BLADDER CANCER DIAGNOSTICS WITH RAMAN CYTOLOGY

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Gold standard in diagnostics for bladder cancer

- Patient presents with frank painless haematuria
- **Cystoscopy**
  - Fluorescence 5-ALA
- Urine cytology
  - Not used independently
Bladder Cancer

Cystoscopic Imaging

Histological Grade

Pathological Staging

Normal cells

Poorly differentiated cancer cells

fat layer

muscle layer

lamina propria

urothelium

bladder

CIS/TIS

Ta

T1

T2

T3

T4
Inside the black box: urine cytology

- Urine cytology
  - 100% sensitive for high grade
  - 20% sensitive for low grade (75% of all cases!)
Inside the black box: Raman cytology
Chemometrics

- Multivariate Statistical Algorithms can detect subtle variations across datasets
  - Classify blind sample
- PCA/LDA allows us to quantify the separation between two groups
- Build up database
  - Healthy cells
  - Low grade
  - High Grade
Previous work

• We conducted a large review of over 70 papers
• Only patient study to date: Shapiro et. al. Journal of European Urology 59 (2011)

<table>
<thead>
<tr>
<th></th>
<th>No. of cases</th>
<th>Detects cancer, n (%)</th>
<th>Correct grade, n (%)</th>
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<tbody>
<tr>
<td>No tumour</td>
<td>116</td>
<td>11 (9.5)</td>
<td>All classified low grade</td>
</tr>
<tr>
<td>Low grade</td>
<td>92</td>
<td>79 (95.8)</td>
<td>68 (73.9)</td>
</tr>
<tr>
<td>High grade</td>
<td>132</td>
<td>132 (100)</td>
<td>130 (95.8)</td>
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• Can we improve on this?
  • Better sensitivity/specificity
  • Suitable for the clinic??
  • Screening?? time taken
Wavelength/Substrates/Stats

- Exhaustive search for the best:
  - Slide Material
  - Laser wavelength
  - Statistical Method/Algorithm

- Also completed considerable work on pre-processing of spectra to improve results
  - Noise removal
  - Wavelength Calibration
  - Background subtraction
Automated Raman Cytology

- Basic system designed/patented
  - Image processing used to scan slide, identify and align cell nuclei with source laser

Figure 1: Automated Raman cytology system set-up

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Next step: Medical Trial

- Fixing study
  - Vial with 50% ethanol
  - ICA to separate ethanol spectrum
  - Test using 5 cell lines and using automated Raman

- Ethical Approval and medical trial 2015-2016 Beaumont Hospital
Future Work

V = 109 μm³, n = 1.401
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