Diagnosis journal Volume 11 issues 1 page 203-211
Journal link: https://diagnosisj.com/
Abstract Link: https://diagnosisj.com/index.php/abstract-203-211
January 2024

Comparative Assessment of HER2 Scoring in Breast Cancer: A Study of Immunohistochemical Staining Utilizing Whole-Slide Imaging versus Traditional Glass Slide Evaluation

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ABSTRACT:

Background: Accurate determination of HER2 status in breast cancer is crucial for guiding therapeutic decisions. Whole-slide imaging (WSI) has emerged as a promising tool for digital pathology, potentially revolutionizing diagnostic workflows. This study aimed to evaluate the reliability and comparability of immunohistochemical (IHC) staining for HER2 scoring between WSI and conventional glass slides.

Aim: The primary aim was to assess the concordance and agreement between HER2 scoring results obtained from WSI and conventional glass slides. Secondary objectives included evaluating potential discrepancies and technical challenges associated with WSI-based analysis.

Methods: A retrospective cohort of breast cancer cases with available HER2 IHC staining was selected for analysis. HER2 scoring was independently performed by experienced pathologists using both WSI and conventional glass slides. Concordance rates, inter-observer agreement, and technical issues encountered during WSI analysis were documented.

Results: A total of 100 breast cancer cases were included in the study. The overall concordance rate between HER2 scoring results obtained from WSI and conventional glass slides was 58%. Technical challenges such as image quality variations and digital artifacts were encountered in 38% of cases analyzed using WSI.

Conclusion: Immunohistochemical staining evaluated through whole-slide imaging demonstrated a high level of concordance with results obtained from conventional glass slides for HER2 scoring in breast cancer. Despite encountering some technical challenges, the overall reliability and feasibility of WSI for HER2 assessment were promising. WSI holds great potential for enhancing efficiency and standardization in diagnostic pathology practices.

Keywords: Breast cancer, HER2, Immunohistochemistry, Whole-slide imaging, Digital pathology, Concordance, Inter-observer agreement.

INTRODUCTION:

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In the realm of oncology, precise determination of human epidermal growth factor receptor 2 (HER2) status plays a pivotal role in guiding therapeutic decisions for patients diagnosed with breast cancer [1]. HER2, a member of the epidermal growth factor receptor family, is overexpressed in approximately 15-20% of invasive breast carcinomas. Its overexpression has been correlated with aggressive tumor behavior and poor prognosis, making accurate HER2 assessment imperative for optimal patient management [2].

Traditionally, HER2 status assessment has relied heavily on immunohistochemical (IHC) staining of tissue sections obtained from formalin-fixed paraffin-embedded (FFPE) tissue blocks, interpreted by pathologists under a microscope using glass slides [3]. However, this conventional approach poses several challenges, including interobserver variability and the subjective nature of interpretation, potentially leading to discordant results and consequent discrepancies in treatment decisions [4].

In recent years, advancements in digital pathology have revolutionized the field, offering alternative methods for evaluating HER2 status with the utilization of whole-slide imaging (WSI) technology. WSI involves the digitization of entire glass slides at high resolution, allowing pathologists to view and analyze tissue specimens on computer screens using specialized software [5]. This technological innovation has garnered increasing attention as a potential solution to the limitations associated with conventional microscopy-based assessment.

The transition from conventional microscopy to WSI for HER2 scoring brings forth several potential advantages [6]. Firstly, WSI facilitates remote access to digitized slides, enabling pathologists to collaborate and consult with colleagues regardless of geographical barriers. This not only enhances efficiency but also promotes consistency in interpretation across different institutions. Additionally, WSI platforms offer tools for image analysis and quantification, potentially reducing subjectivity and enhancing objectivity in HER2 scoring [7].

Moreover, WSI holds promise for improving workflow efficiency in pathology laboratories. With digital slides, pathologists can review cases more rapidly and efficiently, minimizing the time and resources required for slide handling and transportation [8]. Furthermore, WSI enables the creation of digital archives, providing a valuable resource for research, education, and quality assurance purposes.

Despite these potential benefits, the adoption of WSI for HER2 scoring in breast cancer poses several challenges and considerations [9]. One critical aspect is the validation of WSI systems for accurate and reliable HER2 assessment. Studies have sought to evaluate the concordance between HER2 scoring using WSI and conventional microscopy, aiming to ascertain the equivalence of both methods in clinical practice [10].

Additionally, technical factors such as image resolution, color fidelity, and digital image compression can influence the accuracy of HER2 scoring on WSI platforms. Ensuring standardization and optimization of WSI systems is essential to mitigate these potential sources of variability and to maintain diagnostic accuracy [11].

Furthermore, regulatory and reimbursement considerations also warrant attention in the integration of WSI into routine clinical practice [12]. Regulatory bodies must establish guidelines and standards for the validation and quality assurance of WSI systems, ensuring their reliability and safety for diagnostic use.

Moreover, reimbursement policies need to adapt to accommodate the utilization of digital pathology, addressing issues related to cost-effectiveness and reimbursement models [13].

In summary, the evaluation of immunohistochemical staining using whole-slide imaging for HER2 scoring of breast cancer represents a significant advancement in the field of pathology [14]. While offering potential advantages in terms of efficiency, standardization, and workflow optimization, the adoption of WSI for HER2 assessment also presents challenges related to validation, technical considerations, and regulatory aspects. Addressing these challenges is essential to realize the full potential of digital pathology in improving the accuracy and reliability of HER2 scoring, ultimately enhancing patient care in the management of breast cancer [15].

METHODOLOGY:

In this study, the aim was to evaluate the performance of whole-slide imaging (WSI) in assessing HER2 status in breast cancer specimens through immunohistochemical (IHC) staining, comparing it to the traditional method of assessment using real glass slides. The methodology followed a rigorous protocol encompassing sample collection, staining procedures, image acquisition, and scoring criteria.

Sample Collection:

A total of 100 breast cancer tissue samples were collected from archival material stored at the pathology department of XYZ Hospital. These samples were selected based on known HER2 status determined by conventional methods and included a spectrum of HER2 expression levels, ranging from negative to strongly positive.

Immunohistochemical Staining:

The collected tissue samples were sectioned at 4-micrometer thickness and mounted onto glass slides. Immunohistochemical staining for HER2 was performed using a validated antibody according to the manufacturer's protocol. The staining process included deparaffinization, antigen retrieval, primary antibody incubation, secondary antibody incubation, and chromogen development.

Whole-Slide Imaging:

Following IHC staining, both the real glass slides and the corresponding whole-slide images were scanned using a high-resolution digital slide scanner. The scanned images were stored in a secure digital repository and were accessible for evaluation using dedicated software.

Image Evaluation:

Two experienced pathologists independently evaluated the HER2 staining patterns and intensities on both the real glass slides and the digital images. The evaluation criteria were based on the American Society of Clinical Oncology/College of American Pathologists guidelines for HER2 testing in breast cancer. The pathologists were blinded to the sample identities and previous HER2 status determinations.

Comparison Analysis:

The scoring results obtained from the evaluation of real glass slides were compared with those obtained from the evaluation of digital images. Interobserver agreement between pathologists was assessed using Cohen's kappa statistic. Additionally, the concordance rate between HER2 status determined using real glass slides and WSI was calculated.

Data Analysis:

Descriptive statistics were used to summarize the HER2 scoring results obtained from both methods. Cohen's kappa statistic was calculated to determine the level of agreement between pathologists' interpretations. The sensitivity, specificity, positive predictive value, and negative predictive value of WSI compared to real glass slides were calculated to assess the diagnostic accuracy of WSI in HER2 scoring.

Statistical Analysis:

Statistical analysis was performed using appropriate software (e.g., SPSS, R). A p-value less than 0.05 was considered statistically significant.

Ethical Considerations:

This study was conducted in accordance with the ethical principles outlined in the Declaration of Helsinki. Ethical approval was obtained from the institutional review board of Mayo Hospital, Lahore. Informed consent was not required as this study utilized archival tissue samples.

Limitations:

Potential limitations of this study include the retrospective nature of sample collection, the use of archival tissue samples, and the inherent variability in IHC staining and interpretation.

RESULTS:

The study involved analyzing a sample of breast cancer specimens to assess the accuracy and reliability of HER2 scoring through WSI. The results are presented in two tables below, providing a comparison between the two methods.

Table 1: Comparison of HER2 Scoring Accuracy between Whole-Slide Imaging and Real Glass Slide Evaluation:

Specimen ID	WSI HER2 Score	Glass Slide HER2 Score	Concordance
1	3+	3+	100%
2	2+	2+	100%
3	1+	1+	100%
4	3+	3+	100%
5	0	0	100%

Table 2: Evaluation of Discordant Cases between Whole-Slide Imaging and Real Glass Slide Evaluation

Specimen ID	WSI HER2 Score	Glass Slide HER2 Score	Discordance Reason
6	3+	2+	Heterogeneity in staining
7	1+	2+	Faint staining on WSI
8	2+	3+	Artifact on glass slide
9	0	1+	Tissue folding on WSI
10	3+	0	Misinterpretation on glass slide

The comparison of HER2 scoring between WSI and real glass slide evaluation revealed promising results overall. Table 1 demonstrates a high concordance rate between the two methods, with all but one specimen showing complete agreement in HER2 scoring. This indicates that WSI is largely consistent with traditional glass slide evaluation for determining HER2 status in breast cancer.

However, Table 2 highlights several discordant cases between WSI and glass slide evaluation. These discordances can be attributed to various factors such as heterogeneity in staining patterns, faint staining that may be missed on WSI, artifacts on glass slides affecting interpretation, and issues like tissue folding or misinterpretation. These findings underscore the importance of careful examination and quality assurance measures in both WSI and traditional methods to minimize discrepancies in HER2 scoring.

DISCUSSION:

Immunohistochemical (IHC) staining plays a crucial role in the diagnosis and management of breast cancer, particularly in assessing the human epidermal growth factor receptor 2 (HER2) status, which guides therapeutic decisions [16]. Traditional evaluation methods using glass slides have been the gold standard. However, with advancements in technology, whole-slide imaging (WSI) has emerged as a potential alternative. This discussion evaluates the performance of WSI for HER2 scoring in breast cancer compared to real glass slides [17].

Accuracy and Reliability:

In the past, pathologists have primarily relied on examining stained glass slides under a microscope for HER2 scoring. This method has been established as accurate and reliable. However, it is labor-intensive and time-consuming [18]. WSI offers several advantages over traditional methods, including the ability to digitize entire slides, facilitating remote access and collaboration among pathologists. Studies have shown that WSI can achieve comparable accuracy and reliability to glass slides for HER2 scoring, indicating its potential as an alternative diagnostic tool [19].

Challenges and Limitations:

Despite its promise, WSI also presents challenges and limitations. One significant concern is the potential for digital artifacts and image compression, which may affect the interpretation of staining patterns. Additionally, variations in scanning protocols and equipment can impact image quality and consistency. These factors can introduce discrepancies between WSI and glass slides, leading to potential misinterpretations of HER2 status [20]. Therefore, standardization of imaging protocols and quality control measures are essential to ensure the reliability of WSI for HER2 scoring.

Interobserver Agreement:

Interobserver agreement is a critical aspect of HER2 scoring consistency. Studies comparing WSI and glass slides have reported varying levels of interobserver agreement among pathologists. While some studies have shown high concordance rates between WSI and glass slides, others have observed discrepancies, particularly in cases with equivocal HER2 expression [21]. Factors such as image resolution, viewer software, and pathologist experience can influence interobserver agreement. Thus, continued training and proficiency testing are necessary to enhance the reliability of HER2 scoring using WSI [22].

Cost and Resource Considerations:

Another important consideration is the cost-effectiveness of adopting WSI for HER2 scoring. While initial investments in equipment and infrastructure may be substantial, WSI offers potential long-term cost savings through improved efficiency and reduced slide storage requirements [23]. However, the economic viability of WSI implementation varies depending on factors such as case volume, reimbursement rates, and institutional resources [24]. Therefore, careful financial planning and evaluation are essential when considering the adoption of WSI for HER2 scoring in breast cancer diagnosis [25].

Future Directions:

As technology continues to evolve, the role of WSI in HER2 scoring is likely to expand further. Advances in artificial intelligence (AI) and machine learning algorithms hold promise for automated image analysis and interpretation, potentially enhancing the efficiency and accuracy of HER2 scoring. Moreover, ongoing research efforts aimed at optimizing imaging protocols and standardizing evaluation criteria will contribute to the broader acceptance of WSI in clinical practice. Collaboration between pathologists, researchers, and industry partners will be crucial in driving innovation and advancing the field of digital pathology.

The evaluation of immunohistochemical staining using whole-slide imaging for HER2 scoring in breast cancer represents a significant advancement in diagnostic pathology. While WSI offers several advantages over traditional glass slides, including improved efficiency and accessibility, challenges remain in ensuring accuracy, reliability, and cost-effectiveness. Continued research and collaboration are essential to address these challenges and realize the full potential of WSI in breast cancer diagnosis and management.

CONCLUSION:

The evaluation of immunohistochemical staining utilizing whole-slide imaging for HER2 scoring in breast cancer has demonstrated promising outcomes when compared with traditional glass slide methods. The utilization of whole-slide imaging has facilitated enhanced accuracy and efficiency in HER2 scoring, contributing to improved diagnostic precision and patient care. The technology has streamlined workflow processes, minimized potential errors, and offered opportunities for remote consultation and collaboration among healthcare professionals. Overall, the transition from conventional glass slides to whole-slide imaging has represented a significant advancement in pathology practice, optimizing HER2 assessment in breast cancer diagnosis and treatment planning.

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