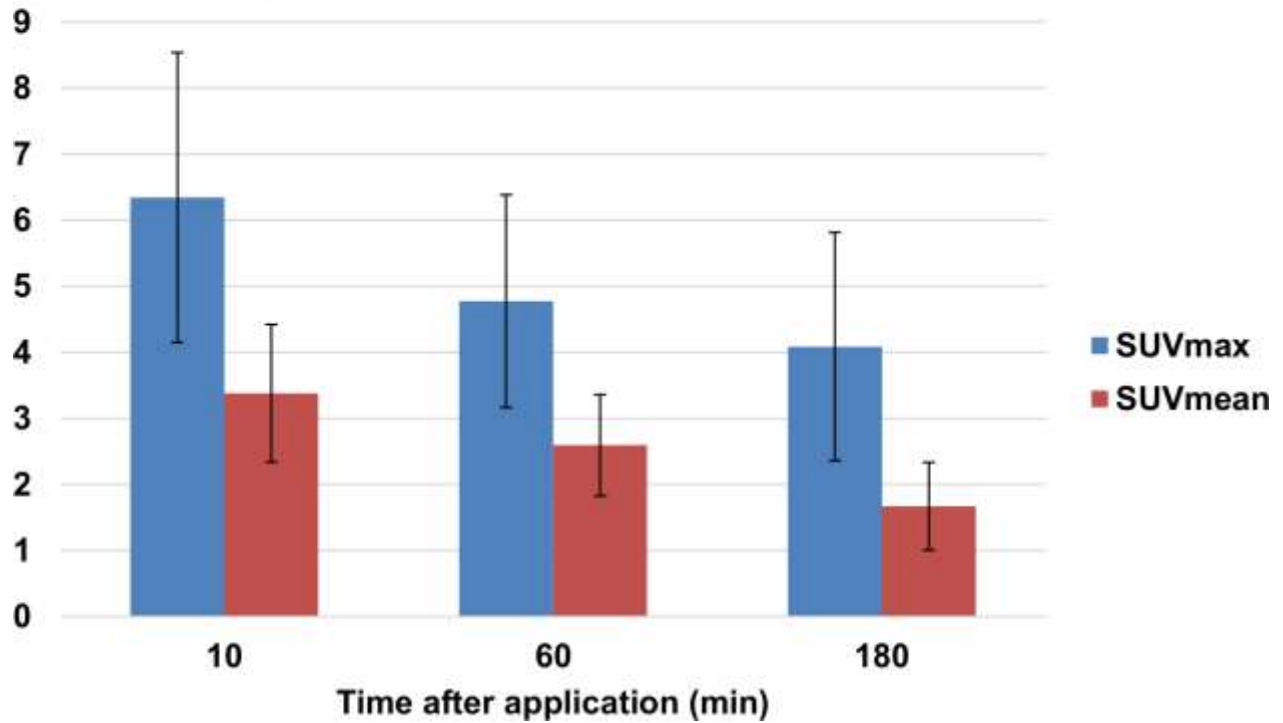
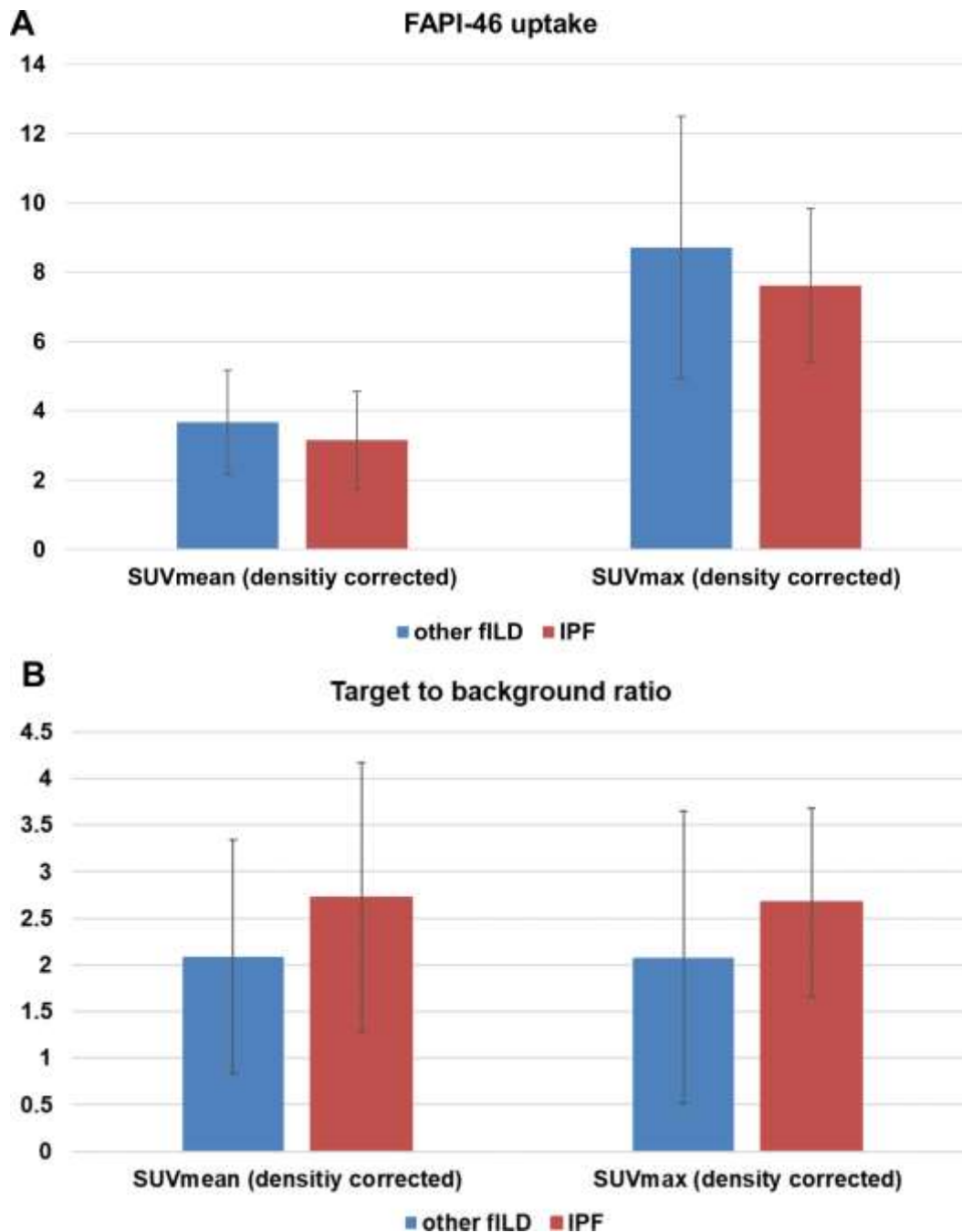


Supplemental figure 1: Representative example of the performed intermodal co-registration of CT and FAPI-PET images. The intensively FAPI-positive tumor manifestations (yellow arrows) located in the basal left lung and on the pleura of the left upper lobe, moderately FAPI-positive fibrotic areas (white arrows) in the basal parts of both lungs and the photopenia of bullae in the apical right lung serve as visual landmarks. Intermodal co-registration leads to identical volumes that allow the comparison of PET- and CT-based parameters.

Background Activity (SUVmax and SUVmean density corrected)

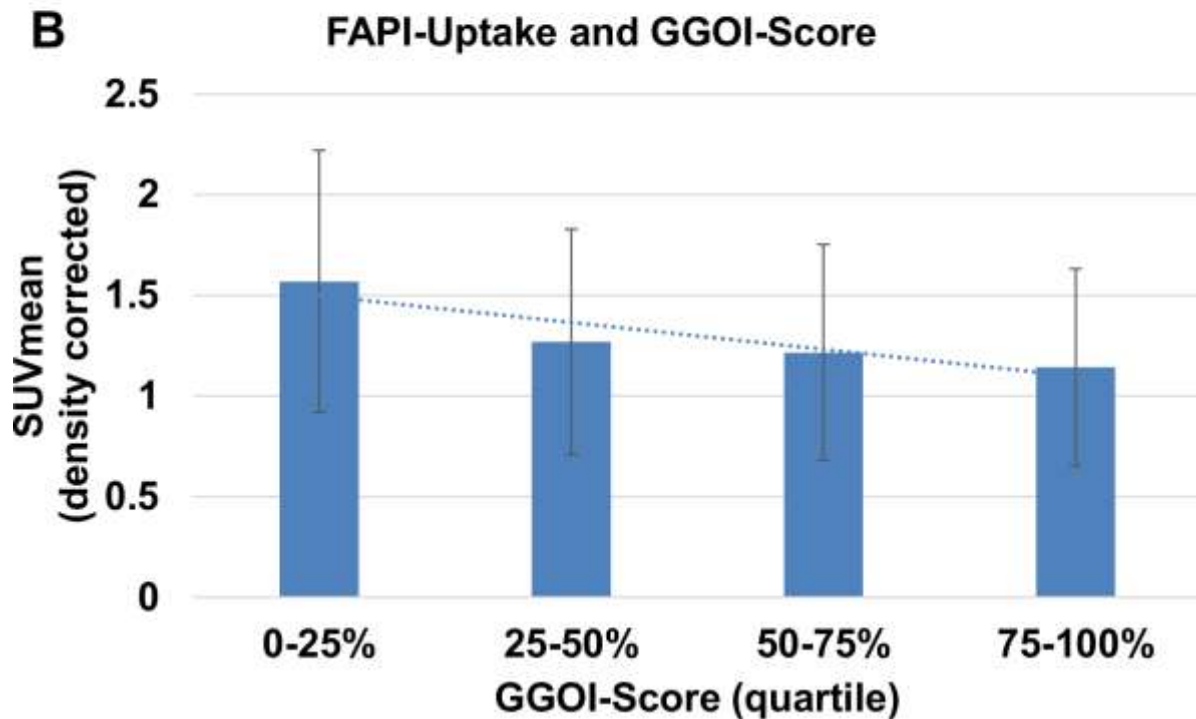
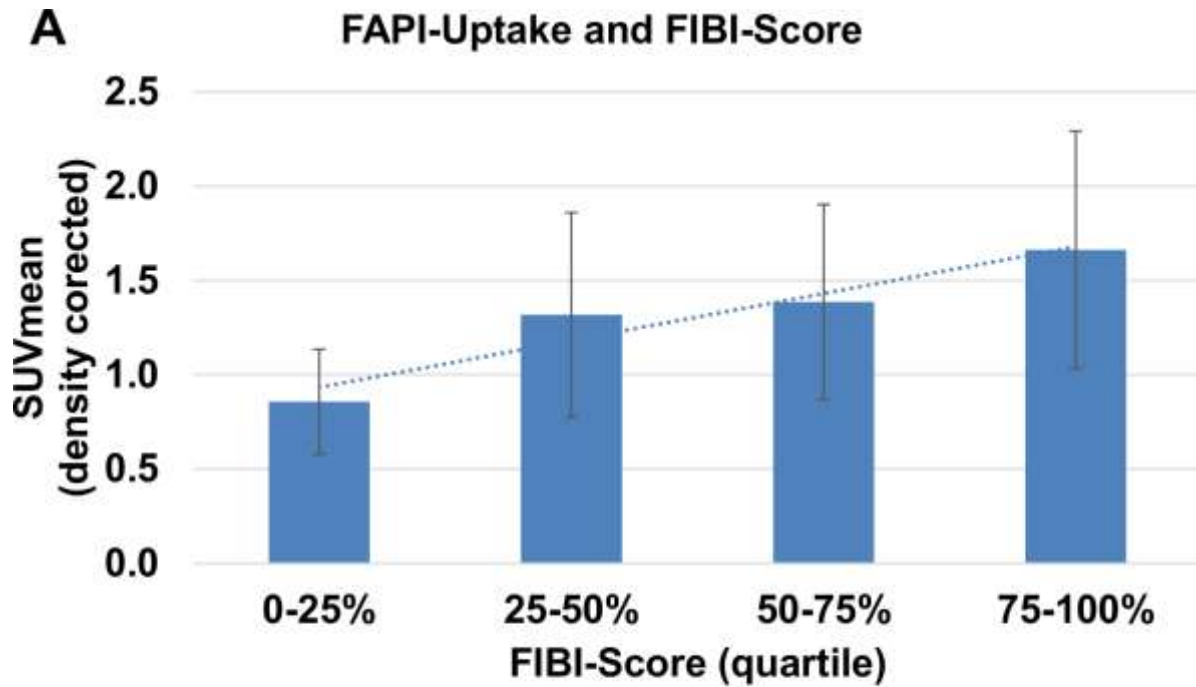


Supplemental figure 2: Average density corrected SUVmax and SUVmean values +/- standard deviation for healthy appearing lung parenchyma in 15 patients 10, 60 and 180 minutes after application of FAPI-46, representing the background activity regarding FAPI-46 uptake.

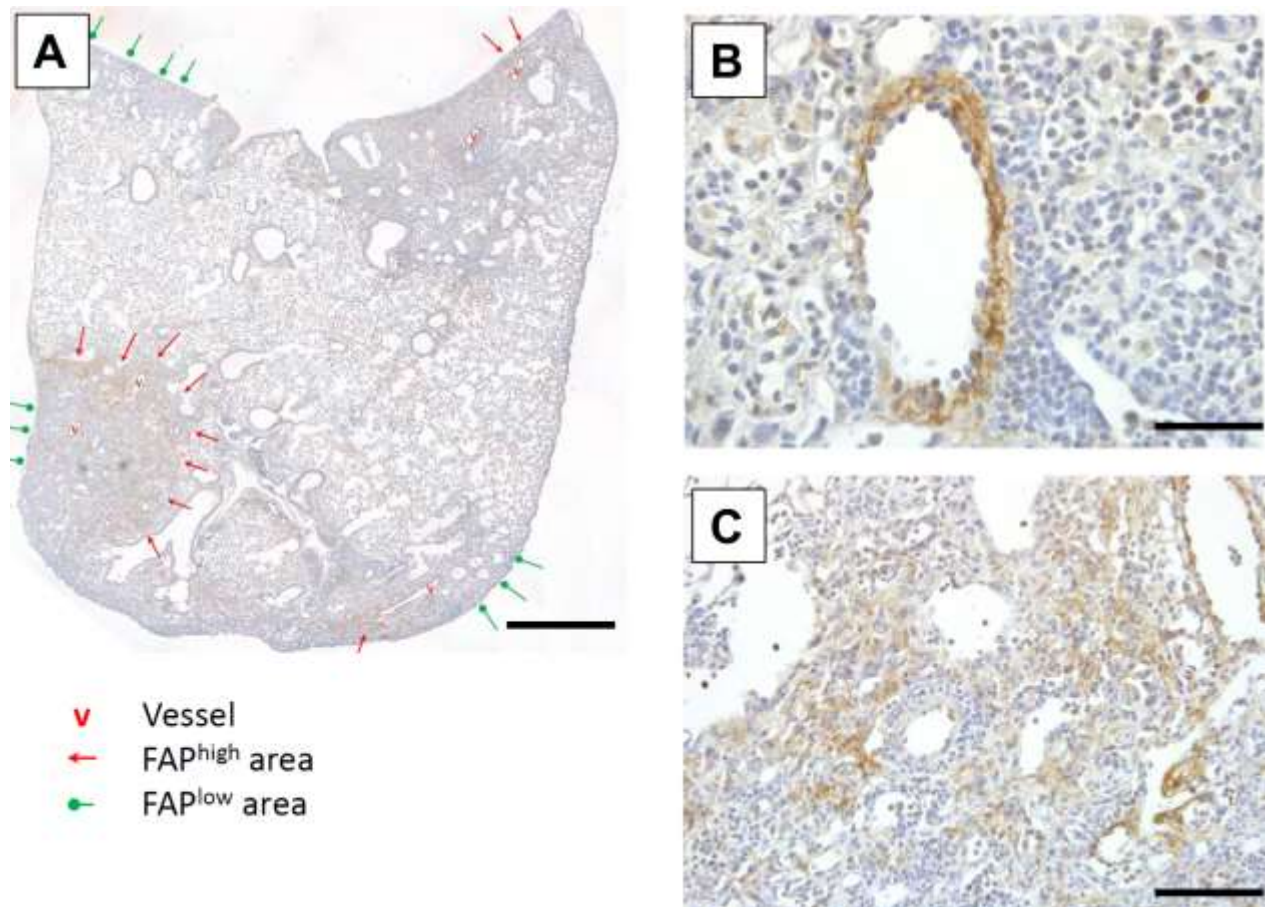


Supplemental figure 3: Comparison of density corrected FAPI-46 uptake (SUVmean and SUVmax) (**A**) and corresponding TBR (**B**) of IPF and other fILDs. We measured the following parameters: Average SUVmean: 3.15 +/- 1.41 (IPF) versus 3.67 +/- 1.50 (other fILD), p-value 0.23, average SUVmax 7.61 +/- 2.22 (IPF) versus 8.71 +/- 3.79 (other fILD), p-value 0.19, average TBR (SUVmean) 2.73 +/- 1.45 (IPF) versus 2.08 +/- 1.25 (other

fILD), p-value 0.13 and average TBR (SUVmax) 2.67 +/- 1.01 (IPF) versus 2.08 +/- 1.57 (other fILD), p-value 0,10.



Supplemental figure 4: Quartile-wise correlation analysis of FAPI-46 uptake (density corrected SUVmean values) and FIB (A) /GGO (B) indices in 75 lobes.



Supplemental figure 5: **A** Exemplary whole lung section of a *Nedd4-2*^{-/-} mouse suffering from IPF-like lung disease immunohistochemically stained for FAP. Red arrows indicate areas with high FAP expression, green arrows indicate areas with low FAP expression. V=blood vessel. Scalebar = 1000 μ m. **B** Exemplary image of perivascular FAP-positive cells. Scalebar = 50 μ m. **C** Exemplary image of parenchymal FAP-positive cells. Scalebar = 100 μ m.

Supplemental Table 1: Clinical features and imaging protocols of 15 ILD patients with suspected lung cancer										
No.	Age	Sex	FVC	DLCO	ILD Subtype	Biopsy technique	ILD pattern	LC Subtype	Tracer	Image acquisition p.i.
1	59	f	2,01 l (62,7%)	DLCO/SB 36,1 % DLCO/VA 61,3%	DIP	none		NSCLC (SCC)	FAPI-46	10,60,180 Min.
2	75	m	1,05 l (37,8%)	DLCO/SB 131,4% DLCO/VA 102,6%	RA-ILD	Surgical Biopsy	NSIP	NSCLC (SCC)	FAPI-46	10,60,180 Min.
3	69	m	2,13 l (51,7%)	DLCO/SB 21,6% DLCO/VA 39,9%	RA-ILD	none		NSCLC (SCC)	FAPI-46	10,60,180 Min.
4	69	f	1,79 l (69,8%)	DLCO/SB 51,5% DLCO/VA 75,6%	IPF	VATS and atypical resection of segments 2,9,10	UIP	LC not proven	FAPI-46	10,60,180 Min.
5	78	f	1,87 l (71,8%)	DLCO/SB 19,6 % DLCO/VA 30,6 %	SSc-ILD	Bronchoscopy	unspecific	LC not proven	FAPI-46	10,60,180 Min.
6	56	m	1,96 l (42%)	DLCO/SB 26,7% DLCO/VA 56,7%	uILD	Surgical Biopsy	UIP	NSCLC (AC)	FAPI-46	10,60,180 Min.
7	70	m	2,66 l (66,3%)	DLCO/SB 32% DLCO/VA 54,2%	IAPAF	none		NSCLC (AC)	FAPI-46	10,60,180 Min.
8	76	m	2,33 l (66,6%)	DLCO/SB 36,6% DLCO/VA 66,6%	IPF	none		NSCLC (SCC)	FAPI-46	10,60,180 Min.
9	71	f	1,58 l (55,5%)	DLCO/SB 28,1%	IPF	Surgical Biopsy	UIP	NSCLC (AC)	FAPI-46	10,60,180 Min.
10	78	m	2,81 l (75,3%)	DLCO/VA 47,9%	IPF	Bronchoscopy	UIP	LC not proven	FAPI-46	10,60,180 Min.
11	74	m	3,07 l (80%)	DLCO/SB 28,2% DLCO/VA 45,4%	IPF	none		NSCLC (SCC)	FAPI-46	10,60,180 Min.
12	77	m	2,55 l (81,6%)	DLCO/SB 49,9% DLCO/VA 69,2%	IPF	1. Bronchoscopy 2. Surgical Biopsy	NSIP transition NSIP/UIP	SCLC	FAPI-46	10,60,180 Min.
13	80	m	2,46 l (77,9%)	DLCO/SB 19,1% DLCO/VA 33,1%	CPFE	none		NSCLC (subtype not determined)	FAPI-46	dynamic 60 min. + 60,180 Min.
14	65	m	4,04 l (88,6%)	DLCO/SB 36,3% DLCO/VA 50,4%	IAPAF	none		NSCLC (SCC)	FAPI-46	dynamic 60 min. + 60,180 Min.

15	71	m	3,54 l (96,5%)	DLCO/SB 49% DLCO/VA 62,5%	Sarcoidosis	TBB	epithelioid cell granuloma	LC not proven	FAPI-46	dynamic 60 min. + 60,180 Min.
<p>Abbreviations: FVC = Forced Vital Capacity, DLCO = Diffusing Capacity of the Lung for Carbon Monoxide, VA = Alveolar Volume, SB = Single Breath, DIP = Desquamative Interstitial Pneumonia, RA-ILD = Rheumatoid Arthritis associated Interstitial Lung Disease, IPF = Idiopathic Pulmonary Fibrosis, IPAF = Interstitial Pneumonia with autoimmune Features, SSc-ILD = Systemic Sclerosis associated Interstitial Lung Disease, CPFE = Combined Pulmonary Fibrosis and Emphysema, uILD = unclassifiable Interstitial Lung Disease, LC = Lung Cancer, NSCLC = Non Small Cell Lung Cancer, SCC = Squamous Cell Carcinoma, AC = Adenocarcinoma, SCLC = Small Cell Lung Cancer, NSIP = Non Specific Interstitial Pneumonia , VATS = Video Assisted Thoracoscopic Surgery, UIP = Usual Interstitial Pneumonia</p>										

Supplemental table 2: density corrected SUV values and target to background ratios (TBR) off 55 fibrotic lesions in 15 patients with various fILD													
Patient number	Localization of fibrotic lesion	10 minutes p.i.				60 minutes p.i.				180 minutes p.i.			
		SUV (density corrected)		TBR (density corrected values)		SUV (density corrected)		TBR (density corrected values)		SUV (density corrected)		TBR (density corrected values)	
		SUVmean	SUVmax	SUVmean	SUVmax	SUVmean	SUVmax	SUVmean	SUVmax	SUVmean	SUVmax	SUVmean	SUVmax
1	RUL	4.122470696	11.68574119	1.962224862	1.878182	3.88601749	10.2274065	1.81111161	2.62232856	0.74793642	2.01383798	3.87317147	3.72297669
	RML	4.844485338	12.35688173	2.305891363	1.986051	3.45704153	9.09536535	1.61118371	2.33207082	0.74793642	2.01383798	2.75963467	1.96869448
	RLL	4.564995799	11.88313546	2.172859169	1.909908	3.22993662	7.53392924	1.50533952	1.93171531	0.74793642	2.01383798	4.35731791	3.31364417
	LUL	4.937648518	12.63323372	2.350235428	2.030467	3.20470274	8.431755	1.49357906	2.16191973	0.74793642	2.01383798	4.35731791	3.39161227
	LLL	4.774612953	12.19896631	2.272633315	1.96067	3.93648525	9.13440125	1.83463254	2.3420797	0.74793642	2.01383798	4.06683005	2.86532761
2	RML	4.218142096	7.990471321	1.024096326	1.046341	3.36164571	5.49113451	1.53564214	1.57947595	1.07581006	2.4313868	3.15516662	2.2307032
	RLL	4.063550501	7.717504909	0.986564	1.010597	6.63304589	11.2329017	3.03005899	3.23104416	1.07581006	2.4313868	7.08619388	5.30651862
	LLL	4.151888555	6.104521568	1.008011043	0.799379	4.19641679	5.71898241	1.9169761	1.64501437	1.07581006	2.4313868	3.80171715	2.4468947
3	RUL	3.570303325	12.68122241	0.679657308	1.211729	3.32133585	10.8222836	0.85046987	1.37560588	2.58955338	4.913906	0.95352522	1.05556319
	RML	4.168285163	15.58733588	0.793491537	1.489417	4.55946696	10.7526869	1.16750893	1.36675954	2.58955338	4.913906	1.33493531	1.63237368
	RLL	5.680827458	17.56877688	1.081425174	1.67875	3.65543472	8.83877826	0.93602009	1.12348519	2.58955338	4.913906	1.10450005	1.48817106
	LUL	3.81653114	13.47379881	0.726530225	1.287462	3.55717035	9.46514838	0.91085826	1.20310225	2.58955338	4.913906	1.15217631	1.46509864
	LLL	3.939645048	16.11572014	0.749966684	1.539906	3.45890597	10.0219218	0.88569643	1.27387297	2.58955338	4.913906	1.13628422	1.44779432
4	RLL	4.046722708	17.69396194	1.745970137	5.000369	8.99848214	33.6942833	5.49016394	11.0113775	1.22178188	2.55056305	6.91754103	10.2353397
	LUL	3.139698653	9.475269445	1.354632003	2.677741	3.70940565	12.8344861	2.2631867	4.1943427	1.22178188	2.55056305	3.38303102	4.24241446
5	RLL	4.661628294	14.03888644	1.722838235	3.190291	2.01690117	6.46232909	1.23055399	2.11190558	1.22178188	2.55056305	1.57790626	2.18298997
	LLL	4.747162759	13.30608742	1.754449946	3.023765	4.00688272	10.1268618	1.69779912	1.48192986	1.40804307	3.79921345	1.85937706	1.96582597
6	RML	5.891261082	13.57279944	1.472390695	2.156954	4.58927846	12.0557879	1.94457224	1.76420221	1.40804307	3.79921345	2.78906559	2.72594534
	RLL	5.917918372	15.14353884	1.479053096	2.406572	3.38248143	8.97847767	1.00078445	2.13094315	1.98725405	3.66242613	1.30629885	1.79627981
	LUL	5.384772572	11.9215093	1.345805069	1.894535	4.22297681	12.9647727	1.24946422	3.07704654	1.98725405	3.66242613	1.43882192	2.03263242
	LLL	5.731317342	15.50601717	1.432416287	2.464176	3.44398109	10.8039773	1.01898053	2.56420545	1.98725405	3.66242613	1.25896918	1.72537403
7	RUL	7.544836319	13.72034047	2.891304038	3.537077	4.05897771	10.8412324	1.20094134	2.57304754	1.98725405	3.66242613	1.70386806	3.0016781
	LUL	7.049468278	13.45043214	2.701470945	3.467495	3.13971578	6.27657323	1.19816576	1.55562785	1.87110078	3.98712383	1.79081261	2.3206437
8	RUL	5.409333836	12.52043519	1.388010343	1.621334	2.97446758	6.87653979	1.1351044	1.70432757	1.87110078	3.98712383	1.38879345	2.39771305
	LLL	5.278673598	9.793922084	1.354483523	1.268264	3.85579131	8.16877546	1.47143163	2.02460389	1.87110078	3.98712383	1.42534065	2.3206437
9	RUL	4.935572787	10.6378189	1.376513778	1.275758	3.45185127	7.79956527	1.31728165	1.93309637	1.87110078	3.98712383	1.47407024	1.97811327
	RLL	5.335754364	11.08730421	1.488123003	1.329663	5.18778762	9.81753519	3.00397814	3.77946757	1.10196147	3.52202069	3.50531972	2.16684449

	LLL	6.936480673	14.87047219	1.934559904	1.783365	4.49608261	8.11647711	2.60344772	3.12460933	1.10196147	3.52202069	2.98874628	1.77630856	
10	RML	4.520426488	10.25791396	2.051069705	2.638895	2.73744518	6.60620458	1.06386455	1.25176588	1.24265568	3.05452265	1.76430672	2.33434146	
	LUL	4.081299344	9.278942922	1.851822934	2.38705	2.29091157	5.32964331	0.89032636	1.00987876	1.24265568	3.05452265	1.43104879	1.76432785	
	LLL	5.631159854	15.87635647	2.555046833	4.084265	4.07566794	11.6055494	1.21817086	1.61116341	2.52724263	6.28504238	1.39104328	1.08422616	
11	RUL	13.26554698	27.02917417	2.789810246	3.254479	4.51565482	12.2583615	1.34967794	1.70179135	2.52724263	6.28504238	1.71779841	1.30410419	
	RML	6.893906306	12.4965015	1.449822647	1.504656	5.5114146	13.5277185	1.64729923	1.87801235	2.52724263	6.28504238	1.91385149	1.49365421	
	RLL	9.470416744	16.72854354	1.991675556	2.01422	3.93672472	11.1340739	1.17664231	1.5457099	2.52724263	6.28504238	1.29768467	1.03494315	
	LUL	9.365963618	20.60126126	1.969708546	2.480519	5.09458493	12.2220942	1.52271358	1.69675647	2.52724263	6.28504238	1.60576808	1.35338719	
	LLL	8.216979233	15.5307958	1.728071438	1.870004	5.91264898	13.0487629	2.54446124	3.70166767	1.64521978	4.34116624	1.78385879	2.05313375	
12	RUL	9.653535333	20.4482863	3.183644091	3.756101	5.05531487	11.3557272	2.17551436	3.221388	1.64521978	4.34116624	1.8266714	2.09663235	
	RML	5.961169284	10.93366844	1.965936904	2.008381	6.6517301	16.0218988	2.8625189	4.54508562	1.64521978	4.34116624	2.29761012	2.45332084	
	RLL	5.071442525	8.653882257	1.672513485	1.589613	3.3176141	7.51761926	2.41071133	2.1790841	0.68725643	1.57606631	3.61316584	4.71039972	
	LUL	3.358718514	6.490411693	1.107673405	1.192209	2.84703054	6.33627909	2.06876646	1.8366566	0.68725643	1.57606631	2.3564125	2.82623983	
	LLL	4.470876963	8.653882257	1.474452678	1.589613	3.22349739	7.01644464	2.34232235	2.03381183	0.68725643	1.57606631	3.17330217	3.48997798	
13	RUL	not available due to dynamic imaging					10.7334511	27.5973769	2.92971336	4.53396979	2.30639047	6.00683043	3.99260191	2.8487371
	RML						5.56549317	14.8813245	1.51911063	2.44485104	2.30639047	6.00683043	1.58494197	1.11981607
	RLL						5.59199552	11.8893122	1.52634449	1.95329369	2.30639047	6.00683043	2.06889372	1.63052716
	LUL						5.45948378	11.6137321	1.49017519	1.90801867	2.30639047	6.00683043	1.59704076	1.12918691
	LLL						5.88352135	14.4089015	1.60591695	2.36723672	2.30639047	6.00683043	1.70592991	1.20415368
14	RUL						2.88450383	10.2565275	1.21523553	2.1646621	1.98768803	5.43846679	1.28169953	1.38120667
	RLL						2.96644997	10.3970279	1.24975927	2.194315	1.98768803	5.43846679	1.43248771	1.44274559
	LUL						2.14698865	8.25439711	0.9045219	1.74210819	1.98768803	5.43846679	1.28169953	1.38120667
	LLL						3.06478532	11.0995297	1.29118775	2.34257953	1.98768803	5.43846679	1.79689248	1.91454391
15	RUL						7.75435833	12.8538635	2.34724603	2.39671904	2.67409064	7.72851975	2.5473222	1.94894304
	RML						4.83507049	7.36699043	1.46357693	1.37364195	2.67409064	7.72851975	1.58624459	1.41089128
	RLL						4.81226355	7.42454504	1.45667327	1.38437353	2.67409064	7.72851975	1.53959034	1.27936752
	LUL						3.05612946	5.16073027	0.92509108	0.96226481	2.67409064	7.72851975	1.03572441	0.91269521
	LLL						3.92279304	6.08160408	1.18743034	1.13397005	2.67409064	7.72851975	1.32498078	1.10798807

Abbreviations: p.i. = post injection, RUL = right upper lobe, RML = right middle lobe, RLL = right lower lobe, LUL = left upper lobe, LLL = left lower lobe

