INNERVE: AUTOMATIC DETECTION OF NERVE FIBERS IN SKIN BIOPSIES

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1 MOTIVATION

- Around 240 000 people suffer from **Small Fiber Neuropathies (SFNs)** in Europe.
- Patients suffering from SFNs experience sensitivity loss and neuropathic pains which ultimately lead to invalidity.
- The diagnosis consists in counting all the small fibers in skin biopsies taken on the patient. This task, done by high qualified medical professionals, is **painful**, **repetitive** and **time-consuming**.
- Consequently, SFNs are still **underdiagnosed**. Proposing tools to facilitate their detection is a major challenge.

2 OBJECTIVES

- Innerve aims at proposing a **computer-aided diagnosis solution for SFNs** by **automating the counting of nerve fibers in skin biopsies.**
- The solution integrates in the physicians' visualization software by displaying the detected fibers for human validation.
- Innerve evolves in a medical context such that **high and reliable results** are required.
- A **thorough analysis** of the model performances is done at each step of the process : epidermis segmentation, fiber detection, and result aggregation.

3 DATA

The input data are **3D immunofluorescent images** acquired from a slide scanner where 2 to 4 samples (from skin biopsies) have been placed on it, see Fig. 1. The image depth corresponds to the focus point of the scanner.

- A total of 86 annotated slides have been provided.
- Images have a very high resolution (~ 100 000 × 40 000 px).
- Images are anonymized with a controlled dedicated algorithm.
- We are interested in the fibers that cross the basal membrane.
  - → A very localized and small region of the input slide.
  - → Fibers are very small; we must keep the full resolution to detect them.

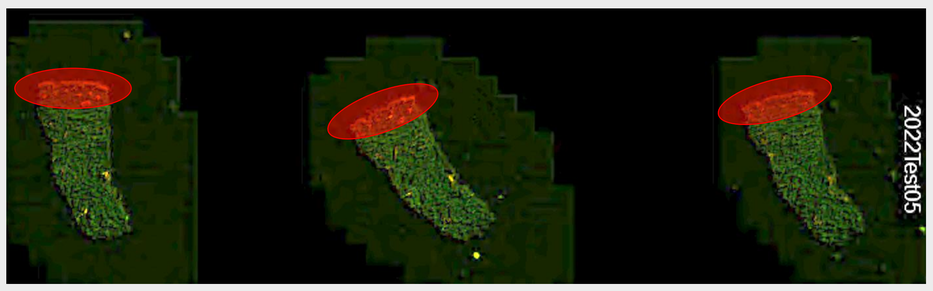

Fig. 1: Example of a scanned slide with 3 samples of skin biopsies. Red circles show the region of interest (i.e., where the crossing fibers are located). Only a small part of the input image is needed.

4 METHODOLOGY & RESULTS

DELINEATION OF THE EPIDERMAL REGION

The epidermal region is our **Region of Interest** (ROI) which it where the fibers are located. We use a DeepLabv3+ segmentation model to detect this part of the image, Fig. 2. Final model gives a **75% Dice Score (DSC)**

SMALL CROSSING FIBERS DETECTION

We use an EfficientDet-D4 object detection model (Fig. 3) trained on patches from the RoI. Qualitative Results are shown in Fig. 4. Final model gives: **AP all = 26% ; AP@50 = 60%**

AGGREGATION OF THE DETECTIONS

The detections should be aggregated through the patches. We use a clustering method based on the distance between the predictions, Fig. 5. **Precision: 72% and Recall: 72%**

PATENTED AI

The presented methodology for detecting crossing nerve fibers in large immunofluorescent images has been patented "procédé de détection automotatisé d'un élément biologique dans un échantillon de tissu."

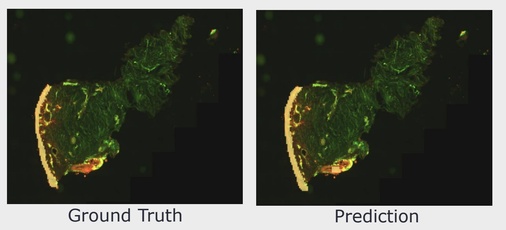

Fig. 2: Segmentation of the epidermis using a DeepLabv3+ [2]. At the left side the ground truth annotation and at the right side the model prediction

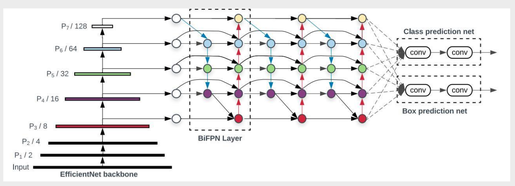

Fig. 3: We choose EfficientDet as our detection model because it gave the best results compared to other

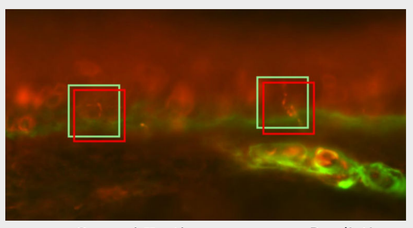

Fig. 4: Fiber detection result on a patch.

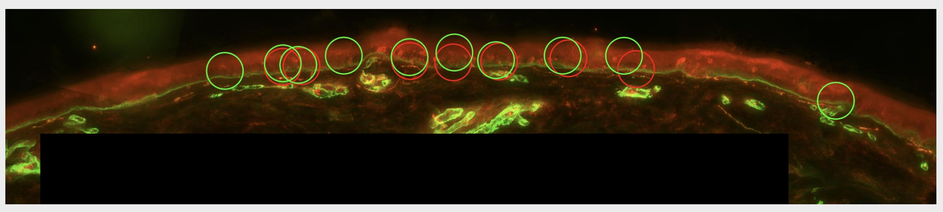

Fig. 5: Detections are aggregated to the slide level with a clustering method

5 CONCLUSION & PERSPECTIVES

CONCLUSION

- Innerve is an AI assisted tool for accelerating the diagnostic of Small Fiber Neuropathies.
- Innerve is an end-to-end solution to process very large medical images.
- Our method is multiple steps and rely on two deep neural networks:
  - A **segmentation model for the epidermis region.**
  - A **detection model for the crossing fibers** near the basal membrane.
- Innerve to be used in a clinical context: Ongoing throughout evaluation with medical professionals for validating that Innerve is as performant as a human annotator.
- Anonymous images made Open Source with **Health Data Hub** support.

FUTURE WORKS

- Fiber detection scores are uncalibrated: ongoing work focus on providing confidence levels on detections for more interpretable results. This problem is addressed in an ongoing PhD thesis.
- The current detection model (EfficientDet) gave the best results compared to other similar models. However, we could use the latest variants based on the recently emerging Transformers architectures.
- The upcoming deployment of Innerve in operational environment of the hospital and the consequent clinical trials with our tool will determine the future technical iterations of our algorithms.

This project is supported by a HDH x BPI grant "IA pour une experience de santé améliorée"