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ELECTRICAL IMPEDANCE SPECTROSCOPY TO MONITOR SALIVARY FUNCTION

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INTRODUCTION

Xerostomia, or dry mouth syndrome, is one of the radiation therapy (RT)-induced side effects experienced by head and neck cancer patients. The severity of xerostomia can be measured using several indirect techniques [1]. The amount of saliva being produced can be measured by placing cotton rolls in the patient's mouth. This technique is quite reliable and sensitive but it is invasive and uncomfortable for the patient [2]. Measuring the electromyographic activity of musculus digastricus, a small muscle under the jaw, is another noninvasive technique for measuring xerostomia and results from this technique correlate well with the cotton roll method [3-4]. However, both methods are indirect measurement techniques that provide results regarding the total activity of all the salivary glands combined. Neither method can provide the health status/activity status of individual salivary glands.

Over recent years, electrical impedance spectroscopy (EIS) has been developed as a simple and reliable, non-invasive technique for the characterization of tissues and tissue function [5]. Numerous studies have been published showing a variety of clinical applications for EIS such as the detection of breast tumors[6] and in regional ventilation monitoring [7]. This current study examines the potential use of EIS as a novel way to monitor salivary gland function. A similar study, involving electrophysiological measurements of parotid gland activity, has been reported previously in the literature but was inconclusive in its findings [8-9].

The developed treatments for xerostomia based upon in vivo electrical impedance involve the electrical stimulation of salivary glands to increase saliva output but these are incapable of monitoring the health status of the salivary glands [10-12].The use of *in vivo* electrical impedance to monitor salivary gland function could potentially help to reduce the impact of xerostomia as a side effect experienced by head and neck cancer patients undergoing radiation treatment. Changes to salivary gland function detected by EIS during the course of radiation treatments could allow the RT plan to be modified to improve sparing of the salivary glands and thereby reduce the severity of xerostomia. This is in keeping with QUANTEC suggestions for the development of new tools and strategies for the prospective recording of specific pathologies after radiation therapy [13].

METHODOLOGY

This study will evaluate the use of *in vivo* electrical impedance to monitor salivary function.

Tissue impedance has been commonly modeled as a parallel RC circuit (Fig.1). R1 depicts the extracellular resistance, R2 the intracellular conduction and C the membrane capacitance.

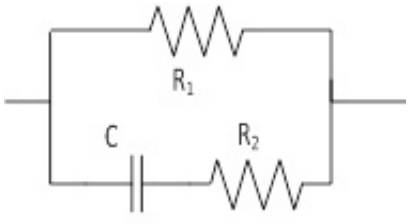

Fig. 1: Three Element RC Model

A commonly used methodology for representing tissue impedance is through Cole-Cole plots [14]. This representation has been used in multi-frequency measurements to classify malignant and healthy tissue[15].

In this preliminary study, one participant was used for all measurements. The subject did not have any history of dry mouth syndrome or salivary gland dysfunction and was not suffering from any cold or flu-like symptoms. The participant was asked not to eat or drink one hour before the experiment.

Impedance measurements were taken using an impedance spectroscope HF2IS from Zurich instruments ("Zurich Instruments"). A two electrode terminal system was used, with the current carrying and signal measuring electrodes being the same [17]. The electrodes were circular, pre-gelled Ag/AgCl 2mm electrodes from Vermed. These are non-polarizable and generate less than 10μV noise, hence preferred for skin surface measurements. The reference electrode was placed just below the ear lobe over the parotid gland and the measuring electrode was placed over the temporomandibular joint, 2cm longitudinally from the reference electrode, providing a good and stable surface signal. The current was limited to 1mA p-p as being within the current limits allowed for human application (IEC601). The considered frequency range was from 8 Hz to 1 MHz; further to overcome the effect of skin impedance, a frequency sweep from 10 KHz to 1 MHz was also used.

Measurements were taken 'at rest' and after activation of saliva production through the use of one of two activators, Lemon juice or artificially flavoured orange tictac®.

DISCUSSION AND RESULTS

Cole-Cole plot representations have been used to compare results. The X-axis of the plots is the real impedance and the Y-axis is the negative imaginary impedance. Three consecutive trials at the same location with the same electrodes showed little variation in the impedance as depicted in Figure 2.

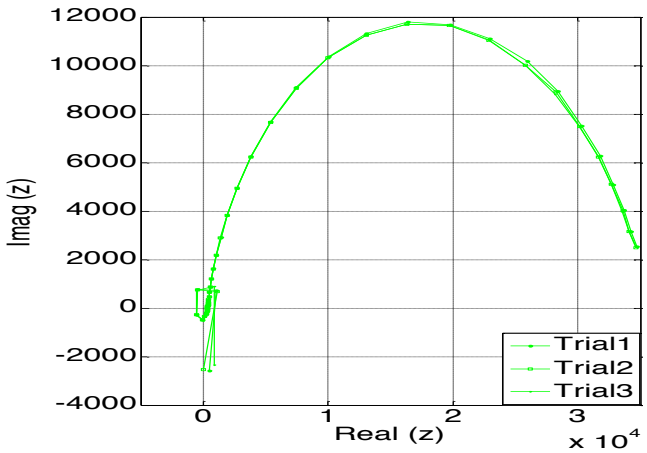

Fig. 2: Three repeated trials for single location

Figure 3 depicts impedance plots for left and right glands in rest and active stages over a frequency range from 1 Hz to 7 MHz. The activator used was lemon juice.

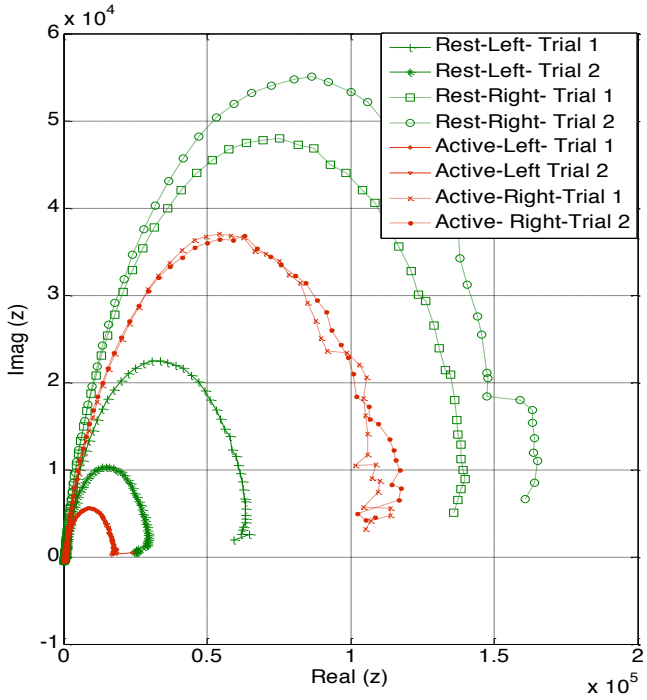

Fig. 3: Cole-Cole plots for contralateral glands

As observed in Figure 3, both right and left side showed a decrease in impedance during the active stage. However, the variability in impedance measurements in the rest stage between the left and right side is quite high and needs to be better analyzed and accounted for. All further experiments were carried out on the left gland only with four measurements being taken, rest stage followed by active stage, then

repeated after an interval of 1 hour (Figure 4). It was observed that the active stage showed lower impedance than rest stage. As saliva increases conductivity, these results were as expected.

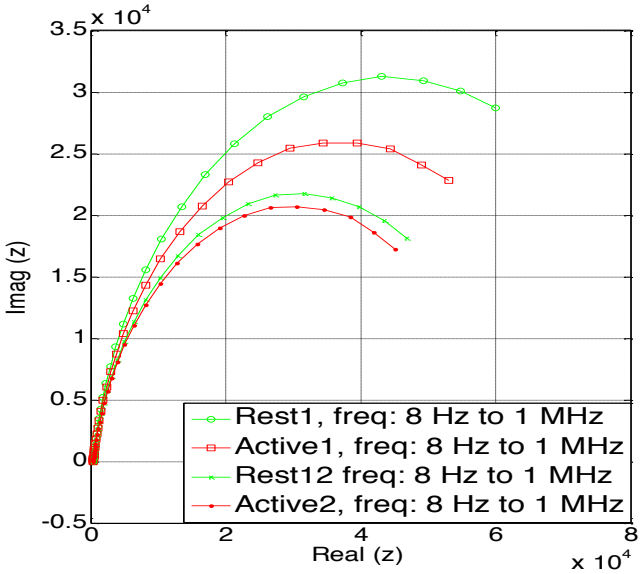

Fig. 4: Consecutive Rest Active Impedance: 8Hz to 1 MHz

Figure 5 depicts the same results in the frequency range 10 KHz to 1MHz. This frequency range has less effect of skin impedance over it. The impedance is decreasing when the glands are activated.

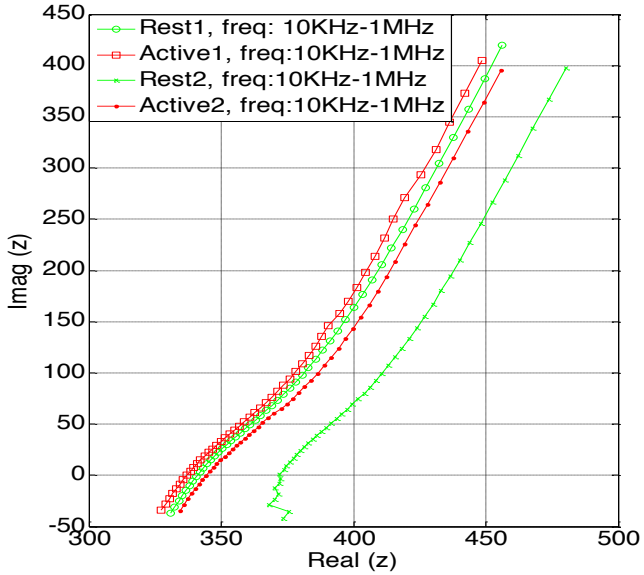

Fig. 5: Consecutive Rest Active Impedance (10KHz to 1 MHz)

A similar procedure was repeated with the second activator, tictac®. This activator is sugar based. The impedance measurements in the frequency range 8Hz to 1 MHz is shown in Figure 6. The impedance in this case increased in active stage. This is attributed to the fact that the tictac activator is sugar-based, with sugar having higher impedance than saliva.

The same activator *tictac* was used to repeat the experiments in the frequency range 10 KHz to 1MHz as shown in Figure 7.

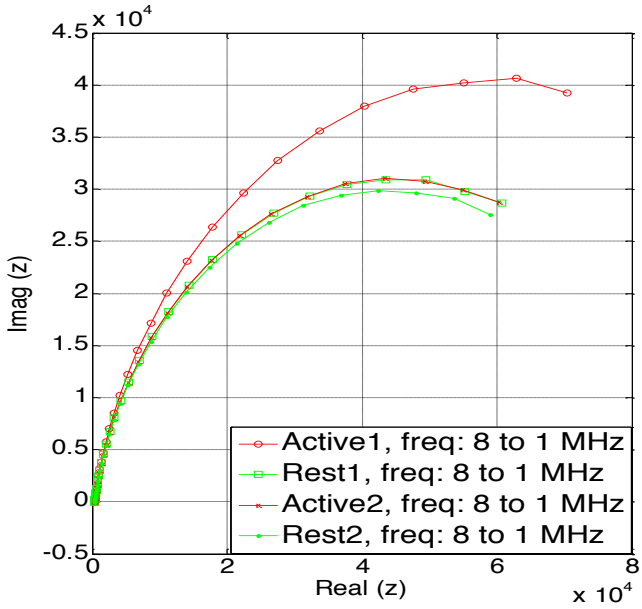

Fig. 6: Consecutive Rest Active impedance for data collected at an interval of one hour

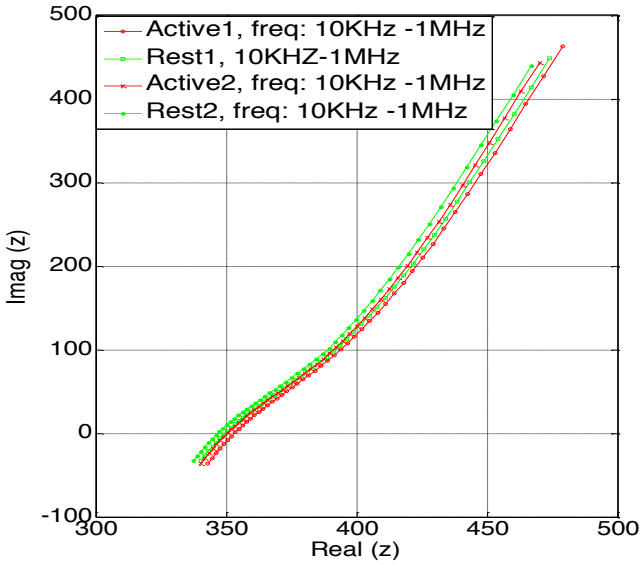

Fig. 7: Consecutive Rest Active impedance for data collected at an interval of one hour

CONCLUSION

This study found a vast amount of variability in the tissue impedance measured using the superficially placed electrodes. It was observed that with time the measured impedance of the tissue tended to drift. The kind of activator used to stimulate salivary activity also affected the measured impedance. The impedance increased when a sweet-based *tictac* activator was used and decreased when a non-sweet-based lemon juice activator was used. This is expected as sugar has higher resistance than saliva. The authors observed that the experimental procedure needed to be more standardized (should saliva be stored, should lemon juice be licked or not, how jaw movement should be minimized). The distance between the electrodes, position of electrodes and pressure over the electrodes should also be kept constant and standardized.

Promisingly, the observed variation in impedance between the rest and the active stage of the salivary glands suggests the usability of EIS in non-invasively measuring saliva production and thus indirectly salivary function. Information learned from this study will be helpful in optimizing *in-vivo* EIS protocols to measure aspects of salivary gland function and morphology in healthy volunteers as part of a larger more comprehensive study. Such a study may eventually include using EIS to measure radiation induced changes in salivary gland function and morphology on patients receiving head and neck radiation therapy, with the goal of guiding radiation therapy optimization algorithms such that salivary gland function can be better preserved.

ACKNOWLEDGEMENT

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