Abstract

A clinical study of the use of impedance spectroscopy in the detection of cervical intraepithelial neoplasia (CIN)[☆]

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Background. A 4-electrode impedance probe, 5.5 mm in diameter (Fig. 1), with 2 electrodes injecting a current of 20 μA and the other 2 electrodes measuring the impedance spectrum, at 8 frequencies has been shown be a promising cervical screening tool [1,2]. Good separation of CIN from squamous epithelium using this probe has been achieved, but separation from immature metaplastic tissue was less defined. Finite element modelling [3] suggests that improved separation of CIN from normal tissue may be achieved using a wider frequency range (Fig. 2). The mark III impedance probe has been designed to take 30 measurements over a frequency range of 2–1200 kHz.

Objective. To assess the performance of the new cervical impedance spectroscopy mark III probe in the separation of CIN from normal tissue.
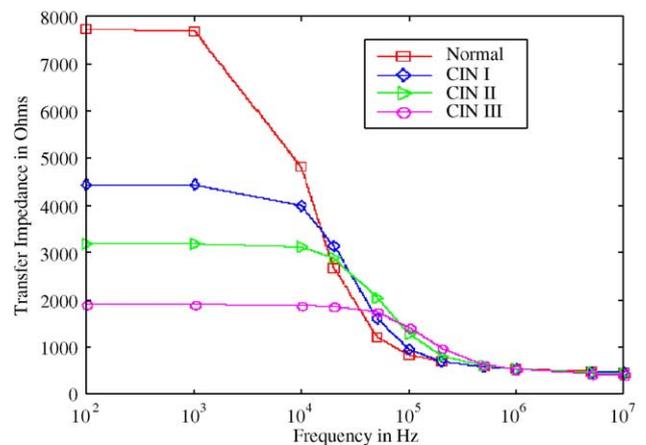
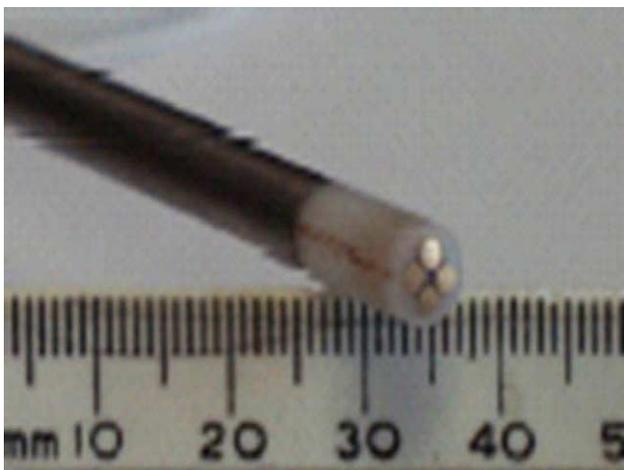Fig. 2. Modelled impedance spectra for tissue types.

Design. Prospective observational study of 176 women referred for colposcopy with an abnormal smear (borderline, mild, moderate or severe dyskaryosis).
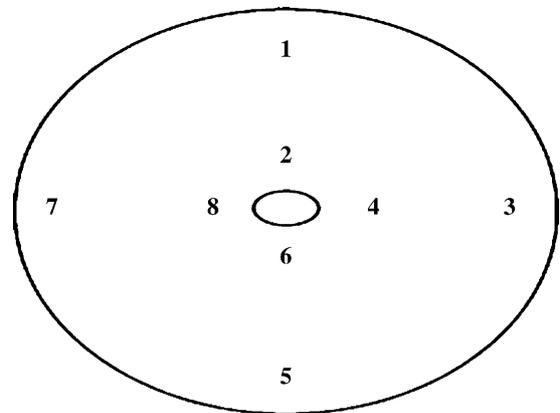
Fig. 1. Impedance probe.

Fig. 3. Measurement points on cervix.

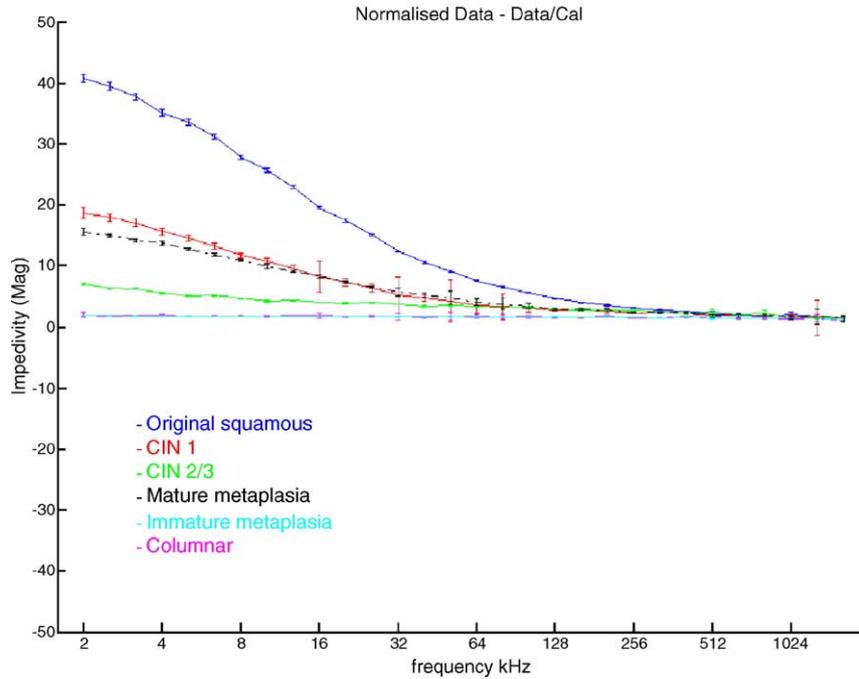☆ Abstract submitted for the Fourth International Cervical Cancer Conference.

Fig. 4. Measured impedance spectra for tissue types.

Method. Electrical impedance spectra were recorded from 8 points on the cervix (Fig. 3). Colposcopy examination and probe positioning were video recorded for analysis to allow classification of each point into different epithelia types. Impedance spectra measured (Fig. 4) were fitted by a method of least square regression to Coles' equation to give parameter R, S, C, Fc and R/S for the different epithelia.

Outcome measures. Cervical impedance derived parameters R, S, C, Fc and R/S in different epithelia and the performance of the probe in identifying women with CIN.

Results. 176 women were assessed. 1360 measurements were classified as squamous epithelium (680), CIN 1 (39), CIN 2/3(178), mature metaplasia (135), immature metaplasia (79) and columnar epithelium (28). From normal epithelium through CIN 1 to CIN 2/3, R decreases significantly ($P < 0.001$ Mann Whitney test) by a factor of 3.2, S increased significantly ($P < 0.0001$ Mann Whitney test) by a factor of 2.0, Fc increases by a factor of 4.5, R/S decreases by a factor of 4.0 and C does not change (Fig. 5).

Mann Whitney tests showed several significant separations ($P < 0.001$). CIN 2/3 can be separated from: normal squamous epithelium (by R, S, C, Fc and R/S); columnar epithelium (by R, S, C, Fc and R/S); and mature metaplastic tissue (by R, S, C, Fc and R/S). Separation of CIN 2/3 from immature metaplasia could not be achieved by any parameter. CIN 1 can be separated from: normal squamous epithelium (by R, S, Fc and R/S); columnar and immature metaplastic tissue (by R, S, C, Fc and R/S); and CIN 2/3 (by R, S, C, Fc and R/S).

Receiver operating characteristics (ROC) curves were derived for separating CIN from normal epithelium (Fig. 6). The area under the curve (AUC) values are given for separating CIN 2/3 (using R, S, C, Fc and R/S respectively) from: original squamous epithelium (0.88, 0.83, 0.63, 0.79 and 0.89 respectively); columnar epithelium (0.68, 0.65, 0.67, 0.67 and 0.69 respectively); mature metaplastic epithelium (0.80, 0.80, 0.69, 0.77 and 0.81 respectively);
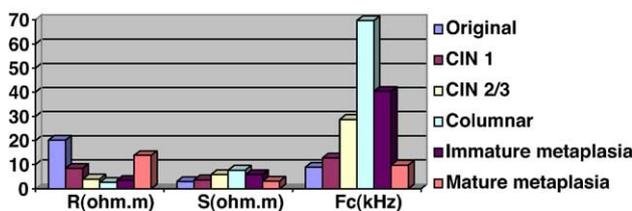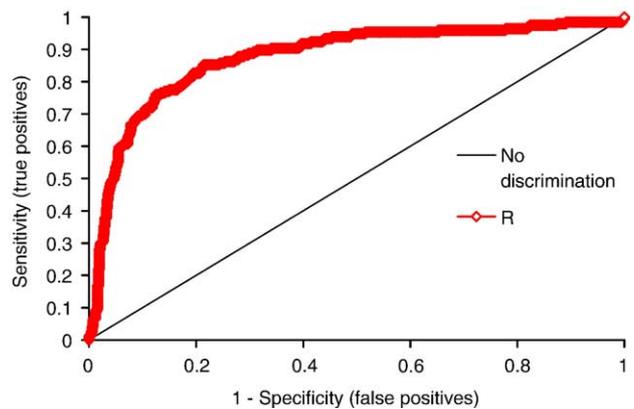

Fig. 5. R, S and Fc values in tissue types.

Fig. 6. ROC curve using R to separate squamous epithelium from CIN2/3 (Area Under Curve = Curve 0.88).

and immature metaplastic epithelium (0.54, 0.51, 0.55, 0.55 and 0.55 respectively).

A per woman analysis using R/S parameter as a discriminant between normal and CIN 2/3 gives sensitivities of 74%, specificity of 53%, positive predictor value of 60% and negative predictor values of 67%.

The positive predictor value of cervical cytology for CIN in our study was 67%.

Conclusions. Cervical impedance spectroscopy has similar sensitivity and specificity to currently used screening tests [4] for the detection of CIN, but with the potential advantage of providing instant results. The new mark III probe improves separation of CIN 2/3 from normal squamous, mature metaplastic and columnar epithelium compared to our previous probe, but could not separate CIN 2/3 from immature metaplastic epithelium. It is a potentially promising tool for cervical screening but further work is needed to improve the probe's ability to separate CIN 2/3 from immature metaplastic tissue, to allow eventual clinical use.

References

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