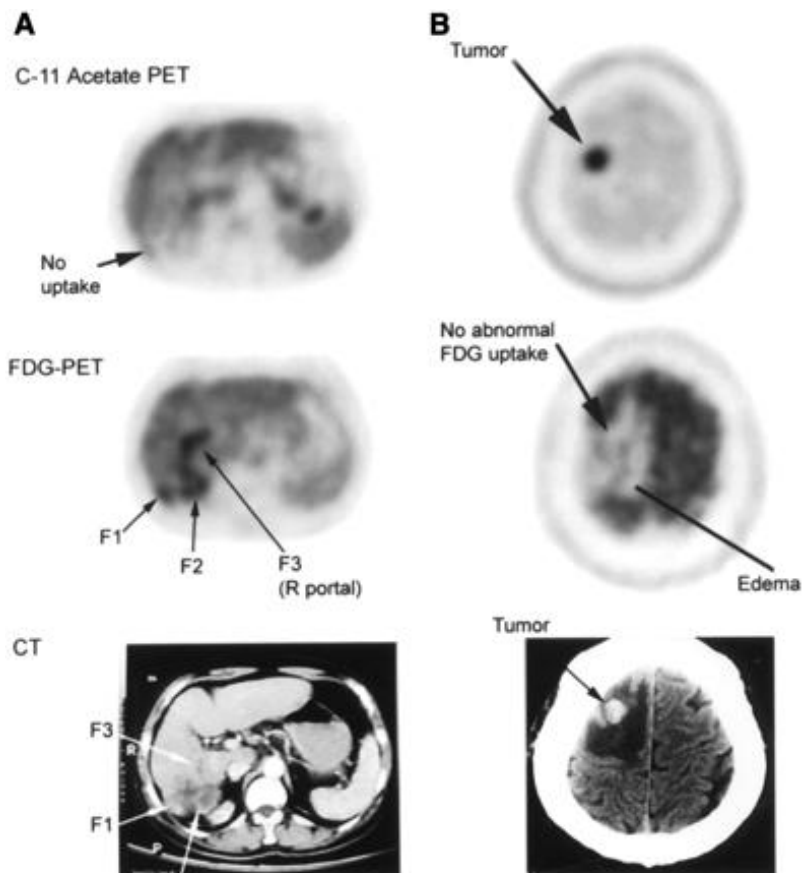


QUALITY CONTROL AND REPRODUCIBILITY IN CLINICAL HYPERPOLARIZED MR

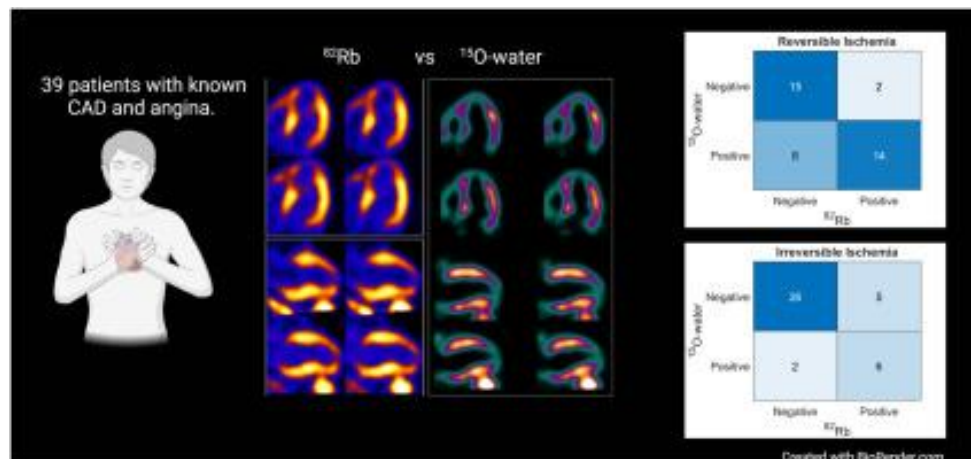
CHRISTOFFER LAUSTSEN



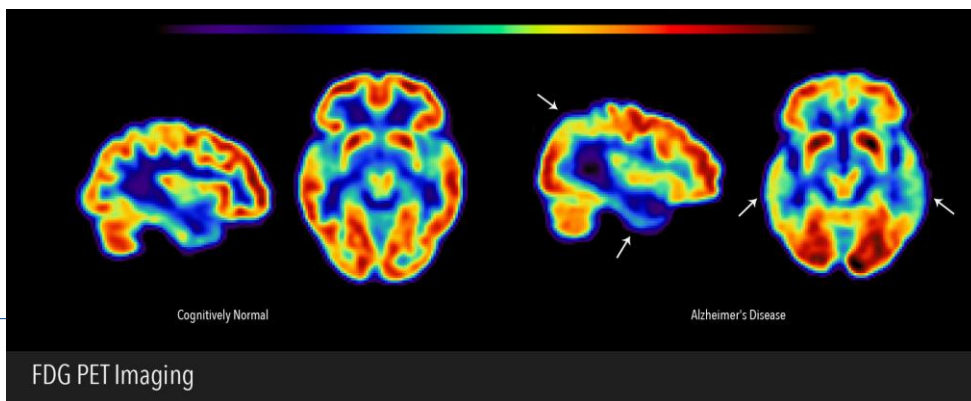
DO WE NEED METABOLIC IMAGING?



Ho CL, Yu SC, Yeung DW. ¹¹C-acetate PET imaging in hepatocellular carcinoma and other liver masses. J Nucl Med. 2003



Quantitative and qualitative comparison of Rubidium-82 and Oxygen-15 water cardiac PET Hoff, Camilla Molich et al. Journal of Nuclear Cardiology, 2024



CAN WE DO IT BETTER HP?

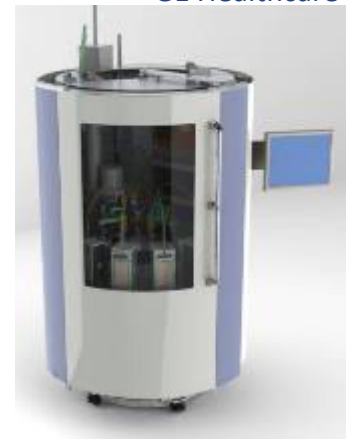
- › Ultra fast (like ^{15}O —water PET), improved metabolism mapping beyond (^{11}C and ^{18}F FDG)
- › First pass hemodynamic and metabolism imaging using hyperpolarized ^{13}C MRI – goes beyond PET/MR

d-DNP hyperpolarised MRS

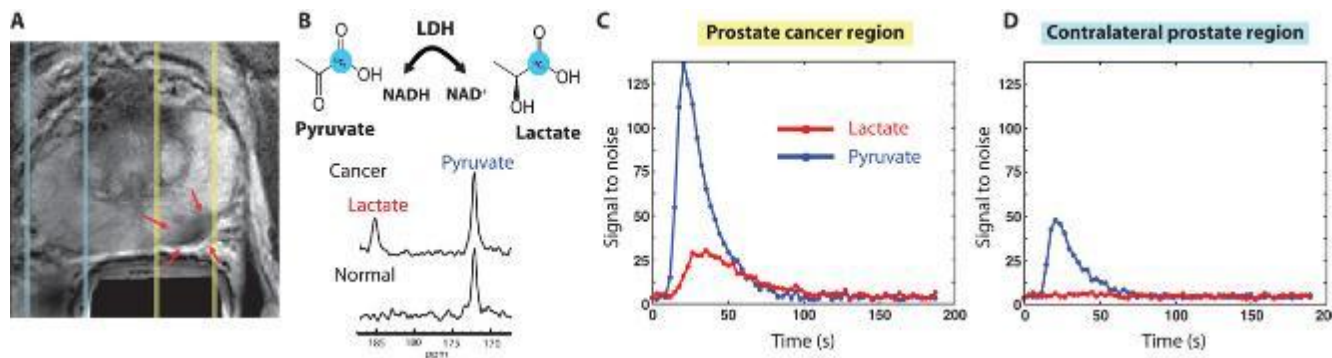
- › Hyperpolarization enhances signal >10,000-fold *in vivo*
- › No ionizing radiation
- › Signals are specific to chemical structures
- › Simultaneous acquisition of several bio-markers
- › Several groups are now doing human studies

Designed for clinical research,
but also useful for animal studies

SpinLab™
GE Healthcare

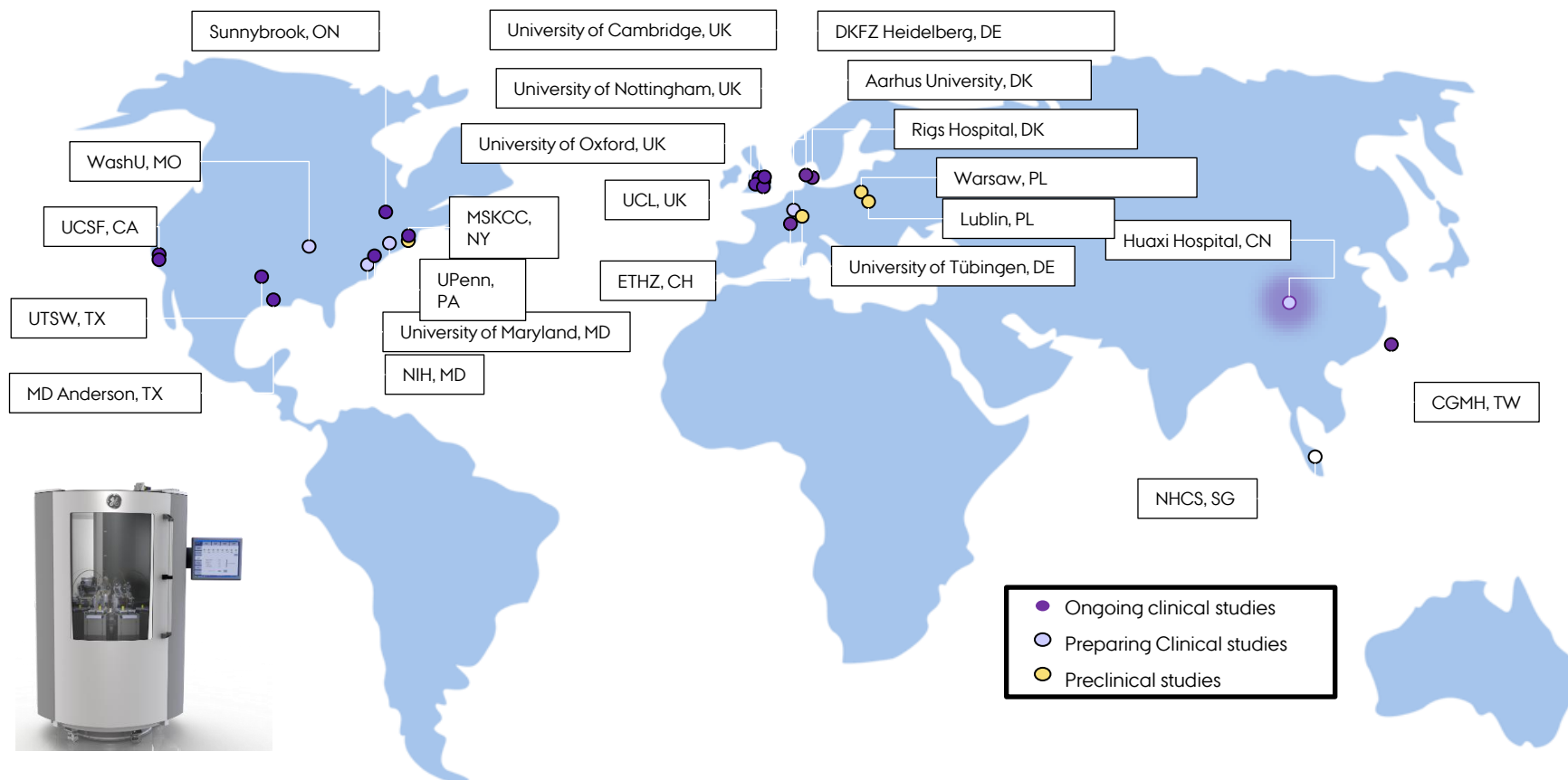


Ardenkjær-Larsen et al,
NMR in Biomedicine 2011



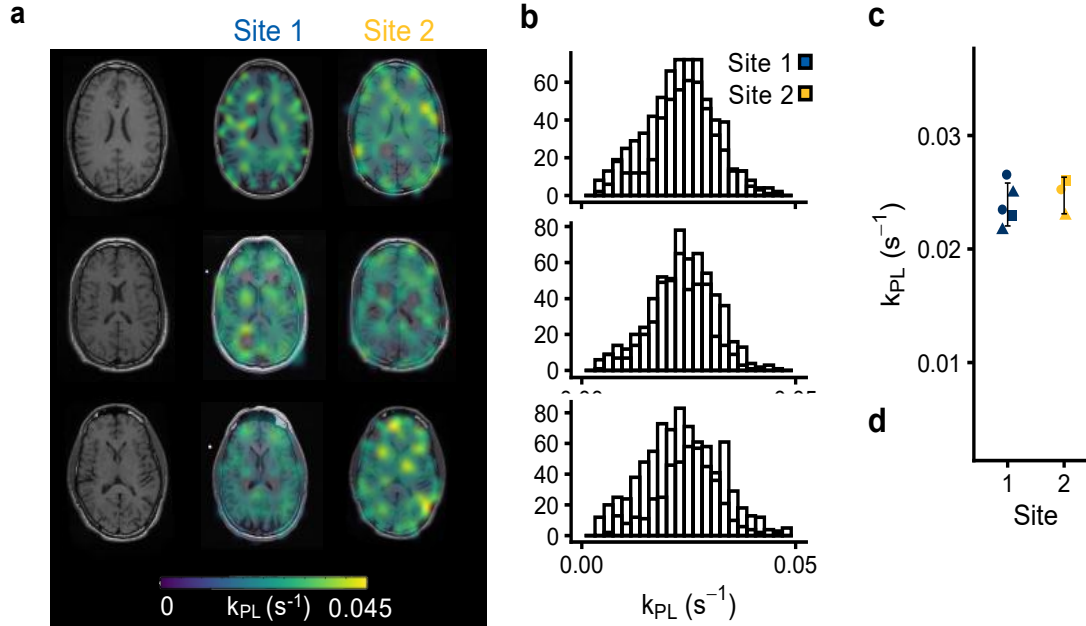
Nelson SJ et al,
Sci Transl Med 2013

SPINlab™ installed base



> 100 publications with human data (> 1500 exams)

CAN WE COMPARE RESULTS ACROSS SITES?



- Travelling male “human” phantoms ($n=3$) imaged repeatedly across two sites
- ICC exam-to-exam = 0.83; ICC site-to-site = 0.71

Type 1 Diabetes DKD (n=9)



15 ml/min > eGFR < 60 ml/min
Albuminuria

Type 1 Diabetes (n=9)

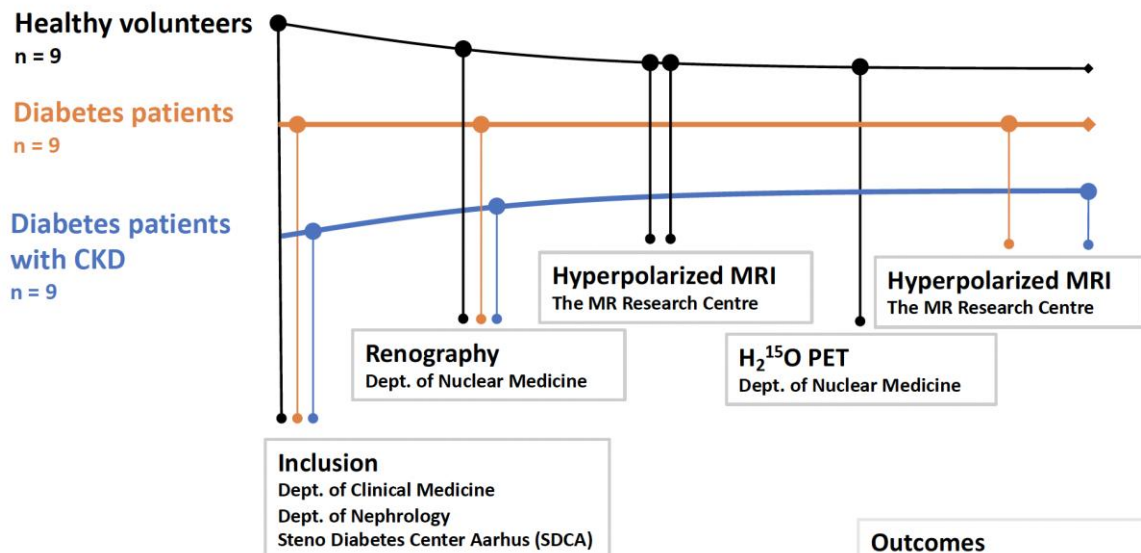


Normal kidney function
No albuminuria

Control Subjects (n=9)



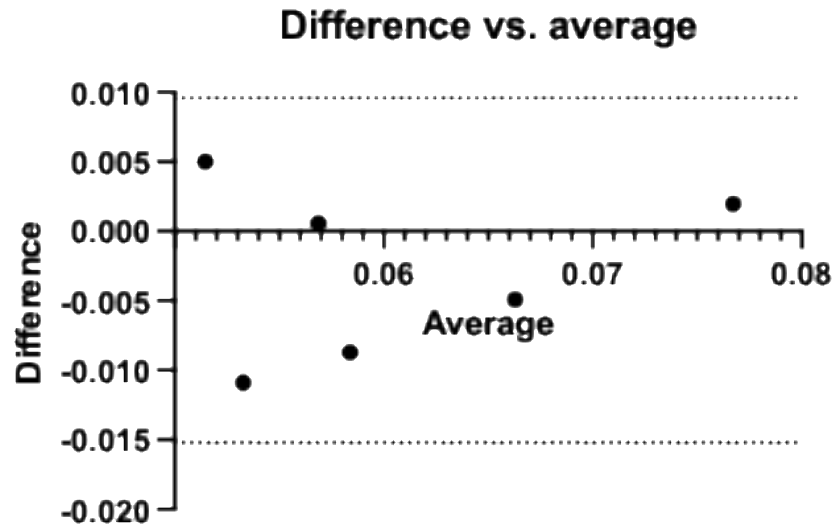
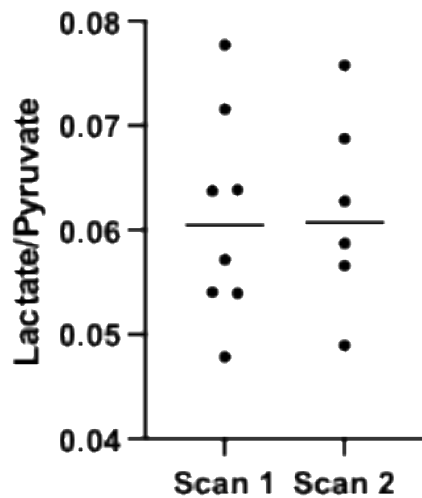
Normal kidney function
No albuminuria



Outcomes

- Metabolic and perfusion MR
- Clinical and paraclinical data from records

REPEATABILITY



THE KILLER APPLICATION PARADOX

- › **Are we looking for tomorrow's value using today's clinical paradigm?** We often assume that a new imaging technology needs a “**killer application**” **before clinical adoption can begin.**
- › The paradox: **we demand evidence within the current clinical paradigm for technologies intended to enable a different clinical paradigm.**

IMPLICATION FOR CLINICAL TRANSLATION

Which clinically important decisions are currently made with insufficient information about tissue metabolism?

- › Start with diseases where advanced imaging can **replace an existing test**.
- › Identify **decision points** where additional biological information could change management.
- › Design trials around **actionability and patient stratification**, not only diagnostic accuracy.
- › Use early clinical trials to establish **where the information changes decisions**, rather than requiring the final use case to be known beforehand.
- › Translation is an **iterative process: technology → biological insight → clinical decision → outcome evidence**.

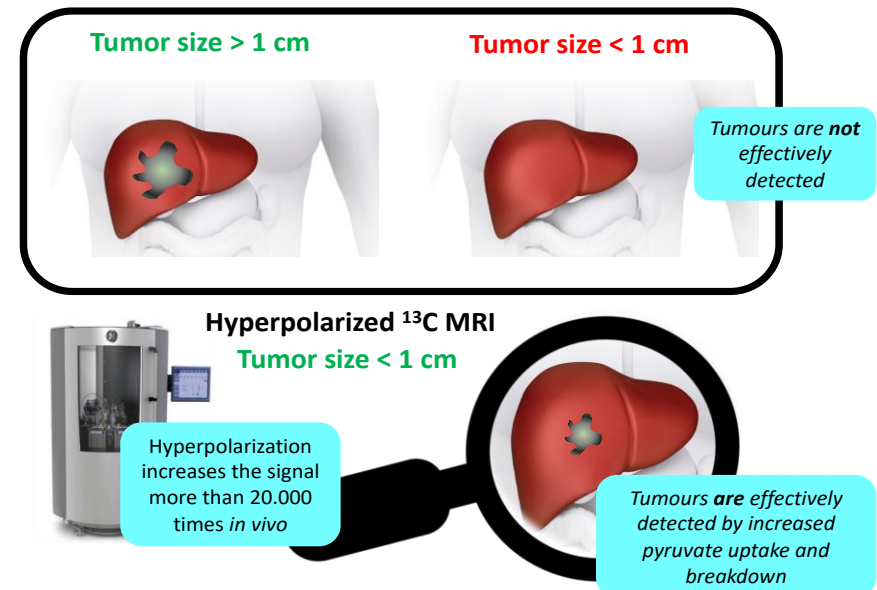


Liver cancer – improving diagnosis and surgery planning

Tumor size	Sensitivity (MRI)
≥ 20 mm	95 % ¹
< 20 mm	62 % ¹
< 10 mm	48 % ²

1. Lesion ≥ 10 mm in a cirrhotic liver
2. Hypervascularity in the arterial phase
3. Washout in the portal venous/late phase

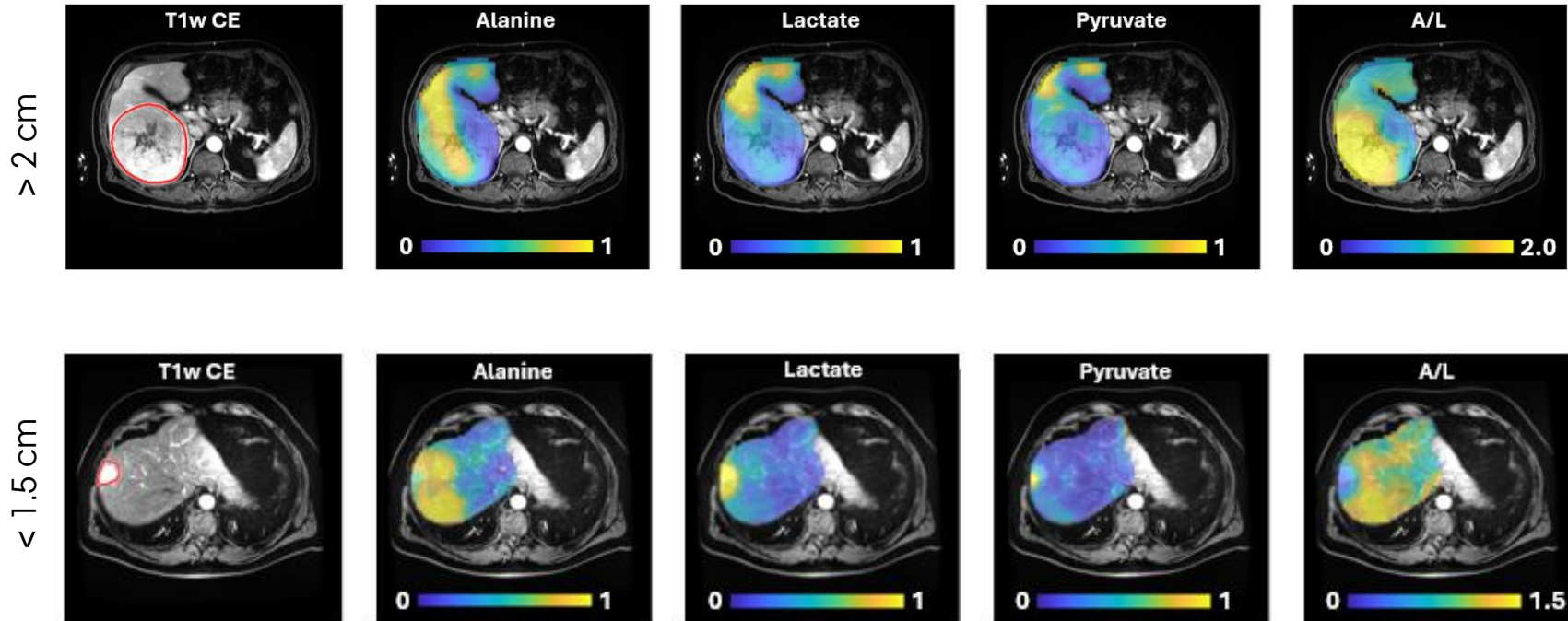
Improving HCC outcome



[1] Galle, P. R. *et al.* EASL Clinical Practice Guidelines: Management of hepatocellular carcinoma *q.* <http://globocan.iarc.fr>. (2018) doi:10.1016/j.jhep.2018.03.019.

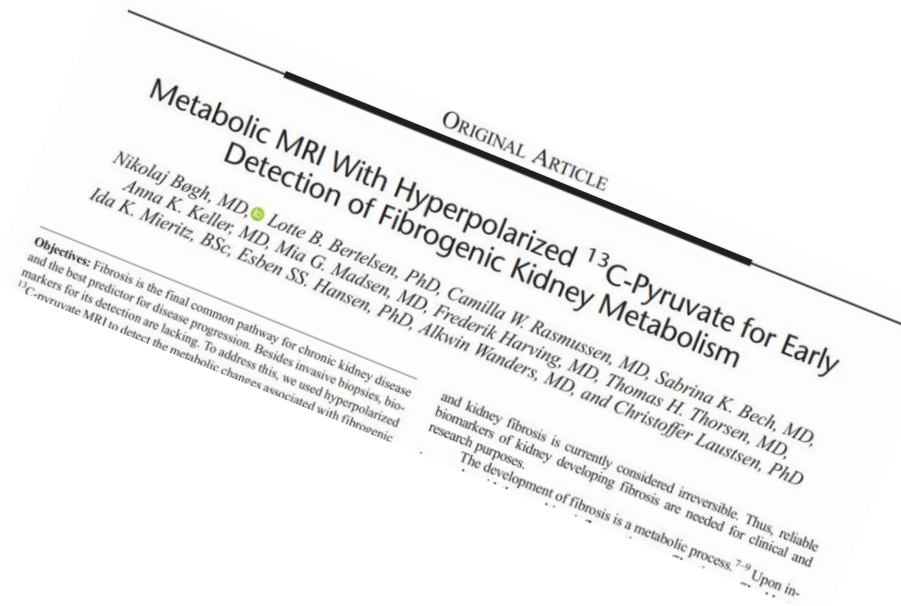
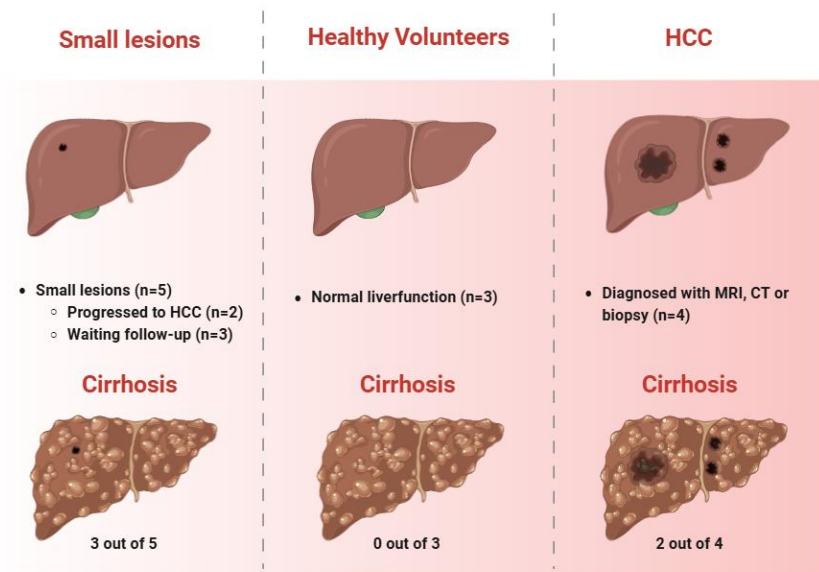
[2] Lee, Y. J. *et al.* Hepatocellular carcinoma: Diagnostic performance of multidetector CT and MR imaging-a systematic review and meta-analysis. *Radiology* **275**, 97–109 (2015).

HEPATOCELLULAR CARCINOMA (HCC)

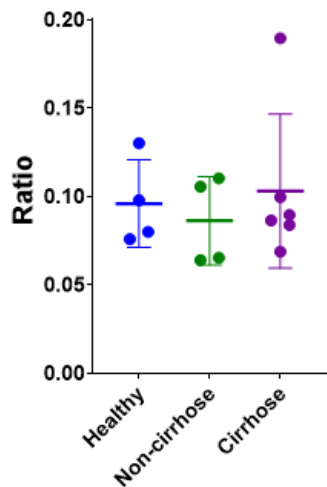


Characteristics	Patients with HCC (n=5)	Patients with Indeterminate lesions (n=5)	Healthy volunteers (n=4)
Age, years, median (range)	64 (62-79)	69 (43-77)	48 (34-68)
Sex, male, n (%)	5 (100)	5 (100)	4 (100)
BMI, kg/m ² , median (range)	25.7 (23.1-34.3)	26.0 (20.9-30.1)	26.4 (20.1-28.4)
Liver disease status			
Cirrhosis, n (%)	3 (60)	3 (60)	N/A
MELD score, median (range)*	9 (6-16)	9 (7-19)	N/A
Child-Pugh class (A/B/C)*	2/1/0	3/0/0	N/A
Etiology of cirrhosis			
- Alcohol	2	1	N/A
- HBV/HCV	0	0	N/A
- MASH	1	1	N/A
- MASH+Alcohol	0	1	N/A

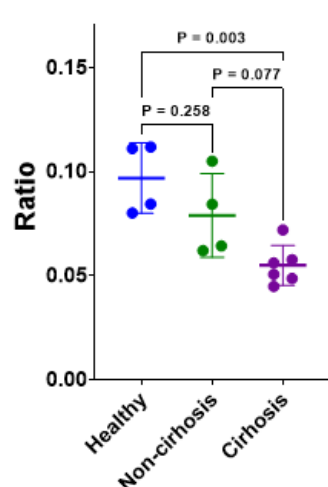
Parameter	T1 in-/out-of-phase (spoiled GRE)	T2 FSE ± FS (SSFSE/FRFSE)	DWI (single-shot SE- EPI)	Dynamic contrast-enhanced T1 (spoiled GRE)
TR (ms)	4.2	4000	6000	4.5
TE (ms)	2.1 / 4.2	90-100	60-70	2.1
Flip angle (°)	12	90-111	90	12
Slice thickness (mm)	5	6	6	5
b-values (s/mm ²)	N/A	N/A	0, 50, 400, 800	N/A
Resp. control	Breath-hold	Breath-hold / navigator	Free-breathing / navigator	Breath-hold
Contrast details / Timing	N/A	N/A	N/A	Dotarem 0.2 mmol/kg @ 3 mL/s + 30 mL saline; arterial (~25 s), portal (~60-70 s), delayed (~3-5 min)



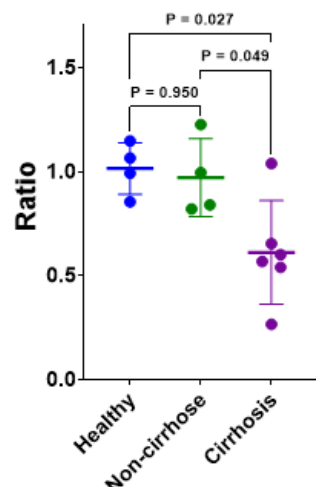
(A) Lactate to pyruvate



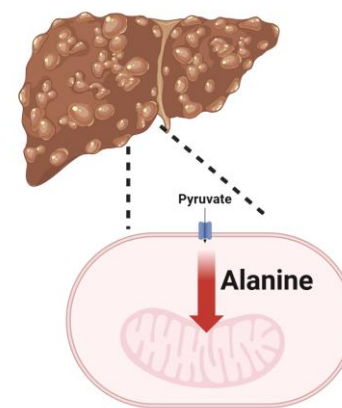
(B) Alanine to pyruvate



(C) Alanine to lactate



Cirrhosis



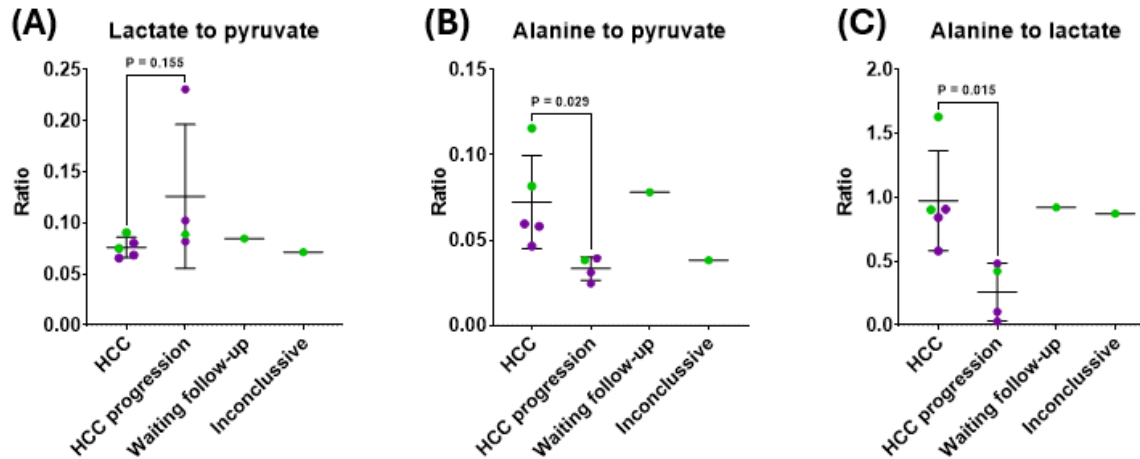
• Healthy

• Non-cirrhosis

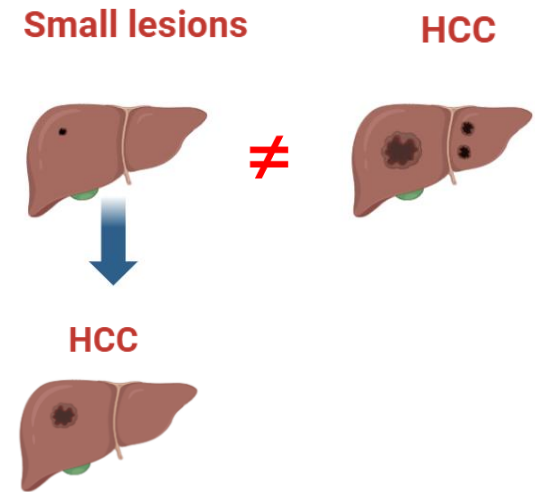
• Cirrhosis

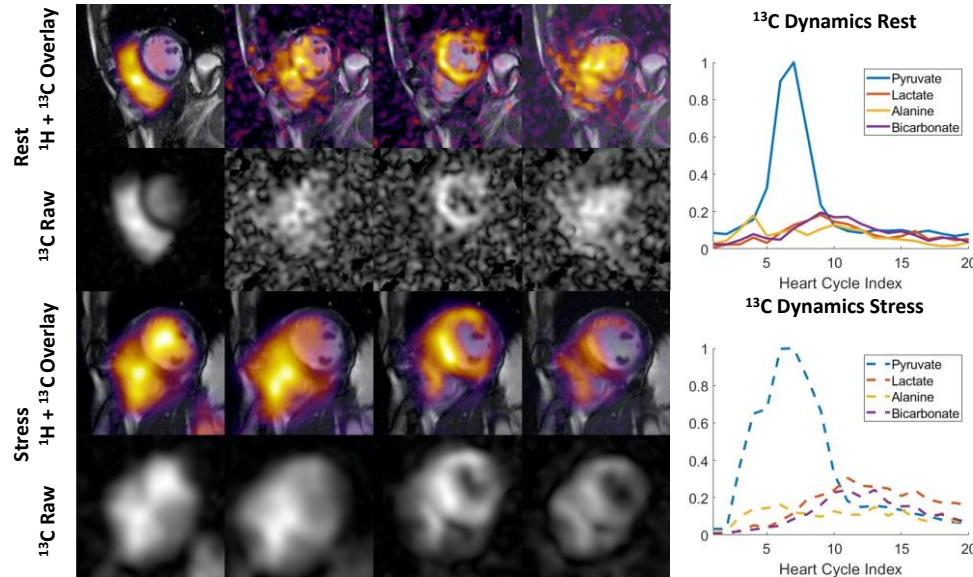
METABOLISM IN LIVER TUMORS?

In progress



● Cirrhose ● Non-cirrhose

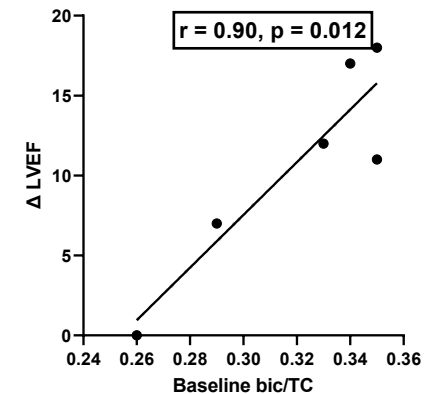
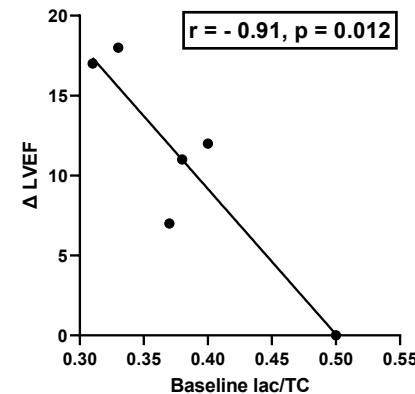
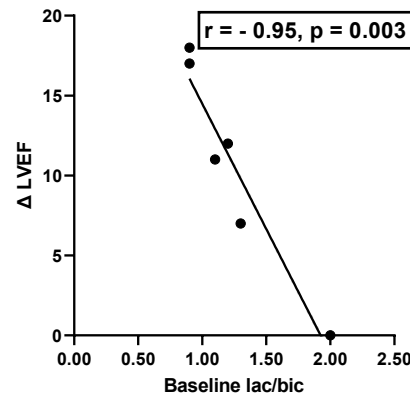




Hyperpolarized ^{13}C -pyruvate
outperforms clinical best
practices myocardial water PET,
MRI and FDG – **without even
trying!**

Joergensen SH, et al. . Hyperpolarized $[1-^{13}\text{C}]$ pyruvate
cardiovascular magnetic resonance imaging identifies metabolic
phenotypes in patients with heart failure. J Cardiovasc Magn
Reson. 2024;26(2):101095.

Joergensen SH, et al. Detection of
increased pyruvate dehydrogenase flux in
the human heart during adenosine stress
test using hyperpolarized $[1-^{13}\text{C}]$ pyruvate
cardiovascular magnetic resonance
imaging. J Cardiovasc Magn Reson. 2022
Jun 6;24(1):34.



THE PILOT EVIDENCE IS THERE; WHAT NOW?

How do we harmonize?

Lessons learned from the renal MRI community

Project background

The project originates from the renalmri network (www.renalmri.org) and builds on the PARENCHIMA MRI standardization efforts

Builds on UKRIN-MAPS results extending them to a pan-European level



SPECIAL ISSUE IN MAGMA

Special issue on **Magnetic Resonance Imaging Biomarkers of Renal Disease**, published in Magnetic Resonance Materials in Physics, Biology and Medicine. Get it here: <https://link.springer.com/journal/10334/volumes-and-issues/33-1>

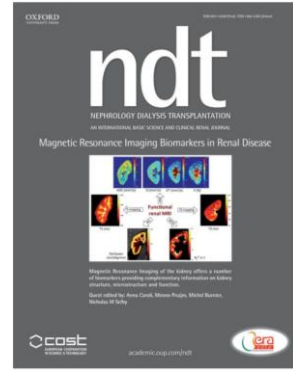
Includes:

- Editorial

- Review papers on phase contrast (open access), hyperpolarization, image registration (open access), renal transplantation.

- Consensus papers (all open access) including a report of the process and recommendations in BOLD, ASL, DWI and T1/T2 mapping of the kidney.

The special issue was produced by working group 1 of PARENCHIMA.



› Position papers

› Delphi consensus framework

› Prospective multi vendor multi center studies

1. Best solution or minimum standard?
2. Indications might restrict the choices
(clinical needs are different than research needs)

3. Sequences/parameters
4. Patient preparation
- Analysis
- Hardware considerations

RESPECT STUDY

Aim: To develop and technically validate a standardised multiparametric renal MRI protocol to be used for personalised CKD management.

The Consortium

3-year project (June 2021 – May 2024)



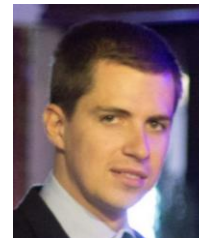
Coordinator: Anna Caroli (Mario Negri Institute, Italy)



Co-PIs: Chris Laustsen (Aarhus University, Denmark)



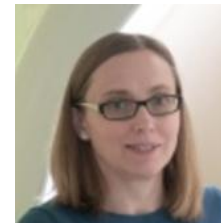
Frank Zoellner (Heidelberg University, Germany)



Maria Fernandez Seara (University of Navarra, Spain)



Constantin Suciu (Siemens, Romania)



Susan Francis (University of Nottingham, UK)

- › **T2.1: Establishment of multiparametric protocol.** Set-up of a physiologically and clinically relevant standardised multiparametric MRI protocol for CKD and harmonisation of the protocol for different MR vendors (GE, Siemens and Phillips, 3T scanners only), following recently published consensus guidelines and taking into account the results of a multi-vendor UK effort (UKRIN-MAPS, led by UoN), which provides a 'roadmap'. The protocol will provide accurate determination of anatomical, diffusion, perfusion, oxygenation as well as tissue relaxation properties
- › **T2.2: Protocol validation.** Phantom evaluation of the standardised MRI protocol by comparing the quantitative values in each site in test-retest experimental setup; MRI acquisition standard operating procedure (SOP) definition.
- › **T2.3: Technical validation in HVs and CKD patients.** Repeated MRI acquisition and analysis in 60 HVs (10 males and 10 females, aged [40-70] years, per centre – IRFMN, UNAV and AU), scanned 4 times, twice in a day few hours apart and again twice in a day about 1 week later, to assess test-retest repeatability and reproducibility; repeated MRI acquisition and repeatability analysis in a subset of CKD patients (3-5 patients in each site, to limit burden to patients), to show MRI feasibility and repeatability in patients and, conditionally (in case of higher intra-person variability in patients than in HVs), in all CKD patients enrolled in the WP4 clinical study.

REVIEW

Current methods for hyperpolarized [1-¹³C]pyruvate MRI human studies

Peder E. Z. Larson^{1,2}   | Jenna M. L. Bernard¹ | James A. Bankson³ |
Nikolaj Bøgh⁴  | Robert A. Bok¹ | Albert P. Chen⁵ |
Charles H. Cunningham^{6,7}  | Jeremy W. Gordon¹  | Jan-Bernd Hövener⁸  |
Christoffer Laustsen⁴  | Dirk Mayer^{9,10} | Mary A. McLean^{11,12}  |
Franz Schilling¹³  | James B. Slater¹ | Jean-Luc Vanderheyden^{5,14} |
Cornelius von Morze¹⁵  | Daniel B. Vigneron^{1,2} | Duan Xu^{1,2} |
the HP 13C MRI Consensus Group

Ongoing pre-clinical consensus work lead by Irene Marco Rius and the EMIM study group

Received: 19 December 2024 | Revised: 25 April 2025 | Accepted: 25 April 2025
DOI: 10.1002/mrm.30570

GUIDELINES

Magnetic Resonance in Medicine

Consensus recommendations for hyperpolarized [1-¹³C]pyruvate MRI multi-center human studies

Shonit Punwani^{1,2}  | Peder E. Z. Larson³  | Christoffer Laustsen⁴  |
Jan VanderMeulen⁵ | Jan Henrik Ardenkjær-Larsen⁶  | Adam W. Autry³ |
James A. Bankson⁷ | Jenna Bernard³ | Robert Bok³ | Lotte Bonde Bertelsen⁴ |
Jenny Che³ | Albert P. Chen⁸ | Rafat Chowdhury^{1,2} | Arnaud Comment⁹ |
Charles H. Cunningham^{10,11}  | Duy Dang³ | Ferdia A. Gallagher¹² |
Adam Gaunt¹³ | Yangcan Gong^{1,2} | Jeremy W. Gordon³  | Ashley Grimmer¹² |
James Grist^{14,15}  | Esben Søvsø Szocska Hansen⁴  | Mathilde Hauge Lerche⁶  |
Richard L. Hesketh¹⁶ | Jan-Bernd Hövener¹⁷ | Ching-Yi Hsieh^{18,19} |
Kayvan R. Keshari^{20,21}  | Sebastian Kozerke²² | Titus Lanz²³ | Dirk Mayer^{24,25} |
Mary McLean^{12,16} | Jae Mo Park^{26,27,28}  | Jim Slater³ | Damian Tyler^{14,15,29} |
Jean-Luc Vanderheyden^{30,31} | Cornelius von Morze³²  | Fulvio Zaccagna^{11,14,33,34,35} |
Vlad Zaha^{34,36}  | Duan Xu³ | Daniel Vigneron³ | The HP 13C MRI Consensus Group

DISCUSSION

› Where are we?

› Multi-center studies are feasible and show relative good agreement across sites

› What do we need to accomplish in the short term

› Retrospective and prepare for prospective multi center studies (share data!!)

› Where do we need to go?

› Harmonize hardware, software and SOP to allow efficient multicenter studies