

Useless and Even Potentially Detrimental, or a Promising Leap into the Future: A Comparative Analysis of Instrumental and Iridological Examination Methods for Breast Tumour Disease

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Abstract

Mechanisms inherent in living organisms that are based on the signalling function of the external receptor zones are probably the most accurate signalling system ever existing. These zones hold a potential to relay information regarding incipient pathological alterations within organs at the disease nascent stages. The contemporary iridology considers the iris as one of five receptor zones endowed with a capability to "inform" about changes within the organism, often long before clinical symptoms are manifested. This study aimed to examine the iris potential to provide information on a presence of tumours in the body on the example of the breast tumor.

During a prospective comparative study of the mammographic, ultrasound and iridological method efficiency in diagnostics of benign and malignant breast tumors, were analyzed 305 female patients (including 10 persons is a comparison group) treated for newly diagnosed benign and malignant breast tumour at an oncology center. It is the first time when a comparative iridological instrumental and morphological correlations were drawn that resulted in a clarified breast topography on the right and left iris; a specific criterion named a T-Criterion was defined that is a marker indicative of breast tumors on the iris (the data is not disclosed due to a

pending patent process) and has two degrees of manifestation: T1-Criterion representing changes on an iris that are more likely associated with benign tumors with no cellular proliferation/hyperplasia; and T2-Criterion representing changes on the iris that are more likely associated with benign tumors with cellular proliferation/hyperplasia, cellular atypia present, as well as tissues with adenocarcinoma cells. The sensitivity of the T2-Criterion-based iridological method was 85.7%, which is comparable with mammography results (87%) and surpasses considerably the ultrasound techniques (69%).

The outcomes of this study have allowed assuming that a certain correlation exists between the nature of structural changes in the breast tissue and responsive changes in the iris structure. These findings prompt reconsidering the iris potential as a possible tumor biomarker.

Keywords: iris, biomarker, tumour, screening, breast, mammography, ultrasonography

Introduction

The global incidence of oncological diseases is continuously growing worldwide, which causes considerable socio-economic damages [1]. The year 2022 witnessed approximately 20 mln novel incidences of cancer and 9.7 mln deaths attributable thereto. Projections suggest that the year of 2050 may see over 35 million new cancer diagnoses, should such tendency persist, a 77% augmentation relative to 2022 [2]. In this scenario, is anticipated an increase in disability and mortality from this disease as well.

Currently, our capacity to influence the incidence of cancer remains limited; however, we can make efforts to try and find solutions to enhance preventive strategies [3] with the aim to slow down, reverse, or stop the cancerous process progression.

A well-established screening practice is one of the primary modalities for cancer prevention and early detection; it is a chain of sequential actions that shape the pathway [4]. Despite the considerable achievements made in reducing the incidence of disability and mortality due to cancer, the screening process has certain limitations:

1. It necessitates a sophisticated organizational framework and entails significant economic expenditures;
2. Its implementation is limited to the target population only;
3. It requires a certain periodic frequency, typically once every 2 years or less;
4. Logistical obstacles;
5. Social inequalities in equitable access to healthcare resources and organized screening programs [4], [5].

In light of the increasing incidence of cancer in younger demographics [6], [7] and the limitation inherent in existing screening methods [4], amplifying the capacity for early diagnosis constitutes a salient priority within the comprehensive cancer control agendas of all World Health Organization (WHO) member nations [8]. Consequently, dynamic developments are currently occurring in the search of methods that are at once straightforward, non-invasive, effective, and economically viable to allow rendering the screening process into an uninterrupted and universally accessible practice [4].

The recent years have been witnessing an increased interest in identifying specific tumor biomarkers that could reveal a presence of malignant processes in the body [9, 10]. Despite significant advances in this area, it has not yet been possible to find a universal biomarker that can completely solve the problem. Within this paradigm, it is pertinent to consider the iris as a prospective candidate for a biomarker. Despite its promising potential, the iris continues to be relatively underexplored.

Iridology (ID, iridodiagnosis), located within the spectrum of alternative medicine [11], encounters both support [12,13] and scepticism [14,15] within the medical community. This contentious ID standing is largely due to the position of ID in the underground of medical sciences and, as a result, a wide access to the practice of iridoanalysis for specialists who do not have medical education. The lack of freely available training resources and a dearth of rigorous clinical and fundamental research in this field, as well as missing standardized protocols for interpretation of iridological findings, and a deficient comprehension of the underlying pathophysiological mechanisms collectively constitute formidable obstacles to the ID assimilation as an esteemed applied diagnostic tool in conventional medical practice.

Embryologically, the iris shares a common neural origin with the brain [12]. It reflects processes taking place in the internal milieu and acts as one of the informative exteroceptive zones that allow signalling about changes in the organs, often long before clinical signs of a disease appear. [12], [13], [16], [17]. The occurrence of these processes is reflected upon the iris via iridosigns [12, 13, 17]. This is facilitated by a well-defined network of annular iridoneural connections in the organism. The principal pathway elements include: an internal organ, conductive neural pathways within the spinal cord, trigeminoreticular neuronal cells of the brainstem, and the iris [12], [18].

The iris serves as a unique map of the human body, wherein each organ is mirrored in a specific position on the iris in a homolateral fashion: the right hemisphere of the body is reflected onto the right iris, and conversely, the left hemisphere corresponds to the left iris [12], [13], [17]. Currently, approximately 30 projection zone schematics are known for human organs. While these schematics are fundamentally similar in their representation of organ-specific zones, it is imperative to acknowledge the existence of minor topographical variances concerning certain organs [12,13].

A multitude of studies in the ID domain undertaken by scientists and doctors around the world has identified and systematized both general and specific patterns exhibited by iris exteroceptors in the context of various somatic pathologies. These findings have been documented in an array of monographs and scholarly articles [12], [17], [19], [20], [21], [22]. Notwithstanding these contributions, the literature search returns merely two publicly accessible publications that examine the iris potential in a complex diagnostic of patients with breast tumors [23], [24]. These studies contained a comparative prospective analysis delineating common iris changes for breast tumors, and identified common iris changes for benign tumors (BT) as well as for breast cancer (BC).

This study was aimed to elucidating prospective capabilities that the iris may provide in screening of breast tumor pathologies. Breast cancer is a critical health concern necessitating heightened scrutiny and reconsideration of preventive methods [25]. It might be posited that for this particular malady, the axiom 'the more screening, the better' is distinctly applicable. This comparative study was focused on identification of localized alterations within the iris projection characteristic of benign and malignant breast

tumors, with the ultimate objective to find a specific marker that evidences a neoplasm presence.

Purpose of the Study:

To study alterations occurring in the iris in patients with diagnosed benign tumors and breast cancer, with the intent to delineate the actual scope of iridodiagnosis as a viable method in screening for neoplastic breast diseases.

Methods

The study design and management were approved by the institutional ethics committee of N.N. Alexandrov National Cancer Centre. The study was pursued in accordance with the Principles of the Declaration of Helsinki.

In terms of time parameters, it was a one-stage study comprising two steps. During the first step, patients were recruited, and examination data were collected.

The patient data compilation was carried out over an interval spanning from November 2018 to October 2020 at the N.N. Aleksandrov National Cancer Centre of Belarus. Analysis of the accumulated data was undertaken during a period between 2021 and 2022.

The inclusion criteria: The study focused on women aged between 18 to 84 years, with a radial or radial-lacunar type of iris, with diagnosed BTs and newly diagnosed BC with stage 0 – IV, who had been examined according to a unified diagnostic protocol for breast diseases. Before surgical or specialized treatment, all examined patients underwent bilateral iridography (IG) with the use of a digital camera.

A group of healthy women was recruited on an outpatient basis as a comparison group. They all passed a clinical examination, breast ultrasonography (USG) and bilateral IG.

The IG presents photographing of the iris using a digital camera, with images of the right and left iris captured under manual camera settings. Colour images of the irises were subsequently analyzed with a set of various software designed for ID analysis.

Thus, the study included 305 women that were divided into three groups:

- Group 1 (106 patients) with BT, aged 18 to 77 years: (37 patients – aged 18-30 years; 18 patients – 31-40 years; 24 patients – 41-50 years; 21 patients – 51 to 60 years; and 6 patients – aged 61 years and older).
- Group 2 (189 patients) with diagnosed BC, aged 31 and 84 years: (20 patients – aged 31-40 years; 26 patients – 41-50 years; 48 patients – 51-60 years; and 95 patients – aged 61 years and older) with BC stage 0-IV (4 patients were diagnosed at stage 0; 63 at stage I; 76 at stage II; 36 at stage III; and 10 at stage IV).
- Group 3 included 10 healthy women at the age ranging between 18 and 22 years who served as a control group for the comparative analysis.

During the second part of the study, following the results of a pathomorphological examination, an iridoanalysis was carried out on the iris correlating with the side of the breast neoplasm. This part involved a comparative assessment of mammographic (MG) and USG findings with the iridogram data, a determination of the iridological sign intensity in relation to the tumor's morphological structure, and a statistical analysis of the results obtained.

Iridological maps developed according to B. Jensen and E.S. Velhover were used for the iridoanalysis.

According to these maps, the right breast is represented on the right iris in segments 8.00-9.00, and the left breast on the left iris corresponds to segments 3.00-4.00.

Analysis focused on specific local iridosigns, namely within the designated iris segment: Toothed Line or Autonomus Ring (AR), Contraction Ring (CR), Pigmentation Spot (PS), Lacunae(L), and T criterion (details are not disclosed due to a pending patent process). Each discerned iridosign underwent a qualitative evaluation quantified on a scale between 0 and 3, where '0' indicates the sign absence or its normal status, and '1', '2', '3' represent the qualitative amount of the sign deviation from the norm. In instances where multiple occurrences of the same iridosign were observed within the segment under study (e.g., two or more lacunae; two or more pigment spots), the sign that demonstrated the highest qualitative deviation was prioritized for consideration. The analysis in the study did not take into account dimensions and configurations of the iridological signs within the examined segment.

Limitations and Assumptions: The statistically small number of persons in the comparison group is due to a specificity of the institution where females were recruited, as well as difficulties with data collection due to ethical considerations. Consequently, this resulted in a disproportionately small patient cohort included in the comparison group.

Mathematical processing and data analysis was carried out using statistical Excel (Microsoft inc., USA), Statistica 10.0 (StatSoft inc., USA), SPSS Statistics 22 software packages.

Research Findings

The Iris Status in Practically Healthy Women (Comparison Group)

In the comparison group, the analysis included both the right and left irises. Females in this group revealed CR on the right and left irises in 100% cases that manifested as concentrically broken arcs. In 65% of instances, these CRs exhibited interruptions at the inception point of the breast segment inferiorly (notably at the 8 o'clock position on the right iris and 4 o'clock on the left) and resumed their trajectory above the breast segment thereafter (commencing from 9 o'clock on the right iris and 3 o'clock on the left iris, respectively); or they manifested an irregular line within the breast segment. While, 35% of the observed cases featured concentrically closed CRs without any discontinuity within the segment of interest. Additionally, four women displayed solitary Ls of varying dimensions on one of the irises, without accompanying changes. The changes revealed in the breast segment area on both the right and left irises are detailed in Table 1.

Table 1: Incidence of Iridological Signs within the Breast Segment Area on the Iris in the Group of Practically Healthy Women (Both Right and Left Irises Included) n=20

Iridosign, % (abs. value)		PS (n=20)	AR (n=20)	L (n=20)	CR (n=20)	T- Criterion (n=20)
Degree of iridosign intensity	Norm	-	100% (20)	25% (5)	-	-
	Not identified					
	1	-	-	-	35% (7)	-
	2	-	-	-	65% (13)	-
	3	-				

The Iris Status in Patients with Benign Breast Tumors

The group of 106 patients diagnosed with breast BT demonstrated numerous iridosigns with qualitative changes. The PS sign of varied degrees of intensity was observed in the absolute majority of instances – 76.1%, while changes on the side of ARs were revealed in 72.6%. Changes were found in all cases (28.3%) when Ls were revealed. Instances when CRs were identified (75.5%) were numerous in nature and demonstrated as disrupted arches. Changes described as T - Criterion (T1 – 38.7%; T2 – 61.3%) were observed in all patients of this group (100%).

Table 2 presents specific changes on the iris revealed in patients with benign breast tumors.

Table 2: Incidence of Iridological Signs within the Breast Segment Area of the Iris in the Group of Patients with Benign Tumors (only iris on the disease side included) n=106

Iridosign, % (abs. value)		PS	AR	L	CR	T - Criterion
Degree of iridosign intensity	Norm		27.4% (29)			
	Not identified	33.9% (36)		71.7% (76)	24.5% (26)	
	1	35.8% (38)	29.2% (31)	15.1% (16)	-	38.7% (41)
	2	27.4% (29)	43.4% (46)	13.2% (14)	75.5% (80)	61.3% (65)
	3	2.9% (3)				

The Iris Status in Patients with Breast Cancer

The analysis of iridograms within the designated segment in the patients with BC revealed a multiplicity of iridosigns varying in their degree of intensity. In most cases, qualitative changes were revealed in PS signs –

67.6%, AR – 86.6%, L – 29.1%, and CR – 56.6%. 99.5% of patients in this group demonstrated the T2 - Criterion. The specific changes on the iris noted in the projection area of the breast in patients with breast cancer are detailed in Table 3.

Table 3: Incidence of Iridological Signs within the Breast Segment Area of the Iris in the Group of Patients with Breast Cancer (only iris on the disease side included) n=189

Iridosign, % (abs. value)		PS	AR	L	CR	T- Criterion
Degree of iridosign intensity	Norm		13.4% (25)			
	Not identified	32.4% (61)		70.9% (134)	43.4% (82)	
	1	30.9% (59)	19.5% (37)	19.9% (38)		0.5%
	2	28.8% (54)	67.1% (127)	9.2% (17)	56.6% (107)	99.5% (188)
	3	7.9% (15)				

Comparison of Tumours by Iridological Signs

Table 4 presents results obtained by a comparison between the three groups by two groups of iridological signs (using the Mann-Whitney criterion at $p \leq 0.05$).

Table 4: Comparison of independent groups of variables by Mann-Whitney criterion (U-criterion).

	PP	AK	Lacunae	NK	T- Criterion
Benign / Malignant	0.421	0.0001 *	0.913	0.345	0.0001 *
Benign / Healthy	0.002	0.001*	0.708	0.111	0.0001*
Malignant / Healthy	0.003	0.001*	0.718	0.123	0.000 *

* $p \leq 0.05$

The comparison of the BT and BC groups by the PS iridosign did not reveal a statistically significant variance ($U=2.456$, $p=0.421$): this sign is presented with comparable prevalence in both benign and malignant breast tumors.

While comparing the BT group with the comparison (healthy) group ($U=2.456$, $p=0.002$), as well as the BC group with the comparison group ($U=2.456$, $p=0.003$) by the selected PS iridosign, a statistically significant difference was revealed that suggests a discernible dependence between the PS presence and pathological processes within the breast tissue.

The L iridosign demonstrated no statistically significant difference across the three examined groups, which is attributable to its equal occurrence rate across all groups ($U=2.456$, at p -values of 0.913, 0.708, and 0.718, respectively).

No statistically significant differences were revealed in regards to the CR iridosign when the three groups were comparing between each other (at $p > 0.05$).

The AR iridosign had varying expression intensities, which explains its obvious statistical difference across the three groups (U-criterion, $U=2.456$, $p=0.001$, and $U=2.456$, $p=0.001$, U-criterion, $U=2.456$, $p=0.001$).

Lastly, when comparing across all three groups by the T- Criterion, statistically significant differences were revealed between the BT and BC groups ($U=2.456$, $p=0.0001$), between the BT and the comparison groups ($U=1.326$, $p=0.0001$), as well as between the BC and the comparison groups ($U=1.126$, $p=0.0001$).

Dependence between Iridological Sign Intensity and Breast Tumor Morphological Structure

The pathomorphological examination of tumor tissue in women with benign and malignant breast tumors revealed changes that were assigned numeric values and classified as follow:

Morphology 0 – normal; Morphology 1 (M1) – benign changes without signs of proliferation/hyperplasia; Morphology 2 (M2) – benign changes with signs of proliferation/hyperplasia; Morphology 3 (M3) – benign changes with proliferation/hyperplasia and/or cells with signs of atypia present; Morphology 4 (M4) – presence of adenocarcinoma cells; Morphology 5 (M5) – no morphological examination was carried out.

PS Iridosign and Morphology

The analysis of interrelations between the breast tumor morphological structure and the PS iridosign revealed a direct moderate correlation. It was noted that PS of intensity degrees 1 and 2 were detected with the same incidence rate in both the BT and BC patient groups. On the contrary, PS iridosigns of intensity degree 3 identified within these groups correlated with inflammatory processes and a marked destruction in the breast tissue.

These findings are presented in Figures 1 and 2.

Fig 1. Correlation between the Pigment Spots Intensity Degree and the Tumor Morphological Structure in Patients with Benign Tumors

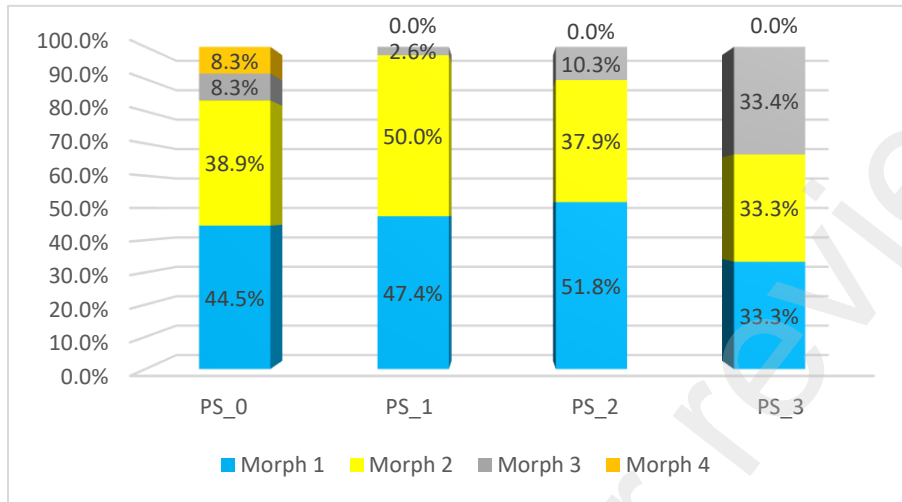
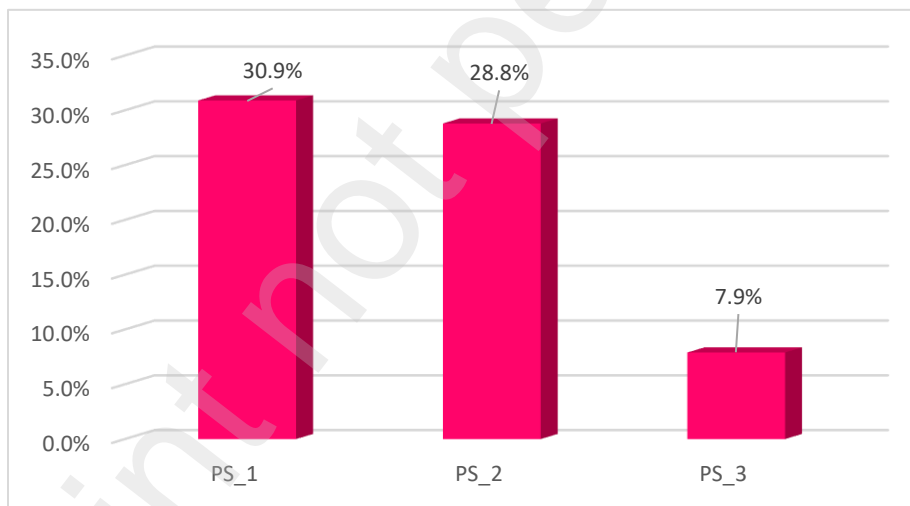


Fig. 2. Correlation between the Pigment Spots Intensity Degree and the Tumor Morphological Structure in Patients with Breast Cancer

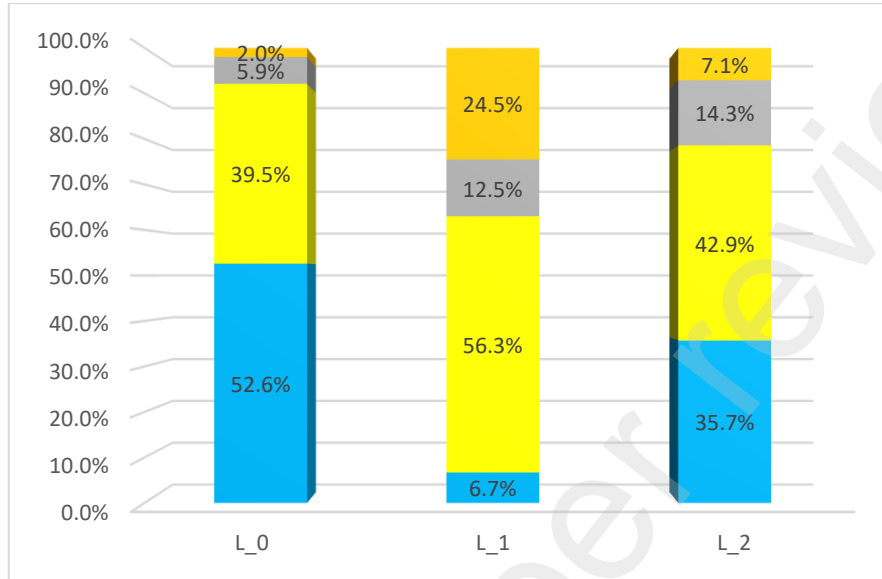


L Iridosign and Morphology

A direct strong correlation was detected between structural changes in the L iridosign and the tumor morphological structure. Qualitative changes in L in the BT group were observed 9 times more often when proliferation/hyperplasia and atypical cells occurred in tumor tissues.

These findings are presented in Figure 3.

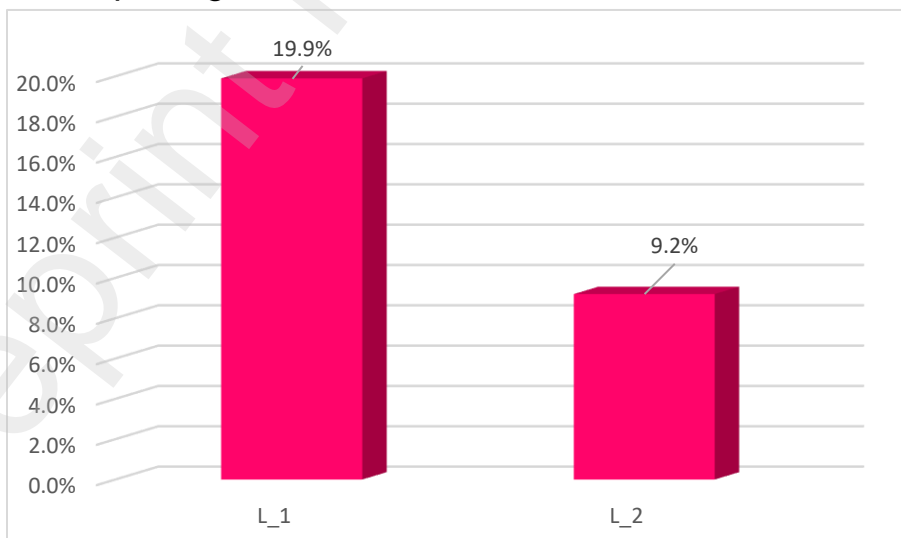
Fig. 3. Correlation between the Lacunae Intensity Degree and the Tumor Morphological Structure in Patients with Benign Tumor



100% of cases in the group diagnosed with BC demonstrated a direct strong correlation between a change in L and a presence of adenocarcinoma cells in the tumor morphological structure.

This information is presented in Figure 4.

Fig. 4. Correlation between the Lacunae Intensity Degree and the Tumor Morphological Structure in Patients with Breast Cancer



AR Iridosign and Morphology

Structural abnormalities in AR correlated with proliferative/hyperplasia changes, atypical cells and adenocarcinoma cells present in the tumor morphological structure.

These findings are presented in the figures below (Figures 5 and 6).

Fig 5. Correlation between the Autonomus Ring Intensity Degree and the Tumor Morphological Structure in Patients with Benign Tumors

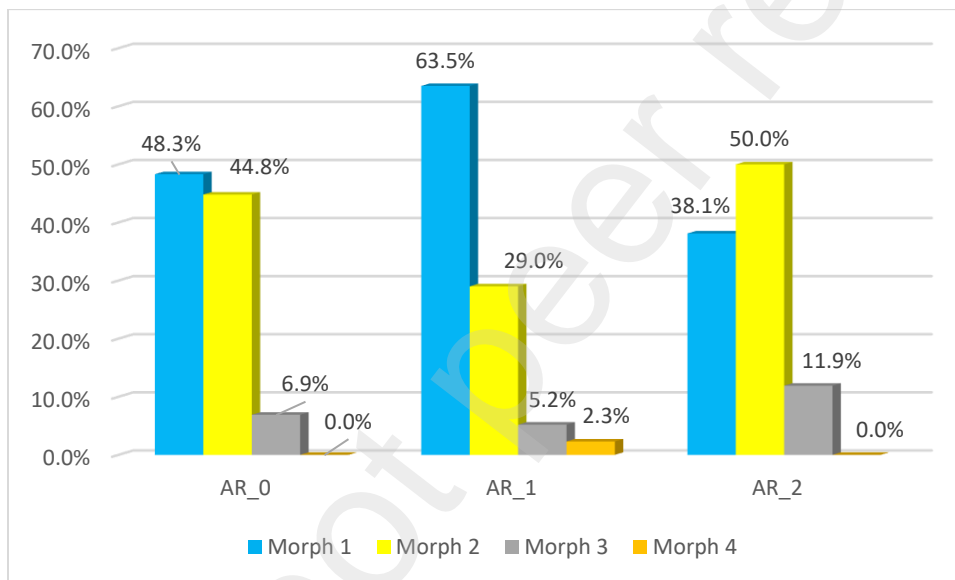
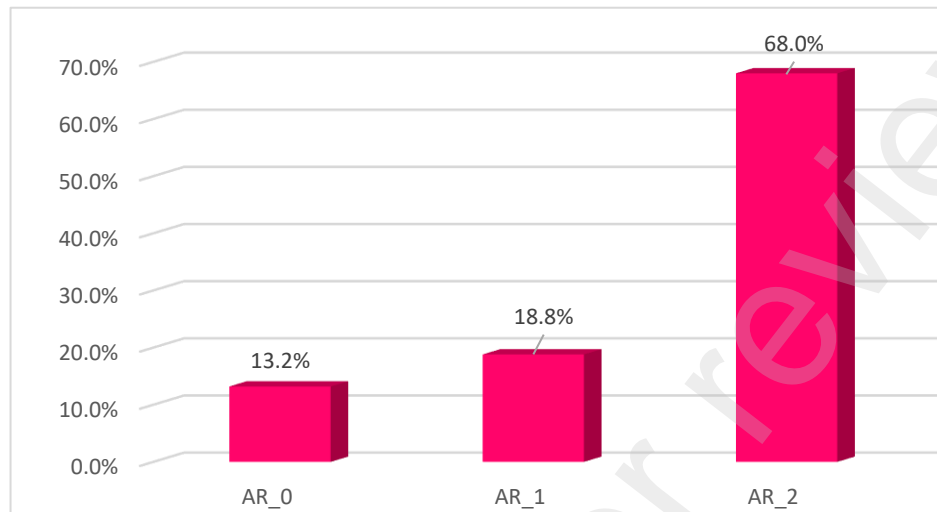


Fig. 6. Correlation between the Autonomus Ring Intensity Degree and the Tumor Morphological Structure in Patients with Breast Cancer



T - Criterion and morphology

A significant correlation was revealed between the nature of structural manifestations in breast tumor tissue and the degree of T - Criterion intensity. The BT group demonstrated a correlation between the breast tissue with no proliferative/hyperplasia signs and the T1 - Criterion in the majority of cases (81.6%), and the T2 - Criterion in 29.2% of cases. Meanwhile, the presence of cellular proliferation/hyperplasia, both with and without cellular atypia, revealed a strong direct correlation with the T2 - Criterion (70.8%). 99.5 % of cases demonstrated a correlation between the breast tissue with adenocarcinoma cells and the T2 - Criterion. These findings are presented in Figures 7 and 8.

Fig. 7. Correlation between the T - Criterion Intensity Degree and the Tumor Morphological Structure in Patients with Benign Tumours

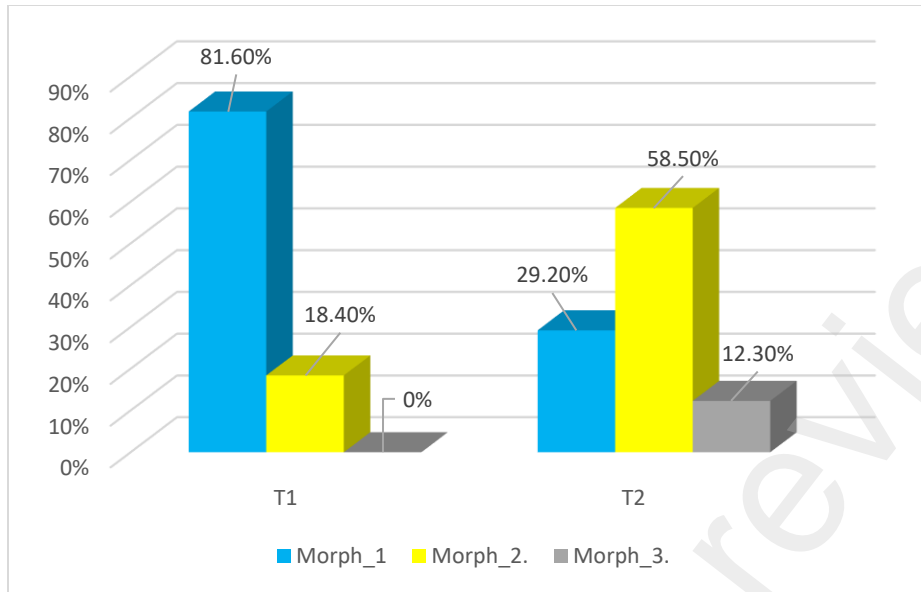
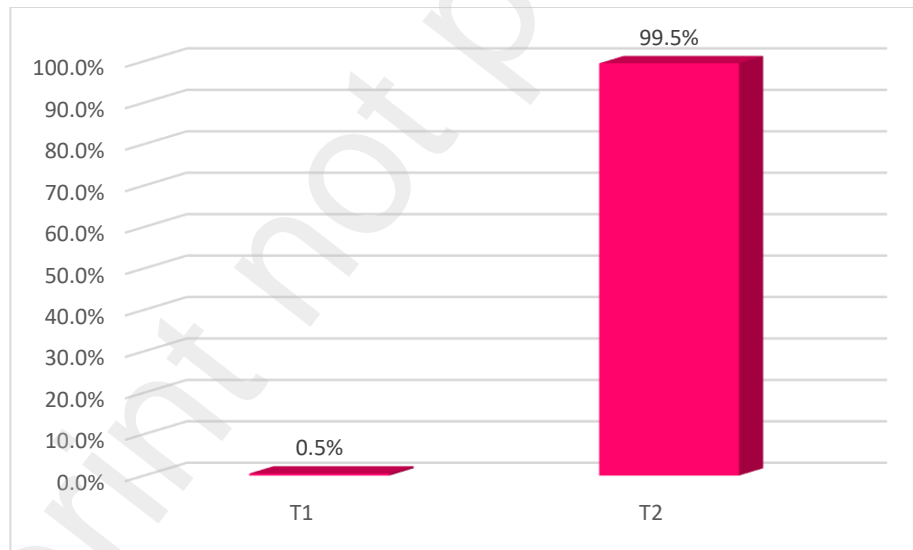


Fig. 8. Correlation between the T - Criterion Intensity Degree and the Tumor Morphological Structure in Patients with Breast Cancer



CR Iridosign and Morphology

It is inexpedient to identify a correlation between the CR iridosign and the tumor morphological structure, as this sign is not specific in the iridodiagnosis.

Instrumental Iridological Parallels in Breast Tumors

The integration of MG and USG findings with pathomorphological assessments juxtaposed with the intricate projection analysis of identified iridological markers allowed elucidating the breast tissue representation on the irises of both eyes (no details are disclosed due to pending patent processes.)

This study appraised the sensitivity of both instrumental and ID test methods. MG and USG were found to have sensitivity of 87% and 69%, respectively, in detecting malignant breast tumors across the evaluated cases.

The ID approach sensitivity was analyzed by the T - Criterion that is specific for tumor processes. Having in mind that the T2 represents a set of changes on the iris that are more likely associated with precancerous changes in tumor tissues and BC, the sensitivity of the ID method was assessed by the degree of the T2 - Criterion intensity. Thus, the ID method demonstrated a sensitivity of 85.7% for both BT and BC groups.

The data obtained from the research allowed drawing a diagram of multiple non-linear regression to quantify the contribution of each iridosign to the overall diagnostic profile.

Within the BT cohort considered from the point of view of multiple regression analysis, we defined a **Y** predictor (Morphology) and predictors **X** – L, AR, PS, CR, and T - Criterion. To this end, we used a stepwise approach to integrate the predictors into the regression equation, which provides a quantitative assessment of every iridosign contribution. The multiple regression analysis of the data produced the following results.

A consistent correlation with a high statistical significance was revealed between the L ($t=2.121$; $p=0.001$) and AR ($t=1.921$; $p=0.045$)

predictors with the Morphology, with the L predictor alone contributing approximately 9% and the combined input of both predictors amounting to roughly 48.0% (based on η^2), underscoring the predictive significance of AR.

Simultaneously, we have found that the T - Criterion (including T1 and T2) emerges as the primary predictive factor. Its inclusion within the regression equation indicated its statistically significant impact on the process of suspected breast tumor ($\eta^2=84.4\%$), which supposes a major diagnostic value of this predictor ($t=2.105$, $p=0.001$).

The stepwise inclusion in the regression equation and the cumulative determination factor of about 20% revealed that the PS and CR predictors ($p=0.061$; $p=0.237$, respectively) did not exert a statistically significant influence on BT diagnostics. Therefore, these predictors were assigned to a group of supplementary predictors in the prognostic assessment for the BT evolution that are relevant during the screening phase.

Furthermore, the multiple regression assessment of the BC group demonstrated a consistent and statistically significant correlation between the AR ($t=3,421$; $p=0,001$), T - Criterion ($t=2,831$; $p=0,035$) predictors and the Morphology indicators, with their collective contribution accounting for approximately 74.0% (based on η^2), which reflects a substantial impact that the intensity degrees of the AR an T - Criterion predictors produce on the Morphology attributes. If we consider the role and impact of the additional prognostic predictors (about 25%), it suggests their more frequent and pronounced occurrence in the presence of malignant pathologies.

Conclusions

1. The comparative analysis of clinical-instrumental data with iridological findings enabled a refinement of the breast topography on the iris, specifying the right breast projection within the 8.00-9.00 segment on

the right iris, and the left breast projection within the 3.00-4.00 segment on the left iris.

2. Changes in the iris occur on the side corresponding to the location of the breast tumor, within the topographically associated segment.
3. The identified T - Criterion serves as an iridological marker for breast tumors, exhibiting two distinct intensity degrees: T1 - Criterion represents a pattern of iridological changes most typically associated with benign tumors in the absence of cellular proliferation/hyperplasia in the breast tissues; T2 - Criterion denotes a set of iridological changes most common to benign tumors with present cellular proliferation/hyperplasia, cellular atypia, as well as tissues with adenocarcinoma cells.
4. The Iridology method sensitivity is comparable with that of mammography, registering at 85.7% and 87%, accordingly. The Iridology method sensitivity is superior to that of ultrasonography – 85.7% and 69%, respectively.
5. The study's findings suggest a discernible correlation between the structural changes within the breast tissue and specific iridosign manifestation.
6. The contribution of every iridological sign and criterion in detection of suspected breast tumors is represented within a multiple non-linear regression framework. The use of this analytical model in a highly specialized software, combined with thorough knowledge and clinical thinking, has a potential to yield informationally consistent outcomes that could identify early and frequently preclinical pathological indicators that may serve as diagnostic tests.

7. The integration of modern technology within iridological practice is supposed to enhance substantially the method sensitivity and specificity, thereby reducing the percent of diagnostic errors.
8. The expansion into broad-based multidisciplinary research endeavors could dispel the "vicious mystical circle" that has historically encircled iridological practice and extricate the Iridology Diagnostic method from obscurity.

Acknowledgement

1. Conflict of interest disclosure: Professor Leonid Putyrski (Former employee (1982-2012) of N.N. Alexandrov National Cancer Centre in Belarus; I asked L.P. for a consultation on clinical breast oncology several times between 2020 and 2023. In 2022, he read a manuscript of completed research (provided to him electronically). He expressed his complete approval and concern for further development of iridological prospects in oncology. There is a risk that, without my permission, he shared the idea and results with his son, Yury Putyrski (former employee (2007-2014) of N.N. Alexandrov National Cancer Centre in Belarus, Szpital Czerniakowski in Poland (from March 1, 2023 – present). The contact with L.P. has been stopped since 27.02.2024. Leonid Putyrski family members and close relatives (including Yury Putyrski at all...) which interests may be affected by the content of manuscript. Competing interest statement: The data of the manuscript could have been disclosed to family members of Pr. Leonid Putyrski without the author's permission.
2. This research did not receive financial support.

3. The conduct of the research was approved by the N.N. Alexandrov National Cancer Centre institutional ethics committee on June 12, 2018 (Lesnoy, Minsk District, Belarus; <https://omr.by>).

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