

Imbio Lung Density Analysis™

Bibliography of Peer-Reviewed Scientific Literature

Regulatory Clearance Notice: Lung Density Analysis (LDA) is FDA Cleared, CE Mark certified and Health Canada Approved. LDA is available for research use only in other regions without regulatory clearance for clinical use.

Indications for Use: The Imbio CT Lung Density Analysis Software provides reproducible CT values for pulmonary tissue, which is essential for providing quantitative support for diagnosis and follow up examinations. The Imbio CT Lung Density Analysis software can be used to support the physician in the diagnosis and documentation of pulmonary tissue images (e.g. abnormalities) from CT thoracic datasets. Three-D segmentation and isolation of sub-compartments, volumetric analysis, density evaluations and reporting tools are provided.

Original paper for LDaf

Galbán, C.J., Han, M.K., Boes, J.L., Chughtai, K.A., Meyer, C.R., Johnson, T.D., Galbán, S., Rehemtulla, A., Kazerooni, E.A., Martinez, F.J. and Ross, B.D., 2012. Computed tomography–based biomarker provides unique signature for diagnosis of COPD phenotypes and disease progression. *Nature medicine*, 18(11), p.1711.

Histological Validation

Vasilescu, D.M., Martinez, F.J., Marchetti, N., Galbán, C.J., Hatt, C., Meldrum, C.A., Dass, C., Tanabe, N., Reddy, R.M., Lagstein, A. and Ross, B.D., 2019. Noninvasive imaging biomarker identifies small airway damage in severe chronic obstructive pulmonary disease. *American journal of respiratory and critical care medicine*, 200(5), pp.575-581.

LDaf associations with outcomes and disease status in COPD

Bhatt, S.P., Soler, X., Wang, X., Murray, S., Anzueto, A.R., Beaty, T.H., Boriek, A.M., Casaburi, R., Criner, G.J., Diaz, A.A. and Dransfield, M.T., 2016. Association between functional small airway disease and FEV1 decline in chronic obstructive pulmonary disease. *American journal of respiratory and critical care medicine*, 194(2), pp.178-184.

Han, M.K., Quibrera, P.M., Carretta, E.E., Barr, R.G., Bleecker, E.R., Bowler, R.P., Cooper, C.B., Comellas, A., Couper, D.J., Curtis, J.L. and Criner, G., 2017. Frequency of exacerbations in patients with chronic obstructive pulmonary disease: an analysis of the SPIROMICS cohort. *The Lancet Respiratory Medicine*, 5(8), pp.619-626.

Boes, J.L., Hoff, B.A., Bule, M., Johnson, T.D., Rehemtulla, A., Chamberlain, R., Hoffman, E.A., Kazerooni, E.A., Martinez, F.J., Han, M.K. and Ross, B.D., 2015. Parametric response mapping monitors temporal changes on lung CT scans in the subpopulations and intermediate outcome measures in COPD Study (SPIROMICS). *Academic radiology*, 22(2), pp.186-194.

Martinez, C.H., Diaz, A.A., Meldrum, C., Curtis, J.L., Cooper, C.B., Pirozzi, C., Kanner, R.E., Paine III, R., Woodruff, P.G., Bleecker, E.R. and Hansel, N.N., 2017. Age and small airway imaging abnormalities in

subjects with and without airflow obstruction in SPIROMICS. *American journal of respiratory and critical care medicine*, 195(4), pp.464-472.

Pompe, E., Galbán, C.J., Ross, B.D., Koenderman, L., Nick, H.T., Postma, D.S., van den Berge, M., de Jong, P.A., Lammers, J.W.J. and Hoesein, F.A.M., 2017. Parametric response mapping on chest computed tomography associates with clinical and functional parameters in chronic obstructive pulmonary disease. *Respiratory medicine*, 123, pp.48-55.

Pompe, E., van Rikxoort, E.M., Schmidt, M., Rûhaak, J., Estrella, L.G., Vliegenthart, R., Oudkerk, M., de Koning, H.J., van Ginneken, B., de Jong, P.A. and Lammers, J.W.J., 2015. Parametric response mapping adds value to current computed tomography biomarkers in diagnosing chronic obstructive pulmonary disease. *American journal of respiratory and critical care medicine*, 191(9), pp.1084-1086.

Labaki, W.W., Gu, T., Murray, S., Hatt, C.R., Galbán, C.J., Ross, B.D., Martinez, C.H., Curtis, J.L., Hoffman, E.A., Pompe, E. and Lynch, D.A., 2019. Voxel-wise longitudinal parametric response mapping analysis of chest computed tomography in smokers. *Academic radiology*, 26(2), pp.217-223.

LDAi Original papers

Müller, N.L., Staples, C.A., Miller, R.R. and Abboud, R.T., 1988. "Density mask": an objective method to quantitate emphysema using computed tomography. *Chest*, 94(4), pp.782-787.

LDAi Validation

Gevenois, P.A., De Maertelaer, V., De Vuyst, P., Zanen, J. and Yernault, J.C., 1995. Comparison of computed density and macroscopic morphometry in pulmonary emphysema. *American journal of respiratory and critical care medicine*, 152(2), pp.653-657.

Madani, A., Zanen, J., De Maertelaer, V. and Gevenois, P.A., 2006. Pulmonary emphysema: objective quantification at multi-detector row CT—comparison with macroscopic and microscopic morphometry. *Radiology*, 238(3), pp.1036-1043.

Madani, A., De Maertelaer, V., Zanen, J. and Gevenois, P.A., 2007. Pulmonary emphysema: radiation dose and section thickness at multidetector CT quantification—comparison with macroscopic and microscopic morphometry. *Radiology*, 243(1), pp.250-257.

Gevenois, P.A., Scillia, P., De Maertelaer, V., Michils, A., De Vuyst, P. and Yernault, J.C., 1996. The effects of age, sex, lung size, and hyperinflation on CT lung densitometry. *AJR. American journal of roentgenology*, 167(5), pp.1169-1173.

Kirby, M., Hatt, C., Obuchowski, N., Humphries, S.M., Sieren, J., Lynch, D.A., Fain, S.B. and QIBA Lung Density Committee, 2020. Inter- and intra-software reproducibility of computed tomography lung density measurements. *Medical physics*, 47(7), pp.2962-2969.

LDAi associations with outcomes and disease status in COPD

Ash, S.Y., San José Estépar, R., Fain, S.B., Tal-Singer, R., Stockley, R.A., Nordenmark, L.H., Rennard, S., Han, M.K., Merrill, D., Humphries, S.M. and Diaz, A.A., 2021. Relationship between Emphysema Progression at CT and Mortality in Ever-Smokers: Results from the COPDGene and ECLIPSE Cohorts. *Radiology*, 299(1), pp.222-231.

LDAi in lung cancer screening

Labaki, W.W., Xia, M., Murray, S., Hatt, C.R., Al-Abcha, A., Ferrera, M.C., Meldrum, C.A., Keith, L.A., Galbán, C.J., Arenberg, D.A. and Curtis, J.L., 2021. Quantitative emphysema on low-dose CT Imaging of the chest and risk of lung cancer and airflow obstruction: an analysis of the National Lung Screening Trial. *Chest*, 159(5), pp.1812-1820.

Hatt, C.R., Oh, A.S., Obuchowski, N.A., Charbonnier, J.P., Lynch, D.A. and Humphries, S.M., 2021. Comparison of CT Lung Density Measurements between Standard Full-Dose and Reduced-Dose Protocols. *Radiology: Cardiothoracic Imaging*, 3(2), p.e200503.

Steiger, D., Siddiqi, M.F., Yip, R., Yankelevitz, D.F., Henschke, C.I., Jirapatnakul, A., Flores, R., Wolf, A., Libby, D.M., Smith, J.P. and Pasmantier, M., 2021. The importance of low-dose CT screening to identify emphysema in asymptomatic participants with and without a prior diagnosis of COPD. *Clinical imaging*, 78, pp.136-141.

LDAf associations with outcomes and disease status in BOS

Galbán, C.J., Boes, J.L., Bule, M., Kitko, C.L., Couriel, D.R., Johnson, T.D., Lama, V., Telenga, E.D., van den Berge, M., Rehemtulla, A. and Kazerooni, E.A., 2014. Parametric response mapping as an indicator of bronchiolitis obliterans syndrome after hematopoietic stem cell transplantation. *Biology of Blood and Marrow Transplantation*, 20(10), pp.1592-1598.

Belloli, E.A., Degtiar, I., Wang, X., Yanik, G.A., Stuckey, L.J., Verleden, S.E., Kazerooni, E.A., Ross, B.D., Murray, S., Galbán, C.J. and Lama, V.N., 2017. Parametric response mapping as an imaging biomarker in lung transplant recipients. *American journal of respiratory and critical care medicine*, 195(7), pp.942-952.

Verleden, S.E., Vos, R., Vandermeulen, E., Ruttens, D., Bellon, H., Heigl, T., Van Raemdonck, D.E., Verleden, G.M., Lama, V., Ross, B.D. and Galbán, C.J., 2016. Parametric response mapping of bronchiolitis obliterans syndrome progression after lung transplantation. *American Journal of Transplantation*, 16(11), pp.3262-3269.