Towards the Development of Non-Invasive Electrical Impedance Spectroscopy-based Oral Cancer Diagnosis System

Malwina Matella[1,4], Rachel Furmidge[2,4], Zhicheng Lin[3,4], Helen Colley[2,4], Craig Murdoch[2,4], Zi-Qiang Lang[3,4], Dawn Walker[1,4]

[1]School of Computer Science, University of Sheffield, UK, [2]School of Clinical Dentistry, University of Sheffield, UK, [3]School of Electrical and Electronic Engineering, University of Sheffield, UK, [4]Insigneo Institute for In Silico Medicine, University of Sheffield, UK

m.matella@sheffield.ac.uk, d.c.walker@sheffield.ac.uk

Keywords: Oral Cancer Diagnosis, Electrical Impedance Spectroscopy, Tissue Engineering, Finite Element Modelling, Machine Learning

1. Introduction

Head and neck cancer remains the seventh most common type of cancer worldwide, with oral squamous cell carcinoma (OSCC) being one of its most prevalent subtypes [1]. In 2020, more than 377,000 new cases of OSCC were reported, resulting in nearly 178,000 deaths [1]. Despite advances in treatment, the overall 5-year survival rate remains low at 54%, largely due to late-stage diagnosis [2]. In contrast, early detection can improve survival rates – up to 90% [2].

2. Description of the problem

The current golden standard in the diagnosis of OSCC is a scalpel biopsy, which is a painful procedure with long turn-around times. Additionally, in the case of mild to moderate dysplasia, the biopsy often needs to be repeated. The low 5-year survival rate associated with the late diagnosis indicates that there is a continuing need for an earlier oral cancer detection or oral cavity screening programme amongst patients of increased risk. One potential solution is a diagnostic tool based upon electrical impedance spectroscopy (EIS), a technology permitting non-invasive and real-time identification of cancerous changes in various biological tissues based on the influence of cellular level tissue structure on the opposition to the flow of an alternating electrical current.

3. Related work

The use of EIS in cancer diagnosis has been investigated from the late 1990s, resulting in the cervical cancer diagnosis commercial device, ZedScan, that demonstrates Area Over the Curve (AUC) of 0.887 for early cervical cancer detection when paired with colposcopy [3]. Our current work relating to the use of EIS in the more complex scenario of early oral cancer detection builds upon a small pilot study exploring the potential for EIS to distinguish cancerous and potentially malignant lesions from healthy oral epithelium in vivo [4]. Despite promising results (significant differences in the EIS of cancer and high-risk lesions versus low-risk lesions and controls), a deeper understanding on the impact of tissue composition and structure in health and pathology on their electrical behaviour is needed before the deployment of EIS in the clinic.

4. Solution to the problem

In the current study, we explore the feasibility of EIS measurement to enhance the diagnosis of oral cancer by integrating tissue engineering (TE), finite element (FE) and machine learning (ML) models to develop a prototype oral cancer detection system. Due to the lack of the necessary certification for the in vivo use of our current EIS instrumentation, TE oral epithelium constructs are cultivated using healthy and cancerous cell lines. EIS measurements are performed on the mature TE samples, which are subsequently prepared for histology. Histology images provide morphological information which are the basis of Virtual Oral Tissues i.e. tissue-specific multiscale FE models. The latter are deployed to investigate the impact of tissue characteristics (morphology and composition) on different EIS spectra features, and to augment the TE-derived EIS dataset for classification study. Four ML models were trained on the simulated spectra and tested on the TE EIS data. Initial results (Fig. 1) show promising agreement between the EIS spectra obtained from TE models and FE simulations, and subsequent classification study results exhibit the best separability using a decision tree model with AUC=0.913 after 100-fold cross validation.

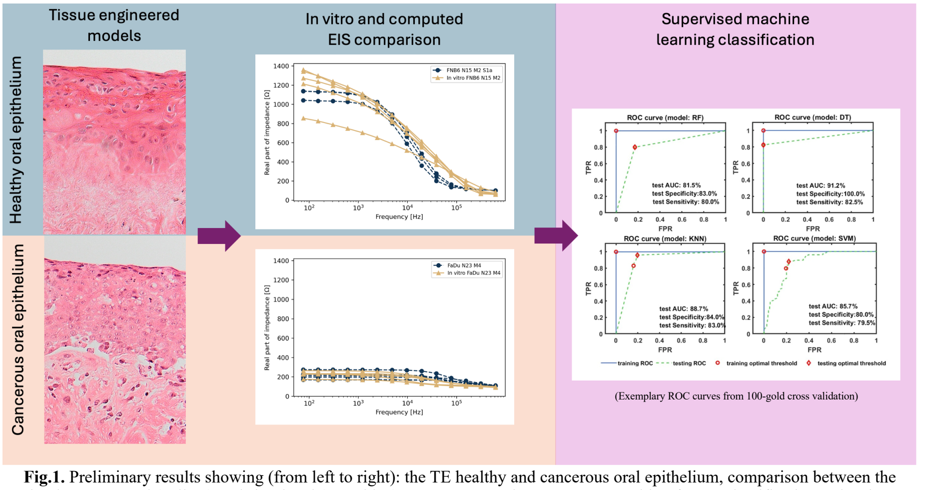

Fig.1. Preliminary results showing (from left to right): the TE healthy and cancerous oral epithelium, comparison between the in vitro measured (yellow) and simulated (navy blue) EIS spectra, and ROC curves resulting from a classification task using different supervised ML models.

5. Conclusions and future work

In this preliminary study, we developed a process combining tissue engineered and computational models to classify healthy and cancerous oral epithelium using electrical impedance spectroscopy. Preliminary data confirmed the utility of the FE modelling and ML in predicting and classifying the EIS spectra of healthy and cancerous oral epithelium constructs. This provides proof-of-concept that ML models informed by simulation-augmented EIS data could ultimately form the basis of a clinical diagnosis method for oral cancer diagnosis. In the future work we plan to adapt the existing framework to explore different stages of dysplasia, to calibrate and validate the FE model given the parameters from histopathology and transmission electron microscopy (TEM) images. Following the required certification for medical devices, the definitive aim will be to carry out a follow-up in vivo study, where additional patient history could enhance the ML classifiers accuracy and interpretability.

Acknowledgements. The authors want to acknowledge Yorkshire Cancer Research for funding this project (YCRSPF/2023/172).

References

[1] Sung H. *et al.*, ‘Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries’, *CA. Cancer J. Clin.*, 71 (3), 209–249, 2021.
[2] Muller P *et al*., ‘Oral Health Foundation: The State of Mouth Cancer UK Report 2020/21.’, Cancer Research UK Cancer Survival Group, London School of Hygiene and Tropical Medicine, 2022. [Online]. Available: Available from http://csg.lshtm.ac.uk/rare-cancers/.Accessed July 2016. www.mouthcancer.org.
[3] Tidy J. A. et al., “Accuracy of detection of high-grade cervical intraepithelial neoplasia using electrical impedance spectroscopy with colposcopy,” *BJOG: An International Journal of Obstetrics & Gynaecology*, 120, 400–411, 2013.
[4] C. Murdoch *et al.*, “Use of electrical impedance spectroscopy to detect malignant and potentially malignant oral lesions,” *International journal of nanomedicine*, 9, 4521–4532, 2014.