Research Square

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Automated analysis of chest CT of bronchiectasis patients with and without NTM infection

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Abstract

Background:

Nontuberculous Mycobacterium (NTM) is thought to contribute to the progression of structural lung disease. In this retrospective observational study, we analyzed CTs of bronchiectasis (BE) disease patients to assess and compare changes in bronchus and artery (BA)-dimensions and mucus plugs (MP) in patients with and without NTM.

Methods:

LungQ-BA measures automatically for each BA-pair: bronchus outer and inner diameter (B_{out} and B_{in}), arterial diameter (A), and bronchial wall thickness (B_{wt}) and computes the ratios; B_{out}/A; B_{in}/A; B_{wt}/A and B_{wa}/B_{oa} (bronchus wall area/bronchus outer area) for each segmental generation. LungQ-MP detects and computes the number and volume of MP. Comparisons between groups: median of B_{out}/A, B_{in}/A, B_{wt}/A and B_{wa}/B_{oa} for segmental generations G_{1-6} and number and volume of MP. Results shown median [IQR] unless stated otherwise.

Results:

120 patients seen in a BE clinic: CTs of 57 NTM- (21-89 years) and 63 NTM+ (age range 31-89 years) met LungQ requirements. For the NTM- from G_{1-6} 161 [75] and NTM+ 170 [97] BA-pairs per CT were analyzed. There were 2 [6] MPs with a volume of 0.09ml [0.36ml] in the NTM- group and 8 [19.5] MPs with a volume of 0.36ml [1.29ml] in the NTM+ group. Both MP number ($p<0.001$) and volume ($p<0.002$) were higher in the NTM+ group compared to the NTM-. No statistically significant differences between the two groups in BA-dimensions and ratios.

Conclusions:

The presence of NTM is associated with double the number of MP and volume compared to the NTM- group, but we observed no difference in BA-dimensions and ratios.

Trial registration:

This was a single center retrospective study of patients managed in our BE program. The study protocol was approved by the Medical University of South Carolina institutional review board. Clinical trial number: not applicable

Background

Bronchiectasis (BE) is a pulmonary condition described as dilated airways (1) and is rising in both incidence and prevalence (2). It is a condition that results from many etiologies and presents with heterogeneous severity. A consequence of BE can be persistent infection of the airways by opportunistic

bacteria, including non-tuberculous mycobacteria (NTM), also a condition of rising incidence and prevalence (3). Many people with BE (pwBE) will have persistent cough and fatigue, among other chronic symptoms, which are also associated with NTM pulmonary disease (NTM-PD). Radiographic features for chest computed tomography (CT) scans that are often used to describe NTM-PD include bronchiectasis, pulmonary nodules, and cavities but specific measures have not been validated and are often subjective descriptions. Radiographic interpretations using artificial intelligence (AI) methods may offer greater specificity as to which pwBE may have NTM-PD, perhaps reducing the need for invasive procedures in those unable to expectorate sputum(4–6). We have looked at a cohort of carefully phenotyped pwBE known to have NTM-PD (or not) to assess AI algorithms to determine whether there are features that are associated with a greater likelihood of having NTM.

Methods

In this retrospective observational study, eligible subjects included those with documented BE by chest computed tomography (CT). We evaluated chest CT images from a cohort of all subjects who were seen in a single institution's BE clinic during a specific 4-month period; this approach was intended to reduce bias, and the cohort has been previously described(7). Subjects with cystic fibrosis (CF) and scleroderma were excluded. For the chest CT analysis, a single chest CT study per subject was evaluated. The chest CT images had to meet the requirements of slice thickness < 1.5mm, no major motion artifacts, and volumetric and continuous acquisition (no missing slices).

Subject demographics, microbiologic data, and pulmonary function data were abstracted from the electronic health record. All subjects had cultures of respiratory specimens (i.e. sputum or bronchoalveolar lavage) and were defined as NTM+/- based on those results; any patient with at least one positive NTM in culture was deemed NTM+. Study data were entered into a Research Electronic Data Capture (REDCap) database by the South Carolina Clinical and Translational Science (SCTR) Institute at the Medical University of South Carolina.

Chest CT images were analyzed using validated artificial intelligence-based algorithms (LungQ®, Thirona, Nijmegen, The Netherlands)(4, 6, 8). A fully automatic Bronchus-Artery (BA) and Mucus Plugging (MP) analysis was used to quantify BA dimensions and ratios and the number and volume of MP. LungQ segments the bronchial tree and identifies for each bronchus the matching artery. For each BA-pair it computes the following diameters: bronchus outer and inner diameter (B_{out} and B_{in}), arterial diameter (A), and bronchial wall thickness (B_{wt}). It then computes the following ratios: B_{out}/A, B_{in}/A, B_{wt}/A and B_{wa}/B_{oa} (bronchus wall area/bronchus outer area) for each segmental generation. We compared the median of all BA-dimensions and ratios B_{out}/A, B_{in}/A, B_{wt}/A and B_{wa}/B_{oa} for segmental generations 1 to 6 (G_{1-6}) and volume and number of MP in subject with and without NTM.

Statistical Analysis

For statistical analysis demographic and clinical characteristics at the time of CT acquisition were summarized. LungQ-BA metrics were derived by computing the medians (IQR) of each variable (BA pair counts, B_{out}, B_{in}, B_{wt}, B_{oa}, and A) for G_{1-6} and their ratios (B_{out}/A, B_{in}/A, B_{wt}/A, and B_{wa}/B_{oa}). Proportions of airways exceeding thresholds like $B_{out}/A > 1.1$, $B_{out}/A > 1.5$ or $B_{wt}/A > 0.14$) and mucus plug (MP; total count and volume [mL]) metrics, were summarized using medians and interquartile ranges (IQR) stratified by NTM status, with visualizations via raincloud plots. For continuous outcomes without marked zero-inflation (e.g., inspiratory lung volume [mL], ratio metrics), normality was first assessed separately within each NTM group using the Shapiro–Wilk test; independent-samples t-tests were applied when $p > 0.05$ in both groups, otherwise non-parametric Wilcoxon–Mann–Whitney rank-sum tests were used. Total MP count (over-dispersed with excess zeros) was analyzed via a model comprising a negative binomial component for non-zero counts and a zero-inflation logistic component. Total MP volume (mL; zero-inflated continuous) employed a zero-inflated log-normal model, with the conditional log-normal component estimating non-zero volume differences and the zero-inflation logit for zero probability. All tests were two-sided ($\alpha = 0.05$) and performed using R.

Results

Subjects

120 subjects (23 [19.17%] males) are included in the analysis. 57 (48%) subjects were defined as NTM- with a mean age of 69.3 years (range 21–89 years); 63 (52%) subjects were NTM + with a mean age of 69.4 years (range 31–89 years); p = NS. The demographic data are shown in Table 1; there were no differences between the groups.

Table 1
Subject demographics

	NTM-	NTM+
N	57 (47.5%)	63 (52.5%)
Mean Age, yrs (SD)	69.3 ± 13.6	69.4 ± 10.9
Female Sex, n (%)	36 (63.2%)	53 (84.1%)
Race, n (%)	74 (86%)	34 (85%)
White/Caucasian	9 (10.5%)	4 (10%)
Black/African American	2 (2.3%)	2 (5%)
Hispanic	1 (1.2%)	0 (0%)
Asian American		
Suspected Etiology for Bronchiectasis	54 (62.8%)	24 (60%)
Idiopathic	13 (15.1%)	8 (20%)
Infection-Related	9 (10.5%)	3 (7.5%)
Autoimmune	3 (3.5%)	2 (5%)
Immune deficiency	3 (3.5%)	0
Congenital defect	2 (2.3%)	1 (2.5%)
Ciliary disease	2 (2.3%)	0
A1AT deficiency	0	2 (5%)
Radiation		
Mean BMI, units (SD)	Mean = 24.1 ± 6.2	Mean = 24.8 ± 5.8
Tobacco History, n (%)	0 (0%)	0 (0%)
Current Smoker	33 (38.4%)	14 (35%)
Former Smoker	53 (61.6%)	26 (65%)
Never Smoker		
History of Infection	23 (26.7%)	15 (37.5%)
Pseudomonas		
SD = Standard deviation, yrs = Years.		

Radiographic measures

Chest CT images were acquired between May 2020 and January 2024. The LungQ BA-analysis detected from G_{1-6} (median [IQR]) 116 [75] BA-pairs for the NTM- group and (median [IQR]) 170 [97] BA-pairs for the NTM + group. The complete descriptive statistics are shown in Table 2. Overall, the comparison of the BA-pairs ratios B_{out}/A, B_{in}/A, B_{wt}/A and B_{wa}/B_{oa} for segmental generations 1 to 6 (G_{1-6}) didn't show any statistically significant differences between the two groups (p-values > 0.05). The proportion of BA-pairs that met the definition of bronchiectasis (i.e. $B_{out}/A > 1.1$) also did not differ between the two groups(9). However, when using a more conservative threshold ratio of 1.5(4, 10), there was a nominally greater proportion of BA pairs that met this definition in the NTM + group (median 40.8%) compared to the NTM- group (median 35.2%) suggesting more severely dilated bronchi in the NTM + group (Fig. 1).

Table 2
LungQ CT Scan Analysis Data

Measure	**NTM-**		**NTM+**	
	Mean (SD)	Median	Mean (SD)	Median
Lung Volume at CT (mL)	4409.68 (1302.52)	4258	4358.33 (995.77)	4374
Total number of bronchi				
B_{in}/A	1.04 (0.2)	1.06	1.06 (0.2)	1.03
B_{out}/A	1.35 (0.2)	1.33	1.37 (0.2)	1.39
B_{wt}/A	0.15 (0.0)	0.14	0.14 (0.0)	0.14
B_{wa}/B_{oa}	0.39 (0.1)	0.38	0.38 (0.01)	0.37
% BA pairs with $B_{out}/A > 1.1$	70.2 (18.6)	75.4	70.4 (18.4)	74.8
% BA pairs with $B_{out}/A > 1.5$	37.2 (18.6)	35.2	38.3 (18.6)	40.8
% BA pairs with $B_{wt}/A > 0.14$	49.4 (22.4)	48.4	48.0 (19.2)	45.9
Number of plugs	6.5 (13.6)	2	16.1 (26.2)	8
Total mucus volume (ml)	0.39 (0.9)	0.09	1.16 (2.2)	0.36
LungQ scores the quantity of mucus plugging as well as Bronchus-Artery (BA) dimensions and ratios. The volume and number of mucus plugs, as well as the median of all BA-dimensions and ratios for segmental generations 1 to 6 (G_{1-6}) were compared between those with and without NTM.				
A = arterial diameter, B_{in} = bronchus inner diameter, B_{oa} = bronchus outer area, B_{out} = bronchus outer diameter, B_{wa}= bronchial wall area, B_{wt} = bronchial wall thickness, SD = standard deviation.				

There were greater number and volume of mucus plugs (MP) in the NTM + group compared to the NTM- group (Table 2). There were statistically significant differences between both MP number ($p < 0.001$) and MP volume ($p < 0.002$) between the two groups. This can be seen graphically in Figs. 2 and 3).

Discussion

Radiographic features of NTM-PD include bronchiectasis, pulmonary nodules, and cavities. We used AI algorithms to look at radiographic features, specifically bronchial dilatation (bronchiectasis), bronchial wall thickness, and mucus plugs to see if there are differences between those pwBE known to have NTM to those without. Using a more conservative measure to define BE we found a nominal difference in the proportion of more severely dilated bronchi in the NTM + group compared to NTM-(10, 11). There was a greater number and volume of mucus plugs in the NTM + group as well. The differences are not striking but it remains to be seen whether these parameters offer any predictive value, which could be tested prospectively.

Since many pwBE may not produce sufficient sputum for culture, a recommendation for bronchoscopy may often follow. Many of these patients will not have NTM present in the airways and so the procedure may offer risk without any benefit. Greater specificity of radiographic features on chest CT may improve the yield of bronchoscopy by reducing the number of patients undergoing the procedure.

There are some limitations to this analysis. The key limitation is the degree of certainty about the presence of NTM in the airways. Although all subjects had respiratory cultures performed for NTM, not all subjects had them collected by bronchoscopy, which could be more sensitive than by sputum alone. There may be other radiographic features (e.g. nodules) that may increase the specificity. The sample size is not large but should be sufficient to see if there are measures of radiographic differences that would differ. In addition, we tried to reduce the bias in selection of patients by including all patients during a specified time period.

Conclusions

In conclusion, although there are some differences in chest CT features associated with NTM in patients known to have bronchiectasis, the differences are not so striking to easily predict who would have a positive culture.

Abbreviations

A
Artery Diameter
AI
Artificial Intelligence
BA
Bronchus Artery

BE
Bronchiectasis
B_{in}
Bronchial Inner Diameter
B_{oa}
Bronchial Outer Area
B_{out}
Bronchial Outer Diameter
B_{wa}
Bronchial Wall Area
B_{wt}
Bronchial Wall Thickness
CF
Cystic Fibrosis
CT
Computed Tomography
G
Segmental Generation
IQR
Interquartile Range
MP
Mucus Plug
NTM
Non-tuberculous Mycobacteria
NTM+
Non-tuberculous Mycobacteria Postive
NTM-
Non-tuberculous Mycobacteria Negative
NTM-PD
Non-tuberculous Mycobacterial Pulmonary Disease
pwBE
Persons with Bronchiectasis
REDCap
Research Electronic Data Capture
SCTR
South Carolina Clinical and Translational Science
SD
Standard Deviation

Declarations

Author Contribution

Federico Mollica and Christina M. Mingora contributed equally to this work and share first authorship. Patrick A. Flume conceived and designed the study. Harm A.W.M. Tiddens, Daan Caudri, Punitkumar Makani and Spenser Staub, contributed to data acquisition, interpretation, and critical revision of the manuscript for important intellectual content. Punitkumar Makani performed the statistical analysis. Federico Mollica performed the primary data analysis and drafted the initial manuscript, with substantial input and revisions from all co-authors. All authors meet the criteria for authorship, approved the final version of the manuscript, and agreed to be accountable for all aspects of the work.

Data Availability

The data can be made available by contacting the author.

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Figures

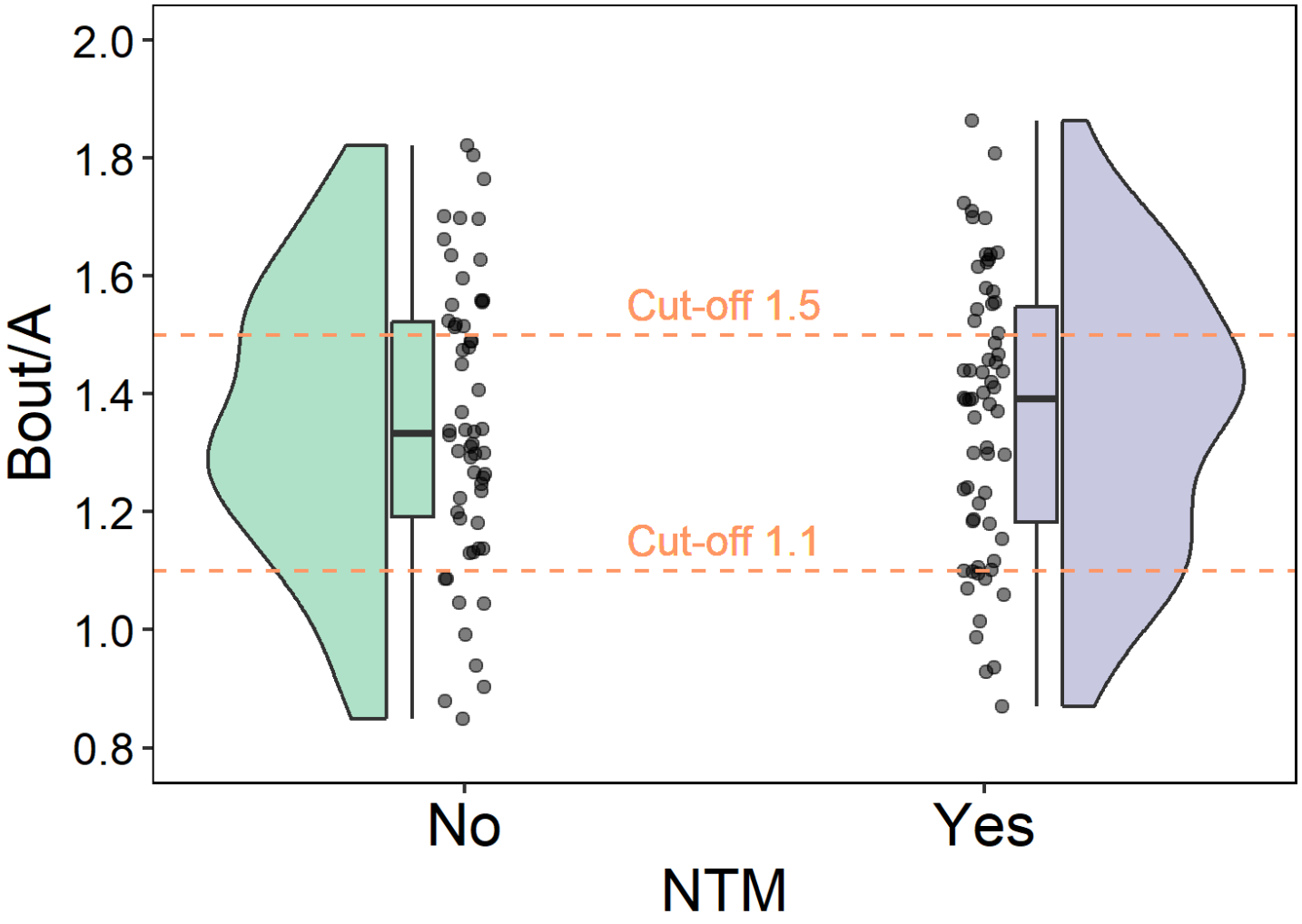


Figure 1

LungQ BA-analysis difference in B_{out}/A for G_{1-6} in NTM- vs NTM+. The dash lines represent the bronchiectasis cut-off of 1.1 and the more conservative cut-off of 1.5.

A = Artery diameter; B_{out} = Bronchial outer diameter; G_{1-6} = Segmental generations 1 to 6.

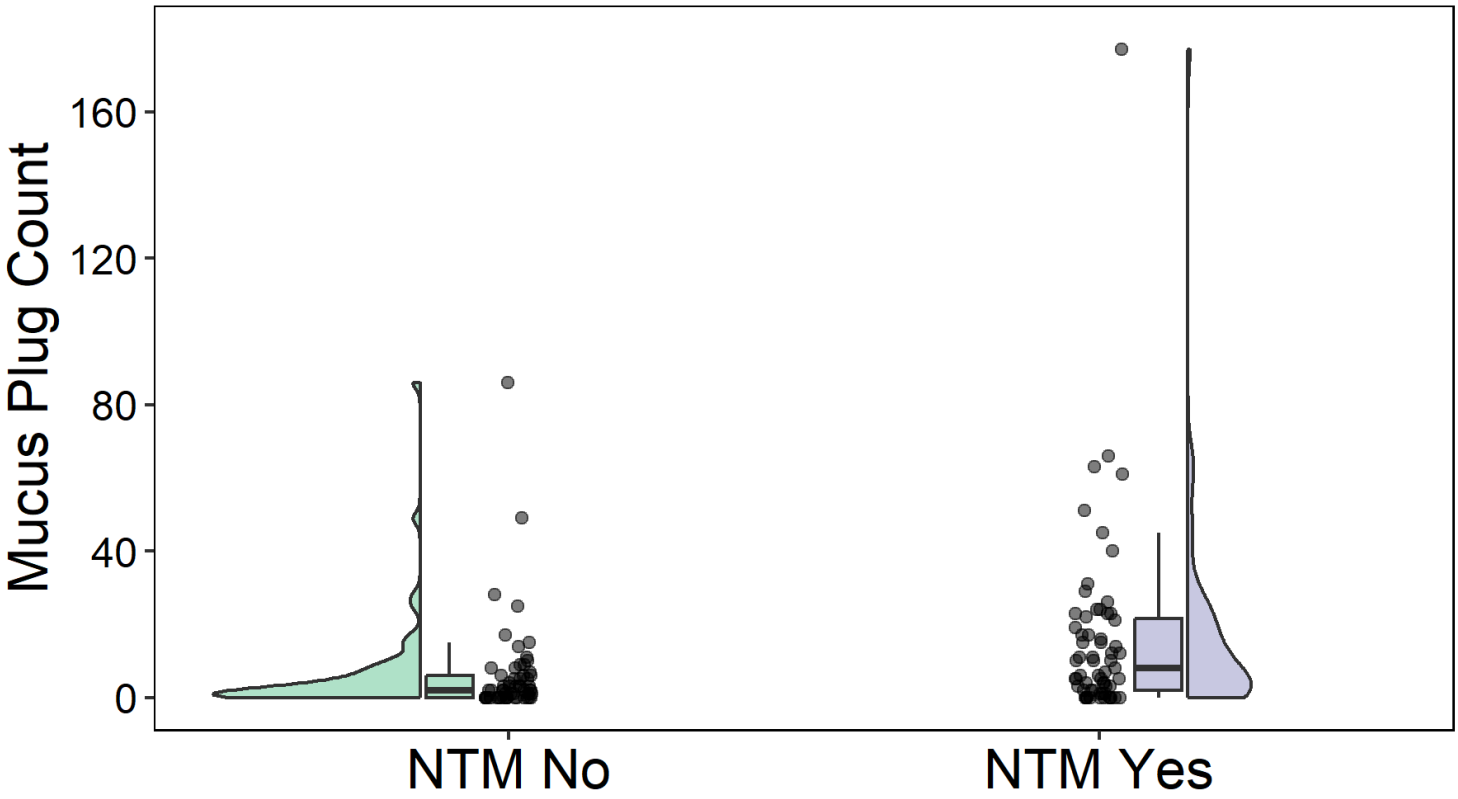


Figure 2

LungQ MP-analysis difference in total number of mucus plugs in NTM- vs NTM+.

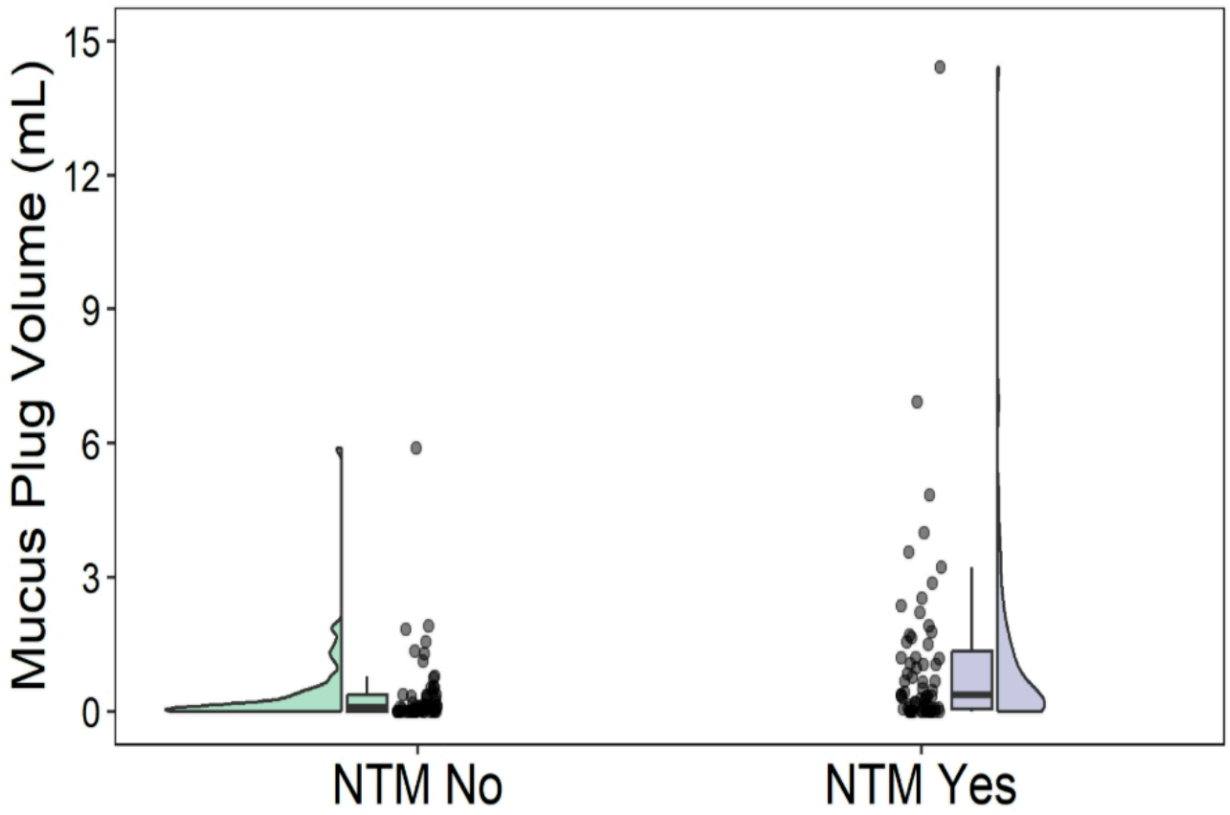


Figure 3

LungQ MP-analysis difference in total volume of mucus plugs NTM- vs NTM+.