Three is enough: Optimization of regions of interest selection for accurate estimation of proton density fat fraction in liver from magnetic resonance images

F. ROCHE[1], F. VINCENT[1], J. MARY[1], S. ZABBATINO[2], S. HOLLAND[2]
1 Medpace, Lyon, France
2 Medpace, Cincinnati, Ohio, United States

1 INTRODUCTION

Proton Density Fat Fraction (PDFF) measured by Magnetic Resonance Images (MRI) is now widely accepted as a biomarker for liver fat fraction in non-alcoholic fatty liver disease (NAFLD) and steato-hepatitis (NASH), correlating highly with both MR spectroscopy and histology of liver biopsies[1].

2 AIM

- Demonstrate that average PDFF (aPDFF) from 3 spatially well distributed Regions Of Interest (ROIs) correlates highly with aPDFF from 9 ROIs placed in each of the 9 Couinaud segments[2] (S) in the liver.
- Obviate more complicated, time-consuming and artifact-prone ROI strategy for liver fat measures.

3 METHOD

- PDFF maps[3] (N=96) were randomly extracted from an anonymized data repository of NAFLD clinical trials (c.f. Fig. 1).

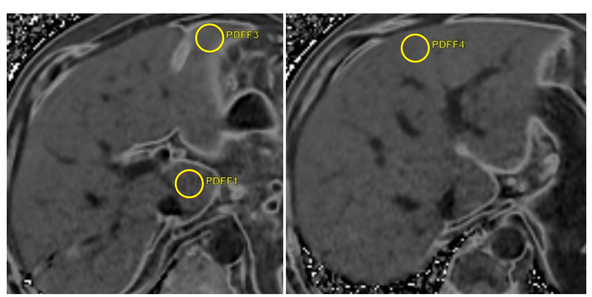

Fig. 1: *Example of PDFF maps with ROIs.*

- ROIs were placed in each of 9 Couinaud segments[2,4] (c.f. Fig. 2 left).
- aPDFF was calculated over the complete set of 9 ROIs and over all combinations of 1 to 8 ROIs[5].

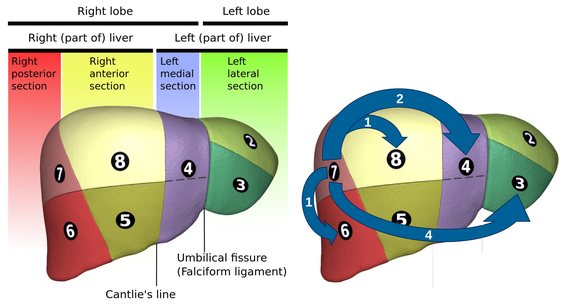

Fig. 2: (left) *Liver segment classification by Couinaud[7] (S4 is split into S4a and S4b, S1 is posterior to S4)*
(right) *Inter-segment distances used for dispersion score calculation.*

- A "Dispersion" score was calculated for each combination of ROIs:
  - It reflects the spatial distribution of the ROIs in the liver.
  - The higher the score, the higher the average distance between the ROIs.
  - It is based on a simple inter-segment distance metric (c.f. Fig. 2 right) which is worth 1 for two contiguous segments (e.g. S6 and S7 or S8 and S5) and reaches a maximum value 4 for the most distant pairs (e.g. S7 and S3 or S6 and S2).
- ROI combinations were split in two groups for analysis:
  - "High": Quartile of ROI combinations with highest dispersion score (e.g. 3 ROIs in S2, S4b and S8 which has a dispersion score of 3).
  - "Low": Other three quartiles (e.g. 3 ROIs in S6, S7 and S8 which has a dispersion score of 1.33).
- aPDFF for each ROIs combination was compared to the aPDFF from 9 ROIs using the following statistical measures:
  - Intraclass Correlation Coefficient (ICC).
  - Absolute Error (AE) in aPDFF expressed in % point.
  - 95% Limits Of Agreement[6] (LOA).

4 RESULTS

- High dispersion performs better than Low for all 3 metrics (c.f. Table 1).

	Disp.	N	ICC (μ)	ICC (σ)	LOA (μ)	LOA (σ)	AE (μ)	AE (σ)
2 ROIs	**High**	8	**0.990**	**1.10^{-3}**	**2.85**	**0.251**	**0.881**	**0.053**
	Low	26	0.985	6.10^{-3}	3.59	0.613	1.06	0.198
3 ROIs	**High**	16	**0.994**	**1.10^{-3}**	**2.30**	**0.232**	**0.696**	**0.082**
	Low	68	0.991	3.10^{-3}	2.63	0.451	0.797	0.141
4 ROIs	**High**	19	**0.996**	**1.10^{-3}**	**1.85**	**0.235**	**0.551**	**0.080**
	Low	107	0.995	2.10^{-3}	2.05	0.350	0.629	0.107

Table. 1: *Summary of statistical measures for 2 to 4 ROIs combination grouped by dispersion (high/low). Other ROIs combination do not show statistical differences.*

- Individual PDFF values are comparable across liver segments (c.f. Fig. 3).

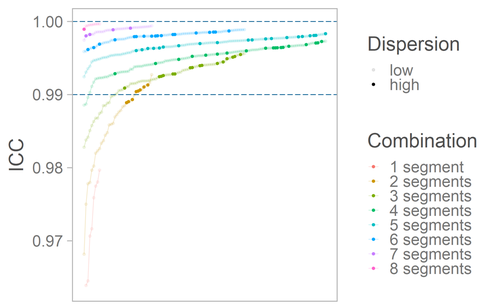

Fig. 4: *ICC score per ROIs combination. Bold dots have the 25% higher dispersion in the combination of ROIs.*

- ROI combinations with higher dispersion score result in higher and stable values of ICC, AE and LOA metrics (c.f. Fig. 4 and Table 1, High dispersion ROIs are bold in Fig. 4).
- aPDFF from more ROIs leads to increased correlation with 9 ROIs for ICC, AE and LOA metrics (c.f. Fig. 4).

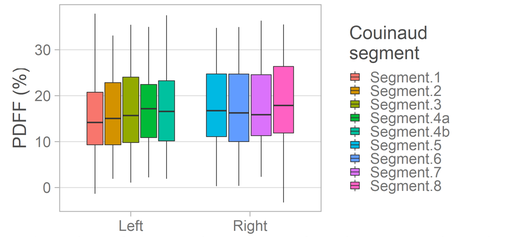

Fig. 3: *Overview of PDFF values per Couinaud segments (N=96).*

5 CONCLUSIONS

- aPDFF over fewer ROIs with the greatest dispersion produces a valid and reliable alternative to using 9 ROIs.
- Fewer ROIs can be placed more efficiently and reliably across the liver (avoiding vessels or artifacts).
- 3 ROIs selected with High dispersion (e.g. S2, S4b and S6) yield >99% agreement with aPDFF calculated over 9 ROIs covering all Couinaud segments of liver.

6 REFERENCES

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7 CONTACT

Tel: +33 4 37 53 09 80 (ext. 25455)
E-mail: f.roche@medpace.com
www.medpace.com