

PathScore™ – An automated Breast Cancer Grading Demonstrator

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Abstract

The project reported here has developed automated computer analysis for grading invasive breast cancer using the Elston and Ellis grading scheme.

The dataset used consisted of 47 samples of invasive carcinoma from the NHSBSP EQA scheme assessed by 733 pathologists. Gland formation, nuclear atypia/pleomorphism, mitotic frequency and overall grade were scored automatically by the system.

Evaluation was against the majority view of all pathologists. The grade allocated by pathologists was usually not unanimously agreed, the level of agreement varied widely. Evaluation showed that PathScore's performance was similar to that of the human pathologists. Overall grade agreement between the Pathologists and PathScore grade was good, although there was some tendency for PathScore to overestimate the severity of Nuclear Pleomorphism. The observed agreement (68.09%) is twice as high as could have been observed by chance. The weighted kappa of 0.591 is statistically very highly significant and there is no evidence of any significant disagreement over any category or its asymmetry. By coincidence the level of agreement on the final grade amongst the pathologists yielded an identical kappa value (kappa = 0.59).

PathScore provides the potential for enhanced objectivity and reproducibility offering a standardized objective and reliable method for histological grading of breast cancer on routine clinical samples.

Breast Cancer

Diagnosis is based on a combination of:

- Radiological, surgical and **pathology assessment**

Pathology assessment is based on detailed evaluation of tissue samples

- Tumour **grade**, size, type
- Lymph node status
- Steroid hormone status
- HER2 status

This forms the basis of the patient's optimal treatment planning

Current Slide Management

Problems with current modes of slide management and analysis:

Glass slides are viewed under the microscope

- Cumbersome
- Can be broken
- Usability is determined by the age of the slide and the quality and timing of the staining

Digitised slides are stored off-line and retrieved to view on line

- Access one slide at a time
- Cannot access multiple slides with ease
- Time intensive

Pathology Analysis

Visual interpretation of complex microscopic images:

- Time consuming
- Liable to inter- and intra-observer variation of up to 50%
- In the NHS National External Quality Assurance scheme
 - The same slide is graded as 1, 2 or 3 by different pathologists

NEQAS work has improved the concordance of this grading from 0.3 Kappa to 0.6; however, the performance still varies. There is a need for a new approach.

Solution:

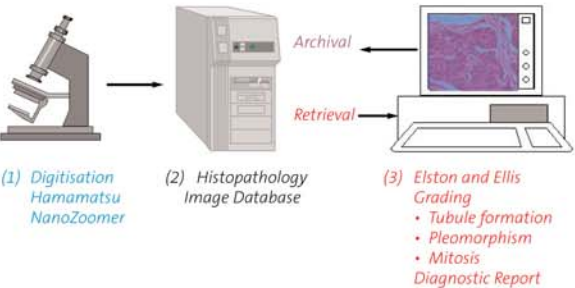
An automated system that provides an objective and reproducible quantitative assessment of the diagnostic features

- Improve the reproducibility and consistency of diagnosis
- Support and complement pathologist's diagnosis
- Increase throughput

The PathScore project has developed automated computer analysis for grading breast cancer using the Elston and Ellis grading scheme.

PathScore™ System

- (1) Whole slides are digitised by the Hamamatsu NanoZoomer scanner and stored in the PathScore database system.
- (2) System is designed to:
 - Manage multiple slides from same and different patients
 - Allow viewing of slides at different resolutions
- (3) Automatic grading of the slide based on the Elston and Ellis grading system and generates a patient's diagnostic report



Data

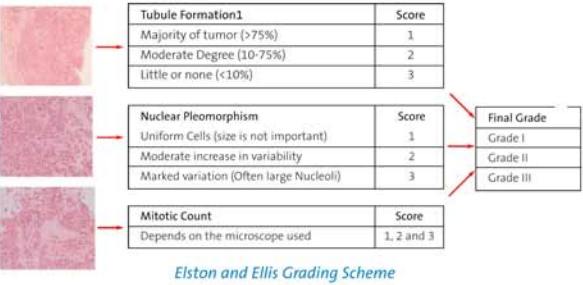
Slides are scanned at:

- x40 resolution
- Sub-sampled for x10 processing when required
- Images are compressed, c.f. raw

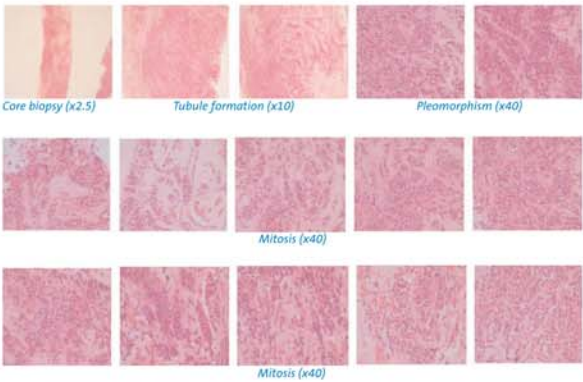
NHS National External Quality Assurance Scheme (NEQAS) program

- 47 cases were used for this evaluation

Automated Breast Cancer Grading



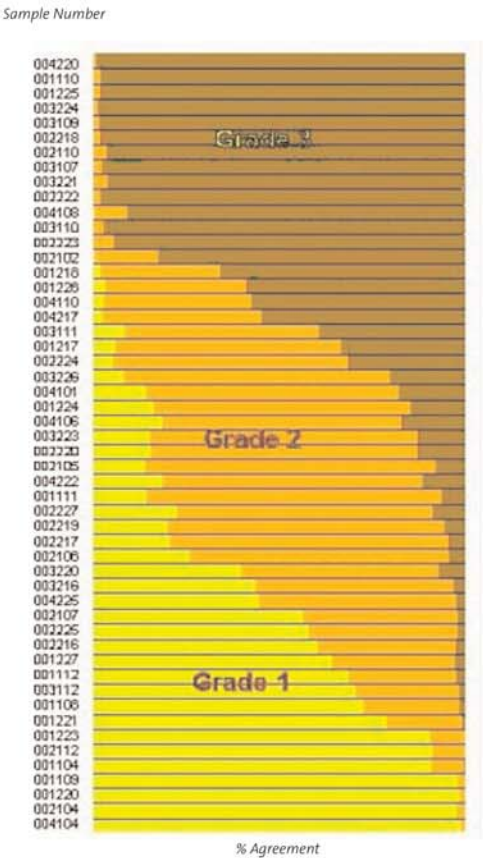
Minimum Patient Grading Data



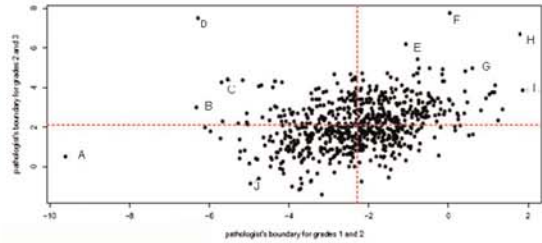
Ground Truth for Evaluation

- The ground truth is based on the scores from 733 pathologists
- Evaluation was thus carried out against the majority view of all pathologists
- The grade allocated by pathologists was usually not unanimously agreed, the level of agreement varied widely.

Pathologists' Agreement



Graphical Representation of Pathologists' Grading

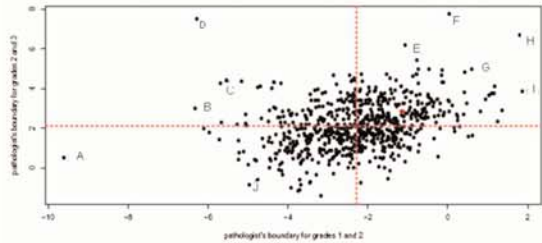


Location of the mean and outliers shown

Observation of Pathologists' Performance

- Pathologist H, marked on the graph, has cut-off values of around +1.75 and +6.75, which are both high compared to the majority. This indicates a reluctance to give grades 2 and 3 (compared to other pathologists) unless s/he judges the tumour to be extremely severe
- Pathologist A has cut-off values of around -9.5 and +0.75, both low compared to the majority. This indicates that a tumour does not have to be very severe at all on the scale before s/he gives a grade of 2 or even 3. In fact, so differently do these two pathologists perceive the scale that any tumour lying between +0.75 and +1.75 on this underlying scale would be given a grade 1 by pathologist H but a grade 3 by pathologist A
- Similarly pathologists C and D display a tendency to give the grade 2 rather than 1 or 3 as would be done by the majority of their peers
- The points on the graph represent an overall view of the rating performance of each pathologist and consequently any differences cannot be attributed to the possible disparities between the slides sent to them, as these could be assumed to be random

PathScore (in red) and 733 Pathologists



Location of the mean and outliers shown

PathScore's Performance

PathScore sits happily within the main cluster of the pathologists PathScore cannot be differentiated from the human pathologists

Conclusions

- The PathScore project has developed automated computer analysis for grading invasive breast cancer using the Elston and Ellis grading scheme
- PathScore provides the potential for enhanced objectivity and reproducibility offering a standardized reliable method for histological grading of breast cancer on routine clinical samples
- Evaluation showed that PathScore's performance was similar to that of the human pathologists
- Overall grade agreement between the Pathologists and PathScore grade was good, although there was some tendency for PathScore to overestimate the severity of Nuclear Pleomorphism
- The observed agreement (68.09%) is twice as high as could have been observed by chance
- The weighted kappa of 0.591 is statistically very highly significant and there is no evidence of any significant disagreement over any category or its asymmetry
- By coincidence the level of agreement on the final grade amongst the pathologists yielded an identical kappa value (kappa = 0.59)