Assessors' report for cIQc Run 11: Breast module (ER, PR and HER2)

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Assessment performed on Saturday, May 1, at Toronto General Hospital

Overview

Cases from this run were drawn from St. John's NFLD, and the tissue microarray was prepared by Nikita Makretsov. Reference staining and FISH for these cases was done at Mt. Sinai Hospital. These were unselected cases of invasive breast cancer. Once again the results of labs participating in this CIQC survey, overall, were excellent.

HER2 testing continues to be excellent, with all participating laboratories showing optimal results, as defined below. In fact, there were only 2 false positive results and no false negative results; on review of the 2 false positive results, the panel of assessors would have considered them to be 2+ staining, indicating that these errors were interpretive rather than technical.

For ER testing, the cores where there was variability in interpretation included one core where normal cells stained positively (core 9); these cells were called positive by some labs, which is understandable given the lack of an H&E stained slide to guide identification of tumor cells. The other core with variable staining was core 3 – this was a case where the number of positive nuclei varied from 1 to 5 for most labs, and it was truly near the 1% threshold for recognition of ER positivity. The variability in interpretation for this core can be attributed to sampling variability in a case. Both the original laboratory interpretation and assessors assigned variable results for this case, depending on the number of positively stained nuclei present. Apart from these two cores there were very few discordant ER results and most of these, based on the assessors' reviews, were interpretive errors, such as weak staining being interpreted as negative.

In the case of PR staining, there were no ER positive cases that were PR positive. Cores 8 and 31, like core 3 for ER, showed borderline positivity. Because different slides showed anywhere from 1-10 cells staining positively, different interpretations were made, based on the 1% cut-off, and both the original laboratory interpretation and assessors assigned variable results for this case, depending on the number of positively stained nuclei present. There were very few tumor cells present for core 24, and it was therefore not considered informative. As for ER, apart from these few problematic cases there were very few "outlier" results otherwise, and most of these, based on assessor review, were interpretive rather than technical errors.

In the results for individual labs, the following definitions were applied:

Optimal result= >90% agreement rate (vs reference)

Suboptimal result= ≤90% agreement rate

Suggested actions based on assessment results:

1) if optimal staining and no missed cores, nothing need be done

2) if optimal staining and one or two of the very weakly staining/equivocal cores were considered negative, nothing need be done (negative results probably reflect sampling)

3) if optimal result (>90% concordance rate) but missed cores that were uniformly positive by reference methods and in other participating labs, we would suggest that this requires immediate attention. CIQC can make additional array slides available for retesting, if this would be of help

4) if suboptimal staining: immediately address the problem. CIQC can make additional array slides available for retesting, if this would be of help

Thank you for your participation in CIQC. We look forward to continuing to improve the service we are able to offer, working with you and the Canadian Association of Pathologists - Association canadienne des pathologistes.

For the next breast cancer biomarker run we anticipate having on-line protocol and results entry on the CIQC website, with instant feedback about your results, available on-line. We hope to unveil this website, which is under construction, at our second annual **Diagnostic Immunohistochemistry meeting, July 8 and 9 in Montreal**, before the CAP meeting. We hope to see you there!

NOTE: Garrattograms for ER, PR and HER2 below reflect results of the self-assessment for most participants. We have recently determined that self-assessment in our program is as acurate as expert assessment. Therefore, these calculations are reflective of your true success in our program. For those rare laboratories that did not submit self-assessment results, we have assessed their slides and these results are calculated based on expert assessment.

Figure 1. ER garrattogram

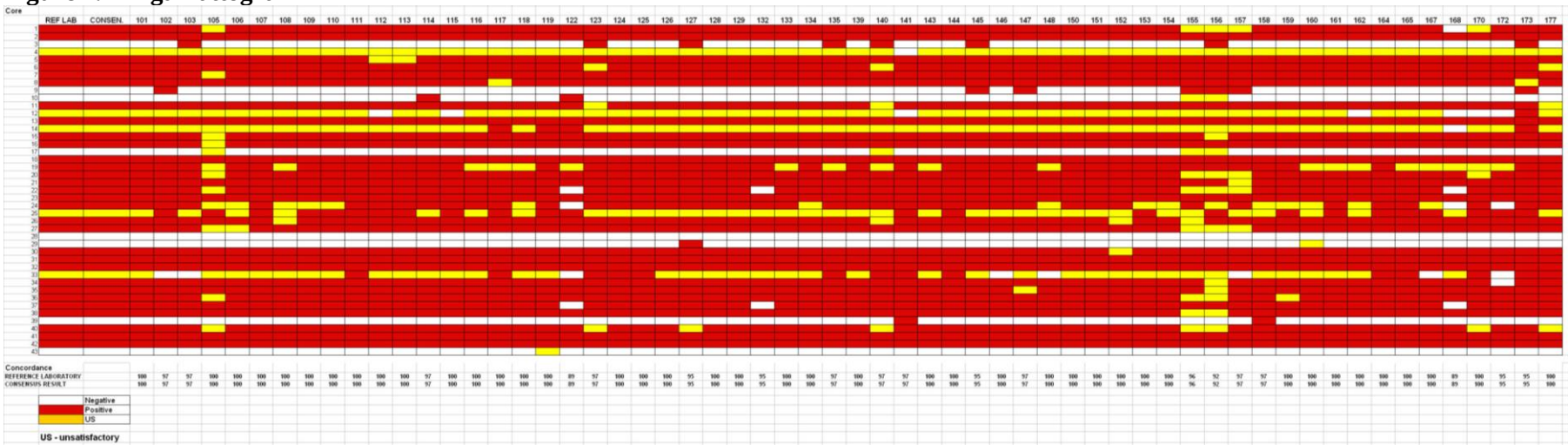

Figure 2. PR garrattogram

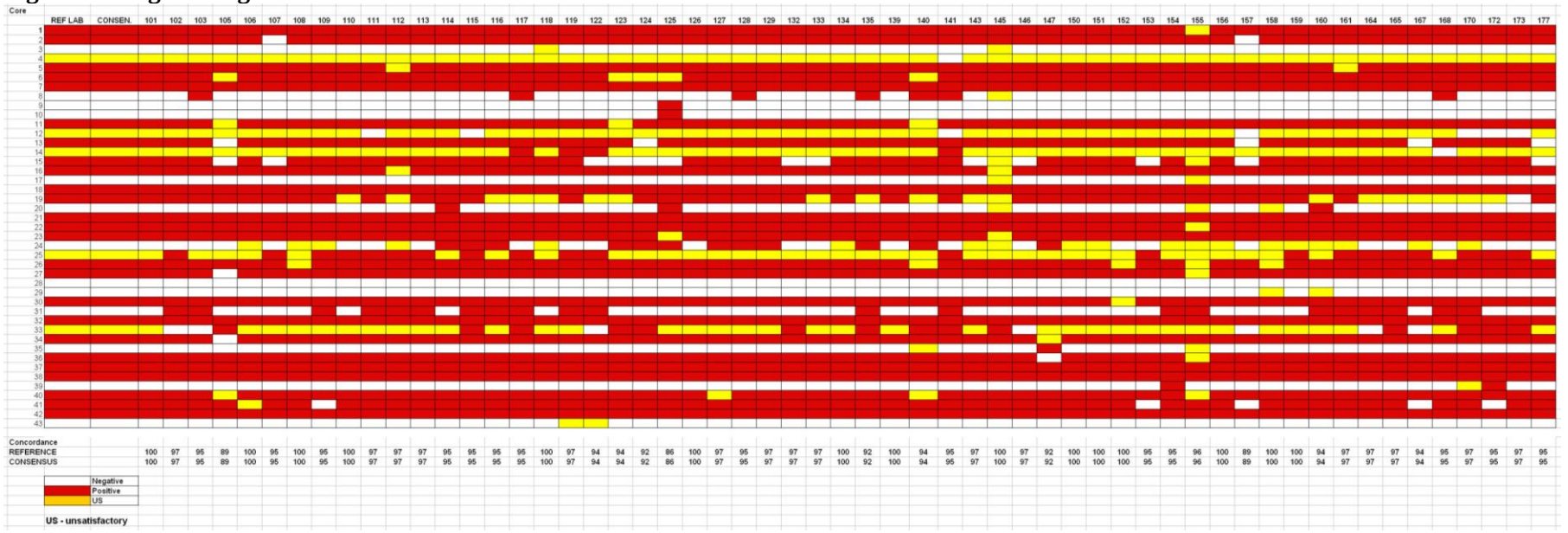

Figure 3. HER2 garrattogram