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Evaluation of two automatic image processing approaches for oligoclonal band detection: an expert system and a deep learning model

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BACKGROUND

Cerebrospinal fluid (CSF) restricted oligoclonal bands (OCB) are the established immunological biomarker for multiple sclerosis (MS) diagnosis

OCBs report persistent intrathecal synthesis of immunoglobulin G (IgG) and are evidence of dissemination in time of neurological damage.

Isoelectric focusing (IEF) and immunoblotting is the gold standard technique to detect OCBs

OCB visual quantification on the resulted IEF migration image is a complex, tedious task subject to misinterpretations and hence has high inter and intra expert variabilities

AUTOMATIC OCB DETECTION

We have developed Expert-IEF, an image processing tool for automatic analysis of IEF migration images with three major processing steps:

Lane segmentation: lane's contours are segmented simultaneously "in ribbon" using an original formulation of open active contours [1]

OCB straightening: distorted OCBs during migration are transformed back into ideal horizontal OCBs via an innovative coupling of a hierarchy of image resolutions to a hierarchy of deformations [2]

OCB detection: we proposed two approaches:

- OCB-ES:** (expert system) an expert knowledge driven model, that requires a prior step of OCBs' relevant feature extraction. Auto-explicative model with comprehensive rationale and results
- OCB-DL:** (Deep Learning) a massive data driven model that has the advantage of extracting OCBs' relevant features autonomously but is not straightforward explainable

AIM

Benchmarking the performance of the two approaches and four experts to detect OCBs, the references being:

- a visual on-membrane expert consensus analysis
- the final classification of the disease

DATA GATHERING

982 CSF lanes (80% training/validation ; 20% test) with :

- Visual on-membrane expert consensus analysis
- Final classification of the disease (at the time of the inclusion) : MS (P, RR), versus control (non-inflammatory central nervous system related disease)

Inclusion criteria: From French cohorts (POLAR, reference NCT02043964) and (Expert-IEF, reference RNIPH-2021-37) Jan 2014 to Dec 2021

Exclusion criteria: (i) mirror pattern (ii) with non-analyzable IgG migration region (highly artifactual or deformed)

EVALUATION METHOD

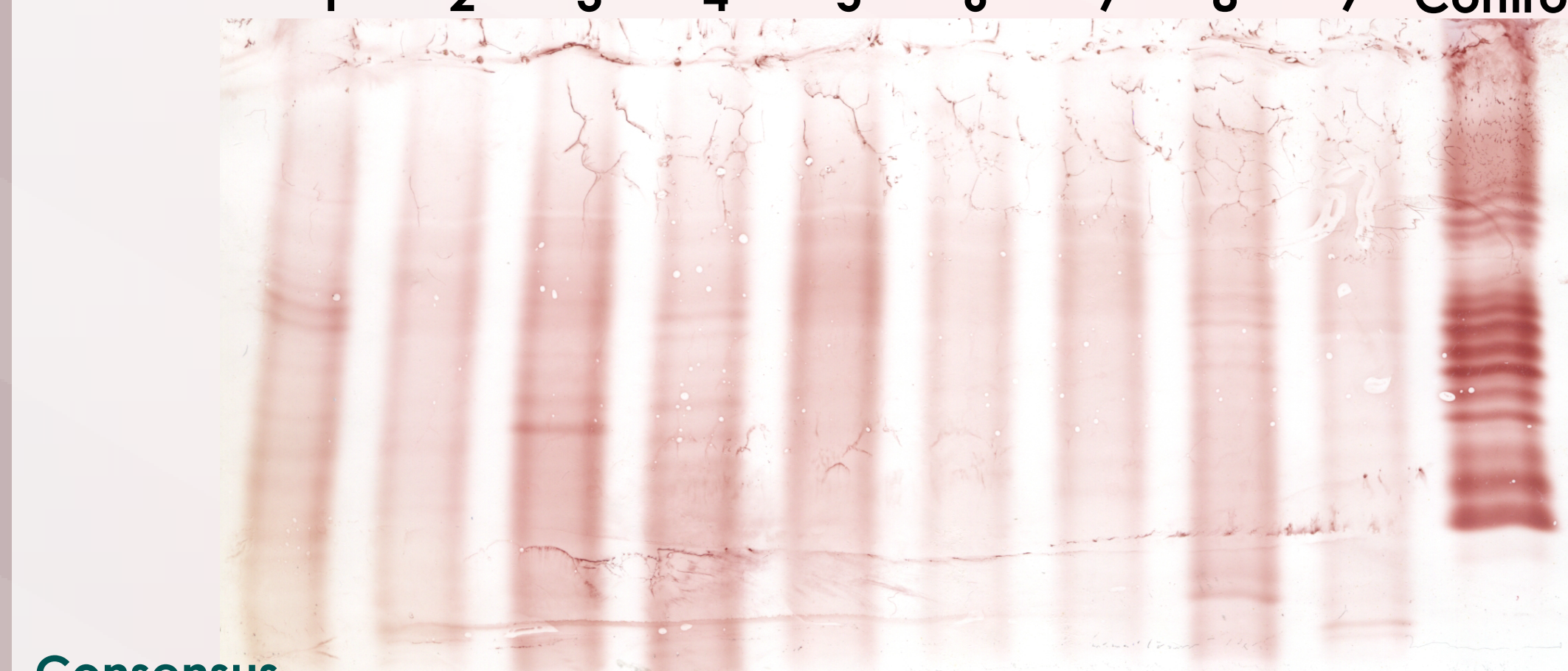
On test dataset (**149 CSF lanes**), we evaluated (i) the two developed approaches (ii) four experts blinded to each other's

Evaluation criteria:

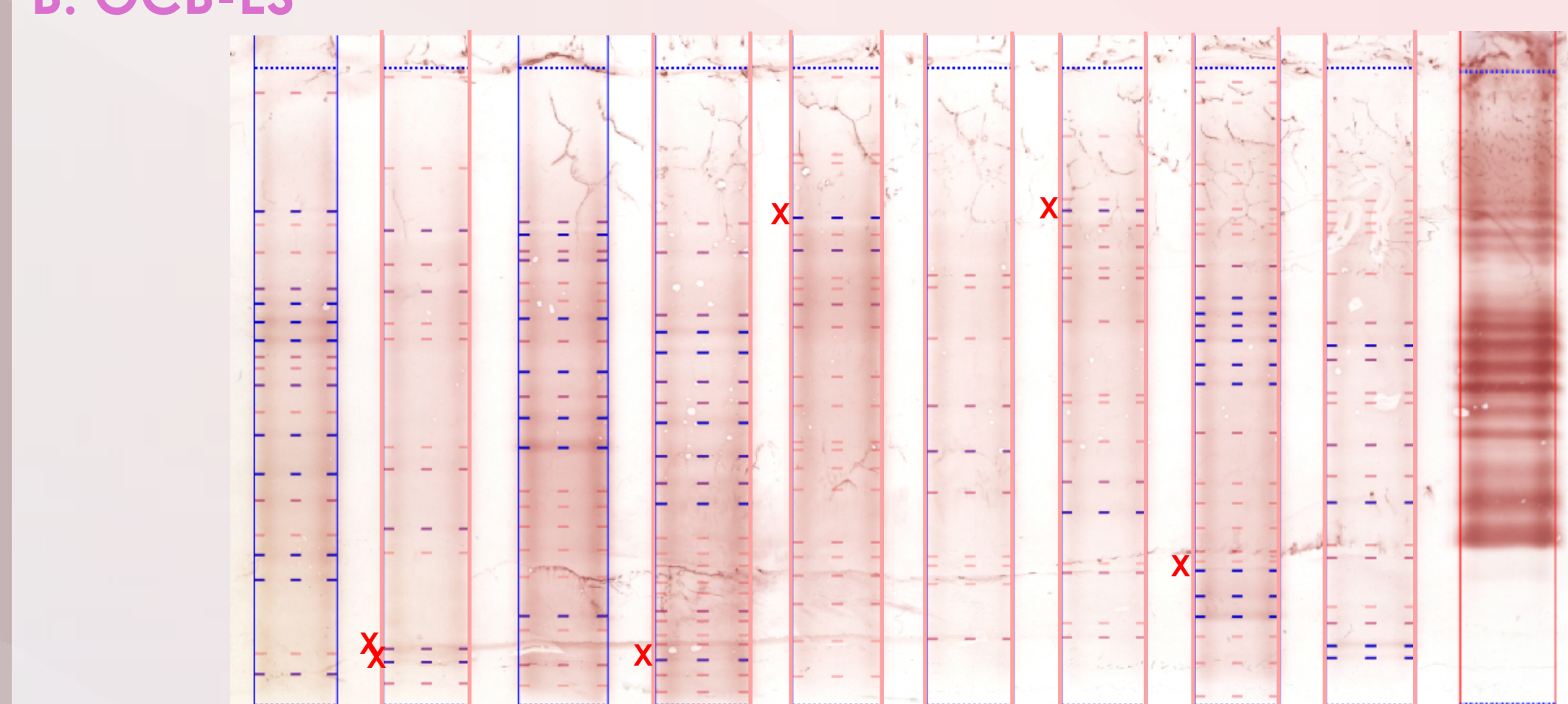
- To reproduce a visual on-membrane expert consensus analysis considered to be the ground truth (≥ 3 OCBs \Rightarrow oligoclonal lane (o) else non-oligoclonal (n))
- To predict the clinical classification (MS vs control; CIS/RIS subjects excluded)

RESULTS

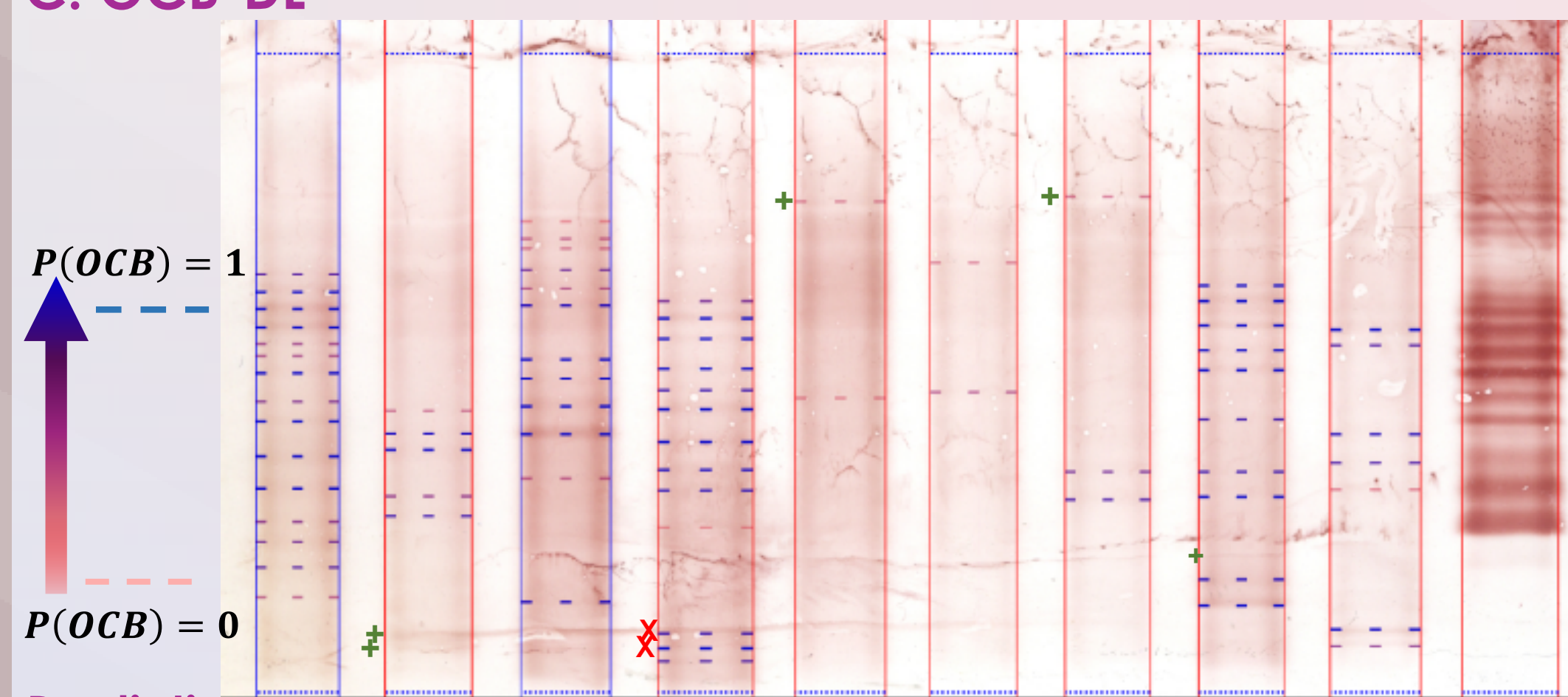
A : raw IEF Lane No 1 2 3 4 5 6 7 8 9 Control



Consensus analysis
B: OCB-ES



Prediction o o o o n n n o o
C: OCB-DL



$P(OCB) = 1$
 $P(OCB) = 0$
+ Correct noticeable classification x Wrong noticeable classification
Fig 1: Results of the two approaches on a CSF IEF image
Acquired using SPIFE 2000 (Helena Laboratories, Texas USA) and IgG IEF kit (Helena Biosciences Europe, Gateshead, UK)



Fig 2: Comparison of performance to reproduce the consensus analysis ($N_o=87, N_n=62$)

When compared to the accuracy of each expert, no significant difference were observed:

with OCB-ES ($\min_i p\text{-value}_{OCB-ES vs expert_i} = 0.17$)

with OCB-DL ($\min_i p\text{-value}_{OCB-DL vs expert_i} = 0.57$)

OCB-ES and OCB-DL reached similar accuracy ($p=0.52$)

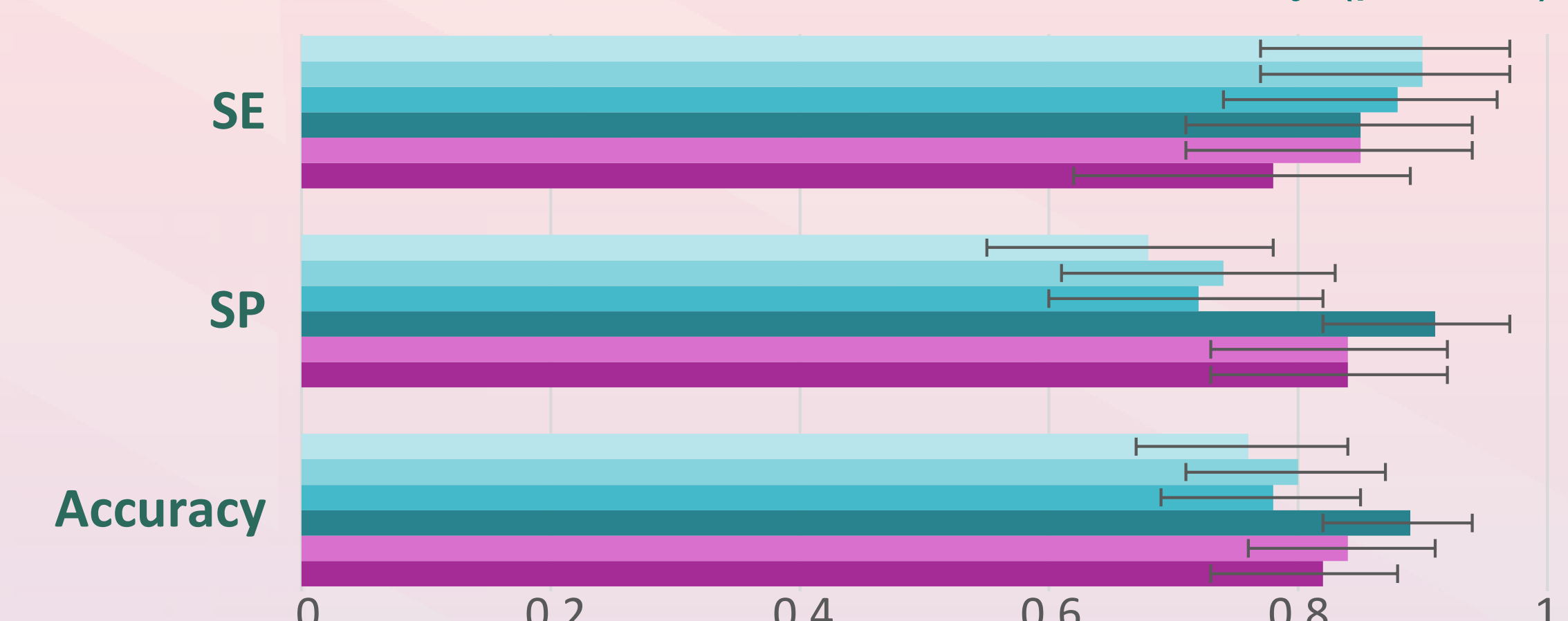


Fig 3: Comparison of performance to predict the clinical classification ($N_{MS}=52, N_{control}=68$)

When compared to the accuracy of each expert, no significant difference were observed:

with OCB-ES ($\min_i p\text{-value}_{OCB-ES vs expert_i} = 0.11$)

with OCB-DL ($\min_i p\text{-value}_{OCB-DL vs expert_i} = 0.096$)

OCB-ES and OCB-DL reached similar accuracy ($p=0.58$)

CONCLUSIONS

- Our developed approaches successfully reproduced the consensus analysis and predicted final classification of the disease **with a level of competence comparable to clinical biologists**
- Expert-IEF is a promising easy-to-use decision support system for OCB detection
- In a future work, both approaches will be combined to make profit of their complementary advantages

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DISCLOSURE

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