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How Does FRD Protect the Cervix?

FRD IS ONE OF THE LATEST AND FASTEST METHODS OF SCREENING FOR CERVICAL CANCER. It is a non-invasive, inexpensive and precise diagnostic tool and has a significant impact on the development of diagnostics and the management of abnormal cytological smear.



Cervical cancer (RSM) is still a significant oncological problem in terms of both primary and secondary prophylaxis, and deepened diagnosis of abnormal cervical cytology. This cancer is the fourth most-diagnosed cancer and the fourth cause of cancer deaths in women with 300,000 deaths in 2018 worldwide (1). In Poland, in 2018, 2,622 new cases were diagnosed in the course of this disease (2).

Incidence and mortality rates for RSM are steadily falling, especially in highly developed countries, particularly due to the elimination of risk factors, by introducing HPV vaccines (1). The truth of socioeconomic and hygienic conditions, reduced population fertility and a decrease in the incidence of sexually transmitted diseases also have an effect on the response patterns of this

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tumor (1,3). RSM screening programs based on Evidence Based Medicine utilize classical cytology, liquid-based cytology (LBC) and detection of the presence of oncogenic HPV viruses in the identification of precancerous states (4).

The methods of cervical cancer prevention include primary prevention tools (avoidance of HPV infection, vaccination against HPV) and secondary prevention (cytological examination, determination of DNA presence of high-zoonococcal HPV viruses and other modern methods of detecting cancerous conditions) (5). Early screening in healthy people aims to conceal the disease early allowing treatment at its initial stage, resulting in lowering mortality (6). Screening tests should have appropriate sensitivity to show the ability of the test to correctly exclude the disease and specificity to show the ability of the test to poorly exclude the disease. Screening testing for cervical cancer is relatively easy due to the availability of the organ for testing and the availability of classification of cancerous conditions.

A PROMISING METHOD

Cytological examination is a recommendation as a basic tool in the prevention of RSM, despite the fact that it is characterized by a high percentage of false negative and false positive results, mainly due to the subjectivity of personnel assessing the size and specifics of smear collection (7). A study of 687 Polish women with histologically confirmed cervical intraepithelial neoplasia (CIN) confirmed its sensitivity at 58.02% and specificity 63.28% (8). For this reason, many studies are currently underway on new tools at the screening stage and in-depth



HOW CAN THE PERIPTIC REACTION PROTECT THE CERVIX?

By overexpressing the folate receptor α in the epithelium of High Grade lesions, the FRD complex binds to the folate receptor, triggering the process of endocytosis. In the cell, methylene blue, after its endocytosis into the epithelial cell, undergoes oxidation, giving a blue, blue-black or black color indicating a CIN2 + lesion.

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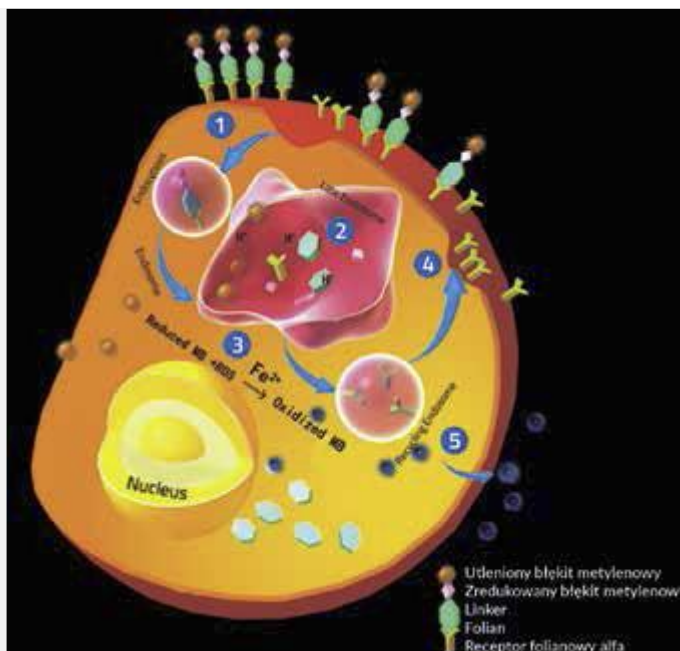


	Image from FRD™ staining	Colposcopy image	FRD™	Cytology	HPV	Biopsy
1			Negative	Normal	Positive	CIN1
2			Negative	LSIL	Negative	Inflammation
3			Negative	LSIL	Positive	CIN1
4			Positive	Normal	Positive	CIN2
5			Positive	ASCUS	Positive	CIN3

diagnostics, which quickly, cheaply and objectively indicate cases requiring the necessary medical intervention. Among the promising techniques, staining methods based on folate receptor - FRD - are mentioned.

FRD COLORING SOLUTION

The FRD (Folate Receptor - mediated Staining Solution) solution consists of folic acid, reduced methylene blue, acetic acid and dimethyl sulfoxide.

Due to the overexpression of the folate receptor in the epithelium with High Grade lesions, the FRD complex binds to the folate receptor, initiating the process of endocytosis. In the cell, methylene blue, after its endocytosis into the epithelial cell, undergoes oxidation, giving a blue, blue-black or black color indicating a CIN2 + lesion. Research involving over 14,000 women showed the sensitivity of this method in detecting CIN2 +

was 85.7%, the specificity was 76.4%, the positive predictive value was 61.3% and the negative predictive value was 92.5% (9). Other studies have confirmed the effectiveness of this method, emphasizing the simplicity of staining and the possibility of immediate results (10, 11). At the 2nd Department and Clinic of Gynecology and Obstetrics, the Medical University of Wrocław is currently conducting



LITERATURE:

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the first clinical trials in Europe to assess the sensitivity of this method in screening towards RSM.

WHAT IS FRD RESEARCH?

Exfoliating cells were taken from the cervix using a single-use tool with a porous sponge (applicator), which is then dipped into the FRD solution. The test is performed during routine sighting. The color of the applicator changes depending on the number of the

folate receptors. It has been proved that abnormal cells have a higher demand for folate receptors, which were actively obtained from the immediate environment.



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In clinical practice, FRD may be considered as a complementary diagnostic tool in screening for the detection of cancerous and neoplastic lesions, as well as for assessing and monitoring the health state of patients with abnormal cytological test results (ASC-US / LSIL), while waiting for repeated test and patients with positive HPV test results but negative cytology test.

APPLICATION

The multitude of currently studied methods of extensive diagnosis in the field of RSM, including the FRD test, is promising and raises hopes that cytology will soon be supplemented with more effective tests. An important advantage of FRD is that it is non-invasive, simple and possible to perform in any gynecological office during a traditional examination, and its result is available in just 60 seconds. This is important because it can be allowed to quickly spread this effective method of cervical screening in Poland, where the incidence of this cancer is still high compared to other European countries.

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