activity curves (TACs) from each VOI as input and compared to the K-value calculated using arterial blood samples as input. Each input VOI was tested on PET data reconstructed with and without resolution modelling.

Results: All five image-derived input VOIs yielded K^*-values that correlated significantly with K calculated using arterial blood samples. A semicircle drawn in the posterior part of the abdominal aorta was the only VOI that was successful for both healthy subjects and patients as well as for PET data reconstructed with and without resolution modelling.

Conclusion: Three-dimensional images of regional metabolic liver function using 20-min 18F-FDGal PET/CT can be made using input data from a semicircle VOI drawn in the posterior part of the abdominal aorta. This method can be used in assessment of patients with parenchymal liver disease and in planning local treatment of liver tumours.

28.

Total hemispheric glycolysis ratio by FDG-PET/CT in gliomas; Evaluating diaschisis and potential prognostic information

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Aim: Diaschisis denotes brain dysfunction remote from a focal brain lesion. We quantified diaschisis ratios and tested the claim that these ratios have prognostic value in glioma patients.

Material and methods: Fifty FDG-PET/CT studies collected prospectively in 5 male and 9 female glioma patients, aged 35-77 years, were compared to scans from 10 healthy controls, aged 43-75 years. Dedicated 3D-segmentation software (ROVER, ABX, Germany) provided "total hemispheric glycolysis" (THG), i.e., the product of segmented metabolic volume and SUVmean in each hemisphere. The hemisphere of likely diaschisis (i.e., the ipsilateral cerebral and the contralateral cerebellar hemisphere) was normalized to the opposite hemisphere to provide the "total hemispheric glycolysis ratio" of cerebrum and cerebellum, i.e.,

THGr(Ce) and THGr(Cb), respectively. Receiver operating characteristics (ROC) provided optimal cut-offs for these variables.

Results: Visual analysis confirmed cerebro-cerebellar diaschisis in 100% of glioblastoma PET studies performed within one year until death. Diaschisis was not observed in healthy controls, who had mean values of THGr(Ce) and THGr(Cb) that significantly exceeded those of patients, i.e., p= 0.0007 and p=0.02, respectively. Median THGr(Ce) averaged 0.62, 0.71, 0.88 in patients surviving less than one year, one to three years, and more than three years, respectively, versus 0.98 in healthy controls. Median THGr(Cb) averaged 0.74, 0.88, 1.01, and 0.96, respectively. The finding of a low THGr (Ce<0.62 or Cb<0.84) agreed almost completely with the presence of diaschisis by visual assessment of cerebrum or cerebellum, i.e., in 16/17 (94%) and 25/26 (96%) of PET scans, respectively. The combination of THGr(Ce) <0.62 and THGr(Cb) <0.84 had a 100% sensitivity and a 78.6% specificity with regard to survival of less than one year for the glioblastoma patients.

Conclusion: We present a novel and feasible quantitative approach for detection of diaschisis in glioma patients. THGr could demonstrate diaschisis in both cerebrum and cerebellum, and optimized cut-off values for THGr(Ce) and THGr(Cb) had a high sensitivity and fair specificity for prediction of survival of less than one year for these glioma patients. The presented semi-automated quantitative approach may allow comparison of similar data obtained at different institutions.

29.

Different cognitional patterns in healthy aging and Alzheimer's disease during brain activation: an activation likelihood estimation-based meta-analysis

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Abstract: Alzheimer disease (AD) is a neurodegenerative disorder which frequently affects cognitional functions. Lately, a large body of neuro-imaging studies have aimed at finding reliable biomarkers of AD for early diagnosis of the disease.

We conducted a systematic review and meta-analysis on functional neuroimaging i.e., positron emission tomography (PET) and functional magnetic resonance imaging (fMRI) studies to find the relationship between cognitional patterns in AD patients and normal elderlies. We meta-analyzed the coordinates of regions related to cognition using Sleuth software and the activation likelihood estimation (ALE) method. We considered p-value map at the false discovery rate (FDR) of P‹ 0.05 thresholds and the clusters with a minimum size of 200 mm3. We used MANGO software to visualize the data. Forty-one articles that assessed the areas activated during cognition in normal elderly subjects and AD patients were met our criteria.

We found that left middle frontal and left precuneus gyri are the most activated areas in cognitional tasks in healthy elderlies and AD patients respectively. In normal elderly subjects and AD patients, comparison of ALE maps and reverse contrast showed that insula and left precuneus were the most activated areas in cognitional aspects respectively.

According to unification of left precuneus activation in cognitional tasks, it seems that this point can be a hallmark in differentiation of AD patients and healthy individuals.