Early Detection of Cervical Intraepithelial Neoplasia
in a Heterogeneous Group of Colombian Women
Using Electrical Impedance Spectroscopy and the
Miranda-López Algorithm

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Abstract. Electrical Impedance Spectroscopy (EIS) allows the study of the electrical
properties of materials and structures such as biological tissues. EIS can be used as a diagnostic
tool for the identification of pathological conditions such as cervical cancer. We used EIS
in combination with genetic algorithms to characterize cervical epithelial squamous tissue in
a heterogeneous sample of 56 Colombian women. All volunteers had a cytology taken for
Papanicolau test and biopsy taken for histopathological analysis from those with a positive
result (9 subjects). ROC analysis of the results suggest a sensitivity and specificity in the order
of 0.73 and 0.86, respectively.

1. Introduction
Cervical cancer is the leading malignancy among Colombian women, where the situation is worse
when compared to South America and Europe [1, 2, 3]. Therefore, cervical cancer in Colombia
is an issue of high concern and the Colombian government is interested in strengthening the
prevention programs implemented in the country [4].

Electrical characterization of cervical tissue has been suggested as a tool for the screening
of cervical cancer [5, 6]. Electrical tissue properties studied through EIS depend upon the
amplitude and frequency of the electrical excitation. For low amplitudes (i.e. electric field
and current density below 1V/cm and 1mA/cm² respectively) electrical properties of tissues
have a linear behavior. At low frequencies (alpha dispersion zone) electrode-tissue properties,
relaxation and polarization of charged spaces dominate. Between frequencies around 1 kHz and
1 MHz (beta dispersion zone) polarization and interfacial relaxation characterizes the electrical
properties of tissue. At higher frequencies (gamma dispersion zone) the dipolar relaxation of
water and other molecules take relevant importance. In the beta dispersion zone it is possible
to study the properties of biological tissues by the induced polarization effect that takes place
at these frequencies [7, 8].

Biologic tissues are characterized by aqueous solution compartments separated by membranes
of cells attached together. These membranes limit the free movement of ions through the
extracellular compartment, determining its macroscopic behavior as a heterogeneous dielectric [7]. As such, they can be modeled by the Cole-Cole semi-empirical equation [9]. Pelton et al [10] suggested an alternative form of Cole-Cole equation that better describes the induced polarization effect:

\[ \rho = \rho_0 \left\{ 1 - m \left[ 1 - \frac{1}{1 + (j\omega\tau)^c} \right] \right\} \tag{1} \]

Where \( \omega \) is the frequency of the excitation, \( \rho_0 \), the resistivity at low frequency, \( \tau \), the time parameter, \( c \), the relaxation parameter and \( m \), the intrinsic chargeability (also called limited polarizability). The intrinsic chargeability, \( m \), characterizes the intensity of the induced polarization effect [11].

In this article, we use the algorithm proposed by Miranda and López-Rivera [12] to obtain the Cole-Cole parameters from real part of the electrical impedance cervical measurements taken in a heterogeneous sample of 56 Colombian women. The results suggest good sensitivity (0.73) and specificity (0.85) when using two different parameters: low frequency resistivity and intrinsic chargeability, respectively.

2. Methods and Materials

The study was approved by the institutional Ethics Committee and women included in it signed a written informed consent. In this study we present the results obtained from a heterogeneous sample of 56 women. Electrical impedance spectrum were measured in cervical tissue in the eight zones showed in figure 1. On each zone impedance spectrum for seven different frequencies between 9.6kHz and 614kHz was measured using the Mark III bioimpedanciometer [5, 13]. A cervical sample for the Papanicolau test was taken from each woman after the electrical measurements were registered. A biopsy and histopathological study of the cervix were performed to women with a positive Papanicoalu test (9 women).

![Figure 1. Zones in cervix were electrical impedance spectrum were measured.](image)

Electrical impedance spectra were processed using the Miranda-López algorithm [12] to obtained the following four parameters of the spectra: intrinsic chargeability (\( m \)), low frequency resistivity (\( \rho_0 \)), central relaxation time (\( \tau \)) and relaxation parameter (\( c \)) for tissue.

In accordance with Bethesda standard for cervical cytology, four classification groups were defined to the screening: normal (NO), low-grade squamous intraepithelial lesion (LSIL), high-grade squamous intraepithelial lesion (HSIL) and cancer (CA). ANOVA and ROC curves were used to analyze the results.
3. Results and Discussion
The real part of the electrical impedance spectrum for measures classified as NO, LSIL, HSIL and CA are showed in figure 2. This figure shown differences in the spectra due to tissue condition. For normal tissue (NO) low frequency resistivity is greater than that of abnormal tissue (LSIL, HSIL and CA), i.e. as tissue become abnormal, a conductive behavior is predominant with a decrease in low frequency resistivity.

![Figure 2. Real part of the electrical impedance spectrum for NO, LSIL, HSIL and CA tissues.](image)

From the four Cole-Cole parameters only the low frequency resistivity ($\rho_0$) and intrinsic chargeability ($m$) show a good behavior as an classifier. ANOVA analysis revealed a statistical differentiation between classification groups and numerical values for $\rho_0$ and $m$ ($p < 0.001$). The sensitivity and specificity were studied by ROC curves for $m$ and $\rho_0$ (figures 3 and 4, respectively). The cut-off point of ROC curve was selected in the form that the best sensibility and specificity were simultaneously achieved, i.e. the point near to the left up corner in the ROC curve. A sensitivity and specificity over 70% and 80%, respectively, were suggested by ROC curves. Because measures were made on a heterogeneous population, the sensitivity and specificity obtained suggest that electrical properties of tissue are not significantly influenced by population heterogeneity.

![Figure 3. ROC curve for intrinsic chargeability ($m$).](image)
4. Conclusions
Electrical impedance spectroscopy was used to study electrical properties of cervical tissue in a heterogeneous population of Colombian women. Cole-Cole parameters were studied as screening tool. Statistical differences between numerical values for parameters $m$ and $\rho$ of Cole-Cole model for normal and abnormal tissue were observed ($p < 0.001$). The area under ROC curves ($A_{ROC} > 0.78$) suggest that these two parameters ($m$ and $\rho$) could be used, in a complementary way, for the screening of cervical cancer in Colombian women.

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References
[1] Lewis, MJ. 2004 A Situational Analysis of Cervical Cancer in Latin America and the Caribbean. (Washington, DC: PAHO/WHO).
[2] WHO/ICO 2010 Information Centre on HPV and Cervical Cancer. Summary report on HPV and cervical cancer statistics in Colombia. 2010. www.who.int/hpvcentre. Accessed the 26/03/2012.
[3] Howlader N. et. al. 2011 SEER Cancer Statistics Review, 1975-2008, National Cancer Institute. Bethesda, MD. http://seer.cancer.gov/csr/1975_2008/. Based on November 2010 SEER data submission, posted to the SEER web site, 2011. Accessed the 26/03/2012.
[4] Palacio-Betancourt D. et. al. 2010 “Plan Nacional para el Control del Cáncer en Colombia 2010-2019, República de Colombia, Ministerio de la Protección Social, Instituto de Cancerología” (http://www.cancer.gov.co/documentos/Plan_nacional_contr_012010.pdf).
[5] Brown B. H. et. al. 2000 Lancet 355 892.
[6] Abdul S et. al. 2005 Gynec. Oncol. 99 S64.
[7] Grimnes S. and Martinsen Ø. G. 2008 Bioimpedance and bioelectricity basics, second edition (Great Britain: Academic Press).
[8] Schwan H. 1957 Electrical properties of tissue and cell suspensions In: Advances in Biological and Medical Physics, editors: J. H. Lawrence and C. A. Tobias (New York: Academic Press) 5 1929-1931.
[9] Cole K. and Cole H. 1971 J. Chem. Phys. 9 341.
[10] Pelton W. H. et. al. 1978. Geophysics 43 788.
[11] Zhdanov M. 2008 Geophysics 73 F197.
[12] Miranda D. and López-Rivera 2008 Physiol. Meas. 29 669.
[13] Wilkinson B. A. et. al. 2002 J. Urology 168 1563.