Novel digital pathology adequacy score benchmarks the performance of pre-analytical method for digital pathology and AI end-to-end tissue assays

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INTRODUCTION

The control and monitoring of pre-analytical conditions is key to minimize the noise and variability of Digital Pathology read-outs in the context of Artificial-enabled Digital Pathology tissue assay used for the assessment of liver biopsies. While modern AI algorithms can compensate for most sources of noise (FibroNest, doi: 10.1111/iv.15768), additional opportunities can be addressed for large studies.

AIM

Inspired by the definition of Adequacy for tissue biopsies, we report the development, validation, and results of a Digital Biopsy Adequacy (DBA) score as a Key Performance Indicator (KPI) to measure liver biopsy pre-analytical quality.

METHOD

The DBA score is a normalized composite score (1 to 10) to evaluate a digital pathology image along three dimensions and 24 features including

(i) Biopsy tissue and glass slide processing (11 features such as area of the biopsy, tissue rupture, folding artifacts, pathologist annotations, and wash quality)
(ii) staining quality (7 features including over or under staining, and vacuole quality)
(iii) digital scanning (6 features including out-of-focus areas, scanning stripes, and dust/debris on slide).

The score is based on a point-based method whereby defects have different penalty weights, such as one single defect can significantly affect the overall score.

The method is consistent with the August 2021 FDA Guidance to Industry and Technical Specifications for Submission of Clinical Trials Data Sets for Treatment of NASH. Bio specimen Findings (BS) domain.

Digital Pathology images are classified as:

- Non-Adequate (DBA<5)
- Minimally Acceptable (5≤DBA<8)
- Acceptable (DBA≥8)

We report aggregated DBA results for N=5227 Digital images processed since 2020 from 13 Phase 2 and 3 MASH studies.

RESULTS

Catalogue of Histological defects

- Biopsy length
- Biopsy width
- Ruptures
- Fragments
- Section Artifacts
- Section Artifacts
- Coverslip bubbles
- Staining Quality
- Ink annotations
- Folding
- Calibration
- Poor Rinsing
- Scanning Stripes
- Calibration

DBA inter-Operator Robustness

- Operator 1: 353 images
- Operator 2: random subset of 99 images

Inter-Class Correlation from MASH – 2 Operators:

<table>
<thead>
<tr>
<th>DBA Score</th>
<th>Not Acceptable</th>
<th>Minimally Acceptable</th>
<th>Acceptable</th>
</tr>
</thead>
<tbody>
<tr>
<td>Min</td>
<td>0%</td>
<td>8%</td>
<td>15%</td>
</tr>
<tr>
<td>Mean</td>
<td>12%</td>
<td>23%</td>
<td>65%</td>
</tr>
<tr>
<td>Median</td>
<td>6%</td>
<td>16%</td>
<td>75%</td>
</tr>
<tr>
<td>STD</td>
<td>14%</td>
<td>16%</td>
<td>25%</td>
</tr>
<tr>
<td>Max</td>
<td>44%</td>
<td>59%</td>
<td>87%</td>
</tr>
</tbody>
</table>

- From one operator scoring 385 images and a second independent operator scoring a random subset of 99 images, the Intra-Class Correlation (ICC) is 0.876 (“excellent”, Cichetti, 1994) and the Linear Correlation is 0.889 (“good”, Koo, 2016).
- We observe significantly different Not Acceptable ratios (Min 0%, Mean 8%, Median 6% Std 10% Max 41%) and Acceptable Ratios (35%, 71%, 79%, 19%, 97%) across studies.
- The main tool causes for non and minimal adequacy are overstaining, sectioning and folding artefacts, which can be resolved by basic quality control procedures and rework. In best class performers demonstrate non-acceptable images can be fully avoided.
- The industry benchmark (13 studies, 5227 images) demonstrates that defect rates (not-acceptable biopsies) can be realistically expected to be below 3% and that the rate of fully adequate digital images be above 80%.

CONCLUSIONS

The use of a KPI for pre-analytical quality in a Digital Pathology end-to-end tissue assay has the potential to significantly improve the Digital Pathology Images used in MASH studies. This KPI should be used to incentivize some pre-analytical laboratories to implement basic Quality Assurance and rework processes.

CONTACT INFORMATION

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