Research Article

Biosensors: Molecular Probing Rejuvenated - A Meta Analysis Research

Aditya Jayan[1]* and Gaurav[2]

[1]*House Surgeon, NSVK Sri Venkateshwara Dental College and Hospital, Bangalore, Karnataka, India*

[2]*Consultant Oral Physician and Maxillofacial Radiologist, Assistant Professor, Department of Oral Medicine and Maxillofacial Radiology, NSVK Sri Venkateshwara Dental College and Hospital, Bangalore, Karnataka, India*

*Corresponding Author: Aditya Jayan, House Surgeon, NSVK Sri Venkateshwara Dental College and Hospital, Bangalore, Karnataka, India.

Abstract

Aim of the Study: To statistically demonstrate the enhanced significance of BIOSENSORS over other comparative investigative procedures for detection of Oral Potentially Malignant Disorders (PMDs) over a decade's timeperiod.

Methodology: Study sample included research articles, based on databases from the COCHRANE collaboration having undergone a definite Randomised Control Trial, on various investigative procedures for Oral Precancer Lesions and Conditions and Oral Cancer itself over the past decade. This included literatures on Toluidine blue, Lugol's iodine, Vizilite, Velscope, Colposcopy and Biosensors. The literature was, assessed analysed and studied, comparison was made based on the various p-values between various techniques on one side and biosensors on the other in terms of sensitivity and specificity. A Meta Analysis of all the modalities including the above mentioned parameters was carried out and advantages and disadvantages documented and compared with those of Biosensors in order to demonstrate the title of the study.

Result: Compared to the 100% sensitivity and specificity of biosensors, the sensitivity and specificity of vital staining techniques were found to be respectively 95% and 81%, whereas the sensitivity and specificity of visual aids were found to be respectively 86% and 78%.

Conclusion: Biosensors definitely came up as the best diagnostic aids and investigative procedures at hand compared to all others existing or tried so far.

Keywords: Biosensors; Meta Analysis; Randomised Contol Trials; Sensitivity; Specificity

Introduction

Oral cancers, as all of us are aware are one of the most significant human maladies in our history. The alarming epidemiological data of various cancers of the human body including the oral cancers ranking 6th amongst all, have been disheartening in the literatures existing so far. It is estimated that there are almost three lakh cases of oral cancer reported worldwide in literature to claim numerous lives annually [1,2]. This malady has been an enigma not only to the patients but also the professionals (oral surgeons, physicianss and oncologists) because cancer is not a disease of a patient alone, but the entire family (physically, psychologically and socioeconomically).

Presently cancers are being diagnosed very late usually at the untreatable stages, thereby increasing the morbidity and mortality rates bringing down the 5 year survival rate drastically [3,4]. Hence

in the present scenario an onus for early diagnosis probably at the molecular or bio molecular level before genotypic conversion takes place, lays the preamble for combating this deadly disease.

The complexity and diversity of cancer etiology and various investigative procedure, has posed many hurdles in meeting the challenge of early diagnoses of cancer thereby to improve the prognosis. Amongst the many early diagnostic tools for the same, a newer biosensor technology has shown the potential to provide fast and accurate results in picking up these gene-conversions at the molecular level thus enhancing the prognostic outcome. It has claimed a sensitivity and specificity of 100% [1,4,6,7].

Hence the present study aims to evaluate the literature for various investigative procedures, to compare their efficacy (dependent on p-values) in terms of specificity and sensitivity index, through a Meta-Analysis with those of biosensors, thus evaluating whether "BIOSENSORS" are indeed a new wave in early stage cancer diagnostics, which could definitely herald a new era in the field of oral oncology diagnosis and treatment planning.

Materials and Methods

Various researches and studies have documented that the Biosensors to be 100% sensitive and specific. With this fact in mind a literature based Meta analysis was carried out in order to fulfil the aim of this study. With the Cochrane collaboration taken as source for authenticated scientific research data, 188 articles were selected having undergone a randomized control trial. Out of these, the articles were screened and finally 88 articles were selected which met the criterion for Meta Analysis. There were 3 groups which were included in our study, viz;

- **Group 1**: Biosensors
- **Group 2**: Vital Staining Techniques (Lugol's iodine, Toluidine blue etc)
- **Group 3**: Visual AIDS (Colposcopy, Vizilite etc).

Group I: Diagnostic kit and the mode of working of biosensors

The kit consists of a silicon or a photonic crystal mounted on a glass slide (Figure 1). The preamble lies in detection of bio molecules like the proteins. A drop of blood is pooled onto the silicon or photonic crystal following which the protein content of the blood is extracted and gets bound to the antibody dot present on the crystals thus exposing the entire panel of proteins on the screen. Then the proteins pertaining to oral cancer (IL-8, AFPs) are segregated

or sorted out and then a chemical solution with a fluorescent tag is added to it. If the protein contains antibodies, it will fluoresce on application of LASER thus demonstrating the presence of dysplasia or malignancy in the body. This procedure claims a 100% sensitivity because these bio molecules of onco proteins can be picked up very early in the processes of onco genesis.
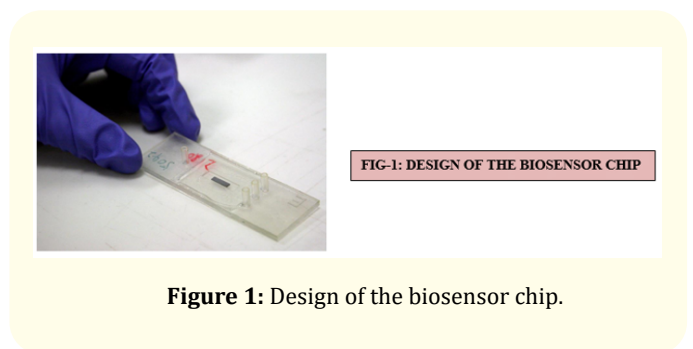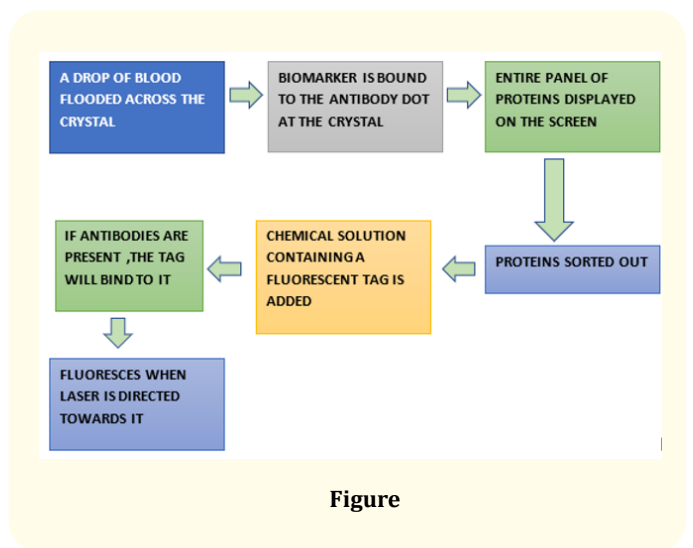

FIG-1: DESIGN OF THE BIOSENSOR CHIP

Figure 1: Design of the biosensor chip.

Figure

Group-Ii: Vital staining techniques

These are the metachromatic vital dyes that may bind preferentially to tissues undergoing rapid cell division (such as inflammatory, regenerative and neoplastic tissue), to sites of DNA change associated with Oral Pre Malignant Lesions or both. The binding results in the staining of abnormal tissue in contrast to adjacent normal mucosa. Since the molecular and genetic analyses are not routine procedures for oral lesions in which biopsies are performed regularly, the main contribution of these techniques is to highlight the oral lesions and to assist the physicians in better locating the surgical margins.
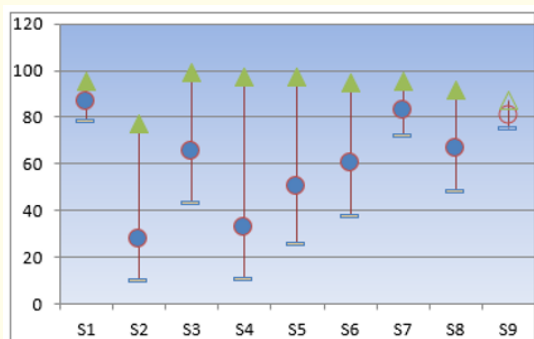
Group-Iii: Visual aids

Several visualization adjuncts are intended for use as adjuncts to the standard visual and tactile oral examination under incandescent light. They function under the assumption that mucosal tissues undergoing abnormal metabolic or structural changes have different absorbance and reflectance profiles when exposed to various forms of light or energy. After receiving an application of acetic acid, sites of epithelial proliferation, having cells with altered nuclear structure, are purported to preferentially reflect the low energy blue-white light emitted by a device generating an "acetowhite" change, thus detecting the signs of dysplasia or malignancy.
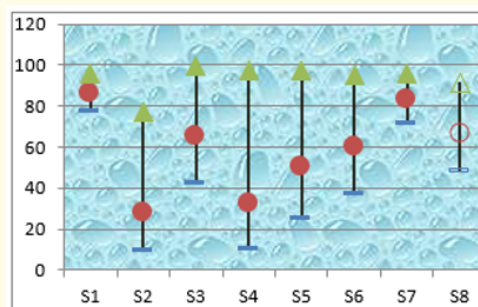
Meta analysis was performed using well defined specific softwares, the one used in this study was Comprehensive meta analysis V5 software.

Results

Meta analysis is a technique of combining the results of many studies in a rigorous and systemic manner to allow us to better assess the prevalence rates of different types of gambling and determine which intervention has the best evidence regarding its effectiveness. A Meta Analysis of all the modalities including the above mentioned parameters was carried out and advantages and disadvantages were documented and compared with those of Biosensors in order to demonstrate the title of the study. The sensitivity (Graph 1) and specificity (Graph 2) of the Vital staining techniques was statistically found to be 95% and 81% respectively where as the sensitivity (Graph 3) and specificity(Graph 4) of the visual aids was found to be 86% and 83% respectively. Finally when all the 3 groups of the study were taken into consideration together, Biosensors proved to be the best amongst all with 100% sensitivity (Graph 5) and specificity (Graph 6) followed by the vital staining techniques and then the visual aids as diagnostic modalities for early detection of pre cancer and cancer.
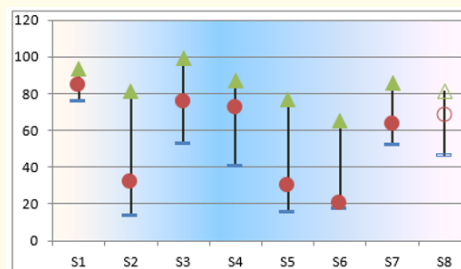

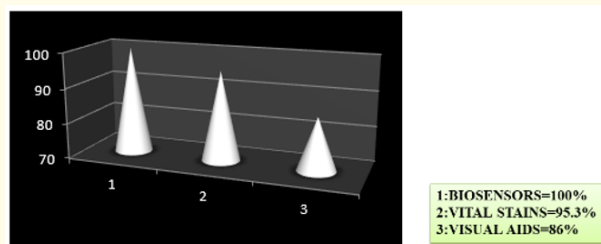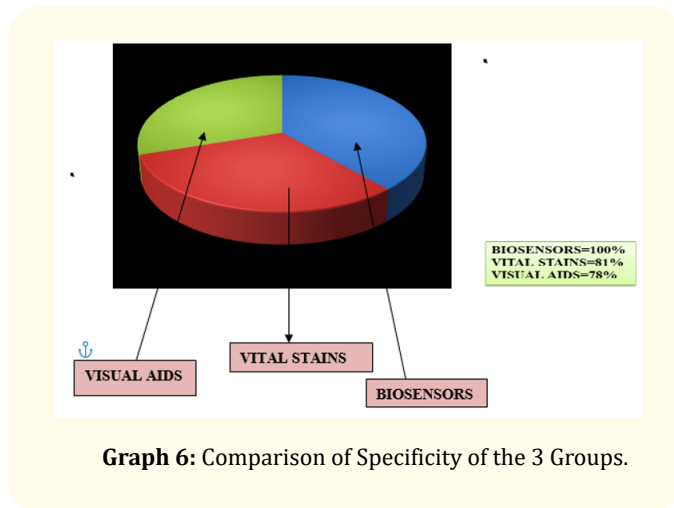**Graph 2:** Specificity of Vital Staining Techniques=81%.
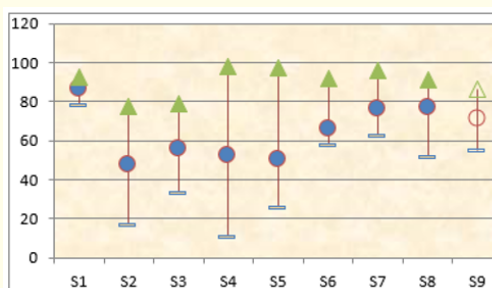
Graph 3: Sensitivity of Visual Aids=86%.

Graph 4: Specificity of Visual Aids=83%.

Graph 5: Comparison of Sensitivity of the 3 Groups.

Graph 1: Sensitivity of Vital Staining Techniques=95%.

Graph 6: Comparison of Specificity of the 3 Groups.

The Meta Analysis graphical representations are depicted after the reference section later in this article.

Discussion

Biosensors work on the principle that the tumors or the cancerous cells elaborate specific onco proteins which can circulate through the bloodstream and can be picked up even at minute concentrations [1,5,8]. These onco proteins are characteristic and are called BIOSENSORS. Biosensor devices are specially designed to detect biological entities by converting biomolecular signals into electrical signals which is further analyzed. This technology has the potential to provide fast and accurate detection which are reliable in, imaging of cancerous cells, monitoring angiogenesis and cancer metastasis [3,7,16].

Staining techniques and other visual aids have been used routinely as early diagnostic tools to pick up Potentially Malignant Disorders. The concept and technology is based on genetic and morphological changes ie changes which have already caused oncoconversion [7-17].

Therefore difference between the above 3 groups is that the Biosensors pick up early biochemical onco conversions whereas other 2 groups pick up functional and morphological conversions. In terms of onco conversion, biosensors prove to be the most significant of all and the same has been proven by our Meta Analysis results.

Conclusion

The development of biosensors is probably one of the most promising ways to solve some of the problems concerning the increasing need to develop highly sensitive, fast and economic methods of analysis in early detection of cancers.

In this regard, biosensors come up as the best weapons of choice in the future of fight against oral cancers.

Bibliography

1. Rasooly A and Jacobson J. "Development of biosensors for cancer clinical testing". *Biosensors and Bioelectronics* 21.10 (2006): 1851-1858.

2. Hu Y. "BRCA1 hormone, and tissue-specific tumor suppression". *International Journal of Biological Sciences* 5.1 (2009): 20-27.

3. Stevens RC., *et al*. "Detection of cortisol in saliva with a flow-filtered portable surface plasmon resonance biosensor system". *Analytical Chemistry* 80 (2008): 6747-6751.

4. Luo CX., *et al*. Lab on a Chip 5.7 (2005):726- 729.

5. Epstein JB., *et al*. "Toluidine blue and Lugol's iodine application in the assessment of oral malignant disease and lesions at risk of malignancy". *Journal of Oral Pathology and Medicine* 21.4 (1992):160-163.

6. Warnakulasuriya KA and Johnson NW. "Sensitivity and specificity of Ora Scan (R) toluidine blue mouthrinse in the detection of oral cancer and precancer". *Journal of Oral Pathology and Medicine* 25.3 (1996): 97-103.

7. Epstein JB., *et al*. "The utility of toluidine blue application as a diagnostic aid in patients previously treated for upper oropharyngeal carcinoma". *Oral Surgery, Oral Medicine, Oral Pathology, and Oral Radiology* 83.5 (1997): 537-547.

8. Ya-Wei C. "Methylene blue as a diagnostic aid in the early detection of oral cancer and precancerous lesion". *British Journal of Oral and Maxillofacial Surgery* 45 (2007b): 590-591.

9. Michaell A Huber., *et al*. "Acetic acid wash and chemiluminescent illumination as an adjunct to conventional oral soft tissue examination for the detection of dysplasia: A pilot study". *Quintessence International* 35 (2004): 378-384.

10. Camile S Faraha and Michael J Mc Culloughb. "A pilot case control study on the efficacy of acetic acid wash and chemiluminescent illumination (ViziLite™) in the visualisation of oral mucosal white lesions". *Oral Oncology* 48 (2007): 820-882.

11. Grodzinski P., *et al.* "Nanotechnology for cancer diagnostics: promises and challenges". *Expert Review of Molecular Diagnostics* 6.3 (2006): 307-318.

12. Banerjee HN and Verma M. "Use of nanotechnology for the development of novel cancer biomarkers". *Expert Review of Molecular Diagnostics* 6.5 (2006):679-683.

13. Wong PN. "*In vivo* toluidine blue staining for the detection of oral cancer and precancer". *PNG Institute of Medical Research* 25 (1982): 278-280.

14. Silverman S Jr and Migliorati C. "Toluidine blue staining and early detection of oral precancerous and malignant lesions". *Iowa Dental Journal* 78 (1992): 15-16.

15. Betz CS., *et al.* "Autofluorescence imaging and spectroscopy of normal and malignant mucosa in patients with head and neck cancer". *American Society for Laser Medicine* 25 (1999): 323-334.

16. Zargi M., *et al.* "Autofluorescence imaging in the diagnosis of laryngeal cancer". *European Archives of Oto-Rhino-Laryngology* 257 (2000): 17-23.

17. Novo M., *et al.* "Chemical instability of 5-aminolevulinic acid used in the fluorescence diagnosis of bladder tumours". *The Journal of Photochemistry and Photobiology B* 34 (1996): 143-148.