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Order No. A91DX-HHS-150290-XC2-4A00 | 02-2016 | © Siemens Healthcare Diagnostics Inc., 2016

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Monitor Residual Renal Function Simply and Accurately

N Latex BTP (Beta-trace Protein) Assay

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The Role of Residual Renal Function in Kidney Dialysis

Chronic kidney disease (CKD) is a major public health problem, and CKD's incidence and prevalence are increasing worldwide. End-stage renal disease (ESRD) is the last stage of CKD, in which dialysis or organ transplant are required to stay alive. ESRD prevalence data shows an alarming trend (see Figure 1): ESRD and dialysis are increasing worldwide.[1] Dialysis is expensive (about $80,000 USD/patient/year), and improved therapy may help in reducing the cost. Home dialysis (peritoneal dialysis) can help to reduce expenditures, as costs are approximately $25,000 USD/patient/year.

In patients undergoing dialysis, contribution of the residual native kidney function, also known as residual renal function (RRF), is highly associated with improved outcomes.[2,3] RRF can be an important marker for monitoring the decline of kidney function, predicting mortality, deciding on peritoneal dialysis versus hemodialysis, and adjusting the dialysis regimen. Maintenance of some level of RRF may also improve quality of life for patients, as it may influence food intake and diet.[3,4] An optimized approach to dialysis can also help to manage costs, because dialysis contributes significantly to overall healthcare expenditures (e.g., $28.6 billion in cost to Medicare in the U.S.[1]).

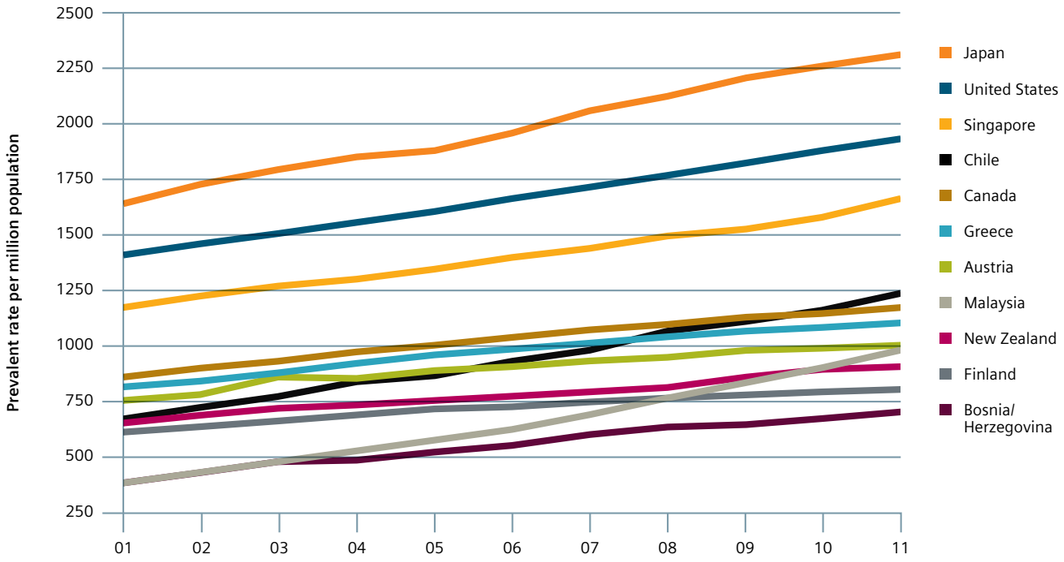

Figure 1. Comparison of unadjusted ESRD prevalence worldwide. All rates are unadjusted. Data from Japan are dialysis only. Graphic modified from 2013 USRDS Annual Data Report Volume 2: Atlas of End-Stage Renal Disease in the United States.[1]

BTP Offers a More Precise Alternative for RRF Determination

The European Best Practice Guidelines on dialysis strategies recommend RRF measurement every 2 months.[5,6] Estimation of the glomerular filtration rate (eGFR) is a reliable measure for determination of CKD. Measurements of analytes such as creatinine or urea in urine are commonly used in order to determine eGFR as well as RRF through creatinine or urea clearance.

However, urea clearance and creatinine measurements have been shown to lack precision in dialysis patients; due to their low molecular weight, these markers are efficiently removed by dialysis membranes (see Figures 2 and 3). In addition, urea and creatinine measurements require a cumbersome, 24–48 hour urine collection, a task that is difficult and inconvenient for many patients. As a result, this collection is performed in fewer than 5% of U.S. hemodialysis patients.[7]

An accurate and convenient method for determination and monitoring of RRF is therefore desirable.

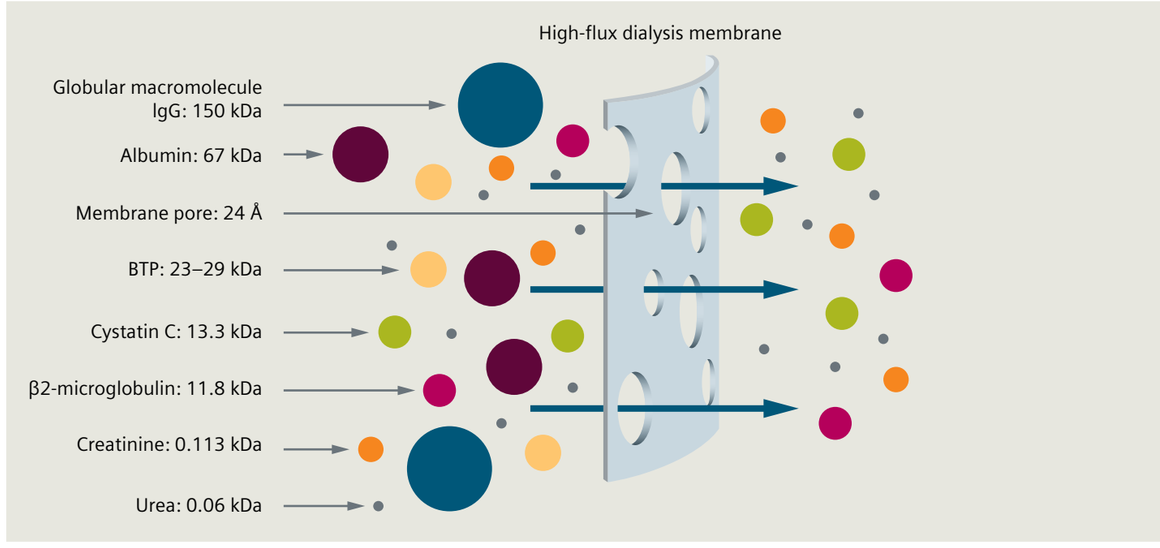

Figure 2. Beta-trace protein (BTP) is freely filtered by the glomerulus, absorbed by renal tubules, and then degraded. With a molecular weight of 24 kDa, BTP is not removed by dialysis. It also does not seem to be affected by the patient's gender, age, weight, diet, fitness, or body composition, and so may represent a more accurate surrogate RRF measurement than creatinine or urea.[8,9]

Beta-trace protein (BTP) is expressed in all tissues (except in ovaries) and can be found in various biological fluids (CSF, plasma, urine).[10] Virtually all BTP is filtered by the kidneys; consequently, its concentration in plasma is mainly dependent on glomerular filtration rate (GFR). Like cystatin C, serum BTP levels increase with decline of kidney function. However, cystatin C may be of limited value in the dialysis setting due to partial removal during dialysis.[11]

BTP is not influenced by thyroid function or the influence of corticosteroids. BTP has been shown to serve as a surrogate marker for RRF in dialysis settings,[12] because it is not removed by dialysis due to its size (Figure 2).

Due to its high concentration in plasma, BTP offers a desirable alternative to urea and creatinine clearance for determination of RRF. BTP also predicts end-stage renal disease more conveniently than creatinine or urea. Unlike other markers—creatinine, cystatin C, and β2-microglobulin—BTP is not filtered out by peritoneal dialysis or hemodialysis machines; therefore results are more accurate, and a true picture of RRF status is provided. This increases confidence in diagnosis when monitoring individual therapies.

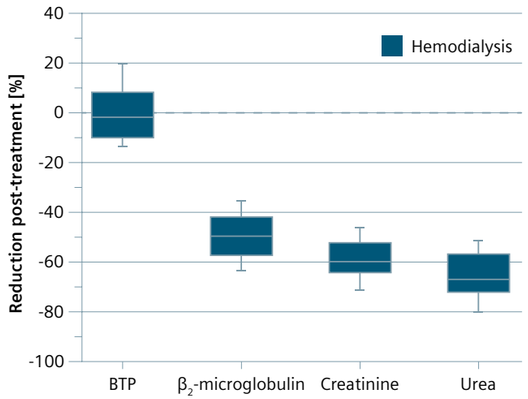

Figure 3. Pre- and post-hemodialysis levels of markers of GFR and RRF (adapted from Gerhardt et al.[12]).

N Latex BTP Assay: The First Marker to Accurately and Simply Estimate RRF Status with One Serum Sample

The N Latex BTP assay from Siemens Healthcare is a fast and accurate screening method for determination of GFR and RRF in serum samples. As a fully automated, random-access assay designed for the Siemens BN™ II and BN ProSpec® Systems, the N Latex BTP assay employs a latex-enhanced, polyclonal reagent with high lot-to-lot reproducibility.

Serum BTP measurement with the N Latex BTP assay combines increased accuracy of RRF determination compared to other methods and much simpler sample retrieval.[13] Compared to the long-term urine-collection method required for measurement of urea and creatinine, BTP determination requires only a single serum sample that can be obtained during routine care of dialysis patients. No special trips or extra tasks are required of patients, and there are no procedures that must be done correctly and consistently by patients to ensure accurate results. Because no extra effort is required on the part of patients, there is greater potential for more patients to be monitored for RRF than the very small number monitored today.

The estimation of RRF by BTP measurement may help support decisions regarding the modality and frequency of dialysis and thus contribute to better patient outcomes.

Shafi et al. proposed the first equation for the direct calculation of RRF from BTP for dialysis patients.[13]

Adult estimated RRF using BTP:[13]

$95 \times BTP^{-2.16}$ (x 1.652 if the patient is male)

(BTP = mg/L; RRF = mL/min/1.73m²)

Figure 4: Estimation of RRF in dialysis patients. RRF is expressed as average of urinary urea and creatinine clearance.

> "BTP provides a promising blood measure of RRF that could facilitate existing recommendations to integrate regular assessment of RKF."
>
> Shafi, et al. Serum BTP and Mortality. Clin J Am Soc Nephrol. 2012.

In addition, several studies have shown that BTP may be a sensitive marker of GFR in specific settings, e.g., transplant recipients or pediatric patients. The CKD Epidemiology Collaboration (CKD-EPI) has also suggested an equation for GFR utilizing BTP (see figure 5).

CKD-EPI equation using BTP:[14]

$eGFR = 55 \times BTP^{-0.695} \times 0.998^{age}$
(x 0.899 if the patient is female)

(BTP = mg/L; eGFR = mL/min/1.73 m²)

Pediatric estimated GFR using BTP:[15]

eGFR = 10^(1.902 + (0.9515 x LOG(1/BTP)))

Figure 5. BTP is an accurate endogenous marker for GFR estimation in both general CKD, and pediatric patient populations as well as in renal transplant receipients.[14-16]

A Significant Advance in RRF Determination

BTP results demonstrate the quality of dialysis management. Therefore, BTP measurement may support individualized therapeutic decisions, such as diet and fluid intake recommendations and whether peritoneal dialysis at home is indicated, leading to better patient outcomes.

- Allow estimation of renal contribution to renal clearance, without urine collection
- Support decisions regarding modality selection
- Adjust dialysis regimen
- Proactively anticipate and manage complications
- Use therapies that preserve RRF
- Test new interventions to preserve RRF
- Simplify clinical trial design
- Support decisions on fluid intake and diet in dialysis patients, thus improving patient's quality of life

Simple and Precise Monitoring of RRF

- Suitable for human serum, heparinized and EDTA plasma, urine, CSF, and nasal or ear secretions containing CSF
- Fully automated, random-access assay
- Low imprecision (total CV <5%)
- Latex-enhanced, polyclonal reagent providing high lot-to-lot reproducibility

Expected values:

	95th Percentile (Median)
BTP in serum	0.70 (0.50) mg/L
BTP in urine	≤3.75 (1.11) mg/L

Beta-trace Protein measurement with the N Latex BTP assay offers simpler sample retrieval and increased accuracy of RRF determination when compared to other methods. For use on BN™ II and BN ProSpec® Systems, it is the first assay to accurately, reliably and simply estimate RRF status with one serum sample. N Latex BTP assay also offers a fast and accurate method to determine leakage of cerebrospinal fluid (CSF) in trauma or head surgery patients.

Two applications—one accurate, convenient, fully automated assay.

Visit siemens.com/BTP or contact your Siemens Healthcare representative for more details.

Conveniently Monitor RRF

The Siemens N Latex BTP assay quickly and easily delivers the results clinicians need to conveniently and accurately monitor RRF and determine appropriate dialysis strategies. With the broadest menu on reliable, dedicated plasma-protein analyzers, Siemens enables confident clinical decisions.

Take advantage of a powerful combination:

The N Latex BTP assay is available on the BN II and BN ProSpec Systems.

BN ProSpec System: Dedicated, compact system offering a consolidated menu of specialty and routine plasma-protein testing.

BN II System: Fully automated analyzer providing confidence in results for mid- to high-volume plasma-protein testing.

The products/features mentioned here are not commercially available in all countries. For regulatory reasons, their future availability cannot be guaranteed. Please contact your local Siemens organization for further details.

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