

# Colour and the Leeds virtual pathology project, 2003-2013

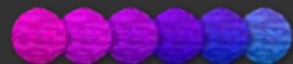
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May 2013

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[www.virtualpathology.leeds.ac.uk](http://www.virtualpathology.leeds.ac.uk)

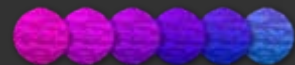
 @LeedsPathology





# Summary

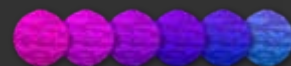
- I. There is variability in colour in pathology imaging
- II. Its important (I think)?
- III. What can we do about it?



# Leeds digital pathology project



- Scanning since 2003
- 4 x Aperio scanners
  - 2AT – 380 slides at a time
  - 2 CS – 5 slides at a time
- Scan 2000 - 5000 slides per month for teaching, education and research
- 180,000 slides scanned
- 100 Terabytes of image data





# All available online, free at

[www.virtualpathology.leeds.ac.uk](http://www.virtualpathology.leeds.ac.uk)



The screenshot shows the homepage of the Virtual Pathology website. At the top, there is a navigation bar with buttons for Public, EQA, Teaching, Slide Library, Research, Clinical Trials, Tissue Banking, and CPD. Below this is a large banner image with the text 'Virtual Pathology' and 'The Virtual Pathology website is home to all our research projects including the Powerwall'. A green circuit board graphic is overlaid on the banner. Below the banner, there are two columns of text. The left column contains a welcome message and a list of links: 'Leeds Powerwall', 'Leeds JISC Collection', and 'EU guidelines for QA in pathology in colorectal cancer screening and diagnosis'. The right column features a YouTube logo and the text 'www.youtube.com/LeedsPathology'. The website is decorated with a row of colorful spheres (purple, blue, green, yellow, orange, red) at the top right and bottom right.

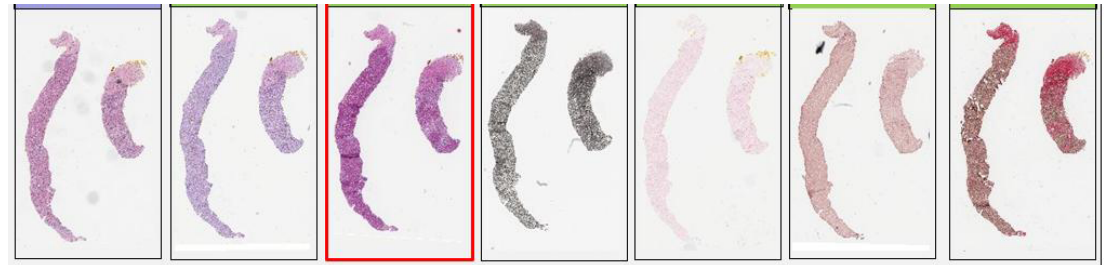
- EQA
- Slide library (5,000 cases)
- Undergraduate teaching
- Postgraduate teaching
- FRCPath examinations
- Clinical trials



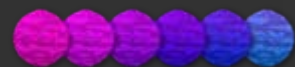


# My perspective

- I'm a practicing pathologist in the NHS
- I chose liver pathology as a subspeciality partly *because I like the colours*



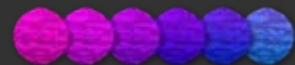
- I run a digital pathology research project - colour was an issue in several of our projects over last 10 years
  - 3D pathology
  - Image analysis
  - High efficiency digital pathology workstation – the Leeds virtual microscope





# Summary

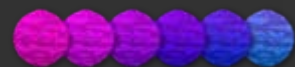
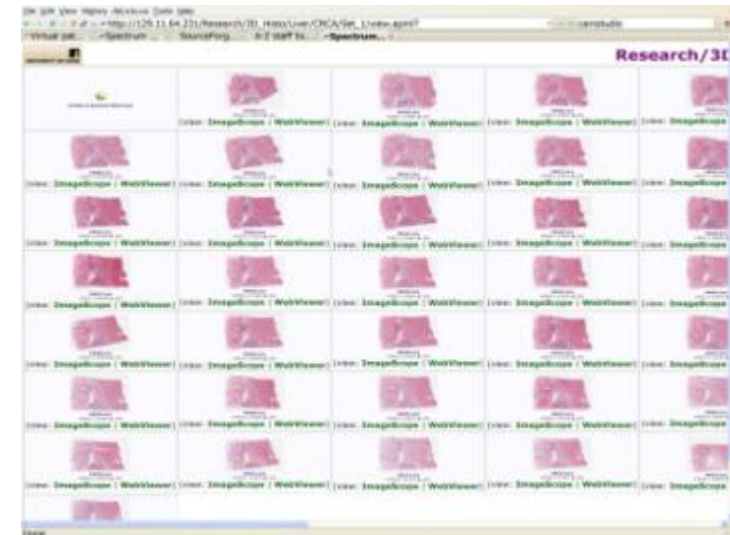
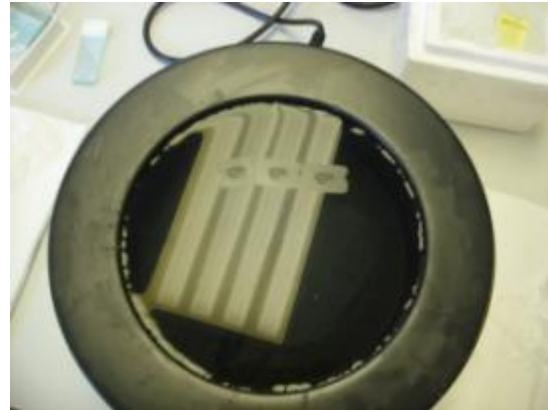
- I. **There is variability in colour in pathology imaging**
- II. Its important (I think)?
- III. What can we do about it?



# 3D histopathology with virtual slides: From sections to scans



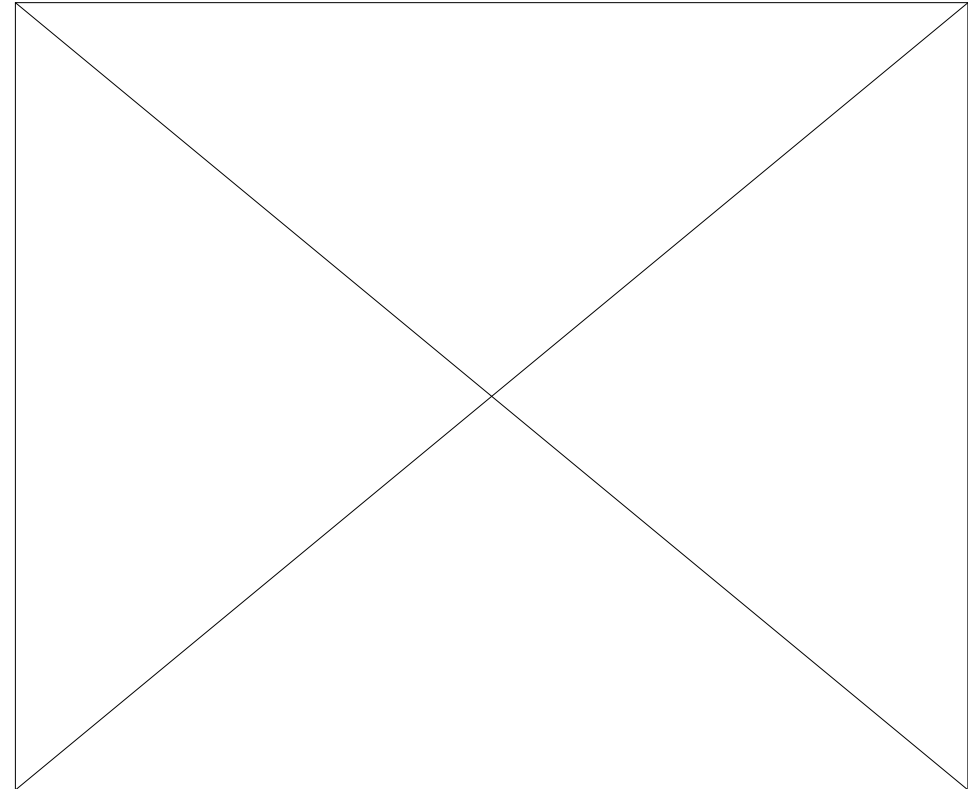
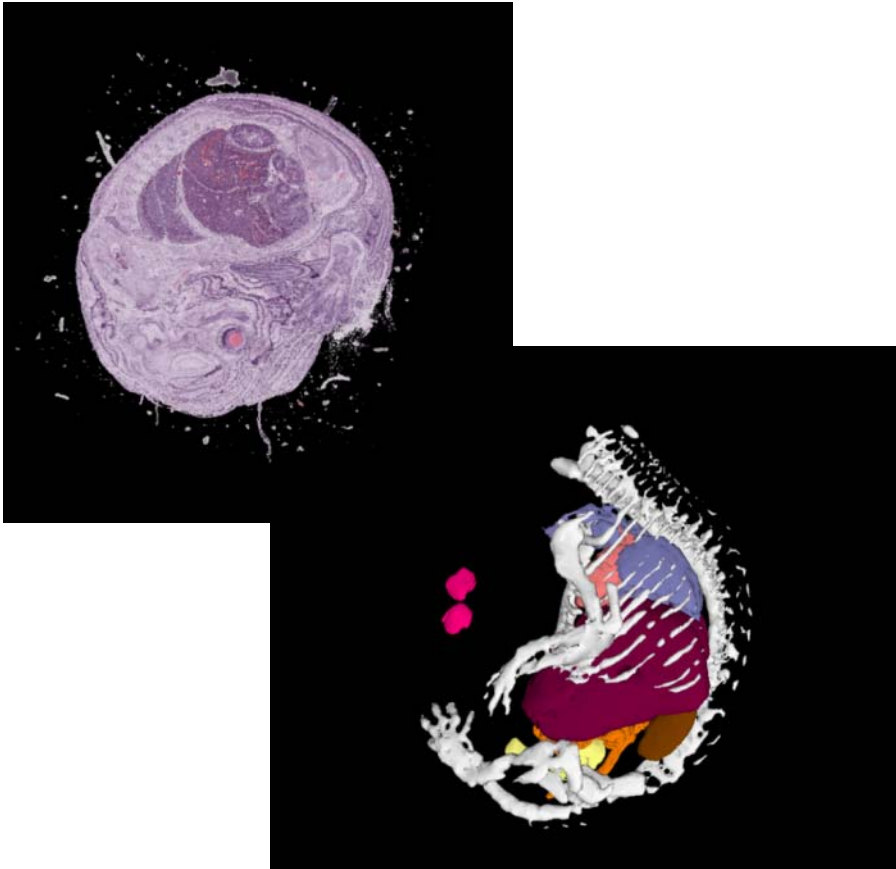
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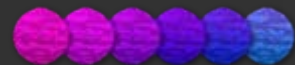
# 3D histopathology with virtual slides



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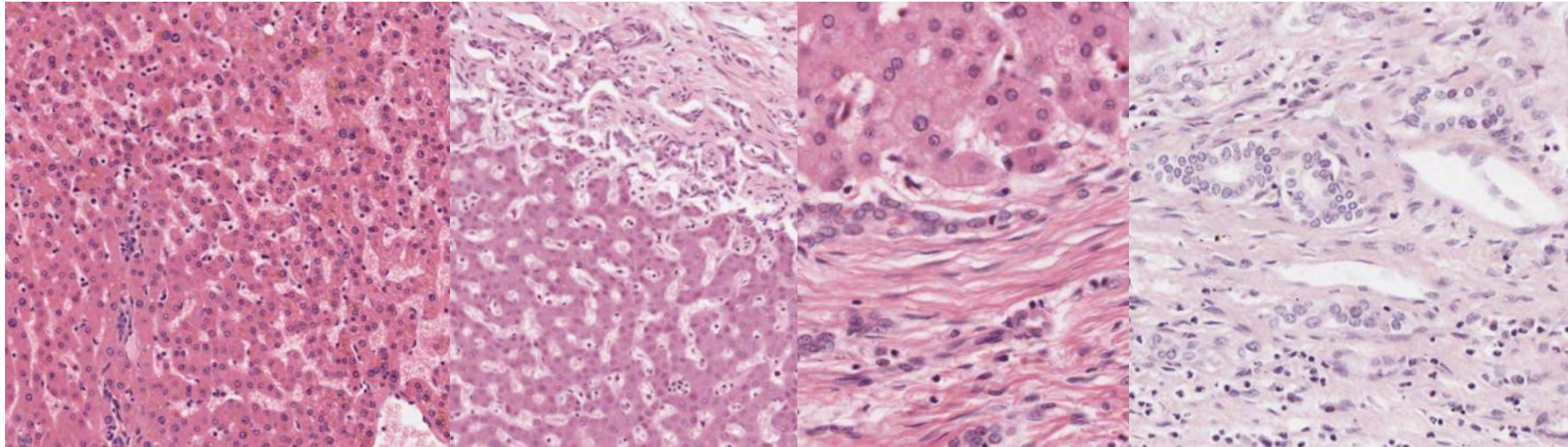


Nicholas Roberts,\* Derek Magee,† Yi Song,† Keeran Brabazon,† Mike Shires,\* Doreen Crellin,\* Nicolas M. Orsi,\* Richard Quirke,\* Philip Quirke,\* and Darren Treanor\*‡, **Toward Routine Use of 3D Histopathology as a Research Tool**, *Am J Pathol*, May 2012





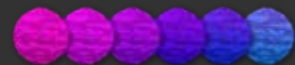
# Colour variability in 3D pathology



Same day

- + Same tissue sample
- + Same stain
- + Same pre-sectioning protocol
- + Same technician
- + Same microtome

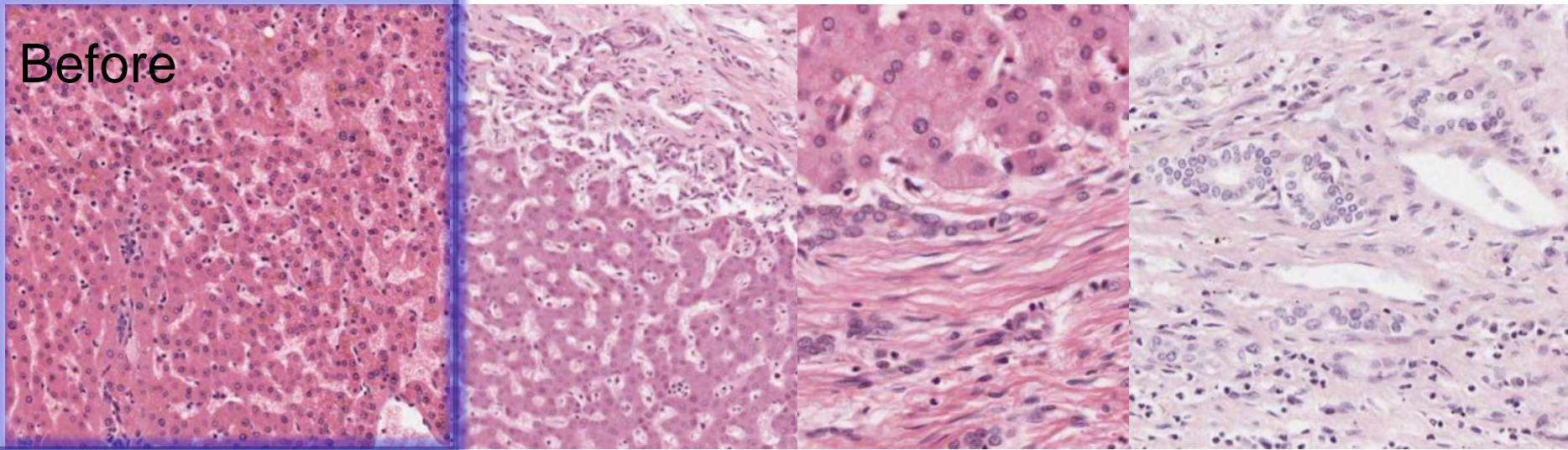
= Different colour



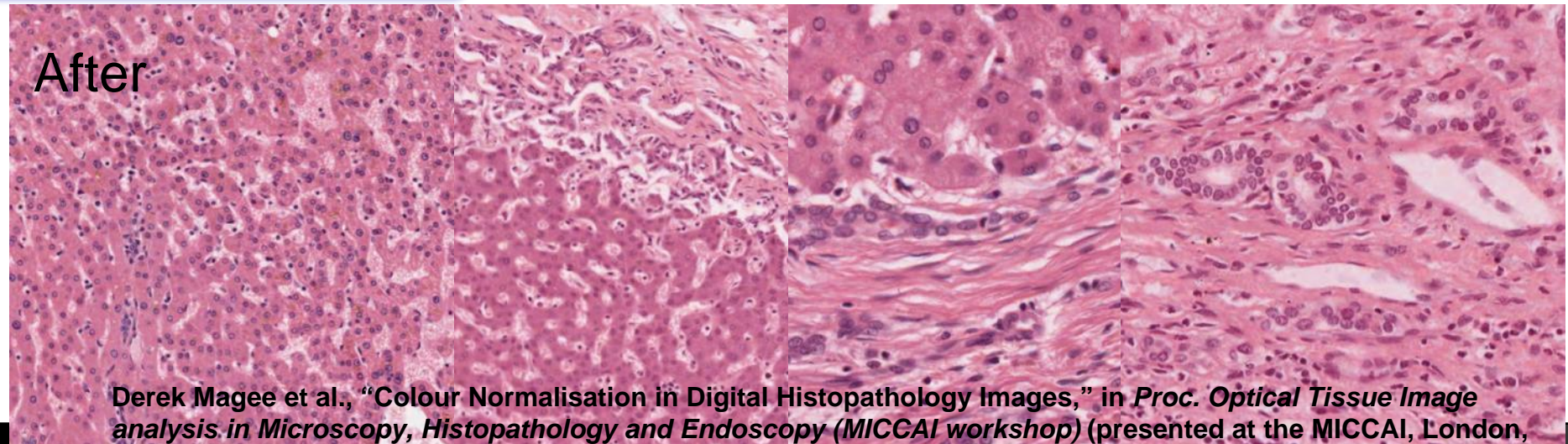
# Colour normalisation used in 3D pathology



Before



After



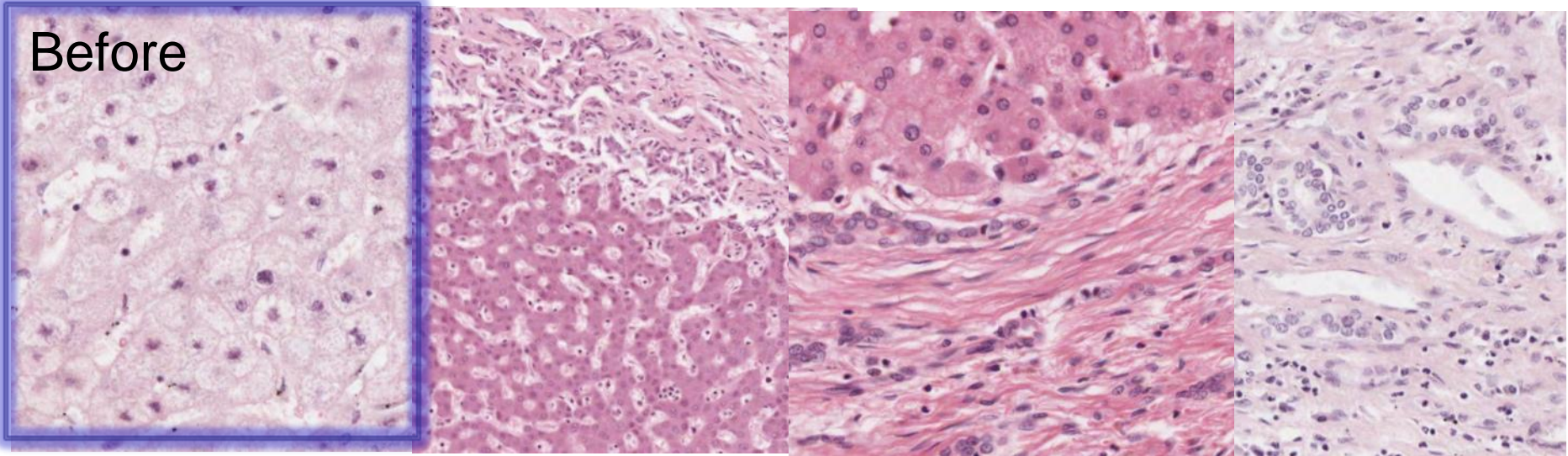
Derek Magee et al., "Colour Normalisation in Digital Histopathology Images," in *Proc. Optical Tissue Image analysis in Microscopy, Histopathology and Endoscopy (MICCAI workshop)* (presented at the MICCAI, London,



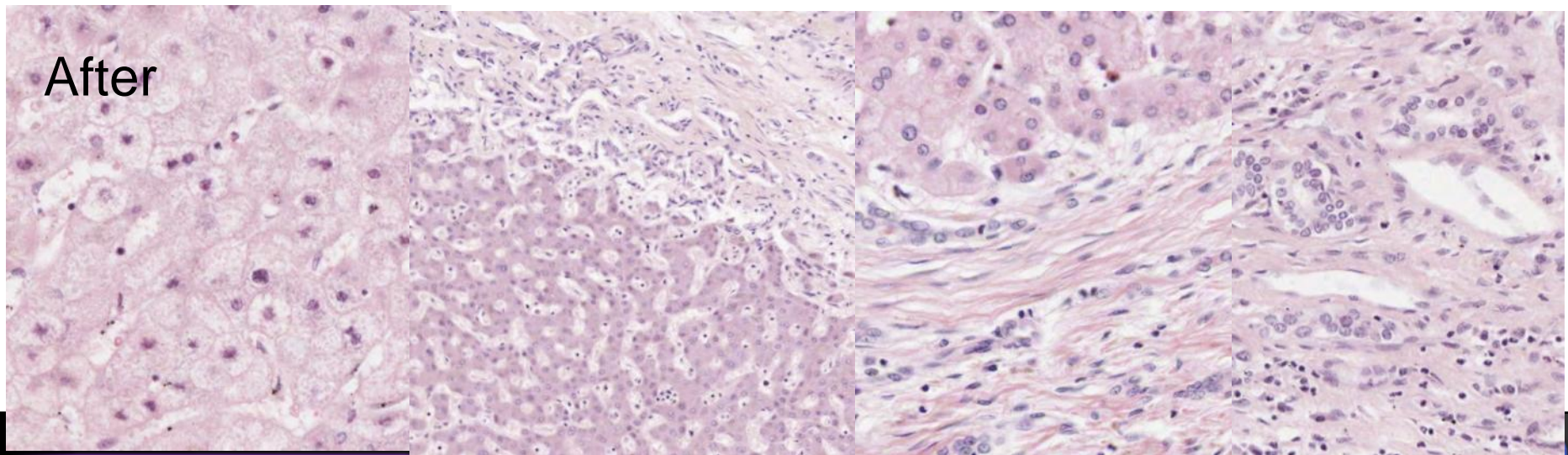


# And again...

Before



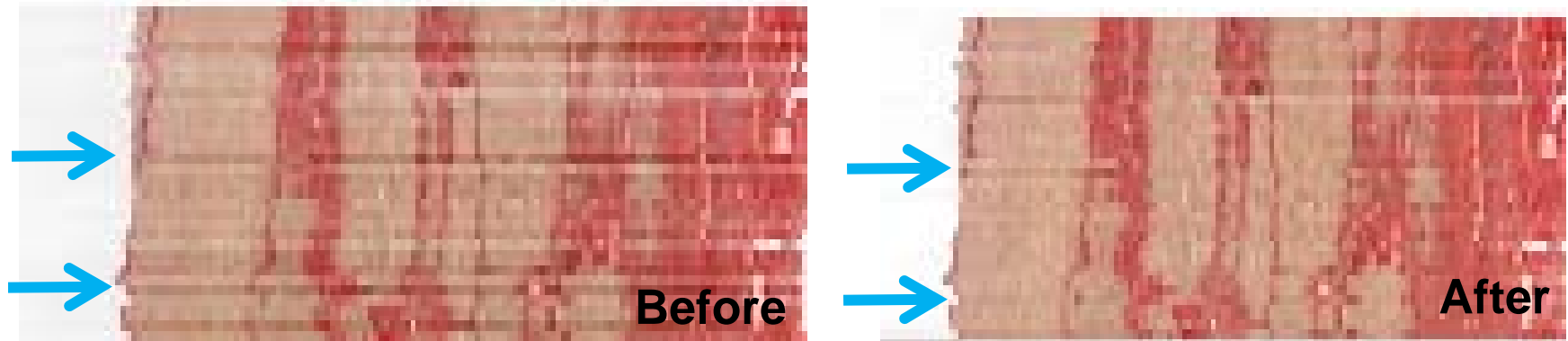
After



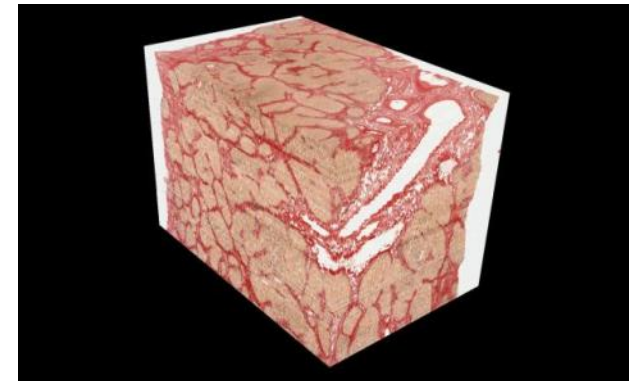


# Colour correction makes a better volume

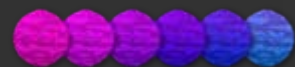
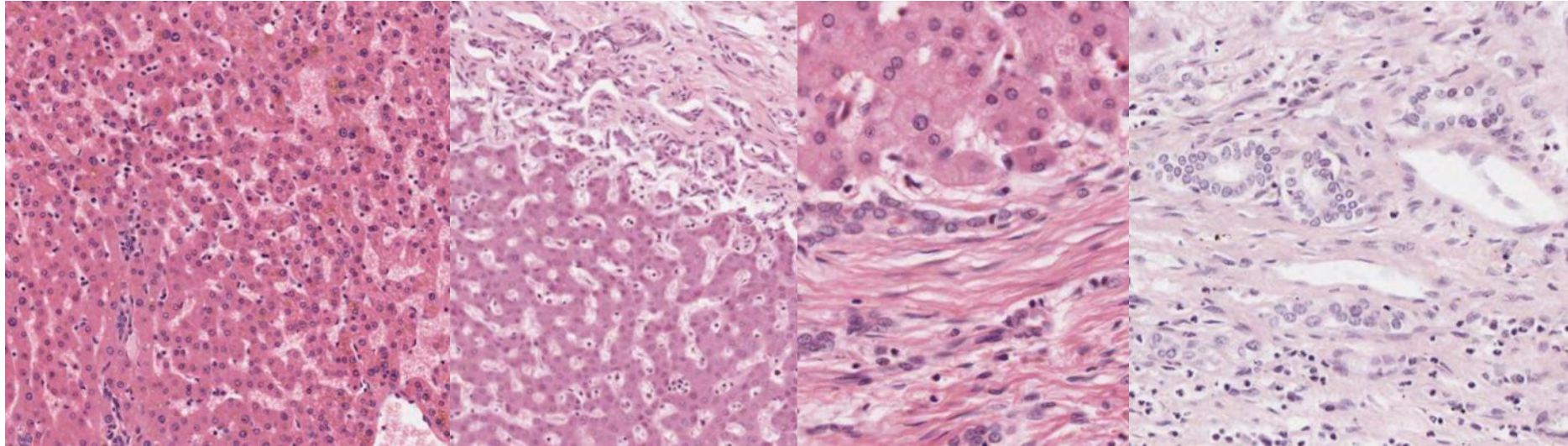
- Correct variability in staining and section thickness.



*Magee D, Treanor D, Crellin D, Shires M, Smith K, Mohee K, et al. Colour Normalisation in Digital Histopathology Images. Proc. Optical Tissue Image analysis in Microscopy, Histopathology and Endoscopy (MICCAI workshop). London; 2009.*

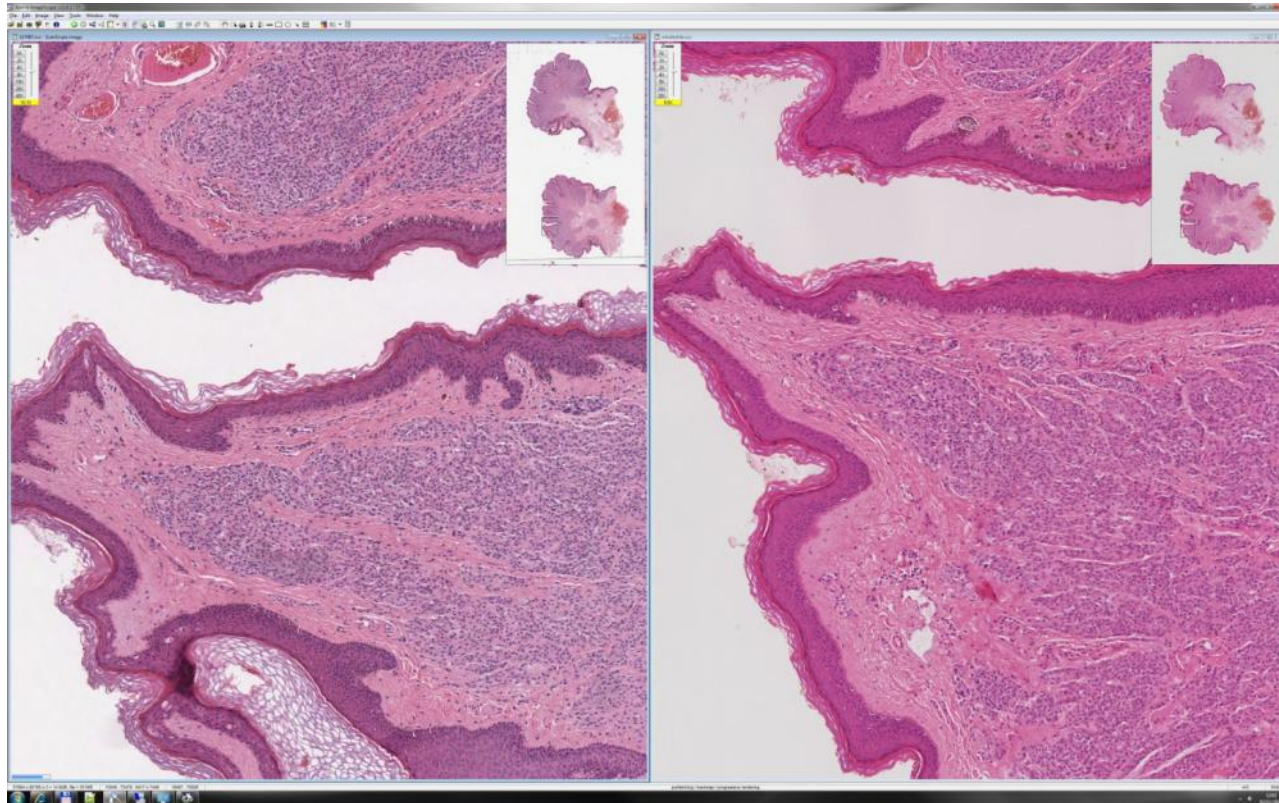


# Same tissue, slightly different section/ stain





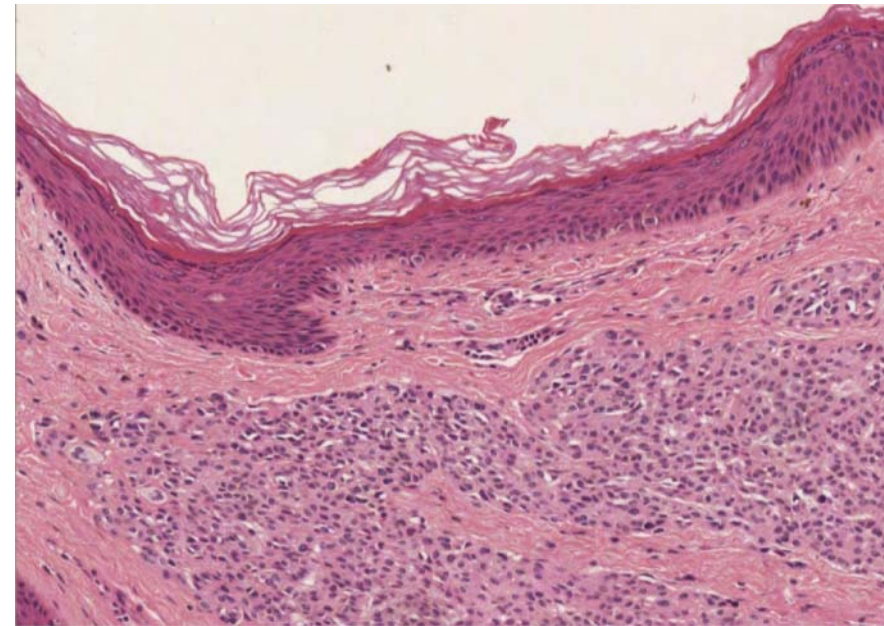
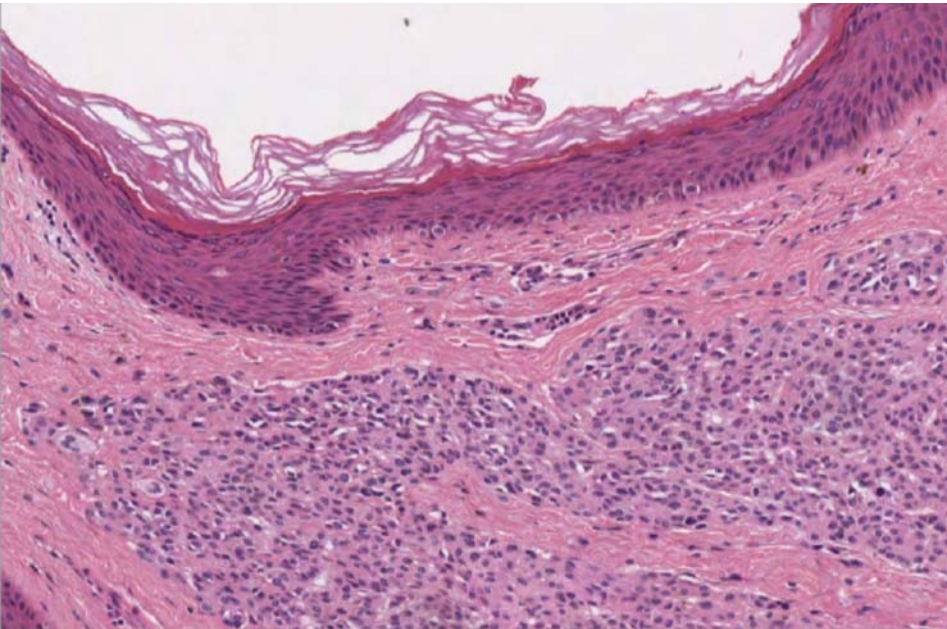
# Same slide, different scanner



- Which is “best”?
  - i.e. Which do you *prefer*?



# Same slide, different software



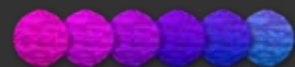
- Irfanview (L); Windows photo viewer (R)





# Summary

- I. There is variability in colour in pathology imaging
- II. Its important (I think)?**
- III. What can we do about it?





# Is colour important to pathologists?



- UK MRC tumour reference collection @ Leeds, 1955

JISC case 00108

Virtual Slides

- Female, 28 years old

**Clinical details:**  
Patient complained of pain and swelling of left lower thigh following mild trauma 5 weeks previously. The lower half of the femur was enlarged with hard rounded masses outside and connected with bone. This was very tender. Following biopsy, a hindquarter amputation was performed. 3 months later there was x-ray evidence of lung metastases. Death occurred 11 months following initial trauma, with painful deposits in the spine. No P.M. Section of femur showed soft, yellowish tumour occupying the medulla of the lower half of the bone, and also rounded whitish encephaloid masses external to the bone and adherent to it.

**Diagnosis:**  
Sections show the characteristic appearance of a liposarcoma with transitional areas between well-differentiated malignant fatty tissue and undifferentiated spindle-cell growth.

**Review diagnosis:**  
Liposarcoma.

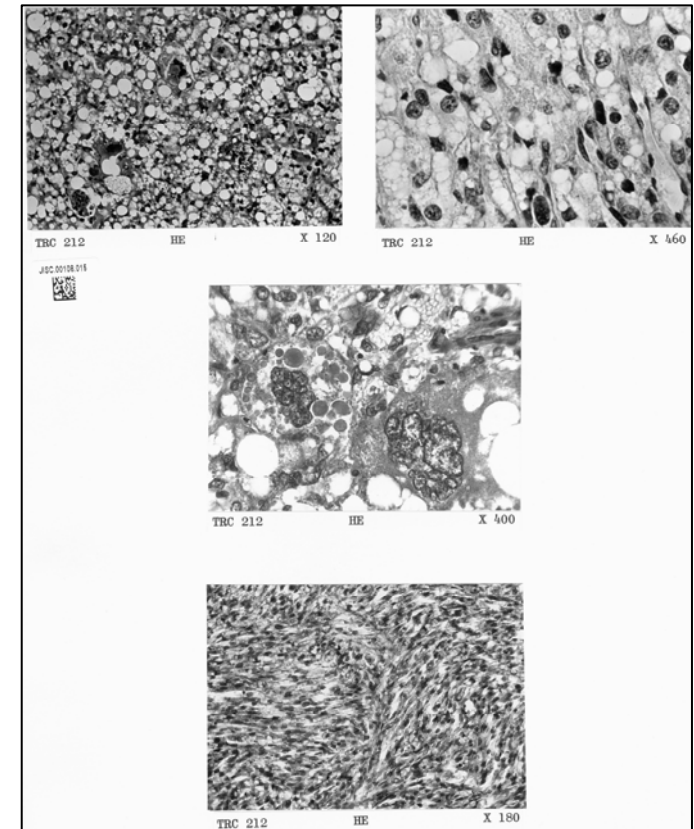
**System:**  
Soft Tissue and Bone

**Specimen:**  
Excision

**Date:**  
p1955

Images - click to enlarge

The virtual slide interface displays a grid of histological images. The top row shows two images: a low-magnification view of a tissue section (left) and a high-magnification view of a spindle cell (right). Below each image are links to 'Open with WebScope' and 'Open with ImageScope'. The second row shows two more images: a low-magnification view of a tissue section (left) and a high-magnification view of a spindle cell (right). Below each image are links to 'Open with WebScope' and 'Open with ImageScope'. The third row shows two more images: a low-magnification view of a tissue section (left) and a high-magnification view of a spindle cell (right). Below each image are links to 'Open with WebScope' and 'Open with ImageScope'. At the bottom of the interface is a small thumbnail grid of all the images.



# Leeds "Powerwall" project: as fast as a microscope



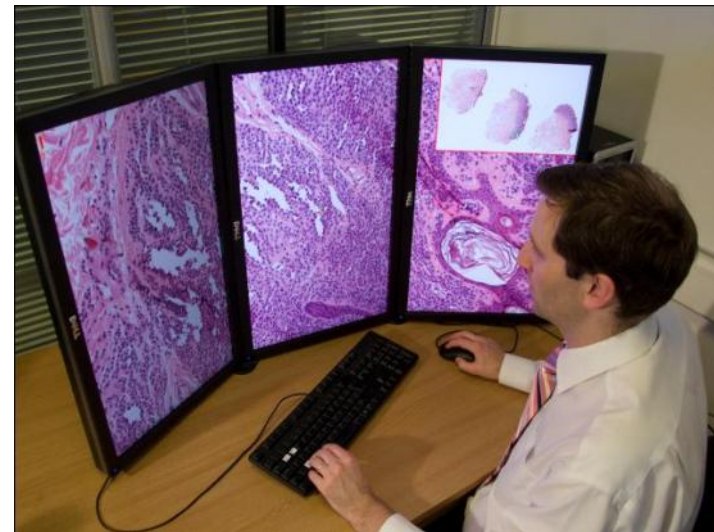
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## Leeds Powerwall



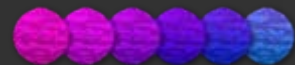
- Collaboration, teaching, discussion

## Leeds virtual microscope v1



- Diagnosis (single user)

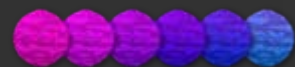
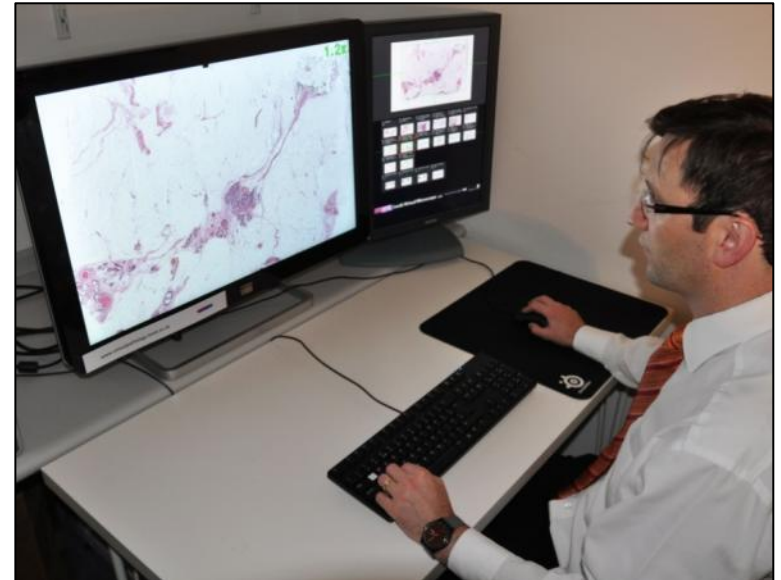
*Off the shelf displays, minimal calibration, no colour calibration*





# Leeds virtual microscope v2

- Medical grade monitors
  - Barco Coronis 6MP plus Nio 3MP
  - Total 9 megapixels
  - Basic calibration only (not per-slide)
  - As fast as a microscope



# Is colour important to pathologists in clinical practice?



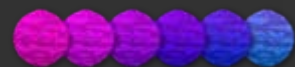
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## NO

- Effect of colour on diagnostic accuracy is **unknown**
  - But little research in the area
- **Huge variability** in microscope components and setup in laboratories seems to be tolerated by pathologists
- Small validation studies of digital pathology **don't mention colour** as a problem

## YES

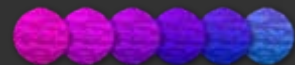
- Badly stained slides are hard to read, **can mislead you**
- Pathologists find stains from other labs harder (slower) to interpret
  - And get “**recuts**” in their own lab for referred cases
- It's important in radiology, printing, photography etc. So **surely** must be important in pathology





# Summary

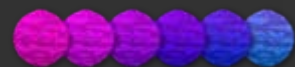
- I. There is variability in colour in pathology imaging
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# So...

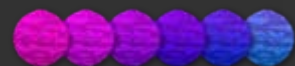
- There is variability between laboratory processes, individual sections, scanners, and software
- We don't know what the effects of variability in colour are, if any,
- But at the very least unfamiliar colours slow our diagnoses, and *may* affect diagnostic accuracy
- We know that calibration of images is important in radiology and printing





# What can we do about it?

- Minimum requirement
  - Different installations of the same virtual slide system from one manufacturer should be consistent
- Better still
  - All systems should reproduce the **same slide the same way**
- In an ideal world
  - Scanners should all replicate what we see down the scope
  - But we don't know if we need that, we don't know what's "good enough"





# So what do you think?

## Acknowledgements

Virtual Pathology in Pathology & Tumour Biology at Leeds Institute of Molecular Medicine

- Phil Quirke
- David Turner, Martin Waterhouse, Mike Hale, Alex Wright, Fraser Lewis, Hannah Dee, Gordon Hutchins
- Nick Roberts, Richard Quirke, Mike Shires, Doreen Crellin, Nick Roberts (technical work)

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- Alex Wright & Andrew Bennett & Yanong Zhu, Pathology and Tumour Biology Group, Leeds Institute of Molecular Medicine, University of Leeds
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Visualisation & human computer interaction

- Roy Ruddle, Rhys Thomas, John Hodrien School of Computing
- Rebecca Randell, Leeds Institute of Molecular Medicine

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- Yorkshire Cancer Research
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[www.virtualpathology.leeds.ac.uk](http://www.virtualpathology.leeds.ac.uk)

