The EPoS staging system is a reproducible 7-tier fibrosis score for NAFLD adapted both to glass slides and digitized images (e-slides)

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INTRODUCTION

• Liver fibrosis stage is the major independent prognostic factor in NAFLD. So far, biopsy is considered the best standard to stage liver fibrosis.

• The NASH CRN staging system (Kleiner, Hepatology, 2005) has been widely used. It is a robust staging system but insufficiently accurate in advanced fibrosis stages (stages 3 and 4) which are most strongly linked to liver-related outcomes.

• Glass slide is the physical support used to assess liver biopsy. Strong technical efforts have been put into transferring histological slide images into electronic files (**e-slides**).

• E-slides can be easily accessed and interpreted from anywhere without the need of the physical support (glass slides), thus facilitating sharing of slides especially for consult review or clinical trials.

AIM

The aims of the study were:

1/ to develop a linear and expanded staging system that mirrors more accurately the different stages of liver fibrosis during NAFLD progression (**EPoS staging system**)

2/ to validate the robustness of the EPoS staging system by assessing observer variation between liver pathologists

3/ to compare staging fibrosis using glass and e-slides in order to assess the reliability of e-slides for staging fibrosis.
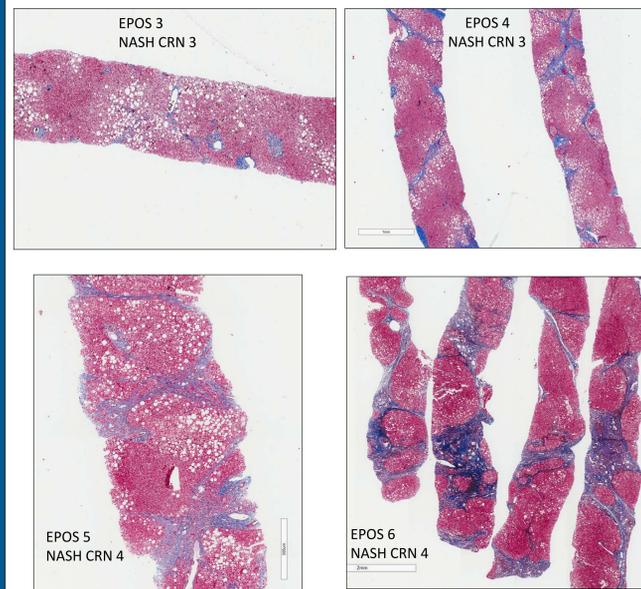
METHOD

• In a first step, 9 European liver pathologists (EPoS Histopathology consortium) jointly reviewed a set of NAFLD liver biopsies to define consensually the various stages of the new EPoS score of fibrosis.

• Then, each participant reviewed independently the same set of 45 NAFLD biopsies (glass slides) with the EPoS staging system to evaluate inter-observer variability.

• Three months later, the glass slides were digitized (e-slides) and re-evaluated electronically by each pathologist, blinded to their first assessment on glass slides.

• The inter-observer agreement was evaluated using Kappa score.

RESULTS

EPoS STAGING SYSTEM

The EPoS staging system includes 7 stages (0 to 6). Compared to NASH CRN, stage 1a, b and c were grouped together while stage 3 and 4 were each expanded into 2 stages. Stage 0 included minimal zone 3 sinusoidal fibrosis or minimal portal fibrosis.

INTEROBSERVER VARIATION OF EPOS STAGING SYSTEM USING GLASS SLIDES

EPoS Kappa score (7-tier) = 0.84 (almost perfect)

EPOS	OBS 1	OBS 2	OBS 3	OBS 4	OBS 5	OBS 6	OBS 7	OBS 8	OBS 9
OBS 1		0,88	0,86	0,85	0,87	0,87	0,77	0,78	0,89
OBS 2	0,88		0,89	0,85	0,89	0,92	0,79	0,83	0,92
OBS 3	0,86	0,89		0,86	0,92	0,9	0,81	0,8	0,91
OBS 4	0,85	0,85	0,86		0,82	0,91	0,87	0,83	0,89
OBS 5	0,87	0,89	0,92	0,82		0,89	0,75	0,75	0,88
OBS 6	0,87	0,92	0,9	0,91	0,89		0,84	0,88	0,93
OBS 7	0,77	0,79	0,81	0,87	0,75	0,84		0,78	0,82
OBS 8	0,78	0,83	0,8	0,83	0,75	0,88	0,78		0,86
OBS 9	0,89	0,92	0,91	0,89	0,88	0,93	0,82	0,86	

Kappa scores by pair of observers after assessment of 45 slides of NAFLD

INTEROBSERVER VARIATION OF EPOS SCORING SYSTEM USING e-SLIDES

e-slide Kappa score = 0.80

	OBS 1	OBS 2	OBS 3	OBS 4	OBS 5	OBS 6	OBS 7	OBS 8	OBS 9
OBS 1		0,83	0,8	0,68	0,8	0,84	0,73	0,81	0,84
OBS 2	0,83		0,81	0,76	0,91	0,84	0,84	0,88	0,88
OBS 3	0,8	0,81		0,76	0,77	0,91	0,8	0,86	0,84
OBS 4	0,68	0,76	0,76		0,79	0,75	0,83	0,79	0,82
OBS 5	0,8	0,91	0,77	0,79		0,84	0,81	0,88	0,89
OBS 6	0,84	0,84	0,91	0,75	0,84		0,82	0,91	0,88
OBS 7	0,73	0,84	0,8	0,83	0,81	0,82		0,83	0,83
OBS 8	0,81	0,88	0,86	0,79	0,88	0,91	0,83		0,85
OBS 9	0,84	0,88	0,84	0,82	0,89	0,88	0,83	0,85	

Kappa scores for pairs of observers assessing 45 e-slides of NAFLD

INTRAOBSERVER VARIATION of EPOS STAGING SYSTEM COMPARING EVALUATION on GLASS SLIDES and e-SLIDES

Mean Kappa Coefficient = 0.85 (range 0.79-0.89)

	OBS 1	OBS 2	OBS 3	OBS 4	OBS 5	OBS 6	OBS 7	OBS 8	OBS 9
K SCORE	0,80	0,85	0,83	0,79	0,85	0,86	0,82	0,86	0,89

Kappa score for each pathologist comparing evaluation on glass slides vs e-slides of 45 NAFLD biopsies

CONCLUSIONS

• The EPoS fibrosis staging system provides an expanded scoring system which might prove useful to assess fibrosis variation in natural history or in short term therapeutic trials.

• The interobserver reproducibility of the EPOS score is excellent between liver pathologists

• E-slides provide material as suitable as glass slides for staging fibrosis as shown by high reproducibility.

• The relevance of the EPoS staging system is currently being evaluated in relation to NAFLD outcome

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