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Combining surface-enhanced Raman scattering (SERS) of saliva and two-dimensional shear wave elastography (2D-SWE) of the parotid glands in the diagnosis of Sjögren's syndrome

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ABSTRACT

In this study, we combine the molecular structural information gained by SERS of saliva samples with the morphological data given by two-dimensional shear wave elastography (2D-SWE) (SuperSonic Imagine, Aixplorer) of parotid glands in the case of n = 31 patients with Sjögren's syndrome (SjS) and n = 22 controls, with the aim to discriminate between the two groups. The overall classification accuracy yielded by a hybrid principal component analysis-linear discriminant analysis (PCA-LDA) model based on both SERS and elastography (81%) was superior to that yielded by SERS spectra alone (75%) and elastography data alone (71%). This preliminary study is the first report on the use of 2D-SWE of parotid glands for the diagnosis of SjS as well as the first to describe the diagnosis of SjS based on the SERS spectra of dried saliva samples, the results suggesting that the strategy of combining the two methods could improve the diagnosis of SjS.

1. Introduction

Primary Sjögren's syndrome (SjS) is an immune cell mediated disease with typical presentation involving dryness of the mouth and eyes, fatigue and polyarthralgia [1]. SjS represents the second most common systemic autoimmune disease after Hashimoto's thyroiditis [2], with incidence estimates ranging between 3 and 11 cases per 100,000 individuals [2,3].

According to the most widely accepted theory termed 'autoimmune epithelitis', SjS is determined by an aberrant inflammatory response mediated by both innate and acquired immunity, primed by the epithelial cells that act as atypical antigen presenting cells and then further expanded by circulating pro-inflammatory cytokines [1]. Consequently, SjS is characterized by a diffuse lymphocytic infiltration of the parotid glands as well as by circulating antibodies against Ro (also called Sjögren's syndrome-associated antigen A (anti-SSA)) and/or La (Sjögren's syndrome-associated antigen B (anti-SSB) [4]. Although much has been discovered about the molecular mechanisms behind SjS, druggable pharmacological targets that could result in disease modifying therapies are still awaited [5].

Besides the classic triad, SjS also presents with general symptoms such as fever and weight loss as well as organ specific complications of the cutaneous, articular, pulmonary, cardiovascular, nephro-urological, nervous and haematological systems, which are present in around 50–60% of cases [6,7]. Interestingly, systemic symptoms can precede the characteristic syndrome, a condition termed occult SjS or non-sicca onset SjS.

SjS is sometimes diagnosed concomitantly with other systemic autoimmune diseases such as systemic lupus erythematosus or rheumatoid arthritis, in which case the SjS is referred to as secondary SjS [8]. An important and potentially life-threatening complication of SjS is represented by lymphoma, which develops predominantly in the major salivary glands, the most common variant being the low-grade extranodal marginal zone B-cell non-Hodgkin lymphoma (also known as mucosa-associated lymphoid tissue (MALT) lymphoma) [9].

Despite extensive evidence demonstrating an impaired quality of life in patients with SjS [10–12], treatment options are scarce and mainly based on clinical experience with other systemic autoimmune diseases and expert opinions [1]. The ocular and salivary manifestations

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