Inter- and intra-laboratory variation in grading of invasive breast cancer: a nationwide study of 33,043 patients in the Netherlands

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Disclosure Information

I hereby declare that I have no conflict of interest
Breast cancer: background

• Most common type of cancer in European women\(^1\)

• Breast cancer management: *it all starts with pathology*
  – Subtype: \textsc{pathology}
  – Prognosis: \textsc{pathology}
  – Treatment: \textsc{pathology}

\(^1\) International Agency for Research on Cancer (WHO), source: GLOBOCON 2018
Breast cancer biomarkers

• Histologic grade
  – B&R (modified)

  – Clinical decisions
    • Chemotherapy
    • Radiotherapy
    • Gene-expression profiling
Reproducibility histologic grading

• No more than moderate\textsuperscript{1-4}

But how are we doing in daily clinical practice?

Real-life data on a Dutch nationwide level

the nationwide network and registry of histo- and cytopathology in the Netherlands

• Synoptic reporting

2. PALGA Foundation, Annual Report 2018
Grading in the Netherlands; 2013-2016 (n=33,792)
Laboratory-level (n=39)

Case-mix: age, tumour size, type of surgery, histologic subtype, ER/PR- and, HER2-receptor status
Grading in the Netherlands; 2013-2016 (n=33,792)

Laboratory-level (n=39)

**Grade II**
- Mean: 47.6%
- Range: 38.4-57.8%

**Grade III**
- Mean: 24.3%
- Range: 15.5-34.3%
Grading in the Netherlands; 2013-2016
Pathologist-level (n=68, 8 laboratories)
Grading in the Netherlands; 2013-2016
Pathologist-level (n=68, 8 laboratories)
Grading variation; does it really matter?

Chemotherapy (n=19,461)

According to the Dutch breast cancer guideline, adjuvant chemotherapy (aCT) is advised for patients with a positive lymph node status (N+), and for patients with a negative lymph node status (N0) with the following characteristics:

- Age < 35 years, except for a grade I tumor < 1 cm
- Age ≥ 35 years with a tumor of 1.1-2 cm and ≥grade II, or a tumor > 2 cm
- HER2 overexpression in a tumor ≥ 0.5 cm

N0: n = 13,077
N+: n = 6,384
HER2+: n = 1,119
HER2-: n = 11,958

< 0.5 cm: n = 43
≥ 0.5 cm: n = 1,076

Grade I: no aCT
Grade II-III: aCT

Conclusion: histologic grading

- Synoptic pathology reports of >33,000 patients

- **Substantial inter- and intra-laboratory variation** in grading of invasive breast cancer in daily clinical practice
  - Not explained by differences in case-mix

- Biomarker of major clinical importance
  - Indication chemotherapy
    - 1 in 3 breast cancer patients
    - 1 in 2 lymph-node negative breast cancer patients

- **Decrease in variation warranted!**

- **Interventions**
  - Feedback reports
  - E-learning
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