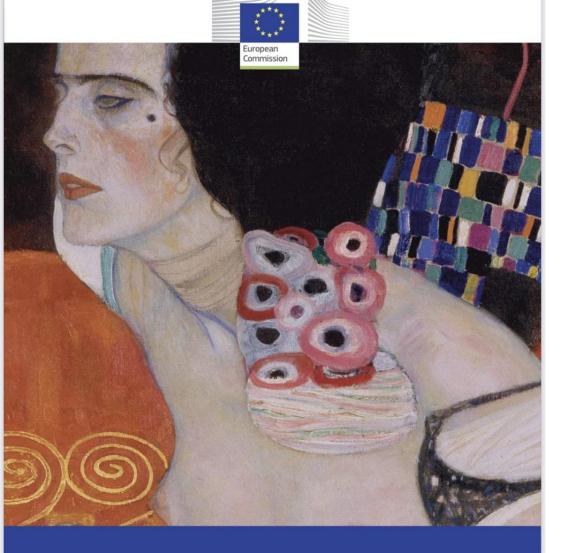
# Специфика при хистопатологичната оценка при скринингови програми

Доц. д-р Свитлана Бачурска, дм Клиника по обща и клинична патология УСБАЛО "Проф. Иван Черноземски", София



## Въведение

- Приемането на официални скринингови програми води до подобрение не само при лечението на ранни, но и напреднали форми на заболявания чрез въвеждането на насоки, стандарти за качество, външна оценка на качество и одит.
- В скрининговите програми трябва да се разработят общи диагностични стандарти, за да се гарантира качество, да се разпознаят области, в които все още липсват достатъчно доказателства и да се инициират висококачествени проучвания, за да отговорите на тези въпроси.



# European guidelines for quality assurance in breast cancer screening and diagnosis

Fourth edition - Supplements

Health and Consumers

#### Produced by the European Working Group on Breast Screening Pathology

- C.A. Wells, Dept. of Cytopathology, University College Hospital, London, United Kingdom
- I. Amendoeira, Dept. of Pathology, Instituto de Patologia & Imunologia Molecular da Universidade do Porto and Hospital S. João, Porto, Portugal
- J.P. Bellocq, Dept. of Pathology, University Hospital Strasbourg, Strasbourg, France
- S. Bianchi, Division of Pathological Anatomy, Dept. of Medical and Surgical Critical Care, University of Florence, Italy
- W. Boecker, Pathologie-Praxis, Hamburg, Germany
- B. Borisch, Dept. of Pathology, University of Geneva, Switzerland
- B. Bruun Rasmussen, Dept. Of Pathology, Herlev Hospital, Herlev, Denmark
- G.M. Callagy, Dept. of Pathology, National University of Ireland, Galway, Ireland
- E. Chmielik, Dept. of Pathology, Maria Sklodowska-Curie Memorial Cancer Center, Gliwice, Poland
- A. Cordoba, Servicio de Anatomía Patológica, Complejo Hospitalario de Navarra, Pamplona, Spain
- G. Cserni, Dept. of Pathology, University of Szeged, Hungary, and Dept. of Pathology, Bács-Kiskun County Teaching Hospital, Kecskemét, Hungary
- T. Decker, Dept. of Pathology, Dietrich Bonhoeffer Medical Center, Neubrandenburg, Germany
- J. DeGaetano, Dept. of Pathology Mater Dei Hospital, Malta
- M Drijkoningen, Dept. of Pathology, University Hospitals Leuven, Leuven, Belgium
- I.O. Ellis, Dept. of Histopathology, Nottingham City Hospital, Nottingham, United Kingdom
- D.R. Faverly, CMP pathology laboratory and CCR Community Reference Center for cancer screening, Brussels, Belgium
- M.P. Foschini, Dept. of Pathology, University of Bologna, at Bellaria Hospital, Bologna, Italy
- S. Frković-Grazio, Dept. of Gynaecological Pathology and Cytology, University Clinical Hospital, Ljubljana, Slovenia
- D. Grabau, Dept. of Pathology, Skåne University Hospital, Lund, Sweden
- P. Heikkilä, Dept. of Pathology, University of Helsinki and HUSLAB, Helsinki, Finland
- E. Iacovou, Dept. of Pathology, Nicosia General Hospital, Cyprus
- J. Jacquemier, Dept. of Molecular Oncology, Institut Paoli Calmettes, Marseille, France
- H. Kaya, Dept. of Pathology, Marmara University School of Medicine, Istanbul, Turkey
- J. Kulka, 2nd Dept. of Pathology, Semmelweis University, Budapest, Hungary
- M. Lacerda, Center for Neuroscience and Cell Biology, University of Coimbra, Portugal
- I. Liepniece-Karele, Riga Eastern Clinical University Hospital, Riga, Latvia
- J. Martinez-Penuela, Dept. of Pathology, Navarra Hospital Complex, Pamplona, Spain
- C.M. Quinn, Dept. of Pathology, St Vincent's University Hospital, Dublin, Ireland
- F. Rank<sup>†</sup>, Dept. of Pathology, Rigshospitalet, Copenhagen University Hospital, Denmark
- P. Regitnig, Institute of Pathology, Medical University of Graz, Austria
- A. Reiner, Institute of Pathology, Danube Hospital, Vienna, Austria
- A. Sapino, Dept. of Biomedical Science and Human Oncology, University of Turin, Turin, Italy
- T. Tot, Dept. of Pathology and Clinical Cytology, Central Hospital Falun, Falun, Sweden
- P.J. Van Diest, Dept. of Pathology, University Medical Center Utrecht, The Netherlands
- Z. Varga, Dept. of Pathology, Institute of Surgical Pathology, University Hospital Zurich, Switzerland
- J. Wesseling, Dept. of Pathology, Netherlands Cancer Institute/Antoni van Leeuwenhoek Hospital, Amsterdam, The Netherlands
- V. Zolota, Dept. of Pathology, Medical School, University of Patras, Rion, Patras, Greece
- E. Zozaya-Alvarez, Navarra Hospital Complex, Pamplona, Spain

European guidelines for quality assurance in breast cancer screening and diagnosis

Fourth Edition

Supplement



## **Pathology update**

# Quality assurance guidelines for pathology



#### Diagnosis Columnar cell ADH/DCIS **Feature** Columnar cell Columnar cell lesion with atypia \*\* hyperplasia change TDLU, acini may be TDLU, acini may TDLU, often microcystically TDLU +/- adjacent ducts **Topography** mildly dilated or of be mildly dilated or dilated acini normal size of normal size Shape of acinar Often rounded acinar Often rounded acini, but Irregularly shaped Irregularly shaped luminal margin spaces, with smooth inner with complex structures luminal margin spaces extending into lumen (see margin Architecture, below) Flat Tufts and mounds **Architecture** Flat or tufted/mounds, not Complex with micropapillary or cribriform structures complex Stratification/ Not present Present May be present May be present multi-layering Luminal Present Present Present May be present secretions often with microcalcifications Small to medium **Nuclear size** Small to medium Small to medium Small to medium **Nuclear shape** Oval, elongated Oval, elongated Often, but not always, Rounded rounded Bland Bland Speckled chromatin pattern Speckled chromatin pattern Nuclear texture may be present is common Uniform Pleomorphism\* Uniform Uniform to moderately Uniform pleomorphic Position of Basally placed Basally placed Often central Central nuclei within cell Nucleoli Not conspicuous Not conspicuous Evident May be evident Mitoses Generally absent Generally absent Generally scarce Generally scarce May be focal or May be focal or May be focal area within Extent May be a focal area within extensive extensive background of non-atypical background of non-atypical CCL CCL: by definition, ADH is small/microfocal



Table 2: Molecular typing of breast cancer based on common immunohistochemical markers (Abd El-Rehim et al., 2005; Goldhirsch et al., 2011)

Molecular intrinsic subtype	Clinico- pathological definition	ER	PR	HER2	Ki67	Basal markers*
Luminal A	Luminal A	+	+ or -	_	Low	
Luminal B	Luminal B (HER2 negative)	+	+ or -	_	High	
Luminal B	Luminal B (HER2 positive)	+	+ or -	Overexpressed	Low or high	
HER2	HER2 positive (non-luminal)	3 <b>—</b> 3	-	Overexpressed	Usually high	+/-
Basal	Triple negative (ductal)	-	-	=	Usually high	+



European guidelines for quality assurance in cervical cancer screening

Second edition - Supplements

**Methods for Screening and Diagnosis** 3.1 **Executive summary** 3.2 Assessment of the performance of screening tests: principles and criteria 3.3 Conventional cervical cytology 3.3.1 Description of conventional cervical cytology 3.3.1.1 Principles of conventional cytology 3.3.1.2 Reading a cervical smear 3.3.1.3 Screening technique and localization 3.3.1.4 Cytological interpretation and reporting 3.3.1.5 Clinical applications of cervical cytology 3.3.1.6 Quality of conventional smears 3.3.2 Performance of conventional cervical cytology 3.4 Liquid-based cytology 3.4.1 Description 3.4.2 Rationale for liquid-based cytology 3.4.3 Recent reviews, meta-analyses and pilot studies 3.4.3.1 Comparison of the test characteristics of liquid-based cytology with the conventional Pap-smear 3.4.3.2 Comparison of the adequacy of liquid-based and conventional smears 3.4.3.3 Pilot projects conducted in Scotland and England 3.4.3.4 Influencing factors

4.1 4.2	Laboratory Guidelines and Quality Assurance Practices for Cytology  Executive summary Introduction	5	Techniques and Quality Assurance Guidelines for Histopathology
<b>4.3 4.3.1 4.3.2 4.3.2.1 4.3.2.2 4.3.3</b>	Personnel and organization General Requirements for cyto-technologists Cyto-technologist Senior cyto-technologist Requirements for other technical laboratory personnel	5.1 5.2 5.3	Executive summary Introduction Punch biopsies
4.3.4 4.3.5 4.3.6 4.4 4.4.1	Requirements for a cyto-pathologist Requirements for administrative personnel Final responsibility Material requirements Buildings, rooms and furniture	5.3.1 5.3.2 5.3.3	Diagnostic goal Macroscopic description Technique
4.4.2 4.5 4.5.1 4.5.2 4.5.2.1	Equipment for staining, microscopes, record systems and teaching materials  Handling and analysis of cervical samples Laboratory preparation  Assessment of the sample: stepwise screening Initial assessment	5.3.4 5.4 5.4.1	Histological diagnosis  Excision biopsies  Diagnostic goals
4.5.2.2 4.5.3 4.5.4 4.6 4.6.1	Samples qualifying for a second screening assessment Workload requirements – primary screening Archiving Recording of results Laboratory information system	5.4.2 5.4.3 5.4.4	Macroscopic description Technique Histological diagnosis
<b>4.6.2 4.6.3 4.7 4.7.1</b> 4.7.1.1	Authorization of results Laboratory response time  Quality management Internal quality management Laboratory quality management (preanalytical quality management)	5.5 5.5.1 5.5.2	Endo-cervical curettage (ECC) Diagnostic goal Macroscopic description
4.7.1.2 4.7.1.3 <b>4.7.2</b> 4.7.2.1 4.7.2.2	Analytical quality management (cytology) Internal continuing education  External quality management  External continuing education  External quality control of screening skills	5.5.3 5.5.4 5.6	Technique Histological diagnosis Immunohistochemistry
4.7.2.3 4.7.3 4.8 4.8.1 4.8.2	Accreditation of the laboratory unit Responsibilities for quality control  Communication Other laboratories General practitioners, gynaecologists and other sample-takers	5.7 5.8	Data collection Quality assurance
4.8.3 4.8.4 4.9	Health authorities Patients References	5.9	References

# Препоръки относно терминология при цервикална цитология

Three-tier classification system (WHO, CIN, NHSCSP)

	Atypical/bor	derline changes	in squamous cell	S	
Normal	HPV infection	Mild/CIN1	Moderate/CIN2 Glandular neop		Cancer
	Atypical/bor	derline changes	in glandular cells		

The Bethesda system

	ASC-US	ASC-H	
Normal	LSIL	HSIL	Cancer
		AIS	
	Atypical changes in glandular co	ells	



Papanicolaou	WHO	CIN (Richart, 1973)	TBS 1991 (Luff, 1992)	TBS 2001 (Solomon & Nayar, 2003)
I	Normal		Ā	Negative for epithelial abnormality
II	Atypia		Infection, reactive repair	
			ASCUS	ASC-US
				ASC-H
	Atypical glandular cell	s	AGUS	Atypical glandular cells
III	Mild dysplasia	Condyloma	LSIL	LSIL
		CIN I	7	
	Moderate dysplasia	CIN II	HSIL	HSIL
IV	Severe dysplasia	CIN III		
	CIS			
	AIS	CGIN	AGUS	AIS
V	Invasive carcinoma			1







### Table 2. The 2001 Bethesda system: terminology for reporting the results of cervical cytology<sup>2</sup>

#### **SPECIMEN ADEQUACY**

- 1. Satisfactory for evaluation (note presence/absence of endocervical/ transformation zone component)
- 2. Unsatisfactory for evaluation . . . (specify reason)
  - Specimen rejected/not processed (specify reason)
  - Specimen processed and examined, but unsatisfactory for evaluation of epithelial abnormality because of (specify reason)

#### **GENERAL CATEGORIZATION (Optional)**

- 1. Negative for intraepithelial lesion or malignancy
- Epithelial cell abnormality
- 3. Other

#### INTERPRETATION/RESULT

- 1. Negative for Intraepithelial Lesion or Malignancy
  - Organisms
    - Trichomonas vaginalis
    - Fungal oganisms morphologically consistent with Candida species
    - Shift in flora suggestive of bacterial vaginosis
    - Bacteria morphologically consistent with Actinomyces species
    - Cellular changes consistent with herpes simplex virus
  - Other non-neoplastic findings (Optional to report; list not comprehensive)
    - o Reactive cellular changes associated with inflammation (includes typical repair)
    - Radiation
    - o Intrauterine contraceptive device
    - Glandular cells status posthysterectomy
    - Atrophy
- . Epithelial Cell Abnormalities
  - Squamous cell
    - Atypical squamous cells (ASC) of undetermined significance (ASC-US)
    - Atypical squamous cells cannot exclude HSIL (ASC-H)
    - Low-grade squamous intraepithelial lesion (LSIL), encompassing: human papillomavirus/mild dysplasia/cervical intraepithelial neoplasia (CIN) 1
    - High-grade squamous intraepithelial lesion (HSIL), encompassing: moderate and severe dysplasia, carcinoma in situ; CIN 2 and CIN 3
    - Squamous cell carcinoma
  - Glandular cell
    - Atypical glandular cells (AGC) (specify endocervical, endometrial, or not otherwise specified)
    - Atypical glandular cells, favor neoplastic (specify endocervical or not otherwise specified)
    - Endocervical adenocarcinoma in situ (AIS)
    - Adenocarcinoma
- 3. Other (List not comprehensive)
  - Endometrial cells in a woman 40 years of age

# European guidelines for quality assurance in colorectal cancer screening and diagnosis. First Edition Quality assurance in pathology in colorectal cancer screening and diagnosis

the Health Programme of the European Union

**Authors** 

P. Quirke<sup>1</sup>, M. Risio<sup>2</sup>, R. Lambert<sup>3</sup>, L. von Karsa<sup>4</sup>, M. Vieth<sup>5</sup>

Institutions

Institutions are listed at the end of article.

Category	Diagnosis		
1	Negative for neoplasia		
2	Indefinite for neoplasia		
3	Mucosal low grade neoplasia		
	Low grade adenoma		
	Low grade dysplasia		
4	Mucosal high grade neoplasia		
	High grade adenoma/dysplasia		
	Noninvasive carcinoma (carcinoma in situ)		
	Suspicious for invasive carcinoma		
	Intramucosal carcinoma		
5	Submucosal invasion by carcinoma		



**Table 7.1** Adaptation of the revised Vienna classification<sup>1</sup> for colorectal cancer screening.

#### 1. NO NEOPLASIA:<sup>2</sup>

Vienna Category 1 (Negative for neoplasia)

#### 2. MUSCOSAL LOW GRADE NEOPLASIA:

Vienna category 3 (Mucosal low-grade neoplasia

Low-grade adenoma

Low-grade dysplasia);

Other common terminology

mild and moderate dysplasia;

WHO: low-grade intra-epithelial neoplasia

#### 3. MUCOSAL HIGH GRADE NEOPLASIA:

Vienna: Category 4.1 – 4.4 (Mucosal high grade neoplasia

high-grade adenoma/dysplasia

Non-invasive carcinoma (carcinoma in situ)

Suspicious for invasive carcinoma

Intramucosal carcinoma);

Other common terminology

severe dysplasia

high-grade intraepithelial neoplasia;

WHO: high-grade intraepithelial neoplasia

TNM: pTis

#### **4. CARCINOMA** invading the submucosa or beyond:

4a. Carcinoma confined to submucsa

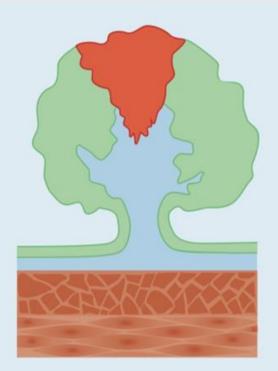
Vienna: Category 5 (Submucosal invasion by carcinoma);

TNM: pT1

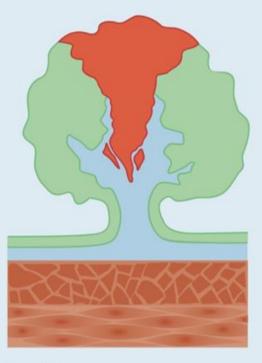
4b. Carcinoma beyond submucosa

TNM: pT2-T4

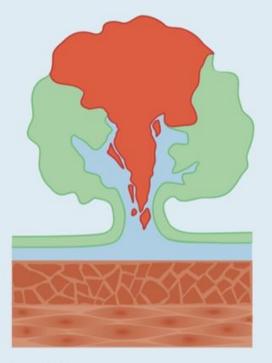
#### Guidelines



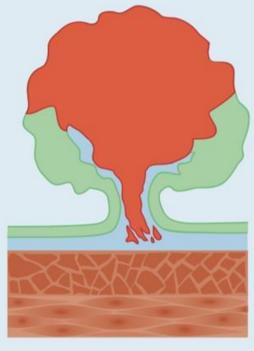
Level 1: Invasion of the submucosa but limited to the head of the polyp.



Level 2: Invasion extending into the neck of polyp.



Level 3: Invasion into any part of the stalk.



Level 4: Invasion beyond the stalk but above the muscularis propria.

**Fig. 7.2** Haggitt levels of invasion in polypoid carcinomas.



**Table 7.2** Modified Dukes stage.

Dukes A	Tumour penetrates into, but not through the muscularis propria (the muscular layer) of the bowel wall.
Dukes B	Tumour penetrates into and through the muscularis propria of the bowel wall but does not involve lymph nodes.
Dukes C	C1:There is pathological evidence of adenocarcinoma in one or more lymph nodes but not the highest node. C2:There is pathological evidence of adenocarcinoma in the lymph node at the high surgical tie.
Stage D	Tumour has spread to other organs (such as the liver, lung or bone).



## Заключение

- В мултидисциплинарен процес е възможно постигане на широк консенсус върху препоръки за осигуряване на качество в патологията при скрининг и диагностика на раковите заболявания.
- Следвайки тези препоръки има потенциал за подобряване на контрола на рак в България чрез подобряване на качеството и ефикасността на процеса на скрининг, приканвайки за менажиране на открити случаи.
- Наличието на единна класификация за докладване на идентифицирани патологични лезии в програмите за скрининг в Европа също има потенциала да подобри международното сътрудничество и обмена на опит в подобряване на качеството и ефективността на грижите за раковите заболявания.

