UCL CENTRE FOR MEDICAL IMAGING

NHS University College London Hospitals NHS Foundation Trust

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Volumetric measurement of Crohn's disease on magnetic resonance enterography: feasibility, clinical utility, and role in assessing biologic treatment response

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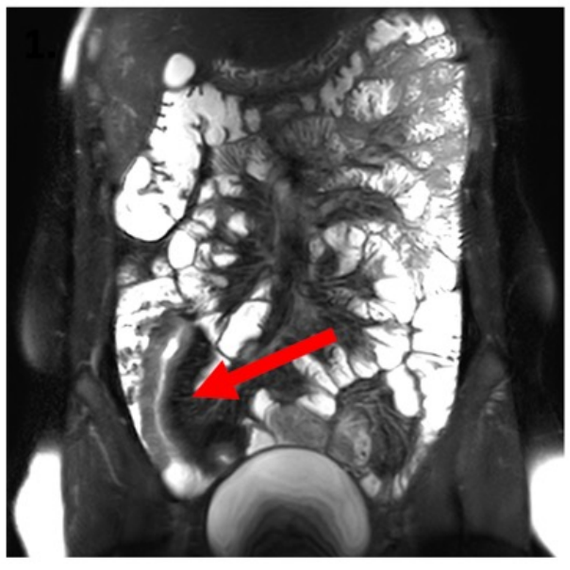
- UKRI Innovate UK (project reference 105860)
- Takeda Pharmaceuticals

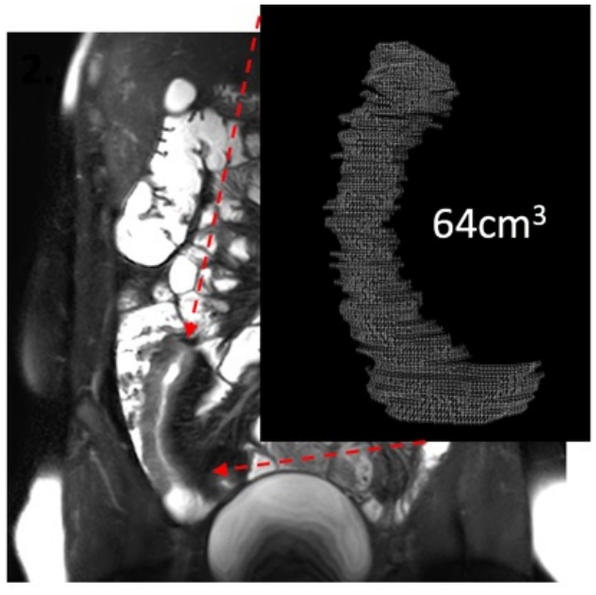
- BB, ABa – employees at Motilent
- AM – CEO of Motilent
- DB – Associate Scientific Director, GI Imaging Lead, Takeda
- ST – shareholder in Motilent

Introduction

- **Magnetic resonance enterography** (MRE)
  - Widely used to assess Crohn's disease (CD) activity and treatment response
  - Subjective interpretation with moderate interobserver agreement
- **Bowel wall thickness** is a key parameter
  - Measured using a single 2D image of the bowel rather than full disease volume
  - Basis for activity scores (e.g., sMARIA)



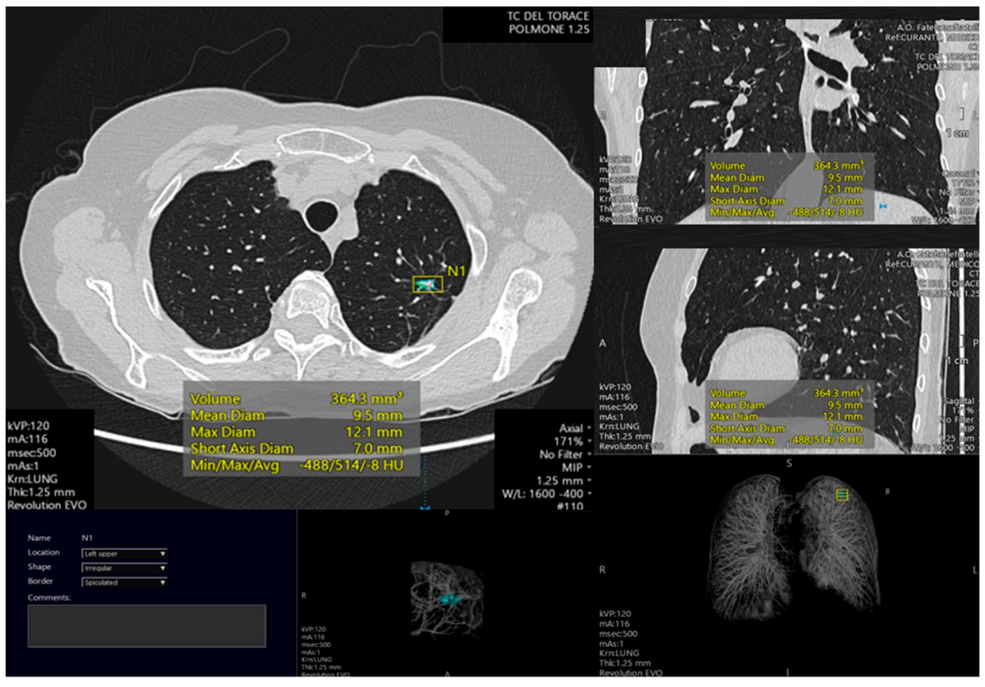
Bowel diameter at single location

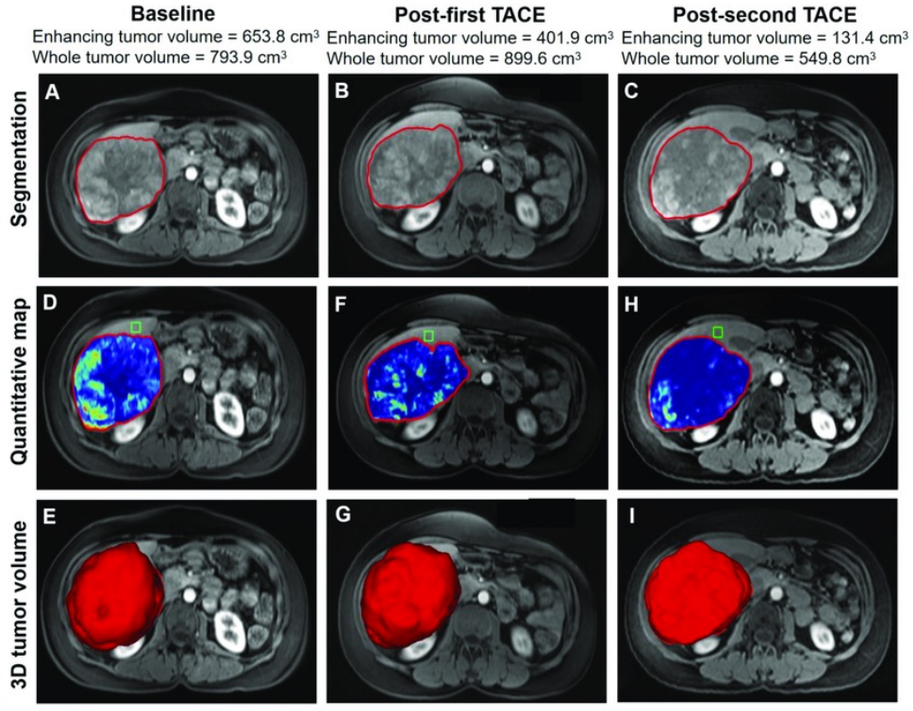


Total disease volume

Introduction 2

- Volumetric evaluation – <u>common but not yet considered for CD activity by MRE</u>
  - Lung nodule assessment
  - Whole-body MRI evaluation of multiple myeloma
  - Tumour volume is more sensitive for detecting therapeutic response

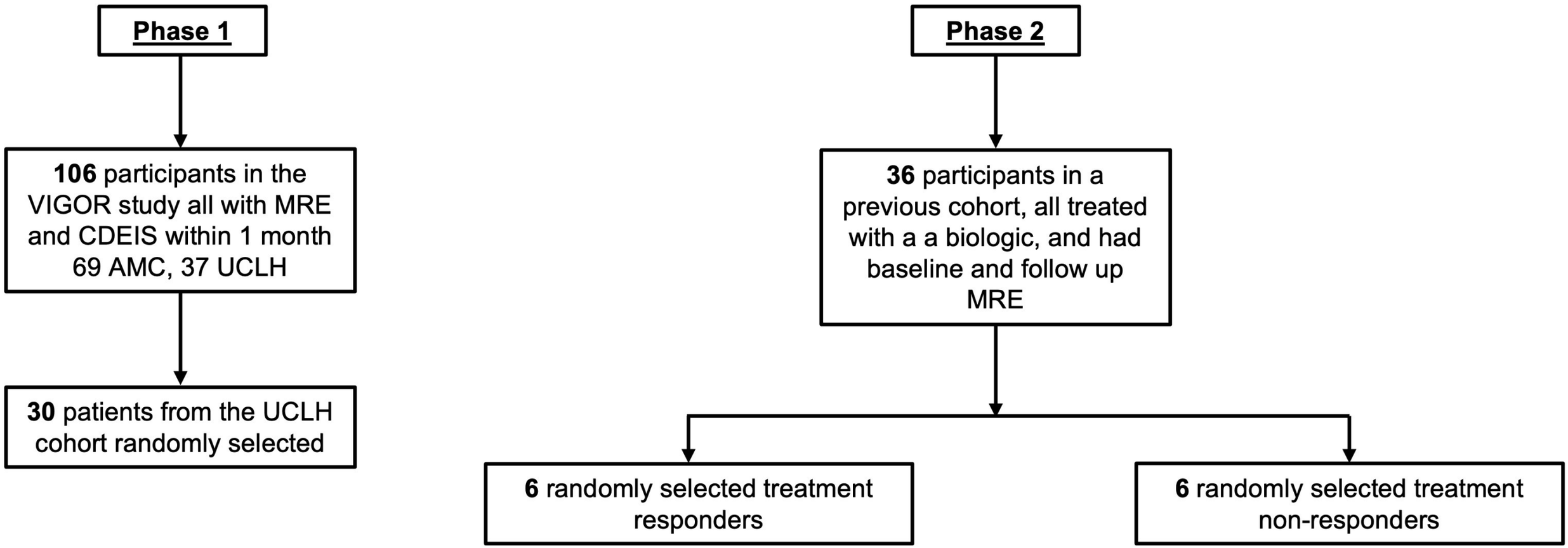




Aims

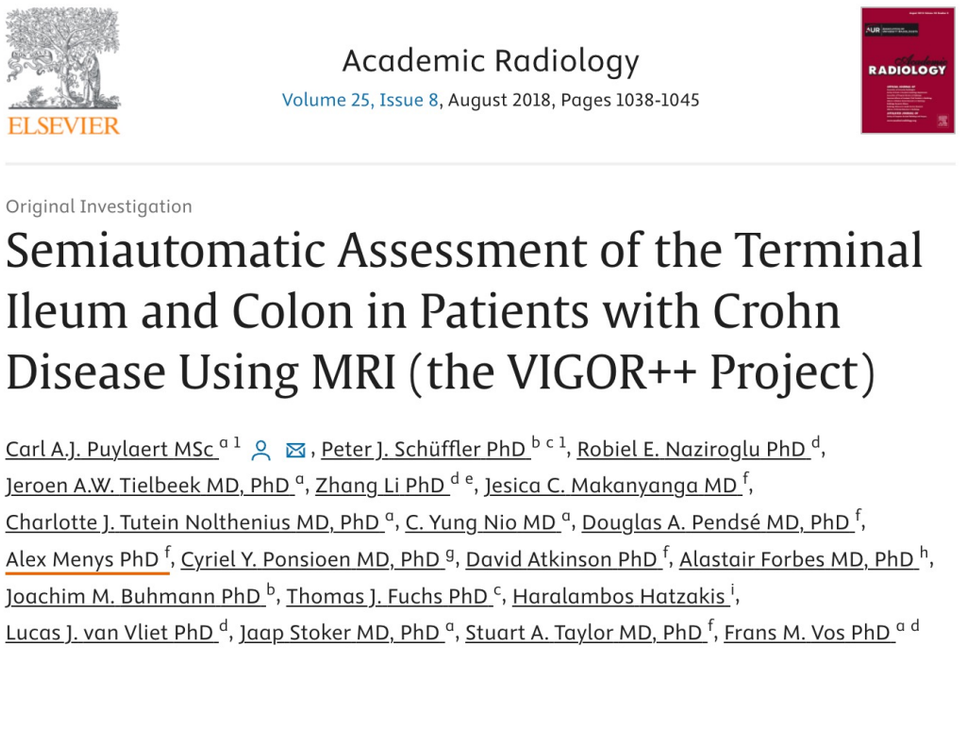
- **Phase 1**
  - Evaluate feasibility and interobserver agreement for quantifying volumetric burden of terminal ileal (TI) CD
  - Compare volumetric CD burden on MRE *vs.* CD activity on endoscopy and sMARIA
- **Phase 2**
  - Assess whether volumetric changes reflect response induced by biologic therapy

Methods


Phase 1
106 participants in the VIGOR study all with MRE and CDEIS within 1 month 69 AMC, 37 UCLH
30 patients from the UCLH cohort randomly selected
Phase 2
36 participants in a previous cohort, all treated with a a biologic, and had baseline and follow up MRE
6 randomly selected treatment responders
6 randomly selected treatment non-responders

Phase I

- 30 consecutive UCLH patients previously recruited to a study developing semi-automated measurements of MRI wall thickness and contrast enhancement (VIGOR)
  - Aged ≥18 years with suspected or known CD
  - Prospectively underwent both MRE and ileocolonoscopy within 2 weeks
- Crohn's Disease Endoscopic Index of Severity (CDEIS) prospectively recorded in TI



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Original Investigation

Semiautomatic Assessment of the Terminal Ileum and Colon in Patients with Crohn Disease Using MRI (the VIGOR++ Project)

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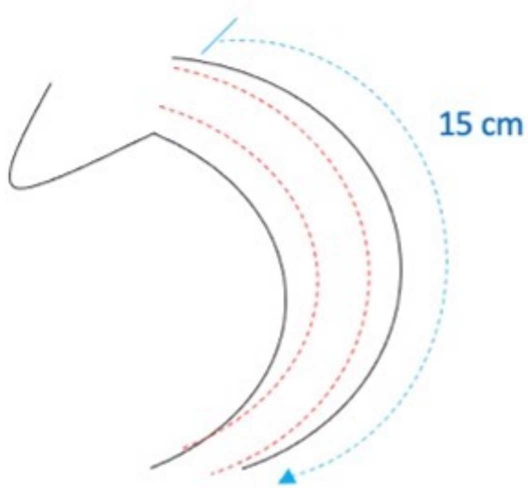
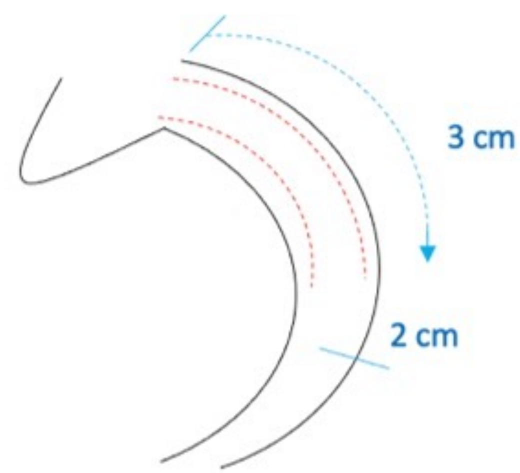
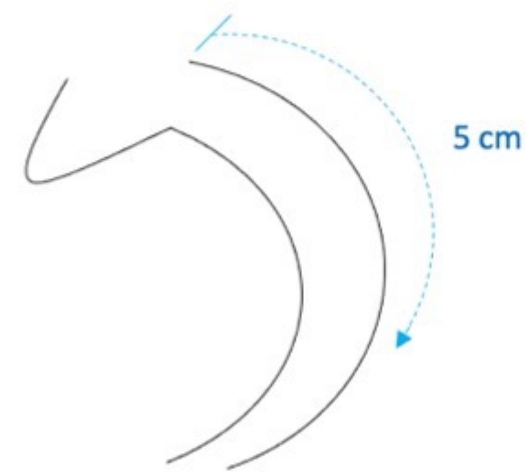
Phase I (Contd.)

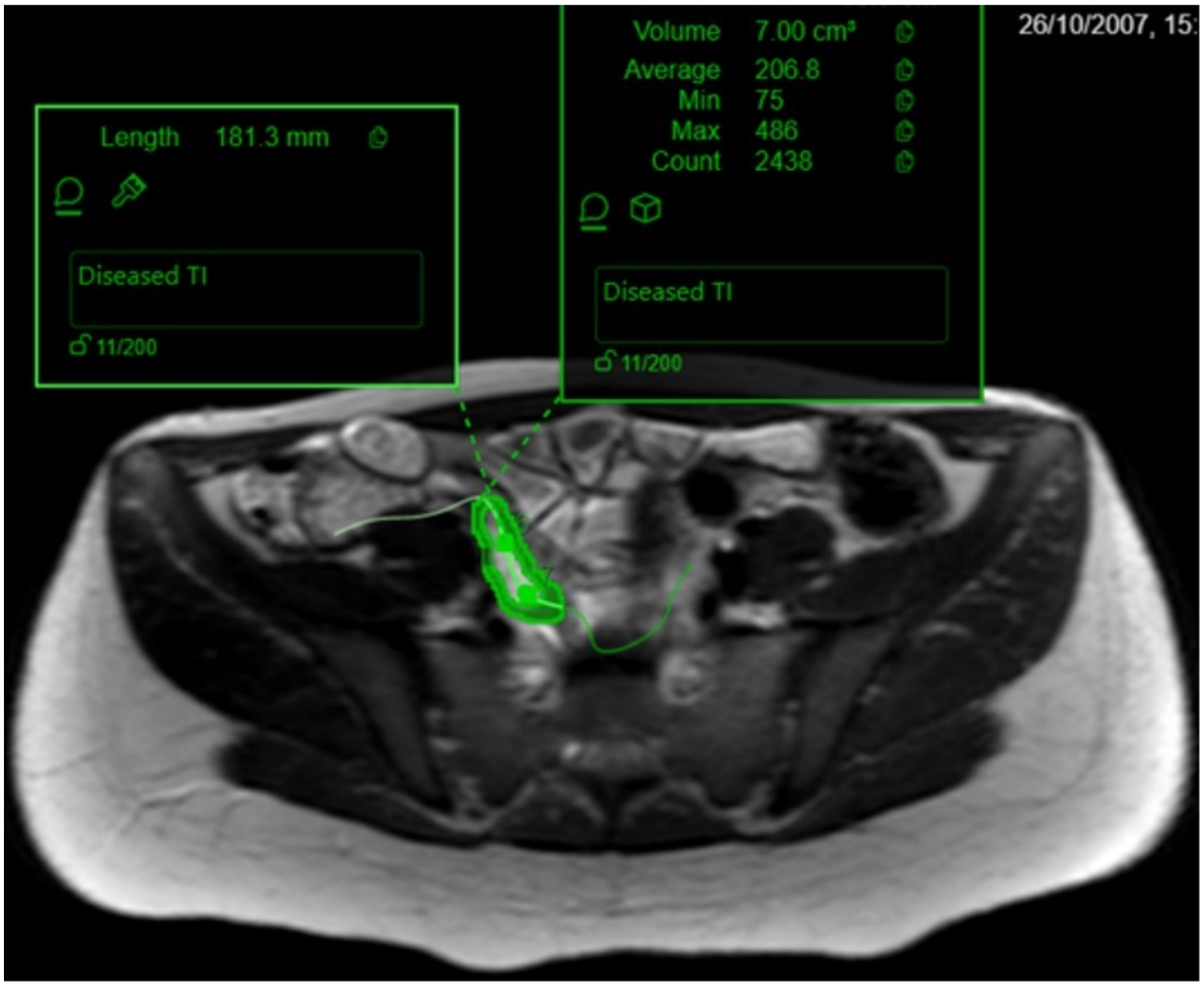
- Online Platform: Anonymised MRE studies were uploaded to Entrolytics (Motilent)
- Centrelines: A Consultant GI Radiologist placed a centreline through the TI lumen that defined the full length of diseased bowel on the T2-weighted non-fat saturated sequence
  - **Coronal or axial** – depending on which best reflected the total disease burden
- Manual Segmentation: Centrelines formed the basis for manual segmentations of diseased bowel wall performed independently by two Consultant GI radiologists (one of whom had placed the original centreline)
  - Segmented all pixels within the **bowel wall from mucosa to serosa**
  - Did **not** include bowel lumen and adjacent structures (e.g., fat and vessels)

Phase I (Contd.)

1. Long segment of disease	2. Short segment of disease	3. Normal segment
		
Segment the abnormal bowel only	Segment the abnormal bowel plus normal bowel to a length of 5 cm in total	Segment 5 cm of normal terminal ileum

Key:
Normal bowel segment
Abnormal bowel segment

Phase I (Contd.)



Phase 2

- Randomly selected data from 12 UCLH patients recruited to a previous study validating an MRE activity score (MEGS)
  - Aged ≥14 years with CD starting anti-TNFα therapy
  - Baseline MRE within 3 months of starting therapy and at least one follow-up MRE no earlier than 3 months after baseline
- Patients categorised as treatment 'responders' or 'non-responders' using physician's global assessment incorporating all available clinical information (blinded to imaging results)

Eur Radiol (2016) 26:2107–2117
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GASTROINTESTINAL

Monitoring Crohn's disease during anti-TNF-α therapy: validation of the magnetic resonance enterography global score (MEGS) against a combined clinical reference standard

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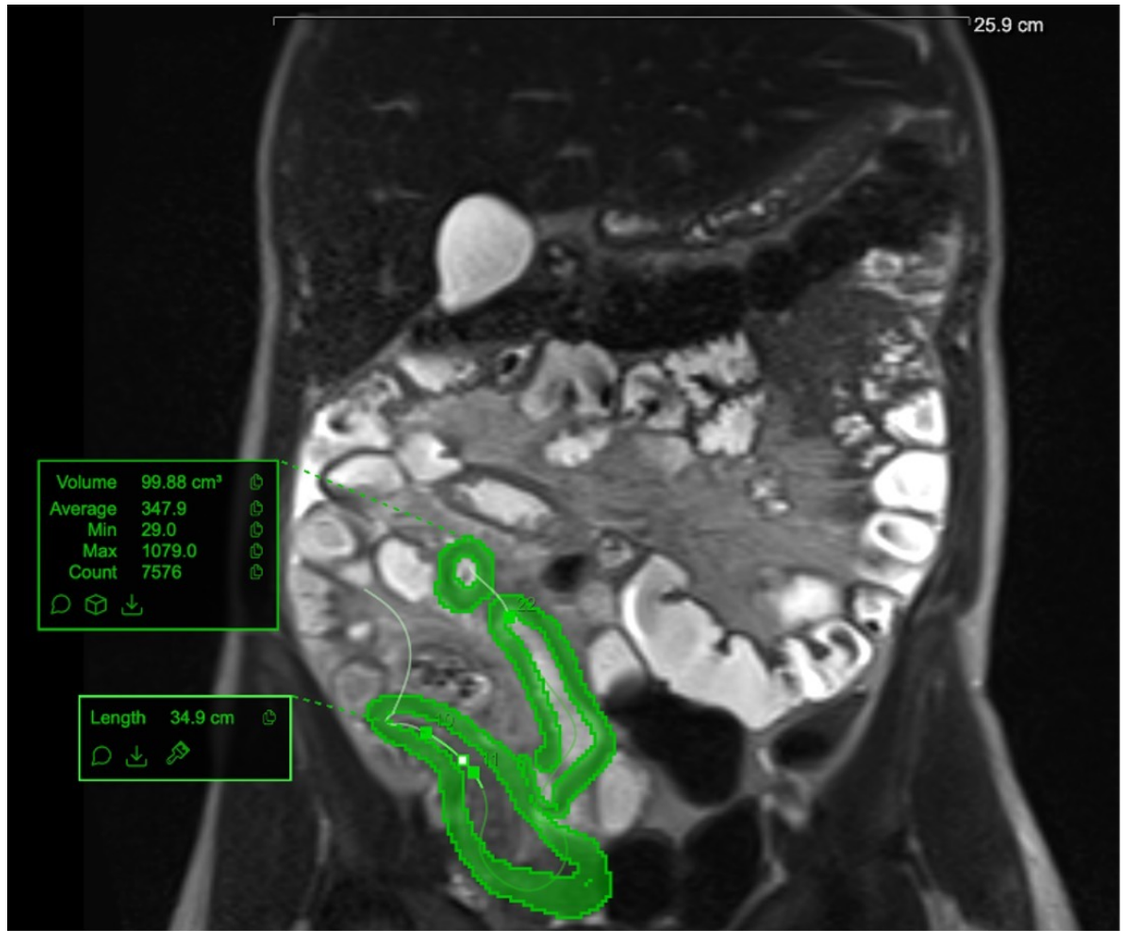
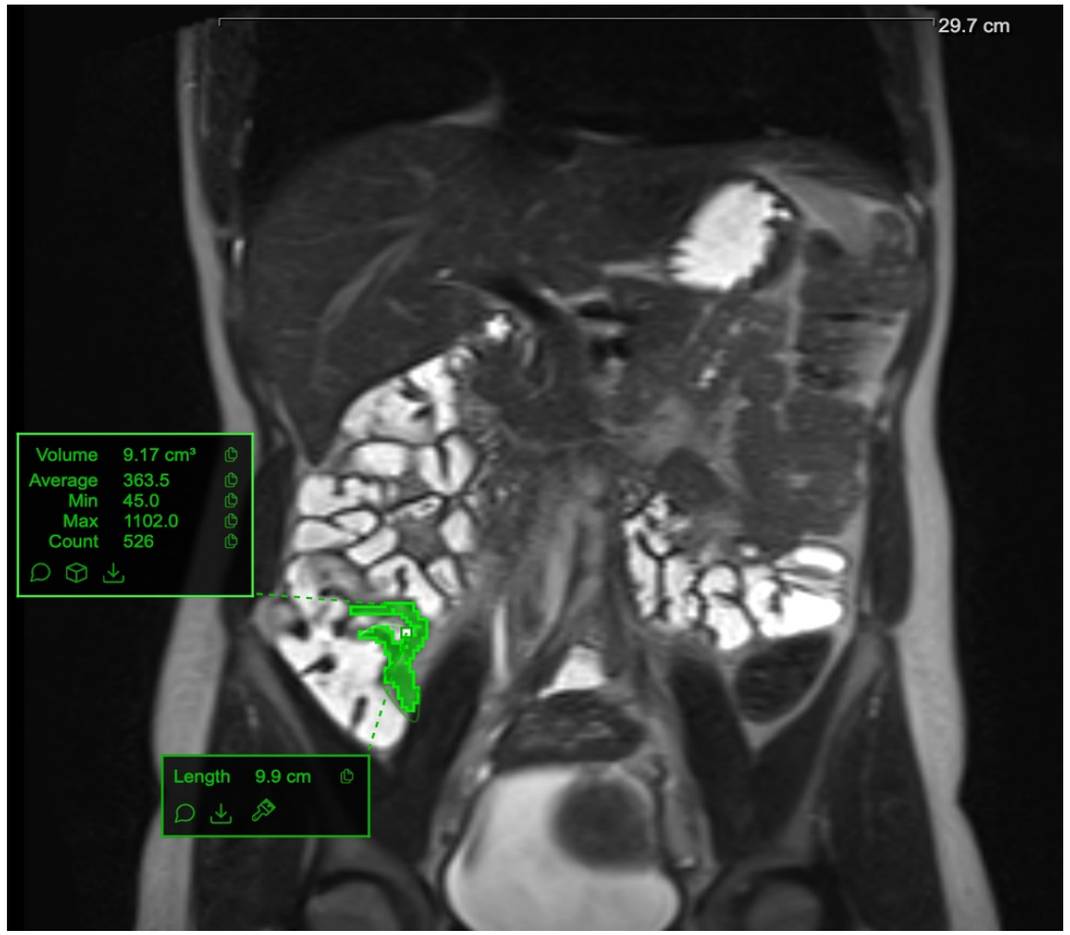
Phase 2 (Contd.)

- A Consultant GI Radiologist placed a centreline and manually segmented TI CD on the pre- and post-treatment MRE using the same methodology as in Phase 1
- Blinded to treatment response classification





Results – Phase I

- 30 patients, median age 29 years, 18 females
- Mean difference of disease volume between the 2 readers was - 3.0 cm^3 (limits of agreement -21.8, 15.9)
- Median time taken to place the polylines was 4 minutes and 41 seconds
- Median time taken to segment bowel wall was of 7 minutes and 50 seconds

Results – Phase I (Contd.)

- Spearman rank correlation coefficient of mean disease volume against CDEIS was 0.54 (95% CI 0.24, 0.84)

		N	R1 disease volume (cm^3)	R2 disease volume (cm^3)	Mean disease volume (cm^3) *
All patients		30	10.1 (3.0, 24.5)	10.2 (4.3, 28.1)	9.9 (4.1, 25.7)
CDEIS	<3	15	5.4 (2.6, 10.2)	7.3 (3.3, 10.1)	5.7 (2.9, 9.8)
	≥3	15	18.7 (10.1, 56.0)	22.5 (12.5, 45.9)	20.9 (11.3, 44.0)
sMARIA	<1	7	2.4 (1.8, 2.6)	3.3 (2.8, 4.3)	2.8 (2.5, 3.1)
	≥1	23	13.5 (7.0, 45.3)	16.5 (9.1, 45.9)	15.0 (8.6, 44.0)

Table. R1 (reader 1), R2 (reader 2), and mean disease volumes by CDEIS and sMARIA

Data are n or median (IQR)

*mean volume of the two readers

Results – Phase 2

Characteristic		Non-responder N=6	Responder N=6	Total N=12
Age		30 (23, 42)	24 (21, 29)	25 (22, 38)
Female		2 (33)	2 (33)	4 (33)
Biologic	Adalimumab	5 (83)	3 (50)	8 (67)
	Infliximab	1 (17)	3 (50)	4 (33)
Pre-existing steroids		1 (17)	3 (50)	4 (33)
Pre-existing immunosuppressant at the time of biologic	Azathioprine	3 (50)	5 (83)	8 (67)
	Methotrexate	1 (17)	0 (0)	1 (8)
	None	2 (33)	1 (17)	3 (25)
Switch from infliximab		1 (17)	0 (0)	1 (8)
Days from MRE to biologic		-38 (-51, -13)	2 (-21, 19)	-17 (-38, 4)
Surgical history	Yes	3 (50)	2 (33)	5 (42)
Montreal A	A1	1 (17)	1 (20)	2 (18)
	A2	5 (83)	4 (80)	9 (82)
Montreal L	L3	5 (83)	3 (50)	8 (67)
	L3 + L4	1 (17)	3 (50)	4 (33)
Montreal B	B1	0 (0)	3 (50)	3 (25)
	B2	4 (67)	2 (33)	6 (50)
	B2 + P	1 (17)	0 (0)	1 (8)
	B3	1 (17)	0 (0)	1 (8)
	B3 + P	0 (0)	1 (17)	1 (8)

Table. Demographic and disease characteristics of responders and non-responders

Data are n (%) or median (IQR). A – Age, B – Behavior, L – Location, P - Perianal

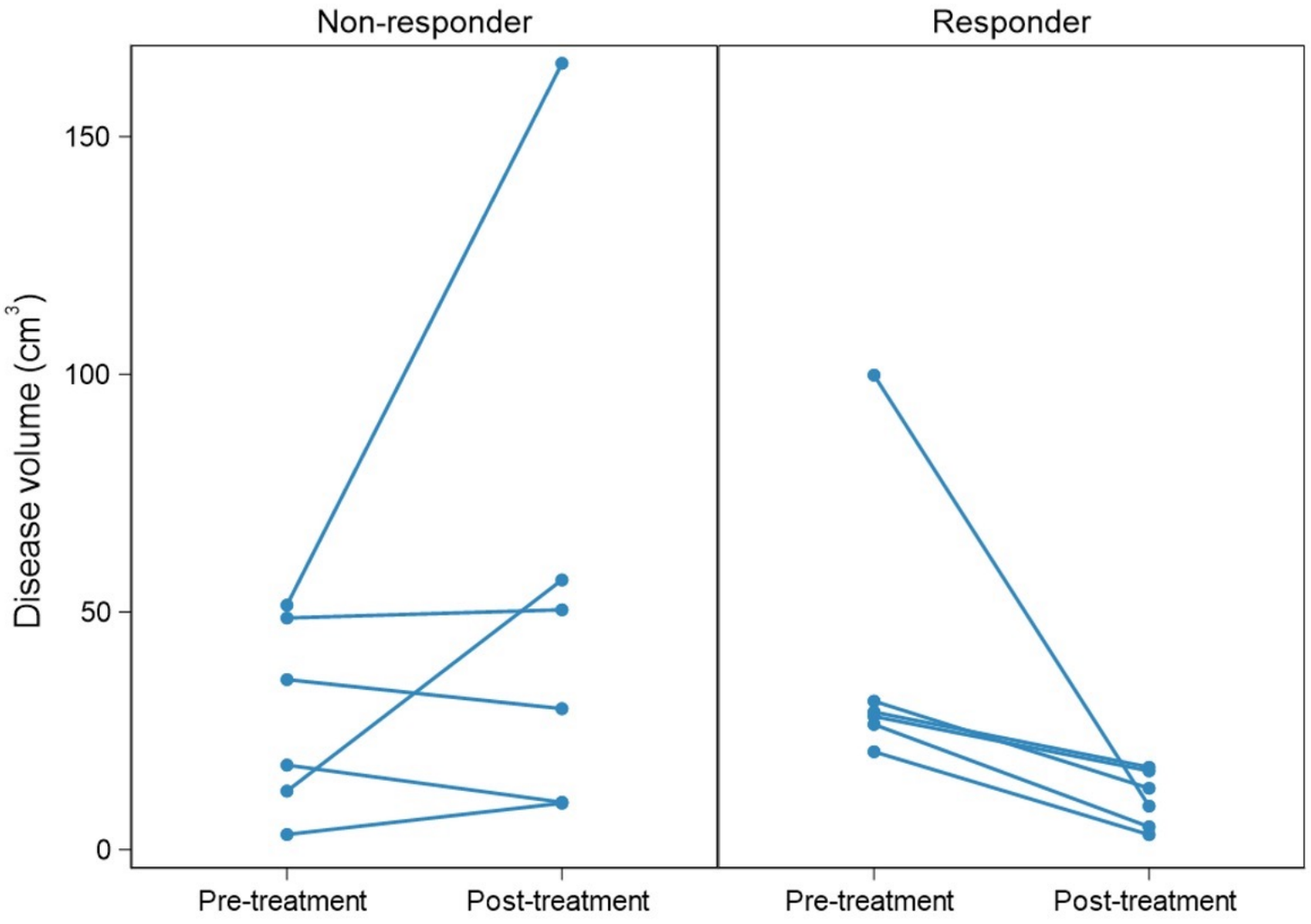
Results – Phase 2 (Contd.)

Responder type	Pre-treatment disease volume (cm^3)	Post-treatment disease volume (cm^3)	Difference in disease volume (post – pre) (cm^3)	p-value
Non-responder	26.8 (12.3, 48.7)	40.1 (10.0, 56.7)	4.2 (-6.1, 44.4)	0.438
Responder	28.5 (26.4, 31.2)	11 (4.8, 16.6)	-17.9 (-21.5, -11.6)	0.031

Table. Difference in pre-treatment and post-treatment disease volumes by responder type

Data are median (IQR)

Results – Phase 2 (Contd.)



Conclusions

- Volumetric measurement of CD activity on MRE is feasible and reproducible
- Volumetric CD burden on MRE relates to CD activity on endoscopy and sMARIA
- Volumetric changes reflect response induced by biologics (i.e., volume reduces in treatment responders but not in clinical non-responders on pre- and post-treatment MRE)
- Novel, objective biomarker worthy of further evaluation

Thank you