

# Development of a Raman-Based Method for the Diagnosis of People with Obstructive Sleep Apnea Syndrome

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Obstructive sleep apnea syndrome (OSAS) is a widespread sleep-related breathing disorder whose diagnosis and monitoring still rely on complex and resource-intensive procedures, in the absence of specific biomarkers<sup>1,2</sup>. In this study, Raman spectroscopy (RS) applied to salivary samples is investigated as a rapid, label-free, and minimally invasive biophotonic approach for OSAS characterization. Saliva represents a highly informative and easily accessible biofluid, composed of approximately 99% water and containing nearly 2300 proteins, enzymes, inorganic salts, and hormones shared with blood, making it a low-cost matrix for clinical investigations<sup>3,4</sup>.

Salivary samples from 51 OSAS patients and 34 healthy controls were analyzed to extract disease-specific Raman molecular fingerprints reflecting global biochemical alterations. In parallel, conventional analytical techniques, including fluorimetric assays and enzyme-linked immunosorbent assays (ELISA), were performed on salivary samples to quantify lactate, cortisol, and superoxide dismutase 3 (SOD3) concentrations.

Raman spectral data were processed using multivariate analysis (MVA), combining principal component analysis with linear discriminant analysis (PCA-LDA), which enabled effective discrimination between groups with an overall accuracy of 82.35% and a receiver operating characteristic area under the curve of 0.88. Among the discriminant spectral features, the Raman band at 920 cm<sup>-1</sup>, attributed to lactic acid, exhibited an increased spectral contribution in OSAS samples. No correlation was observed between the area under the curve (AUC) of the lactic acid Raman peak and lactate concentration measured by fluorimetric assay. Moreover, cortisol and SOD3 levels were higher in OSAS patients compared to controls. Overall, salivary Raman spectroscopy provides a robust molecular fingerprint of OSAS and represents a promising spectroscopic tool for non-invasive diagnosis, monitoring, and personalized clinical management. Further validation in larger cohorts is warranted.

## References

- [1] Lv, R.; Zhang, Y.; Dong, N.; Wang, X.; He, Y.; Yue, H.; Yin, Q. *Sig. Transduct. Target. Ther.* **2023**, 8, 218.
- [2] Iannella, G.; Pace, A.; Bellizzi, M.G.; Magliulo, G.; Greco, A.; De Virgilio, A.; Croce, E.; Gioacchini, F.M.; Re, M.; Costantino, A.; et al. *Diagnostics* **2025**, 15, 1088.
- [3] Carlomagno, C.; Bertazioli, D.; Gualerzi, A.; Picciolini, S.; Banfi, P.I.; Lax, A.; Messina, E.; Navarro, J.; Bianchi, L.; Caronni, A.; et al. *Sci.Rep.* **2021**, 11, 4943.
- [4] Laxton, C.S.; Peno, C.; Hahn, A.M.; Allicock, O.M.; Perniciaro, S.; Wyllie, A.L. *Lancet Microbe* **2023**, 4, e837–e850.