

# A Novel Real-Time Immunoassay for Differentiation of TBE Infection from Vaccination

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## 1. Introduction

Tick-borne encephalitis (TBE) remains a significant public health concern in Switzerland, with approximately **200–450 cases reported annually**. Vaccination represents the most effective preventive measure and has substantially reduced the incidence of severe disease in endemic regions. However, **vaccine failure occurs in approximately 3% of vaccinated individuals<sup>1</sup>**, making the diagnosis of TBE infection sometimes challenging.

Current serological assays mainly detect IgM and IgG antibodies against the envelope protein E, but **cannot distinguish between antibodies induced by vaccination and those resulting from natural infection**. Consequently, interpretation of serological results can be difficult, particularly in vaccinated patients presenting with neurological symptoms compatible with TBE.

**Aim:** Evaluate whether anti-NS1 IgM and IgG detection using the novel real-time immunoassay (ElioDX™, Elionova AG) can differentiate natural TBE infection from vaccine-induced antibody responses.

## 2. Methods

A total of **208 human serum and plasma samples** were included in this study. Participants were categorized according to their vaccination and infection status:

- Unvaccinated / uninfected individuals
- Patients with confirmed TBE infection
- Vaccinated individuals (1 to > 3 vaccine doses)

→ Samples were analyzed using the **ElioDX™ real-time immunoassay** for detection of: **anti-NS1 IgM & anti-NS1 IgG**

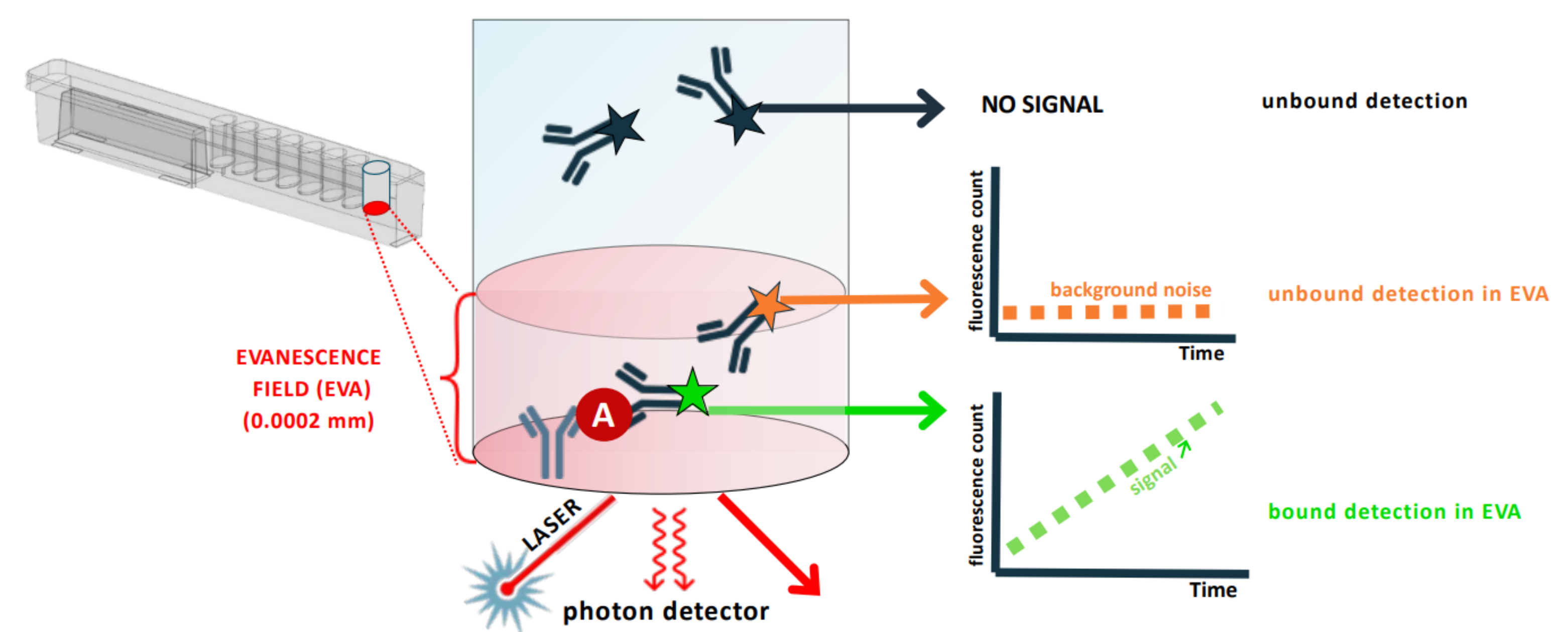
## 3. Results

To overcome this limitation, a new approach based on antibodies against NS1 has been used<sup>2,3</sup>. The **non-structural protein 1 (NS1)** is:

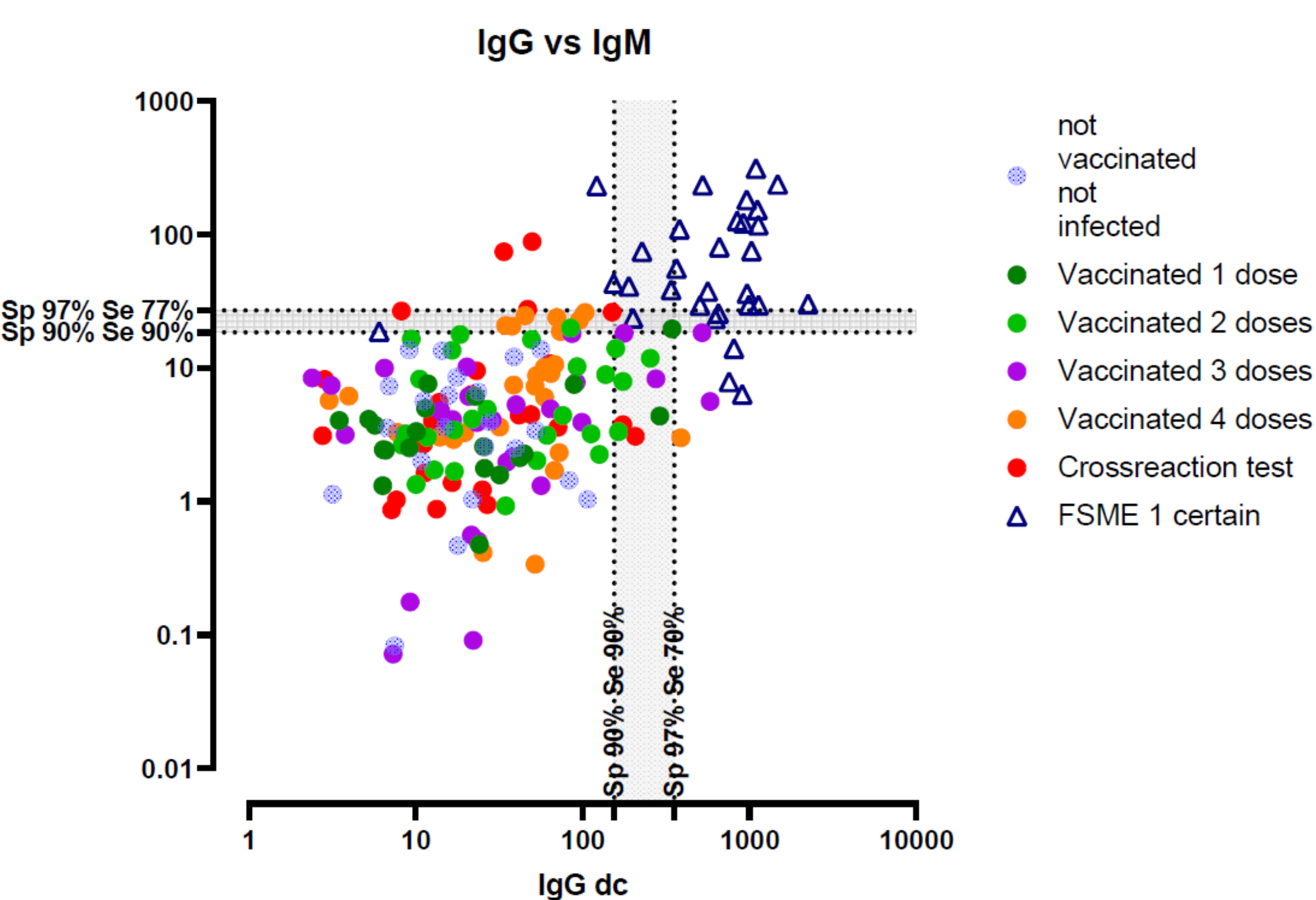
- A highly immunogenic and conserved glycoprotein
- Essential for viral replication
- A potential marker of natural infection
- Present only in trace amounts in inactivated TBE vaccines<sup>4,5,6</sup>

→ During vaccination, the virus used is inactivated → no TBEV replication → likely no production of NS1 protein and/or NS1-specific antibodies

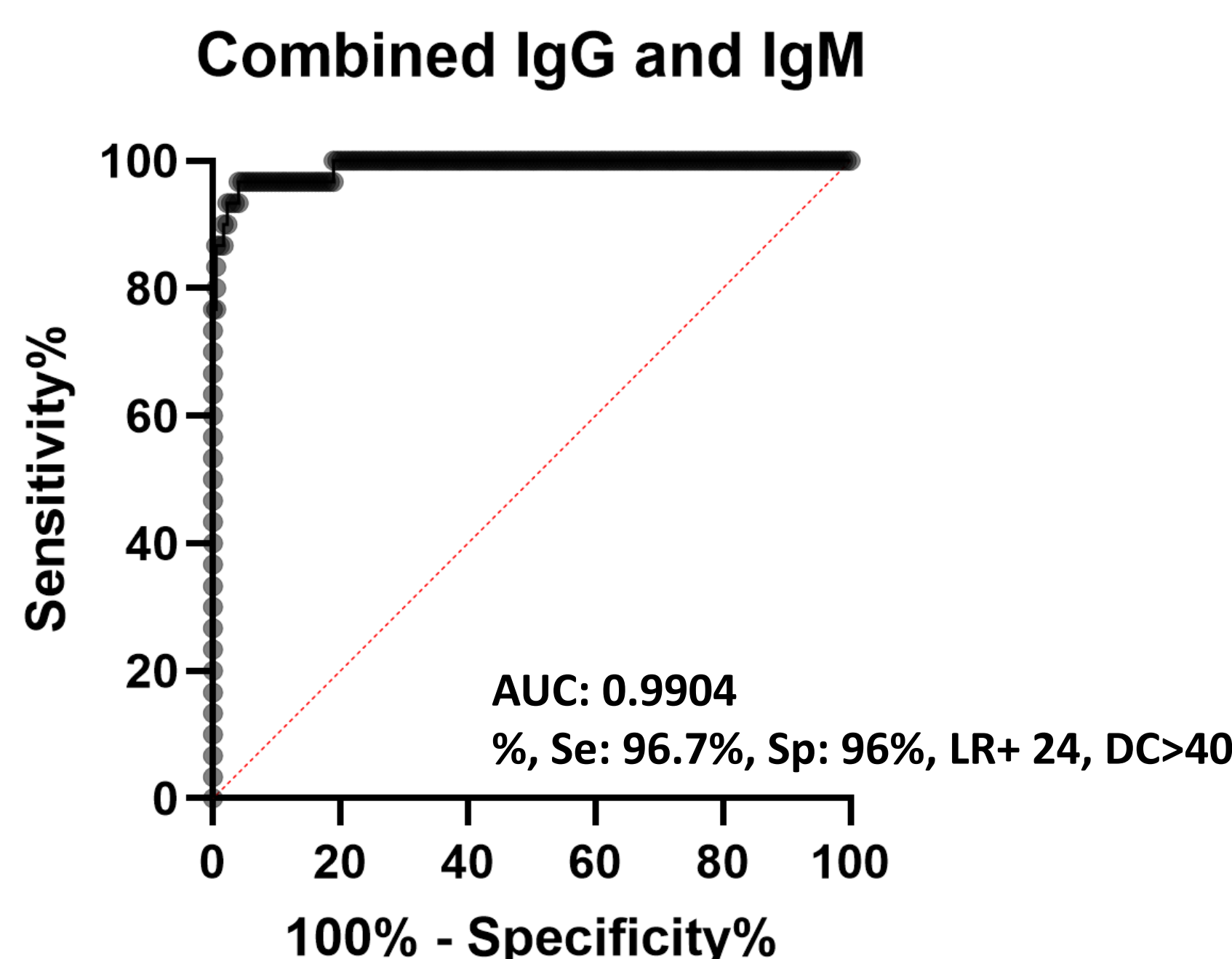
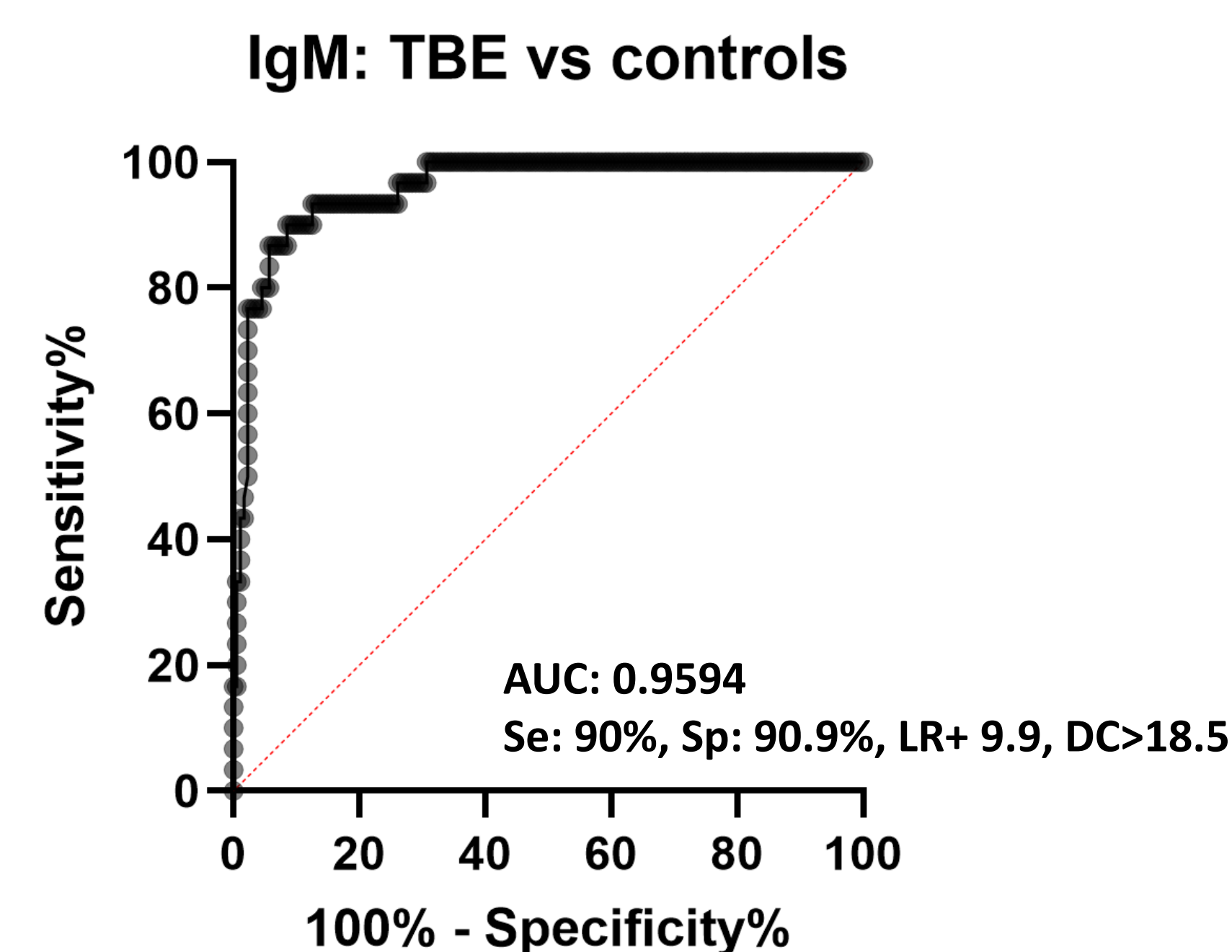
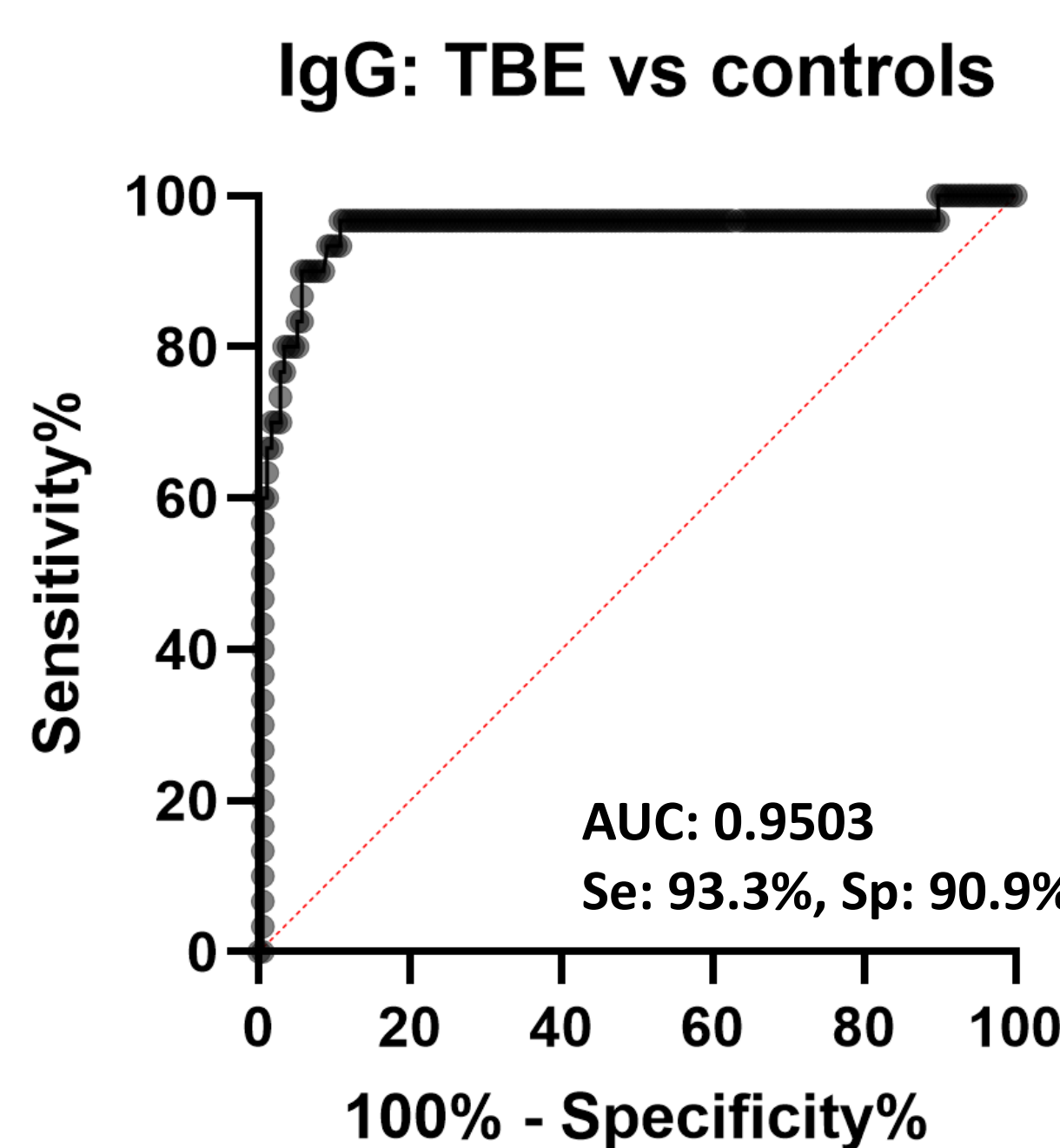
→ Detection of **anti-NS1 antibodies** may provide a useful approach to **distinguish natural infection from vaccine-induced immunity**



**ElioDX™: real-time immunoassay** based on fluorescence waveguide laser evanescent illumination, providing high precision, rapid results (10 min), and a wash-free workflow.



The assays demonstrated **a clear separation between infected and unvaccinated or vaccinated individuals**.



Using a predefined cut-off, the anti-NS1 assays showed good performance: IgG (Se 93.3%, Sp 90.9%) and IgM (Se 90%, Sp 90.9%).

**Combined IgM/IgG detection further improved accuracy** (Se 96.7%, Sp 96%) and provided reliable differentiation between natural infection and vaccine-induced immunity.

## 4. Conclusions

- Combined detection of anti-NS1 IgM and IgG antibodies represents a **reliable and promising strategy for differentiating natural TBE infection from vaccine-induced immunity**.
- The **ElioDX™ real-time immunoassay** provides a **rapid, sensitive, and highly specific diagnostic tool** that may significantly improve the interpretation of serological results in vaccinated individuals.
- This approach may facilitate more accurate diagnosis of suspected TBE cases in vaccinated patients.

### Perspectives:

- Prospective evaluation of anti-NS1 antibody responses in patients
- Development of probability-based diagnostic interpretation combining laboratory results with clinical data
- Evaluation of anti-NS1 antibodies in cerebrospinal fluid
- Further optimization of the assay to improve diagnostic sensitivity