Could Hyperpolarised Xenon and Proton MRI techniques be key in the assessment of Drug Induced Interstitial Lung Disease?

A novel research study assessing bleomycin in patients being treated for testicular cancer.

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Background

Drug induced interstitial lung disease (DI-ILD) can be caused by over 350 drugs including chemotherapy and immunotherapy agents. DI-ILD is thought to be underdiagnosed worldwide and if diagnosed can lead to a restriction in treatment options. Currently, diagnosis is achieved through assessing the temporal relationship between symptoms and drug exposure. Standard investigative tools include CT imaging and lung function analysis, however they have limitations.

Aim

We propose that MRI imaging using Hyperpolarised Xenon and Proton MRI techniques, alongside quantitative CT imaging, could provide both functional and structural information in the diagnosis and prognosis of DI-ILD which would be an improvement upon existing measurements and help determine best clinical practice.

Method

A single centre prospective study between The University of Sheffield imaging department (POLARIS), Sheffield University Hospital Foundation Trust and in collaboration with Translational Imaging in Drug Safety Assessment European Consortium (TRISTAN).
Patients diagnosed with testicular cancer undergoing Bleomycin, Etoposide and Platinum (BEP) chemotherapy are being recruited. Recruitment started October 2022. Currently 4 participants enrolled, target of 21.
Participants reviewed at timepoints as per the study schedule shown in Table 1. Information obtained at each visit is shown in Table 2: clinical assessment, pulmonary function tests (PFTs) and MRI.

Table 1

Table 1: Study Schedule

Visit	Baseline Visit V1	1st Follow Up Visit (V2)	2nd Follow Up Visit (V3)	3rd/Final Follow Up Visit (V4)
Treatment	Pre-chemotherapy	Post Chemotherapy Cycle 1	Post Chemotherapy Cycle 3 or 4	Post Chemotherapy
Timeline		Week 3-4	Week 10-12	Week 36
Assessment	Clinical Assessment PFTs MRI CT (Standard care)	Clinical Assessment PFTs MRI CT (Standard care)	Clinical Assessment PFTs MRI CT (Standard care)	Clinical Assessment PFTs MRI C T (extra care)

Table 2

Table 2: Information obtained at each study visit

Event	Baseline	3-4 weeks	10-12 weeks	6 months post bleomycin treatment
	V1	V2	V3	V4
Informed consent	x			
Screening / Review of eligibility criteria	x	x	x	x
Clinical assessment	x	x	x	x
Vital signs	x	x	x	x
Full blood count (normal clinical practice)	x	x	x	x
Questionnaires				
MRC dyspnoea scale	x	x	x	x
Leicester cough questionnaire	x	x	x	x
Lung Function Tests				
FVC	x	x	x	x
FEV1	x	x	x	x
DLCO	x	x	x	x
Imaging				
^{1}H MRI	x	x	x	x
^{129}Xe MRI	x	x	x	x
CT scan (part of normal practice except visit 4)	x	x	x	(optional)

Example results from Participant 1

Pulmonary function tests

Pulmonary Function Test Participant 1

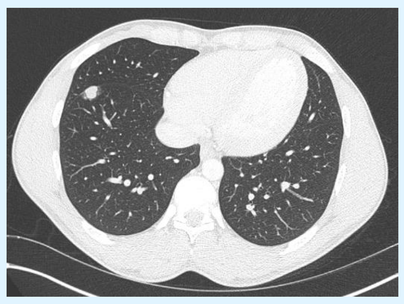
FEV1			FVC			FEV1/FVC		
litre	% predicted	z-score	litre	% predicted	z-score	%	% predicted	z-score
4.71	99.01	-0.08	5.76	99.55	-0.04	81.8	98.85	-0.16

TLCO			KCO			VA		
mmol/(min*kPa)	% predicted	z-score	mmol/(min*kPa*L)	% predicted	z-score	litre	% predicted	z-score
14.35	123.58	1.62	2.11	126.45	2.02	6.81	97.25	-0.25

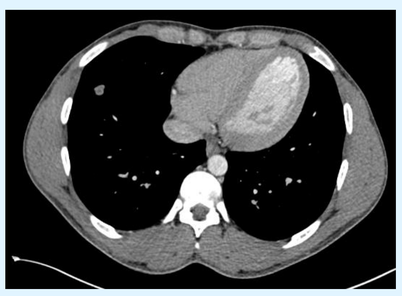
Pulmonary function tests within expected range

CT images A and B.

A



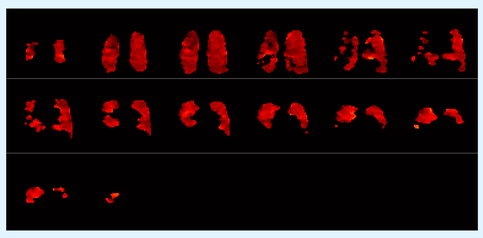
B



CT scans demonstrate lung metastases.

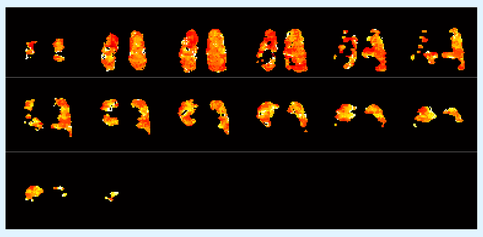
Hyperpolarised Xenon Apparent Diffusion Co-efficient (ADC) and mean diffusive length scale (Lm_D) Maps. Images C and D

C



Mean whole lung ADC ~ 0.035±0.010 cm²/s
Healthy ADC ~ 0.03 cm²/s

D

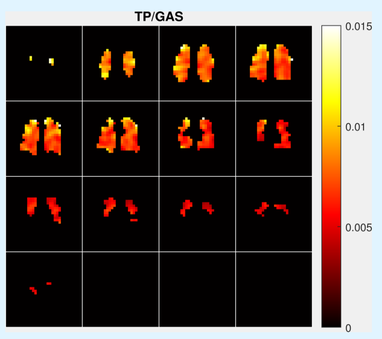


Mean whole lung Lm_D ~ 286±67 µm
Healthy Lm_D ~ 260 µm

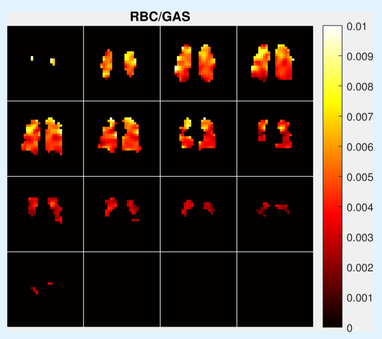
Image C and D demonstrate a mildly increased ADC and Lm_D. An increase in these values may suggest reduced alveolar integrity. Participant 1 is known to have lung metastases.

Signal ratio maps of Xenon in differing physiochemical compartments: Tissue Plasma (TP):Gas, Red Blood Cell (RBC): Gas and RBC:TP. Image E, F and G.

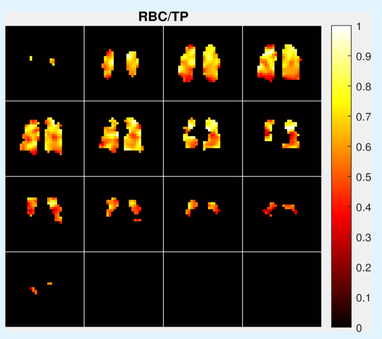
E



F



G



Images E, F and G demonstrate an efficient RBC to TP ratio. In severe fibrotic disease a reduced RBC and increased TP would be expected. In inflammatory disease similarly RBC:TP may be affected.

Take away points

- An unmet need in investigations to determine DI-ILD diagnosis.
- MRI could provide both structural and functional data which could complement existing strategies.
- Recruitment ongoing and consideration of widening participant cohort.
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Conclusion

This is novel research to determine whether functional MRI imaging can potentially help identify DI-ILD. This could help avoid or minimise adverse long-term pulmonary outcomes and subsequently help guide oncological treatment choices. If changes are demonstrable, this could be expanded to assess for potential effects in newer immunotherapy agents or checkpoint inhibitors. Further recruitment may be required.

National Germ Cell Group
NGCG Conference Glasgow 24th April 2023
The University Of Sheffield.
POLARIS Pulmonary, Lung and Respiratory Imaging Sheffield
Polarised Imaging Systems
TRISTAN TRANSLATIONAL IMAGING IN DRUG SAFETY ASSESSMENT