

# Summary of Changes Implemented in Revised Manuscript

Below, we summarize the changes and additions incorporated into the revised version of the manuscript.

## 1. Limitations Section

- Added explicit discussion of limitations:
  - Small dataset size and lack of direct pathologist comparison, which may affect generalizability.
  - Future work will expand validation across multi-center cohorts and integrate multimodal data to enhance clinical relevance.

## 2. Statistical Analyses

- Expanded statistical evaluation of cellular density and fibre composition differences:
  - **Cell Density:** Kruskal–Wallis  $H = 13.64$ ,  $p = 0.0034$ ; post-hoc tests confirmed significant differences (Grade 2 vs Grade 3:  $p = 0.026$ ; Grade 3 vs Grade 4:  $p = 0.009$ ).
  - Zone-wise analysis showed strong positive correlation ( $r = 0.692$ ) between superficial (Zone 1) and deep (Zone 2) regions. Cell density consistently declined with increasing fibrosis grade (Fig. \ref{fig:cell\_density\_box}), consistent with reduced fibroblast activity in advanced fibrosis.
  - **Fibre Composition:** Kruskal–Wallis  $H = 17.26$ ,  $p = 0.00063$ ;  $\epsilon^2 = 0.385$  (large effect size). Post-hoc analysis confirmed Grade 2 vs Grade 3:  $p = 0.0037$  as a major point of separation.
  - **Correlation Analysis:** fine fibrils ( $\rho = -0.63$ ,  $p = 0.00001$ ); bundled fibres ( $\rho = +0.63$ ,  $p = 0.00001$ ), supporting biological consistency.

## 3. Training Protocols and Reproducibility

- Detailed training settings have been added:
  - **Fibrosis classification:** Cross-Entropy loss, Adam optimizer (LR =  $1e-4$ , cosine scheduler, weight decay 0.1), batch size 24, 15 epochs.

- **Segmentation:** Composite BCE + Dice + Jaccard loss, Adam optimizer (LR =  $1e-4$ , ReduceLROnPlateau scheduler, weight decay  $1e-6$ ), batch size 16, 50 epochs on  $256 \times 256$  patches.
- Commitment to reproducibility: the codebase and trained weights are being cleaned and will be publicly released before final submission.

#### **4. Fibrosis Region Detector**

- Added missing description of the fibrosis region detector:
  - A lightweight CNN (two convolutional layers with ReLU, followed by a 2-layer MLP) trained on  $\sim 250$  labeled patches (fibrosis vs non-fibrosis).
  - Achieved 94.2% accuracy on a held-out test set.
  - Used exclusively for isolating connective tissue regions prior to downstream analysis.