The Kristin Henry Lecture

Colorectal cancer screening: extraordinary conundra for pathology

Professor Neil A Shepherd
Gloucester & Cheltenham, UK

Edinburgh Pathology 2013
Friday, 21 June 2013
British Division of the International Academy of Pathology (BDIAP)
George Cunningham and the George Cunningham Lecture of the BDIAP

2005  Christopher Elston
2007  Michael Wells
2009  Geraint Williams
2011  Claude Cuvelier

‘He was the inspiration behind the formation of the British Division of the International Academy of Pathology in 1961’
The Cunningham Medal, British Division of the International Academy of Pathology, November 2010

Gloucestershire Cellular Pathology Laboratory
The BDIAP Kristin Henry Lecture

1982-90	Treasurer, BDIAP
1995-96	President, BDIAP
1982-	Member of Council, BDIAP
1997	Cunningham Medal, BDIAP
2009	President’s Medal, BDIAP
The BDIAP Kristin Henry Lecture

2005-08  Chair, IAP Finance Committee

2008-11  Chair, IAP Education Committee
Presidents of the IAP

1982-1983

2010-2012

Gloucestershire Cellular Pathology Laboratory
The Kristin Henry Lecture

Colorectal cancer screening: extraordinary conundra for pathology

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Edinburgh Pathology 2013
Friday, 21 June 2013
Methods of bowel cancer screening

- sigmoidoscopy
- colonoscopy
- faecal screening
  - FOB
  - FIT
- molecular
- blood screening

Issues
- efficacy
- cost
- service provision
- compliance and uptake
Cancer screening in the European Union
Report on the implementation of the Council Recommendation on cancer screening (FOBt)
## FOBT programme characteristics: Europe

<table>
<thead>
<tr>
<th>Country</th>
<th>Region(s)</th>
<th>Program type</th>
<th>Size of target population</th>
<th>Type of FOBT</th>
<th>Year program began</th>
<th>age range (years)</th>
<th>Screening interval (months)</th>
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CRC screening programmes

- great variation between programs
- great variation in ability to report data
  - report values, values reported
  - within/between modalities, between countries, by program type
- difficult to compare programs
- Europe generally good at reporting screening measures
  - some programs still unable to report basic measures
  - distinguish between prevalent and incident screens
In the UK, it’s not just England’s BCSP…..

Cancer Screening Programmes

Bowel Screening

Scottish Bowel Screening Programme

NICH

Northern Ireland Cancer Network
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Welcome to the Spring 2010 edition of In the Loop, the newsletter designed to keep colleagues delivering the NHS Bowel Cancer Screening Programme up to date with news and progress from within the community.

This is your newsletter so please let us know of any local news and events by emailing us at press.office@nhscancerscreening.co.uk: call on 020 7400 4499.

We’d especially love to hear about any activities you’re running that are aimed at engaging with hard-to-reach groups. Sharing innovative ideas will help deliver best practice and a better service for all.

Bowel Cancer Screening Roll Out Update

The nationwide roll out of the NHS Bowel Cancer Screening Programme is now almost complete. As of February the roll out is 98 per cent complete. By December 2009 just over 5 million testing kits had been sent out since the programme began and nearly 3 million kits returned.

More than 4,400 cases of bowel cancer have been detected in that time and nearly 20,000 polyps removed by colonoscopy.

The map below shows how far the NHS Bowel Cancer Screening Programme has been rolled out across the country.

Rolll out of the Programme

- Fully Live
- Partially Live
- Not Live
Welcome to the Summer 2010 edition of In the Loop, the newsletter designed to keep colleagues delivering the NHS Bowel Cancer Screening Programme up to date with news and progress from within the community.

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Editor:
Professor Julietta Patrick CBE
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New study on flexible sigmoidoscopy published

New research led by Imperial College London has been published claiming that the introduction of flexible sigmoidoscopy in the UK could save thousands of lives. The study, which was conducted over a 15 year period, claims that the use of flexible sigmoidoscopy can reduce bowel cancer incidence by a third.

The study, published in the Lancet in April, volume 357, page 9736, showed that a single flexible sigmoidoscopy examination in men and women aged between 55 and 59 reduced bowel cancer mortality by 43% and bowel cancer incidence by 33% in the group that had the examination compared with the uninvited control group. The trial followed more than 175,000 people in a randomised trial over an average period of 11 years, of whom 40,674 received sigmoidoscopy.

"This trial is the first to show the real benefit of flexible sigmoidoscopy in preventing bowel cancer. We have a tremendous opportunity to use this procedure to push bowel cancer back down the league table of cancer cases in the UK."

Harpreet Kuma, Cancer Research UK's Chief Executive

The implications of the study and the possible introduction of flexible sigmoidoscopy screening will be carefully looked at by the NHS Cancer Screening Programmes and Prof. Sir Mike Richards.
Flexible sigmoidoscopy screening in England

- May 2010    Wendy Atkin publishes Flexiscope trial results
- Oct 2010    PM announces Flexi-sig programme to commence
- Jan 2011    ‘Improving Outcomes’ strategy for cancer published
- Jan 2011    Pathfinder sites offering Flexi-sig screening to people aged 55 years
- April 2011  National Screening Committee approves Flexi-sig screening
- 2013        Pilot sites functional
- Early 2014  Likely first centre opening
Bowel cancer screening: the subconcious musings of a Gloucestershire pathologist: circa November 2006

- most of it will be a pathological doddle
- 130 extra polyps a year - mainly adenomas and HPs - piffle
- a few more cancer resections but lots of easy Dukes As
- and Julietta is going to give us a wad of dosh to do it.....
CRC screening as a driver for enhanced service quality: pathology

- classification of dysplasia
  
mild, moderate and severe to low grade and high grade
Influence of pathology on post-adenoma surveillance
Why is there no pathological data in there and why do we bother recording it in BCSS?

- dysplasia formerly graded mild, moderate and severe
- poor levels of inter-observer agreement in practice
- now two grades: low grade and high grade
High grade dysplasia

recognition based primarily on ARCHITECTURE:

COMPLEX glandular crowding and irregularity

PROMINENT budding

CRIBRIFORM ‘back-to-back’ glands

INTRALUMINAL papillary tufting

low power diagnosis - epithelium is thick, blue, disorganised and ‘dirty’
The importance of high grade dysplasia in adenomas in BCSP

• levels of inter-observer agreement for severe dysplasia/high grade dysplasia have been poor (variation of 2% to 25% in FS trial) – so it doesn’t appear in BSG guidelines

• and yet studies (Atkin, NP study) have shown it is an important marker for metachronous cancer risk

• so we need to agree criteria and get it right

• then it will be an important marker for cancer risk in the future
CRC screening as a driver for enhanced service quality: pathology

- classification of dysplasia
  mild, moderate and severe to low grade and high grade

- metaplastic polyp to hyperplastic polyp

- use of performance indicators and quality measures to drive up colorectal cancer reporting quality, especially through EQA

Williams GT, Quirke P, Shepherd NA. RCPath guidelines for the reporting of colorectal cancer, 2007
Setting UK BCSP pathology standards
The four big issues in BCSP pathology

• the diagnosis of adenocarcinoma on biopsy

• serrated pathology & what do we do about it – expected but not the amount nor the diagnostic difficulties

• polyp cancers (pT1 disease) & what we do about it – expected but not he management difficulties

• the large adenomatous polyp of the sigmoid colon – expected but not the amount nor the diagnostic difficulties
Basil C Morson, doyen of GI pathologists

“It’s your job to control surgeons”

- very conservative with cancer diagnosis

- intramucosal adenocarcinoma not a diagnosis allowed in the colorectum

- you have to see submucosal involvement
The diagnosis of colorectal cancer on biopsy

- intramucosal carcinoma not allowed as a diagnosis in the UK
- those cases are called ‘high grade dysplasia’
- lymphatics in mucosa not capable of delivering metastatic disease
- you don’t want a large specimen by return of post.......

- biopsies may not show definite submucosal tissue
- provides considerable difficulties (certainly for UK pathologists)
Why can’t all rectal biopsies be like this?
The diagnosis of colorectal cancer on biopsy: a local audit (Gloucester, 2012)

One year of MDTMs: 253 cases with a clinical diagnosis of cancer (not including suspicious polyps)

9.6% suspicious but not diagnostic because of a lack of obvious submucosal involvement

4.2% further biopsies not required because biopsies confirmed primary glandular neoplasia and clinical and imaging features demanded resection (mainly colon)

5.4% required further biopsies – 75% of those cases were RECTAL
The four big issues in BCSP pathology

- the diagnosis of adenocarcinoma on biopsy

- serrated pathology & what do we do about it – expected but not the amount nor the diagnostic difficulties

- polyp cancers (pT1 disease) & what we do about it – expected but not he management difficulties

- the large adenomatous polyp of the sigmoid colon – expected but not the amount nor the diagnostic difficulties
What is serrated pathology?

- a distinctive morphological appearance in the large intestinal mucosa
- with specific molecular fingerprints
- but varied endoscopic and macroscopic features
- and a variable but highly significant neoplastic potential
- representing the most important advance in our understanding of colorectal cancer development in the last decade
Sessile serrated adenoma/polyp/lesion

- right-sided
- may be difficult to see/detect at endoscopy
- controversies over classification and management
Observer agreement in the diagnosis of serrated polyps of the large bowel

N A C S Wong, L P Hunt, M R Novelli, N A Shepherd & B F Warren

Department of Histopathology, Bristol Royal Infirmary and Department of Clinical Sciences at South Bristol, University of Bristol, Bristol; Department of Histopathology, University College London Hospitals, London; Department of Histopathology, Gloucestershire Royal Hospital, Gloucester and Department of Cellular Pathology, John Radcliffe Hospital, Oxford, UK

- experienced histopathologists show only moderate concordance in diagnosis of serrated lesions (k value 0.49)
Observer agreement in the diagnosis of serrated polyps of the large bowel

1N A C S Wong, L P Hunt, 1M R Novelli, 2N A Shepherd & B F Warren
Department of Histopathology, Bristol Royal Infirmary and 1Department of Clinical Sciences at South Bristol, University of Bristol, Bristol, 2Department of Histopathology, University College London Hospitals, London, 3Department of Histopathology, Gloucestershire Royal Hospital, Gloucester and 4Department of Cellular Pathology, John Radcliffe Hospital, Oxford, UK

• experienced histopathologists show only moderate concordance in diagnosis of serrated lesions (k value 0.49)

“Nice way” of saying we struggle to differentiate between the different serrated lesions
Proximal serrated lesions

• proximal serrated polyp: 13% in US screening population

• rate may be increasing

• proximal HPs ≥10mm: 7% in UK follow up population

• miss rates for HPs > adenomas

East JE et al. Aliment Pharmacol Ther 2008; 28,:768-76
Proximal serrated lesions

- detection enhanced by chromoendoscopy

- and by narrow band imaging

Hurlstone 2004; Lapalus 2006;
Le Rhun 2006;
Adler 2009; Adler 2010
Natural history of sessile serrated ‘adenomas’

- asymptomatic population, 50-75 yrs, screening colonoscopy, N=3121

- 7.9% had proximal large (> 10mm) non-dysplastic serrated polyps (NDSP)

- more likely than those without proximal NDSP to have advanced neoplasia (17.3% vs 10.0%) at baseline

- large proximal NDSP and no neoplasia at baseline 3.14 times more likely to have subsequent neoplasia

Schreiner M et al. Gastroenterology 2010; 139: 1497–1502
## Serrated lesions

### Table 1. Proposed New Guidelines for Serrated Polyps

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<th>Lesion found</th>
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<td>Serrated polyposis&lt;sup&gt;b&lt;/sup&gt;</td>
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</tr>
<tr>
<td>Serrated polyp with any cytological dysplasia</td>
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<tr>
<td>Serrated polyp proximal to the splenic flexure</td>
<td>3</td>
</tr>
<tr>
<td>Serrated polyp ≥10 mm</td>
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<tr>
<td>Serrated polyps &lt;10 mm and distal to the splenic flexure</td>
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</tr>
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Noffsinger AE. Ann Rev Pathol Mech Dis 2009; 4: 343-64
Serrated lesions: pathological lesions

- small left sided, conventional hyperplastic polyp – common (30% of polyps in BCSP)

- larger right sided ‘sessile serrated lesion’ – less common, easily missed but increasingly recognised

- serrated adenoma – left-sided, 1-7% of adenomas

- larger left-sided (but rare) filiform serrated adenoma – less than 0.1% of adenomas

- serrated adenocarcinoma

- secondary serration – stromal lesions, lipomas, etc – rare

- ulcerative colitis
What does this mean for clinical management?

- typical small hyperplastic polyps (about 25-30% of all BCSP polyps): no specific follow-up

- larger (> 10mm) and multiple hyperplastic polyps in left colon: colonoscopy, enhanced surveillance

- right sided serrated lesions:
  attentive colonoscopy with ? chromoendoscopy, NBI, etc
  depends on age, comorbidity, family history, etc
  sessile serrated lesions > 1cm - excise and surveillance as for adenomas of equivalent size

- serrated adenomas – as traditional adenomas but ? faster progression to aggressive left-sided neoplasia
The four big issues in BCSP pathology

- the diagnosis of adenocarcinoma on biopsy

- serrated pathology & what do we do about it – expected but not the amount nor the diagnostic difficulties

- polyp cancers (pT1 disease) & what we do about it – expected but not the management difficulties

- the large adenomatous polyp of the sigmoid colon – expected but not the amount nor the diagnostic difficulties
The malignant polyp: pathological considerations

• is it really malignant?

• how common is this problem?

• when should we recommend resection after removal of a malignant polyp?
Dukes stage distribution for symptomatic cancer

- Stage D: 25%
- Stage C: 34%
- Stage B: 33%
- Stage A: 8%
Dukes stage distribution for screen-detected cancers

- True A: 26%
- C: 26%
- B: 25%
- Polyp cancers: 22%
- D: 1%
# pT1 cancers in BCSP

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**TOTAL NUMBER CANCERS**

1710

**TOTAL NUMBER pT1**

281

**PERCENTAGE pT1**

16.4

BCSP 10,000 cancers

1,700 pT1s

10-20 per year per per Centre
The malignant polyp: pathological considerations

• is it really malignant?
  can the endoscopist tell?
  can the pathologist tell?

• how common is this problem?

• when should we recommend resection after removal of a malignant polyp?
The polyp harbouring malignancy....
The question

Can the pathologist tell?

Is this cancer in the submucosa or is it the benign phenomenon of epithelial misplacement?
Epithelial misplacement in intestinal polyps

- misplacement of epithelium into the submucosa and beyond is a potent mimic of malignancy
- Peutz-Jeghers polyps in the small intestine
- polypoid mucosal prolapse
- small hyperplastic polyps in the left colon and rectum
- larger serrated polyps in the right colon (especially into lympho-glandular complexes) and in serrated polyposis
- adenomas in the colon and rectum
Peutz-Jeghers syndrome
Polypoid mucosal prolapse

- lower rectal/anal most common: inflammatory cloacogenic polyp

- epithelial (villous) hyperplasia traps the unwary into calling them large villous adenomas

- epithelial misplacement (colitis/proctitis cystica profunda) can cause overdiagnosis of cancer

- may be seen in association with diverticulosis, at stomas, in SUMPS, etc
Inflammatory cloacogenic polyp (polypoid mucosal prolapse at the anorectal junction) with florid proctitis cystica profunda
Epithelial misplacement in hyperplastic polyps

Gloucestershire Cellular Pathology Laboratory
Inverted hyperplastic polyps

Sobin, 1985; Shepherd, 1991; Yantiss et al, 2001

Gloucestershire Cellular Pathology Laboratory
64M. BCSP. Descending colonic polyp

- adenomatous epithelial misplacement in a lympho-glandular complex
- just like in inverted hyperplastic polyps...
Epithelial misplacement in intestinal polyps

- misplacement of epithelium into the submucosa and beyond is a potent mimic of malignancy
- Peutz-Jeghers polyps in the small intestine
- polypoid mucosal prolapse
- small hyperplastic polyps in the left colon and rectum
- larger serrated polyps in the right colon (especially into lympho-glandular complexes)
- adenomas, ESPECIALLY LARGE ONES IN THE SIGMOID COLON
Shepherd-Williams classification of difficult BSCP polyps

• definite epithelial misplacement (remember 85% are in the sigmoid colon)

• definite cancer

• definite epithelial misplacement and cancer (don’t make this diagnosis too often, please)

• haven’t a clue whether this is epithelial misplacement or cancer (I think even Professor Williams will be making this diagnosis every now and then)
Epithelial misplacement/cancer and difficult BSCP polyps

- the most extraordinary diagnostic conundrum I have seen (or, perhaps, recognised!) in my professional career
- low levels of inter-observer agreement amongst ‘general’ pathologists
- not perfect inter-observer agreement amongst ‘experts’
- surely matched only by melanocytic lesions of the skin......
Epithelial misplacement versus polyp cancer: more nightmares!

- meeting of Regional Leads for BCSP, Leeds, Feb 2013: specifically to look at prognostic indicators in polyp cancers, organised by Professor Phil Quirke, Lead Pathologist for BCSP

- review of 60 cases from two well-known centres in UK, putatively of polyp cancers

- in only 41 did the majority agree with the diagnosis of polyp cancer: 19 were thought to be epithelial misplacement

- inter-observer levels of agreement on important prognostic parameters in polyp cancers less than optimal

- and this was ‘experts’.......
Epithelial misplacement in adenomas

• 85% in sigmoid colon

• unusual in rectum (unless there has been previous meddling)

• same epithelium as surface, accompanied by lamina propria, haemosiderin deposition

• what about misplaced epithelium at the diathermy margin?

• intense pathological mimicry of invasive cancer
There is a very important adage in pathology: why make two diagnoses when one will do?
Pathological conundra in BCSP

- epithelial misplacement mimicking cancer

- 85% in sigmoid colon

- selected into BSCP as these are large prolapsing adenomatous polyps that bleed

- can be very difficult and some almost impossible

- require ‘Expert Board’ and BCSP-funded research

- but some are more straightforward and yet may be miscalled by pathologists....
BCSP Expert Board

• established in 2008 (NAS, GTW, BFW)

• three pathologists – you need a majority for this highly subjective and difficult assessment

• N A Shepherd, D S A Sanders & M R Novelli

• funded (IT, postage, secretarial support) in England by BCSP (thanks, Julietta)

• opportunity for education and research into difficult EM v Ca cases
Review mechanisms for difficult BSCP/BSW cases

BSCP/BSW local reporting pathologist

↓

Review by local/network BSCP/BSW GI pathologists

↓

Review by regional lead for BSCP/BSW Pathology

↓

National Expert Board
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## BCSP Expert Board

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<th>Category</th>
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<td>Cases referred to Expert Board</td>
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<td>Complete agreement between originating pathologist &amp; EB</td>
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<td>Original diagnosis equivocal but EB diagnosis certain</td>
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<td>Diametrically opposite diagnosis: originating pathologist &amp; EB</td>
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<td>Less than 100% agreement between members of Expert Board</td>
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<td>Both epithelial misplacement and cancer</td>
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Differentiating epithelial misplacement from adenocarcinoma

- 87% in SC. Elsewhere if previous instrumentation/surgery. DC & other parts occasionally
- rectum rare unless previous meddling
- lamina propria accompaniment
- haemosiderin
- mucus lakes
- continuity of epithelium
- similar cytology and architecture
- muscular proliferation and mucosal prolapse changes
- evidence of acute necrosis
- isolated glands
- budding
- vascular invasion and/or poor differentiation
Epithelial misplacement – continuity
67M. BCSP. Sigmoid colonic polyp. Diathermy artefact disconcerts...

- the changes of epithelial misplacement can be made to look much worse by diathermy artefact
- and it’s at that margin
Gloucestershire Cellular Pathology Laboratory

67M. BCSP. Sigmoid polyp. Previous biopsies and now polypectomy – it’s the company it keeps
BCSP polyps – we need to keep our minds open....

• 62M. Sigmoid colonic polyp – difficult endoscopic resection (left) – site tattooed

• subsequent perforation and resection (left)

• do we allow epithelial misplacement in the muscularis propria?
Artefactual epithelial misplacement
‘Enhancement’ of dysplastic change with inflammation and superficial ulceration
Misplacement of high grade dysplastic & non-neoplastic epithelium

Previous biopsies and tattooing
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Descending colonic polyp
Previous attempted removal

Additional difficulty of morular change
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- morphology different
- definite desmoplastic reaction
- definitely submucosal
| Variable (seen by 5 GI pathologists) | Cancer but very difficult | Equivocal | Equivocal |
### Cancer

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‘low power lens, high power brain’
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</tbody>
</table>
Epithelial destruction in EM, mimicking budding, because of inflammation & necrosis

| Cancer | Epithelial misplacement | Epithelial misplacement | Epithelial misplacement |
Equivocal

EM and ‘intramucosal adenocarcinoma’

‘Superficial adenocarcinoma’

‘Can’t make a firm diagnosis here’
What helps......

- lamina propria accompaniment
- haemosiderin
- mucus lakes
What helps......

- site: 87% in SC. Elsewhere if previous meddling. DC and other parts occasionally: rectum very rare unless meddling

- continuity between surface component and submucosal component (we live in a 3D world...)

- similar cytology and architecture

- muscular proliferation and mucosal prolapse changes

- evidence of acute necrosis
What helps.....

- why make two diagnoses? – if there is classical misplacement in one area......

- isolated glands
- budding
- desmoplastic reaction
- true vascular invasion (!)
Some questions

• have we finally gone mad?

• we have always been pretty conservative when it comes to the diagnosis of colorectal cancer (thanks, Basil) (cf the Far East)

• but surely these are cancer?

• is cancer in continuity ‘twixt its mucosal and submucosal components always, sometimes or never?
The development of adjuncts to aid in the diagnosis of epithelial misplacement

Epithelial misplacement in colonic adenomatous polyps and its differentiation from adenocarcinoma: the role of immunohistochemistry, infra-red spectroscopy and three dimensional reconstruction techniques

Carey D, Kendall C, Stone N, Shepherd NA

Gloucester Biophotonics Unit, Gloucestershire Royal Hospital, Gloucester, GL1 3NN and Gloucestershire Cellular Pathology Laboratory, Cheltenham General Hospital, Sandford Road, Cheltenham, GL53 7AN, UK

‘........ works well in the easy cases but doesn’t in the difficult ones’

Rhonda Yantiss, personal communication
Immunohistochemistry

• antibodies suggested as useful in the literature: e-cadherin, collagen IV, p53, MMP1, Ki67

• all tested in series of EM and cancer

• only collagen IV showed promising results in our hands
Immunohistochemistry: collagen 4 staining, cont'd

• in EM, there was continuous basement membrane staining for collagen 4 in 100% of the EM samples in both submucosal and surface epithelial tissue

Surface epithelial tissue  Submucosal epithelial tissue
Immunohistochemistry: collagen 4 staining, contd

- cancer cases displayed discontinuous or absent collagen IV staining
- significant differences for EM versus cancer
- but the assessment is subjective
3D reconstruction

- 200 6μ sections continuous sections cut from 10 cases of cancer and 11 of EM (technical issues!)

- computerised volume rendering undertaken in Leeds

- technique is very labour-intensive, even with sophisticated IT available in Leeds and hence small numbers.....
Epithelial misplacement
Epithelial misplacement
3D volume rendering: connected component analysis

- 3D volumes made, the epithelium segmented and the number of 26 3D connected components recorded.
3D volume rendering and connected component analysis

![3D Volume Rendering and Connected Component Analysis Graph](image-url)
3D reconstruction, volume rendering and connected component analysis

• excellent connectivity for epithelial misplacement between superficial and submucosal components, as one might predict from our 2D world of pathology

• BUT early polyp cancer also shows remarkable connectivity

• analysis by the Mann Whitney U stats found no significant differences

• cases deliberately selected to avoid poorly differentiated carcinomas......
Infrared (IR) spectroscopy: advantages

- more objective

- the lab has experience in various analytical techniques including Raman spectroscopy, IR spectroscopy and confocal microscopy

- for this study, IR epithelium-specific spectroscopy was considered the most likely to be useful

- methodology applicable to simple formalin-fixed, paraffin-embedded tissue with simple section cutting and a digital staining technique that allows images analogous to their standardly stained counterparts

- areas, identified by a pathologist, selected and their associated spectra collected

- the spectra analysed in a multivariate, PCA-fed LDA model
IR spectroscopy

For the cancer cases DNA, glycogen and the specific vibrational modes of some phosphate groups were important.

For the EM samples, lipid molecules and the C=O stretching mode of DNA were important.
IR spectroscopy

- the spectra were analysed in a multivariate, PCA fed LDA model

- classification correctly differentiated 85% of 10 samples of cancer from 90% of 11 cases of EM

- after ‘leave one region out’ cross validation, the EM and cancerous samples were correctly differentiated 80% of the time
Epithelial misplacement in colonic adenomatous polyps and its differentiation from adenocarcinoma: the role of immunohistochemistry, infra-red spectroscopy and three dimensional reconstruction techniques

- despite the literature, immunohistochemistry not particularly helpful except, perhaps, for collagen 4 staining, although this is subjective

- 3D reconstruction demonstrates the very considerable connectivity of epithelial misplacement

- but it is also present in early/polyp cancers that are not poorly differentiated

- infra-red spectroscopy is readily applicable to standardly prepared histological sections and does show promise in this area
Pathological conundra in BCSP

- epithelial misplacement mimicking cancer

- 85% in sigmoid colon

- selected into BSCP as these are large prolapsing adenomatous polyps that bleed

- can be very difficult and some almost impossible

- require ‘Expert Board’ and BCSP-funded research
The future and the answer

Cancer Screening Programmes

Bowel Cancer Screening Programmes
Acknowledgements

Duane Carey
Catherine Kendall
Nick Stone
Hugh Barr

Nick Roberts
Darren Trainor
Phil Quirke
Acknowledgements

Professor Geraint Williams
Professor Bryan F Warren
15 April 1958 to 28 March 2012
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Acknowledgements

Professor Julietta Patnick, CBE
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