

# Manifesto on Optimal Pathology



## Note: about the optimal breast cancer pathology manifesto

This manifesto was prepared by a European Breast Cancer (EBC) Council working group and launched at the European Breast Cancer Conference in Glasgow on 20 March 2014.

It sets out optimal technical and organisational requirements for a breast cancer pathology service, in the light of concerns about variability and lack of patient-centred focus.

It is not a guideline about how pathology services should be performed. It is a call for all in the cancer community – pathologists, oncologists, patient advocates, health administrators and policymakers – to check that services are available that serve the needs of patients in a high quality, timely way.

EBC Council welcomes all feedback on this first version, which is a working document that will be edited to produce a final version, and will also inform a more detailed position paper.

Please email [Davi.Kaur@ecco-org.eu](mailto:Davi.Kaur@ecco-org.eu) with suggestions.

The members of the working group are:

- Alberto Costa (scientific director, European School of Oncology, Milan, Italy)
- Emiel Rutgers (head of surgery, The Netherlands Cancer Institute)
- Elizabeth Bergsten Nordström, president, Europa Donna, Europe's breast cancer advocacy organisation
- Tibor Tot, associate professor of pathology, Uppsala University, and head of laboratory medicine at Central Hospital Falun, Dalarna, Sweden
- Giuseppe Viale (director, department of pathology, European Institute of Oncology, Milan, Italy)

## Breast cancer pathology - a manifesto for optimal care

**This manifesto calls for:**

**High quality, timely breast cancer pathology services that meet the needs of cancer patients and oncologists**

**By:**

- **Ensuring a full range of diagnostic and prognostic pathology services is available**
- **Promoting professional development for pathologists and their technicians, and full integration with multidisciplinary working in cancer care**
- **Organising hospital pathology services to deliver timely information for decision making and ensuring that pathologists are part of the team visible to patients**
- **Monitoring and reporting undue variability in pathology results nationally and internationally**
- **Introducing quality standards and reporting that are focused on services and care for breast cancer patients**
- **Promoting pathology as a vital and major discipline with substantial career potential in clinical practice and translational research**

## **Introduction**

Pathology is a medical speciality that underpins decision-making in many crucial steps of cancer care. Pathologists in many countries are medical doctors who are responsible for a wide – and rapidly growing – range of diagnostic reports on tissue that supports detection and characterisation of disease, and informs the treatment and care carried out by surgeons, oncologists, radiotherapists and other health professionals in the cancer team.

Pathologists play a vital role in managing all types of cancer but their work can be compromised by lack of resources, training and multidisciplinary teamwork in hospitals, and a lack of commitment to a patient-centred, accountable service at national level. They are often the ‘invisible’ members of the oncology team and should be available to meet patients and explain reports.

This manifesto sets out optimal requirements for a pathology service for breast cancer, but the principles are applicable to oncology generally. It is a call for all involved – pathologists, oncologists, patients, advocates, healthcare administrators and policymakers – to check and improve where necessary this vital discipline.

## **The need for optimal pathology in breast cancer**

Surgeons and oncologists rely on pathology reports to carry out treatment on breast cancer patients. They need to be confident that the reports are as accurate as possible for patients and doctors to make decisions on the type of surgical operations to carry out and the use of chemo- and radiotherapies – and also if there is no need for treatment.

They also need accurate information to make decisions on possible follow-up operations and to monitor how treatments are going, and healthcare systems and researchers need high-quality specimens provided by pathologists for research and possible future care for patients.

But currently there are concerns about the quality of pathology services. Specifically:

- They can vary to a considerable extent in the accuracy of assessing parameters important for treatment decision-making
- Few countries are monitoring and assessing this variability
- Most pathology departments are general and may lack pathologists experienced in the increasingly complex area of breast pathology, and may also lack sufficient volume of cases to develop and maintain expertise
- Quality assurance in breast cancer pathology, and pathology generally, is mostly focused on laboratory systems and minimal acceptable standards, and not on the needs of patients and health service commissioners
- In many countries there is a shortage of pathologists.

Data that are available on variability show that as many as xx% of breast cancers specimens are given a different diagnosis when sent for second opinion, and about x% result in major changes in treatment. There can be major discordance in immunohistochemical and molecular tests. *[exact sources to come as position paper is prepared]*

It is recognised that cancer pathology is not an exact science – much depends on the expertise and judgement of pathologists in interpreting specimens and test results that now span traditional microscopic examination, to high volume laboratory testing of molecular receptor expression, to genetic testing. Further, pathology should be part of a multidisciplinary team, and not isolated from decision-making.

It is also recognised that there are limitations on what can be expected from pathology services. Many are under great pressure, with some national systems handling hundreds of millions of requests a year, and it is unrealistic to, for example, call for mandatory second opinions on routine breast cancer biopsies.

But as other parts of the breast team come under closer scrutiny with their own guidelines, pathologists – and breast cancer patients – should also benefit from the criteria set out in two parts of this manifesto, which is aimed at defining a high quality service centred on the patient, and which is within the reach of all countries.

It covers:

- Essential diagnostic and prognostic services that should be available in a timely manner
- Organisation, from individual to national level, that promotes high quality, timely services.

## **Part 1: Optimal breast cancer pathology – essential diagnostic and prognostic services**

Pathologists need to provide:

- Accurate and detailed diagnosis of breast cancer from the examination of the specimen
- Prognostic parameters from this morphological examination
- Molecular parameters that determine therapeutic decision making and predict the patients' response to the applied therapy
- Evaluation of the efficacy of surgical and oncological treatment.

Specifically, the main types of service are:

- Preoperative diagnosis of needle biopsy specimens from primary tumour or metastases
- Frozen section diagnosis during an operation to assess sentinel lymph node status and surgical margin status, if needed
- Detailed analysis of the operation specimen from the breast, lymph nodes or metastatic sites

- Interpretation of the findings after neoadjuvant therapy (drug therapy given before a surgical operation)
- Presenting findings to multidisciplinary meetings to correlate with radiological images and so give the best clinical picture.

The following are the main parameters that should be assessed in a timely and high quality way by breast cancer pathology services. In each case, it is stated why the parameters are important.

### **Tumour type**

It is a fundamental task to determine the histological tumour type and subtypes according to established criteria in the World Health Organization (WHO) histological classification of tumours of the breast (low-risk or high-risk benign lesions, non-invasive tumours, invasive carcinomas of not special type or special types, other tumours) – information that has high prognostic value.

### **Tumour size**

Tumour size is one of the key parameters for determining prognostic outlook and is usually measured by pathologists from the surgical specimen. In addition to tumour size, disease extent corresponding to the volume of the tissue, including all the components of the cancer, is of clinical significance.

### **Tumour grade**

This is further histological analysis of tumour differentiation according to a defined scale (the Bloom-Richardson grading system as modified by Elston and Ellis). Prognostic value lies in the degree of abnormality from normal tissue.

### **Lymph node status**

Pathologists also carry out microscopic examination of removed lymph nodes to detect or verify suspected spread of breast cancer cells to the nodes. The same applies to specimens from other organs where the spread of cancer cells is suspected. *Metastatic tumour spread to distant organs or spread to lymph nodes are the most powerful prognostic parameters in breast cancer.*

### **Operative margins**

From surgical specimens, pathologists take measurements of the margins of tissue around the tumours to determine if a second operation is required to completely remove all the components of the tumour. Residual tumour tissue increases the risk of local relapse (cancer recurring in the breast) after surgery.

### **Peritumoral vascular invasion**

This is a histological examination of the vessels around tumours to detect or rule out presence of cancer cells within them. The presence of tumour cells could indicate spread to the lymph nodes and steps towards metastasis.

### **Multi-focality/centricity**

Multifocal means more than one tumour in one breast quadrant, multicentric is more than one tumour in two or more quadrants. The presence of multiple tumours increases the risk of cancer spread and pathologists should work with surgeons and radiologists to provide treatment plans for these often complex situations.

### **Hormone receptor status (ER/PR)**

Immunohistochemical tests for detecting expression of oestrogen and progesterone receptors (ER and PR) in the cancer cells are essential to provide prognostic information and predict suitability

for endocrine therapy.

### **HER2 status**

Immunohistochemical and molecular tests for human epidermal growth factor receptor 2 (HER2) also provides prognostic information and may indicate that targeted drug therapy should be offered.

### **Ki67 labelling index**

This is another immunohistochemical test that is a marker of cell proliferation and may show a fast-growing tumour and indicate sensitivity for cytostatic agents such as endocrine therapies.

In addition, these services are likely to be needed in future:

### **Gene profiling**

This is a promising tool that may become a standard of care as a prognostic tool. There are particular approaches that must be followed to produce samples suitable for gene profiling.

### **Biobanking**

Collecting samples of primary and metastatic tumour tissue, blood or bone marrow for ongoing and future research is becoming an integral part of routine breast pathology services.

## **Part 2: Optimal breast cancer pathology – organisation**

This section of the manifesto lists optimal organisational factors for pathology from individual to national level.

### **Individuals – professional expertise and development requirements**

- A high level of competency in all aspects of breast pathology, including both classical morphological and modern molecular/genetic aspects, according to current guidelines
- Continuous education and improvement of diagnostic skills
- Understanding of the clinical consequences of every detail in the pathology report
- Networking with experts for discussing professional views

### **Departmental requirements**

- Access to all relevant clinical information for each patient
- Full attention to breast specimens and a team of technicians that provides high quality breast preparations
- Day-to-day multidisciplinary teamworking, such as with detailed correlation between radiology and pathology, and with molecular biology and pathology
- Understanding of the capabilities and limitations of imaging methods, biopsy modalities and histopathology techniques
- Pathologists should be part of the patient-facing team and available to explain reports to patients
- At least, an informal system for obtaining or giving second opinions on selected cases, involving experts at external institutions

## Hospital requirements

- ECC 2015
- ECCO  
website