Deployment of Paige's Pan-Cancer, image recognition neural network as a digital triage system for prioritising routine specimen reporting in north Wales

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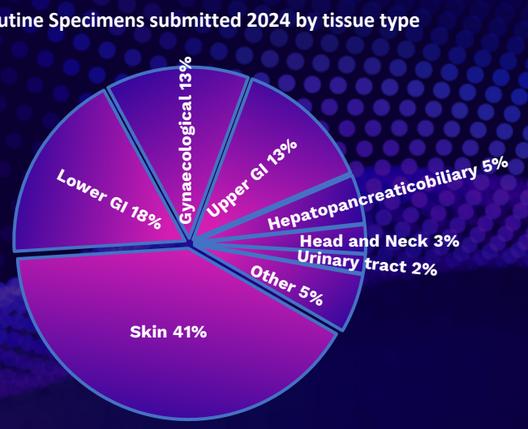
Background:

Each year the Betsi Cadwaladr University (BCU) Health Board receives over 40,000 histology samples and just under half of those are designated as clinically benign. Some samples can take up to 3 months to reach the desk of a pathologist before being reported. 0.2% (206) of routine specimens are diagnosed as an unexpected malignancy. As histology reporting undergoes digital transformation and whole slide images become more commonplace, now is an opportune time to trial artificial intelligence to sift through routine slides, detect and prioritise cases to be seen by pathologists sooner. Paige Pan-Cancer AI provides a novel solution to detect areas suspicious of malignancy and pre-malignant lesions.

Skin – 34743 (41%)
Lower GI – 15456 (18%)
Gynaecological – 11511 (13%)
Upper GI – 11108 (13%)
Hepatopancreatic biliary – 3960 (5%)
Head and neck – 2317 (3%)
Urinary tract – 1541 (2%)
Other – 4748 (5%)

Figure 1: relative proportions of routine specimens as per their tissue type.



Design:

An audit of all routine cases submitted to the Betsi Cadwaladr University Health Board's cellular pathology service was conducted to ascertain the rate of unexpected malignancy and proportions of tissue types submitted as routine. Following this, the team began phase one of the pilot, whereby 30 non-neoplastic and 30 neoplastic cases were selected from the lab's digital archive of cases submitted as routine and scanned via the GT450 slide scanner from Leica; weighted relative to the tissue types of cases received throughout the year. Case inclusion was hand selected by the project lead to maximise the variety of clinical entities and because a randomised selection method would be used in phase two. These whole slide images were anonymised using a 3rd party anonymisation tool for 'svs files' and uploaded to Paige's server. The images were viewable on PaigeFullFocus within the hour alongside an AI detection indicator for malignancy, point of interest and cancer tissue map overlay. Concordance between reporting consultants and Paige's Pan-Cancer AI was calculated.
The second phase of the pilot involved 150 clinically live cases submitted as routine and not yet seen by a pathologist. Physical slides are to be selected at random; slides are excluded from scanning if the quota for their tissue type has been exceeded. Cases are then distributed equally between 10 consultants, filtered only by whether the consultant was validated to report that tissue type. The Pan-cancer algorithm prioritises images suspicious for cancer over non-suspicious slides and consultants report routine cases in descending order of prioritisation. Consultants viewed the cases on a browser-based image platform using departmentally standardised LG medical grade monitors. Following the reporting of the 150 cases, accuracy of the algorithm will be assessed by the project lead correlating the pathologist diagnosis verses the prediction. A positive predictive value for neoplasm, sensitivity and specificity can be calculated as well as qualitative data such as whether the point of interest was centred on the tumour and whether the algorithm assisted the reporting process.

Results:

Of the 21,000 routine cases reported in 2014, 206 contained unexpected malignancy, the majority of these were skin tumours, and of those melanocytic tumours were the most prolific. As part of phase one of the pilot 60 cases were uploaded, all 30 slides containing tumour were flagged as suspicious for malignancy. Of the 30 cases not containing tumour, 5 were flagged as suspicious for malignancy. The false positives included a benign colon and benign ileum, with a point of interest centred over a lymphoid aggregate. A duodenal biopsy was flagged at the site of a stereotypical villi. Skin samples representing inflammatory dermatological conditions such as granuloma faciale, subacute spongiotic dermatitis and capillaritis all localised the point of interest to lymphoid aggregates. Notably a stomach biopsy demonstrating infection with H. Pylori bacteria, atrophic gastritis and intestinal metaplasia was correctly flagged by the algorithm due to the premalignant nature of intestinal metaplasia.
The pan cancer algorithm demonstrated a 100% sensitivity rate for detection of malignant and premalignant lesions within 18 different tissue types. Specificity of the algorithm was 83% within the 30 test cases.
Figure 2 demonstrates Paige's Pan-Cancer algorithm to detect an unexpected metastasis of ovarian serous adenocarcinoma within a routine reversal of a stoma formation

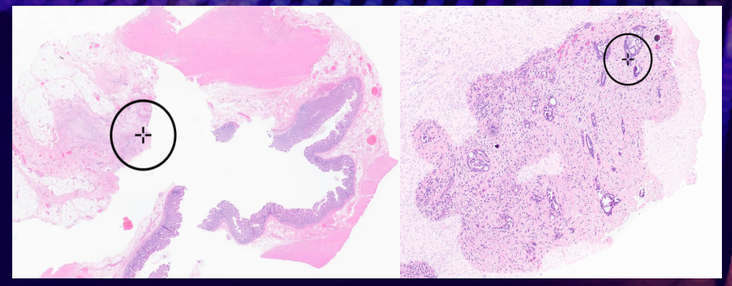


Figure 2: WSI of large bowel resected as routine reversal of Hartmann's procedure. Pan-Cancer algorithm correctly detects and localises a small deposit of metastatic serous adenocarcinoma

Progress, milestones and challenges:

Beginning in august 2024, the initial 4 months of the project involved discussions between Paige, BCU research department and Betsi cellular pathology department. The subject of debate was regarding the nature of the project as either research requiring ethical approval and submission of an Integrated Research Application system form, a late product trial with limited publishing opportunities or a service improvement project. The latter option of service improvement project was agreed on the basis that introduction of a novel intervention within an existing NHS service to measure improvement was covered by the NHS Health Research Authority's definition of service improvement and therefore required no ethics waiver. Following this, the research agreement and study amendment was evaluated and discussed with the project facilitator. Data protection impact assessments agreed with Paige were then discussed with BCU information governance department. Although the data servers receiving images are based within the UK, the information governance department were concerned that GDPR compliance was at risk given Paige's international base in the USA. As such the project required consultation with BCU cybersecurity and the completion of a digital mandate with BCU digital, data and transformation service to provision bandwidth, dedicated ports and technical support.

Prior to intervention, discussions among stakeholders including secretarial and laboratory staff were required to ensure a smooth workflow for continued use of the algorithm once the project was completed. The task of training and accreditation of pathologists was also included within the remit of the project facilitated by Paige staff.
During the final months of the project testing of the algorithm could begin. Third party software was utilised to anonymise data in line with NHS research protocol involving patient data. After selecting the cases, uploading of data, validation and evaluation of the algorithm's performance could be performed by the project lead.

Discussion:

The result from this limited pilot demonstrates the potential for an algorithm to detect neoplasms with great sensitivity in clinically routine specimens and illustrate the areas of highest suspicion to the reporting pathologists. Phase two of the project will involve 150 live cases of routine specimens with the aim of demonstrating feasibility within a functioning pathology department. The main desired attribute of a pan-cancer algorithm was high sensitivity; the future challenge will be optimising specificity without compromising sensitivity. The algorithm demonstrated the ability to accurately assess benign lymphocyte rich tissues without false positives yet the presence of lymphoid aggregates in tissues such as skin and duodenum triggered the suspicion of malignancy. This suggests that the algorithm is capable of interpreting features in context of the tissue type despite no external labelling by researchers.

It is hoped that completion of the project will open the door to new opportunities involving artificial intelligence within the discipline of pathology. One such aspiration is to utilise the infrastructure established to attempt a more detailed AI powered evaluation of whole slide images to present pathologists with a list of differential diagnoses based upon the microscopic details as well as any data provided from integrated lab information systems.

Aside from the technical achievements demonstrated by Paige, this pilot highlighted the logistical challenges of implementing artificial intelligence within an NHS environment. A consensus of understanding regarding the nature of new innovations is vital for any trust hoping to introduce similar artificial intelligence solutions. Understanding the structure of a health board's research and innovation body is hampered by the non-standardised nature of each trust, making the challenge for new innovators more difficult than one might assume. The tools required to introduce AI powered interventions do exist within the NHS, yet their utility is limited by the difficulty it takes to find them. Often the bureaucratic mechanisms in place to protect patients and their data have the effect of stifling innovation within the NHS. Additionally, it is the author's experience that culture within the NHS observes artificial intelligence with scepticism, partly because of the experience with the limited capabilities of aging informatics systems and the ever-present threat of data breaches when using third party software.

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The author herby declares no conflict of interest in the research conducted and publication of this academic material.