Automated Ki67 hot-spot detection and analysis

Mieke Zwager
MD, PhD student
Department of Pathology
University of Groningen, University Medical Center Groningen
The Netherlands
Background

Ki67

- Nuclear protein
- Expressed during cell cycle
- Prognostic and predictive in breast cancer
Background

Standardised manual Ki67 hot-spot scoring
• Select one high-power field with highest staining rate
• Count up to 500 cells
• Type-writer pattern
• Median scoring time: 6 minutes (4-8)

Background

Hot-spot scoring

• Visual identification is difficult
• Labour-intensive
• Inter- and intra-observer variability
  • Inter-observer reproducibility/ICC of 0.8
Background & Objective

Digital image analysis
• Automated detection and scoring
• Standardised and reproducible

Objective
• Compare manual Ki67 hot-spot scoring and detection with digital image analysis (DIA)

Methods

102 breast carcinomas

Manual hot-spot detection and scoring
Methods

Manual hot-spot detection and scoring

DIA manual hot-spot

Automated hot-spot detection and scoring
Automated hot-spot selection and analysis

1. Tumor identification
2. DCIS vs. invasive tumor discrimination
3. Ki67 quantification
4. Heat map creation
5. Hot spot identification
6. Ki67 quantification within hot spot
Manual Ki67 hot-spot correlation is suboptimal

$R^2 = 0.78$
Manual and DIA scores of the manual ROIs strongly correlate

\[
R^2 = 0.90
\]
Automated Ki67 hot-spot analysis leads to higher proliferation indices

Mean Ki67 hot-spot score

- Observer 1
- Observer 2
- DIA

Mean Ki67 hot-spot score
Conclusion

Automated Ki67 hot-spot detection and analysis is a reliable method that leads to higher hot-spot Ki67 proliferation indices
Acknowledgments

UMCG/UG
• Dr. Bert van der Vegte
• Dr. Timco Koopman
• Henk Buikema

Visiopharm
• Dr. Henrik Klingberg
• Dzenita Omanovic
• Dr. Andreas Schønau