Supplementary material

Table S1: Specialities of the histopathologists pathologists in this study.

Key: Urology Germ cell (UGC), Bladder/Kidney/Penile (BKP), Gastrointestinal (GI), Head & Neck (H&N). Renal is medical renal biopsies.

Pathologist	Specialities		
1	UGC	BKP	
2	UGC	BKP	Prostate
3	UGC	BKP	Prostate
4	Prostate		
5	BKP	Breast	
6	Breast		
7	Breast		
8	Renal		
9	Renal		
10	GI	Liver	
11	GI		
12	GI		
13	GI		
14	GI		
15	H&N		
16	Skin		
17	Skin		
18	Skin		
19	Gynaecology	Respiratory	
20	Gynaecology		

Table S2: Technical issues encountered.

Scanning related issues	
Time waiting for slides to be scanned	○ Prolonged scanning times for larger sections. ○ Rescanning poor quality slides.
Slides in the wrong order	○ Slides scanned out of order they were embedded.
Tissue not scanned / scanned in multiple	○ Not all levels scanned. ○ Tissue out of the field of scanning. ○ Glass slide broke in lab couldn't be scanned. ○ Same slides in a case scanned more than once.
Quality of scans	○ Areas out of focus e.g. due to minor tissue folds, tissue at edge of coverslip, wax obscuring view ○ Fatty tissue or mucous too faint, scans feel 'empty'. ○ Staining quality: slides were pale (issue for both GS & WSI, overcome with colour adjustment on WSI). ○ Poor detail on delicate collagen features. ○ Certain features require high quality scanning e.g. mitotic figures, intraepithelial lymphocytosis (GI), so had to be rescanned if poor quality. ○ Distortion of artefacts magnified on digital e.g. drying artefact.
Portal related issues	
	○ Portal running slowly, especially for larger images and during network peak use times. ○ Pathologist was 'logged in and out of the portal'. ○ Reporting tab doesn't always save pathologist's notes. ○ No clinical details available on portal.
Virtual private network (VPN) related issues	
	○ 'Virtual desktop program degrades image quality and can be very slow'. ○ Trust's virtual private network (VPN) access allows image quality but variable connections.

Table S3: Areas of potential pitfalls with the digital platform by speciality

Speciality	Potential pitfalls	Frequency of comments
General	Interpretation of special stains in suspected infection	20 (renal, GI, liver)
	Differentiating reactive atypia from dysplasia in an inflammatory background	17 (BKP, breast)
	Identification of mitoses	15 (breast, GI, liver)
	Assessment of dysplasia (tendancy to overcall low grade)	9 (BKP, breast, GI)
	Identification of necrosis	6 (BKP, renal, liver, gynae)
	Identification of perineural invasion	3 (prostate, skin)
	Identification of inflammatory cells such as neutrophils and plasma cells, especially if crushed	3 (UGC, prostate, BKP)
	Identification of lymph nodes, especially in fat	3 (prostate, breast)
	Assessment of lymphovascular invasion	2 (UGC)
	Identification of subtle amyloid deposits	1 (renal)
Urology Germ Cell	Identification of spermatogonia	10
	Identification of germ cell neoplasia in situ (GCNIS)	2
	Identification of rete testis invasion	2
	Differentiating seminoma vs solid pattern embryonal carcinoma	1
Prostate	Identification of prostatic intraepithelial neoplasia (PIN)	4
	Identification of atypical small acinar proliferation (ASAP)	3
	Identification of lymph node micrometastasis	1
	Identification of extra prostatic extension	1
Bladder/kidney/penile	Grading of dysplasia in urothelial carcinoma when at low grade / high grade borderline	13
	Identification of flat carcinoma in situ	1
	Identification of foreign material	1
Breast	Interpretation of immunohistochemistry (as it is positivity amplified digitally) particularly interpretation of Her 2 at borderline between 1+/2+	16

	Assessment of pleomorphism	1
	Identification of intraductal proliferations e.g. atypical ductal hyperplasia	1
	Identification of calcium oxalate	1
	Identification of small mucinous tumour	1
Renal	Immunofluorescence not available digitally	5
	Identification of spikes and lucencies on silver stain	5
	Identification of glomerular tip lesions	1
	Identification of basement membrane abnormalities	1
GI	Identification of paneth metaplasia	2
	Identification of helicobacter pylori identification on Tol blue stain	1
	Grading severity of inflammatory bowel disease	1
	Interpretation of special stains e.g. EVG	1
	Identification of intestinal metaplasia	1
	Melanin vs haemosiderin	1
Liver	Interpretation of orcein stain	9
	Intraductal lesions e.g. intraductal papillary neoplasm of the bile duct: dysplasia assessment and invasive foci identification	1
	In situ lesions in the pancreas: assessment of invasion	1
	When high power required: Diffuse type adenocarcinomas Post neoadjuvant therapy cases	2
	Interpretation of Perl's stain (paler on digital)	1
	Identification of siderosis	1
H&N	Identification of fungi	2
Skin	Identification of interface change	2
	Immunofluorescence not available digitally, so cannot fully report inflammatory cases digitally	1
Gynaecology	Interpretation of immunohistochemistry (as positivity amplified)	1
Respiratory	Assessment of PD-LI expression	1
	Identification of giant cells	1

	Identification of IgG4 positive plasma cells	1

Table S4: Diagnostic areas noted to be easier on the digital platform.

Speciality		Potential situations	
General		Assessment of overall anatomy	4 (prostate, UGC, skin)
		Assessment of tumour distribution	1 (prostate)
		Assessment of dysplasia	2 (HN, GI)
		Identification of inflammatory cells (neutrophils, lymphocytes)	3 (GI)
		Identification of lymphovascular invasion	3 (UGC, GI)
		Assessment of lymph nodes	3 (breast)
Urology Germ Cell		Identification of atrophy	1
		Identification of myelomonocytic cells in stroma	1
		Identification of rete testis invasion	1
		Identification of hilar soft tissue	1
Prostate		Identification of a small focus of adenocarcinoma	6
		Identification of a benign focus	1
Bladder/kidney/penile		Identification of ova	1
		Identification of sinus vein invasion	1
		Identification of papillary adenoma	1
Breast		Interpretation of Her2 strong positive/negative, borderline weak 1+/0* or 2+/3+	2
Renal		Assessment of IgA positivity	2
		Identification of amyloid on congo-red stain	2
		Identification of basement membrane ruptures on Silver stain (crisper & clearer)	1
		Interpretation of C4d stain (more contrast between clear background & stained areas)	1

		Interpretation of immunoperoxidase slides (crispier, more contrast)	1
		Interpretation of kappa to lambda slides (crispier staining & stacking images)	1
		Identification of v1 lesions of active T cell mediated rejection	1
		Identification of oxalate crystals	1
		Identification of long spikes & CR +’ve	1
		Identification of viral inclusions	1
		Identification of acute glomerular thrombotic microangiopathy	1
GI		Identification of viral inclusions	2
		Identification of candida	2
		Interpretation of MMR staining	2
		Identification of pinworms	1
		Identification of florid helicobacter pylori	1
		Identification of melanosis	1
Liver		Identification of megamitochondria	1
		Interpretation of orcein stain	1
		Assessment of vascular invasion	1
H&N		Interpretation of immunohistochemistry (extremely clear, including HPV in situ hybridisation)	1
		Identification of perineural invasion	1
		Assessment of tumour extent and infiltration	1
Skin		Assessment of routine general practice specimens including basal cell carcinoma was quicker	1

Table S5: Key examples of situations where digital pathology assisted histopathologists.

		Frequency of comments
Workflow related	Facilitates double reporting	21
	Enabled remote working	2
Multidisciplinary team (MDT)	Allows sharing cases in MDT discussion	7
Interface related or technical	Taking measurements	90
	Low power overview	38
	Wider field of view	6
	Easily switch between H&E, special stains and report	13
	Able to link immunohistochemistry images using the slide tool	12
	Able to make annotations	7
	Small biopsy assessment is easier and quicker	3
	Clearer resolution including some immunostains	3
Education	Facilitates working with and teaching trainees	2

Table S6: Issues reported to have arisen due to use of the digital interface

	Disadvantages of digital interface	Frequency of comments
Interface related	Time consuming to screen large areas	38
	Navigation around the slide more difficult	3
Ergonomic related	Wrist pain from examination of extra-large blocks.	1
	Looking at a screen for long periods can be very tiring.	1

Table S7: Pathologist's diagnostic confidence

		Digital slides		Glass slides	
Pathologist	Speciality	Mean diagnostic confidence (0-7)	Range	Mean diagnostic confidence (0-7)	Range
N/A	Across specialities	6.8	1-7	6.9	1-7
1	Urology Germ cell	5.8	5-7	6.6	6-7
	Blad/Kid/Pen	6	4-7	6.4	5-7
2	Urology Germ cell	6.9	4-7	6.9	5-7
	Prostate	6.9	5-7	6.8	6-7
	Blad/Kid/Pen	6.7	5-7	6.7	5-7
3	Prostate	6.8	1-7	7	5-7
	Blad/Kid/Pen	7	7-7	7	7-7
	Urology Germ cell	6.8	6-7	6.9	6-7
4	Prostate	6.8	5-7	7	7-7
5	Breast	6.7	1-7	7	5-7
	Blad/Kid/Pen	6.7	1-7	7	6-7
6	Breast	6.8	1-7	6.9	5-7
7	Breast	6.8	2-7	7	7-7
8	Renal	6.6	4-7	6.8	5-7
9	Renal	6.9	6-7	6.9	6-7
10	GI	6.8	5-7	7	6-7
	Liver	6.8	5-7	6.9	6-7
11	GI	7	6-7	7	6-7
12	GI	6.6	2-7	6.8	4-7
13	GI	7	7-7	7	7-7
14	GI	7	5-7	7	6-7
15	H&N	6.8	3-7	7	6-7
16	Skin	6.9	1-7	7	6-7
17	Skin	7	1-7	7	1-7
18	Skin	6.4	4-7	6.6	5-7

19	Gynae	7	6-7	6.9	1-7
	Resp	7	6-7	7	6-7
20	Gynae	6.9	5-7	9	6-7

Table S8: 'Results of Stage 2 pathologist views'. Diagnostic preferences of pathologists by speciality. Pathologist confidence scores on digital reporting vs glass reporting.

Pathologist	Preferred method of reporting – Digital (%)	Preferred Method of Reporting – Glass (%)	Preferred Method of Reporting - Either
Averages across the 8 specialities	41	8	51
Urology Germ cell	55.7	12.0	31.7
Prostate	77.0	8.3	14.7
Blad/Kid/Pen	44	9	48
Breast	61.3	6.3	32.3
Renal	7.5	7	85.5
GI	40.6	12.6	46.6
Liver	89.0	3.0	7.0
H&N	0.0	2.0	98.0
Skin	22.3	8.0	67.3
Gynaecology	4.5	4.0	91.0
Respiratory	0.0	1.0	97.0

Table S9: Summary of all the data. A - Poor quality image. B1 -Serious error with fundamental aspects of the case. B2 – Significant error in supplementary parameter. B3 – Minor error in supplementary parameter. N/A – no clinical impact.

Speciality (path-ologists)	**Time taken (average)**	**Total cases viewed**	**Cases per pathologist viewed (average)**	**Cases with discordances (number of cases)**	**Technical deferral rate (%)**	**Discordance B1**	**Discordance B2**	**Discordance B3**	**Discordance N/A**	**Digital was preferred method (% of cases)**	**Glass was preferred method in this (% of cases)**	**Either digital or glass were the preferred method (% of cases)**
Across all specialities	11.9 months	3777 cases	135 cases	49 cases 1.3% of cases	2.6%	0 cases	3 cases 0.1% of cases	16 cases 0.4% of cases	30 cases 0.8% of cases	41%	8%	51%
Urology germ cell	12.8 months	149 cases	50 cases	1 case	2%	0 cases	0 cases	1 case	0 cases	56%	12%	32%
Prostate	8 months	173 cases	58 cases	8 cases	2.9%	0 cases	0 cases	3 cases	5 cases	77%	8%	15%

Blad/Kid/Pen	8.5 months	244 cases	61 cases	13 cases	1.6%	0 cases	2 cases	5 cases	6 cases	44%	9%	48%
Breast	6.8 Months	660 cases	220 cases	10 cases	3.5%	0 cases	0 cases	2 cases	8 cases	61.3	6.3	32.3
Renal	15.4 months	138 cases	69 cases	2 cases	0%	0 cases	0 cases	1 case	1 case	7.5%	7%	85.5%
Gastrointestinal	14 months	1188 cases	238 cases	9 cases	2.7%	0 cases	1 case	1 case	6 cases	40.6	12.6	46.6
Liver	18.9 months	99 cases	99 cases	1 case	15%	0 cases	0 cases	0 cases	1 case	89	3	7
Gynaecology	16 Months	180 cases	90 cases	0 cases	0.6%	0 cases	0 cases	0 cases	0 cases	4.5	4	91
H&N	2.4 months	87 cases	87 cases	0 cases	5.8%	0 cases	0 cases	0 cases	0 cases	0	2	98
Skin	14.6 months	726 cases	242 cases	6 cases	1.2%	0 cases	0 cases	3 cases	2 cases	22.3	8	67.3

Respiratory	6.2 months	133 cases	133 cases	0 cases	0%	0 cases	0 cases	0 cases	1 case	0	1	97

Figure S1: Cases with discordances (% of total cases)