INTRODUCTION
In previous Functional Respiratory Imaging (FRI) trial (Int J Chron Obstruct Pulmon Dis. 2016;11:1533-1541), pulsed inhaled nitric oxide (iNO) was shown to cause an acute vasodilating effect in 6 severe WHO Group 3 PH associated with COPD patients on long-term oxygen treatment (LTOT). In a follow up telephone call patients reported improvement in their symptoms up to 24 hours after a one-time 20-minute treatment with pulsed iNO. Therefore, a follow up study was designed to investigate the clinical relevance of this vasodilation with respect to changes in exercise tolerance and hemodynamics after chronic treatment with iNO.

AIM
To evaluate the relevance of vasodilation to changes in exercise tolerance among PH-COPD patients undergoing chronic pulsed iNO treatment.

METHODS
This study recruited 10 PH-COPD patients on long-term oxygen therapy (LTOT). Pulsed iNO was provided by the INOpulse® delivery system. For all patients, acute vasodilatation under pulsed iNO, is assessed by FRI before starting a 4-week treatment with iNO (>12h/day). Exercise tolerance, hemodynamics and perception of SOB were measured at baseline and after 4 weeks treatment with iNO (n=7).

RESULTS
All 10 patients experienced acute increases in blood vessel volumes following iNO treatment (+4.2%, p=0.03, Figure 1). There was a significant association (p<0.01) between ventilation and vasodilatation during iNO therapy, suggesting that regions with better ventilation experience more vasodilatation. The patients who completed 4 weeks of iNO therapy experienced reductions in pulmonary arterial pressure (-19.9%, p=0.02) (Figure 2) and had a 50.7±4.4 meter increase in 6MWD (p=0.04) (Figure 3). In addition of 7 subjects reported improvement in SOB at rest and with exercise. The therapy was well tolerated with no safety concerns. There were no changes in SpO2, FVC, FEV1, or Arterial Blood Gases.

CONCLUSION
FRI analyses demonstrate regional dilatation of blood vessels in the lungs following acute pulsed iNO treatment. Vasodilatation occurs in well-ventilated areas as supported by the correlation with lobar ventilation. There were significant reductions in pulmonary artery pressures and improvements in 6MWD and SOB with four weeks of treatment with iNO. Chronic iNO therapy has the potential to significantly increase exercise tolerance and shortness of breath in COPD patients with PH.

References

Table 1: Patient Characteristics.

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<thead>
<tr>
<th>Age (years)</th>
<th>sPAP (mmHg)</th>
<th>6MWD (meters)</th>
<th>FVC (%) pred.</th>
<th>FEV1 (%) pred.</th>
<th>PaO2 (mmHg)</th>
<th>PaCO2 (mm Hg)</th>
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<tr>
<td>64±9</td>
<td>59±20</td>
<td>271±166</td>
<td>81±17</td>
<td>40±16</td>
<td>71±10</td>
<td>41±7</td>
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Figure 1: Chronic change in Blood Vessel Volume During iNO Administration Compared to Baseline.

Figure 2: Chronic change in mean pulmonary artery pressure that reversed after 2 weeks off iNO.

Figure 3: Chronic change in 6MWD Volume During iNO Administration Compared to Baseline.