Assay Performance Summary: Thyroglobulin, LC/MS-MS

Introduction

The use of liquid chromatography/mass spectrometry (LC/MS-MS) for accurate quantification of thyroglobulin (Tg) in the presence of thyroglobulin antibody (TgAb) has been well described in clinical laboratory literature. It is designed to overcome TgAb interference through the use of enzymatic digestion (discussed below).[1] More recently, such LC/MS-MS measurements have proven to facilitate serum Tg measurements in monitoring for recurrent thyroid cancer—particularly in TgAb-positive patients.[2] Historically, Tg is measured by immunometric assay (Tg-IMA), as currently offered by LabCorp, which has a limit of quantitation (LOQ) as low as 0.1 ng/mL. However, this method may be susceptible to TgAb interference for patients with positive TgAb. Alternative assays using radioimmunoassay (RIA) and LC/MS are less prone to TgAb interference but are often less sensitive than Tg-IMA.[2]

The LabCorp Method

In contrast, **Thyroglobulin by LC/MS-MS** (Tg-LC/MS-MS), developed by LabCorp, has an LOQ of 0.2 ng/mL in serum and is currently one of the most sensitive methods designed for interference-free quantification of Tg. This sensitivity is comparable to LabCorp's thyroglobulin by immunometric assay (Tg-IMA), which currently has an LOQ of 0.1 ng/mL.

LabCorp's Tg-LC/MS-MS assay involves heat-aided denaturation of samples, followed by trypsin digestion. This process is designed to disrupt protein-antibody interactions, which reduces the potential for TgAb interference. Based on this design, LabCorp's Tg-LC/MS-MS assay has been shown to provide accurate measurement of thyroglobulin in both the absence and presence of TgAb. When TgAb-negative (<1 IU/mL) and TgAb-positive (≥1 IU/mL) serum specimens were spiked with known amounts of thyroglobulin, accurate Tg-LC/MS-MS measurements were obtained in all samples regardless of TgAb concentration (Figure 1). In contrast, Tg-IMA measurements showed a reduction in the ability to measure Tg as TgAb concentrations increased.

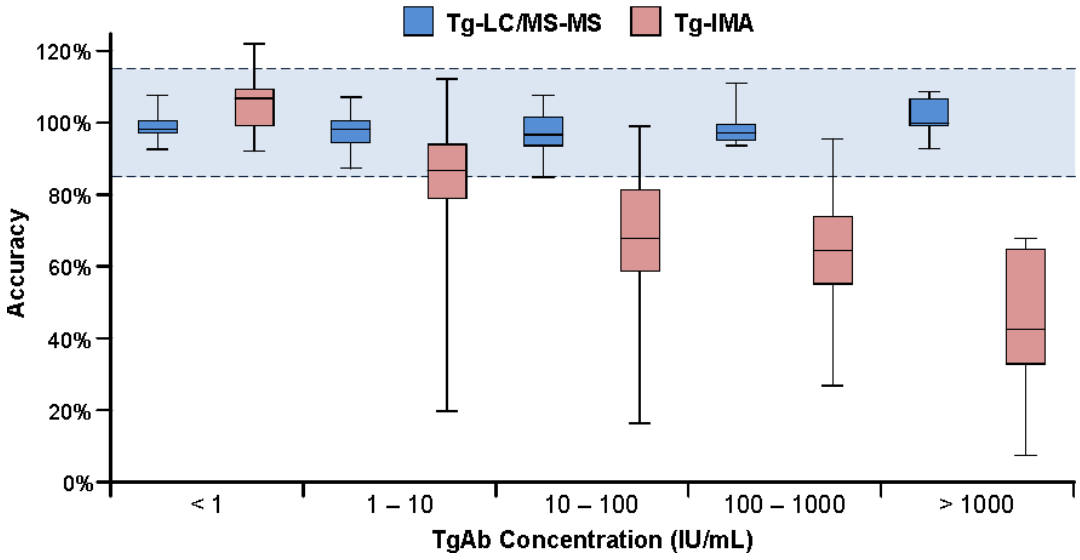

Figure 1 — Accuracy of thyroglobulin LC/MS-MS and IMA measurements in TgAb-negative (<1 IU/mL) and TgAb-positive (≥1 IU/mL) serum specimens spiked with known amounts of exogenous thyroglobulin.[3]

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Assay Correlation

LabCorp's Tg-LC/MS-MS and Tg-IMA measurements demonstrate agreement in the absence of TgAb (Figure 2). In comparing results from TgAb-negative specimens (<1.0 IU/mL), thyroglobulin measurements by the IMA and LC/MS assays showed good correlation, with a slope of 0.95. Both the Tg-LC/MS-MS and Tg-IMA assay standards are traceable to the international reference standard, BCR457.[4] Differences in TgAb-positive patients, therefore, may be related to expected interference in Tg-IMA measurements (Figure 2).

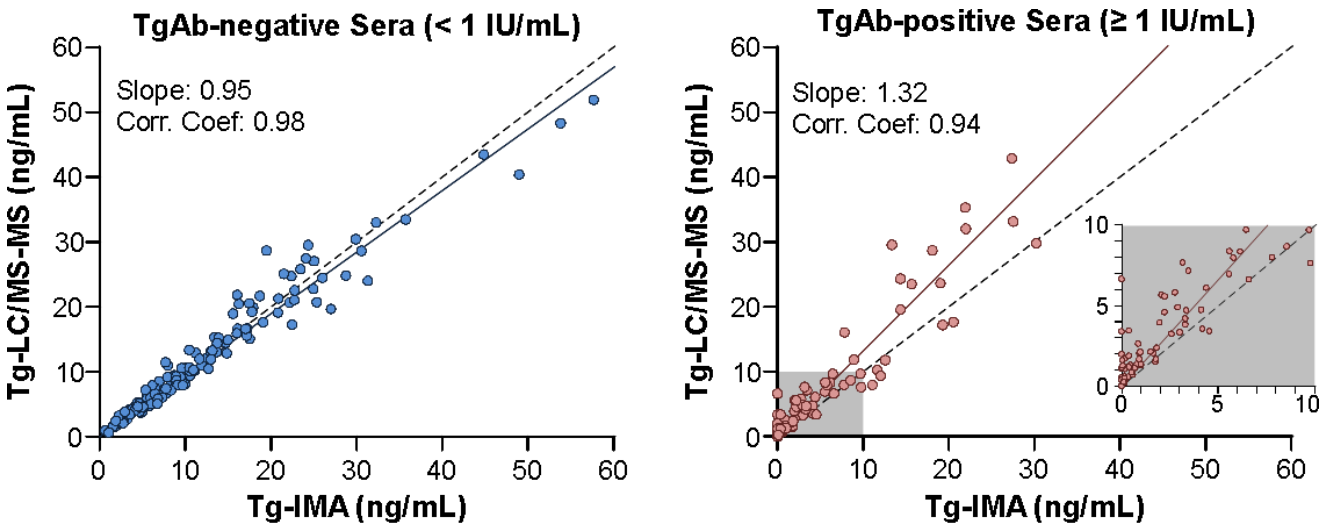

Figure 2 — Comparison of thyroglobulin IMA and LC/MS-MS measurements in TgAb-negative serum specimens (left) and TgAb-positive serum specimens (right).[3]

References

1. Hoofnagle AN, Becker JO, Wener MH, Heinecke JW. Quantification of thyroglobulin, a low-abundance serum protein, by immunoaffinity peptide enrichment and tandem mass spectrometry. *Clin Chem*. 2008 Nov; 54(11):1796-1804. PubMed 18801935

2. Netzel BC, Grebe SKG, Carranza Leon BG, et al. Thyroglobulin (Tg) testing revisited: Tg assays, TgAb assays, and correlation of results with clinical outcomes. *J Clin Endocrinol Metab*. 2015 Aug; 100(8):E1074-E1083. PubMed 26079778

3. LabCorp. Internal data on file.

4. Iervasi A, Iervasi G, Bottoni G, et al. Diagnostic performance of a new highly sensitive thyroglobulin immunoassay. *J Endocrinol*. 2004 Aug; 182(2):287-294. PubMed 15283689

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