Evaluation of the Atellica IM Thyroglobulin (Tg) Assay*

Schiavoni L, Bradley K, Carbone L, Higgins C, Iaconelli E, St-Onge S, Yang Y, Zhao Z, Dauscher C.
Siemens Healthcare Diagnostics Inc., Tarrytown, NY, U.S.

siemens-healthineers.com

Clinical Brief

*Not available for sale in the U.S. Product availability may vary from country to country and is subject to varying regulatory requirements.

SIEMENS Healthineers

Evaluation of the Atellica IM Thyroglobulin (Tg) Assay*

Introduction

Thyroglobulin (Tg) has an important role in monitoring patients with differentiated thyroid cancer following successful removal of all thyroid tissue by total thyroidectomy with or without radioiodine ablation. In these patients, serum Tg is expected to decrease to undetectable levels (e.g., <0.2 ng/mL). Detectable and/or rising concentrations of serum Tg following total thyroidectomy may be indicative of persistent or recurrent disease. Due to residual tissue in patients treated with lobectomy, serum Tg levels will remain at measurable levels.

Thyroglobulin assays with a functional sensitivity <0.05 ng/mL provide the opportunity to detect changes in Tg levels earlier. Early detection may allow patients to remain on thyroid replacement therapy (without TSH stimulation) prior to Tg testing.[1]

Single measurement of Tg close to the limit of detection is of minimal value in assessing disease status. Serial determinations are required and should be referenced to the postsurgical baseline Tg result when possible. Evaluation of increasing Tg levels over time is more clinically important.[2]

A limiting factor in the use of serum Tg measurements is the presence of Tg autoantibodies (aTg) found in some patients. These antibodies may interfere with measurements of Tg and cause falsely high or falsely low values. Any changes in serum Tg concentration should be interpreted in consideration of the total clinical presentation of the patient, including clinical history, data or imaging from additional testing, and other appropriate information.[3]

**Not available for sale in the U.S.*
Product availability may vary from country to country and is subject to varying regulatory requirement.

Assay Principle

The Atellica® IM Tg Assay is a fully automated, one-step sandwich immunoassay using acridinium ester chemiluminescent technology, which uses constant amounts of two monoclonal antibodies. The first antibody, in the Lite Reagent, is a mouse monoclonal anti-human Tg antibody labeled with acridinium ester. The second antibody is a biotinylated mouse monoclonal anti-human Tg antibody that is bound to streptavidin-coated paramagnetic latex particles in the Solid Phase. A direct relationship exists between the amount of Tg present in the patient sample and the amount of relative light units (RLUs) detected by the system.

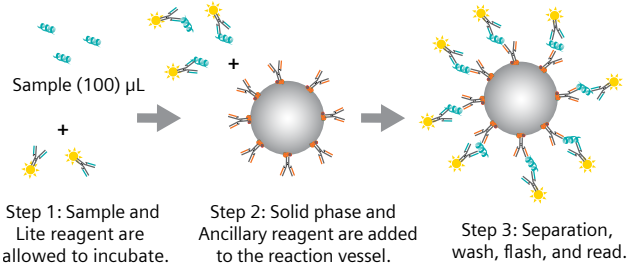

Figure 1. Atellica IM Tg Assay format.

Table 1. Assay attribute summary.

Sample Volume	25 µL
Time to Result	34 minutes
Specimen Types	Serum, plasma (lithium heparin and EDTA)
Measuring Interval	1.8–1000 IU/mL
Limit of Detection	1.3 IU/mL
Limit of Quantitation	1.8 IU/mL
Hook Effect	No hook effect up to 50,000 IU/mL

Experimental Design

Limit of quantitation (LoQ)

- CLSI protocol EP05-A3[4]
- Six serum pools, two runs/day for 20 days
- One reagent lot
- Within-laboratory precision calculated by analysis of variance (ANOVA)
- LoQ calculated as the lowest level at which the 95% upper confidence limit of within-laboratory CV is ≤20%

Linearity

- CLSI protocol EP06-A[5]
- 11 samples, tested n = 6
- One reagent lot
- Analysis by percent bias from weighted linear regression

Specimen equivalence

- CLSI protocol EP09c-ed3[6]
- 53 matched sets, including 5 spiked
- Samples containing anti-Tg were excluded
- One reagent lot
- Analysis by Passing-Bablok

Precision

- CLSI protocol EP05-A3[4]
- Nine samples, two runs/day for 20 days
- Bio-Rad LIQUICHEK Tumor Marker Control and six patient serum pools
- One reagent lot
- Data calculated by analysis of variance (ANOVA)
- Data reported as the upper 95% confidence limit

Interference

- CLSI protocol EP07-ed3[7]
- Two analyte test levels, 0.100–0.300 ng/mL and 20,000–30,000 ng/mL, tested n = 5
- Analysis by percent bias

Method comparison study

- CLSI protocol EP09-ed3[6]
- 126 native remnant serum samples spanning 0.080–119 ng/mL
- Samples containing anti-Tg were excluded
- Tested in singlicate on one Atellica® Immunoassay Analyzer and one Beckman ACCESS 2 system
- One reagent lot on each system
- Analysis by Passing-Bablok

Results

Limit of quantitation

Functional sensitivity of <0.050 ng/mL (at a within-lab precision ≤20% CV) was achieved for the assay, with a limit of quantitation of 0.041 ng/mL.

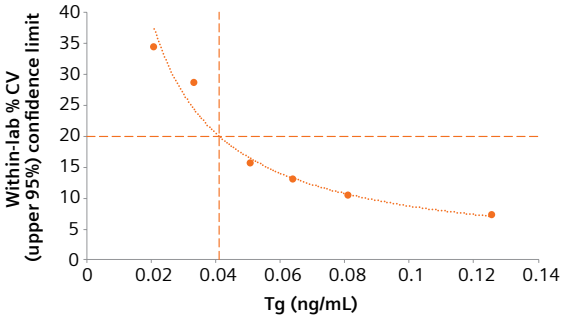

Figure 2. LoQ determination.

Assay linearity

Linearity of the assay was achieved within the measuring interval of 0.050–150 ng/mL. The percent bias from the weighted linear fit was <10%, or <0.090 ng/mL, across the assay range.

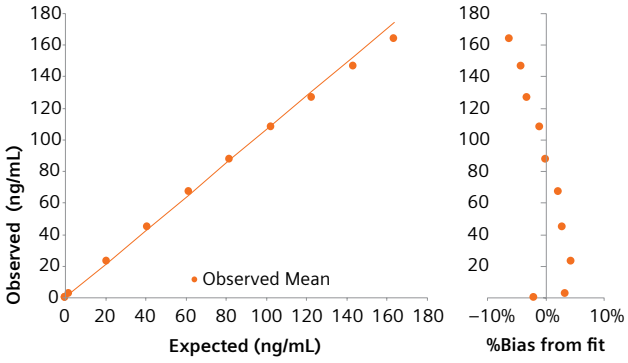

Figure 3. Assay linearity and %bias from fit.

Sample type equivalence

Sample equivalence was demonstrated among serum, lithium heparin plasma, and EDTA plasma.

Table 2. Regression statistics.

	SST vs. Serum	EDTA Plasma vs. Serum	Lithium Heparin Plasma vs. Serum	PST vs. Serum
Slope	1.02	0.99	0.99	0.99
Y-int (ng/mL)	–0.041	–0.049	0.021	0.026
r	0.999	0.999	0.987	0.992
n	53			
Range	1.597–141.997 ng/mL			

Precision

The precision of the assay met our design requirements. The 95% upper confidence limit for repeatability ranged from 1.5 to 6.2% CV. The 95% upper confidence limit for within-lab precision ranged from 3.0 to 9.8% CV.

Table 3. Precision.

Sample	Mean (ng/mL)	Repeatability	Within Lab
Serum pool 1	0.157	6.2%	9.8%
Serum pool 2	1.611	2.1%	4.5%
Serum pool 3	6.121	1.7%	3.0%
Serum pool 4	25.135	2.8%	3.8%
Serum pool 5	78.925	1.5%	3.4%
Serum pool 6	136.364	2.3%	3.5%
QC level 1	3.830	3.1%	4.7%
QC level 2	42.669	3.6%	4.7%
QC level 3	120.576	3.0%	4.3%

Interferences

The Atellica IM Tg Assay was tested for interferences from the substances listed in Table 4. No significant interference (<7%) was observed for the substances in Table 4.

Table 4. Potential interferents.

Acetaminophen	Iodide
Acetylsalicyclic acid	Octreotide acetate
AFP	Perchlorate
Amiodarone	Prednisolone
Biotin at 3500 ng/mL	Propranolol
Carbimazole	Propylthiouracil
Fluocortolone	Rheumatoid factor
FSH	Silwet L720
Hydrocortisone	TBG
Ibuprofen	Thiamazole
Imatinib (TKI)	Total protein
Immunoglobulin G (IgG)	Triglycerides
Immunoglobulin M (IgM)	VEGF

Method comparison study

The Atellica IM Tg Assay demonstrated acceptable correlation r = 0.983 to the Beckman ACCESS 2 Thyroglobulin assay.

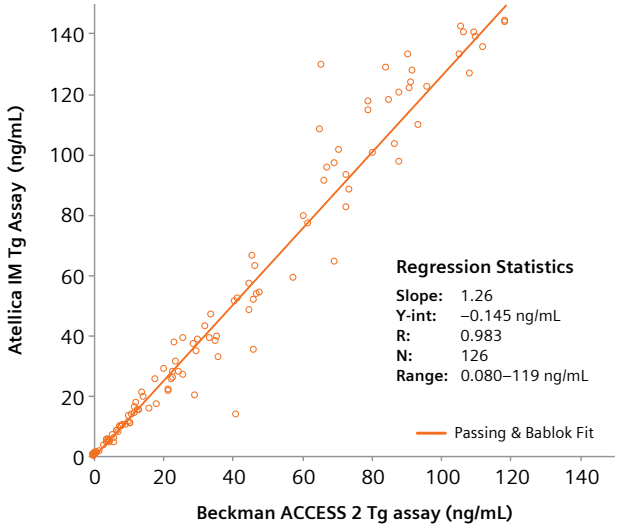

Figure 4. Regression analysis.

Conclusion

The new Atellica IM Tg Assay combines strong analytical performance with second-generation functional sensitivity for the detection of thyroglobulin.

- Fully automated assay on the Atellica IM Analyzer with results in 34 minutes for serum and plasma samples
- LoQ of 0.041 ng/mL
- Repeatability ≤6.2%; within-lab precision ≤9.8%
- No interference to 3500 ng/mL biotin
- Good correlation (Pearson correlation coefficient = 0.983) with the Beckman ACCESS 2 Thyroglobulin assay

At Siemens Healthineers, our purpose is to enable healthcare providers to increase value by empowering them on their journey toward expanding precision medicine, transforming care delivery, and improving patient experience, all made possible by digitalizing healthcare.

An estimated 5 million patients globally benefit every day from our innovative technologies and services in the areas of diagnostic and therapeutic imaging, laboratory diagnostics, and molecular medicine, as well as digital health and enterprise services.

We are a leading medical technology company with over 120 years of experience and 18,000 patents globally. Through the dedication of more than 50,000 colleagues in 75 countries, we will continue to innovate and shape the future of healthcare.

Product availability may vary from country to country and is subject to varying regulatory requirements. Please contact your local representative for availability.

References:

1. Haugen BR. 2015 American Thyroid Association management guidelines for adult patients with thyroid nodules and differentiated thyroid cancer: what is new and what has changed? Cancer. 2017;123(3):372-81.
2. Cooper DS, Doherty GM, Haugen BR, et al. Revised American Thyroid Association management guidelines for patients with thyroid nodules and differentiated thyroid cancer. Thyroid. 2009 Nov;19(11): 1167-1214.
3. Spencer CA. Clinical review: clinical utility of thyroglobulin antibody (TgAb) measurements for patients with differentiated thyroid cancers (DTC). J Clin Endocrinol Metab. 2011;96(12):3615-27.
4. Clinical and Laboratory Standards Institute. Evaluation of the linearity of quantitative measurement procedures: a statistical approach; approved guideline. EP06-A. Wayne, PA: CLSI; 2003.
5. Clinical and Laboratory Standards Institute. Measurement procedure comparison and bias estimation using patient samples; approved guideline—third edition. EP09c-ed3. Wayne, PA: CLSI; 2018.
6. Clinical and Laboratory Standards Institute. Evaluation of precision of quantitative measurement procedures; approved guideline—second edition. EP05-A2. Wayne, PA: CLSI; 2004.
7. Clinical and Laboratory Standards Institute. Interference testing in clinical chemistry; approved guideline—third edition. EP07-ed3. Wayne, PA: CLSI; 2018.

Siemens Healthineers Headquarters
Siemens Healthcare GmbH
Henkestr. 127
91052 Erlangen, Germany
Phone: +49 9131 84-0
siemens-healthineers.com

Published by
Siemens Healthcare Diagnostics Inc.
Laboratory Diagnostics
511 Benedict Avenue
Tarrytown, NY 10591-5005
USA
Phone: +1 914-631-8000

Published by Siemens Healthcare Diagnostics Inc. · Order No. 30-21-DX-618-76 · 03-2021 · ©Siemens Healthcare Diagnostics Inc., 2021