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Since publication of their article, the authors report no further potential conflict of interest.

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Evidence of Adult Lung Growth in Humans

TO THE EDITOR: Butler et al. (July 19 issue)¹ describe a 48-year-old woman in whom apparent-diffusion-coefficient data derived from helium-3 magnetic resonance imaging (MRI) suggested new (versus hyperexpanded) alveoli in regions of

new lung growth. This patient also had improved pulmonary function 15 years after pneumonectomy. The helium-3 apparent-diffusion-coefficient maps and posterior–anterior apparent-diffusion-coefficient differences were not reported but have been previously evaluated in childhood lung development² and chronic obstructive pulmonary disease.³ It is important to note the patient's history of smoking because the heterogeneous and reduced alveolar depth measurements reported may in fact indicate mild emphysema.

We report a heterogeneous apparent diffusion coefficient in another former smoker. Seven years after lobectomy, this 60-year-old patient did not have improved pulmonary function (Fig. 1). The apparent diffusion coefficient was age-appropriate⁴ for a person who had never smoked, although an elevated apparent diffusion coefficient was observed in the right upper lung with the posterior–anterior apparent-diffusion-coefficient gradient reversed as compared with previous findings.³ Although we cannot rule out new lung growth in this older patient, these findings are consistent with alveolar expansion or emphysema. We think apparent diffusion coefficients and their regional differences are important when evaluating lung growth because MRI-derived alveolar dimensions based on the model and assumptions of Haefeli-Bleuer and Weibel⁵ may not completely explain abnormal morphologic features in the lungs after surgery in former smokers.

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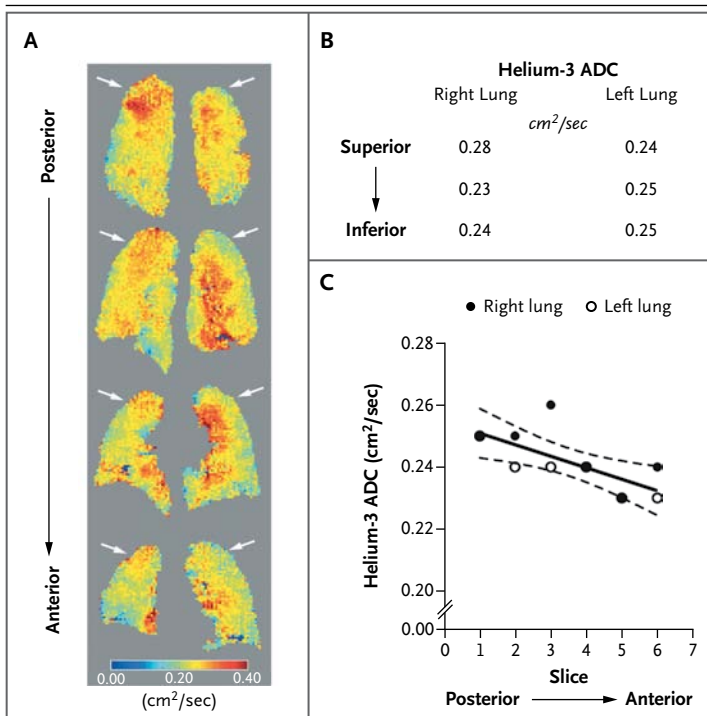


Figure 1. Heterogeneous Apparent Diffusion Coefficient in a Former Smoker.

Panel A shows four central coronal slices obtained with helium-3 magnetic resonance imaging in a 60-year-old female former smoker with a 44-pack-year history who had quit smoking 8 years previously and had undergone lobectomy of the right upper lung 7 years previously. The forced expiratory volume in 1 second (FEV₁) was 76% of the predicted value, the ratio of FEV₁ to forced vital capacity was 0.98, and the carbon monoxide diffusing capacity was 86% of the predicted value. The white arrows highlight areas with a greater apparent diffusion coefficient (ADC) in the right upper lung than in the left upper lung. Panel B shows helium-3 ADC values from the superior portions of the lungs to the inferior portions. Panel C shows posterior-to-anterior regions of interest in the right and left lung ($r=0.71$, $P=0.01$).

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DOI: 10.1056/NEJMc1209904

TO THE EDITOR: Butler et al. provide radiologic data on new lung growth after pneumonectomy with overall enlargement of the remaining lung, including an increase in tissue density and alveolar number. They confirm previous *in vitro* studies¹ suggesting that human lungs harbor stem cells that can replace 30% of the parenchyma even if no functional coupling between the old and the newly developed structures is detected. Moreover, blood gas analysis and pulmonary hemodynamic assessment supporting perfusion and ventilation were not reported. No correlation between functional improvement and insertion of a volume expander was provided; this maneuver probably caused the functional changes shown in Figure 2 of their article, in which data on peaks in lung volumes obtained from computed tomography were mostly related to the insertion of a volume expander. Did hypoxemia or pulmonary hypertension contribute?

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No potential conflict of interest relevant to this letter was reported.

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THE AUTHORS REPLY: Kirby et al. raise some important questions and remind us of the care necessary in interpreting data from new technology such as diffusion MRI. In our study, we used multiple magnetic-field gradients to dissect the helium-3 diffusion signal into values to derive

the radial dimension of the acinar airways (R) and the effective alveolar depth (h). Both measures of regional lung dimensions rely on the use of multiple magnetic-field gradients to detect the signal corresponding to R and h and the fitting of these heterogeneous signals to a model of molecular diffusion (in this case, helium-3) in the distal airspace.¹ The data provided by Kirby et al. are intriguing, but they are insufficient to fit to a detailed microstructural model. We agree that it would be interesting to build on these data by comparing values of R and h in lung regions both near to and remote from a lobectomy. Similarly, we need more detailed investigations involving both normal² and emphysematous lungs.

We share the interest of Frati and Venuta in the mechanism of lung growth in our patient. We are particularly intrigued by our patient because the lung growth occurred without apparent therapeutic manipulation, probably as a natural process of repair and regeneration. The patient's improvement on spirometry and in functional activity suggests that the new lung growth was integrated both structurally and functionally.

The trigger for growth remains a mystery. There was no time when this patient had persistent hypoxemia, nor were there any clinical or echocardiographic signs of pulmonary hypertension. The unique clinical features of our patient were the clinically significant postoperative mediastinal shift, the strong chest wall capable of generating high inspiratory force, and the high level of routine exercise activity. Although these observations suggest the importance of parenchymal stretch as a trigger for lung growth, considerably more research needs to be done to explore this possibility.

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Since publication of their article, the authors report no further potential conflict of interest.

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