Author's response to reviews

Title: Preservation of biomolecules in breast cancer tissue by a formalin-free histology system

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Author's response to reviews:

Dr. Deborah Saltman,
Editorial Director
BMC Clinical Pathology
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RE: MS#1945273621135923

Dear Dr Saltman,

We are submitting the revised manuscript and in the following we have addressed the reviewer concerns.

Reviewer- Dr Liotta

1- Figures 3 and 4 were modified in response to the reviewer previous suggestion to show the scatter plot of all samples for RNA and DNA. Figure 3 shows higher yield for RNA but similar yield for DNA in UFPE samples compared to FFPE. Figure 4 shows higher copy number (3 to ten fold) in UFPE samples. However, as we have stated in the manuscript, each makers seems to show a different dynamic range.

2- The manuscript was edited for language clarity and grammatical errors.

3- We expanded the HER2 IHC studies in Discussion section:

For example, therapeutic decision is based on HER2 3+ positive results by IHC or evidence of amplification by FISH. Since performance of FISH as a primary test is prohibitively expensive, many institutions use a two-tier system of performing IHC as the first step and FISH as the second step. Cases with Her2-IHC score of 2+ are considered equivocal and are not treatment-candidate.
These cases need to be confirmed by FISH and must show amplification in order to receive Herceptin. In our study, 7 formalin-fixed samples had 2+ IHC score; three of these cases had 3+ score in parallel UMFIX section (all showed amplification by FISH) and two had 2+ score (one with amplification by FISH, figure 2B). Therefore UFPE samples had lower number of equivocal HER2 IHC score compared to FFPE samples. Since all of the 3+ IHC positive UFPE cases were also positive by FISH, there was no false positive result that might affect therapeutic decision based on HER2 IHC score of UFPE tissue. On the other hand, fewer cases with equivocal IHC scores in UFPE blocks means decrease in laboratory workload to perform FISH studies to validate these results. This might decrease the financial burden of performing more expensive FISH assay to confirm the equivocal IHC results. Clinical application of HercepTest performed on tissues fixed in molecular fixative need to be further studied in a larger series of cases and correlated with the response to Herceptin.

I am looking forward to hearing from you.

Sincerely yours

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