Berkeley School of Public Health

FORUM for Collaborative RESEARCH

Session III

Existing NAFLD/NASH Pediatric Research Across the Atlantic

Panel discussion

Piotr Socha

The Children’s Memorial Health Institute
Warsaw
Poland

Diagnostic approach to NAFLD

Diagnosis of Nonalcoholic Fatty Liver Disease in Children and Adolescents: Position Paper of the ESPGHAN Hepatology Committee

*Pietro Vajro, †Selvaggia Lenta, ‡Piotr Socha, §Anil Dhawan, ||Patrick McKiernan, #Ulrich Baumann, **Ozlem Durmaz, ††Florence Lacaille, ‡‡Valerie McLin, and ¶Valerio Nobili

JPGN 2012

Risk factors	Liver steatosis	Exclusions
• Obesity • BMI • Waist circ.	• US • ↑ALT • Other… • Liver biopsy	• Wilson d. • Alph-1-ATD • Other…

Children's Memorial Health Institute

When liver biopsy can be avoided for diagnostic purposes

Diagnosis	Liver biopsy-typical findings?	Biochemical/molecular testing
Wilson disease	No	Yes
LAL-deficiency	Yes	Yes
ATD	Not very specific	Yes
Galactosemia	No	Yes
Fructosemia	No	Yes
Beta-oxidation defects	No	Yes
Mitochondrial DNA depl.	Can be helpful, quantification of mDNA	Yes
DILI	Can be helpful	No
HCV	No	Yes

Only histology indicates severity of the disease

NAFLD	NASH	Cirrhosis
		
Steatosis	Steatosis Inflammation	Inflammation Fibrosis
Benign?	**Moderate**	**Severe**

Children's Memorial Health Institute

Omega-3 fatty acids in treatment of NAFLD

THE JOURNAL OF PEDIATRICS • www.jpeds.com ORIGINAL ARTICLES

Omega-3 Fatty Acids Therapy in Children with Nonalcoholic Fatty Liver Disease: A Randomized Controlled Trial

Wojciech Janczyk, MD[1], Dariusz Lebensztejn, MD, PhD[2], Aldona Wierzbicka-Rucińska[3], Artur Mazur, MD, PhD[4], Joanna Neuhoff-Murawska[1], Paweł Matusik, MD[5], and Piotr Socha, MD, PhD[1]

Methods

- Multicenter RCT
- 76 patients aged 12,8 y (5,9-18,4)
- Supplemented 450-1300mg/day DHA/EPA 3:2 or placebo
- Duration: 6 months

Primary outcome

- Decrease of ALT by 30% of ULN

Results:

- No change in ALT, insulin resistence and steatosis on US
- Significantly decreased AST, GGTP and increased adiponectine
- No offect on BMI z-score, waist circumference z-score

J Pediatr 2015

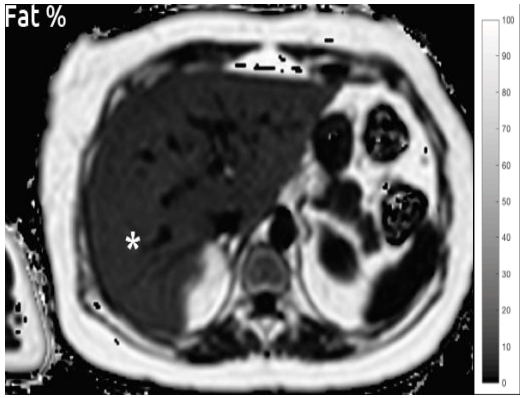
Children's Memorial Health Institute

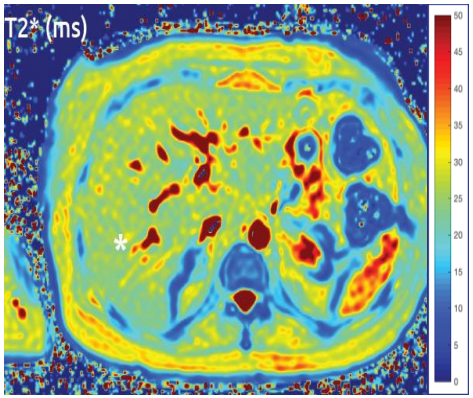
Questions for clinical trials

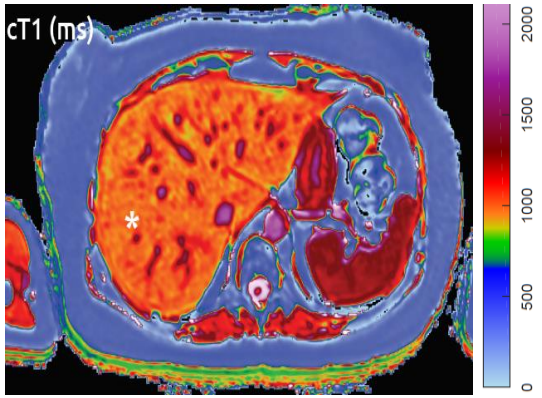
- Liver biopsy as an end point?
  - not feasible in children
  - not optimal- biased by sampling error
  - surrogate markers needed
- How to describe liver damage
  - US- limited sensitivity and specificity
  - Imaging methods do not include inflammation

Children's Memorial Health Institute

MRI-based liver tissue characterisation







MRI-PDFF

Chemical shift-based method for water-fat separation
Shown to correspond to histological measures of ***steatosis***

T2* map

MR relaxation time

Shown to decrease with increased
hepatic iron overload

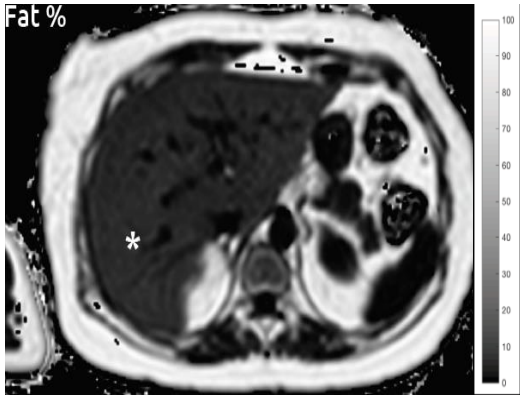
Corrected T1

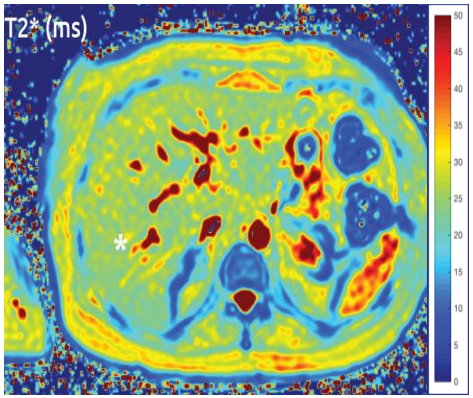
Free-water content in tissue
Shown to increase in ***inflammation and fibrosis, when corrected for hepatic iron***
Reported as LIF Score (0-4)

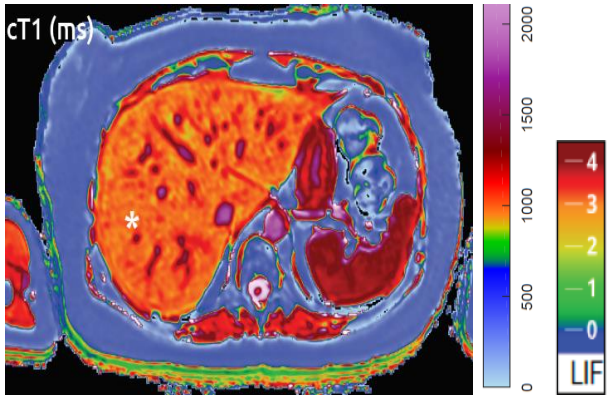
Children's Memorial Health Institute

LiverMultiScan Discover

A virtual biopsy using Liver*MultiScan*



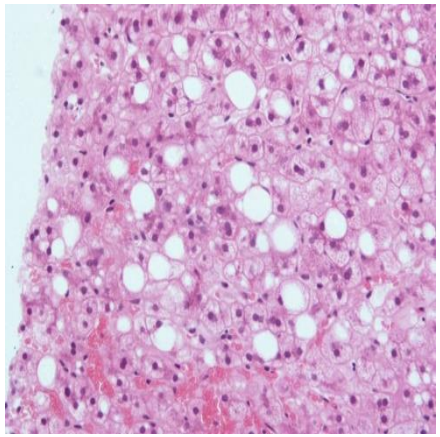


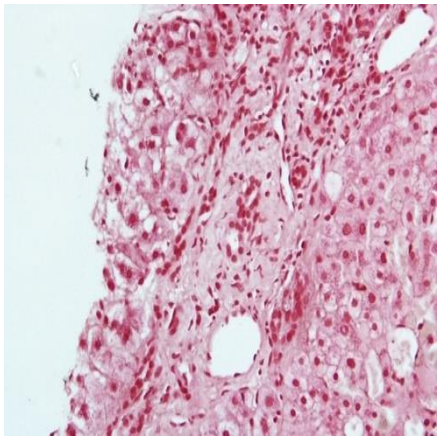


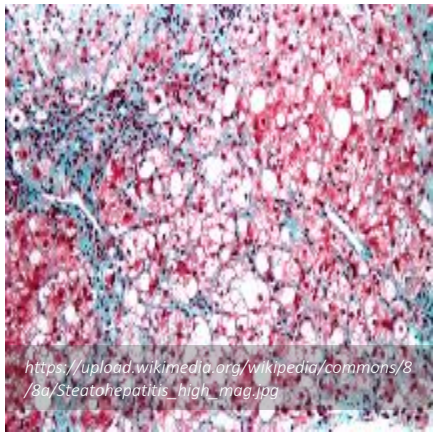
MRI-PDFF → Steatosis

T2* map → Iron

Corrected T1/LIF score → Inflammation and Fibrosis







Children's Memorial Health Institute

LiverMultiScan Discover

Kids4LIFe

Multiscan compared to liver biopsy

- Children with various liver diseases
  - Liver biopsy
  - Multiscan
  - Clinical data
  - Lab data
  - US
- Healthy controls
  - Multiscan
  - Lab data

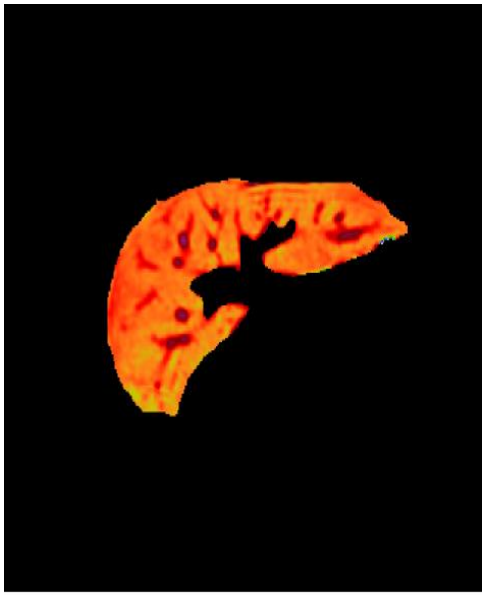
Children's Memorial Health Institute

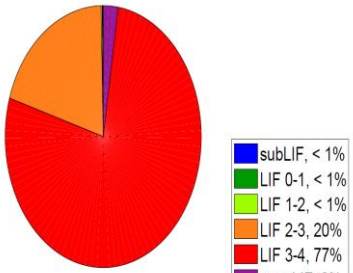
eurostars™

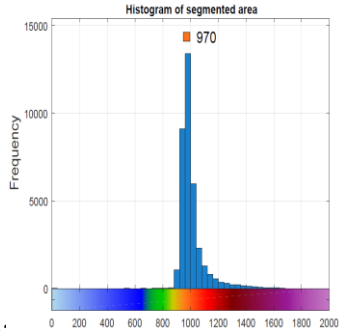
European Commission

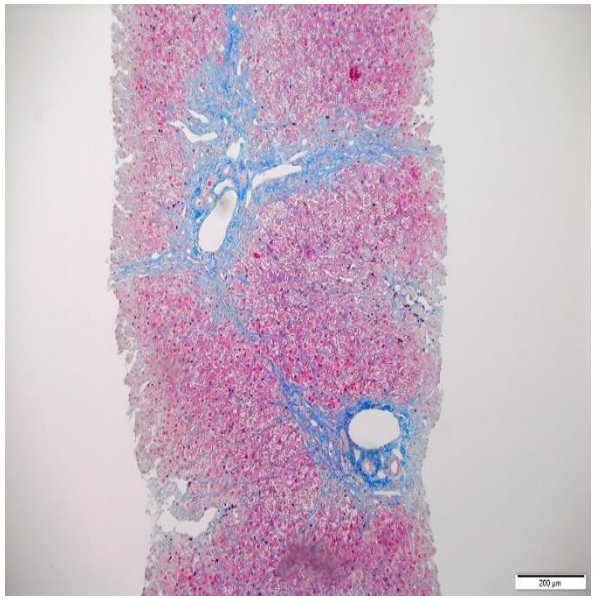
Case Study: Autoimmune hepatitis

12 year old male recently diagnosed (not receiving therapy)
Referred for liver biopsy, pathology review included NAFLD assessment (NAS Score)







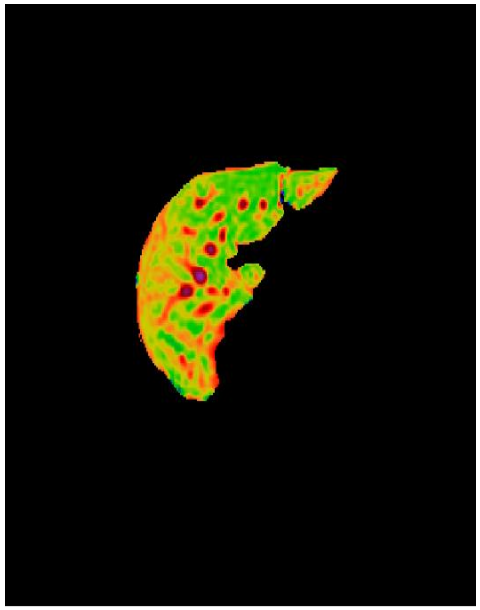


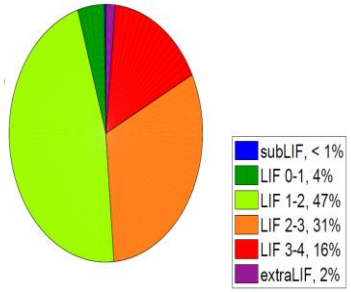
Date of Procedure	16th Feb 2017	
Fat (%)	0.7	[normal range: <5.6%]
Iron (mg/g)	0.9	[normal range: <1.8mg/g²]
Median LIF Score	3.08	
Modal cT1 (ms)	970	

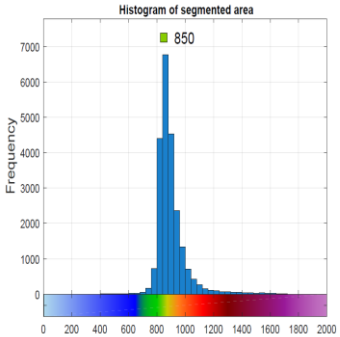
Date of Procedure	21st Feb 2017
Steatosis Grade	0
Lobular Inflammation	3
Portal Inflammation	3
Ballooning	0
Fibrosis	3

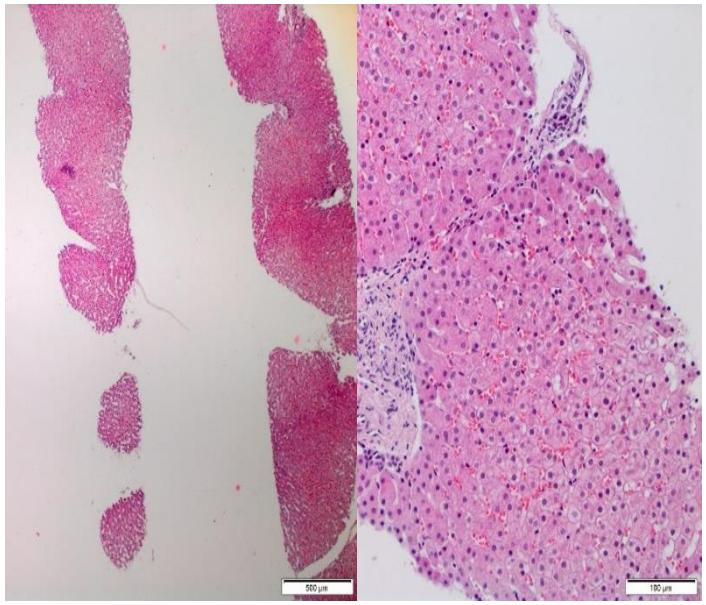
Case Study: Autoimmune hepatitis

16 year old female, treated with Azathioprine







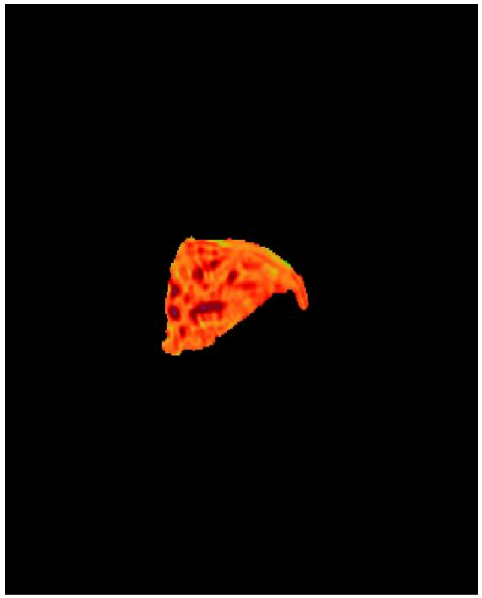


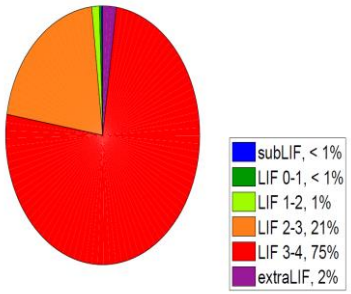
Date of Procedure	18th Jan 201.	
Fat (%)	3.2%	[normal range: <5.6%]
Iron (mg/g)	0.8	[normal range: <1.8mg/g2]
Median LIF Score	1.97	
Modal cT1 (ms)	850	

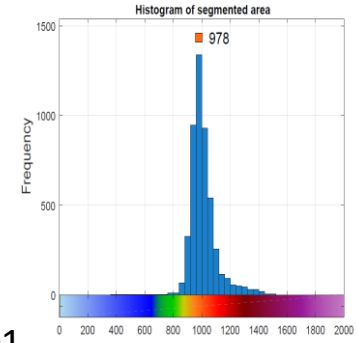
Date of Procedure	19th Jan 2017
Steatosis Grade	0
Lobular Inflammation	1
Portal Inflammation	2
Ballooning	0
Fibrosis	1c

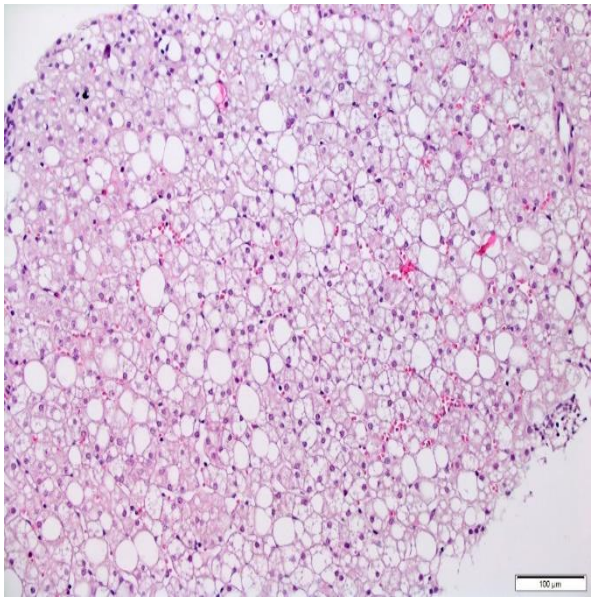
Case Study: Wilson's Disease

7.5 year old female, on Zincteral
Referred for assessment due to persistent high ALTs on Therapy









Date of Procedure	25th Jan 201	
Fat (%)	32.6%	[normal range: <5.6%]
Iron (mg/g)	1.4	[normal range: <1.8mg/g2]
Median LIF Score	3.08	
Modal cT1 (ms)	987	

Date of Procedure	26th Jan 2017
Steatosis Grade	3
Lobular Inflammation	1
Portal Inflammation	1
Ballooning	2
Fibrosis	2