International Scientific Committee of Radionuclides in Nephro-Urology
(ISCORN)

Abstracts Part 2 - Methodology (M1 - M19)

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M1 - TEACHING SINGLE-SAMPLE PLASMA CLEARANCE OF 51CR-EDTA

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Objective: The present teaching program was made to overcome young students difficulties in understanding the single-sample plasma clearance technique. The program is based on a simplified one-compartment model for the measurement of glomerular filtration rate (GFR) and is not expected to produce exact values.

Methods and results:

1) Illustration: Plasma clearance = Injected dose / Area under curve (AUC).
   Teaching point: AUC is the same in patients with equal GFR.
2) Illustration: Plasma disappearance curves in patients with equal size (distribution volumes=Vd) and GFR ranging from 20-140 ml/min.
   Teaching point: At low GFR plasma concentration decreases slowly and AUC is large.
3) Illustration: Patients with different Vd but equal GFR=80 ml/min.
   Teaching points: a) Plasma concentration is initially lower in patients with a large Vd and the decrease in plasma concentration is slower. b) Plasma concentration is nearly the same in all patients at a certain point in time. c) If the plasma sample is taken earlier or later then correction for differences in Vd is necessary.
4) Illustration: Plasma disappearance curves in patients with different Vd but equal GFR (30 and 110 ml/min).
   Teaching point: The plasma disappearance curves intersect earlier in patients with high GFR and later when GFR is low.
5) Illustration: Optimum sampling time as a function of GFR.
   Teaching point: Time for optimal sampling is very late when GFR is less than 10 ml/min.

(Curves will be shown).

Conclusion: The program has been presented with success.

M2 - RENAL DECONVOLUTION AS AN INTERCONNECTING PRINCIPLE

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Objective: To investigate two new uses for renal deconvolution: (A) incorporating non-negativity and monotonicity constraints as a means of facilitating subtraction of the extravascular component (EV) from the input function and (B) without constraints as a key to elimination of the influence of renal function on both renal output efficiency (ROE) and normalized residual activity (NORA).

Methods: (A) An iterative technique was used to minimize the difference between reconvolution of the retention function (RF) with the input and the background subtracted renal curve, thus providing an EV subtracted input function from which the clearance normalized for plasma volume, C/V, was calculated. The technique was tested (i) using Hybrid phantoms and (ii) in a set of 50 adult patient studies in which C/V was also calculated by a proportional subtraction method. (B) A virtual RF was used to encode the renal response for each kidney. Reconvolution with a chosen standard input function resulted in the decoding of the response and formation of a new renal curve from which normalized ROE and NORA were measured.

Results: (A) (i) C/V values had mean (standard error) of 90% (2.5%) expected value. (ii) C/V values from deconvolution and proportional methods correlated linearly ($r=0.89;p<.001$). (B) Pre-normalization, NORA showed a higher dependence on renal function than ROE. Post-normalization, ROE and NORA were linearly correlated ($r=-.99;p<.001$).

Conclusion: (A) Subtraction of EV from the input function is possible without prior specification of a subtraction factor. (B) Equivalent values for ROE and NORA can be obtained independent of renal function.

M3 - MEASUREMENT ERROR OF REPEATED GFR DETERMINATION BY SINGLE-SAMPLE METHOD AND GAMMA CAMERA UPTAKE METHOD WITH Tc-99m-DTPA.

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Background: The single-sample method after single injection of T-99m- DTPA has been proved to be more accurate for the determination of GFR than the gamma camera uptake method. The purpose of this study was to assess their measurement error of repeated GFR on the same subject.

Materials and Methods: The study was performed on 20 normal subjects (men/women = 19/1; age range = 23 to 55 ys with median of 33 ys). The renal scintigraphy with Tc-99m-DTPA was repeated on the same subject within a month apart (range 6 from 35 days with median = 14 days). The GFR was determined by single-sample method (Christensen-Groth's algorithm, GFRcg) and a gamma camera uptake method (Gates' algorithm, GFRgates). Split renal function (SRF) by the gamma camera uptake method, serum creatinine (S-Cr) and BUN were also measured. Linear regression and one-way analysis of variance (one-way ANOVA) tests between pairs of observations were evaluated by a commercially available software (JMR v.4.0.5J, SAS Institute). The probability less than 0.05 was considered significant.

Results: Correlation coefficient of GFRcg, GFRgates, the right SFR (SRFr), S-Cr and BUN between pairs of observations was 0.775, 0.473, 0.577, 0.764 and 0.621, respectively (all in $p<0.05$). The repeatability (= 2.77 x within-subject standard deviation, Bland JM and Altman GD, *BJM* 1996; 31;1654) of CGRcg, CGRgates, SRFr, S-Cr and BUB was 34.1 ml/min/1.73 m^2, 48 ml/min/1.73 m^2, 8.5 %, 0.276 mg/dl and 9.18 mg/dl, respectively. The subject absolute difference ((|1^{st} measurement – 2^{nd} measurement|)/(subject mean) x 100 %) between repeated measurements was 5.8 % in GFRcg, 14.6 % in GFRgates, 4.8 % in SRFr, 6.0 % in S-Cr and 16.4 % in BUN.

Conclusion: The gamma camera uptake method is less reliable and repeatable than the single-sample method for the determination of GFR using Tc-99m-DTPA. It is reliable for the determination of the SRF rather than the global renal function.

M4 - COMBINATION OF TWO INDEPENDENT METHODS FOR ESTIMATION IN ADULTS OF THE GLOMERULAR FILTRATION RATE (GFR) IN Tc-99m DTPA RENOGRAPHY.

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Objectives: (1) To design an alternative and robust method (the rate constant method) for GFR estimation in Tc-99m DTPA renography which is independent of the conventional Gates' method, (2) To combine the rate constant method and Gates' method for calculation of a pooled GFR, and (3) To compare the reliability of the pooled estimate *separately* with the reliability of the reference method using Cr-51 EDTA plasma samples.

Methods: The rate constant method is based on Tc-99m DTPA renographies lasting 40 min in which regions of interest (ROIs) are manually created over selected parts of certain blood pools (e.g. heart, lungs, spleen, and liver). For each ROI the corresponding time-activity curve was generated and exposed to a monoexponential fit in the time interval 10 to 40 min postinjection. Following an iterative procedure comprising usually 5-10 manually created ROIs, the monoexponential fit with the maximum rate constant in min^{-1} was used for estimation of GFR.

Results: In a patient group of 54 adults in whom GFR was determined from the reference method, the standard errors of estimate (SEE) of the pooled estimate were 5.9, 8.3 and 11.7 ml/(min ≅ 1.73 m^2) for GFR equal to 30, 60 and 120 ml/(min ≅ 1.73 m^2). The corresponding SEE values of the reference method were assumed to be 3.0, 4.6 and 9.2 ml/(min ≅ 1.73 m^2). Hence, the *separate* SEE values of the pooled estimate were calculated to be 5.0, 6.9 and 7.1 ml/(min ≅ 1.73 m^2).

Conclusions: The reliabilities of the pooled GFR estimate *separately* and of the reference method are of the same magnitude. Therefore, Tc-99m DTPA renographies lasting 40 min may replace the reference method for GFR determination provided that adequate gamma camera facilities are available. In addition, the renography is considerably less time consuming, requires fewer resources from patient and staff and it yields clinical information on single kidney GFR, renal morphology and renal outflow. Finally, experimental errors in the pooled GFR are easier to detect than in GFR using the reference method.

M5 - A UNIFIED APPROACH TO RADIOPHARMACEUTICAL CLEARANCE ESTIMATION FROM ONE OR MORE PLASMA SAMPLES

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Bayesian statistical methods offer a robust means of fitting compartmental models to plasma time-activity curves. Here we present a computer program based on a Bayesian model that can calculate clearance from any number of plasma samples drawn at arbitrary time intervals.

Methods. A Bayesian compartmental model was fitted to clinical data for Tc99m-MAG3, Tc99m-EC, I131-OIH, Tc99m-DTPA, and Yb169-DTPA to obtain Bayesian parameter estimates. The program uses these retrospective parameters as prior estimates to calculate clearance from prospective data, again using a Bayesian model. The method is scaled for body size and is intended for children as well as adults.

Results. Clearance estimates calculated from only one or two plasma samples were found to closely approximate more exact results using multiple samples.

Conclusions. When only one or a few points are available, the program fills in needed information from a Bayesian prior probability distribution based on previous clinical data. When many points are available, the new data overwhelm the prior probability, and the results are similar to conventional curve fitting but with less sensitivity to bad data points and less risk of fitting failure.

M6 - BAYESIAN COMPARTMENTAL MODELS FOR Tc99m-ETHYLENE DICYSTEINE

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Introduction. Bayesian statistics provide a robust method for fitting compartmental models that can be used for simplified one- and two-sample clearance measurements after intravenous bolus injection of tracer. We applied this method to the renal agent Tc99m-ethylenedicysteine (EC), which has properties similar to the more widely used agentTc99m-MAG3.

Methods. Multisample plasma clearance data (5-8 samples between 2-5 and 60-90 minutes) were obtained after bolus intravenous injection of Tc99m-EC. The data were fitted by a Bayesian compartmental model in which all 82 subjects were included simultaneously, forcing the compartmental parameters to be similar (but not identical) between patients of similar size. This achieved a kind of data smoothing that facilitated fitting 3 compartments.

Results. Parameters were calculated for both 2- and 3-compartment models. These parameters were then used for 1-, 2-, and multisample clearance calculations. Clearances for individual subjects were lower using 3 compartments than 2 compartments, by an average of 28 ml/min/1.73m^2.

Conclusions. The 3-compartment model, presumably more accurate since it allows closer fit to the measured data, led to lower clearance than the conventional 2-compartment model. The Bayesian model can also be used to estimate clearance using only one or two plasma samples.

M7 - BLOOD OXYGEN LEVEL-DEPENDANT MAGNETIC RESONANCE IMAGING IN RENAL ARTERY STENOSIS.

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Objective: In magnetic resonance (MR) imaging, the paramegnetic molecule desoxyhemoglobin (dHb) induces signal attenuation in T2*-weighted sequences as opposed to diamagnetic oxyhemoglobin. This attenuation is measured by the Blood Oxygen Level-Dependant (BOLD) method to estimate indirectly renal oxygen content. In hypoxia, BOLD signal is increased due to an increased tissue concentration of dHb. Nevertheless, the BOLD method has never been evaluated in renal artery stenosis (RAS). This study was therefore designed to test if BOLD can detect renal hypoxia induced by RAS.

Methods: RAS was induced in 8 pigs by an occluder placed on the right renal artery. Renal blood flow (RBF) was measured continuously with an US probe. BOLD signal was measured as the slope of the logarithm of MR signal (that decreases linearly with echo time) depending on tissue dHb content. BOLD signal was measured in regions of interest drawn in the cortex (C) and medulla (M) on both kidneys. BOLD signal was measured at baseline (BL) and at the lower limit of RBF autoregulation. BOLD was then repeated during sequential decreases in RBF to 80, 60, 40, 20, 10, 0% (S80 to S0) of BL value for 15 min, and during recovery, at 5min interval.

Results: At BL, BOLD signals were not significantly different between the right and the left C and M (RC = 19.3±1.9, RM = 17.3 ±2.0, LC = 16.4 ±0.8, LM = 17.1 ±1.5 /s, $p = 0.63$). In the right kidney, BOLD signal increased during occlusion significantly ($p<0.0001$) to a maximum of 33.8 ±2.0/s (+79%) in the RC, 29.8 ±2.3/s (+78%) in the RM at total occlusion. After the release, BOLD signal returned to BL values (RC=19.2 ±1.7, RM=17.7 ±2.5) within 15 min.

Conclusion: This study shows that BOLD signal is significantly increased by a RAS. As the method is completely non-invasive, this study provides a strong rational for developing the BOLD method for the detection and evaluation of renal hypoxia induced by RAS in humans.

M8 - RENAL HEMODYNAMICS AND FUNCTION DURING CHRONIC AND PARTIAL UNILATERAL URETERAL OBSTRUCTION.

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Objective: The changes in renal hemodynamics and function induced by chronic and partial unilateral ureteral obstruction (UUO) remain unknown because of the lack of non-invasive quantitative methods for measuring single kidney function. Electron Beam Computed Tomography (EBCT) is a functional imaging method that allows the non-invasive quantification of renal regional volume, blood flow and glomerular flow rate (GFR) of the single kidney. The aim of this study is to describe chronic changes in renal function induced by a partial UUO in pigs.

Methods: EBCT was performed 4 weeks after the insertion of a rubber ring (16 to 20 Fr) around the left ureter of 21 three-month old pigs, including 4 sham-operated animals. Obstruction was graded as severe when cortex and medulla were indistinguishable on EBCT, moderate in case of intra-renal dilation and mild in cases of exclusive extra-renal dilation. GFR and regional perfusion were estimated by modelling parenchyma regional opacity, after dye injection.

Results: GFR, regional volume and perfusion were not modified in pigs with mild (n=6) and moderate obstruction (n=6), as compared to shams. In severe obstruction (n=7), both the obstructed and the contralateral kidney volume increased significantly (+139%, $p=0.02$ and +44%, $p=0.02$, respectively). Cortical blood flow and GFR per unit weight were significantly reduced (-76%, $p=0.002$ and -71%, $p<0.0001$) in the obstructed kidney and significantly increased (+72%, $p=0.01$ and +37%, $p=0.02$) in the contralateral kidney.

Conclusion: The results of this study with EBCT show that, after one month of obstruction, significant hemodynamic and functional changes occur mainly in the pigs with severe obstruction. Moreover, the contralateral kidney compensate by hypertrophy for the functional loss of the obstructed kidney.

M9 - CORRELATION OF INTRA-RENAL CAVITY VOLUME WITH RENAL HEMODYNAMICS AND FUNCTION DURING URETERAL OBSTRUCTION

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Objectives : During unilateral ureteral obstruction (UUO), a significant correlation between functional or histological renal parameters and the quantitative measurement of dilation of the renal pelvis (ultrasound or CT-scan) has not been demonstrated. These linear measurements may not describe accurately the structural changes induced by UUO. Electron Beam Computed Tomography (EBCT) is a functional imaging method that allows the quantification of renal regional volume, blood flow and glomerular filtration rate (GFR) of the single kidney non invasively. EBCT also allows the measurement of the total volume of intra renal cavities. The aim of this study is to test if the intra renal cavity volume, as measured tri-dimensionally, by EBCT correlates with renal hemodynamics and function.

Methods: An EBCT was performed 4 weeks after the insertion of a rubber ring (16 to 20 Fr) around the left ureter of 21 three-month old pigs, including 4 animals without the ring as controls. The intra renal cavity volume was given by the product of integrated intra-renal area on abdominal transversal slices and slice thickness (6mm). GFR and regional perfusion were estimated by modeling parenchyma regional density, after dye injection.

Results: In the obstructed kidney, there was a significant correlation between intra renal cavity volume and the regional perfusion ($r=0.79$, $p<0.0001$), glomerular filtration rate expressed by gram of tissue ($r=0.83$, $p<0.0001$) and the cortical volume ($r=0.80$, $p<0.0001$).

Conclusions: This study with EBCT shows a significant correlation between modifications in renal functional parameters and an increase in volume of intra-renal cavity during ureteral obstruction, when cavities are measured tri-dimensionally. This study suggests that this quantitative parameter may useful to evaluate the impact of obstruction on renal function.

M10 - ELECTRON BEAM COMPUTED TOMOGRAPHY MEASUREMENTS OF CHANGES IN RENAL HEMODYNAMICS AND FUNCTION INDUCED BY RENAL ARTERY STENOSIS.

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Objective: Changes in single kidney hemodynamics and function induced by renal artery stenosis (RAS) remain hard to explore because of the lack of a non-invasive and quantitative method. Electron Beam Computed Tomography (EBCT) is a functional imaging method that allows for non-invasive quantification of the regional volume, blood flow, glomerular flow rate (GFR), and intra-tubular concentration capacity (ITC) of the single kidney distal to a stenosis. The aim of this study was to test the feasibility of obtaining those measurements in humans with renal artery stenosis.

Methods: Significant RAS was diagnosed by MRI or conventional angiography, and Doppler ultrasound in 5 patients with RAS due to fibromuscular dysplasia (FMD), but with preserved renal function (creatinine $\leq$1.5 mg/dL). Regional perfusion, GFR and ITC were estimated by modelling parenchyma regional opacity, after dye injection.

Results: As compared to the contralateral kidney, the stenotic kidney had significant cortical atrophy (31.6±3.2 cc vs 39.4±1.9 cc, p=0.045) without a change in medullary volume. Cortical blood flow was slightly decreased, but this has not reached statistical significance (131 vs 168 ml/min, p=0.15), and cortical perfusion remained unchanged (4.1 vs 4.2 ml/min/g). Medullary blood flow and perfusion were also unchanged. A 40% decrease in GFR has not reached statistical significance (16.8 vs 26.8 ml/min, p=0.11). ITC (proximal and distal tubule, Henle's loop) were not changed in the stenotic kidney.

Conclusion: This study demonstrates the feasibility of obtaining measurements of renal hemodynamics and function with EBCT in humans. The preliminary results suggest that in patients with RAS due to FMD at a degree usually considered significant, atrophy of the kidney may precede renal functional alterations.

M11 - Validation Of Renal Oxidative Metabolism Measurement By Positron Emission Tomography With ^{11}C Acetate.

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Objective: Ischemic nephropathy is becoming the first cause of end stage renal disease. However its exploration, either in research or in clinical practice, is limited by the lack of non invasive measurement of functional parameters, such as oxidative metabolism (OM). OM can be estimated as the acetate turnover in the Krebs cycle, which is measured in positron emission tomography after 11C labelled acetate injection (AcPET). For myocardial OM, the AcPET methodology is strongly established, but this method has never been validated for renal OM. The aim of this study is the validation of AcPET compared to renal oxygen consumption (ROC).

Methods: In 10 pigs, ROC was measured as the product of arterio-venous oxygen concentration difference by renal blood flow. Acetate turnover was estimated by PET as the slope of the linear regression between time and the logarithm of cortical acetate concentration after a 4.5 mCi injection of C11 labelled acetate. Changes in ROC were induced by different combinations of interventions, either mechanical (renal artery constriction) or pharmacological (dopamine, hypertonic saline, furosemide and acetazolamide).

Results: As expected, ROC varied on a wide range from 0.15 to 0.77 ml 0_2/l (> 5 fold). AcPET varied in the also in a wide range from 0.025 to 0.188 /min (> 7 fold). There was a very significant correlation ($p < 0.0001$, $r = 0.82$) between ROC and AcPET (AcPET = 0.228*ROC – 0.0065).

Conclusion: This study demonstrates for the first time the ability of PET to non invasively and quantitatively measure kidney cortical oxidative metabolism. This method could be relevantly used to measure renal OM in ischemic nephropathy and the impact of treatments.

M12 - RELATIVE RENAL FUNCTION MEASUREMENT : WHICH IS THE MOST CRITICAL PARAMETER ?

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Objective : The aim of that work is to identify the most critical parameter in the process of relative renal function measurement. The studied parameters are :

- the choice of radiopharmaceutical : ^{99m}Tc-DTPA or ^{99m}Tc-MAG3
- the choice of the calculation method : surface method as recommanded by international committee versus slope method
- the choice of the time measurement : the beginning of the relative renal function calculation after bolus injection versus cardiac peak activity

Methods : we studied 14 patients (preliminary data) using dynamic renal scintigraphy with ^{99m}Tc-DTPA (7 patients) or ^{99m}Tc-MAG3 (7 patients). The time duration for one image was 5 seconds. The calculation of the relative renal function was made with 15 seconds steps. Before any relative renal function calculation, we made a renal background correction. All studies were performed by the same observer. The statistical analysis of the results use Friedman test.

Results : The Friedman test shows significant variations of the relative renal function according with the measurement delay after the cardiac peak activity. In that peliminary study, these variations seem to be randomly distributed with ^{99m}Tc-MAG3. In opposite, with ^{99m}Tc-DTPA the variations seem to be time dependant.

Conclusion : these preliminary results are advocating for a well defined time measurement to evaluate the relative renal function.

M13 - SIMULTANEOUS 111IN- DTPA AND 99MTC-MAG3 FUNCTIONAL IMAGING IN CHILDREN.

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Objective. Respective value of DTPA and MAG3 for renal functional renal evaluation in children and newborns ?

Methods. 34 children were studied. Mean age was 24 months (range 15 days to 14 years). 23 were less than 1 year old. 15 were diagnosed with ureteropelvic junction, 9 with primary megaureter and 5 with other urological diseases. DTPA labelled with 111-Indium (925 KBq/Kg) and MAG3 labelled with 99mTechnetium (4625 kBq/Kg) were injected simultaneously. Double isotope dynamic acquisition lasted for 30 minutes with 1 image every 15 seconds in a 64x64 format and appropriated zoom. 0.5 mg/Kg of Furosemide were injected at 20 minutes. Signal/noise ratios (S/N) and relative clearances were measured on early images (30 seconds to 2 minutes). Maximum activity (Max), time to peak (TP), activities at 20 (A20) and 30 (A30) minutes as well as diuretic response (DR=(A20-A30)/A30) were measured on each renogram after scaling to the early cardiac activity.

Results. S/N were significantly higher for MAG3 than for DTPA ($p<0.0001$). However, this difference was less on the right side due to some liver uptake of MAG3. This phenomenon was correlated with young age ($p=0.002$). Relative clearances were not significantly different between the 2 tracers with no significant impact of the side of the abnormal kidney. TP were identical but MAG3Max was twice DTPAMax ($p<0.0001$). MAG3 DR was 15% higher than DTPA ($p<0.0001$) due to a higher A20 and identical A30 values.

Conclusion. This study confirms the superiority of MAG3 over DTPA for renal functional evaluation in young children.

M14 - QUANTITATION OF DIFFERENTIAL RENAL BLOOD FLOW AND RENAL FUNCTION USING DYNAMIC CONTRAST ENHANCED MRI IN RATS

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Objectives: Measurement of different aspects of individual kidney function is important in the diagnosis and management of renal diseases. The low-molecular-weight gadolinium diethylenetriaminepenta-acetic acid (Gd-DTPA) has physiological properties comparable to the meta-stable ^{99m}Tc-DTPA. As DTPA is excreted completely and exclusively by glomerular filtration, the paramagnetic contrast agent Gd-DTPA reflects kidney filtration, transit through the tubules and drainage into the bladder. The aim of the present study was therefore determine whether the differential renal blood flow (DRBF) and differential renal function (DRF) could be estimated for single-slice Gd-DTPA enhanced MRI in conjunction with the mathematical strategy behind the differential renal blood flow, differential renal function (clearance) approaches developed for gamma camera studies.

Methods: A Patlak-Rutland approach was used to estimate differential renal blood flow (DRBF) and differential renal function (DRF) using Gd-DTPA-BMA enhanced MRI. DRBF and DRF were estimated in rat kidneys under three different experimental conditions: 1) transient renal artery occlusion (TRAO); 2) partial unilateral ureteral obstruction (PUO); and 3) sham operated control rats (SHAM). A bolus of Gd-DTPA-BMA was given intravenously during a dynamic single slice T1-weighted gradient echo sequence, which allowed calculation of concentration from signal intensity values.

Results: Calculations based on the raw signal intensity showed that DRBF was decreased in both PUO (44±1%; $p<0.05$) and in TRAO (38±1%; $p<0.05$) compared with SHAM (52±1%). Converting the signal intensity into a measure of Gd-DTPA-BMA concentration did not substantially alter these findings (PUO: 40±3%; TRAO: 35±2%; SHAM 49±1%). Likewise, DRF decreased in both PUO (43±4%; $p<0.05$) and TRAO (39±3%; $p<0.05$) compared with SHAM (48±2%). Converting the signal intensity into measurements of Gd-DTPA-BMA concentration revealed similar findings (PUO: 41±5%; TRAO: 34±5%; SHAM: 49±2%). PUO and TRAO data were all markedly lower as compared with SHAM, statistical analysis revealed significant differences.

Conclusions: Our results suggest that DRBF and DRF can be adequately assessed from the acquired single slice Gd-DTPA-BMA enhanced signal intensity using time activity curves in rats without absolute quantitation of Gd-concentration.

M15 - URETERAL OBSTRUCTION IS ASSOCIATED WITH DECREASED INTRARENAL OXYGEN CONTENT MEASURED BY BOLD MRI

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Objectives: Urinary tract obstruction is a common disorder during both childhood and adolescence. Blood oxygenation level dependent (BOLD) magnetic resonance (MR) imaging provides a measure of deoxyhemoglobin. Thus, BOLD MR imaging measures the intrarenal partial pressure of oxygen (pO2) indirectly. The purpose of this study was therefore to examine the relationship between the apparent relaxation rate (R2*), measured by BOLD imaging, and simultaneously measured absolute values of pO2 by an oxygen sensitive microelectrode. Secondly, intrarenal pO2 levels were measured during and after release of unilateral ureteral obstruction (UUO).

Methods: Adult Danish Landrace pigs were used and oxygen sensitive microelectrodes were inserted into renal parenchyma. Different arterial and intrarenal levels of pO2 were obtained by stepwise changing the percentage of the respirator supplied oxygen-to-nitrogen ratio. Pigs were subjected to 24 h UUO by inserting a catheter through the mid-ureter with the tip placed in the renal pelvis and the other end of the catheter closed with a stop-gauge.

Results: When the inhaled oxygen fraction was 5-70%, R2* was approximated to vary linearly with pO2 levels (cortex: $\Delta R2^*/\Delta pO2=-1.2$ $ms^{-1}kPa^{-1}$ and medulla: $\Delta R2^*/\Delta pO2=-1.7$ $ms^{-1}kPa^{-1}$), indicating that reduction in arterial pO2 levels predominantly affects the amount of medullary deoxyhemoglobin. UUO caused a marked reduction in medullary pO2 (1.9±1.1 kPa vs 4.1±0.6 kPa, P=0.032), which normalized after release of obstruction (3.3±1.2 kPa vs. 4.2±0.7 kPa, N.S.).

Conclusion: BOLD MR imaging provides reliable non-invasive estimates of renal oxygen content and the technique may provide a useful additional tool in the diagnostic strategy in cases with suspected ureteral obstruction.

M16 - CONVOLUTION OF RENOGRAMS AND DECONVOLUTION USING LAPLACE TRANSFORMS.

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Objectives: (1) To understand better the shape of a renogram depending on the shape of the renal input curve and the distribution of renal transit times, (2) To understand better how the important renal *mean* transit time is defined and determined, (3) To investigate the accuracy and robustnesss of the deconvolution method as regards propagation of errors in the renograms originating, for example, from irregular renal outflow, and (4) To determine the accuracy of prolonged renal mean transit times as function of the duration of the renography.

Methods: Convolution of renograms was made using nine different sum-of-exponential renal input functions (with or without a bolus term at injection time) and eight different models of the renal impulse response function. Simulations of the renograms were also made with Gaussian distributed noise and noise spikes superimposed on the renograms. Admittedly, the writing of the computer program for deconvolution with Laplace transforms is comprehensive.

Results: Deconvolution based on Laplace transforms yields very accurate deconvoluted renal impulse response functions using error-free renograms. The direct deconvolution algorithms using Laplace transforms is not particularly sensitive to propagation of errors in the renogram.

Conclusion: Deconvolution using Laplace transforms is recommended for use not only in renal applications but as a general tool for direct determination of the distribution of transit times. The condition that the input function must be represented by a sum-of-exponential expression is satisfied in most nuclear medicine applications.

M17 - A NEW FORMULA FOR MEASURING 99mTc EC CLEARANCE

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Objective: Numerous simplified formulas have been proposed for estimating clearance of renal radiopharmaceuticals. Russell et al. (JNM 1996) have proposed a new approach to measure 99mTc-MAG3 clearance using single plasma sample which is based on dimensional analysis. This study aimed to test the accuracy of same method for estimating 99mTc-EC clearance.

Methods: Data of 62 subjects were included in this study. Reference 99mTc-EC clearance values from 6-10 samples were calculated using the Sapirstein's method. Reference values were scaled to body surface area.
The following equation was used; Ct/W= ln (pW) (C=clearance of 99mTc-EC (mL/min), t(min)=sampling time, W(kg)=weight, p=plasma concentration expressed as the fraction of administered dose per liter). The calculated ln(pW) values were plotted against the Ct/W values. Using the polynomial analysis, the following formulas were obtained for several sampling times.
Ct/w (40 min) = 259.34 - 196.19 X + 36.47 X2
Ct/w (45 min) = 264.10 - 202.78 X + 41.06 X2
Ct/w (50 min) = 266.89 - 206.90 X + 44.3 X2
Ct/w (55 min) = 268.62 - 207.52 X + 45.19 X2
Ct/w (60 min) = 269.32 - 203.59 X + 25.45 X2 X=Ln (pW)
When the estimated clearance values scaled to body surface area were compared with the reference 99mTc-EC clearance value, close agreement was observed.

Sampling time	correlation coef.	residual s.d
40	0.962	27.32
45	0.968	25.47
50	0.972	24.17
55	0.973	23.68
56	0.973	23.69
57	0.973	23.72
58	0.973	23.83
59	0.973	23.95

Conclusion: The formula presented here provides low residual standard deviation and good correlation in the estimation of 99mTc-EC clearance using single plasma sample obtained from 50-60 minutes.

M18 - THE INFLUENCE OF BACKGROUND SUBTRACTION PROTOCOLS ON RANDOM ERRORS IN RENOGRAPHY ANALYSIS

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Purpose: Background subtraction in renography is valuable in improving the accuracy of assessing renal function from radiopharmaceutical uptake. However different subtraction protocols can give rise to different results. This study aims to compare the random variation obtained with two different methods of subtraction and two different ROI locations.

Methods: Renal uptake at 1.5 min was assessed in twenty MAG3 renograms using (a) a simple one-stage subtraction and (b) a two-stage protocol involving separate subtraction of extra- and intra-renal components using deconvolution analysis. The two protocols were used with two different background region locations and varying size of the renal ROI. The variability of results was assessed for each protocol and the values compared.

Results: The difference between background-subtracted counts (C_b) for the two background locations, was significantly lower for two-stage (4.4%) than for one-stage (9.3%) subtraction ($p<0.001$). The difference between the background locations was evaluated for the two-stage background protocol. There was no systematic difference between background-subtracted counts for central and peri-renal ROIs. The variation of background-subtracted counts when ROI size was changed by one pixel (4.5 mm) in radius, was significantly lower for the central background ROI (3.1%) compared to the peri-renal ROI (5.4%) ($p<0.01$).

Conclusion: Variation in renal uptake values is reduced by use of separate subtraction of extra- and intra-renal components and use of a central rather than a peri-renal ROI. The higher variability for the peri-renal ROI results from the more rapid variation in counts per pixel in background ROIs towards the edge of the patient.

M19 - Quantitative measurement of renal function using contrast enhanced MRI: an initial experience.

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Objectives: Magnetic resonance imaging (MRI) has recently demonstrated potentials for determination of single-kidney GFR indexes, giving measures that are proportional or in correlation with GFR measures based on radiopharmaceutical techniques. These studies have most often been conducted using rapid dynamic acquisition followed by an instant bolus of Gd-DTPA that is known to excrete exclusively through glomerular filtration. Based on this approach, this survey communicates a novel strategy to obtain quantitative measures on total kidney GFR founded on currently available system performance and dedicated post-processing algorithms.

Methods: MRI was performed with a 1.5 T Philips system, where data perception and reception were performed with a phased-array radiofrequency coil. Five patients with various renal disorders were included in this initial study. A strong T1 weighting was obtained using a saturation recovery prepulse prior to a 3D fast-gradient-echo scheme with minimum TR and TE, allowing 5 consecutive slices to be obtained in less than 2 seconds. Imaging was performed in the coronal plane traversing both the longitudinal axis of the kidneys and aorta. Signal intensities were converted into measures of MR using: 1) known relaxation rates and relaxivity constants of Gd-DTPA of renal parenchyma, 2) estimated amount of injected dosage that reaches the renal parenchyma, and 3) a known pulse sequence expression that describes changes in signal intensity. Next, a volume scan was performed to derive the parenchymal volume of each kidney. The second part involving the quantification of GFR (in units of ml/min/cm^3) was calculated by two methods: 1) deconvolution analysis based on the indicator dilution theory (slightly modified compared to the original approach presented by Østergaard et al) [1], and 2) the Patlak-Rutland-plot approach [2]. In both cases, a signal intensity curve of the abdominal aorta was used as the arterial input function (AIF). The delay that exists from blood entering the arterial ROI to its arrival in the kidney was accounted for by time-shifting AIF accordingly. In the final step, an estimate of the capillary to large vessel hematocrit ratio was multiplied to these results to derive GFR (in units of ml/min) per single kidney. Estimations of the total GFR were compared with those derived by the empirical Cockroft-Gault formula.

Results: The total kidney GFRs of the 5 patients are here presented in brackets to identify: renal disease, GFR measured with Cockroft-Gault formula, GFR measured with deconvolution, GFR measured with the Patlak approach) with units in ml/min. Data are: patient 1 (ureteric obstruction, 62, 57, 59); patient 2 (allograft, 45, 44, 42), patient 3 (renal artery stenosis, 70, 80, 62), patient 4 (normal, 65, 69, 54), and patient 5 (renal artery stenosis, 121, 91, 95).

Conclusions: This study demonstrated, for the first time, a strategy to derive GFR based on dynamic Gd-DTPA enhanced MRI of the kidney. Bear in mind that our

findings revealed a number of differences between GFR values measured by this technique and those calculated by the empirical Cockroft-Gault formula. This is likely explained by several factors, including a need for: 1) movement compensation, 2) better intrarenal delineation (segmentation techniques), 3) accurate conversion of signal intensity into measures of Gd-DTPA concentration, 4) verification of relaxivity constants, and 5) better knowledge about large vessel and capillary hemotocrit. Secondly, the Cockroft-Gault formula is not considered being an exact reference as opposed to calculations based on inulin or creatine-clearance. Nonetheless, we believe that our proposed method can be further developed to become an attractive tool for investigation of clinical important studies of the kidney, allowing non-invasive measures of GFR values comparable with those derived from currently available methods.

References: 1. Østergaard L, Magn Reson Med 36:726-36, 1996. 2. Pedersen M, Magn Reson Med 51:510-7, 2004.