Devices for cervical cancer screening: a narrative review

Dispositivos para rastreamento de câncer cervical: uma revisão narrativa

Dispositivos para el cribado del cáncer de cuello uterino: una revisión narrativa

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Nirliane Ribeiro Barbosa
PhD student in Biotechnology
Institution: Universidade Federal de Pernambuco
Address: Recife, Pernambuco, Brasil
E-mail: nirliane.barbosa@ufpe.br

Ana Caroline Melo dos Santos
PhD in Health Sciences
Institution: Faculdade UNIRB Arapiraca
Address: Arapiraca, Alagoas, Brasil
E-mail: anamelodossantos1105@gmail.com

Susiane Lima Feitosa
Specialization in Nursing
Institution: Faculdade Raimundo Marinho
Address: Penedo, Alagoas, Brasil
E-mail: prof.susiane.feitosa@frm.edu.br

Cristiane Araújo Nascimento
PhD in Biotechnology
Institution: Universidade Federal de Alagoas, Campus Arapiraca
Address: Arapiraca, Alagoas, Brasil
E-mail: crisnasci@arapiraca.ufal.br

Elaine Virgínia Martins de Souza Figueiredo
PhD in Biotechnology
Institution: Universidade Federal de Alagoas - campus Arapiraca
Address: Arapiraca, Alagoas, Brasil
E-mail: elaine.figueiredo@arapiraca.ufal.br
ABSTRACT
This research aimed to describe the scientific and patent literature on devices for visual inspection of the cervix in cancer screening. The searches were performed without time restriction in the PUBMED, ScienceDirect and Scopus databases. For patent review, the technological bases named The Lens, Patentscope/WIPO¹, Espacenet, USPTO², and INPI³ were used. Based on the strategy (“Cervix Uteri” AND Neoplasms AND “Equipment and Supplies” AND Patent), sixty-four articles were identified, of which 61 were excluded and 03 selected for analysis. Considering four combinations of the terms “Schiller”, “lugol”, “iodine”, “cervical cancer test”, “device”, “gynecological test”, “sponge”, “cervical”, “cervical test”, “Schiller’s test” and “diagnostic”, three hundred and sixty-three patents were returned, of which 22 dealt with devices. Of these, nineteen were duplicates and 03 were selected for analysis. Considering the 03 articles and 03 patents selected for analysis, only 03 met the study objective, being 01 granted patent and 02 scientific articles. However, none of them represents a tool for the practice of visual inspection of the cervix through Schiller's test and visual inspection with acetic acid. Thus, the study showed the need for the development of new technologies focused on the practice of visual inspection of the cervix and strengthening of cervical cancer screening.

Keywords: Gynecological Examination, Cervix Uteri, Equipment and Supplies, Patent.

RESUMO
Esse estudo tem como objetivo descrever a literatura científica e patenteária sobre dispositivos para inspeção visual do colo uterino no rastreamento do cancer. As buscas

¹ WIPO – World Intellectual Property Organization
² USPTO – United States Patent and Trademark Office
³ INPI – Brazilian National Institute of Industrial Property
foram realizaas sem restrição de tempo nas bases de dados PUBMED, ScienceDirect e Scopus. Para a revisão de patentes, foram usadas as bases tecnológicas The Lens, Patentscope/WIPO, Espacenet, USPTO, e INPI. Com base na estratégia (“Cervix Uteri” AND Neoplasms AND “Equipment and Supplies” AND Patent), sessenta e quatro artigos foram identificados, dos quais 61 foram excluídos e 03 selecionados para análise. Considerando quatro combinações dos termos “Schiller”, “lugol”, “iodine”, “cervical cancer test”, “device”, “gynecological test”, “sponge”, “cervical”, “cervical test”, “Schiller’s test” e “diagnostic”, trezentos e sessenta e três patentes foram encontradas, das quais 22 tratavam de dispositivos. Destas, dezenove eram duplicatas e 03 selecionadas para análise. Considerando os 03 artigos e 03 patentes selecionados para análise, apenas 03 antederam ao objetivo do estudo, sendo 01 patente concedida e 02 artigos científicos. Entretanto, nenhum deles representa uma ferramenta para a prática de inspeção visual do colo uterino através do teste de Schiller e da inspeção visual com ácido acético. Assim, o estudo mostrou a necessidade para o desenvolvimento de novas tecnologias voltadas para a prática da inspeção visual do colo do útero e fortalecimento do rastreamento do câncer cervical.

**Palavras-chave:** Exame Ginecológico, Colo do Útero, Equipamentos e Provisões, Patente.

**RESUMEN**
Este estudio tiene como objetivo describir la literatura científica y de patentes sobre dispositivos para la inspección visual del cuello uterino en el cribado del cáncer. Las búsquedas se realizaron sin restricción de tiempo en las bases de datos PUBMED, ScienceDirect y Scopus. Para el examen de las patentes se utilizaron las bases tecnológicas The Lens, Patentscope/WIPO, Espacenet, USPTO e INPI. Con base en la estrategia (“Cuello Uterino Y Neoplasias Y "Equipos e Insumos" Y Patente), se identificaron sesenta y cuatro artículos, de los cuales 61 fueron excluidos y 03 seleccionados para análisis. Considerando cuatro combinaciones de los términos "Schiller", "lugol", "yodo", "prueba de cáncer de cuello uterino", "dispositivo", "prueba ginecológica", "esponja", "cervical", "prueba cervical", "prueba de Schiller" y "diagnóstico", se encontraron trescientas sesenta y tres patentes, de las cuales 22 se referían a dispositivos. De estos, diecinueve fueron duplicados y 03 fueron seleccionados para su análisis. Considerando los 03 artículos y 03 patentes seleccionadas para el análisis, solo 03 precededieron al objetivo del estudio, 01 patente concedida y 02 artículos científicos. Sin embargo, ninguno de ellos representa una herramienta para la práctica de la inspección visual del cuello uterino mediante el test de Schiller y la inspección visual con ácido acético. Así, el estudio mostró la necesidad del desarrollo de nuevas tecnologías dirigidas a la práctica de la inspección visual del cuello uterino y al fortalecimiento del tamizaje del cáncer cervicouterino.

**Palabras clave:** Examen Ginecológico, Cuello del Útero, Equipos y Suministros, Patent.
1 INTRODUCTION

Cervical cancer is the fourth most common neoplasm and the fourth leading cause of death among women worldwide (Who, 2020; Pimple, Mishra, 2022). Screening for this disease is part of public health programs in Brazil (Brasil, 2019; INCA, 2019). For this screening to be effective, in addition to minimal coverage of the female population and care flowcharts, the quality of gynecological exams is essential. Thus, visual inspection of the cervix with acetic acid (VIA), at a concentration of 3%-5%, and the Schiller’s test, performed with 2% Lugol’s solution, are important examinations for observing the integrity of the epithelial tissues of the cervix and vagina. These are part of the gynecological assessment during screening and require skilled human resources and appropriate technology (Zanini, 2021).

However, when performing the gynecological examination, there are many obstacles for the professional who conducts the procedure, being essential a person to help with the necessary materials or, at least, an installation that facilitates access and movement throughout the examination. In this context, there is a gap regarding technologies that meet this need in a more effective way. There is a lack of products that are previously prepared and individually packaged for use in gynecological examinations, especially for visual inspection in Schiller's and VIA tests.

Thus, the use of technological devices is an important strategy for the agility and comfort of professional practice, which is not found in the reality of gynecology services. Therefore, our objective was to describe the scientific and patent literature on devices for visual inspection of the cervix in cancer screening. Our hypothesis is that there is a scarcity of patents and scientific publications on devices for visual inspection of the cervix in cancer screening.

Based on this study, it is intended to provide a portfolio of devices focused on visual inspection of the cervix, thus helping professionals to facilitate their routine when performing this procedure.
2 MATERIAL AND METHODS

This is a narrative review in partnership with the Research Program for SUS (PPSUS), through the public call nº 06/2016, provided by the Research Support Foundation of the State of Alagoas.

Through the CAPES Periodicals Portal, searches were carried out in July 2022 in the following technological bases: “The Lens”, “Patentscope”/ “World Intellectual Property Organization” (WIPO), “United States Patent and Trademark Office” (USPTO), “Espacenet” and “Brazilian National Institute of Industrial Property” (INPI, as per its Portuguese acronym). Search strategies were used in all searched databases, with four different combinations of terms: “Schiller”, “lugol”, “iodine”, “cervical cancer test”, “device”, “gynecological test”, “sponge”, “cervical”, “cervical test”, “Schiller’s test” and “diagnostic”. The first combination: ((Schiller OR lugol OR iodine) AND (cervical test) AND device). The second combination: ((Schiller OR lugol OR iodine) AND (gynecological test) AND device). The third combination: ((Schiller OR lugol OR iodine) AND sponge AND cervical AND device). Finally, the fourth combination: ((Schiller’s test) AND iodine AND (cervical test) AND diagnostic AND device).

Inclusion criteria encompassed patents for accessory devices for gynecological examination or treatment, excluding duplicates. There were no time, language or country restrictions. After returning from the patent search, the title and abstract were first assessed. Then, the full text was assessed, in order to map the patents that returned from the searches. The documents that met the inclusion criteria were eligible for the data extraction stage and were analyzed.

The eligibility process was organized into a PRISMA 2020 flowchart (PRISMA, 2020). The collected data were title, publication number, IPC (international patent code), IPC classification, country of origin, country of filing, inventors, and classification sectors. The data were organized into a Microsoft Excel® spreadsheet, version 2010, grouped, and then forwarded for analysis and discussion. No technological prospection program or software was used after extracting the results of the included patents and grouping the relevant findings.
Scientific searches were carried out in September 2022 in the PUBMED, ScienceDirect and Scopus databases, based on the search strategy (“Cervix Uteri” AND Neoplasms AND “Equipment and Supplies” AND Patent).

The inclusion criteria encompassed articles published in the studied scientific databases, with no time, language or country restrictions, and that described accessories or devices used for visual inspection of the cervix in cancer screening.

The articles that returned were assessed by means of the titles and abstracts. Considering the eligibility criteria, the articles were selected for analysis, according to the extraction of data from the articles: title, author/year, country of origin, journal, study design and studied product design.

The data collected from the scientific databases were organized into a Microsoft Excel® spreadsheet. The extracted data were stored in the spreadsheet, and the results were grouped and formatted. Finally, the Parsifal® program was used to analyze the scientific data (Parsifal, 2021).

3 RESULTS AND DISCUSSION

A total of 363 patents were identified, 341 of which were ineligible and 22 registers that met the inclusion criteria. After assessment, only 03 patents were selected, being 01 patent eligible in the study. In the scientific searches, 64 articles returned, of which 61 were excluded and 03 selected for analysis, being 02 articles included in the study, as displayed in Figure 1.
Table 1 describes the characterization of the patent registers identified from four different combinations for searching the studied technological bases, and how many patents dealt with devices related to visual inspection of the cervix and the number of patents included in the study. Thus, 08 patents were registered in The Lens database, with 02 devices and 01 selected for the study; 264 patents were registered in Patentscope/WIPO, with 14 devices and 04 selected patents; there were 19 patent registers
in Spacenet, with 05 devices and 04 selected; no registers were found in the INPI base with any of the combinations; 72 patent registers were found in USPTO, with 01 device, which was selected for the study.

Accordingly, 10 device registers were selected for the study, 07 devices being duplicates of registers and, therefore, 03 registered devices selected for analysis in the study.

Table 1 – Number of devices found in the patent search on visual inspection of the cervix in cervical cancer screening, according to combinations and technological bases

<table>
<thead>
<tr>
<th>Combinations</th>
<th>The Lens</th>
<th>Patentscope/WIPO</th>
<th>Bases</th>
<th>Source: designed by the authors, 2023</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. ((Schiller OR lugol OR iodine) AND (cervical test) AND device)</td>
<td>00/00/00</td>
<td>24/07/02</td>
<td>08/03/02</td>
<td></td>
</tr>
<tr>
<td>2. ((Schiller OR lugol OR iodine) AND (gynecological test) AND device)</td>
<td>00/00/00</td>
<td>00/00/00</td>
<td>00/00/00</td>
<td></td>
</tr>
<tr>
<td>3. ((Schiller OR lugol OR iodine) AND sponge AND cervical AND device)</td>
<td>08/02/01</td>
<td>10/04/01</td>
<td>02/01/01</td>
<td></td>
</tr>
<tr>
<td>4. ((Schiller’s test) AND iodine AND (cervical test) AND diagnostic AND device)</td>
<td>00/00/00</td>
<td>230/03/01</td>
<td>09/01/01</td>
<td></td>
</tr>
</tbody>
</table>

Caption: QD= total number of patents / QDIS= number of devices/ DS= selected devices

Considering the eligibility criteria for inclusion of the devices in the patent and removing the registered duplicates, 03 patent devices were obtained for the study: 1) Device for treatment of a body canal and adjacent surfaces; 2) Apparatus for photodynamic therapy and photodetection; 3) Electrospray catheter (Table 2).
These three devices were filed in the United States. Although their countries/places of origin and years were respectively: Australia (2020), South Korea (2009) and the Aveitas LTD company (2020). Of the three filings, one has a patent granted and the other two only have a submitted patent. All devices were submitted in the area of human needs, with the respective classification of the International Patent Code (IPC) referring to: 1) device for introducing media into the body for treatment purposes; 2) device for therapy and diagnosis by applying radioactive material to the body; 3) spraying apparatus.

Table 2 – Characterization of devices of the patents selected for the study on visual inspection of the cervix in cervical cancer screening

<table>
<thead>
<tr>
<th>Title</th>
<th>Authors/inventors/year</th>
<th>Country of origin/company</th>
<th>Country of filing</th>
<th>IPC</th>
<th>Area</th>
<th>Brief description of the invention</th>
</tr>
</thead>
<tbody>
<tr>
<td>Device for treatment of a body canal and adjacent surfaces</td>
<td>McCloskey, 2020</td>
<td>Australia</td>
<td>United States of America</td>
<td>A61M31/00 (Devices for introducing or retaining media, e.g., remedies, in cavities of the body)</td>
<td>Human necessities / Devices for introducing media into, or onto, the body.</td>
<td>A device for treatment of a canal associated with an orifice includes a flexible stem portion adapted for insertion along the canal and having an expandable member carried by the stem portion at or adjacent the distal end. Application of interest is the in situ inactivation of human papillomavirus (HPV).</td>
</tr>
<tr>
<td>Apparatus for photodynamic therapy and photodetection</td>
<td>Kang Uk and Papayan Garri. V, 2009</td>
<td>South Korea</td>
<td>United States of America</td>
<td>A61N 5/06 (using light - A61N 5/01 takes precedence)</td>
<td>Human necessities / Radiation therapy (devices or apparatus applicable to both therapy and diagnosis applying radioactive material to the body A61M 36/00).</td>
<td>An apparatus for photodynamic therapy and fluorescence detection, in which a combined light source is provided to illuminate an object body and a multispectral fluorescence-reflectance image is provided to reproduce various and complex spectral images for an object tissue, thus performing effective photodynamic therapy for various diseases.</td>
</tr>
<tr>
<td>Electrospray catheter</td>
<td>Maguire Michael; Finnegan Shane, 2020</td>
<td>Avectas LTD</td>
<td>United States of America</td>
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<tr>
<td>CN111032134A</td>
<td></td>
<td></td>
<td>A61M15/02 (with activated or ionized gases; Ozone-inhalators)</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>A61M25/00 (Catheters; Hollow probes)</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>B05B5/00 (Electrostatic spraying apparatus; Spraying apparatus with means for charging the spray electrically; Apparatus for spraying liquids or other fluent materials by other electric means).</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

An apparatus includes a catheter, and an electrode and methods of delivering molecules to eukaryotic cells using such an apparatus. The catheter defines a fluidic channel and has a distal opening. The electrode is within the fluidic channel and is spaced a distance from the distal opening of the catheter. The catheter is arranged to prevent direct contact between any electrode of the apparatus and tissue. Related apparatus, systems, techniques and articles are also described.

Following the search strategy (“Cervix Uteri” AND Neoplasms AND “Equipment and Supplies” AND Patent) in the studied databases, 64 articles were identified, being 03 in PUBMED, 56 in Science Direct and 05 in Scopus, as displayed in Table 3. Of the articles found, only the 03 from PUBMED are related to devices, which were selected for the study.
Table 3 – Number of articles found in the scientific search on devices for visual inspection of the cervix in cervical cancer screening, according to search strategy and databases

<table>
<thead>
<tr>
<th>Search String</th>
<th>PUBMED QD/QDIS/DI</th>
<th>Science Direct QD/QDIS/DI</th>
<th>Scopus QD/QDIS/DI</th>
</tr>
</thead>
<tbody>
<tr>
<td>(&quot;Cervix Uteri&quot; AND Neoplasms AND “Equipment and Supplies” AND Patent)</td>
<td>03/03/03</td>
<td>56/00/00</td>
<td>05/00/00</td>
</tr>
</tbody>
</table>

Caption: QD= total number of patents / QDIS= number of devices/ DI= devices included

Source: designed by the authors, 2023

The three scientific articles selected for the study, published between 2015 and 2017, originated in the United States: 1) Design and preliminary analysis of a vaginal inserter for speculum-free cervical cancer screening; 2) Design of a Novel Low-Cost Point of Care Tampon (POCkeT) Colposcope for Use in Resource-Limited Settings; 3) Image-Guided High-Dose Rate Brachytherapy in Cervix Carcinoma Using Balloon Catheter and Belt Immobilization System (Table 4).

The designs of the included studies sequentially comprised: 1) exploration of different speculum designs for cervical cancer screening, using 3D computer-aided design software for simulating mechanical tests. Two designs were tested with 15 volunteers regarding the assessment of the uterine cervix, comfort and usability compared to the standard speculum; 2) comparative study between the Pocket colposcope, with components designed to fit into a tampon inserted into the vagina to capture images of the uterine cervix, and commercially available colposcopes. The Pocket colposcope has resolving power, color resolution accuracy, minimal lens distortion, and illumination comparable to commercials, based on in vitro and in vivo pilot results; 3) development and use of a balloon catheter constructed by gluing a short inflatable tube to a long regular catheter with an open end, through which the contrast agent will be injected in image-guided high-dose rate brachytherapy in cervix carcinoma. The balloon catheter was used by 21 patients undergoing treatment, with potential results for a solution in this type of treatment. Device designs described are displayed in Table 4.
Table 4 – Characterization of the scientific articles selected for the study on devices for visual inspection of the cervix in cervical cancer screening

<table>
<thead>
<tr>
<th>Title</th>
<th>Authors/year</th>
<th>Country of origin</th>
<th>Journal</th>
<th>Study design</th>
</tr>
</thead>
<tbody>
<tr>
<td>Design and preliminary analysis of a vaginal inserter for speculum-free cervical cancer screening</td>
<td>Asiedu et al., 2017</td>
<td>United States of America</td>
<td>PLOS ONE</td>
<td>Three main designs were explored (a mechanical billed expander, a silicone expander and a probe inserter) using 3D computer-aided design (CAD) software and performed mechanical testing simulations on each. Designs were rapid prototyped and tested using a custom vaginal phantom across a range of vaginal pressures and uterine tilts to select an optimal design. Two final designs were tested with fifteen volunteers to assess cervix visualization, comfort and usability compared to the speculum and the optimal design.</td>
</tr>
<tr>
<td>Design of a Novel Low-Cost Point of Care Tampon (POCk eT) Colposcope for Use in Resource-Limited Settings</td>
<td>Lam et al., 2015</td>
<td>United States of America</td>
<td>PLOS ONE</td>
<td>The components of the POCk eTCenoscope are designed to fit within the form factor of a Tampon, can be inserted into the vagina to capture images of the cervix. The POCk eTCenoscope’s concentric LED ring provides comparable white and green field illumination at a fraction of the electrical power required in commercial colposcopes.</td>
</tr>
<tr>
<td>Image-Guided High-Dose Rate Brachytherapy in Cervix Carcinoma Using Balloon Catheter and Belt Immobilization System</td>
<td>Fan et al., 2016</td>
<td>United States of America</td>
<td>Technology in Cancer Research &amp; Treatment</td>
<td>The balloon catheter is constructed by gluing a short inflatable tube to a long regular open-end catheter. Contrast agent (10 cm³) is injected into the inflatable end, which is affixed to the tandem and ring applicator, to displace the posterior vaginal wall. The belt immobilization system consists of a specially designed bracket that can hold and fix itself to the applicator, a diaper-like Velcro fastener package used for connecting the patient’s pelvis to the bracket, and a buckle that holds the fasteners to stabilize the whole system.</td>
</tr>
</tbody>
</table>

Source: designed by the authors, 2023

The visual inspection test is highlighted as a complementary method for cervical cancer screening. The effectiveness is related to its low cost and the easy and fast interpretation that it provides, helping health professionals in clinical practice (Feitosa et al., 2020). Furthermore, cervical cancer screening plays a key role in terms of reducing the morbidity and mortality from this disease (Mulmi et al., 2022). However, resources for the practice of this method are scarce. It is noted that it has not been a priority that
these resources be made available for women’s health and gynecology services, and even less in primary health care services (Cerqueira et al., 2022).

In this patent and scientific review on devices for visual inspection of the cervix in cancer screening, exclusively 06 devices met the eligibility criteria in this study. After performing component analysis, it was identified that only 03 devices were published containing components for visual inspection of the cervix in cancer screening.

Among the 03 devices selected according to the purpose of the study, 01 is registered into a granted patent (US8382812B2) and 02 published in scientific articles, respectively: 1) Apparatus for photodynamic therapy and photodetection; 2) Design and preliminary analysis of a vaginal inserter for speculum-free cervical cancer screening; 3) Design of a Novel Low-Cost Point of Care Tampon (POCkeT) Colposcope for Use in Resource-Limited Settings. It can be assured that these three devices offer advanced technology components using photodetection and 3D computer-aided design software, which indicates the convergence of the devices under development.

It is curious that none of the instruments already used in the practice of visual inspection of the cervix appear in the search conducted in this study, not even the standard material recommended for gynecological consultation, collection of material in coloproctology and for colposcopy, such as specula, forceps, spatulas and colposcope. In addition, there is no device that represents an auxiliary instrument for the practice of visual inspection of the cervix through Schiller’s and visual inspection with acetic acid tests.

Particularly, visual inspection with acetic acid is a cheap and effective method to identify cancerous lesions at an initial stage for early intervention, and it is recommended for low-income countries (Hayumbu et al., 2021). Therefore, in a resource-limited setting, it is necessary to agree on the need to improve programs for cervical cancer screening using visual inspection of the cervix.

Considering the reality of gynecology services, the findings of this study warn us of the need for innovation in these services, in order to provide more resources focused on agility and quality in terms of performing visual inspection of the cervix, as well as comfort during professional practice.
4 CONCLUSION

Given the hypothesis of the study regarding the scarcity of patents and scientific publications on devices for visual inspection of the cervix in cancer screening, it is affirmed that it is true. However, it is important to indicate the use of those already approved, support innovative low-cost ideas, and rethink about the protocols applied in this procedure.

It should also be noted that there are limitations in this study, referring to the time frame of the search in technological databases until June 2022 and in scientific databases until September 2022, which may restrict the data.

Accordingly, it is recommended to contribute to the development of appropriate and necessary materials in this field of practice, acquiring a portfolio of devices for visual inspection of the cervix to facilitate the routine of health professionals and expand access to these technologies.

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