



A promising technique to improve and expand the practice of colposcopy to help the global fight against cervical cancer

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Cervical cancer affects women worldwide, although two predominant scenarios are observed. The first occurs in countries that have reduced mortality with organized screening programs and currently are reaching high coverage of human papillomavirus (HPV) vaccination in preadolescents and adolescents (1-3). Based on real-life data, it is already possible to observe and project a progressive drop in both cervical cancer cases and precursor lesions for the next decades (4-6). In those regions, is expected a progressive debate focused on improving screening and diagnosis methods, such as biomolecular tests and colposcopy performance (7,8).

The second scenario is related to low and middle-income countries, which account for at least 80% of cervical cancer cases detected annually (9). This higher concentration is due to the insufficient or non-existent provision and access to preventive measures such as vaccination and screening, highlighting the global disparities (10). In those regions, efforts are focused on providing less costly and easy-to-perform methods, and emphasizing high coverage HPV vaccination at early ages. When vaccinating girls up to 15 years of age, a substantial impact is expected to reduce mortality from cervical cancer. The World Health Organization (WHO) has considered vaccination a primary global goal since 2019 (11).

Even with scientific evidence and tools already available, there are disparities in technology use among regions. Currently, many women cannot be benefited from early

diagnosis and experience a cure for early-stage cervical cancer. They experience barriers such as lack of knowledge, access to screening and diagnosis programs, and facilities. Demonstration studies on organizing screening programs using biomolecular tests showed promising results and cost-effectiveness (12-15).

Colposcopy is a step in cervical cancer prevention, enabling the diagnosis of precursor lesions or early invasive cancer diagnosis after a positive screening test. It is an outpatient exam usually performed by gynecologists and well tolerated by women after sexual debut. The cervix is visualized and evaluated in detail during a gynecological exam. The colposcope has good lighting linked to magnifying lenses. After applying common reagents on the cervix surface, such as acetic acid or iodine solutions, suspicious areas are identified to guide biopsies or excisional procedures. Colposcopy's performance depends on adequate equipment and the examiner's experience, with a non-negligible degree of subjectivity (16,17).

In low-income regions and rural or remote areas, where the prevalence of cervical cancer is usually high, colposcopy is not available. Screening is performed by a low complex test, the 'visual inspection' (VI), with lighting and the use of colposcopy reagents, acetic acid (VIA), or compound iodine solution (Lugol's iodine, VILI), with limited results (18,19).

The colposcopy exam has some limitations associated with the colposcope device, colposcopist experience, and the reduced capacity to identify lesions in the cervix

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channel or if the squamocolumnar junction (SCJ) is not fully assessed. In the attempt to control the subjectivity of the colposcopic evaluation or the lack of experience of the colposcopist, in a linked paper, Mei and colleagues (20) report the initial results of an adjunctive procedure aiming to improve the colposcopy accuracy to define the places to be biopsied. The researchers developed an algorithm based on bioimpedance information measured on the cervix surface through a device with a pen and sensor at the tip. The tissue electrical impedance is related to the capacitance and resistance to the flow of electrical current, which varies according to tissue composition. The goal was to map areas of risk on the surface of the cervix under unarmed vision before colposcopy and thus assist in pointing out the best place for a biopsy.

In an initial phase, the impedance was measured by collecting hundreds of records at different points on the cervical surface. Using a graph neural network, the researchers performed a correlation with the histopathological result, which allowed the researchers to build an algorithm with 100% agreement between bioimpedance and histopathology. Subsequently, the algorithm was tested in another 21 samples as a validation subgroup, and the agreement achieved was 18/21 cases (86%). This high-performance index, far above those achieved by most colposcopy studies (16,17), is a promising result that might help colposcopy performance, controlling part of the subjectivity and the lack of experience of the examiner (20).

The excellent results demonstrated, even with only 21 samples studied in the validation phase, indicate the continuity of the studies, which needs to move forward and clarify other points. Detailing some of them, in 222 samples (67.7% of 328), coming from 46 of 83 (55%) patients, it was not possible to evaluate the bioimpedance. This limitation needs to be overcome. The fact reported by the authors that the impedance assessment did not reach the predefined criteria in a high proportion of the samples can be an obstacle to the routine use of this technology. Besides the author's justifications, maybe the pen used is sensitive to the variation in pressure applied to the sensor, which may vary between operators, and the coupling of the sensor to the cervix surface may not have been full, due to differences in contours. Another important point is a detailed evaluation of the one case of cervical lesion not indicated by the impedance measurement, which can help to define the cases more suitable for this technique. Finally, another critical

point in current colposcopic assessments not addressed with this new technology is the non-applicability in a common situation of cases with SCJ not fully visualized. We hope that continuity in the development of the technique, the equipment accessories, and a better understanding of the measured impedances, will be able to expand its use in these more critical situations.

The panorama of cervical cancer issue that causes the death of one woman every two minutes in the world is dynamic and particular to each country or region. Besides the challenge to define which scenarios this type of innovation would fit, certainly it will require additional studies to expand the number of applicable cases, correct possible human interference, and evaluate the reproducibility in other environments and cost-effectiveness. Congratulations to the researchers of this technology that is allowing us to see the possibility of expanding its possible use and we hope, without restrictions.

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References

- Vaccarella S, Lortet-Tieulent J, Plummer M, et al. Worldwide trends in cervical cancer incidence: impact of screening against changes in disease risk factors. *Eur J Cancer* 2013;49:3262-73.
- Kyrgiou M, Arbyn M, Bergeron C, et al. Cervical screening: ESGO-EFC position paper of the European Society of Gynaecologic Oncology (ESGO) and the European Federation of Colposcopy (EFC). *Br J Cancer* 2020;123:510-7.
- Kim JJ, Burger EA, Sy S, et al. Optimal Cervical Cancer Screening in Women Vaccinated Against Human Papillomavirus. *J Natl Cancer Inst* 2016;109:djw216.
- Hall MT, Simms KT, Lew JB, et al. The projected timeframe until cervical cancer elimination in Australia: a modelling study. *Lancet Public Health* 2019;4:e19-27.
- Lei J, Ploner A, Elfström KM, et al. HPV Vaccination and the Risk of Invasive Cervical Cancer. *N Engl J Med* 2020;383:1340-8.
- Patel C, Brotherton JM, Pillsbury A, et al. The impact of 10 years of human papillomavirus (HPV) vaccination in Australia: what additional disease burden will a nonavalent vaccine prevent? *Euro Surveill* 2018;23:1700737.
- Giorgi Rossi P, Carozzi F, Federici A, et al. Cervical cancer screening in women vaccinated against human papillomavirus infection: Recommendations from a consensus conference. *Prev Med* 2017;98:21-30.
- Rebolj M, Cuschieri K, Mathews CS, et al. Extension of cervical screening intervals with primary human papillomavirus testing: observational study of English screening pilot data. *BMJ* 2022;377:e068776.
- Arbyn M, Weiderpass E, Bruni L, et al. Estimates of incidence and mortality of cervical cancer in 2018: a worldwide analysis. *Lancet Glob Health* 2020;8:e191-203.
- Vale DB, Teixeira JC, Bragança JF, et al. Elimination of cervical cancer in low- and middle-income countries: Inequality of access and fragile healthcare systems. *Int J Gynaecol Obstet* 2021;152:7-11.
- WHO. World Health Organization. Global strategy to accelerate the elimination of cervical cancer as a public health problem. 17 November 2020. (Internet). WHO: Geneva; 2020. Available online: <https://www.who.int/publications/i/item/9789240014107>
- Mezei AK, Armstrong HL, Pedersen HN, et al. Cost-effectiveness of cervical cancer screening methods in low- and middle-income countries: A systematic review. *Int J Cancer* 2017;141:437-46.
- Vale DB, Silva MT, Discacciati MG, et al. Is the HPV-test more cost-effective than cytology in cervical cancer screening? An economic analysis from a middle-income country. *PLoS One* 2021;16:e0251688.
- Teixeira JC, Vale DB, Campos CS, et al. Organization of cervical cancer screening with DNA –HPV testing impact on early-stage cancer detection: a population-based demonstration study in a Brazilian city. *Lancet Reg Health Am* 2022;5:100084.
- Rebolj M, Mathews CS, Pesola F, et al. Age-specific outcomes from the first round of HPV screening in unvaccinated women: Observational study from the English cervical screening pilot. *BJOG* 2022;129:1278-88.
- Khan MJ, Werner CL, Darragh TM, et al. ASCCP Colposcopy Standards: Role of Colposcopy, Benefits, Potential Harms, and Terminology for Colposcopic Practice. *J Low Genit Tract Dis* 2017;21:223-9.
- Davies KR, Cantor SB, Cox DD, et al. An alternative approach for estimating the accuracy of colposcopy in detecting cervical precancer. *PLoS One* 2015;10:e0126573.
- Syrjänen K, Naud P, Derchain S, et al. Comparing PAP smear cytology, aided visual inspection, screening colposcopy, cervicography and HPV testing as optional screening tools in Latin America. Study design and baseline data of the LAMS study. *Anticancer Res* 2005;25:3469-80.
- Catarino R, Schäfer S, Vassilakos P, et al. Accuracy of combinations of visual inspection using acetic acid or lugol iodine to detect cervical precancer: a meta-analysis. *BJOG* 2018;125:545-53.
- Mei L, Meng J, Wei D, et al. Diagnostic test of bioimpedance-based neural network algorithm in early cervical cancer. *Ann Transl Med* 2022;10:471.

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