10.1148/radiol.2017160532

Appendix E1

Details of MR Image Acquisition

Patients were imaged by using a whole-body clinical 1.5-T MR imaging unit (GE HDx; GE Healthcare, Milwaukee, Wis) with a quadrature transmit-receive vest coil tuned to 48.65 MHz for ^{3}He imaging (Clinical MR Solutions, Brookfield, Wis) and a quadrature transmit-receive body coil for proton imaging. Patients were trained in the breathing maneuver outside the MR imaging unit before imaging and once more inside the MR imaging unit before administration of the hyperpolarized ^{3}He.

Helium was polarized on site to approximately 25% by using a rubidium spin-exchange polarizer (GE Healthcare, Amersham, England). Patients inhaled 350 mL ^{3}He mixed with 650 mL N_2 from a Tedlar bag (Jensen Inert Products, Coral Springs, Fla) from functional residual capacity. Ventilation (^{3}He) and anatomic (^{1}H) images were acquired back-to-back during one breath hold covering the same volume (20). Table 1E shows an overview of the specific imaging parameters used

Challenges in Calculating Treatment Response Maps

Quantifying regional ventilation changes between longitudinal time points is a challenge in lung imaging because of patient repositioning and differences in lung volume between acquisitions. The problem of lung volume variation between separate breaths has been highlighted previously (20) in the calculation of %VV, where acquisition of proton images and ventilation images in separate breaths has been shown to considerably influence the reliability of %VV. Here, %VV was calculated from ventilation and anatomic images acquired within the same breath to avoid this problem. When calculating treatment response maps, image registration with the same-breath ^{1}H anatomic images was used to overcome differences in lung volume of ventilation images acquired at different breath holds and patient movement between time points. This process reduces image registration errors introduced by morphologic changes in gas distribution in the ventilation images that arise from response to treatment. Registration of images in this way then allows regional comparison of ventilation changes and TRM over multiple time points.

Images were acquired with the patient in a similar position within the coil and by using the same sequence parameters each time, allowing a comparison of relative changes in image intensity. It is acknowledged that lung units with very low ventilation, resulting in a long time constant for gas wash-in, may not be captured with a single-breath ventilation imaging method (26).

Error in the Calculation of ΔR

The quantification of treatment response is sensitive to the amount of hyperpolarized gas inhaled. It is assumed that a total of 1 L (350 mL ^{3}He and 650 N_2) is precisely dispensed and fully inhaled. Patients are trained in the inhalation process before entering the imaging unit to assure a successful emptying and inhalation of the contents of the bag of gas. When dispensing the gas, a typical dispense accuracy of ±25 mL in the volume of the bag can be achieved. The contribution

of the inhaled bag volume to the calculation of the local voxelwise ventilation fraction can be derived from Equation (1) of the main text as follows:

$$R(r) = \frac{I(r)}{V_{voxel}} \cdot \frac{V_{bag}}{I_{tot}}, \quad (E1)$$

where I(r) is the regional image intensity, V_{voxel} is the volume of a voxel, and V_{bag} is the volume of the bag containing the hyperpolarized ^{3}He mixture (1 L).

This allows a simple error estimation of how the bag volume V_{bag} contributes to the error in voxelwise estimate of fractional ventilation:

$$\frac{\partial R}{|R|} = \sqrt{\left(\frac{\partial V_{bag}}{V_{bag}}\right)^2} = 2.5\% . \quad (E2)$$

Thus this results in a propagated error in voxel fractional ventilation of less than 2.5%. As the treatment response measurement, $\Delta R(r)$ is the result of a subtraction of two ventilation fractions (R(r) from two images), the maximum potential error is compounded to 3.5%.

The effect of image registration on $\Delta R(r)$ was not investigated. Nevertheless, the above discussion shows how effects were mitigated, and it can therefore be assumed that effects from misregistration are negligible.

Reference

26. Marshall H, Deppe MH, Parra-Robles J, et al. Direct visualisation of collateral ventilation in COPD with hyperpolarised gas MRI. Thorax 2012;67(7):613–617.

Table E1: Summary of MR Imaging Parameters

Imaging Type	Sequence	Repetition Time (msec)	Echo Time (msec)	Flip Angle (degrees)	Bandwidth (kHz)	Field of View (cm)	Matrix Size	Pixel Size (mm)	Section Thickness (mm)
Ventilation (^{3}He)	SPGR	3.6	1.1	8	62.5	38.4 × 30.7	128 × 102	3 × 3	10
Anatomic (^{1}H)	SSFP	2.4	2.4	50	167	38.4 × 38.4	128 × 64	3 × 6	10

Note.—SPGR = spoiled gradient echo, SSFP = balanced steady-state free precession.

Table E2: Overview of Outcome Measures in Terms of FEV_1 Change in Each Patient with Asthma Who Was Imaged

Patient No./Age (y)/Sex	Height (m)	Weight (kg)	BMI (kg/m^2)	GINA	Prebronchodilator				Postbronchodilator				FEV_1 Change (mL)
					%VV	VV (mL)	FEV_1 (%)	FVC (%)	%VV	VV (mL)	FEV_1 (%)	FVC (%)	
1/49/F	1.58	96.1	38.5	4	79.62	3518	41.39	75.47	91.54	3552	57.95	88.88	400
2/54/F	1.58	96.6	38.7	5	86.27	4496	32.74	54.34	92.05	4669	61.11	94.26	650
3/63/F	1.6	88.5	34.6	4	87.21	3208	70.40	83.20	89.54	3302	76.46	86.72	130
4/53/F	1.66	109	39.6	5	92.95	3297	73.71	85.88	92.54	3442	82.07	91.39	220
5/41/F	1.61	65.7	25.3	4	93.06	3363	53.76	62.97	96.20	3301	69.85	77.13	790
6/65/M	1.75	90.4	29.5	4	94.78	4327	72.38	83.95	93.46	4517	76.19	81.98	1130
7/41/M	1.73	77	25.7	4	94.10	4766	96.81	114.07	97.95	5228	101.86	115.60	440
8/59/F	1.59	62.7	24.8	5	88.35	3959	95.22	118.33	95.53	4245	107.91	122.91	120
9/45/F	1.71	96.1	32.9	4	94.14	4928	114.21	137.97	96.08	4305	126.42	142.80	190
10/62/M	1.74	87.8	29	4	81.26	4746	43.52	94.59	78.43	4553	50.72	101.22	280
11/45/M	1.74	88.3	29.2	2	82.23	5070	71.87	100.39	91.36	4992	103.06	121.00	370
12/73/M	1.65	70.3	25.8	5	57.51	3498	41.40	69.50	60.56	3562	34.16	67.36	230
13/66/M	1.8	75.1	23.2	4	73.88	4224	27.28	68.65	79.15	4674	31.18	71.89	1150
14/36/M	1.67	84.3	30.2	3	97.17	4519	100.36	105.45	97.58	4098	106.11	105.91	−180
15/60/F	1.57	61	24.7	4	94.14	4186	121.82	123.75	98.35	5214	127.05	126.54	130
16/44/M	1.69	82.2	28.8	4	87.55	3314	77.69	77.88	95.26	3133	81.98	85.87	210
17/52/F	1.52	51.4	22.2	4	99.10	3478	100.76	114.38	99.28	3711	100.76	110.37	110
18/21/F	1.66	85.6	31.1	4	92.54	3526	84.33	108.82	97.93	4291	90.04	115.11	150
19/34/M	1.73	109.5	36.6	4	84.79	3775	51.48	79.10	90.19	3934	59.55	85.22	0
20/60/M	1.67	61.1	21.9	4	87.11	4260	46.76	82.01	85.10	3966	53.20	90.34	190

Note.—BMI = body mass index, GINA = Global Initiative for Asthma classification.

Table E3: Overview of All Outcome Measures in Terms of TRM in Each Patient with Asthma Who Was Imaged

Patient No./Age (y)/Sex	Height (m)	Weight (kg)	BMI (kg/m^2)	GINA	TRM						Baseline Variability Mean ΔR_B (%)
					Positive Net ΔR_{TR} (mL)	Positive Net ΔR_{TR} (%)	Negative Net ΔR_{TR} (mL)	Negative Net ΔR_{TR} (%)	Net ΔR_{TR} (mL)	Net ΔR_{TR} (%)	
1/49/F	1.58	96.1	38.5	4	222.9	22.29	79.38	7.94	143.5	14.35	9.33
2/54/F	1.58	96.6	38.7	5	351.1	35.11	54.45	5.45	296.7	29.67	5.38
3/63/F	1.6	88.5	34.6	4	178.6	17.86	83.49	8.35	95.11	9.51	5.30
4/53/F	1.66	109	39.6	5	158.2	15.82	101.9	10.19	56.37	5.64	6.63
5/41/F	1.61	65.7	25.3	4	266.7	26.67	67.87	6.79	198.9	19.89	3.48
6/65/M	1.75	90.4	29.5	4	122.6	12.26	125.8	12.58	–3.204	–0.32	4.72
7/41/M	1.73	77	25.7	4	137	13.70	79.13	7.91	57.9	5.79	3.70
8/59/F	1.59	62.7	24.8	5	196.8	19.68	85.5	8.55	111.3	11.13	3.06
9/45/F	1.71	96.1	32.9	4	243.9	24.39	141.7	14.17	102.2	10.22	2.47
10/62/M	1.74	87.8	29	4	326.2	32.62	99.2	9.92	227	22.70	5.15
11/45/M	1.74	88.3	29.2	2	279.4	27.94	67.15	6.72	212.3	21.23	3.93
12/73/M	1.65	70.3	25.8	5	155.1	15.51	53.71	5.37	101.4	10.14	10.77
13/66/M	1.8	75.1	23.2	4	175.5	17.55	65.61	6.56	109.9	10.99	2.49
14/36/M	1.67	84.3	30.2	3	113.5	11.35	96.29	9.63	17.22	1.72	3.52
15/60/F	1.57	61	24.7	4	292.6	29.26	181.1	18.11	111.4	11.14	4.91
16/44/M	1.69	82.2	28.8	4	223.6	22.36	117.2	11.72	106.4	10.64	4.68
17/52/F	1.52	51.4	22.2	4	120.8	12.08	96.87	9.69	23.92	2.39	1.93
18/21/F	1.66	85.6	31.1	4	215.6	21.56	91.74	9.17	123.9	12.39	6.04
19/34/M	1.73	109.5	36.6	4	208	20.80	90.97	9.10	117	11.70	4.88
20/60/M	1.67	61.1	21.9	4	201.8	20.18	113.7	11.37	88.18	8.82	2.34

Note.—BMI = body mass index, ΔR_B = baseline variability, ΔR_{TR} = treatment response, GINA = Global Initiative for Asthma classification.