Research Article

Mouse cursor movement and eye tracking data as an indicator of pathologists' attention when viewing digital whole slide images

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Abstract

Context: Digital pathology has the potential to dramatically alter the way pathologists work, yet little is known about pathologists' viewing behavior while interpreting digital whole slide images. While tracking pathologist eye movements when viewing digital slides may be the most direct method of capturing pathologists' viewing strategies, this technique is cumbersome and technically challenging to use in remote settings. Tracking pathologist mouse cursor movements may serve as a practical method of studying digital slide interpretation, and mouse cursor data may illuminate pathologists' viewing strategies and time expenditures in their interpretive workflow. **Aims:** To evaluate the utility of mouse cursor movement data, in addition to eye-tracking data, in studying pathologists' attention and viewing behavior. **Settings and Design:** Pathologists (*N* = 7) viewed 10 digital whole slide images of breast tissue that were selected using a random stratified sampling technique to include a range of breast pathology diagnoses (benign/atypia, carcinoma *in situ*, and invasive breast cancer). A panel of three expert breast pathologists established a consensus diagnosis for each case using a modified Delphi approach. **Materials and Methods:** Participants' foveal vision was tracked using SensoMotoric Instruments RED 60 Hz eye-tracking system. Mouse cursor movement was tracked using a custom MATLAB script. **Statistical Analysis Used:** Data on eye-gaze and mouse cursor position were gathered at fixed intervals and analyzed using distance comparisons and regression analyses by slide diagnosis and pathologist expertise. Pathologists' accuracy (defined as percent agreement with the expert consensus diagnoses) and efficiency (accuracy and speed) were also analyzed. **Results:** Mean viewing time per slide was 75.2 seconds (SD = 38.42). Accuracy (percent agreement with expert consensus) by diagnosis type was: 83% (benign/atypia); 48% (carcinoma *in situ*); and 93% (invasive). Spatial coupling was close between eye-gaze and mouse cursor positions (highest frequency Δx was 4.00px (SD = 16.10), and Δy was 37.50px (SD = 28.08)). Mouse cursor position moderately predicted eye gaze patterns (Rx = 0.33 and Ry = 0.21). **Conclusions:** Data detailing mouse cursor movements may be a useful addition to future studies of pathologists' accuracy and efficiency when using digital pathology.

Key words: Digital whole slide images, digital pathology, eye-tracking, interpretive behavior, visual attention

INTRODUCTION

Little is known about pathologists' visual scanning behavior when assessing pathological specimens. Studying the visual search behavior of pathologists is challenging; technical and logistical obstacles, such as the difficulty of placing a recording device in a traditional light microscope, have impeded research that would illuminate pathologists' interpretive processes. The advent of digital whole slide imaging (WSI) affords researchers the opportunity to study the interpretive behavior of pathologists in innovative ways.

Digital images are becoming ubiquitous in many areas of medicine and are now widely used in medical education, including national board certification.[1,2] Trends in digital pathology are expected to mirror trends in digital radiology where the use of digital images is now widespread.[2-4] The workflow associated with the use of WSI for pathologic assessment is significantly different than the workflow required to interpret traditional glass slides under a microscope, and thus diffusion of digitized slides into clinical practice may drastically alter pathologists' interpretive behavior.[5-10] Studying pathologists' interpretive behavior and accuracy using this new digital medium is both timely and clinically significant.

Studies that have examined pathologists' behaviors when looking at digitized slides have relied on eye-gaze tracking technology[11,12] to determine patterns of visual attention. Because eye-tracking studies are logistically complicated and costly, prior studies have been limited by small sample sizes. In contrast, mouse cursor movement data, which has been used as an "implicit indicator of interest" in studies of Web search behavior,[13] can be gathered on a large-scale at relatively low cost. Although the resolution of the information required to understand Web search behavior is significantly lower than that required to understand digital slide interpretation, and the level of spatial and temporal granularity of mouse cursor movement data as a predictor of pathologists' attention is relatively limited compared to that of eye-gaze movement,[14] it may still provide general insight into pathologists' attention as evidenced by their movements, clicks and zoom behavior, and their total time spent viewing a given slide. Consequently, mouse cursor data may help us understand image characteristics and regions of interest that inform pathologists' interpretations. Additionally, data on interpretive time and viewing strategies will help pathologists, practice managers, and health services administrators predict and plan for ways, in which the incorporation of digital pathology may affect clinical efficiency.

Expanding on innovative methods of measuring visual behavior proven effective in other high-stakes work settings, such as aviation,[14-17] we present a study that assessed pathologists' interpretive visual search performance by analyzing both their mouse cursor and eye-gaze movement while they viewed digitized whole slide images of pathological specimens. We explore the potential of mouse cursor tracking data to elucidate pathologists' interpretive practices.

MATERIALS AND METHODS

Test Set

The test set was composed of 10 digital whole slide images scanned in the TIFF format using an iScan Coreo Au digital slide scanner at 40x magnification.[18] The glass slides used to develop the digital WSI were drawn from a larger test set that was developed for an ongoing National Cancer Institute funded breast pathology study and included one glass slide per case. The specimens were obtained from cancer registries participating in the Breast Cancer Surveillance Consortium (BCSC) in Vermont and New Hampshire.[19,20] BCSC procedures are HIPAA compliant, and all registries have a Federal Certificate of Confidentiality to protect the identities of research subjects and the physicians and facilities that contribute data to the BCSC.[21] The women enrolled in BCSC registries provided prior consent to BCSC investigators allowing their archived tissue samples to be used for research; thus, the research subjects were not re-consented for the development of the test set. The women were >40 years of age at the time of breast biopsy.

Three pathologists with expertise in breast pathology independently interpreted each of the glass slides in the test set. Using a modified Delphi approach,[22,23] these three experts held consensus meetings to determine a consensus "gold standard" diagnosis for each case.

As our goal is to study the interpretive accuracy and viewing behavior over a broad scope of cases, and as we are most concerned with errors in the diagnosis of carcinoma, half of the cases included were invasive or in *in situ* carcinoma. A stratified sampling technique was used to select the test cases from this larger BCSC data to include a range of diagnoses. The final test cases for our study included two non-proliferative, two proliferative, one atypical lobular hyperplasia (ALH), two ductal carcinoma *in situ* (DCIS; nuclear grade 2), one lobular carcinoma *in situ* (LCIS), and two invasive breast cancer specimens. Diagnoses with clinically similar treatments were grouped together into three overarching diagnostic categories: Benign/atypia, carcinoma *in situ*, and invasive [Table 1]. The slides were randomized, and each participant viewed the 10 slides in the same order with no time constraints.

This study was approved by the Human Subjects Division at the University of Washington (#41467) and Tufts University (#1109018).

Table 1: Breakdown of cases comprising the three diagnostic categories

Diagnostic category	Example specific assessment	# Of test cases
Benign/Atypia	Non-proliferative	2
	Proliferative	2
	Atypical lobular hyperplasia (ALH)	1
Carcinoma *in situ*	Lobular carcinoma *in situ* (LCIS)	1
	Ductal carcinoma *in situ* (DCIS)	2
Invasive	Invasive breast cancer	2
	Total	10

Participants

We recruited a convenience sample of seven physicians with a range of experience in pathology from the Seattle, Washington region to participate in the study. The range of participants' experience comprised pathology residents with limited experience in breast pathology ($n = 3$), faculty members who specialized in dermatopathology and general anatomic pathology respectively ($n = 2$), and pathology faculty members who specialized in breast pathology ($n = 2$). Informed consent was obtained from all participants.

Logistics

We recruited pathologists to interpret a series of breast pathology specimens and recorded their eye-gaze and mouse cursor movements throughout their interpretations. Pathologists' accuracy and time spent on each slide were noted, and the recorded cursor position was then compared to the recorded eye-gaze position by measuring the distance between the cursor and eye positions at each point in time.

Each of the participants independently examined the slides during a single, approximately 30-minute session. The slides were presented using a digital slide viewer developed for the larger national study, and displayed on a 19" LCD monitor running at 1280×1024 resolution. The experimenter used an auxiliary monitor positioned to the right of the viewing monitor. At the start of each session prior to data collection, the eye-tracker was calibrated by participants' sequential fixation on nine visual targets that appeared on the screen. Room lighting was kept constant throughout each session and between individual participant sessions. Subjects familiarized themselves with the virtual slide viewer and eye-gaze tracker with a sample digital whole slide image of breast tissue before beginning their evaluation of the 10 test cases. Research staff spent a few minutes instructing participants on how to manipulate the images using the viewer's on-screen controls, and the buttons and scroll wheel on the computer mouse prior to beginning data collection. Participants were not told that their mouse cursor movements were being tracked.

Upon loading, the images were displayed at low resolution (1.0x) in the upper left quadrant of the viewer. Immediately upon loading each image, research staff verbally instructed participants to manually click the on-screen control that caused the image to be displayed at full screen. Data acquired during the initial slide set up (i.e., when the slide was not yet at full screen) were discarded from analyses. The participants were able to view each digital whole slide image at up to 60x magnification using the computer mouse scroll function. The participants provided a diagnosis for each digital whole slide image using a standardized histological assessment form.

Eye Tracking and Mouse Cursor Tracking

Participants' eye-gaze movements were tracked using the SensoMotoric Instruments RED remote eye-tracking system v.2.7.13 (SensoMotoric Instruments, Boston, MA).[24] Eye-gaze position and mouse cursor clicking event data were recorded and logged at a sampling rate of 60 Hz using SensoMotoric Instruments' iView Software and Experiment Center. Eye-gaze was calibrated using a nine-point calibration before the beginning of the study to ensure the accuracy of the remote eye-tracker (to approximately <0.5° visual angle). Mouse cursor position was logged with custom software written using MATLAB 7[25] and the Psychophysics Toolbox extensions.[26,27] A two-dimensional Cartesian coordinate system was applied to the virtual slide viewer (x- and y-coordinates), and the coordinates of the cursor position were recorded and logged at a sampling rate matching the screen refresh rate (60 Hz).

Analysis

Eye-movement data was pre-processed, and further analyses were conducted using MATLAB. First, missing eye-gaze position values and artifacts, as in the case of blinks, were replaced using cubic spline interpolation. Second, since the cursor position was sampled only when the cursor was moved more than a pixel, eye-gaze data were collected at an inherently higher sampling resolution relative to cursor data. To temporally align the two data streams at the higher sampling density, cursor position was calculated for each eye-gaze data point by extracting the cursor position coordinates recorded at the closest time point less than or equal to the eye position time stamp. In other words, if the cursor hadn't moved from time T-1 to time T, it wasn't updated at time T, but the cursor position sampled at the earlier time stamp (e.g., T-1) provided accurate position information with precise temporal correspondence to the eye-gaze position at time T. This resulted in x- and y-coordinates for both eye-gaze and mouse cursor position at a given time; note that this method simply aligns the two raw data streams into a single temporally synchronous data set. Then, all data acquired outside of the sample slide presentation and

where the mouse cursor or eye-gaze *x*-coordinate was less than 0 (i.e., when the cursor or eye was on the experimenter's auxiliary monitor) were excluded from further analyses; note that this was exceedingly rare. Eye-gaze and mouse cursor position were analyzed using regression-based analyses and distance comparisons, both by slide diagnosis type and collapsed across all slides.

Eye-gaze typically leads cursor movement,[28] so a time lag was applied to the eye-gaze time series to see if there is an improvement in the relationship between cursor movements and clicking events. However, adjusting the time series to account for this lag produced no increase in the predictive value of mouse cursor position in accounting for eye gaze patterns.

Diagnostic accuracy was evaluated by viewing time and participant expertise (resident, general faculty, breast specialist) for a decoupling in the relationships between eye-gaze, cursor movement, and clicking events.

RESULTS

Slide Viewing and Diagnostic Accuracy by Diagnosis Type

Because of the small sample sizes, we used non-parametric tests for analyses; Friedman analyses of variance (ANOVAs) and Wilcoxon's matched pairs tests were used to evaluate within-subject comparisons, and Kruskal-Wallis ANOVAs were used for between-subject analyses.

Viewing times varied significantly, $\chi^2(2) = 8.00$, $P < 0.05$, Kendall Coeff of Concordance = 0.57, by categorical diagnosis (invasive; carcinoma *in situ*; benign/atypical) as shown in Table 2. Cases for which the diagnosis falls between benign and invasive often represent more challenging diagnostic areas within diagnostic pathology. More specifically, viewing times were shortest for the slides that showed invasive breast cancer (M = 44.37 sec, Median = 38.75 sec) and longer for carcinoma *in situ* (M = 79.16 sec, Median = 86.53 sec) and benign/atypical cases (M = 85.16, Median = 76.04 sec). Carcinoma *in situ* cases were viewed for longer durations than invasive cases, $z(6) = 2.20$, $P < 0.05$, and benign/atypical cases also elicited longer viewing times than invasive cases, $z(6) = 2.37$, $P < 0.05$. There was not a significant difference in viewing time between benign/atypical and carcinoma *in situ* cases ($P = 0.61$). Viewing times did not vary as a function of participant experience ($P = 0.16$).

Further, accuracy varied significantly by diagnostic category as shown in Table 2, $\chi^2(2) = 12.00$, $P < 0.01$, Kendall Coeff of Concordance = 0.86. In general, carcinoma *in situ* cases elicited the lowest diagnostic accuracy as compared to invasive cases, $z(6) = 2.37$, $P < 0.05$ and benign/atypical cases, $z(6) = 2.37$, $P < 0.05$. There was no difference in diagnostic accuracy between benign/atypical and invasive cases ($P = 0.35$). Accuracy did not vary as a function of participant experience

Table 2: Mean accuracy (average % agreement with expert consensus diagnosis) and viewing time (seconds) by image diagnostic category and participant experience

Participants' experience level	Benign/Atypia		Carcinoma *in situ*		Invasive		All	
	Accuracy	Time	Accuracy	Time	Accuracy	Time	Accuracy	Time
Breast specialist	90	87.75	50	64.70	100	45.43	80	72.37
General faculty	80	44.67	33	62.17	75	13.00	65	43.56
Residents	80	110.43	56	100.12	100	64.58	77	98.17
Overall	83	85.16	48	79.16	93	44.37	74	75.20

Table 3: Regression analysis of mouse cursor position as a predictor for eye-gaze position in x-and y-coordinate space by slide type and participant experience

Betas (slopes)	Benign/Atypical		Carcinoma *in situ*		Invasive		All	
	X	Y	X	Y	X	Y	X	Y
Breast specialist	0.42	0.27	0.39	0.25	0.39	0.22	0.41	0.26
General faculty	0.36	0.37	0.43	0.38	0.46	0.46	0.41	0.37
Residents	0.40	0.16	0.27	0.22	0.36	0.24	0.36	0.18
Overall	0.39	0.25	0.35	0.27	0.40	0.30	0.39	0.26
R-values								
Breast specialist	0.34*	0.22*	0.27*	0.29*	0.40*	0.24*	0.33*	0.24*
General faculty	0.34*	0.33*	0.35*	0.28*	0.52*	0.34*	0.36*	0.31*
Residents	0.36*	0.15*	0.24*	0.21*	0.31*	0.25*	0.32*	0.18*
Overall	0.35*	0.19*	0.27*	0.24*	0.37*	0.24*	0.33*	0.21*

*P<0.01

(P = 0.37). For cases of invasive cancer, all participants, with the exception of one pathologist in one case, agreed with the consensus diagnosis. The three cases of carcinoma *in situ* proved more challenging; no participant agreed with the consensus diagnosis in all three cases (accuracy M = 0.48, Median = 0.33), and only three participants agreed with the consensus diagnosis for two of the three carcinoma *in situ* cases.

Mouse Cursor Position and Eye-Gaze Position

To assess whether mouse cursor movements can be used independently to grossly index patterns of visual attention, we conducted regression analyses to assess whether mouse cursor position predicts eye-gaze position in x- and y-coordinate space [Table 3]. Overall, mouse cursor data showed the strongest predictive value along the x-dimension (Rx = 0.33) relative to the *y*-dimension (Ry = 0.21). Similarly, regression slopes (i.e., beta coefficients) for both x- and y-coordinate space were significantly greater than zero (Mx = 0.39, My = 0.26; P < 0.001), a pattern that was consistent for all participants.

Distance between the cursor and eye-gaze position (px; pixels) was calculated as Δx (distance between the cursor x-coordinate and eye-gaze x-coordinate) and Δy (distance between cursor y-coordinate and eye-gaze y-coordinate).[28] Frequency distributions plotting Δx and Δy are depicted in Figures 1a and 1b. Collapsed across participants, the highest frequency Δx was 4.00px (SD = 16.10), and Δy was 37.50px (SD = 28.08), demonstrating that cursor and eye-gaze position were generally close together along the *x*-coordinate over time, but relatively loosely coupled along the *y*-coordinate.

Euclidean distance ($\sqrt{(\Delta x)^2 + (\Delta y)^2}$) was calculated and plotted in Figure 1c. Collapsed across participants, mean Euclidean distance between gaze, and mouse cursor position was 318.56px (approx. 3.7 inches), and the median was 292.70px. Euclidean distance did not vary by slide type (P < 0.05). As seen in Figure 1c, the highest frequency Euclidean distances were generally between 0-200 pixels. On average, the cursor position tended to be slightly below and to the right of eye-gaze amongst all subjects. [Figure 2] The computer mouse itself was always positioned to the right of the monitor, and data on participants' handedness was not collected.

DISCUSSION

In this study, we gathered and analyzed detailed data on simultaneous eye-gaze and mouse cursor movement as pathologists interpreted digital whole slide images and found a medium predictive value of mouse cursor movements in accounting for eye gaze behavior (R_x = 0.37 and R_y = 0.27). This relationship was strongest along the *x*-axis and was not improved by introducing a time lag.

Participants quickly and accurately diagnosed the cases of invasive breast cancer; once they noted the histologic features of invasive breast cancer, their visual search was over. In contrast, cases classified as benign and atypia were associated with both longer average viewing time and lower diagnostic accuracy (benign/atypia: overall diagnostic accuracy (83%), mean viewing time (85.16 sec); invasive breast cancer: overall diagnostic accuracy (93%), mean viewing time (44.37 seconds)). This can be expected as these non-invasive pathologic cases can be more difficult to interpret because a thorough review is required to rule-out the presence of a clinically significant lesion.[29]

Notably, the highest frequency Δx was 4.00px (SD = 16.10), and Δy was 37.50px (SD = 28.08) when collapsed across participants, demonstrating a close spatial coupling between eye-gaze and mouse cursor positions along the *x*-coordinate, and a relatively loose coupling along the *y*-coordinate. A possible explanation for the difference between Δx and Δy is that users place the cursor above or below their gaze to prevent it from distracting visual analysis or partially obscuring the image. Users will often keep the cursor slightly offset from where they are viewing the image, as to not occlude that particular part of the screen.[30] Studies in human computer interaction have shown that pointer orientation affects performance,[31,32] and the design of the arrow-headed mouse cursor itself, which in this case, pointed upward and to the left, may encourage this method of viewing.[33,34]

While we have not found any studies that explicitly track the combination of eye-gaze and cursor movement to examine the visual search behaviors of pathologists in digital pathology, a few innovative studies have evaluated eye tracking or image manipulation tracking. Other studies that have used eye tracking to understand pathologists viewing behavior have presented images to the pathologists via a variety of graphical user interfaces including Power Point slides and virtual microscopy.[35,36] Information on visited sites within the image and time spent in each area can be used to understand scanning patterns of physicians and regions of the image that attract their attention.[12,37] In general, investigators at the forefront of research in this area of studying physicians' assessment of virtual whole slide images have involved up to five participants.[12,36-39] If data on pathologists' interpretive behavior could be captured over the Internet using Web-based applications, the numbers of participants could be much higher.

A limitation of our study is that our methodology and analyses do not allow us to effectively distinguish between foveal (central) and para-foveal (peripheral) attention towards image elements; of course, we note that pathologists, particularly experts, rely strongly on both central and peripheral vision to examine aspects
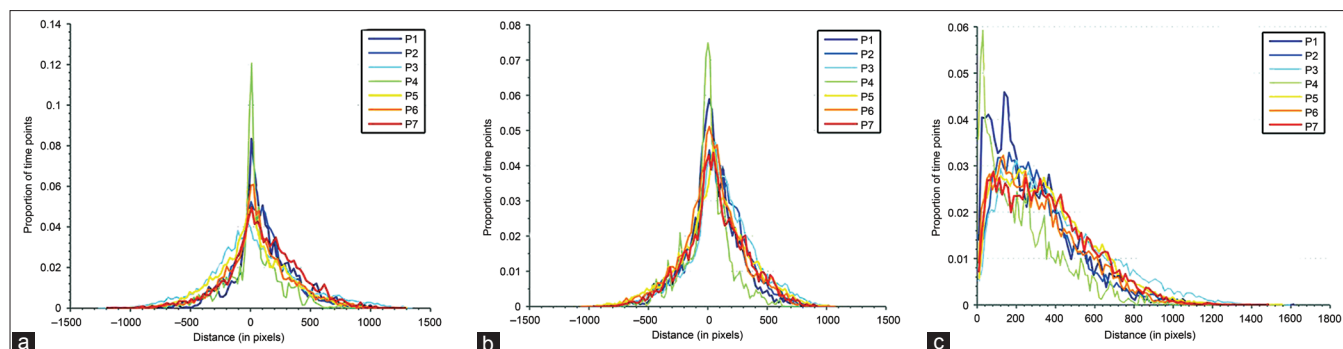
Figure 1: Distance between eye-gaze and cursor position: X-coordinates, y-coordinates, and Euclidean distance for all participants (P1-P7); (a) Distribution of the distance between eye-gaze and cursor position: X-coordinates for all participants (P1-P7); (b) Distribution of the distance between eye-gaze and cursor position: Y-coordinates for all participants (P1-P7); (c) Euclidean distance between eye-gaze and cursor position for all participants (P1-P7)
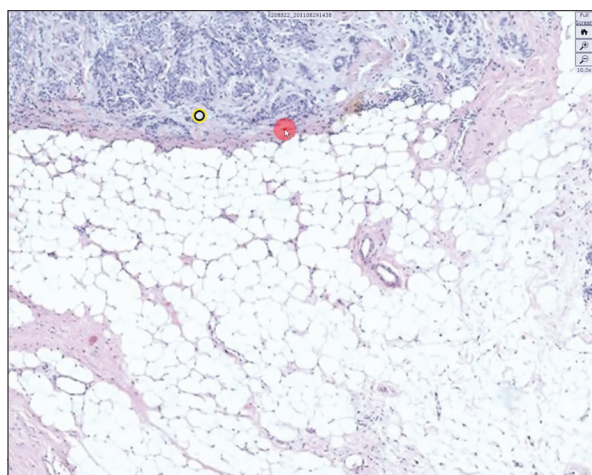

Figure 2: Screen shot of digital image viewer showing participant's concurrent eye (yellow/black circle) and mouse cursor position (red)

of the entire digital whole slide image.[12] Therefore, our methodology and analyses may not reveal some of the complex dynamics of true pathologist visual scanning behavior. Further, some gaze-cursor asynchrony might be attributed to tagging behavior, which involves temporarily leaving the mouse cursor in an area of potential interest while using the eyes to briefly examine other image regions.[40] Interestingly, the present results suggest that while pathologists may be employing a tagging strategy to efficiently compare different regions of interest on the slide, in general, they tend to keep their gaze relatively close to the cursor in monitor space, a behavior that may be learned because the design of the viewer centers the image on the mouse position as higher zoom level is activated when using the mouse scroll wheel. Additionally, individual differences in cursor manipulation by pathologist (i.e. neglecting the cursor while interpreting the images) may bias the results toward certain behaviors; consequently, data from a single pathologist might not reflect the general cursor manipulation behavior exhibited by all pathologists. Additionally, participants' behavior may vary as a function of their experience viewing WSI, but our study was limited in that data on participants'

experience with WSIs was not collected. Future studies would add to the literature by exploring the possible association between WSI viewing experience and specific viewing and cursor manipulation behaviors.

The slide test set from the present study also posed two important limitations: (1) the test set was relatively small, comprising only 10 digitized breast pathology slides, and (2) the composition of the test set included a high proportion of breast pathology cases that are difficult to interpret (e.g., carcinoma *in situ*). In addition, this study collected detailed data on eye and mouse cursor movement along both *x*- and *y*- axes, but data on participants' level of zoom (movement along the z-axis) was not collected. Given that zoom level changes the physical distance between eye gaze and mouse cursor positions, level of zoom could be considered in future studies.

Eye-tracking studies within the domains of aviation, airport security screening, and radiology have proven useful in understanding how to improve performance of visual search tasks.[14-17,41] While eye-tracking studies are relatively new in the field of medicine, preliminary findings are promising. For example, novice radiologists showed improved performance after viewing a representation of an expert radiologist's visual search pattern prior to interpreting the same image.[41]

Likewise, if a correlation between eye-gaze and cursor movements were established, results from mouse cursor studies could also possibly inform future educational interventions that aim to improve pathology trainees' diagnostic behavior, and determining if certain types of cursor behaviors are associated with more efficient and accurate diagnoses of cases could be beneficial in educating pathologists on efficacious scanning practices as the field moves into the digital era.

Future studies would look to further expand on the efficacy of cursor tracking as a complement to eye tracking when gauging pathologist attention to particular image regions. For example, examining the strength of eye and cursor

correlation over different types of cursor behavior (inactive cursor, mouse clicks, using the cursor for tagging specific areas of interest) would be important in deciding the predictive value of cursor behavior in determining user interest, especially because these behaviors vary by user. This would be beneficial in understanding if specific cursor behaviors should be isolated when studying users' attention remotely via the Web. For example, long periods of time in which the cursor is static may indicate that the user has stepped away from the interface for a "lunch break." The exclusion of "lunch break" data is not relevant for our study, because research staff monitored pathologists throughout each session, and we observed no such periods of cursor stasis. However, in the event cursor data were gathered over the Web, we would recommend that researchers establish criteria for evaluating and possibly excluding long periods in which the mouse is static. Additionally, time-stamped data on when pathologists begin and end zooming may provide further information on the true area they have selected for diagnostic analysis.

Our study adds to the understanding of how pathologists interpret whole digital biopsy slides by examining concurrent data on both eye-gaze and cursor movement. In summary, we examined spatial coupling between eye-gaze and mouse cursor positions, and found a medium correlation overall between mouse and eye movement ($R_x = 0.33$ and $R_y = 0.21$). Determining if mouse cursor movement data are a reliable indicator of physician attention and diagnostic behavior has important implications for large-scale studies of pathologists' interpretive behaviors; our results suggest that mouse cursor movement might have the potential to aid in the identification of behaviors associated with diagnostic accuracy, interpretive errors, and efficient screening practices. These are critical factors to study as digital imaging technology diffuses into the practice of diagnostic pathology.

ACKNOWLEDGEMENT

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