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Title: The influence of emphysema heterogeneity on the magnitude of benefit following endoscopic thermal vapor ablation (InterVapor™) in patients with heterogeneous emphysema

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Body: Introduction: Endoscopic thermal vapor ablation (InterVapor™) has been demonstrated to induce lung volume reduction through the local delivery of heated water vapor to targeted lung segments. We examined patient subgroups based on emphysema heterogeneity for differential responses. Methods: Subgroup analysis from a single-arm trial of InterVapor (single upper lobe treatment at 10 cal/g of tissue) in patients with upper lobe predominant emphysema. Inclusion criteria: FEV₁ 15%-45% predicted, RV>150%, TLC>100%, 6 minute walk distance (6MWD)>140 m, DLCO>20%. Primary efficacy endpoints: FEV₁ ≥12% or SGRQ ≥-4 units at 6 months. Secondary efficacy: lung volumes (body plethysmography, HRCT), mMRC dyspnea, and 6MWD. Endpoints were analyzed for associations (Pearson correlation) and categorized based on tertiles of heterogeneity index (HI) (lower to upper lobe tissue to air ratio from HRCT). Results: 44 patients received InterVapor. Demographics: 50% men, age 63 years, FEV₁ 0.86 L (31% predicted), SGRQ 59 units, 6MWD 300 m. Results at 6 and 12 months (mean change from baseline):

	HI<1.45 (n=15)	HI 1.45 - ≤1.90 (n=15)	HI>1.90 (n=14)
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	6 mo	12 mo	6 mo	12 mo	6 mo	12 mo
Lobar reduction (%)	34	31	44	44	66	59
RV (mL)	-203	-88	-311	-304	-753	-559
FEV1 (mL)	119	67	139	94	168	96
FEV1 (%Δ)	16	9	14	10	21	12
mMRC	-0.64	-0.67	-0.93	-0.54	-1.17	-1.36
6MWD (m)	34	2	65	19	40	36
SGRQ (units)	-15	-6	-13	-12	-14	-14

Conclusion: Efficacy from InterVapor for the treatment of heterogeneous emphysema appears to increase with increasing HI (i.e. upper lobe predominance). HI should be considered when projecting the magnitude of benefit after InterVapor.