Review Article

Lite Image Analysis Module Salivary Diagnostic Tool - A Review

ABSTRACT

Background: Saliva is a versatile biofluid that can help in detecting any oral or systemic disease of an individual. Saliva seems to be clinically an informative biofluid for easy prognosis of a disease and clinical or laboratory diagnosis of oral as well as many systemic diseases. It has some specific soluble biological markers that can be considered as an ideal approach for early detection of diseases.

Aim: This paper is intended to review on one of the recent developments in point of care salivary diagnosis that is the Lite Image Analysis Module.

Conclusion: Thus, this technology primarily helps in a rapid assessment of salivary biomarker levels signifying the probable systemic and oral condition of an individual both in quantitative as well as qualitative manner. Adopting a simple and quick technique, LIAM can be used effortlessly in some rural remote areas as well where advanced high technology laboratories have not yet reached.

Clinical Significance: It is one of the recent advancements in the world of salivary diagnosis LIAM (Lite Image Analysis Module) that is a portable, light, hand-held scanning device which magnificently integrates a distinct analyte identification system that detects the type of analytes being tested and transfer the report straight to a smartphone or a Bluetooth devices.

KEY WORD:

LIAM, Lateral Flow Test, Non-invasive, Oral disease, Point of care salivary diagnostics, Saliva, Super•SAL, VerOFy®

INTRODUCTION

Early phase detection of human diseases like cancer, cardiovascular and metabolic disorders turns out to be a challenging situation in a healthcare setting. Most of them require specialised clinical assessment along with some laboratory testing as well. Salivary diagnostic could pave a path as an effective medium for the early diagnosis of these diseases.[1] The clinical importance of saliva can have a varied range starting from the forensic field to drug monitoring followed by diagnosis of various local as well as systemic diseases.[2]

Saliva proves to be an indicator to determine the status of the human body since time immemorial. Back in China, it was told by ancestors that if an individual was suspected to be guilty he will definitely fail to swallow a mouthful of dry rice. It was based on the concept that due to anxiety and probably guilt a person might not be able to form a dry rice bolus and swallow it since a feeling of guilt will reduce the production of saliva required for easy swallowing. Eventually reports flourished that the saliva flow rate of parotid depends on various factors like nervousness, morality, decision and introversion.[3]

As it is known Saliva reflects the body's health as it comprises hormones, proteins, enzymes which are also often present in standard blood tests to identify any disease. Our salivary glands produce approximately 600 ml/day of saliva that comprises of various organic and inorganic components whose imbalance can lead to a variety of systemic diseases.[4,5] The saliva of mouth is made up of salivary gland secretions, gingival crevicular fluid, transudates of mucosa, various microbes, debris of food as well as desquamated cells of epithelia.[6] However, unlike blood, collection of saliva is easy, less painful to patients, less infectious for healthcare provider during handling and approximately most of the analytes that are in blood are also found in saliva.[7,8]

Most of the times it turns out to be a challenge to diagnose any systemic diseases without the use of additional invasive investigations. To tackle these conditions, medical experts are identifying disease biomarkers which are non-invasive and will give a quick diagnosis of any

condition. Over the past few years, newly emerging salivary diagnostic tools have shown a remarkable impact in the field of biomedical research and clinical diagnosis.

However, as previously mentioned unlike blood, salivary diagnostics offers a simple, cheap, atraumatic and stress-free procedure for disease detection as biomarkers[9] present in the saliva can be very useful for early detection of diseases at an initial stage of the disease to prevent harmful consequences. Such as salivary cortisol levels to access the disorders of adrenal cortex, p53, lactate dehydrogenase biomarkers to detect any malignancy and HIV antibodies, Mycobacterium tuberculosis to detect any viral or bacterial infections, these biomarkers are present in both saliva and serum. [1]

Presently, many manufacturers produce saliva collections devices for obtaining stimulated and unstimulated saliva.[6] One of the newly emerging devices used along with the saliva collection device developed by the Oasis Diagnostics® known as Litebox Image Analysis Module (LIAM™) which is a small hand held saliva collection tool that can provide immediate quick results from its sample.

LITEBOX IMAGE ANALYSIS MODULE [LIAM]

LIAM™ (Lite Image Analysis Module) is a compact portable device using VerOFy® technology. After the assessment of the saliva sample, the data can be forwarded to any Bluetooth device or a smartphone. This tool is light weight, easy to use, and is battery powered. Due to its unique features, it is easy to handle and can be used in remote locations[10] This tool mainly focuses on VerOFy® technology. It comprises of immunochromatographic test strips that produces quick results of the collected saliva sample with effective delivery of results. The good thing about this tool is that it can used even in far off inaccessible locations due to its easy to carry feature.

BENEFITS OF LIAM

- Evaluation of biomarker levels of saliva
- Disease status
- Assessment of cortisol level of saliva, testosterone levels, biomarkers of various hormone

ARMAMENTARIUM OF LIAM MODULE (Figure. 1)

i) LIAM device
ii) VerOFy Cartridge
iii) Super •SAL (Figure. 2)
    a. Compression tube
    b. Sample volume indicator
    c. Absorbent pad
iv) Disposable pipette
v) Sample collection tube (Eppendorf tube)

PROCEDURE FOR COLLECTION OF SALIVA SAMPLE [11]

The patient is refrained from consumption of food, drinking, tobacco smoking or using mouth rinsing products for about 10 mins before the collection of the sample. The patient was asked to sit in an upright position and requested to pool the whole unstimulated saliva in the mouth, followed by placement of the Super•SAL collection device absorbent pad horizontally in the oral cavity (Figure.3a), after adequate saliva sample was absorbed the sample volume indicator turned red (Figure.3b), up to 2ml of saliva could be collected. Followed by the placement of absorbent pad into the compression tube in an upright position, the plunger is pushed slowly downward at a rate of not more than 2-3 drops/second (Figure.3c), which eliminates any additional unnecessary particulates that can compromise the Lateral Flow Test. The collected saliva sample is then transferred into the Eppendorf tube, the sample is inverted several times to ensure a homogenous mix, with the help of a disposable pipette filtered saliva is transferred from the Eppendorf tube to the right and left well of the cartridge (Lateral flow strip) about 7 drops and wait for about 20 minutes to let the sample flow in the LFT, the cartridge is ready to be analysed via LIAM.Results can also be forwarded to any Bluetooth capable smartphone or laptop.

PROCESSING OF THE SAMPLE[12,13]

Lateral Flow Test (LFT) System (Figure.4)

Saliva from the Super•SAL is examined with the Lateral Flow Test, the first section is a testing compartment that includes two LFT strip. The sample pad acts as a storage site that delivers saliva into the conjugate pad, that is present just below the housing sample well. The dried conjugate then uses saliva as a medium for its hydration. Now the free and conjugate bound analyte in the sample reacts with the europium fluorescent particle-based conjugates that is present in the VerOFy LFT. Later the reacted conjugate that is obtained from the conjugate pad is collected by the nitrocellulose membrane, this membrane then fixes the reacted product on the two capture zones that contains bands. The primary bands contains the restrained antibody for the analyte to be found in the given saliva sample. The second band contains a group of molecules that did not adhere to the primary bands. Due to the capillary action acting on the strip the fluid is continuously being pulled from the nitrocellulose membrane to the absorption pad.

LIAM

The second section is Lite Image Analysis Module which is a fluorescent LFT strip reader that can analyse and transfer the information to another device with the help of Bluetooth connectivity. The Lateral flow test strip after being exposed to the saliva sample, is then inserted to the module, the module then excites the nitrocellulose membrane to ultra violet light in a specific direction to ensure proper image analysis. The module then displays the data in picogram per millilitre units and transfers the information to a Bluetooth enabled devices.

Shirtcliff et al.[12] on 2015 conducted a study with the help of Lateral flow technology cortisol device that is capable of measuring the cortisol level in the saliva minutes after collection of the sample as compared to the traditional immunoassays that usually takes days to months for

the cortisol results. In the study 29 adults were selected and their saliva sample were collected in the morning and afternoon by passive drool and Super•SAL™ Extra Collection Device and later the sample were assayed with the help of LFT and traditional enzyme-immunoassay. The study revealed good correlation between the collection methods and the cortisol levels assayed with the help of LFT and enzyme-immunoassay.

FUTURE INVESTIGATIONS

Salivary biomarker for

- Alzheimer's dementia
- Idiopathic Parkinson's disease
- Sleeping disorders
- Mullerian-inhibiting hormone

ADVANTAGES OF LIAM

- Non-invasive
- Quick
- User friendly
- Easily accessible even in inaccessible remote areas
- Assessment of various diseases from a single saliva sample

CONCLUSION

This paper provides a gist of salivary biomarker detection both qualitatively and quantitatively signifying the probable status of disease of an individual using a portable device LIAM. Therefore, LIAM is and will be an efficient portable saliva detection substitute for use in cities as well as specially in remote far off areas where latest technologies like advanced equipments as well as infrastructures like highly equipped laboratories are not easily accessible. Not many research papers are published yet regarding this device emerging a need for more research about it in the near future.

COMPETING INTERESTS DISCLAIMER:

Authors have declared that no competing interests exist. The products used for this research are commonly and predominantly use products in our area of research and country. There is absolutely no conflict of interest between the authors and producers of the products because we do not intend to use these products as an avenue for any litigation but for the advancement of knowledge. Also, the research was not funded by the producing company rather it was funded by personal efforts of the authors.

REFFERENCE

1. Malathi N, Mythili S, Vasanthi HR. Salivary Diagnostics: A Brief Review. ISRN Dent. 2014;1(1):1-8.
2. Madalli VB, Basavaraddi SM, Burde K, Horatti P. Saliva-A diagnostic tool. IOSR J Dent Med Sci. 2013;11(6):96-99.
3. Costa PT, Chauncey HH, Rose CL, Kapur KK. Relationship of parotid saliva flow rate and composition with personality traits in healthy men. Oral Surg, Oral Med, Oral Pathol. 1980;50(5):416-422
4. Roi A, Rusu L, Roi C, Luca R, Boia S and Munteanu R. A New Approach for the Diagnosis of Systemic and Oral Diseases Based on Salivary Biomolecules. Dis Markers.2019;3(4)1-11.
5. Shah S. Salivaomics: The current scenario. J Oral Maxillofac Pathol 2018;22(3):375-381
6. Khurshid Z, Zafar MS, Najeeb S, Zohaib S. Human Saliva: A Future Diagnostic Tool. EC Dent Sci.2016; 3(6):635-636.
7. Saikia J, Pachipulusu B, Govindaraju P, Das D. Assessment of superoxide dismutase levels in saliva among tobacco and non-tobacco users - A cross sectional study. J Adv Med Dent Scie Res.2019;7(12): 66-72.
8. Malhotra T, Sachdeva A, Bhateja S, Arora G. Salivary biomarkers as a diagnostic tool. J Surg Allied Sci 2019;1(1):1-4.
9. Martina E, Campanati A, Diotallevi F, Offidani A. Saliva and oral diseases. J. Clin. Med. 2020;9(2):466.

10. Oasis Diagnostics®. 2020. *Verofy® & LIAM™ - Oasis Diagnostics®*. [online] Available at: <https://4saliva.com/products/verofy/> [Accessed 26 April 2020]
11. Filgen.jp.2020.[online]Availableat:<https://filgen.jp/Product/Bioscience4/Oasis/SSAL-601.pdf> [Accessed 26 April 2020].
12. Shirtcliff EA, Buck RL, Laughling MJ, Hart T, Cole CR, Slowey PD. Salivary cortisol results obtainable within minutes of sample collection correspond with traditional immunoassays. Clin Ther. 2015;37(3):505-514.
13. Miocevic O, Cole CR, Laughlin MJ, Buck RL, Slowey PD and Shirtcliff EA. Quantitative lateral flow assays for salivary biomarker assessment: A review. Front. public health.2017;5(1):133.

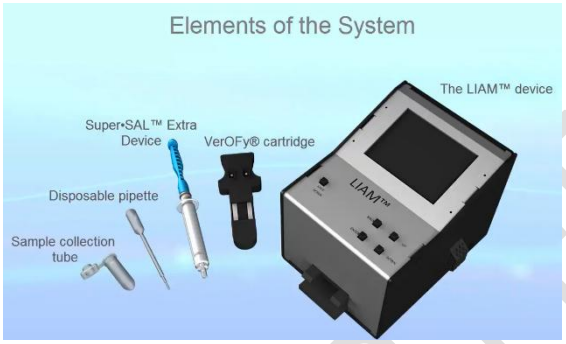

FIGURE: 1

FIGURE: 2

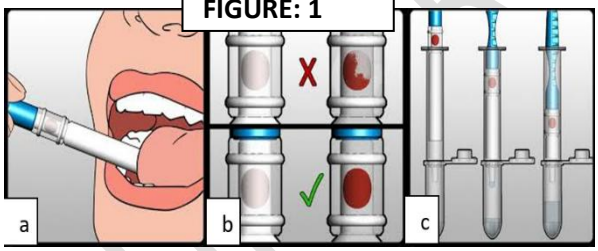

FIGURE: 3 (a,b,c)

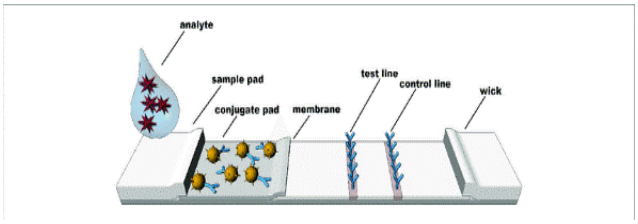

FIGURE: 4

FIGURE LEGEND:

Figure 1: LIAM reader and the test housing in which the VerOFy LFT strips are inserted, LFT – Lateral Flow Test; LIAM – Litebox Image Analysis Module. [11]

Figure 2: Components of Super•SAL device. [11]

Figure 3a: Super•SAL collection device, absorbent pad placed horizontally. [12]

Figure 3b: Sample volume indicator turns red. [12]

Figure 3c: Place the absorbent pad into the compression tube, slowly push the plunger downward at a rate of not more than 2-3 drops/second. [12]

Figure 4: Lateral Flow Strip. [13]