

New WHO classification of breast tumours – as published in 2019

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At the end of 2019, a new classification of breast malignancies was published by the World Health Organization (WHO). Popular name of the classification is the "blue book" and it derives from the colour of its cover. New classification was made available after 7 years from the previous one. In 2019 the WHO introduced new disease entities: mucinous cystadenocarcinoma and tall cell carcinoma of reverse polarity. The most recent classification also contains classification of the microscopic evaluation of ductal carcinoma in situ (DCIS) and of the evaluation of the parameters necessary to define the tumour grade of breast cancer as well as predictive or prognostic parameters. All of above mentioned changes are presented and commented on in the article.

Key words: breast cancer, WHO classification, mucinous cystadenocarcinoma, tall cell carcinoma of reverse polarity

Introduction

At the end of 2019, a new classification of breast cancers was published by the World Health Organization (WHO). The previous classification, binding until then, had been published in 2012. Therefore, the new, fifth edition of this classification, whose popular name, the "blue book", derives from the colour of its cover, comes after 7 years and introduces noteworthy changes. These changes are not as revolutionary as those introduced in the fourth edition (2012), yet studies which concern such an important issue, as breast cancer definitely is, are worth reporting on an ongoing basis.

General WHO characteristics of cancers

In all current WHO classifications, each cancer is described in the same manner, including, among others:

- diagnostic criteria,
- typical microscopic characteristics,
- accompanying molecular lesions.

The objective of this description of specific cancers in the WHO classification is to provide coherent international diagnostic standards.

In the era of digitalisation and in the presence of the pandemic which reduces both interpersonal contacts and the custom of sharing books, it seems especially worthwhile to purchase an annual subscription – an option which has been introduced by the WHO this year, and which gives access to the most recent classifications in digital form: (<https://tumourclassification.iarc.who.int/welcome/>).

The subscription price (currently 100 EUR annually) does not seem very high, especially given the price of a paper version of one book. Currently, the purchase of the subscription allows access to nine books (their most recent editions), which discuss the tumours of the gastrointestinal (GI) tract, breasts, endocrine system, eyeballs, skin, head and neck, central nervous system, soft tissues and bones, haematopoietic and lymphatic tissues (beta version).

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Currently, online access to these publications does not have to be recommended to anyone: the benefits are clear. Digitalisation has allowed progress in “digital pathology” and image analysis systems. Thanks to this, pathologists worldwide have access to microscopic images with much better resolution than those published in traditional, paper books.

The first conclusion that arises from a comparison of the book and the current, digital version of the breast cancer classification is that the latter has a clearer chapter layout. A reduced number of chapters in the 2019 edition results from the fact that all epithelial breast tumours are discussed in one large chapter. Additionally, pathological lesions developing within the breast are discussed in a more logical way – beginning with completely benign lesions, through pre-cancerous lesions and ending with non-malignant and malignant tumours. Each disease entity is described in the same, regularly repeating manner, so the reader can easily find all the necessary information.

What is also worth noting is the attempt to unify various classifications. And thus, the tumours which occur in many organ systems (such as neuroendocrine, haematological and mesenchymal tumours) are described in separate chapters of the book(s). Moreover, the criteria for the evaluation and diagnosis of these tumours proposed by the WHO are the same, regardless of the tumour location.

Apart from these general modifications to the method of establishing diagnostic criteria and other information concerning specific morphological units within the breast and also presenting them to the reader, **the recent edition of the WHO classification contains a lot of new data, even including new disease entities.**

New entities, introduced in the current WHO classification of breast cancers

In 2019 – in the currently binding classification of breast cancers – the WHO introduced new disease entities:

- mucinous cystadenocarcinoma, and
- tall cell carcinoma of reverse polarity.

Mucinous cystadenocarcinoma is a rare form of breast cancer, whose microscopic picture resembles pancreatic or ovarian cancers – the dominating forms are cystic spaces with papillary structures. For a clinician, one important note is that this is a triple negative tumour – in its cells, no expression of oestrogen, progesterone or HER2 protein is found. This property allows this rare form of cancer to be differentiated from the classical mucinous cancer which is characterised by the expression of these hormone receptors.

Tall-cell carcinoma of reverse polarity is a cancer whose cytological properties resemble the papillary carcinomas which develop in the thyroid gland. This type of cancer grows as a solid tumour, creating papillary structures within its architecture. It is included in the parotid type tumours and is also, with regards to its molecular properties, a triple negative tu-

mour (usually no hormone receptors and no HER2 expression are found in the cancer cells).

Selected modifications of the current WHO classification of breast cancer

The most recent classification also contains significant (especially for pathologists) classifications of the microscopic evaluation of ductal carcinoma *in situ* (DCIS) and of the evaluation of the parameters necessary to define the tumour grade of breast cancer as well as predictive or prognostic parameters.

In comparison with the previous edition of the classification of the breast cancers, **the manner of evaluation of tumour grade in the case of ductal breast carcinoma *in situ* (DCIS) has been modified.** Previously, when evaluating this parameter, a pathologist took into consideration both the architecture of the epithelial lesions and the degree of the nuclear atypia. Now, it has been agreed that, for larger compliance of the diagnoses made by various doctors, it is necessary to take into consideration only the morphology of the cells and their nuclei, because the architecture of the lesions vary between specific grades and is not as homogenous as the morphology of the cancer cells. The structures created by cancer cells within the lumens of the ducts may be considered, yet is not necessary for determining the DCIS grade. The distinction between low, medium and high grade remains unchanged.

The next parameter which must be mentioned in the context of the recent classification is the **evaluation of tumour-infiltrating lymphocytes** (TILs). The authors of the classification decided not to include data concerning TILs in the obligatory panel of the parameters under evaluation, but they clearly point out that the micro-environment of the tumour plays a very important role and that an evaluation of the intensity of the host response to the presence of the infiltrating carcinoma – i.e. the amount of the infiltration of lymphatic cells within the cancer tissue – is a recognised prognostic factor for the response to neo-adjuvant treatment in triple negative breast cancers and in HER-positive cancers. At the same time, it is emphasised that this parameter should be an element of clinical studies (taking into consideration existing international guidelines for its evaluation) and, within the progress of the system of digital evaluation of microscopic images, allowing for the standardisation of the entire procedure, this should become a routinely evaluated parameter the value of which should be presented in the case of infiltrating breast cancers.

One significant issue here is also the diagnosis of medullary type cancers. The classification from 2012 listed three types of such cancers of the breast gland. In the current edition, the authors have decided to give up this distinction and specify only one cancer type: no special type (NST) with characteristic morphological properties. This is **invasive carcinoma NST with basal-like and medullary pattern.** The reasons for this decision were as follows:

- the limited repeatability of diagnoses of the previous types of the cancer out of many pathologists,
- the overlapping features of the described cancers with cancers with a molecularly confirmed profile of basal carcinoma and the cancers connected with a *BRCA1* gene mutation.

For clinical reasons, it is now believed that the cancers discussed belong rather to a spectrum of various breast cancers in whose architecture numerous TILs are found, but they do not make up a separate disease entity.

In spite of the extensive debate which has been going on for many years among pathologists dealing with the diseases of the breast, the authors of the classification discussed here, have maintained, in its newest edition, the nomenclature of the lobular breast cancers. Therefore, the term lobular carcinoma *in situ* (LCIS), can still be used, although it is emphasized that both the classical form of LCIS, and atypical lobular hyperplasia (ALH) are merely risk factors and they are non-obligatory precursors of infiltrating cancer. In spite of the lack of adequate data, the authors of the classification, only recommend the resection of the breast lesions in which the pathologist has described a hyperplasia of the types florid LCIS or pleomorphic LCIS. This is meant to reflect the biological diversity of the latter neoplasias and their more aggressive character.

In the above, very brief and obviously unobjective summary of the changes in the recent WHO classification, I have tried to discuss those issues which are significant from a clinical point of view and reflect the rapidly changing medical reality, now strongly dominated by new technologies. In the era of interdisciplinary oncology, the nomenclature must be unambiguous and clear for other members of the oncological multidisciplinary team.

Conflict of interest: none declared

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References

1. Breast Tumours, WHO Classification of Tumours, 5th Edition, ed. WHO Classification Editorial Board, 2019.