Correlation of the ERPF with the Extraction Fraction
Values of Technetium-99m Mercaptoacetyltriglycine

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Objective: The objective of this study was to determine if a correlation exists between the effective renal plasma flow (ERPF) and the extraction fraction (EF) using 99mTc MAG3 in children. This EF has been previously described with 99mTc DTPA. However, the renal imaging agent of choice has become 99mTc MAG3.

Material and Method: The study was approved by The Children’s Hospital of Philadelphia’s institutional review board. Informed consent was also obtained. A retrospective study of 29 children (16 males, 13 females) of ages 1 month to 19.5 years who underwent 99mTc MAG3 renal scintigraphy from September 2001 to December 2001 was analysed. EF values were calculated with and without attenuation correction in each kidney by determining the counts in a region of interest, correcting for background and comparing the counts with the injected dose. The EF was compared to the ERPF calculated using the Schlegel’s method. The correlation between the EF and the ERPF, corrected and non-corrected for soft tissue attenuation, were determined and were identified by using linear regression analysis.

Results: There was significant correlation between the ERPF and the EF with (r = 0.62, p < 0.05 on the left, r = 0.51, p = 0.005 on the right) than without attenuation correction (r = 0.54, p = 0.003 on the left, r = 0.42, p = 0.022 on the right).

Conclusion: These results indicate a correlation of the ERPF calculated using the Schlegel’s method with EF obtained from a 99mTc MAG3 renal scintigraphy. The EF may be the good alternative parameter for calculation of renal function, potentially more practical in pediatric patient and the ERPF for 99mTc MAG3 using the established software program based on Schlegel’s formula.

Keywords: Extraction fraction, Mercaptoacetyltriglycine, Estimated renal plasma flow, Renography, MAG3

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Technetium-99m Mercaptoacetyltriglycine (MAG3) was introduced as a replacement for Iodine-131 Orthoiodohippurate (OIH) for renography studies and measurement of renal function, especially in infants and children due to the favourable dosimetry and excellent imaging qualities of the compound[1,2]. For quantification of renal function using radionuclides, several techniques have been reported as references[6,7].

Gamma camera based methods are a potentially advantageous alternative because they do not require blood sampling. Effective renal plasma flow (ERPF) is also used to monitor renal function. The ERPF can be calculated with a gamma-camera based method by using Schlegel’s formula[8], which is often implemented in commercially available software packages. However, the limitation of this method is that it was originally demonstrated for OIH clearance, which is not suitable in clinical practice for infants and children.

The EF has previously been described as a good indicator for individuals as well as for global kidney function[9]. The authors routinely determine an EF.
with MAG3 as a parameter of renal function for each kidney, expressed from the activity accumulated during minute 1 to 2 after injection as a percentage of the injection dose. To date, no study has reported the correlation between the ERPF based on Schlegel’s formula and the EF for MAG3 in a camera based technique.

To assess the correlation between $^{99m}$Tc MAG3 ERPF and EF by the gamma camera based method in children, the authors compared the ERPF calculated with Schlegel’s method and the EF calculated as a percentage of the injected dose and to determine if the $^{99m}$Tc- MAG3 ERPF could be used directly as a measure of renal function in clinical practice.

Material and Method

The study was approved by The Children’s Hospital of Philadelphia’s institutional review board and informed consent was obtained. There is no financial conflict of interest. This study was performed during one of the authors’ (Chanisa Chotipanich) study, supported by International Atomic Energy Agency (IAEA) fellowship at Hospital of the University of Pennsylvania, Philadelphia, Pennsylvania.

Patient population

A retrospective study of the patients who performed $^{99m}$Tc MAG3 renal scintigraphy from September 2001 to December 2001 was analysed. Fifty-eight renal units in 29 patients (16 boys, 13 girls), age 1 month to 19.5 years (mean age, 2.20 years; median age, 0.45 years), were studied after having received informed consent. Patient data are shown in Table 1.

Dose injection

The syringe with the radioactive dose of $^{99m}$Tc MAG3 was counted by placing it in the centre of the

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<th>%EF LT</th>
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% cEF= % extraction fraction with attenuation correction
field of view for exactly 30 centimetres below a large FoV gamma camera (ADAC-SKYLIGHT) fitted with a low energy high resolution collimator. Ten-second image acquisition of the syringe was obtained pre and post injection.

**Imaging procedures**

Gamma camera renography was performed on a dual head gamma camera (ADAC-SKYLIGHT) with a low energy high-resolution collimator, and a 20% window centred over the 140 keV photo peak of $^{99m}$Tc. Patients remained supine on the bed above the gamma camera and were hydrated with a saline solution at 10 to 20 drops per minute during the exam. Following the intravenous injection of 74-148 MBq of $^{99m}$Tc MAG3, the image data were collected in a 128x128 matrix at 1 second per frame in the initial 1 minute and, thereafter, at 30 seconds per frame for 50 minutes.

**Data analysis**

EF for each kidney was determined from summation of all frames between 1 and 2 or 1 and 3 minutes included, after the injection. Renal and perirenal background regions of interest (RoIs) were drawn manually around each kidney (Fig. 1). The background corrected count in each kidney was obtained with and without attenuation correction.

**Determination of extraction fraction (EF)**

The extraction fraction was calculated for each kidney according to the protocol of Children’s Hospital of Philadelphia as follows:

$$\text{EF} = \frac{((1-2 \text{ min kidney counts-Background}) \times Y)}{\text{Pre-post syringe count} \times 6} \times 100,$$

where Y is the depth correction factor calculated from the following equation:

$$\text{Depth correction factor} = \frac{\text{patient’s height in centimetre}}{\text{patient’s weight in pounds}}.$$

and 6 is used to convert the count from 10 second to 1 minute frames

**Determination of effective renal plasma flow (ERPF)**

The ERPF was calculated according to the protocol (method for ERPF analysis of Schlegel) with software provided by ADAC based on the following:

$$\text{ERPF} = \frac{5.029 \times \text{Body Surface Area} \times R}{\text{Body Surface Area} = \frac{\text{Weight (kg)^0.425}}{\text{Height (cm)^0.725}}} \times 0.007184,$$

and R is the predicted 30-minute return of the injected nuclide, defined as:

$$\text{Predicted Return} = \frac{\text{Individual kidney uptake}}{\text{Total uptake and calculated on each side}}.$$

The uptake is calculated as follow:

$$\text{Uptake} = \frac{\text{Background-corrected counts}}{(\text{Raw Counts} - \text{Background counts} \times \frac{\# \text{pixels in kidney ROI}}{\# \text{pixel in Background ROI}})}.$$

Kidney depth was estimated from the correlations:

Right Kidney Depth = \(\frac{13.3 \times \text{Weight (kg)}}{\text{Height (cm)}} + 0.7\)

Left Kidney Depth = \(\frac{13.2 \times \text{Weight (kg)}}{\text{Height (cm)}} + 0.7\)

**Statistic analysis**

From this database, the authors estimated the correlation between ERPF and EF for both kidneys with and without attenuation correction. Data was analysed using SPSS version 14 (SPSS, Chicago, IL). 95% confidence intervals were presented. A p-value of less than 0.05 was considered to indicate a statistical significance. Pearson correlation coefficients were correlated for comparison between the ERPF and EF with and without attenuation correction. Simple linear regression models were fitted.

**Results**

The results are summarized in Table 1. Regression curves are shown in Fig. 2 and 3. The ERPF of both kidneys was found to correlate with the EF with attenuation correction, with a correlation coefficient of 0.62 for the left kidney and 0.51 for the right kidney.

![Fig. 1 Regions of Interest (ROIs) for each kidney with background surrounding the individual kidney](image-url)
The regression lines of left and right kidney were expressed by the equation: $Y = 21.357X + 90.15$, $r^2 = 0.386$, $p < 0.05$, 95%CI; 0.009, 0.027 and $Y = 18.644X + 117.65$, $r^2 = 0.257$, $p = 0.005$, 95%CI; 0.005, 0.023, respectively. If the EF is calculated without attenuation correction is analysed; the correlation coefficient is 0.54 for the left kidney, 0.42 for the right kidney. The equations of the left and right kidneys were $Y = 26.231X + 113.95$, $r^2 = 0.29$, $p = 0.003$, 95%CI; 0.004, 0.018 and $Y = 21.236X + 143.84$, $r^2 = 0.18$, $p = 0.022$, 95%CI; 0.001, 0.016, respectively.

**Discussion**

When available, Technetium-99m Mercapto-acetyltriglycine (MAG3) is the radiopharmaceutical agent of choice for renal scintigraphy in the evaluation of pediatric nephrourological disease\(^{10-12}\). However, there have been few studies discussing quantification of renal function with \(^{99m}\)Tc MAG3 in children\(^{10-18}\), particularly with a gamma camera based method\(^{19-21}\).

The index for renal function obtained with a \(^{99m}\)Tc MAG3 study for clearance, however, is not often familiar to clinicians and needs to be converted to effective renal plasma flow (ERPF). Higher protein binding, higher plasma concentration, lower plasma clearance and smaller volume of distribution\(^{13-16}\) create high quality imaging; however, the calculation of the ERPF cannot be obtained directly from \(^{99m}\)Tc MAG3. Therefore, a “correction factor” has been used to translate MAG3 clearance into estimated ERPF values\(^{17}\).

Another drawback of \(^{99m}\)Tc MAG3 is that software packages of gamma-camera based methods to calculate the ERPF are validated only for OIH.

Quantitative assessment of renal function is a major role of radionuclide renography and several methods have been reported to estimate MAG3 clear-
ance\textsuperscript{(21-25)} as an index of renal function. Techniques based on the gamma camera acquisition and computer post-processing, are reportedly less accurate than methods based on plasma clearance\textsuperscript{(26)}.

The EF is a good indicator to determine renal function. The EF correlates well with the glomerular filtration rate (GFR) as determined by the clearance from the blood of \textsuperscript{99m}Tc Diethylenetriaminepentaacetic acid (DTPA) with a correlation coefficient of 0.92\textsuperscript{(9)}. Kilingsmith\textsuperscript{(27)} compared the renal uptake of \textsuperscript{99m}Tc MAG3 at 1-2 minutes as a percent of the injected dose in 36 patients studied at least 2 days apart and reported excellent correlation (r = 0.99). Finally, Kazuo\textsuperscript{(20)} reported that the renal uptake per injected dose (%RU) of the 1-min post injection correlates well with plasma clearance by a single blood sample method as the reference, using MAG3 (r = 0.910). The authors routinely measured and reported the differential renal function in terms of MAG3 EF, defined as the activity of radio-tracer present in the ROIs during the passage of the bolus 1 to 2 minutes after injection, expressed as a percentage of the injected dose. For the calculation of renal uptake from the injected dose, several factors are important, including the amount of injected dose, the definition of the region of interest (ROIs), the calculation of renal depth, the value chosen for the effective linear attenuation coefficient of 140 keV photons in the body and correction for background activity. The actual effects of these factors on the estimation of absolute renal uptake have been described by a number of authors\textsuperscript{(28-31)}. Attenuation correction will lead to more accurate measurement of renal function using \textsuperscript{99m}Tc MAG3.

In the present study EF values were obtained with and without attenuation correction in each kidney. The region of interest corresponds to the renal contour and is corrected for background. The injected dose was measured and compared to ERPF values based on Schlegel’s method\textsuperscript{(8)}. In the presented results, 58 kidneys in the 29 patients showed a better correlation between ERPF and EF with attenuation correction (r = 0.62 on the left, r = 0.51 on the right) than without it (r = 0.54 on the left, r = 0.42 on the right).

**Fig. 3** Correlation between ERPF of left kidney as determined by Schlegel’s formula and EF (A) with attenuation correction (B) without attenuation correction.

The actual effects of these factors on the estimation of absolute renal uptake have been described by a number of authors\textsuperscript{(28-31)}. Attenuation correction will lead to more accurate measurement of renal function using \textsuperscript{99m}Tc MAG3.

In the present study EF values were obtained with and without attenuation correction in each kidney. The region of interest corresponds to the renal contour and is corrected for background. The injected dose was measured and compared to ERPF values based on Schlegel’s method\textsuperscript{(8)}. In the presented results, 58 kidneys in the 29 patients showed a better correlation between ERPF and EF with attenuation correction (r = 0.62 on the left, r = 0.51 on the right) than without it (r = 0.54 on the left, r = 0.42 on the right).
Study limitation

The current study was also limited by the small number of patients included. Therefore, it might have decreased the authors’ powers to detect the true difference. Further study should be undertaken with a larger sample size.

Conclusion

The authors found statistically significant correlation between ERPF measurements based on Schlegel’s method and EF using MAG3. The EF can be used as an alternative parameter for the calculation of renal function and is meaningful in long-term follow up care of pediatric patients with renal involvement. Moreover, the ERPF for 99mTc MAG3, obtained from the software program based on Schlegel’s formula, can be used directly as a measure of renal function.

Acknowledgements

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References


ความสัมพันธ์ระหว่างค่า Effective renal plasma flow และ Extraction fraction โดยใช้ 99mTc-MAG3

ชนิสา โอติพานิช, مارك อิเกอร์สัน, เจนเซนฟ คาน, เทพ เบนจิมิน, ดักลัส แผนนิ่ง, แมริสัน ชาร์ล็อต

วัตถุประสงค์: เพื่อศึกษาความสัมพันธ์ระหว่างค่า ERPF และ EF โดยใช้ 99mTc-MAG3

วัสดุและวิธีการ: ทำการศึกษาไปในหลังผู้ป่วยเด็กจำนวน 29 รายที่มารับการตรวจที่ The Children's Hospital of Philadelphia ในระหว่างเดือนกันยายน พ.ศ. 2544 ถึงเดือนธันวาคม พ.ศ. 2544 โดยเป็นผู้ชาย 16 ราย ผู้หญิง 13 ราย อายุเฉลี่ย 2.2 ปี (1 เดือนถึง 19.5 ปี) ศึกษาโดยวิธีการตรวจ Renal scintigraphy (99mTc-MAG3) โดยที่ค่า EF ที่วิเคราะห์ได้มาจากวิธีการตรวจแก้ไขและไม่ตรวจแก้ไขภูมิคุ้มกันรังสี (attenuation) ของไตในแต่ละข้าง ปรีบปรกความสัมพันธ์ระหว่างราคา EF กับค่า ERPF จากผลลัพธ์วิเคราะห์ Linear regression analysis

ผลการศึกษา: มีความสัมพันธ์ระหว่างค่า ERPF กับค่า EF ที่ตรวจแก้ไขภูมิคุ้มกันรังสี (attenuation) ของไตในแต่ละข้างอย่างมีนัยสำคัญทางสถิติ โดยมีค่าสัมประสิทธิ์สัมพันธ์ (r) เท่ากับ 0.62 ของไตซ้าย และ 0.51 ของไตข้างขวาตามลำดับ

สรุป: การศึกษาข้างต่อข้างว่า ERPF ที่คำนวณโดย Schlegel’s method และค่า EF ที่ใช้ 99mTc-MAG3 มีความสัมพันธ์กันอย่างมีนัยสำคัญทางสถิติ ดังนั้นค่า EF น่าจะถูกพิจารณานำมาใช้ในการหาการทำงานของไตในผู้ป่วยเด็ก และในขณะเดียวกันสามารถใช้ Schlegel’s method ในการหาค่า ERPF จาก 99mTc-MAG3 renal scan