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Lindsay Mathew
Miranda Kirby
Donald Farquhar
Christopher Licskai
Giles Santyr

See next page for additional authors

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CASE REPORT

Hyperpolarized $^3$He functional magnetic resonance imaging of bronchoscopic airway bypass in chronic obstructive pulmonary disease

Lindsay Mathew PhD¹,², Miranda Kirby BSc¹,², Donald Farquhar MD³, Christopher Licskai MD³, Giles Santyr PhD¹,², Roya Etemad-Rezai MD⁴, Grace Parraga PhD¹,²,⁴, David G McCormack MD¹

A 73-year-old exsmoker with Global initiative for chronic Obstructive Lung Disease stage III chronic obstructive pulmonary disease underwent airway bypass (AB) as part of the Exhale Airway Stents for Emphysema (EASE) trial, and was the only EASE subject to undergo hyperpolarized $^3$He magnetic resonance imaging for evaluation of lung function pre- and post-AB. $^3$He magnetic resonance imaging was acquired twice previously (32 and eight months pre-AB) and twice post-AB (six and 12 months post-AB). Six months post-AB, his increase in forced vital capacity was <12% predicted, and he was classified as an AB nonresponder. However, post-AB, he also demonstrated improvements in quality of life scores, 6 min walk distance and improvements in $^3$He gas distribution in the regions of stent placement. Given the complex relationship between well-established pulmonary function and quality of life measurements, the present case provides evidence of the value-added information functional imaging may provide in chronic obstructive pulmonary disease interventional studies.

Key Words: Airway bypass; Chronic obstructive pulmonary disease; Hyperpolarized $^3$He magnetic resonance imaging

L’imagerie par résonance magnétique fonctionnelle par $^3$He hyperpolarisé de la dérivation des voies respiratoires par bronchoscopie en cas de maladie pulmonaire obstructive chronique

Un ex-fumeur de 73 ans atteint d’une maladie pulmonaire obstructive chronique de phase III d’après la Global Initiative for Chronic Obstructive Lung Disease a subi une dérivation des voies respiratoires (DVR) dans le cadre de l’essai EASE sur les endoprothèses des voies respiratoires par explosion et était le seul sujet de l’essai EASE à subir une imagerie par résonance magnétique ($^3$IRM) par $^3$He hyperpolarisé pour évaluer la fonction pulmonaire avant et après la DVR. Il avait subi une IRM par $^3$He deux fois auparavant (32 mois et huit mois avant la DVR) et deux fois après la DVR (six et 12 mois après). Six mois après la DVR, l’augmentation de sa capacité vitale forcée était de 12 % inférieure aux valeurs prédites, et il avait été classé comme ne répondant pas à la DVR. Cependant, après la DVR, il a également présenté des améliorations aux indices de qualité de vie, au test de marche de 6 minutes et des améliorations de la distribution de gaz par $^3$He dans les foyers d’installation des endoprothèses. Étant donné le lien complexe entre la fonction pulmonaire bien établie et les mesures de qualité de vie, ce cas démontre l’information à valeur ajoutée que peut fournir l’imagerie fonctionnelle dans le cadre d’études d’intervention sur les maladies pulmonaires obstructives chroniques.

1Imaging Research Laboratories, Robarts Research Institute; 2Department of Medical Biophysics; 3Division of Respirology, Department of Medicine, 4Department of Medical Imaging, University of Western Ontario, London, Ontario

Correspondence and reprints: Dr Grace Parraga, Imaging Research Laboratories, Robarts Research Institute, PO Box 5015, 100 Perth Drive, London, Ontario N6A 5K8. Telephone 519-913-5265, fax 519-913-5260, e-mail gep@imaging.robarts.ca

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and in the left upper lobe (Figure 1, lower left panel) with further improvements, specifically in the right lower lung observed 12 months post-AB (Figure 1, lower right panel). The visually apparent ventilation improvements in the right lower and left upper lobes were in the same regions where stents were originally placed. There were also other areas of regionally improved gas distribution (arrows), and all of these visually apparent changes in gas distribution corresponded to 3He MRI VV increases of 3.2 L at six months and 4.2 L at 12 months post-AB. At the same time, other surrogate measures of functional capacity including 6 min walk distance (6MWD), the St George’s Respiratory Questionnaire (SGRQ) score and cycle ergometry time showed improvements six months post-AB (6MWD increased by 78 m, SGRQ score decreased by 38 and cycle ergometry time improved by 334 s). Along with improvements in quality of life measures, the diffusing capacity of carbon monoxide (DLCO) nearly doubled between the pre-AB and 12-month post-AB time points (Table 1).

### DISCUSSION

AB is an investigational procedure that involves the creation of extra-anatomical passages reinforced by a drug-eluting stent in the airway wall, with stents delivered using Doppler-guidance to avoid pulmonary vasculature in airway regions where the stents are inserted. The aim of AB is to artificially connect the segmental airways to adjacent lung tissue, thereby allowing trapped gas to be exhaled. Bronchoscopic lung volume reduction methods, such as AB, provide a minimally invasive alternative to lung volume reduction surgery with the goal of improving COPD quality of life, pulmonary function and survival (10-12). Unfortunately, for many of these approaches, significant improvements in intermediate end points such as FEV₁ and residual volume/total lung capacity have not been realized postintervention (13-15) and, occasionally, these results are discordant with symptomatic or other functional improvements.

| Table 1 | Pulmonary function and 3He magnetic resonance imaging measurements pre- and post-airway bypass |
|---------|------------------------------------------------------------------------------------------------|
|         | Pre-airway bypass                                                                 | Months                     | Post-airway bypass                                |
| FEV₁, L | 1.2                                                                                   | 0.8                        | 0.9                         | 1.1                         | 1.2                        | 1.2                        | 1.1                         | 1.2                         |
| FEV₁, % predicted | 32                                   | 23                        | 27                         | 32                         | 34                        | 35                        | 33                         | 35                         |
| FVC, L  | 3.2                                                                                   | 2.3                        | 2.6                         | 3.2                        | 3.6                        | 3.6                        | 3.5                         | 3.8                         |
| FVC, % predicted | 66                                   | 49                        | 57                         | 68                         | 77                        | 78                        | 76                         | 81                         |
| FEV₁/FVC, % | 37                                   | 34                        | 35                         | 35                         | 32                        | 33                        | 32                         | 31                         |
| RV, L   | 5.2                                                                                   | 5.2                        | 5.6                         | 4.4                        | 5.0                        | 4.5                        | 4.7                         | 5.0                         |
| RV, % predicted | 193                                  | 200                       | 213                        | 169                        | 190                       | 169                       | 198                        | 189                        |
| TLC, L  | 8.4                                                                                   | 8.0                        | 8.6                         | 7.8                        | 8.2                        | 8.2                        | 8.3                         | 8.5                         |
| TLC, % predicted | 111                                  | 107                       | 115                        | 104                        | 114                       | 110                       | 108                        | 114                        |
| RV/TLC  | 0.62                                                                                  | 0.65                       | 0.65                        | 0.57                       | 0.60                       | 0.55                       | 0.56                        | 0.58                        |
| IC, L   | 1.8                                                                                   | 1.6                        | 1.6                         | 2.1                        | 2.3                        | 2.3                        | 1.8                         | 2.8                         |
| DLCO, mL/min/mmHg | –                                   | –                         | 9.2                        | 9.9                        | 14.6                       | 16.9                       | 14.6                        | 18.7                        |
| DLCO, % predicted | –                                   | –                         | 26                         | 28                         | 42                        | 48                        | 42                         | 53                         |
| mMRQ    | –                                                                                     | –                         | –                           | 2                         | 1                         | 0                         | 1                           | 1                           |
| 6MWD, m | –                                                                                     | –                         | –                           | 288                       | 315                       | 330                       | 366                        | 330                        |
| SGRQ    | –                                                                                     | –                         | –                           | 65                        | 27                        | 27                        | 27                         | 31                         |
| CE, s   | –                                                                                     | –                         | 750                        | –                          | –                         | 1084                       | –                           | –                           |
| WL TCV, L | 7.3                                   | 6.3                       | –                           | –                          | –                         | 8.5                       | 8.1                         |                             |
| WL VV, L | 5.4                                   | 1.6                       | –                           | –                          | –                         | 4.8                        | 5.8                         |                             |
| WL PVV, % | 73                                   | 26                        | –                           | –                          | –                         | 57                        | 72                         |                             |
| WL VDV, L | 2.0                                   | 4.7                       | –                           | –                          | –                         | 3.6                        | 2.4                         |                             |
| WL VDP, % | 27                                   | 74                        | –                           | –                          | –                         | 43                        | 28                         |                             |

6MWD 6 min walk distance; CE Cycle ergometry; DLCO Carbon monoxide diffusion capacity of the lung; FEV₁ Forced expiratory volume in 1 s; FVC Forced vital capacity; IC Inspiratory capacity; mMRQ Modified Medical Research Council; PVV Per cent ventilated volume; RV Residual volume; SGRQ St George’s Research Questionnaire; TCV Thoracic cavity volume; TLC Total lung capacity; VDP Ventilation defect per cent; VDV Ventilation defect volume; VV Ventilated volume; WL Whole lung.
We highlighted hyperpolarized $^3$He MRI in a single case of COPD in an exsmoker who underwent AB. Results of pulmonary function tests and $^3$He MRI suggest a decline in lung function over the pre-AB, two-year time period. Post-AB however, significant improvements in gas distribution were visually and quantitatively apparent after six months and 12 months, including increases in VV and PVV. Regional changes in ventilation were visualized throughout the lung, even in regions not associated with stent placement, perhaps due to redistribution of ventilation following the release of trapped gas. It is worth noting that the most visually prominent changes occurred in the right lower and left upper lobes – the same regions where stents were originally placed. The resultant changes in VV and PVV were much greater than the smallest detectable difference previously estimated for $^3$He MRI (5) based on a reproducibility study in COPD. Although $^3$He MRI was not available immediately preceding AB, which would have enabled identification of ventilation improvements that were due to stent placement alone, the imaging results obtained provided functional information that was in agreement with 6MWD, SGRQ and mMRC, as well as DLCO, but not with spirometry and plethysmography measurements. Perhaps unexpectedly, both DLCO and PVV continued to increase post-AB, evidenced by large changes between six- and 12-month post-AB time points. These relatively late changes post-AB suggest continued improvements in gas distribution post-AB that coincided with improved gas transfer. The intriguing coincidence of improved $^3$He gas distribution, DLCO and quality of life measures that endured 12 months post-AB in the only EASE trial subject for whom $^3$He MRI was performed certainly generates new hypotheses to test – especially with respect to the use of imaging to guide stent placement and track regional changes in lung function.

The high cost and limited availability of $^3$He MRI prohibits its prospective routine use in clinical research and its translation to clinical practice (16). However, its high short-term reproducibility (1) and sensitivity (5,6), coupled with the intriguing findings in longitudinal (6) and other acute COPD therapy studies (5), suggest that hyperpolarized noble gas imaging may be an ideal tool for visualization and quantitative evaluation of functional differences in COPD post-therapeutic intervention. The results of the present case study highlight the advantage of including functional MRI techniques such as hyperpolarized $^{129}$Xe MRI (17,18) or conventional $^1$H MRI (19) in COPD interventional studies, and suggest the application of these types of imaging in interventional studies may offer new insights into regional physiological changes in COPD following treatment.

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