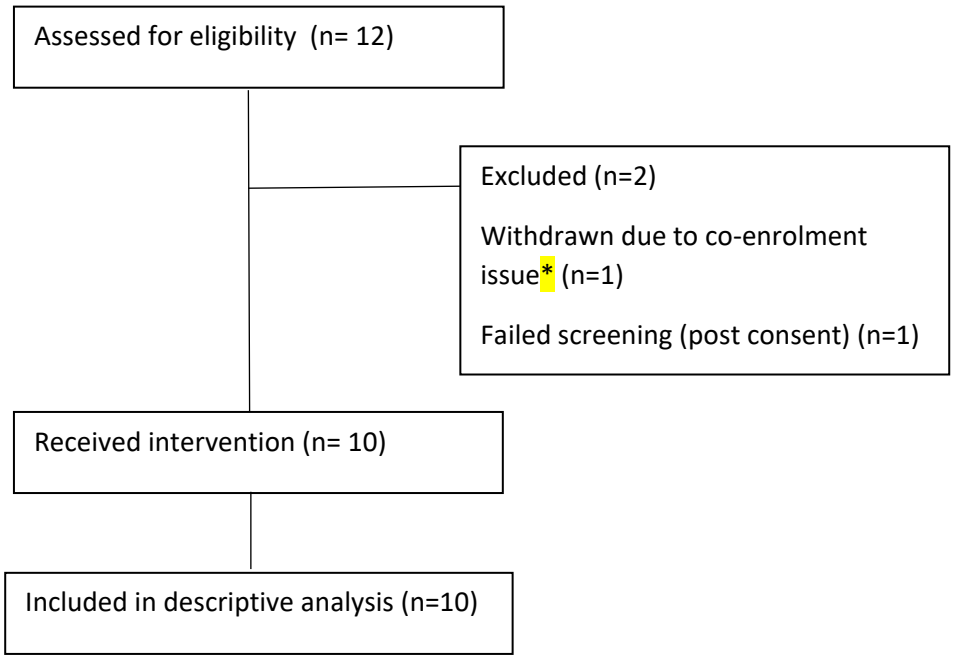
LungSpy End of Study Results

Probing molecular signatures in human lung disease using novel optical technologies

Table 1: Study Objectives and Endpoints

OBJECTIVES	ENDPOINTS
PRIMARY	
To demonstrate safety and feasibility of optical technologies outlined in Appendices 1-3 in patients undergoing a clinically indicated bronchoscopy	**Safety** will be assessed using: Routine clinical monitoring • pre-and post-procedure pulse, temperature, BP and cardiorespiratory exam • O_2 saturation during bronchoscopy procedure • Pre discharge (from bronchoscopy) BP, temp and pulse • Recording adverse events that occur up to 4 hours post procedure (pre discharge) and 24 hours post procedure **Feasibility** will be demonstrated by the visualisation of anatomical regions of the lungs to enable navigation on the imaging systems
SECONDARY	
Detect and characterise pathological targets and signatures using optical technologies detailed in Appendices 1-3.	Using data obtained to characterise: • Bacterial presence and inflammatory signatures • Malignant signatures Compare diseased areas with control areas/tissue
Where relevant, obtain in vivo fluorescence lifetime signatures and/or ex vivo fluorescence lifetime signatures and clinical pathology results.	Where relevant, comparison of the in vivo fluorescence lifetime signatures with ex vivo fluorescence lifetime signatures.
Demonstrate capability of investigational imaging fibres to collect sufficient distal micro Alveolar Lavage (AL) samples for PCR analysis.	Collect a sufficient volume of AL using the optical fibre and perform PCR analysis to identify presence and subtype of specific pathogens
Compare Smart Probe results with biological analysis of BAL sample to determine reliability and sensitivity	Compare SmartProbe signatures with lavage sample results to determine feasibility of pathogen detection and SmartProbe target engagement.

Participant Flow:



Overview of study participants:

Consent and Demographics

12 participants consented to the trial between 06Jun2022 – 21Jul2022:

- 2 Withdrawn (by study team)
  - 1 withdrawn due to co-enrolment issue (*could not confirm with other trial if co-enrolment was permitted)
  - 1 failed screening (post consent)
- 10 participants proceeded to bronchoscopy
  - 3 females
  - 7 males

All the participants that were eligible for the study post screening, went on to have the imaging procedure.

Bronchoscopies and Medical History

In all cases, bronchoscopies were elective with additional research procedure (no research only bronchoscopies).

Indications for bronchoscopy were:

- 4 for cancer
- 3 for inflammation
- 3 for infection

The table below, Table 2, provides a summary of the participants, the clinical and research procedures undertaken and the outcome/results.

Table 2: Participant and Procedure Summary

Participant Number	Clinical Details	Clinical Procedure Undertaken	Planned LungSpy Procedure	Performed LungSpy Procedure	LungSpy Imaging System Used	Imaging Agents used	Does data obtained allow comparison between negative control area and target area?	Comments	Device Deficiencies	Safety Reporting		Outcomes	
										AEs	If AE reported, did any meet SAE criteria?	Primary	Secondary (number of endpoints met)
LS001	Female, 57 yrs. Possible RUL cancer – to allow tissue diagnosis. **Clinical results:** Confirmed adenocarcinoma.	Navigation with radial EBUS – biopsy, brush and wash.	Image tumour (RUL) with Kronoscan, then image normal lung in different lobe.	As planned	KronoScan	None	No	N/A as label free tumour imaging only	1	No	N/A	Yes	0 (2 N/A)
LS002	Female, 49 yrs. Follow up of Nontuberculous mycobacterial pulmonary infection. **Clinical results:** E.coli grown from BAL culture.	Bronchoscopy of posterior segment of RUL and wash.	Image segment with Kronoscan	As planned	KronoScan	None	No	Negative control area not used	0	No	N/A	Yes	0 (3 N/A)
LS003	Male, 67 yrs. LUL lesion – possible cancer. **Clinical results:** Biopsy confirmation of squamous cell cancer.	Olympus slim scope, radial EBUS, fluoroscopy and navigation to guide procedure. FNA biopsy and brush.	Image segment with Kronoscan and a control segment	Image of control segment	Kronoscan	None	No	Unable to pass through slimscope on this procedure	0 (no deficiency reported but issues with advancing panoptes recorded – see deficiency table for details)	No	N/A	Yes	0 (2 N/A)

LS004	Male, 63 yrs. LUL lesion – suspected cancer. **Clinical results:** Biopsy proven NSCLC – favouring adenocarcinoma	Olympus slim scope, radial EBUS and guide sheath. FNA, biopsy, brush and wash.	Image segment with Kronoscan and a control segment, with NAP	Image of control segment, attempted image of the lesion – unable to despite fibre changes.	Kronoscan	NAP	No	Baseline control images taken. Unable to obtain images of abnormal area due to fibre issues	3	No	N/A	Yes	0 (2 N/A)
LS005	Male, 75 yrs. LUL nodules, possibly infective, sample to identify cause. **Clinical results:** Mycobacterium avium	Bronchoscopy and wash (RML)	Image segment with Kronoscan with NAP	As planned	KronoScan	NAP	Yes	Pre and post NAP images obtained	1	No	N/A	Yes	1 (2 N/A)
LS006	Male, 83 yrs. Investigation of RLL mass, possibly cancer. **Clinical results:** Squamous cell cancer.	Bronchoscopy, biopsy, brushings and wash.	Image segment with Kronoscan and control area.	As planned	KronoScan	None	Yes	Control area (bronchus) and tumour images obtained	0	No	N/A	Yes	2 (2 N/A)
LS008	Female, 73 yrs. Pulmonary fibrosis, sampling for investigation of infective cause. **Clinical results:** Normal.	Bronchoscopy and BAL (RML).	Image segment with Versicolour with NAP.	As planned	Versicolour	NAP	No	No negative control area	1	Yes (4)	No	Yes	0 (2 N/A)

LS009	Male, 75 yrs. Possible infection, sampling to identify infective cause. Yeast and Haemophilus identified.	Bronchoscopy and BAL (RML)	Image segment with Versicolour with NAP	As planned	Versicolour	NAP	No	No negative control area as target	3 (none used on participant – detected at set-up stage)	Yes (2)	No	Yes	1 (2 N/A)
LS011	Male, 60 yrs. Investigation of possible cause of cough, thought to be infection. **Clinical results:** Normal	Bronchoscopy and BAL	Image segment with Kronoscan wit NAP.	As planned	KronoScan	NAP	No	No negative control area used	0	No	N/A	Yes	1 (2 N/A)
LS012	Male, 77 yrs. Interstitial Lung Disease – to exclude infection as cause. **Clinical results:** Normal	Bronchoscopy and BAL (RML).	Image segment with Kronoscan with NAP.	As planned but no usable images obtained	KronoScan	NAP	No	No negative control area used	0	Yes	Yes	Safety Only	0 (2 N/A)

Table 3: Details of the clinical monitoring undertaken pre, during and post procedure for all participants.

Participant number	Time point	HR	BP	Temp	Oxygen Saturations
LS-001	Pre bronch	69	153/82	36.3	98
	During bronch	72	151/82		99
	Post bronch – 15 mins	81	137/82	36.1	99
	Post bronch – 30 mins	81	139/79	36.1	99
	Post bronch – 1 hour	71	129/76	36.2	100
	Discharge from bronch suite	77	119/71	36.2	97
LS-002	Pre bronch	103	132/84	36.5	99
	During bronch	88	129/85		99
	Post bronch – 15 mins	71	128/85	36.5	100
	Post bronch – 1 hour	59	126/85	36.6	97
	Discharge from bronch suite	62	135/85	36.6	97
LS-003	Pre bronch	64	138/65	35.9	98
	During bronch	58	127/68		97
	Post bronch – 15 mins	56	126/68	35.9	97
	Post bronch – 45 mins	56	131/65	36.1	96
	Post bronch – 1 hour	62	141/63	36.2	99
	Discharge from bronch suite	60	128/67	36.2	98
LS-004	Pre bronch	82	109/76	36.5	96
	During bronch	77			93
	Post bronch – 15 mins	77	111/76	36.3	97
	Post bronch – 30 mins	76	135/79	36.7	96
	Post bronch – 45 mins	77	116/75	36.5	96
	Post bronch – 1 hour	72	119/79	36.7	97
	Discharge from bronch suite	82	102/67	36.9	95
LS-005	Pre bronch	48	149/74	36.1	100
	During bronch	52			100
	Post bronch – 15 mins	47	101/71	36.1	99
	Post bronch – 45 mins	47	118/76	35.9	99
	Discharge from bronch suite	46	115/72	36.3	100
LS-006	Pre bronch	80	134/71	36.2	98
	During bronch	60	118/71		100
	Post bronch – 15 mins	70	151/84	36.0	98
	Post bronch – 30 mins	58	124/71	36.2	94
	Post bronch – 1 hour	52	109/56	36.1	97
	Discharge from bronch suite	75	137/83	35.7	96
LS-008	Pre bronch	77	153/92	36.0	96
	During bronch	90	113/68		98
	Post bronch – 15 mins	71	156/90	35.7	97
	Post bronch – 30 mins	69	149/91	35.6	94
	Post bronch – 45 mins	67	154/96	36.0	96
	Post bronch – 1 hour	72	164/93	35.8	93
	Discharge from bronch suite	67	138/76	35.8	97
LS-009	Pre bronch	70	132/78	36.6	95
	During bronch	50			96
	Post bronch – 15 mins	61	106/70	36.5	93
	Discharge from bronch suite	58	112/69	36.3	99
LS-011	Pre bronch	61	134/77	37	96
	During bronch	67	145/79		95
	Post bronch – 15 mins	67	109/76	36.2	95
	Discharge from bronch suite	54	121/81	36.6	98
LS-012	Pre bronch	62	135/73	35.7	92
	During bronch	69	120/69		94
	Post bronch – 15 mins	80	96/60	36.2	95
	Post bronch – 30 mins	68	82/47	35.8	92
	Post bronch – 45 mins	68	93/60	36.1	93
	Discharge from bronch suite	81	110/65	36.1	83

For Table 3, the measurements taken at the pre-bronchoscopy timepoint are the measurements that were assessed at baseline and used in the analysis of the primary outcome measure for safety.

PRIMARY OBJECTIVES/ENDPOINTS

The primary objective of the trial was ***to demonstrate safety and feasibility of optical technologies outlined in Appendices 1-3 in patients undergoing a clinically indicted bronchoscopy***.

The endpoints for the primary objective were split into safety and feasibility, and all participants were assessed on both to determine if the primary objective of the study was achieved.

Safety was assessed using routine clinical monitoring

- pre-and post-procedure pulse, temperature, BP and cardiorespiratory exam
- O_2 saturation during bronchoscopy procedure
- Pre discharge (from bronchoscopy) BP, temp and pulse
- Recording adverse events that occur up to 4 hours post procedure (pre discharge) and 24 hours post procedure

Outcome Measures:

Table 4 Outcome Measures: A summary of which outcome measures were met by each participant

Participant Number	Primary Endpoints		Secondary Endpoints*			
	Safety	Feasibility	1	2	3	4
LS001	YES	YES	NO	NO	N/A	N/A**
LS002	YES	YES	NO	N/A	N/A	N/A**
LS003	YES	YES	NO	NO	N/A	N/A
LS004	YES	YES	NO	NO	N/A	N/A
LS005	YES	YES	YES	N/A	NO	N/A**
LS006	YES	YES	YES	YES	N/A	N/A
LS008	YES	YES	NO	N/A	NO	N/A
LS009	YES	YES	YES	N/A	NO	N/A**
LS011	YES	YES	YES	N/A	NO	N/A
LS012	YES	NO	NO	N/A	NO	N/A**

* Secondary Outcome Measures:

1. Detect and characterise pathological targets and signatures using optical technologies detailed in appendices 1-3
2. Where relevant, obtain in vivo fluorescence lifetime signatures and/or ex vivo fluorescence lifetime signatures and clinical pathology results
3. Demonstrate capability of investigational imaging fibres to collect sufficient distal micro alveolar lavage (AL) samples for PCR analysis
4. Compare smart probe results with biological analysis of BAL sample to determine reliability and sensitivity

N/A** - Bacterial smartprobes (BAC2 & BAC3) not available to be used in the study.
Had BAC2 and BAC3 been released for use, these participants would have been imaged using them.

Table 5 Adverse Events: Table of all anticipated and unanticipated serious adverse events (life-threatening) and other adverse events (non-life threatening) for all 10 participants.

Participant Number	Date of Bronchoscopy	Interventions received	Event	SAE	Severity	Causality	Start Date	Outcome	
								End Date	Ongoing at final visit?
LS-008	27 Jun 2022	Versicolour, Panotes 1.0 & NAP	Vomiting	No	Mild	Unrelated	27 Jun 2022	27 Jun 2022	N/A
			Nausea	No	Mild	Unrelated	27 Jun 2022	27 Jun 2022	N/A
			Headache	No	Mild	Unrelated	27 Jun 2022	27 Jun 2022	N/A
			Headache	No	Mild	Unrelated	28Jun 2022	N/A	Yes
LS-009	30 Jun 2022	Versicolour, Panotes 1.0 & NAP	Nausea	No	Mild	Unrelated	30 Jun 2022	01 Jul 2022	N/A
			Headache	No	Mild	Unrelated	30 Jun 2022	01 Jul 2022	N/A
LS-012	21 Jul 2022	KronoScan, Panoptes 1.0 & NAP	Intermittent hypoxia and pyrexia	Yes (Required overnight stay in hospital)	Mild	Unrelated	21 Jul 2022	22Jul 2022	N/A

For safety, AE reporting was included as an endpoint for this particular objective. Any events up to 24 hours after the procedure were recorded. Across these first 10 participants 7 AEs were reported, one of which met SAE classification (participant required to be admitted to hospital for observation overnight, was discharged home the following day). All events were assessed to be **mild** and **unrelated** to the procedure/research. One event was ongoing at the end of the participants final follow up visit, all others were resolved prior to or at final visit.