A system for automated screening for cervical cancer

Medicinsk

Visiondag

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Visible Diagnostics A/S

Outline of presentation

- Why screen at all?
- The Pap test
- Automation
- Competition
- Our approach

Why screen at all?

Cervical cancer statistics

A major killer and global healthcare problem

- Cervical cancer is the second most common cancer among women worldwide.
- In developing countries, cervical cancer is the leading cause of death from cancer.
- Annually, about 370.000 new cases of cervical cancer occur worldwide.
- This cancer kills around 230.000 each year.
- Cervical cancer develops slowly and has a detectable and treatable precursor condition known as dysplasia.
- It can be prevented through screening at-risk women and treating women with precancerous and cancerous lesions.
- The Pap smear test was designed to identify abnormalities and is the most widely used screening test for cervical cancer. It is placed under a microscope and examined by a cytotechnologist for signs of abnormality.
- In many Western countries, cervical cancer screening programs (based on cytology - Pap smears) have reduced cervical cancer incidence and mortality by as much as 90 percent.

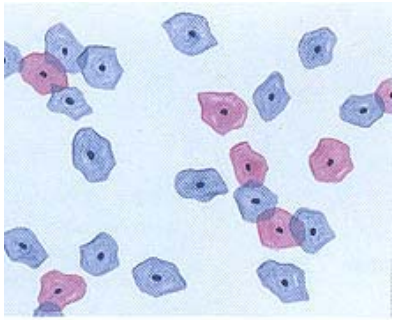
The Pap test

The Pap Test

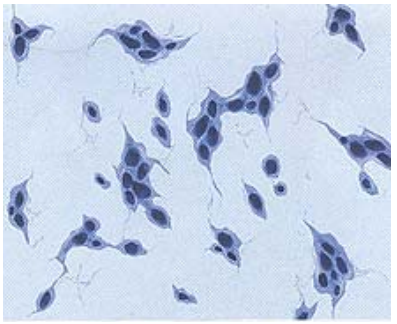
- Developed 50 years ago
- Involves collecting a sample of cells from the cervix
- Smears analysed by cytotechnologist trained to recognise tumour cells
- Test most effective when cervical cancer is at its earliest stage of development

Reading the slides

Reading the slides at the laboratory



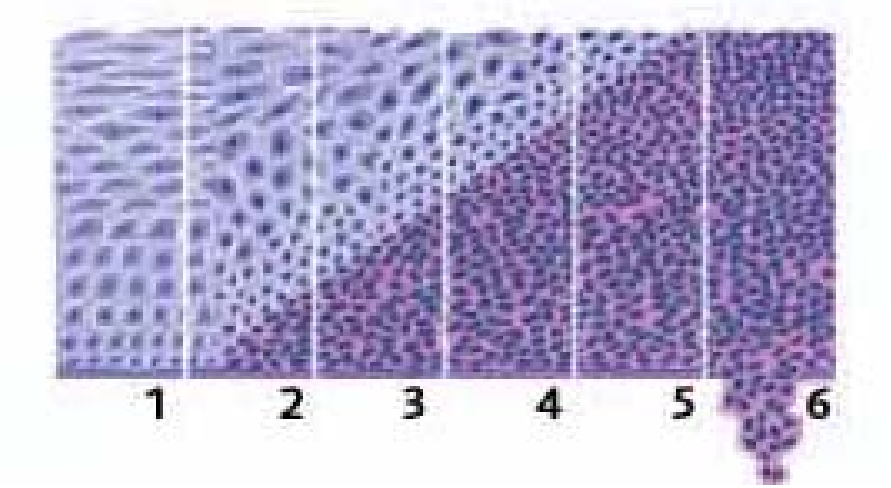
Normal cells



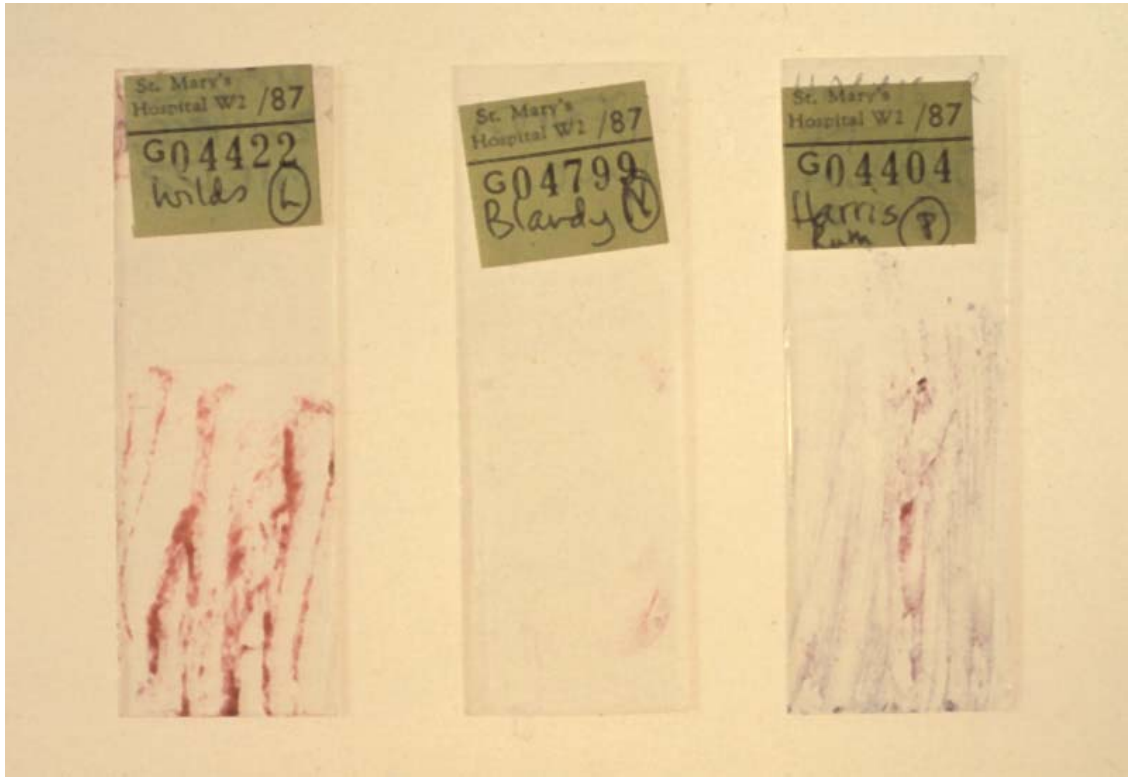
Abnormal cells

What do abnormal results mean?

The Pap test (or Pap smear)



1. Normal.
2. Mild dysplasia (LSIL or CIN 1).
3. Moderate dysplasia (HSIL or CIN 2).
4. Severe dysplasia (HSIL or CIN 3).
5. Carcinoma in situ (HSIL or CIN 3).
6. Cervical cancer, or invasive cervical cancer, occurs when abnormal cells spread deeper into the cervix or to other tissues or organs.


St. Mary's Hospital W2 /87
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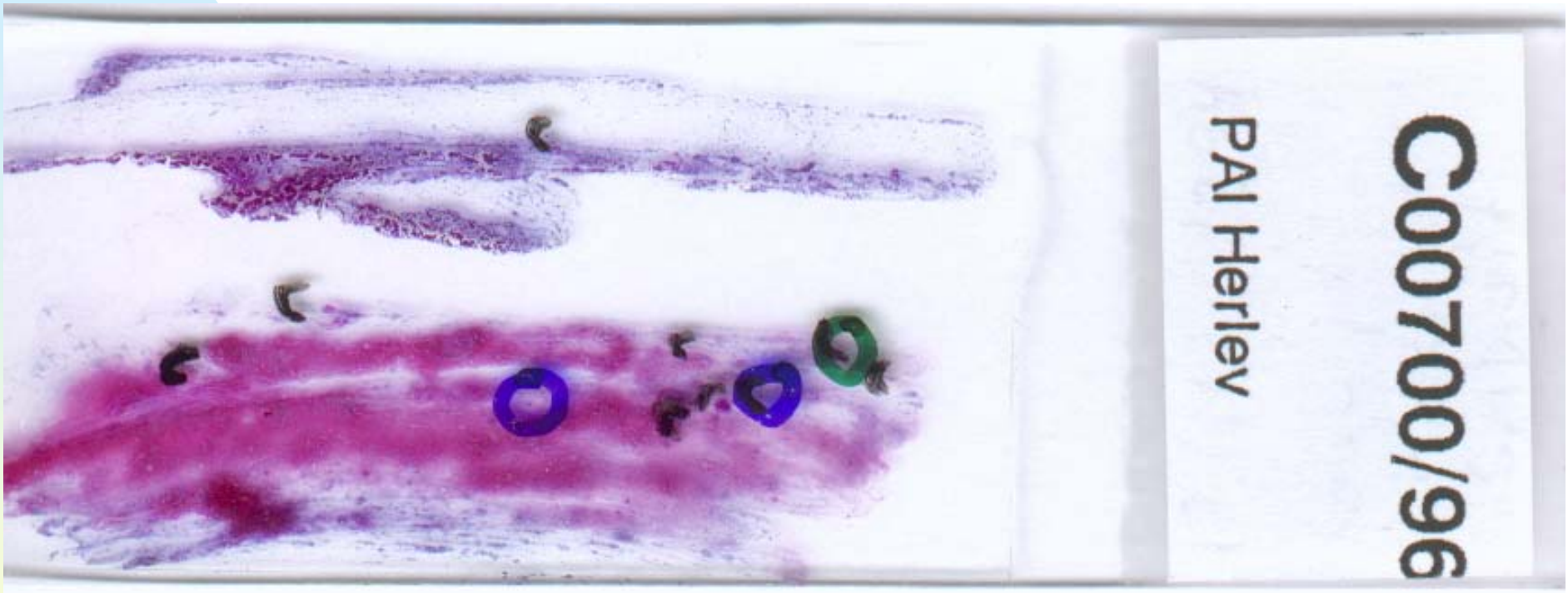
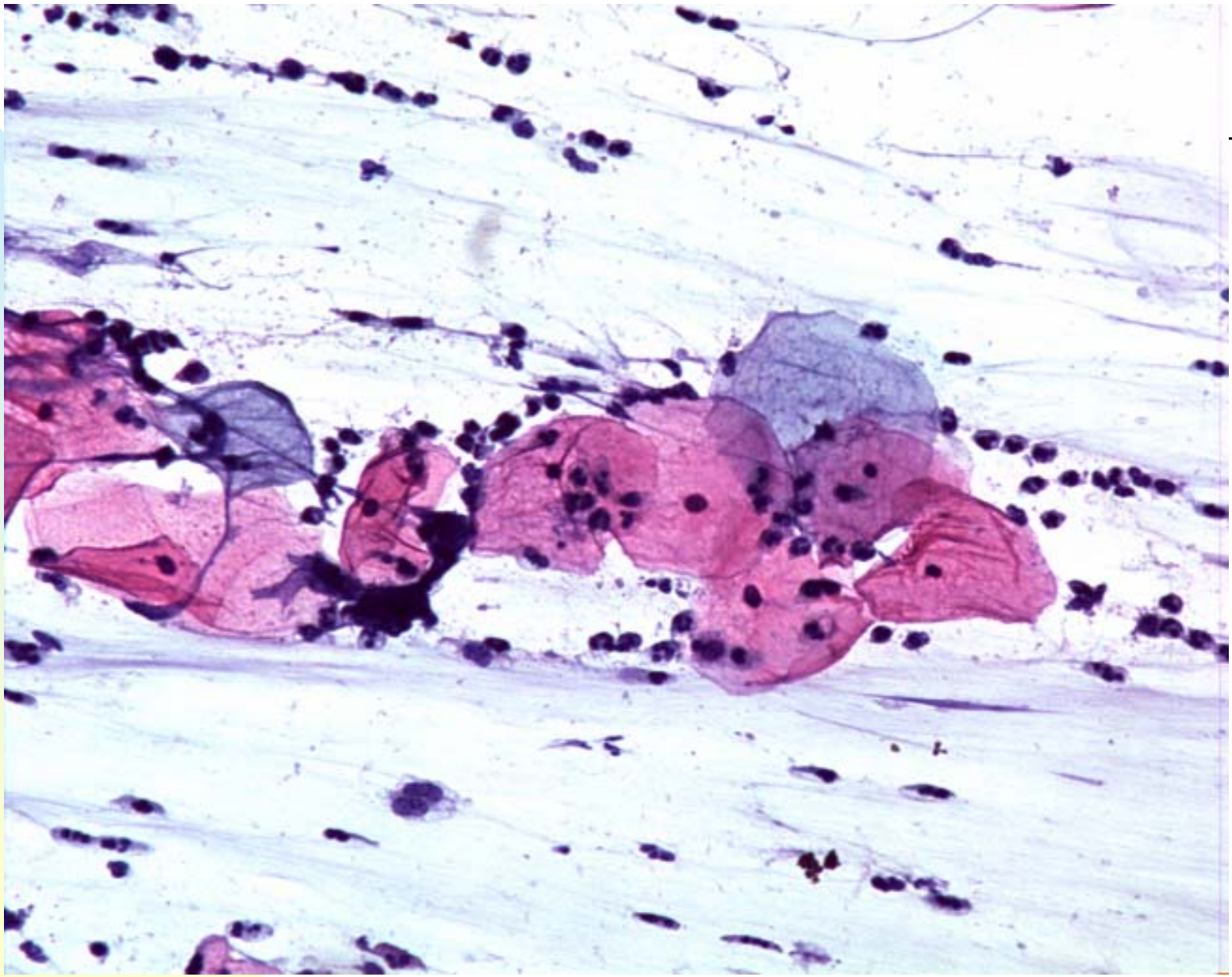
Blandy
St. Mary's Hospital W2 /87
G04404
Harris

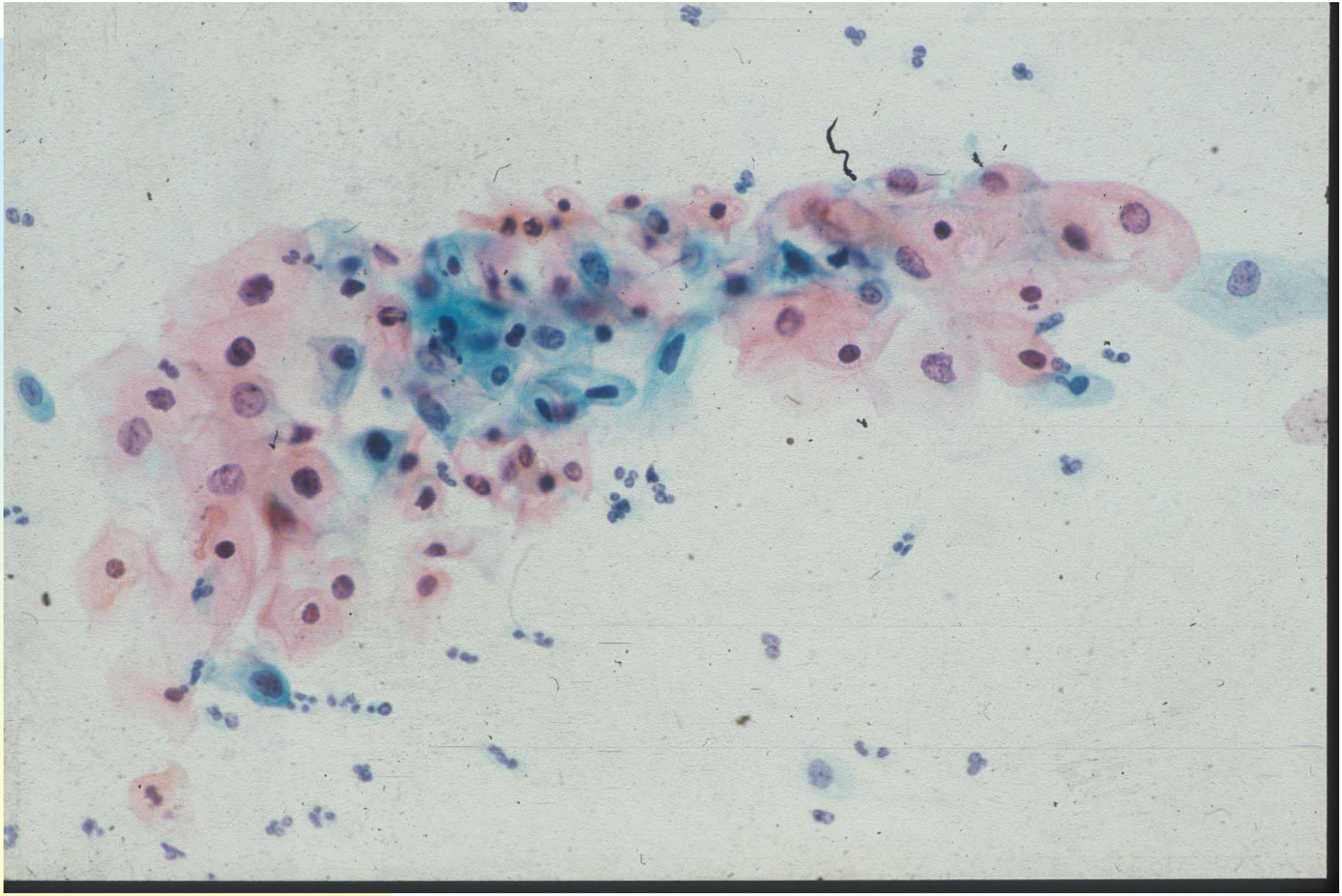
Slide



Normal cells



Abnormal cells



Automation

Need for automation

- Primary screening is repetitive, labour intensive , time consuming task subject to errors of interpretation (7-10% abnormal smears missed)
- Quality assurance measures are of limited value
- Shortage of trained cytotechnologists

The market size

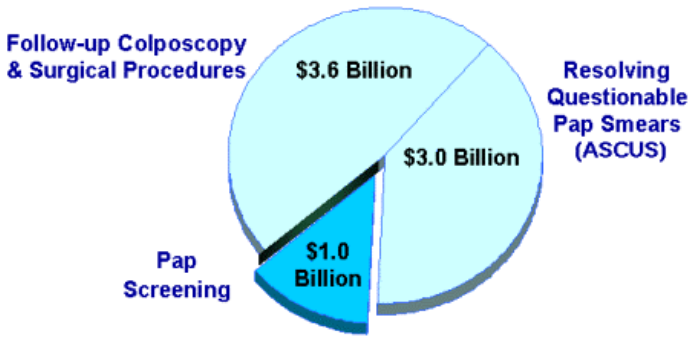
The size of the potential market opportunity

A patented technology that helps cervical cancer prevention naturally has a huge market potential.

The market size for an automated screening system for detection and classification of Pap smears:

- An estimated 160 million Pap smears are performed annually in the industrialised world.
- Approximately 55 million are done in the USA.

Current clinical management of cervical cancer leads to
US health care spending of $7.6 Billion Annual expenditures



Problems associated with automated image analysis systems

- Segmentation
- Feature extraction (morphometric densitometric, colorimetric, texual and contextual)
- Decision strategy for classification of smears
- Need to meet international standards for automated cervical screening

Competition

Competition

Tripath Imaging

- Colour information is ignored altogether
- Many of the image processing steps are sensitive to noise
- Dependency on a large number of controlling parameters (optimisation difficult)
- Not applicable to high risk groups (now required by FDA)
- NFR at max. 25% (batch dependent)

Our approach

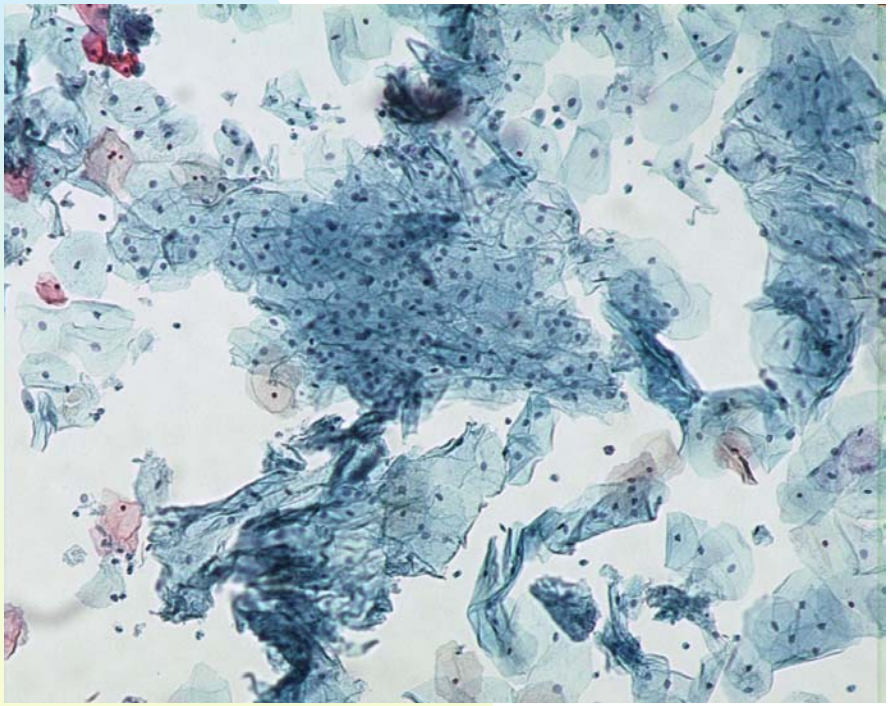
The ”Visible Diagnostics” Approach

1. Image acquisition
2. Colour standardisation and segmentation*
3. Nucleus identification and delimitation*
4. ‘Natural’ classification technology*
5. Cell measurement
6. Slide grading*
7. Slide categorisation

* Patented or patent pending

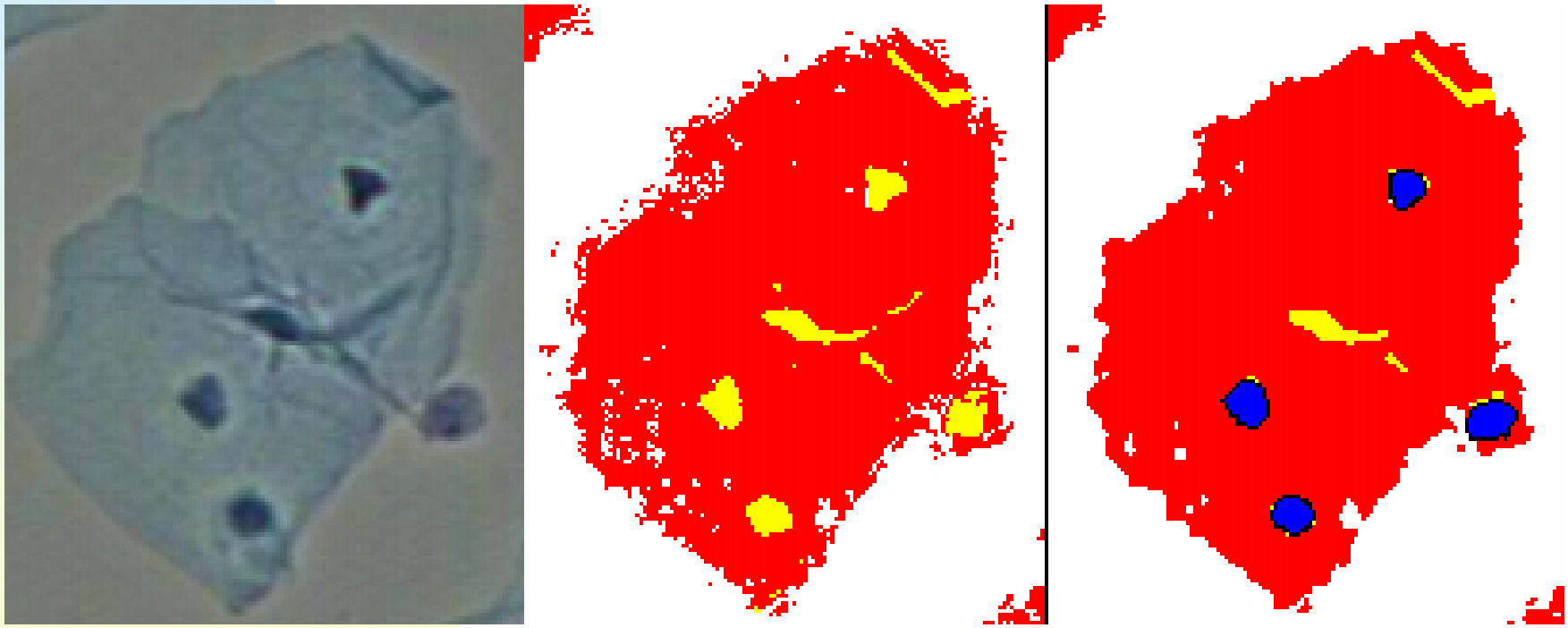
CCS System

Colour Standardisation and Segmentation



- Colour standardisation
- Colour segmentation

Nucleus Identification and Delimitation



Left: Image subset, background corrected

Center: Same, after color segmentation

Right: Same, after nucleus identification and delimitation

‘Natural’ Classification Technology

- Instance based algorithm: direct reference to expert databases
- Detailed rendering of class boundaries
- Non-adjacent parts of parameter space may belong to the same diagnostic class
- Similarity-based non-metrics

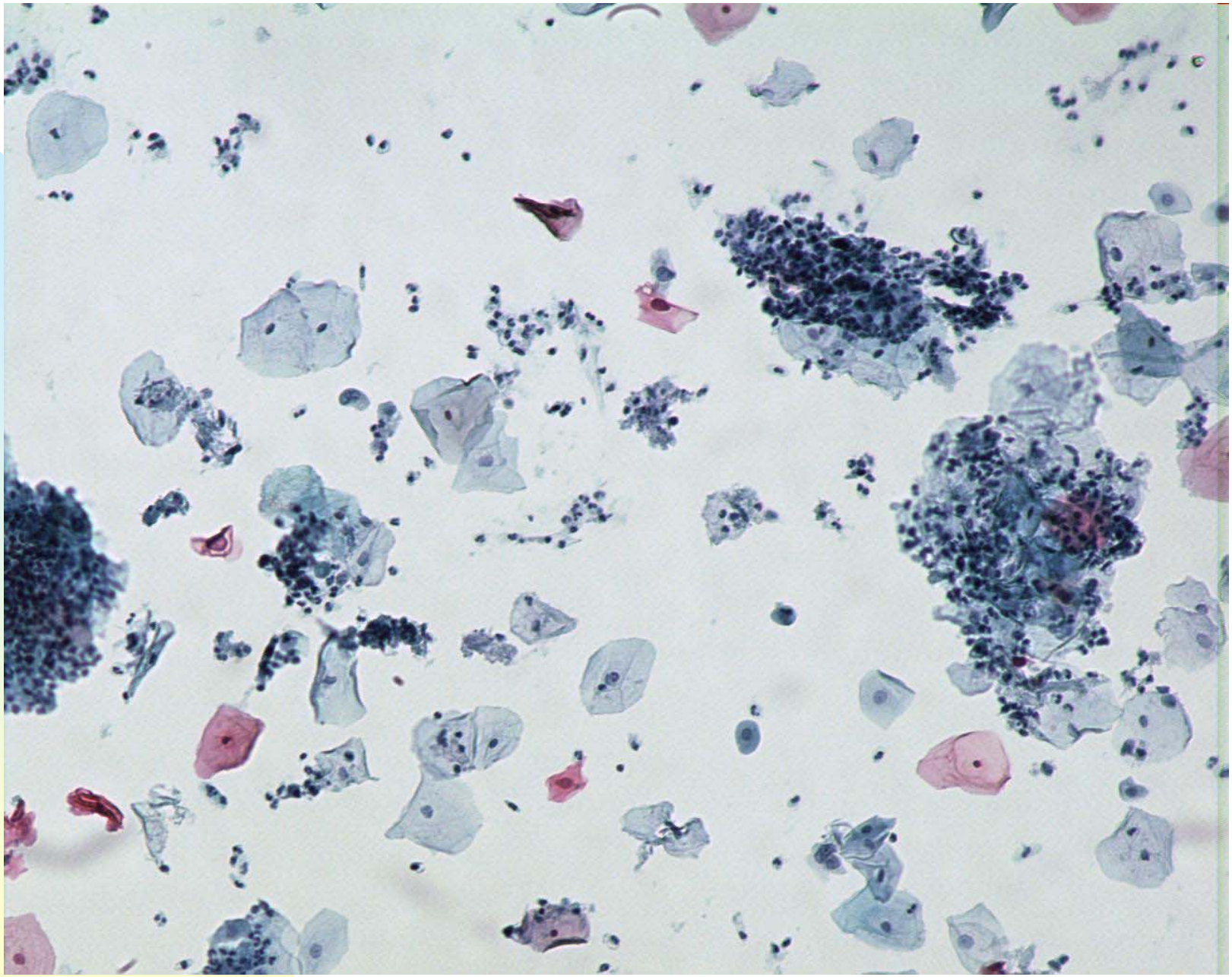
Cell Measurements

- Large number of measurements (ca. 100) on nucleus and cytoplasm:
  - Dimensions
  - Shape
  - Texture and colour
  - Optical density
  - Etc.

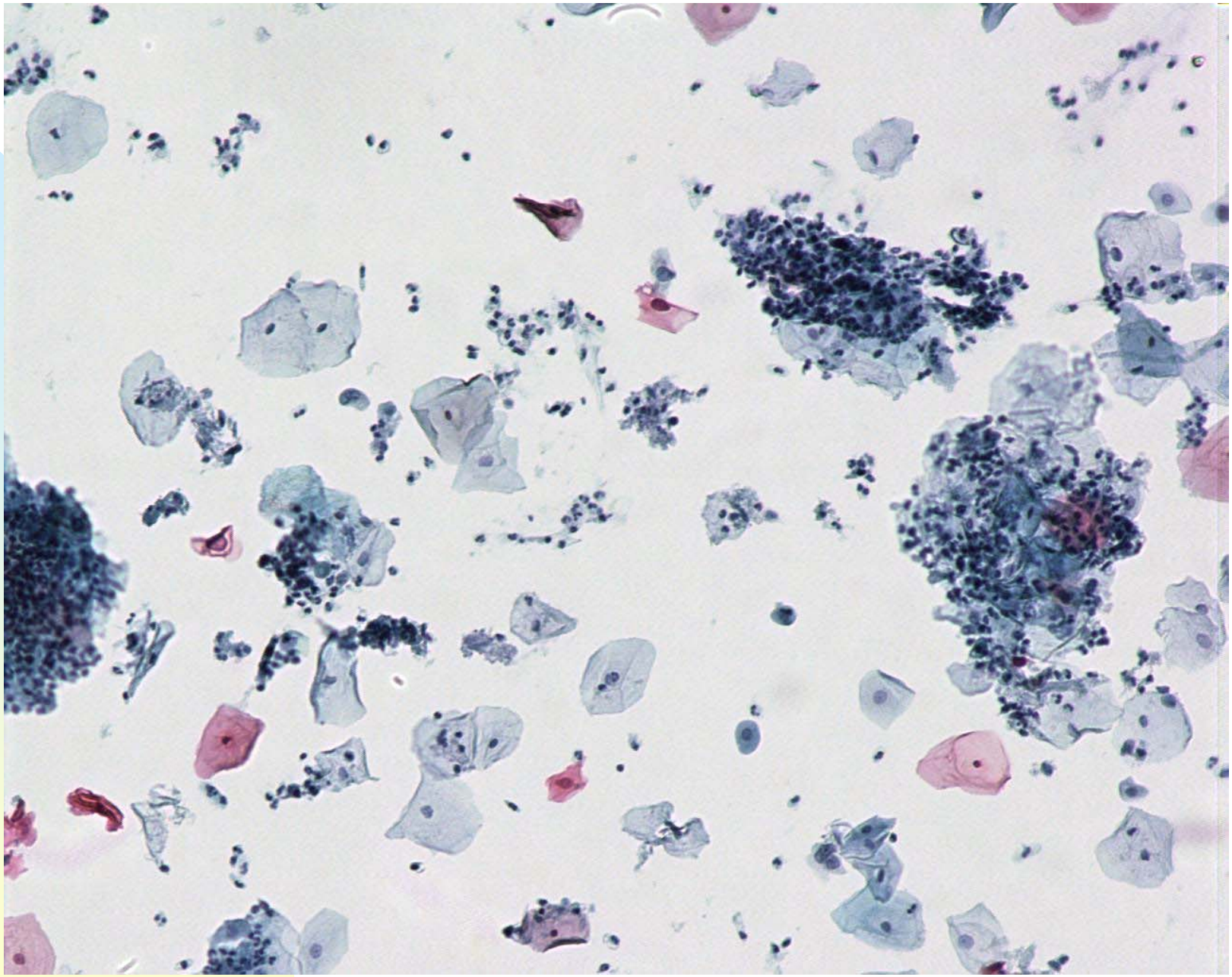
Technology and system highlights

- Unique colour image and nucleus segmentation technology
- Unique data mining (parameter selection & classification) technology
- High NFR fraction (50+%)
- Results independent of batch context
- Results independent of preparation method

Colour image, raw

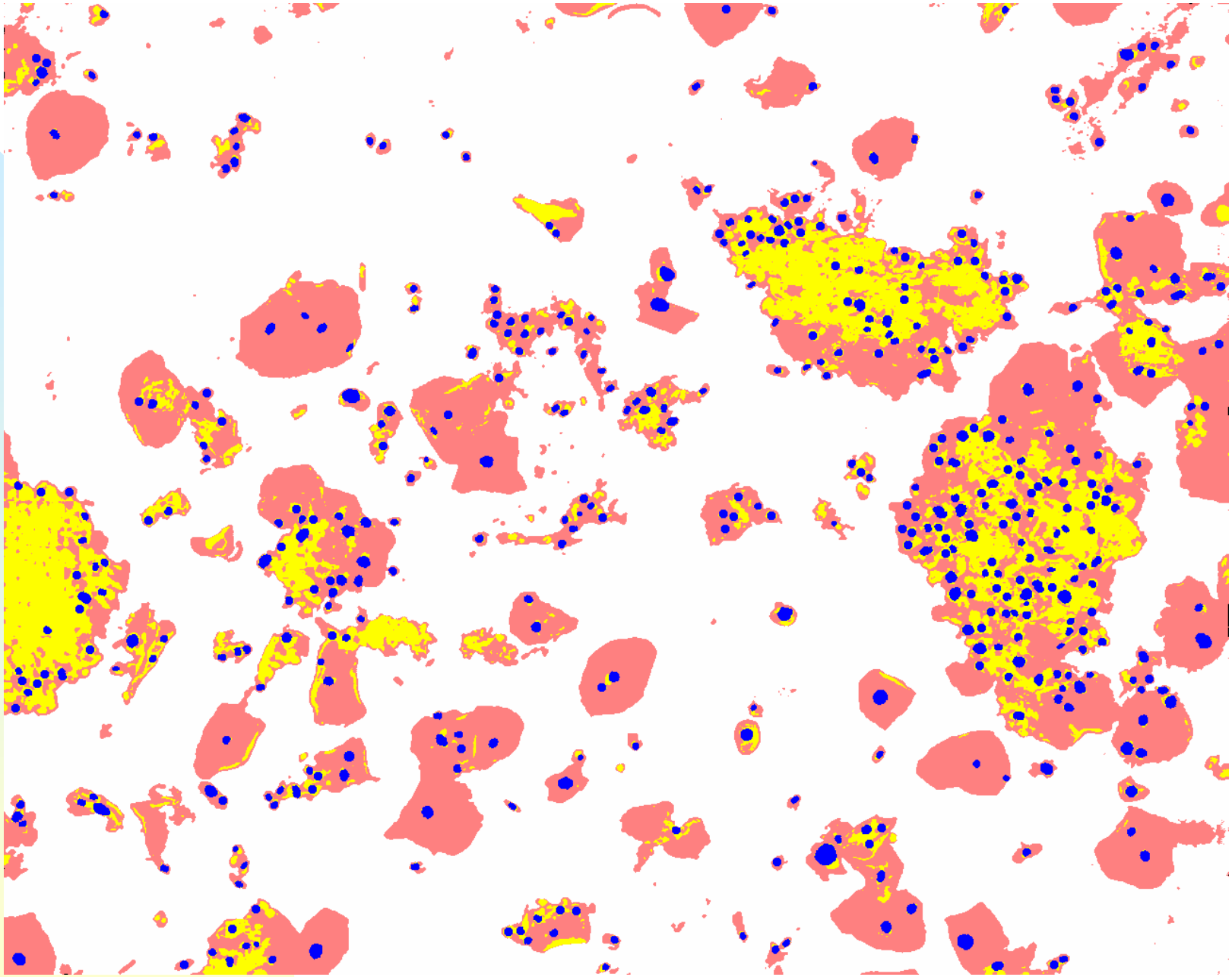


Colour image, background corrected



Symbolic image, colour classified

Symbolic image, nucleus detection



Some numbers

- Resolution: 0.66 micron
- Samples size: 19 mm diameter (314 $mm^{2)}$ or 20 by 55 mm rectangular (1100 mm^2)
- Image size: 1300 x 1030 x 0.66^2 x 0.95^2 = 0.53 mm^2 or 600 images per sample, alternatively 2075 images per sample

More numbers

- 1 CPU analyses one ThinPrep (circular smear in 30 minutes)
- Capacity is scalable: 10 CPU's analyse 480 smears per day
- Uncompressed sample data size: 2.16 Gb (TP) or 7.5 Gb (conventional)

How did we get (t)here?

- 1993, Dimac was founded
- - 1998 colour based image analysis of ”all” sorts
- 1998-99 NanoScan (EC)
- 1998-2001 Aphrodite (Danish)
- 2001-04 Autoscreen (EC)
- 2003 Venture Capital injected and Visible Diagnostics spun out from Dimac

The Autoscreen project

- Critical evaluation of the CCS System (Visible Diagnostics) which sorts smears into two categories only

  -- for review (?abnormal)

  -- not for review (definitely negative)

- Participating centres :UK, Denmark and Italy

- Study involves analysis of 24000 cervical smears It compares results of manual screening with results of automated screening.
- Study meets European Standards for in vitro diagnostic medical devices

- Potential value for primary screening of cervical smears

Select significant attributes for your forecaster