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of the vagus nerve varies substantially between patients and is far deeper than 1·5 cm in most individuals. A human anatomical study recorded the mean depth among 51 vagus nerves at 3·62 cm (SD 0·94), and the vagus nerve depth of the 14 rheumatoid arthritis patients enrolled in our study ranged from 2·19 cm to 4·69 cm (mean 3·40 cm).[4] Given the anatomy of the human cervical vagus nerve, it is very difficult to predict whether or not it can be stimulated using a transcutaneous device.

There could well be a place for non-invasive vagus nerve stimulation for the treatment of patients with rheumatoid arthritis, but its adoption will require investigation and documentation of clinical effectiveness derived from well designed, placebo controlled clinical studies.

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1 Genovese MC, Gaylis NB, Sikes D, et al. Safety and efficacy of neurostimulation with a miniaturised vagus nerve stimulation device in patients with multidrug-refractory rheumatoid arthritis: a two-stage multicentre, randomised pilot study. *Lancet Rheumatol* 2020; **2:** e527–38.

2 Yap JY, Keatch C, Lambert E, Woods W, Stoddart PR, Kameneva T. Critical review of transcutaneous vagus nerve stimulation: challenges for translation to clinical practice. *Front Neurosci* 2020; **14:** 284.

3 Mourdoukoutas AP, Truong DQ, Adair DK, Simon BJ, Bikson M. High-resolution multi-scale computational model for non-invasive cervical vagus nerve stimulation. *Neuromodulation* 2018; **21:** 261–68.

4 Hammer N, Löffler S, Cakmak YO, et al. Cervical vagus nerve morphometry and vascularity in the context of nerve stimulation—a cadaveric study. *Sci Rep* 2018; **8:** 7997.

SARS-CoV-2 serological cross-reactivity with autoantibodies

In their report on the detection of IgM and IgG antibodies against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in patients with autoimmune diseases, Teng and colleagues[1] found that the serological test that they assessed showed no cross-reactivity with autoantibodies present in patients with autoimmune disease. However, several potential confounding factors should be considered when assessing the study findings. Hypogammaglobulinaemia (reduced serum immunoglobulin concentrations) might result in false negative antibody test results; therefore, quantitative serum immunoglobulin measurements should be used to interpret SARS-CoV-2 serology results, along with knowledge of any patient history of immunodeficiencies.[2] The rheumatoid factor range and titre of autoantibodies related to systemic lupus erythematosus and Sjögren's syndrome should be considered, as serology assay interference might only occur at relatively higher serum rheumatoid factor or autoantibody concentrations. Whether the potential interference effects of specimen haemolysis, icterus, and lipaemia on the assay used have been evaluated by the authors is unclear.[3] Importantly, heterophile antibodies or human antianimal antibodies, which have a prevalence of 0·17%–40% in the general population,[4] can potentially interfere with antibody-based assays, causing positive or negative interference depending on the assay design, and their presence should be ruled out before reaching a conclusion on the potential assay cross-reactivity with autoantibodies.[2] The minimum number of specimens to identify clinical specificity should depend on the intended test population.[2] For population-based screening with low seroprevalences, the specificity needs to be greater than 99% with small confidence intervals to ensure a high positive predictive value.[2] To achieve such a high positive predictive value would require a negative control population greater than 750 people or 2000 people, depending on the statistics used.[2] In contrast, specificity might not need to be as high when testing groups with higher pretest probabilities, for example, convalescent plasma donors.[2] In addition, knowledge of storage conditions for the serum specimens, particularly those that were collected before the COVID-19 pandemic, would be useful to rule out preanalytical errors due to specimen stability.[2] The sensitivity of lateral flow immunoassays is generally limited by the dissociation constant of the antibody–antigen conjugate and by the colorimetric read-out.[5] If Teng and colleagues[1] have observed that the overall testing sensitivity for the kit that they assessed was 89% (352 of 397), then this limitation should be considered when evaluating the absence of SARS-CoV-2 serology assay cross-reactivity with autoantibodies. If important limitations are not thoroughly examined during an investigation of serology assay cross-reactivity with autoantibodies, the specificity of an assay might be a clinically significant overestimation, which might potentially be the case here.[2]

I declare no competing interests.

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1 Teng J, Dai J, Su Y, et al. Detection of IgM and IgG antibodies against SARS-CoV-2 in patients with autoimmune diseases. *Lancet Rheumatol* 2020; **2:** e384–85

2 Farnsworth CW, Anderson NW. SARS-Cov-2 serology: much hype, little data. *Clin Chem* 2020; **66:** 875–77.

3 Tang MS, Hock KG, Logsdon NM, et al. Clinical performance of two SARS-CoV-2 serologic assays. *Clin Chem* 2020; **66:** 1055–62.

4 Morton A. When lab tests lie...heterophile antibodies. *Aust Fam Physician* 2014; **43:** 391–93.

5 Koczula KM, Gallotta A. Lateral flow assays. *Essays Biochem* 2016; **60:** 111–20.