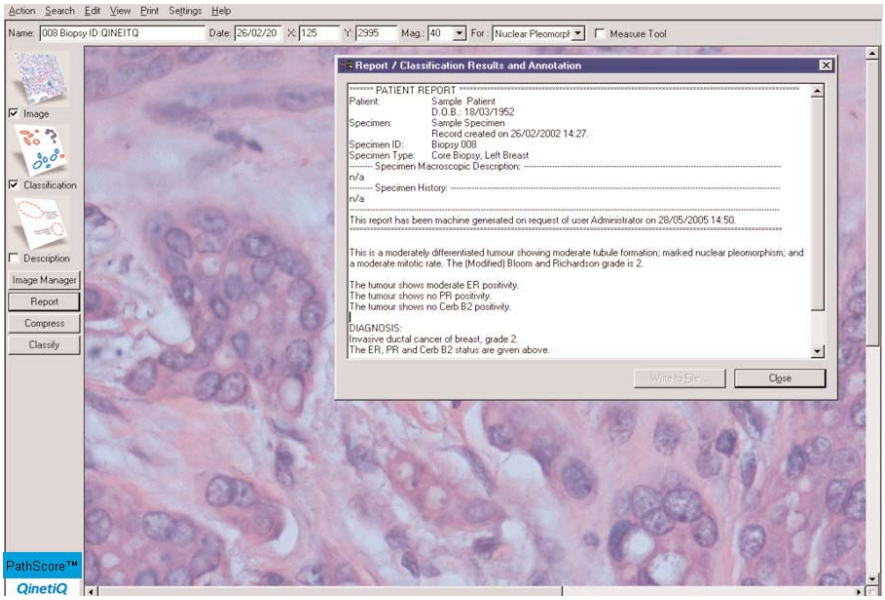
Automated Histopathology Breast Cancer Analysis and Diagnosis System



An automated histopathology breast cancer analysis system

- Breast cancer grading
- Oestrogen receptor (ER) and progesterone receptor (PR) scoring
- HER2 scoring
- Electronic patient report generation
- Supporting trials performed
- Patents

The QinetiQ Automated Histopathology Breast Cancer Analysis and Diagnosis System (Pathscore™) has been developed to provide an automated and objective system to grade breast cancer and score ER, PR and HER2 to support the pathologist's diagnosis, patient prognosis and treatment planning.

Diagnostic Features Analysed

- Breast Cancer Grade:
  - Tubule formation
  - Nuclear pleomorphism
  - Mitotic count
- ER and PR score
- HER2 score

Background

Breast cancer is one of the most common cancers in women worldwide. The diagnosis is made using a combination of radiological, surgical and pathological assessment. The latter involves a detailed evaluation of tissue samples by the histopathologist that establishes the diagnosis and provides prognostic information (tumour size, grade, type, lymph node status, steroid hormone and HER2 status). The optimal treatment can be planned for the patient on the basis of this information.

The Problem

Pathological analysis of tissue samples entails visual interpretation and quantification. This is a subjective process and, given that many new molecular markers may come into the diagnostic and therapeutic realm, it may become an even more time-consuming process. The problem is made acute by the shortage of pathologists. An automated and objective histopathology analysis system would support this pathological assessment.

The Solution –

Automated Pathology Assessment

QinetiQ, in collaboration with the University of Oxford, has developed an automated objective histopathological analysis system which produces a quantified grading of breast cancer. The system uses state-of-the-art image processing technologies to carry out a fully automated analysis. It generates an automatic tumour grade and score for ER, PR and HER2 as assessed by immunohistochemistry.

The system has been clinically evaluated on 100 patients at the Histopathology Department of the John Radcliffe Hospital and Oxford and Cambridge Universities. The performance of the automatic analysis is similar to the performance of human pathologists – with three participating pathologists in the study. The unique approach offered by QinetiQ is equally applicable to the analysis of other tissues and bio-markers.

The system is based on state-of-the-art defence technology capabilities built up by research carried out under the Ministry of Defence Corporate Research Programme. The novel technologies which lie at the core of the system are covered by a suite of patents which are equally applicable to other tissue types.

Pathological Assessment

The automatic system carries out Elston and Ellis grading, ER and PR scoring and HER2 scoring.

Breast Cancer Grading

The Elston and Ellis breast cancer grading system, shown in Table 1, uses the histological characteristics of the breast carcinoma. The cancer grade is calculated by adding the individual scores for each diagnostic feature (Table 2).

Tubule Formation	Score
Majority of tumour (>75%)	1
Moderate Degree (10-75%)	2
Little or none (<10%)	3

Nuclear Pleomorphism	Score
Uniform Cells	1
Moderate increase in cell size and moderate variability in cell size and shape	2
Marked increase in cell size and variation in cell size and shape	3

Mitotic rate	Score
Measurement depends on the microscope used	1,2 and 3

Table1: Elston and Ellis grading Scheme

Final GRADE	Score*	5-year survival	7-year survival
Grade I, well differentiated	3-5 points	95%	90%
Grade II, moderately differentiated	6-7 points	75%	65%
Grade III, poorly differentiated	8-9 points	50%	45%

Table 2: Survival scores

**Score is calculated by addition of the individual scores for tubule formation, pleomorphism, and mitotic rate.*

Scoring of ER and PR

ER and PR status are overall weak prognostic factors in breast cancer. Their main use is in predicting response to endocrine therapy. Approximately 60% of ER-positive tumours respond to hormonal manipulation with Tamoxifen and have an improved prognosis. When assessment of PR is added the prediction of response is better - almost 80% of ER-/PR-positive breast cancers will respond to this therapy, whereas only 10% that are ER-/PR-negative will respond to the treatment.

Scoring of HER2

About 25-33% of breast cancers overexpress a cell surface membrane bound protein called Human Epidermal Growth Factor Receptor Protein2 (HER2) largely as a result of amplification of the HER2/neu gene. Altered expression of this protein is both a prognostic, associated with high tumour grade and reduced survival, and predictive factor, associated with reduced response to certain chemotherapy regimes and Tamoxifen. Detection of over-expression of the HER2 protein by immunohistochemistry is a recommended method of assessing the receptor status and guiding treatment with the appropriate antibody - the humanised monoclonal antibody Herceptin.

The technology is licensed to Zi Medical plc.

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