

Application of Bioimpedance in Community Screening and Early Detection of Oral Potentially Malignant Disorders

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Research Article

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Abstract

Background

Oral squamous cell carcinoma (OSCC) represents a significant global disease burden, particularly in India. OSCC is frequently preceded by oral potentially malignant disorders (OPMDs) such as leukoplakia, erythroplakia, oral submucous fibrosis (OSMF), and oral lichen planus (OLP). Early detection of OPMDs via non-invasive point-of-care bioimpedance analysis can prevent malignant transformation and significantly reduce mortality.

Methods

A prospective case-control community screening study evaluated 85 participants divided into study groups (n = 55; Leukoplakia = 15; Erythroplakia = 10; OSMF = 15; OLP = 15) age/sex- matched healthy controls (n = 30). Electrical bioimpedance parameters – phase angle (ϕ), imaginary part of impedance (X), real part of impedance (R), and total impedance (Z)– were measured at 15Hz and 45kHz using a precision AD5934 impedance analyzer with a tetrapolar surface electrode probe. Histopathological correlation (dysplasia vs. non-dysplasia) was conducted post-biopsy. Data were analyzed using independent Student's t-test and one-way ANOVA.

Results

Bioimpedance measurements revealed significant reduction in total impedance (Z) and real part of impedance (R) across all OPMD groups compared to controls at both 15Hz and 45kHz ($p < 0.05$). Dysplastic tissue exhibited markedly lower phase angles (-10.30° vs. -15.40° at 15Hz; -45.43° vs. -60.99° at 45kHz) and reduced total impedance $910,096\ \Omega$ vs. $13,490\ \Omega$ at 15Hz) compared to healthy control tissues.

Conclusion

Multi-frequency Bioimpedance spectroscopy effectively differentiates normal oral mucosa from OPMDs and dysplastic tissues. It serves as a rapid, reliable, objective and non-invasive decision support tool for community-based screening.

Background

Among developed nations, cancer stands second after coronary disorders as the principal cause of death [1]. Globally, Oral squamous cell carcinoma (OSCC) ranks sixth among all malignancies [2]. India accounts for approximately one-third of total global OSCC cases, posing a formidable public health challenge in developing economies [2]. Annually, nearly 77,000 new cases are diagnosed and 52,000

deaths are recorded in India alone, constituting the highest mortality rate in Asia [3, 4]. Globally, international classification estimates record over 300,373 diagnosed cases and 145,353 deaths due to oral cancer [5].

OSCC is frequently preceded by histopathologically distinctive mucosal precursor lesions termed 'oral potentially malignant disorders' (OPMDs) [6]. Key OPMDs include leukoplakia, erythroplakia, oral submucous fibrosis (OSMF) and oral lichen planus (OPL) [6]. Early identification, accurate diagnosis, and timely management of OPMDs prevent their transformation into overt malignancy [1]. While advanced diagnostic techniques- including exfoliative/ liquid-based cytology, brush biopsy, vital staining and visually enhanced light scopes (VELScope)- enhance risk stratification, electrical bioimpedance analysis offers a unique non-invasive, objective technique [7, 8].

Bioimpedance quantifies tissue impedance by applying a low-intensity sinusoidal electric-current, yielding vital data regarding tissue electrochemical properties, cellular hydration, membrane integrity and tissue structure [8]. In clinical oncology, bioimpedance has been successfully applied to evaluate body composition, monitor nutritional status, determine disease prognosis and demarcate surgical margins [1, 9, 10]. In electrical terms, impedance (**Z**) represents total obstruction to alternating current flow and comprises real resistance (**R**) from extra/intracellular fluids and capacitive reactance (**X**) from cell membrane [8]. The complex impedance is expressed as: $Z = R + jX$

Historically, Thomasset pioneered bioimpedance for total body water estimation using needle electrodes [11, 12], while Nyboer introduced quad-surfaced electrodes [13]. Subsequent studies by Morimoto et al. [14], Emtestam et al. [15], Lee et al. [16], Glickman et al. [17], Aberg et al. [18], Halter et al. [19], Balasubramani et al. [20], Sarode et al. [21] and Tatullo et al. [9] established electrical impedance as a highly reliable tool for differentiating neoplastic from healthy tissue in breast, prostate, skin, cervix and oral lesions [9, 14–21].

Methods

Study Design and ethical approval

This prospective prospective case-control study was conducted in the Department of Oral Pathology and Microbiology, Sharad Pawar Dental College and Hospital, Datta Meghe Institute of Higher Education & Research (Deemed University), Sawangi (Meghe), Wardha, India. The study protocol was approved by the Institutional Ethics Committee of Datta Meghe Institute of Medical Sciences (Deemed to be university (DMIMS(DU) IEC/2023/726, dated 15/02/2023).

Study Population and Eligibility

This study evaluated 55 subjects with clinically diagnosed OPMDs referred to the department following community screening health camps, along with 30 age- and sex- matched healthy controls..

- **Inclusion criteria:** Patients presenting with clinical features of Leukoplakia, OSMF, OLP, or Erythroplakia confirmed by provisional examination during community camps.
- **Exclusion Criteria:** Patients wearing cardiac pacemakers or electrical implanted devices, and those unwilling to provide informed consent.

The study group ($n = 55$) was sub- categorized as follows:

1. **Group 1:** Leukoplakia ($n = 15$)
2. **Group 2 :** Erythroplakia ($n = 10$)
3. **Group 3:** Oral submucous Fibrosis ($n = 15$)
4. **Group 4 :** Oral Lichen Planus ($n = 15$)
5. **Group 5:** Control Group ($n = 30$; age- and sex- matched healthy individuals)

Clinical diagnostic criteria

1. **Leukoplakia Group ($n = 15$):** Defined as a white/ grey plaque or patch of uncertain risk that cannot be scraped off and cannot be characterized as any other specific diseases [23].
2. **Oral Submucous Fibrosis (OSMF) Group ($n = 15$):** Categorised by palpable fibrotic bands, mucosal balancing, intolerance to spicy foods, and restricted mouth opening classified according to Lai et al. criteria: Stage 1 (> 35 mm), Stage 2 (30–35 mm), Stage 3 (20–30 mm), Stage 4 (< 20 mm) [24, 25].
3. **Oral Lichen Planus (OLP) Group ($n = 15$):** Included patients with bilateral white striations, papules, plaques, erosions, or bullae primarily affecting the buccal mucosa, tongue of gingiva [26].
4. **Erythroplakia Group ($n = 10$):** Included patients presented with bright red, velvety, well-demarcated mucosal plaques positioned at a slightly lower level than surrounding normal mucosa [27].

Data collection methods and Bioimpedance measurements

Bioimpedance analysis was performed using a high-precision AD5934 Impedance Converter Network Analyzer (Analog Devices, USA). Prior to clinical measurements, system calibration was confirmed in standard saline solution with reference conductivity accuracy of $\pm 0.2 \Omega$. Patient oral temperatures were verified using a calibrated clinical thermometer before and after bioimpedance acquisition (range: 35.7°C to 38.6°C).

Measurements were conducted non-invasively using a single-use tetrapolar surface probe featuring four 1mm diameter silver electrodes mounted in a square configuration (2 mm inter-electrode spacing) on a wooden applicator spatula. Excitation AC signals at dual frequencies (15 Hz low frequencies and 45 kHz high frequency) were applied. An on-board 12-bit Analog-to-Digital Converter (ADC) digitized the tissue current response, and an integrated Digital Signal Processor (DSP) performed Discrete Transform (DFT) algorithms to output Real (**R**) and Imaginary (**I**) impedance components [8, 22]. The phase angle (θ) and total impedance (**Z**) were calculated accordingly.

Following non-invasive bioimpedance assessment, all OPMD patients underwent diagnostic tissue biopsy for histopathological examination as per standard ethical protocol to determine the presence or absence of epithelial dysplasia [21]. Dysplastic features evaluated included drop-shaped rete ridges, cellular pleomorphism, nuclear hyperchromatism, altered nuclear-cytoplasmic ratio, loss of polarity and atypical mitotic figures [21].

Data Analysis Techniques

Quantitative continuous data were processed and summarized as mean parameter values across excitation frequencies (15 Hz and 45kHz). Differences between OPMD study subgroups and healthy control subjects, as well as comparison between dysplastic and non-dysplastic tissues, were statistically analyzed using Student’s independent t-test and one-day Analysis of Variance (ANOVA). A p-value < 0.05 was considered statistically significant.

Results

Demographic characteristics and Systemic data

The study cohort comprised 85 individuals (55 OPMD patients and 30 healthy controls). Age distribution across subgroups showed: Leukoplakia (40–55 years), Erythroplakia (52-60years), OSMF (20–40 years), OLP (50–65 years), and Control Group (25–55 years). Oral cavity temperatures remained stable across all evaluations (35.7°C to 38.6°C).

Bioimpedance electrical parameters across OPMD subgroups

Comparative measurements of Phase Angle (θ), Imaginary part of Impedance (**X**), Real part of Impedance (**R**), and total impedance (**Z**) at 15Hz and 45kHz are summarized in Tables 1–4.

Table 1
Phase angle(θ) at 15Hz and 45 kHz.

Frequencies	Control(Ω)	Leukoplakia (Ω)	Erythroplakia (Ω)	OSMF(Ω)	OLP(Ω)
15 Hz	-13.99	-15.30	-15.43	-21.82	-13.45
45kHz	-51.32	-56.89	-56.18	-58.07	-47.57

Table 2
Imaginary Part of Impedance (X) at 15Hz and 45 kHz.

Frequencies	Control(Ω)	Leukoplakia (Ω)	Erythroplakia (Ω)	OSMF (Ω)	OLP(Ω)
15 Hz	-3651	-2601	-2551	-2391	-2500
45kHz	-631	-478.2	-476	-431.3	-465.5

Table 3
Real part of impedance(R) at 15Hz and 45 kHz.

Frequencies	Control(Ω)	Leukoplakia (Ω)	Erythroplakia (Ω)	OSMF(Ω)	OLP(Ω)
15 Hz	14030	12390	12401	13497	12205
45kHz	525.9	476.3	476.1	587.0	468.4

Table 4
Total Impedance(Z) at 15Hz and 45 kHz.

Frequencies	Control(Ω)	Leukoplakia(Ω)	Erythroplakia(Ω)	OSMF(Ω)	OLP(Ω)
15 Hz	51470	12295	13101	13142	12104
45kHz	820.0	728.7	779.9	884.0	789.1

Bioimpedance parameters and Histopathological dysplasia correlation

Histopathological evaluation revealed dysplastic changes in 12 patients and non-dysplastic OPMD in 43 patients. Comparison between dysplastic OPMD, and control tissues demonstrates progressive bioimpedance reduction in dysplastic lesions (Tables 5–8)

Table 5
Phase angle (Φ) by histopathological dysplasia grading.

Frequency	Dysplasia Present (Ω)	Dysplasia Absent(Ω)	Control(Ω)
15Hz	-10.30	-14.26	-15.40
45kHz	-45.43	-56.07	-60.99

Table 6
Imaginary part of Impedance (X) by dysplasia grading.

Frequency	Dysplasia Present (Ω)	Dysplasia Absent(Ω)	Control(Ω)
15Hz	-2146	-2745	-2776
45kHz	-498.21	-5801.16	-598.25

Table 7
Real part of Impedance (R) by dysplasia grading.

Frequency	Dysplasia Present (Ω)	Dysplasia Absent(Ω)	Control(Ω)
15Hz	10275	11465	13496
45kHz	345.72	467.45	578.05

Table 8
Total Impedance (Z) by dysplasia grading.

Frequency	Dysplasia Present (Ω)	Dysplasia Absent(Ω)	Control(Ω)
15Hz	10096	12395	13490
45kHz	396.09	47122	617.40

Discussion

Core Findings

The primary finding of this investigation is that bioimpedance spectral parameters – specifically total impedance (Z), resistance (R), Phase angle (ϕ) – are significantly lowered in OPMD tissues compared to normal oral mucosa, with the most pronounced reduction observed in histopathologically verified dysplastic tissues ($Z = 10,096 \Omega$ in dysplastic vs. $13,490 \Omega$ in controls at 15Hz). Cell membranes consist of phospholipid bilayers embedded with proteins, acting as capacitive barriers with leaky ion channels, while intracellular and extracellular fluids act as resistive conductors [13, 11]. Malignant transformation and dysplasia induce severe structural alterations, including disrupted cell orientation, increased cell packing density, altered nuclear- cytoplasmic ratios, breakdown of cell membrane semi-permeability and elevated intr-/extra-cellular water and electrolyte content [13, 11]. These architectural disruptions diminish capacitive reactance and resistance, causing a characteristic decrease in overall electrical impedance across low (15 Hz) and high (45 kHz) excitation frequencies [11, 12].

Our observations align closely with findings reported by Walker et al. [28], who demonstrated significantly lower bioimpedance in premalignant cervical epithelium relative to normal tissues. Similarly, Sarode et al.[10, 21] identified marked reduction in bioimpedance at 20 Hz and 50 kHz in OPMDs and OSCC compared to normal controls, noting that erythroplakia, Leukoplakia and OSMF exhibited statistically significant impedance drops, whereas OLP demonstrated moderate reductions [10]. Tatullo et al. [9] also verified bioimpedance variations in OLP subtypes, showing marked decrease in erosive forms due to mucosal disruption. Furthermore, Ching et al. [29] confirmed bioimpedance sensitivity in screening squamous cell carcinoma of the tongue.

Study Limitations

Certain limitations must be considered. First, the total sample size ($n = 85$ overall; $n = 10$ in the erythroplakia subgroup) is moderate, necessitating caution before generalizing cut-off thresholds across larger populations. Second, surface electrode positioning and localized tissue moisture/saliva variations can introduce mild contact resistance fluctuations. Third, bioimpedance measurements reflect localized electrical property averages and cannot completely replace formal scalpel biopsy and histopathological grading.

Future implications and community relevance

in developing nations, OPMDs precede the vast majority of OSCC cases [1–4]. Conventional community screening is limited by clinical subjectivity and inability to detect early sub-surface dysplasia, while scalpel biopsy is invasive, painful and unfeasible at rural health camps [7, 29] Point-of-care bioimpedance analysis using portable, low-cost micro-converters (such as the AD5934) provides real-time, non-invasive diagnostic decision support. It reduces patient anxiety, facilitates immediate repeat measurements and enables objective triage, referring high-risk dysplastic OPMDs for immediate biopsy and early detection [29].

Conclusion

Bioimpedance analysis is a highly promising, objective, rapid and non-invasive modality for evaluating OPMDs and detecting mucosal dysplasia. The marked reduction in bioimpedance parameters (Z , R , ϕ) in dysplastic tissues highlights its potential as an adjunct tool during routine community health screening camps, facilitating early diagnosis and timely management of oral precancers.

Abbreviations

ADC: Analog-to-digital Converter; **ANOVA**: Analysis of Variance; **BCC**: Basal Cell Carcinoma; **CIN**: Cervical Intraepithelial Neoplasia; **DFT**: Discrete Fourier Transform; **EIS**: Electrical Impedance Scanning; **ICD**: International Classification of Diseases; **OLP**: Oral Lichen Planus; **OPMD**: Oral Potentially Malignant Disorders; **OSCC**: Oral Squamous Cell Carcinoma; **OSMF**: Oral Submucous Fibrosis; **SOP**: Standard Operating Procedure.

Declarations

Ethical approval and Consent to participate

The study protocol was approved by the Institutional Ethics Committee of Datta Meghe Institute of Medical Sciences (Deemed to be university) (DMIMS(DU) IEC/2023/726, dated 15/02/ 2023). Informed written consent was obtained from all individuals participants prior to screening and procedures.

All experiments were performed in accordance with relevant guidelines and regulations.

The study was carried out in compliance with the Declaration of Helsinki.

The written informed consent was acquired from the patients regarding use of their data and archival tissue samples.

Consent for Publication

Not applicable.

Availability of Data and Materials

The datasheets analysed during the current study are available from the corresponding author upon reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Author's Contribution

Study concept and design- Dr. Rashtwar Kaushiki & Dr. Hande Alka

Data collection- Dr. Sonone Archana

Data analysis and interpretation- Dr. Patil Swati and Dr. Pakhale Aayushi

Drafting of manuscript- Dr. Rashtwar Kaushiki & Dr. Hande Alka

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Declaration of generative AI and AI-assisted technologies in the writing process

During the preparation of this work the authors used ChatGPT 5/ Grammarly in order to improve the English language and readability of the manuscript. After using this tool/service, the author reviewed and edited the content as needed and takes full responsibility for the content of the published article.

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Figures

Figure1: Comparison of Mean total Impedance (Z) across control and OPMD groups at 15 Hz and 45kHz.

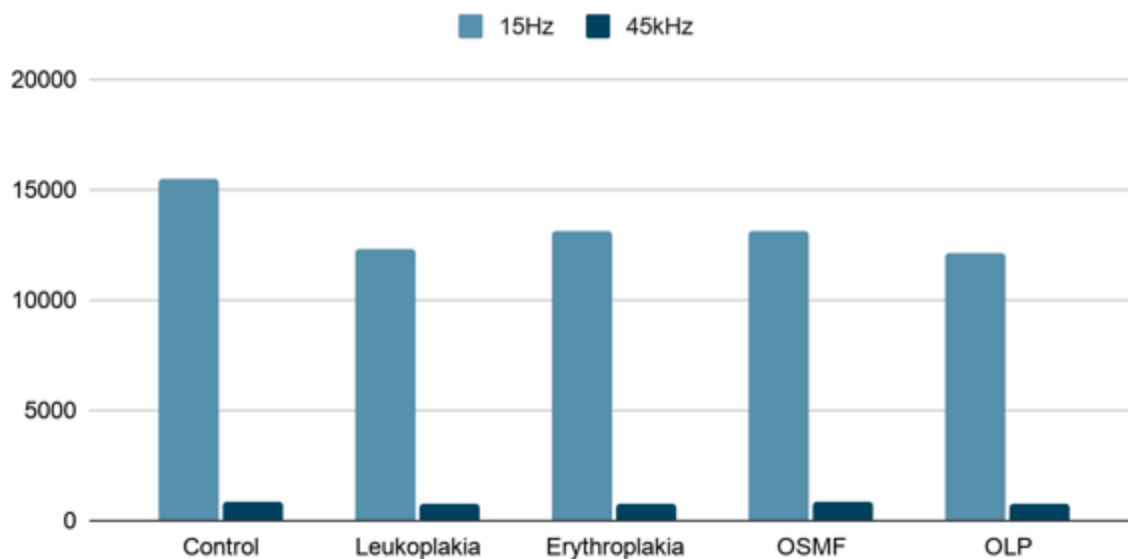


Figure 1

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Figure 2: Significant Bioimpedance (Z) suppression in dysplastic OPMD tissue vs. non-dysplastic OPMD and

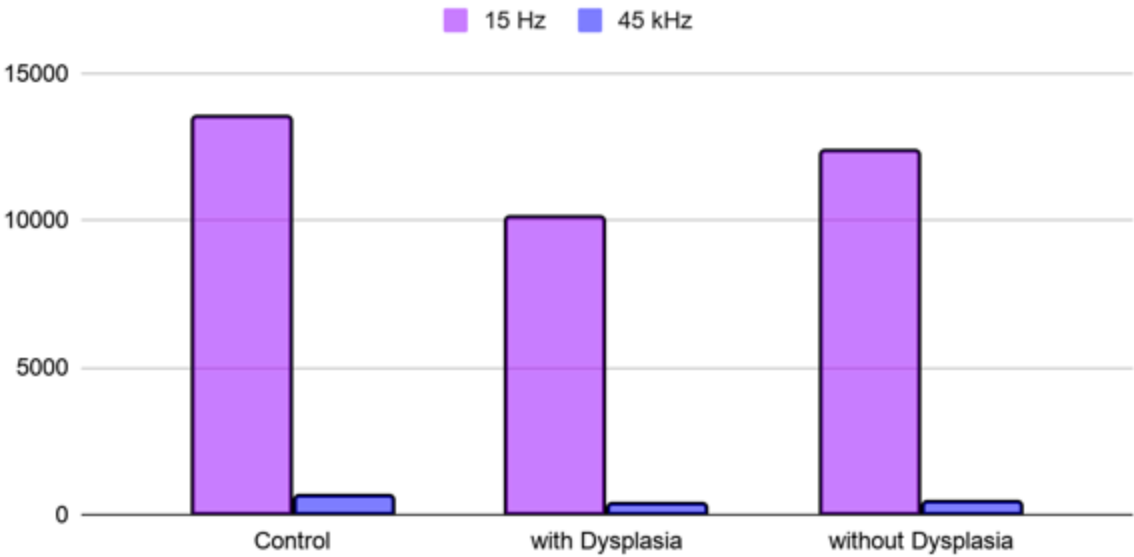


Figure 2

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