Computational pathology versus manual microscopy: comparisons based on workflow simulations of breast core biopsies

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Background

Pathology diagnosis currently relies upon manual review of microscope slides, one at a time and in order from A to Z. Computational pathology now permits a new kind of diagnosis, using machine vision and machine learning to intelligently assist pathologists. Termed pathologists' computer assisted diagnosis (pCAD), such a system would automatically preview whole slide images (WSIs), identify diagnostic regions of interest (ROIs), and interactively display triaged ROIs to the pathologist for expert decisions.

Although breast core biopsies are considered to be quick cases, they are challenging due to the high stakes and potential for diagnostic disagreement, especially with atypical lesions. Herein we compare real glass slide reviews with simulated computer-assisted reviews in order to determine whether pCAD could be expected to improve pathologist productivity.

Design

A pathologist reviewed breast core biopsies (three H&E levels per block). Audio recordings were analyzed for time measurements of slide movements (i.e. time per field of view) and narration (i.e. which slide was placed onto microscope stage).

To model pCAD, assumptions were made: 1) pCAD could reliably find diagnostic ROIs; 2) a pathologist could review all three H&E levels simultaneously onscreen; 3) the first five ROIs would be diagnostic; and 4) the remaining non-diagnostic ROIs could be reviewed more rapidly.

For each case, time data for the five slowest fields of view (FOVs) were used for the first five ROIs; the remaining fields of view were then included as non-diagnostic, rapid ROIs taking 0.5 seconds each. Simulated review time was divided by 3 to account for simultaneous review of H&E levels. A two-sample t-test was used to assess results.

Results

The cases included a variety of benign, atypical and malignant cases (n=25 cases). Complete, detailed time data was captured (Table 1). Average time to manually review a biopsy case was 221.6s (standard deviation 141.3s). Average simulated time to analyze a biopsy case was 98.0s (standard deviation 50.6s), a statistically significant 55.8% reduction ($p < 0.0005$, Table 2).

Table 1. Representative time data derived from an audio recording. The biopsy consisted of one tissue block (three H&E levels) and the diagnosis was invasive carcinoma.

Slide	Starting Time (minutes:seconds)	FOV per slide	Time per FOV (s) x Number of such FOVs	Time per slide (s)
1A level 1	0:08s	25	0.5s x 25 2s x 1 7s x 1	24s
1A level 2	0:35s	17	0.5s x 17	6s
1A level 3	0:44s	20	0.5s x 18 1s x 2	8s

Table 2. Summary of time data for glass slide reviews (measured times) and for pCAD (combination of simulated and measured times)

	Mean	Standard deviation
Time (glass slides, seconds)	221.6	141.3
Time (pCAD, seconds)	98.0	50.6
Time Saved (seconds)	123.7	
Reduction (%)	55.8%	p=.000266

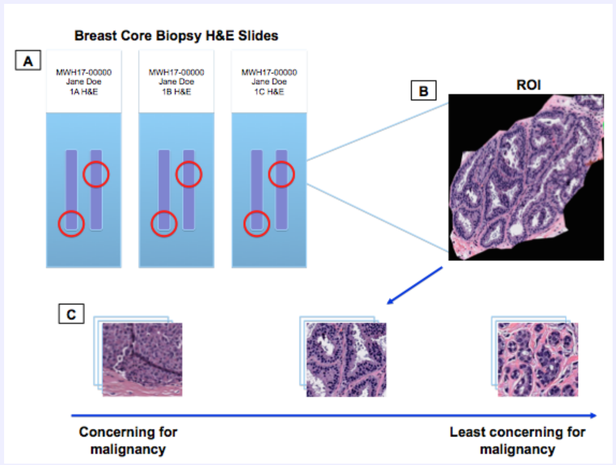

Figure 1. pCAD previews and triages slides (A), identifying ROIs (B) that are shown to the pathologist in order of diagnostic salience (C).

Conclusions

There are an estimated 1.6 million breast biopsies each year in the US, and all of these microscope slides are manually reviewed. This is a fabulous opportunity for computational pathology; extrapolation of our data suggests pCAD could save more than 50,000 pathologist-hours annually in the US, plus there may be additional benefits such as improved concordance and accuracy of diagnoses

While full pCAD is hypothetical, it will not be so for long. Existing computational pathology pipelines are already capable of analyzing entire breast WSIs for atypia and carcinoma, using spatial statistics and machine learning techniques.

Manually driving a microscope is a highly optimized glass slide workflow, but it is a poor choice for digital pathology. Rather, pCAD offers teleportation directly to the diagnostic decisions that only an expert pathologist can render. This study is a critical foundation as it provides data about how pCAD workflow could be designed and applied to real diagnostic work.

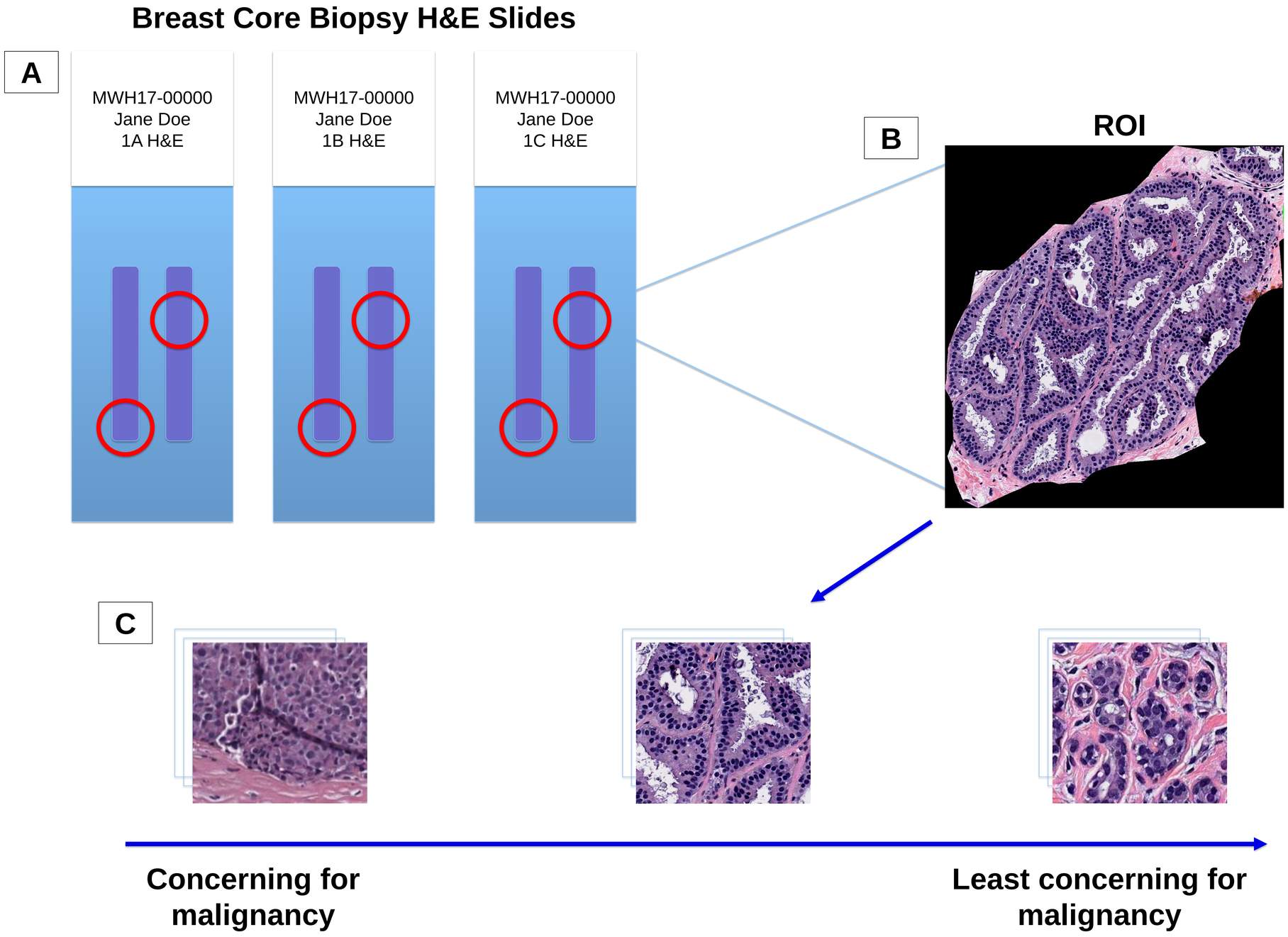

Figure 1. pCAD system previews and triages slides (A), identifying ROIs (B) to be shown to pathologist (B) in order of diagnostic salience, i.e areas of malignancy shown initially, followed by less concerning areas (C).