Evaluation of the Atellica IM Thyroglobulin (Tg) Assay*


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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

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**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.

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

**Step 1:** Sample and Lite reagent are allowed to incubate.  
**Step 2:** Solid phase and Ancillary reagent are added to the reaction vessel.  
**Step 3:** Separation, wash, flash, and read.
Experimental Design

Limit of quantitation (LoQ)
- CLSI protocol EP05-A3⁴
- 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-A⁵
- 11 samples, tested n = 6
- One reagent lot
- Analysis by percent bias from weighted linear regression

Specimen equivalence
- CLSI protocol EP09c-ed3⁶
- 53 matched sets, including 5 spiked
- Samples containing anti-Tg were excluded
- One reagent lot
- Analysis by Passing-Bablok

Precision
- CLSI protocol EP05-A3⁴
- Nine samples, two runs/day for 20 days
- Bio-Rad LIQUICHECK 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-ed3⁷
- 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-ed3⁶
- 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.

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

Table 2. Regression statistics.

<table>
<thead>
<tr>
<th></th>
<th>SST vs. Serum</th>
<th>EDTA Plasma vs. Serum</th>
<th>Lithium Heparin Plasma vs. Serum</th>
<th>PST vs. Serum</th>
</tr>
</thead>
<tbody>
<tr>
<td>Slope</td>
<td>1.02</td>
<td>0.99</td>
<td>0.99</td>
<td>0.99</td>
</tr>
<tr>
<td>Y-int (ng/mL)</td>
<td>-0.041</td>
<td>-0.049</td>
<td>0.021</td>
<td>0.026</td>
</tr>
<tr>
<td>r</td>
<td>0.99</td>
<td>0.99</td>
<td>0.987</td>
<td>0.992</td>
</tr>
<tr>
<td>n</td>
<td></td>
<td></td>
<td>53</td>
<td></td>
</tr>
<tr>
<td>Range</td>
<td></td>
<td></td>
<td>1.597–141.997 ng/mL</td>
<td></td>
</tr>
</tbody>
</table>

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.

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

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       |
| Acetylsalicylic acid | Octreotide acetate |
| AFP              | Perchlorate  |
| Amiodarone       | Prednisolone |
| Biotin at 3500 ng/mL | Propranolol  |
| Carbimazole      | Propythiouracil |
| 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.

![Regression analysis graph](image)

**Regression Statistics**
- **Slope:** 1.26
- **Y-int:** -0.145 ng/mL
- **R:** 0.983
- **N:** 126
- **Range:** 0.080–119 ng/mL

**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 $\leq 6.2\%$; within-lab precision $\leq 9.8\%$
- No interference to 3500 ng/mL biotin
- Good correlation (Pearson correlation coefficient = 0.983) with the Beckman ACCESS 2 Thyroglobulin assay
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References: