Publication List

Perspectum

1. **Rial, B., *et al*. (2011). Rapid quantification of myocardial lipid content in humans using single breath hold 1H MRS at 3 Tesla. *Magnetic Resonance in Medicine*, 66(3), 619- 624.**
   Cardiac lipid levels measured using rapid single breath-hold ^{1}H-magnetic resonance spectroscopy (^{1}H-MRS) at 3T were in excellent correlation with results obtained by averaging over seven multiple breath-holds in 15 healthy volunteers. This study demonstrates that single breath-hold ^{1}H-MRS at 3T is a rapid and reliable method to quantify myocardial lipids.

2. **Banerjee, R., *et al*. (2014). Multiparametric magnetic resonance for the non-invasive diagnosis of liver disease. *Journal of Hepatology*, 60(1), 69-77.**
   First clinical validation on 79 subjects, showing how Liver*MultiScan* can stage chronic liver disease and has high diagnostic accuracy for assessment of liver fibrosis, steatosis and haemosiderosis. This is the first demonstration of a non-invasive test to differentiate early stages of fibrosis from normal liver.

3. **Banerjee, R., *et al*. (2015). Evidence of a Direct Effect of Myocardial Steatosis on LV Hypertrophy and Diastolic Dysfunction in Adult and Adolescent Obesity. *JACC: Cardiovascular Imaging*, 8(12), 1468-1470.**
   This study using ^{1}H-magnetic resonance spectroscopy (^{1}H-MRS) and cardiovascular MRI in 128 adults and 22 adolescents showed that even in the absence of other comorbidities, adult and childhood obesity is related to cardiac steatosis and that increased myocardial triglyceride content (MTGC) is related to diastolic dysfunction, with a stronger effect in males for the latter. The findings suggest that cardiac steatosis occurs early in obesity and has significant effect in childhood.

4. **Pramfalk, C., *et al.* (2015). Sex-specific differences in hepatic fat oxidation and synthesis may explain the higher propensity for NAFLD in men. *Journal of Clinical Endocrinology and Metabolism*, 100(12), 4425-33.**
   Men have a higher prevalence and greater risk of NAFLD compared with women despite similar levels of hepatic fat content, as measured by Liver*MultiScan*. This is potentially driven by sex- specific differences in fatty acid metabolism.

5. **Hodson, L., *et al*. (2015). Menopausal Status and Abdominal Obesity Are Significant Determinants of Hepatic Lipid Metabolism in Women. *Journal of the American Heart Association: Cardiovascular and Cerebrovascular Disease*, 4(10), e002258.**
   The first study to report that abdominal obesity in women, as well as weight gain in post-menopausal women, are major drivers of very low density lipoprotein (VLDL) secretion, which may increase risk of cardiovascular disease. Liver*MultiScan* was used to measure hepatic fat content of 58 women.

6. **Pavlides, M., *et al*. (2016). Multiparametric magnetic resonance imaging predicts clinical outcomes in patients with chronic liver disease. *Journal of Hepatology*, 64(2), 308-315.**
   Liver*MultiScan* demonstrated 100% negative predictive value (NPV) for liver-related clinical outcomes, in 112 patients monitored for up to 40 months. This holds prognostic potential for stratification of patients to facilitate clinical management and clinical trials.

7. **Rider, O., *et al.* (2016). Investigating a liver fat: arterial stiffening pathway in adult and childhood obesity. *Arteriosclerosis, Thrombosis, and Vascular Biology*, 36(1), 198-203.**
   Study on 77 adults and 18 children showing that hepatic fat, as measured by Liver*MultiScan*, is related to increased aortic stiffness in both adults and children. Hepatic fat content is a potential therapeutic target to treat the elevated vascular risk in obesity, which requires reliable biomarkers for monitoring response to treatment.

8. **Blake, L., *et al.* (2016). Decision analytic model of the diagnostic pathways for patients with suspected non-alcoholic fatty liver disease using non-invasive transient elastography and multiparametric magnetic resonance imaging. *BMJ Open*, 6(9), e010507.**
   The inclusion of Liver*MultiScan*, either as an adjunct to or replacement of transient elastography (TE) in the diagnostic pathway of NAFLD, may lead to cost savings for the NHS by reducing the number of liver biopsies required. When used in place of TE and liver biopsy, Liver*MultiScan* remains cost-effective up to a price of £672.

9. **Levelt, E., *et al.* (2016). Ectopic and visceral fat deposition in lean and obese patients with type 2 diabetes. *Journal of the American College of Cardiology*, 68(1), 53-63.**
   Liver*MultiScan* showed elevated hepatic fibroinflammatory and fat levels in asymptomatic patients with type 2 diabetes, suggesting significant NAFLD and NASH. This highlights an urgent need – and potential application of the technology – in screening, staging and monitoring diabetic liver disease.

10. **Eddowes, P., *et al.* (2017). Utility and cost evaluation of multiparametric magnetic resonance imaging for the assessment of non-alcoholic fatty liver disease. *Alimentary Pharmacology & Therapeutics*, 47(5), 631- 644.**
    Liver*MultiScan* accurately identified patients with steatosis, stratified those with NASH and reliably excluded clinically significant liver disease with superior negative predictive value (83.3%) t compared to transient elastography (42.9%) and ELF (57.1%). For the risk stratification of NAFLD, Liver*MultiScan* was cost effective and, combined with transient elastography, had the lowest cost per correct diagnosis.

11. **Wilman, H.R., *et al*. (2017). Characterisation of liver fat in the UK Biobank cohort. *PloS One*, 12(2), e0172921.**
Liver*MultiScan* was used to measure hepatic fat in 4,949 participants in the UK Biobank with a success rate of 96.8% and acquisition time of 3 minutes, demonstrating feasibility to screen large populations potentially cost-effectively.

12. **Pavlides, M., *et al.* (2017). Multiparametric magnetic resonance imaging for the assessment of non-alcoholic fatty liver disease severity. *Liver International*, 37(7), 1065-1073.**
Liver*MultiScan* had a higher success rate on 71 NAFLD patients (95%) compared to transient elastography (59%) and showed high accuracy for the diagnosis of NASH and ballooning. This demonstrates potential application in patient management as well as a surrogate endpoint in clinical trials.

13. **Tunnicliff, E.M., *et al.* (2017). A model for hepatic fibrosis: the competing effects of cell loss and iron on shortened modified Look-Locker inversion recovery T1 (shMOLLI-T1) in the liver. *Journal of Magnetic Resonance Imaging*, 45(2), 450-462.**
Validation of the technology underpinning cT1, showing that iron correction of liver T1 values produces more accurate measures of hepatic fibro-inflammation.

14. **Pavlides, M., *et al.* (2017). Interobserver variability in histologic evaluation of liver fibrosis using categorical and quantitative scores. *American Journal of Clinical Pathology*, 147, 364-369.**
Assessment of liver fibrosis by digital imaging analysis of Collagen Proportionate Area (CPA) followed by visual assessment of CPA, is more robust than visual analysis alone with improved agreement between pathologists.

15. **Breen, D. (2018). Multiparametric magnetic resonance imaging for early detection of diffuse liver disease. *Biomarkers in Medicine*, 12(2), 105-106.**
An overview of Liver*MultiScan* from the perspective of a radiologist, highlighting its advantages over liver biopsy and other non-invasive methods, as well as cost-effectiveness.

16. **McDonald, N., *et al.* (2018). Multiparametric magnetic resonance imaging for quantitation of liver disease: a two-centre cross-sectional observational study. *Scientific Reports*, 8(9187), 1-10.**
Liver*MultiScan* had superior technical success rate (98.1%) even in obese subjects compared to transient elastography (85%). The technique had excellent repeatability and reproducibility and also demonstrated good diagnostic accuracy in detecting hepatic fibroinflammation, fat and iron.

17. **Hoy, A.M., *et al.* (2018). Non-invasive assessment of liver disease in rats using multiparametric magnetic resonance imaging: a feasibility study. *Biology Open*, 7, bio033910.**
Liver*MultiScan* accurately quantified levels of hepatic fibroinflammation, fat and iron in preclinical models.

18. **Mojtahed, A., *et al.* (2018). Reference range of liver corrected T1 values in a population at low risk for fatty liver disease: a UK Biobank sub-study with an appendix of interesting cases. *Abdominal Radiology*, 44(1), 72-84.**
This study established the reference range of cT1 values for a large healthy UK population, which has potential to serve as a benchmark of normality for future studies and enables cT1 as a quantitative imaging biomarker for studies in liver health and disease.

19. **Mole, D.J., *et al.* (2018). Study Protocol: HepaT1ca - An observational clinical cohort study to quantify liver health in surgical candidates for liver malignancies. *BMC Cancer*, 18(1), 890.**
This ongoing trial will refine the technology and clinical application of Liver*MultiScan* in quantifying pre-existing liver health and predicting post-intervention outcomes following liver resection in cancer.

20. **Harrison, S., *et al.* (2018). Utility and variability of three non-invasive liver fibrosis imaging modalities to evaluate efficacy of GR-MD-02 in subjects with NASH and bridging fibrosis during a phase-2 controlled study. *PloS One*, 13(9), e0203054.**
cT1 showed superior reproducibility (CoV 3.1%) compared to the other non-invasive liver tests used in this NASH clinical trial: magnetic resonance elastography (CoV 11%) and transient elastography (40%). This underscores utility of cT1 in monitoring longitudinal change in NASH patients.

21. **McKay, A., *et al.* (2018). Measurement of liver iron by magnetic resonance imaging in the UK Biobank population. *PloS One,* 13(12), e0209340.**
Liver*MultiScan* was used to measure hepatic iron levels in 9,108 participants of the UK Biobank study, demonstrating feasibility of large population studies in liver iron with this technique.

22. **Hutton, C., *et al.* (2018). Validation of a standardized method for liver fat and T2* quantification. *PloS One*, 13(9), e0204175.**
Technical validation of the Liver*MultiScan* technique (LMS IDEAL) to measure hepatic fat. LMS IDEAL had high accuracy and excellent reproducibility across major MR vendors and field strengths, over a wide range of values. Perspectum is the only imaging provider with the IDEAL technique standardised across Siemens, GE and Philips scanners.

23. **Li, Q., *et al*. (2018). Current status of imaging in nonalcoholic fatty liver disease. *World Journal of Hepatology*, 10(8), 530-542.**
Review of imaging methods for NAFLD risk stratification and management, including multiparametric MRI (Liver*MultiScan*), MR Elastography and Ultrasound Elastography.

24. **Mozes, F.E., *et al*. (2018). Mapping tissue water T(1) in the liver using the MOLLI T(1) method in the presence of fat, iron and B(0) inhomogeneity. *NMR in Biomedicine*. 32(2), e4030.**
Describes a method for computing a "water T1" by correcting the MOLLI T1 for the confounding influence of iron, fat and frequency offsets. This has the potential to improve the characterisation of fibro-inflammatory liver disease.

25. **Bachtiar, V., *et al.* (2018). Repeatability and reproducibility of multiparametric magnetic resonance imaging of the liver. *PloS One*, 14(4), e0214921.**
Technical validation of Liver*MultiScan* demonstrating good reproducibility and repeatability for quantifying liver tissue characteristics across different MR vendors and field strengths. Standardised biomarkers with low variability, like Liver*MultiScan*, are crucial for reliable readings in multicentre clinical trials.

26. **Dillman, J. *et al.* (2019). Diagnostic performance of quantitative magnetic resonance imaging biomarkers for predicting portal hypertension in children and young adults with autoimmune liver disease. *Pediatric Radiology*, 49(3), 332–341.**
Evaluates the utility of quantitative MRI biomarkers including elastography and cT1 mapping for predicting portal hypertension in a paediatric population. Liver and spleen stiffness, along with liver cT1, predict radiologic portal hypertension with good accuracy.

27. **Castera, L. *et al.* (2019). Noninvasive assessment of liver disease in patients with nonalcoholic fatty liver disease. *Reviews in Basic and Clinical Gasteroenterology and Hepatology*, 156, 1264-1281.**
Review of non-invasive methods for assessing liver disease in NAFLD and how they could be used in clinical practice. Highlights the key issues of differentiating NASH from simple steatosis and identifying advanced fibrosis.

28. **Harrison, S.A. *et al.* (2019). NGM282 improves liver fibrosis and histology in 12 weeks in patients with nonalcoholic steatohepatitis. *Journal of Hepatology*, 71(4), 1198–1212.**
Results from a Phase 2 NASH trial showing that Liver*MultiScan* (cT1) can detect drug efficacy in as little as 6 weeks to serve as an early go/no-go signal. cT1 predicted responders versus nonresponders as well as correlated with histology and serum biomarkers, underscoring effectiveness in longitudinal monitoring in NASH patients.

29. **Wilman, H.R., *et al.* (2019). Genetic studies of abdominal MRI data identify genes regulating hepcidin as major determinants of liver iron concentration. *Journal of Hepatology*, 71(3), 594–602.**
In this study, 3 genetic variants that are linked to an increased risk of developing higher liver iron content were identified. The same genetic variants were shown to be linked to higher risk of many diseases, but they may also be associated with some health advantages. Finally, genetic variants associated with waist-to-hip ratio were used as a tool to show that central obesi ty is causally associated with increased liver iron content.

30. **Bagur, A., *et al.* (2019). Magnitude-intrinsic water–fat ambiguity can be resolved with multipeak fat modeling and a multipoint search method. *Magnetic Resonance in Medicine*, 82(1), 460–475.**
Technical validation of a Liver*MultiScan* technique (MAGO) for measurement of liver fat. MAGO showed excellent accuracy and reproducibility across different MR vendors at different field strengths. Technically challenging cases were processable with MAGO, demonstrating robustness of the technique.

31. **Levick, C., *et al.* (2019). Non-invasive assessment of portal hypertension by multi-parametric magnetic resonance imaging of the spleen: A proof of concept study. *PloS One*, 14(8), e0221066.**
This proof of concept study aimed to evaluate the diagnostic accuracy of Liver*MultiScan* in the assessment of portal hypertension with comparison to other non-invasive technologies. Spleen cT1 showed to be a promising biomarker of portal pressure that outperformed other non-invasive scores.

32. **Gilligan, L.A., *et al.* (2020). Differentiating pediatric autoimmune liver diseases by quantitative magnetic resonance cholangiopancreatography. *Abdominal Radiology*, 45(1), 168–176.**
MRCP+ parameters and serum biochemistry values were assessed for performance in discriminating primary/autoimmune sclerosing cholangitis (PSC/ASC) from AIH in paediatric population. All but one quantitative MRCP parameter were significantly different between cohorts and predictive of diagnosis. No laboratory values were significantly different between cohorts. Study indicates that MRCP+ provides good discrimination of PSC/ASC from AIH and has the potential to provide numerous imaging biomarkers of autoimmune liver disease.

33. **Chakravarthy, M.V., *et al.* (2020). Nutrition and nonalcoholic fatty liver disease – Current perspectives. *Gastroenterology Clinics*, 49 (1), 63–94.**
This proof of concept study aimed to evaluate the diagnostic accuracy of Liver*MultiScan* in the assessment of portal hypertension with comparison to other non-invasive technologies. Spleen cT1 showed to be a promising biomarker of portal pressure that outperformed other non-invasive scores.

34. **Goldfinger, M., *et al.* (2020). Quantitative MRCP Imaging: Accuracy, repeatability, reproducibility, and cohort-derived normative ranges. *Journal of Magnetic Resonance Imaging*, 52(3), 807–820.**
Technical validation of quantitative MRCP (MRCP+), demonstrating that quantitative MRCP, especially as compared with current qualitative MRCP, could reduce subjectivity, enable measurement of duct diameter throughout the biliary tree, and automatically detect candidate strictures and dilatations with a high degree of sensitivity and specificity. Quantitative MRCP therefore improves upon the current "gold standard" of noninvasive imaging of the biliary tree.

35. **Parisinos, C, A. *et al.* (2020). Genome-wide and Mendelian randomisation studies of liver MRI yield insights into the pathogenesis of steatohepatitis. *Journal of Hepatology*, 73(2), 241–251.**
This study highlights the association between two metal ion transporters and cT1, indicating an important new mechanism in steatohepatitis. Future studies are needed to determine whether interventions targeting the identified transporters might prevent liver disease in at risk individuals.

36. **Dilman, J, R., *et al.* (2020). Relationship between magnetic resonance imaging spleen T1 relaxation and other radiologic and clinical biomarkers of liver fibrosis in children and young adults with autoimmune liver disease. *Abdominal Radiology*, Advance online publication.**
In this study, splenic T1 relaxation was found to be associated with other radiologic and clinical biomarkers of liver fibrosis, including radiologic portal hypertension, in children and young adults with AILD.

37. **Cruz, M., *et al.* (2020). New boundaries of liver imaging: from morphology to function. *European Journal of Internal Medicine*, Advance online publication.**
This review of functional imaging techniques applied to liver imaging emphasizes how modern approaches combine morphological and functional information to provide noninvasive surrogate biomarkers of many focal and diffuse liver diseases.

38. **Hydes, T. J., *et al.* (2020). Mechanisms, screening modalities and treatment options for individuals with non-alcoholic fatty liver disease and type 2 diabetes. *Diabetic Medicine*, Advance online publication.**
This review of screening and treatment options for patients with type 2 diabetes and non-alcoholic fatty liver disease (NAFLD) emphasizes the link between these two diseases.

39. **Jayaswal, A., *et al.* (2020). Prognostic value of multiparametric magnetic resonance imaging, transient elastography and blood-based fibrosis markers in patients with chronic liver disease. *Liver International*, Advance online publication.**
Liver*MultiScan*'s noninvasive MRI biomarker cT1 was shown to predict clinical outcomes in 197 liver disease patients, to outperform FibroScan's transient elastography and FIB-4, and have similar performance to invasive liver biopsy. FibroScan was no longer predictive when high technical failure rate was accounted for.

40. **Thomaides-Brears, H. B., *et al.* (2020). Multiparametric MR mapping in clinical decision-making for diffuse liver disease. *Abdominal Radiology*, Advance online publication.**
This review of techniques for clinical decision making in diffuse liver disease highlights the advantages of Liver*MultiScan*'s cT1 with superior NASH diagnostic ability compared with MRE which requires additional hardware and is confounded by even mild iron overload and inflammation, and DWI which currently lacks standardisation.