



Bronchiectasis- COPD Overlap Syndrome

BCOS- it matters

Tony De Soyza

anthony.de-soyza@ncl.ac.uk



Aims

- Highlight why BCOS occurs
- Define why the diagnosis BCOS should be sought
 - & Refute the counter argument
 - case examples
- Some suggestions on what is needed in terms of research & management of these patients

Why must COPD and Bronchiectasis overlap?

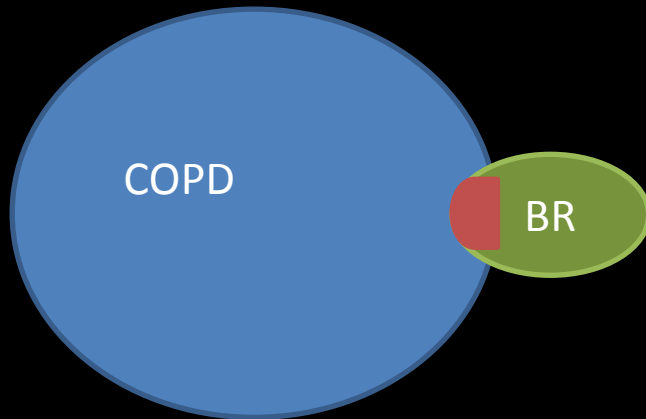
- COPD is a common neutrophilic lung disease affecting approximately 5-10% of the population. It is characterised by functional changes (airflow obstruction)
- Bronchiectasis is a rarer neutrophilic lung disease characterised by structural changes in airway calibre (dilatation) affecting 0.1-0.5% of population

Do we have reliable tests to distinguish COPD and Bronchiectasis?

- Yes;
 - In the absence of bronchial dilatation that is permanent then bronchiectasis is excluded
- No;
 - We don't robust scoring that is reproducible with limited observer variability on CT
 - Bronchial wall thickening/ modest dilatation / definite bronchiectasis

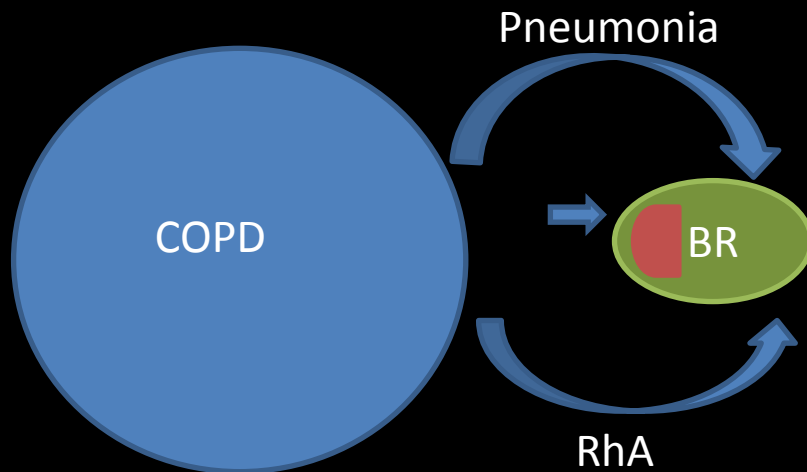
Loebinger et al ERJ 2009
McDonnell et al Resp Med
2012

Models to explain BCOS



Co-incidence

Two events independent of each other happening in the same patient



Causality

One disease process in % of susceptible individuals leads to the second condition

Mechanistically could COPD lead to bronchiectasis?

- Pathogenesis & Aetiology of bronchiectasis without smoking:
 - Neutrophilic lung inflammation
 - Post infectious bronchiectasis
 - Reflux/ micro aspiration
 - Auto-immunity
 - Impaired immunity
 - Impaired mucociliary clearance
 - Neutrophil elastase, TNF and Il-8
 - Matrix metalloproteinases (MMP)

Mechanistically could COPD lead to bronchiectasis?

- Pathogenesis & Aetiology of bronchiectasis without smoking:

	Demonstrated as a component of COPD
– Post infectious bronchiectasis	√
– Reflux/ micro aspiration	?
– Neutrophilic lung inflammation	√
– Auto-immunity	?
– Impaired immunity	√
– Impaired mucociliary clearance	√
– Neutrophil elastase, TNF and Il-8	√
– Matrix metalloproteinases (MMP)	√

Can we reliably define bronchiectasis as being caused by COPD?

- NO:
- Prevalence of bronchiectasis is higher in aged populations
 - Smoking was more prevalent 40 yrs ago
- Presence of airflow obstruction, recurrent infective exacerbations and bronchial wall dilatation could be independent of the smoking history...

How common is BCOs?

COPD cohorts

- O'Brien Thorax 2000 UK 29% (n= 110- primary care pts)
- ECLIPSE cohort EU,US <5% (n=2164)
- Stewart et al COPD gene ATS 2012 20% (n=3758)
- Patel *et al* AJRCCM UK 50% (n=54)
- Baker *et al* J. COPD UK 2014 69% (n=496)
- Baker et al Abstract ATS 2011 19% (n=882)

Reported in Bronchiectasis series:

- Pasteur et al AJRCCM 2001 0%
- Anwar et al Resp Med 20%

Is there a typical CT appearance that helps us define BCOS?

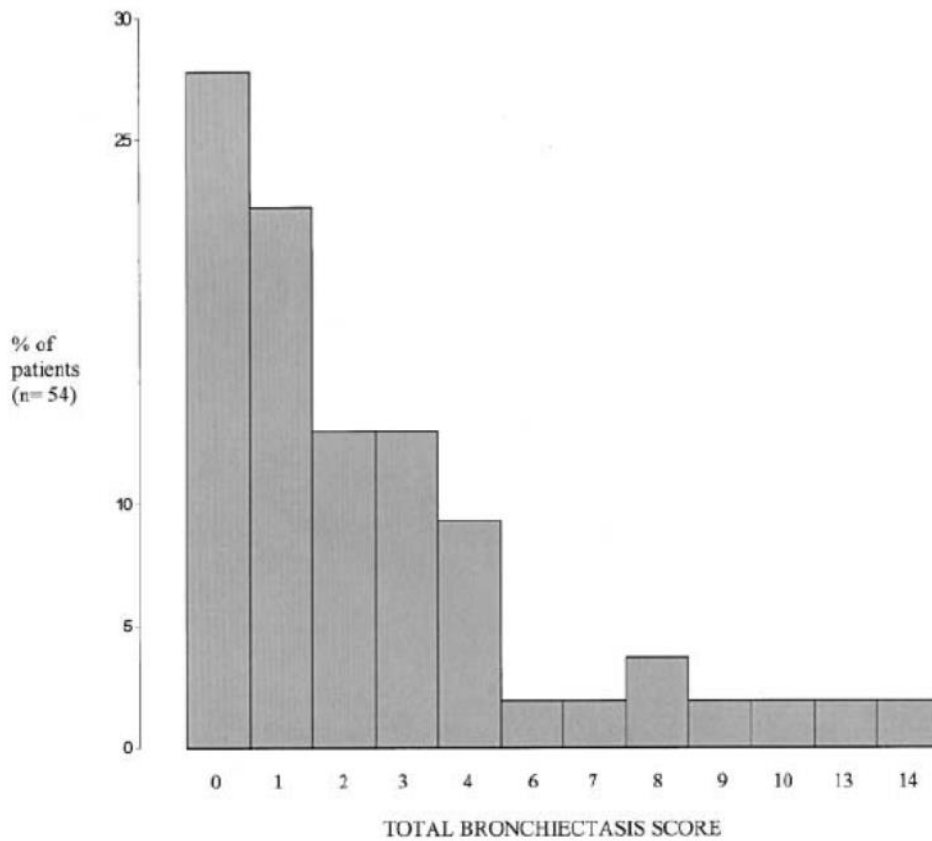
- Many Bronchiectasis doctors quote “mild basal cylindrical bronchiectasis” -
- Patel *et al* AJRCCM 2004
 - Twenty-seven of 54 patients (50%) had bronchiectasis on HRCT, most frequently in the lower lobes (18 of 54, 33.3%).

Bronchiectasis in COPD

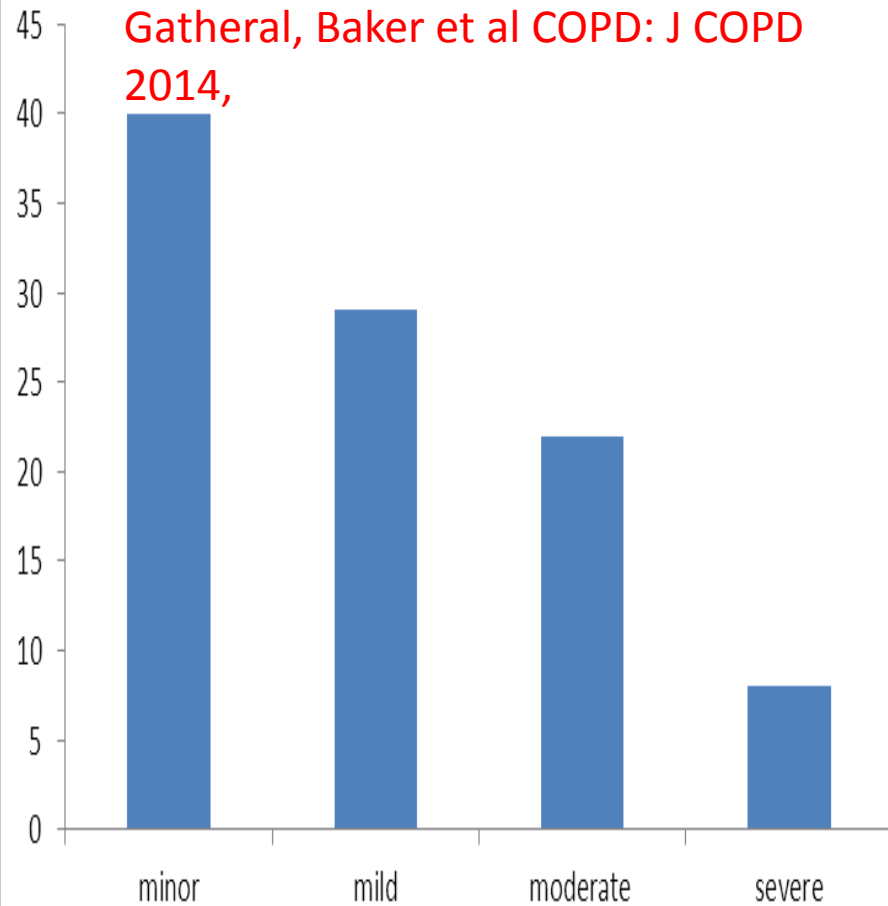
- S. London, UK : 406 patients (71 ± 11 years, 56% male, FEV1 52 ± 23% predicted)
- 278 (69%) patients had bronchiectasis:
 - minor, 112 (40%);
 - mild, 81 (29%);
 - moderate, 62 (22%);
 - severe 23 (8%).

Baker et al COPD: Journal of Chronic Obstructive
Pulmonary Disease Dec 2014

Patel, Vlahos, Wilkinson, *et al.*: CT Scanning and COPD Exacerbations



Gatheral, Baker et al COPD: J COPD 2014,



So BCOS exists- but does it matter?

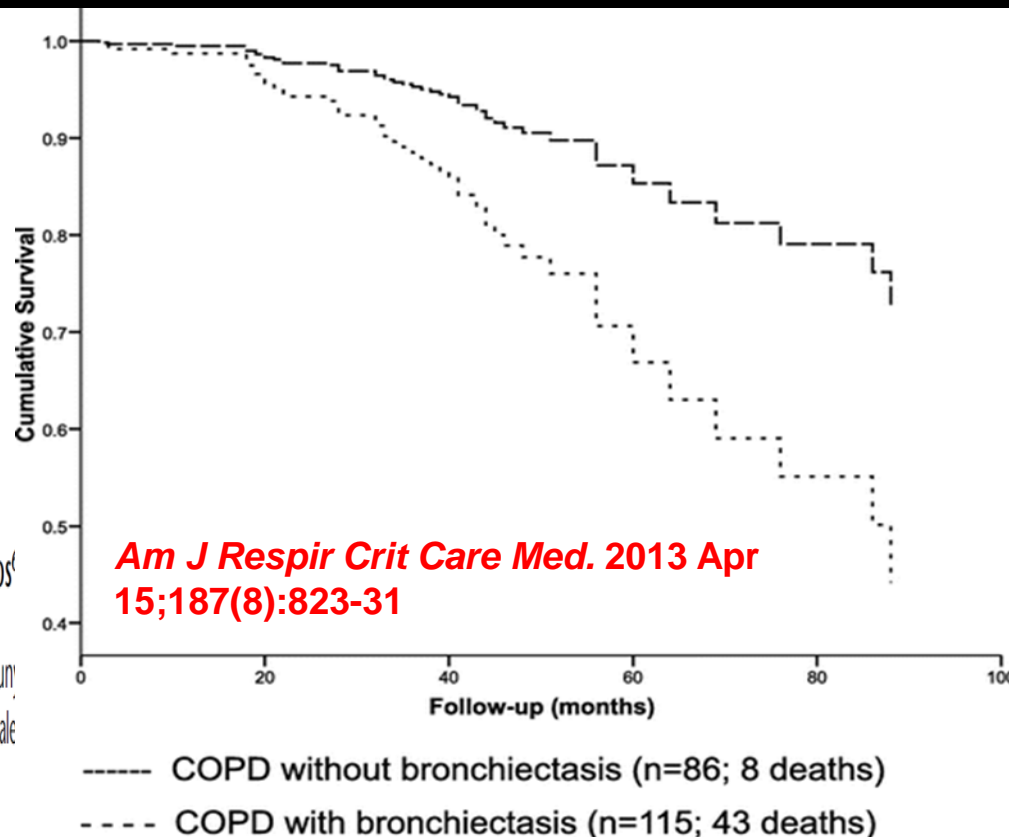
- Mortality: Belgian Cohort of BR; significant numbers with COPD
 - 5yrs f/up: Overall mortality was 20% but 50% mortality in BCOS (HR = 2.12; p = 0.038)
- Patel *et al* BCOS vs COPD
 - higher levels of airway inflammatory cytokines,
 - lower airway bacterial colonization,
 - higher sputum interleukin-8 levels
 - longer symptom recovery time at exacerbation

Does Bronchiectasis matter in COPD?

Prognostic Value of Bronchiectasis in Patients with Moderate-to-Severe Chronic Obstructive Pulmonary Disease

Miguel-Angel Martínez-García^{1,2}, David de la Rosa Carrillo³, Juan-José Soler-Cataluña⁴, Yolanda Donat-Sanz⁴, Pablo Catalán Serra⁴, Marco Agramunt Lerma⁵, Javier Ballestín⁵, Irene Valero Sánchez¹, María Jose Selma Ferrer¹, Anna Roma Dalfo⁶, and Montserrat Bertomeu Valdecillos⁴

¹Pneumology Service, Polytechnic and University La Fe Hospital, Valencia, Spain; ²CIBERes, CIBER de Enfermedades Respiratorias, Burjassot, Spain; ³Pneumology Unit, Platón Hospital, Barcelona, Spain; ⁴Internal Medicine Service and ⁵Radiology Service, Hospital General de Requena, Valencia, Spain; ⁶Radiology Department, Platón Hospital, Barcelona, Spain



Does Bronchiectasis matter in COPD?

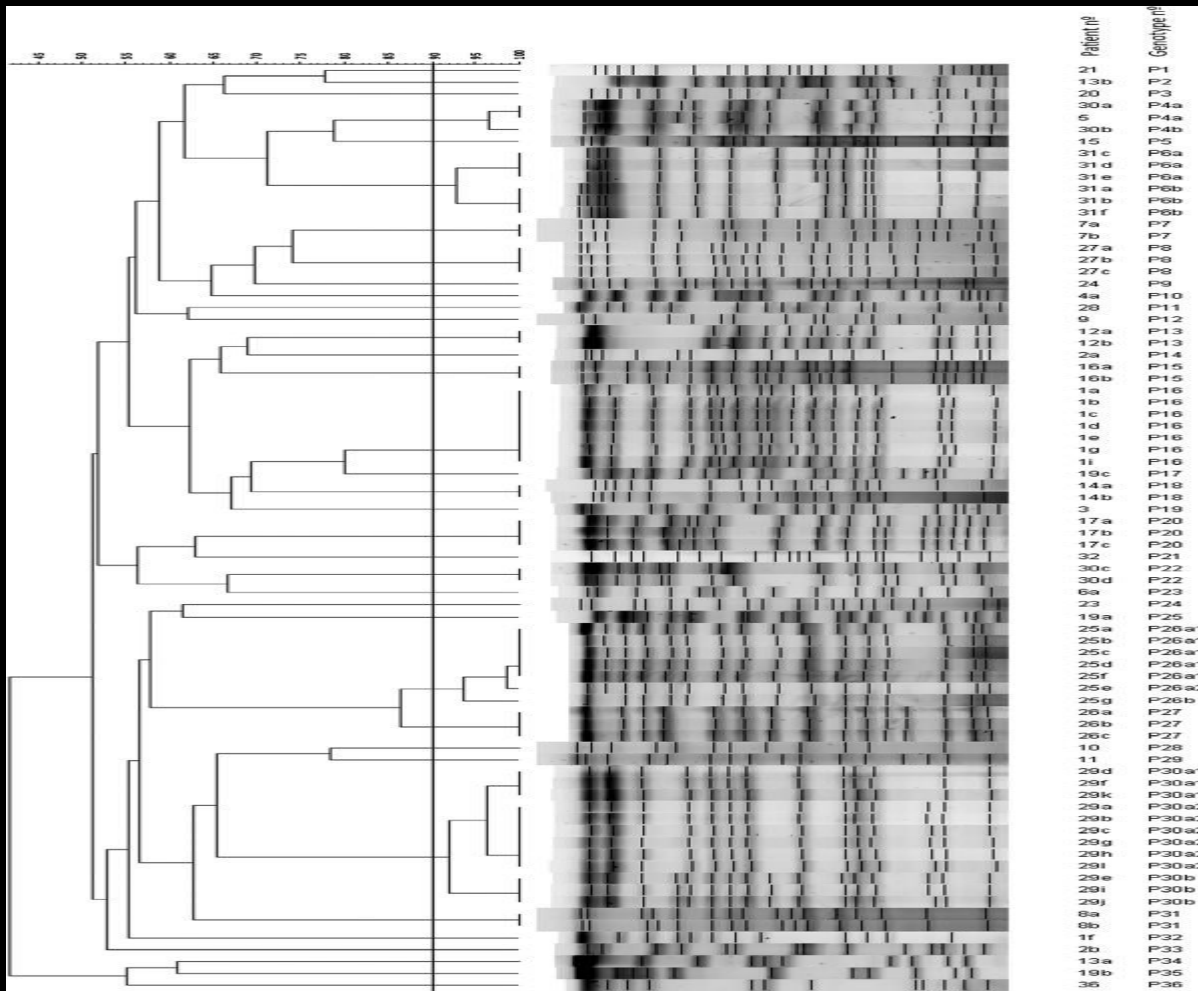
- B-COS independently determined
 - sputum isolation of *Pseudomonas aeruginosa* (Odds ratio (OR) 1.39 (95% CI 1.07 to 1.80), $p = 0.013$)
 - atypical mycobacteria (OR 2.44 (95% CI 1.04 to 5.69), $p = 0.04$),
 - annual respiratory admissions ($p = 0.044$) and inpatient days ($p < 0.001$),
 - did not predict survival ($p = 0.256$).

Predictors of Pseudomonas in COPD...

Factor	OR	95% CI	P value
Bronchiectasis score (>5)	9.8	1.7 - 54.8	0.009
Antibiotic prescriptions/year	1.7	1.1 – 2.5	0.008
Days of hospital stay	1	0.9 - 1	0.3
Corticosteroid courses/year	0.7	0.5 – 1.2	0.2

Gallego et al BMC
Pulm Med. 2014;
14: 103.

Do BCOS patients harbour the same Ps aer isolates?



Standards of care... should we look for BCOS in COPD?

- In bronchiectasis
 - Physiotherapy training (ACBT) is recommended
 - Nebulised antibiotics eg gentamicin
 - ?Lower threshold for long term macrolide therapy than COPD
- BCOS diagnosis may also prompt;
 - Aetiological testing as per BTS guidelines
 - Screening for Non Tuberculous mycobacteria (NTM)

COPD Treatments not to be used in BCOS

- Inhaled steroids (?)
- Endobronchial valves and Endobronchial coils
- Single lung transplant (but bilateral lung transplant can be used)

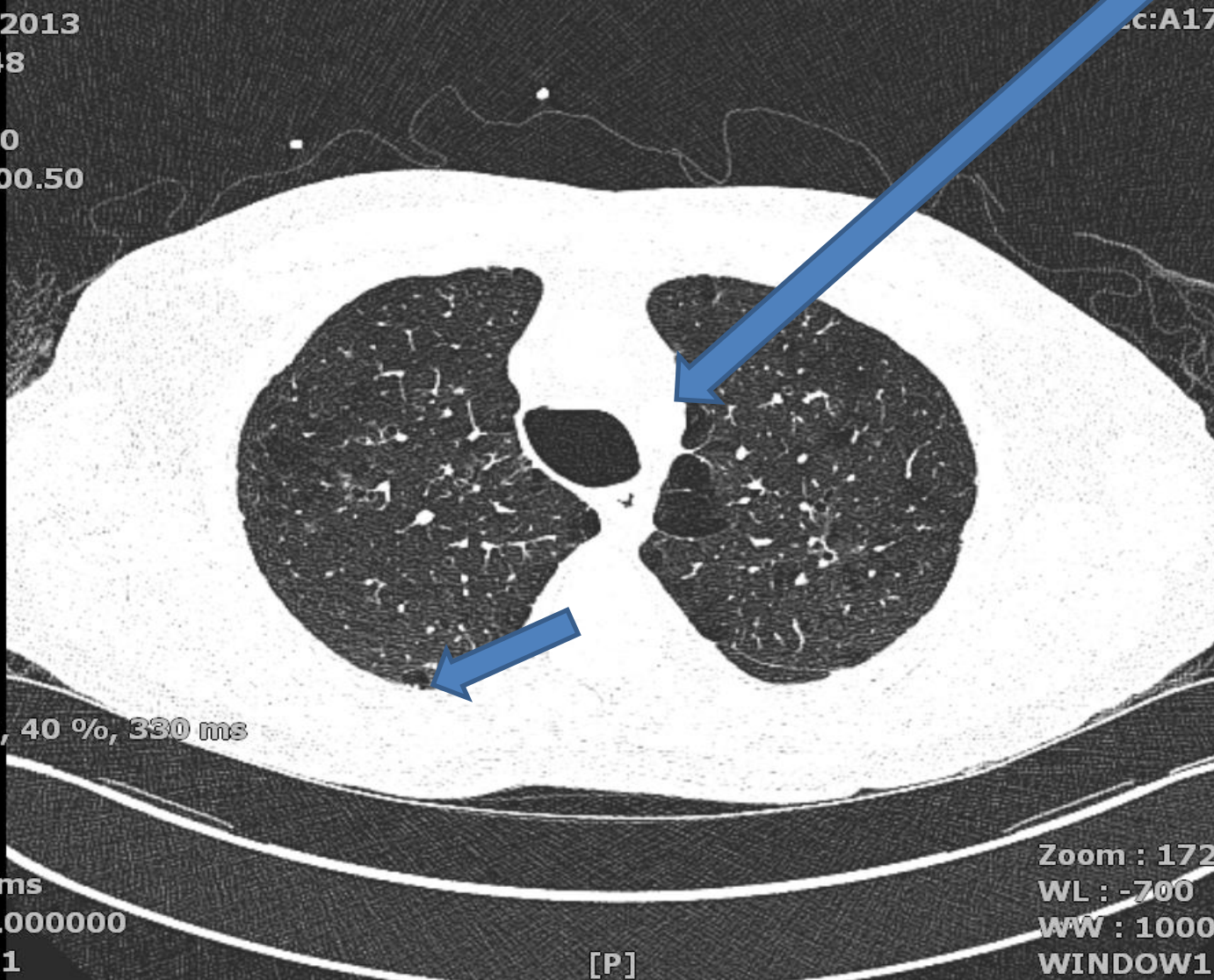


Case 1 B-COS?

03/04/2013
14:04:48

SL : 1.00
SP : 1100.50

PP:HFS



68 yr old
smoker
6th
admission
in 12
months
Sputum
volume 30
mls / day
or more

77 bpm, 40 %, 330 ms

TI 330 ms
kV:120.000000
mAs:111

Zoom : 172.6
WL : -700
WW : 1000
WINDOW1

Case 1 Basal cuts

F0000986260

03/04/2013

14:05:03

SOMATOM Definition AS

Acc:A17529628

Srs:2

Img:23

SL : 1.00

SP : 981.50

PP:HFS



[L]

63 bpm, 40 %, 330 ms

18cm

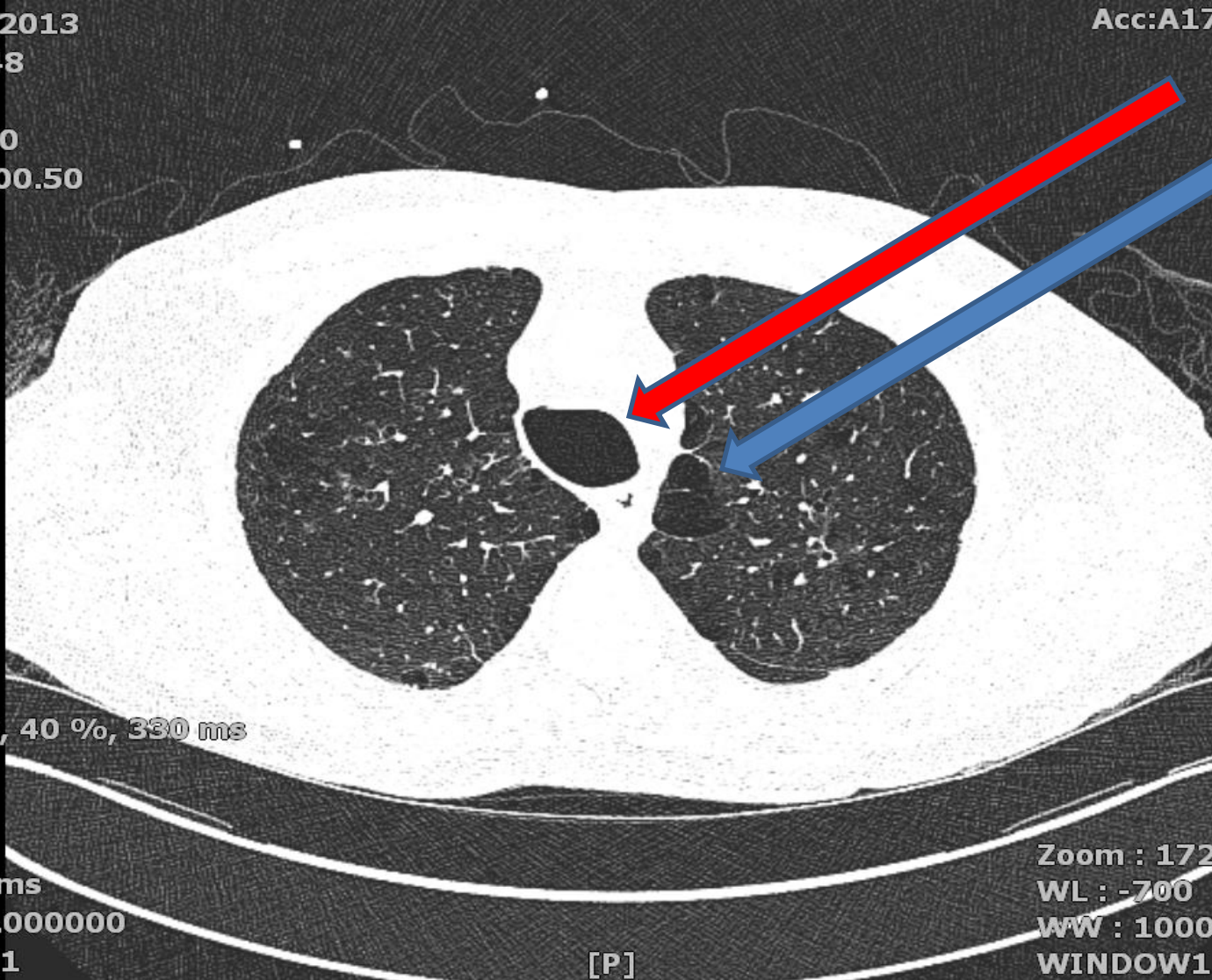
Case 1 B-COS?

03/04/2013
14:04:48

Acc:A175

SL : 1.00
SP : 1100.50

PP:HFS



77 bpm, 40 %, 330 ms

TI 330 ms
kV:120.000000
mAs:111

Zoom : 172.6
WL : -700
WW : 1000
WINDOW1

[P]

Case 1

03/04/2013

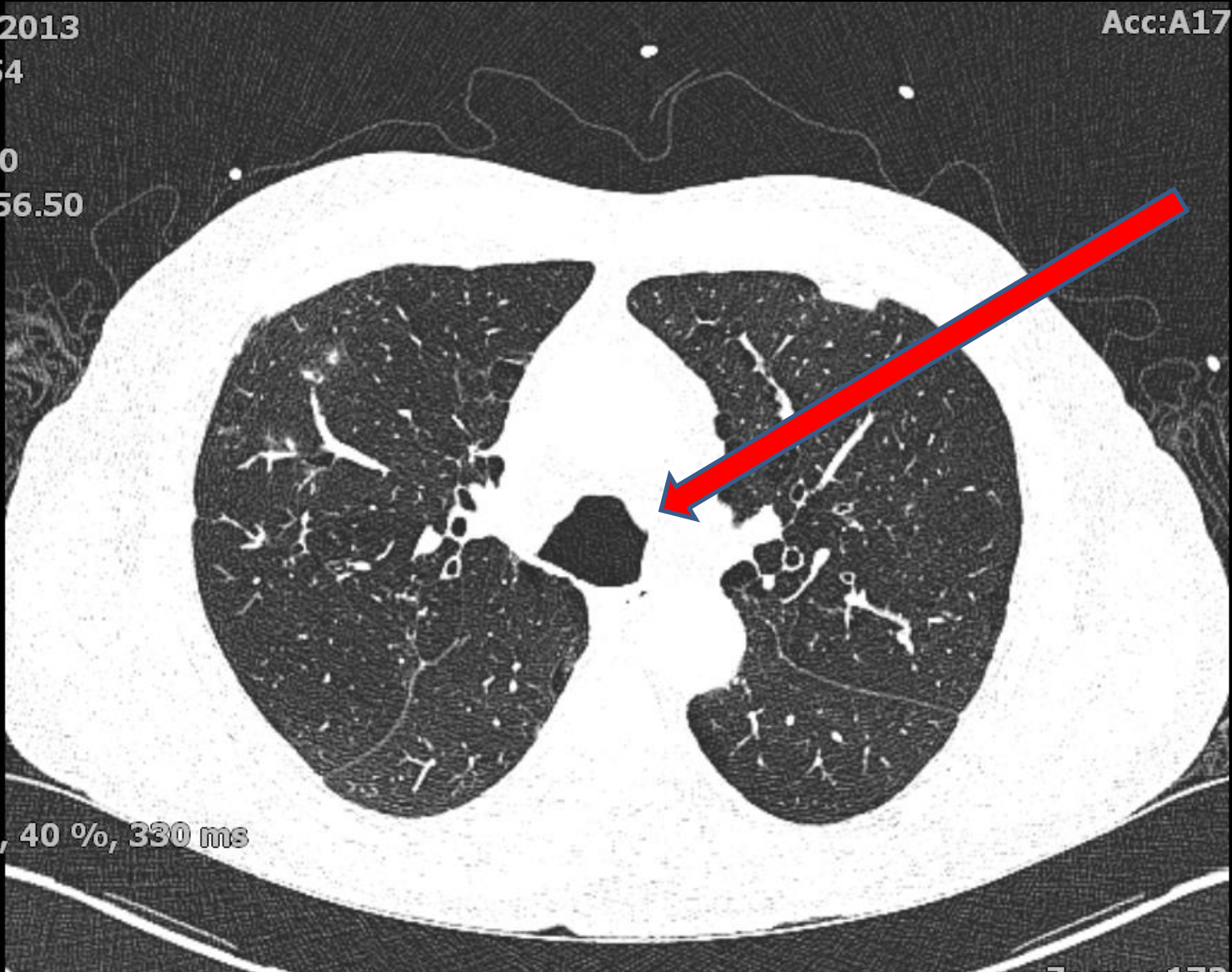
Acc:A175

14:04:54

SL : 1.00

SP : 1056.50

PP:HFS



63 bpm, 40 %, 330 ms

Case 1

- Careful history as child recurrent LRTI
- Mounier Kuhn syndrome PLUS emphysema
- Bronchiectasis and then COPD..?

Case 2: COPD 2012

22/08/2012

13:27:32

SL : 3.00

SP : -182.00

PP:HFS

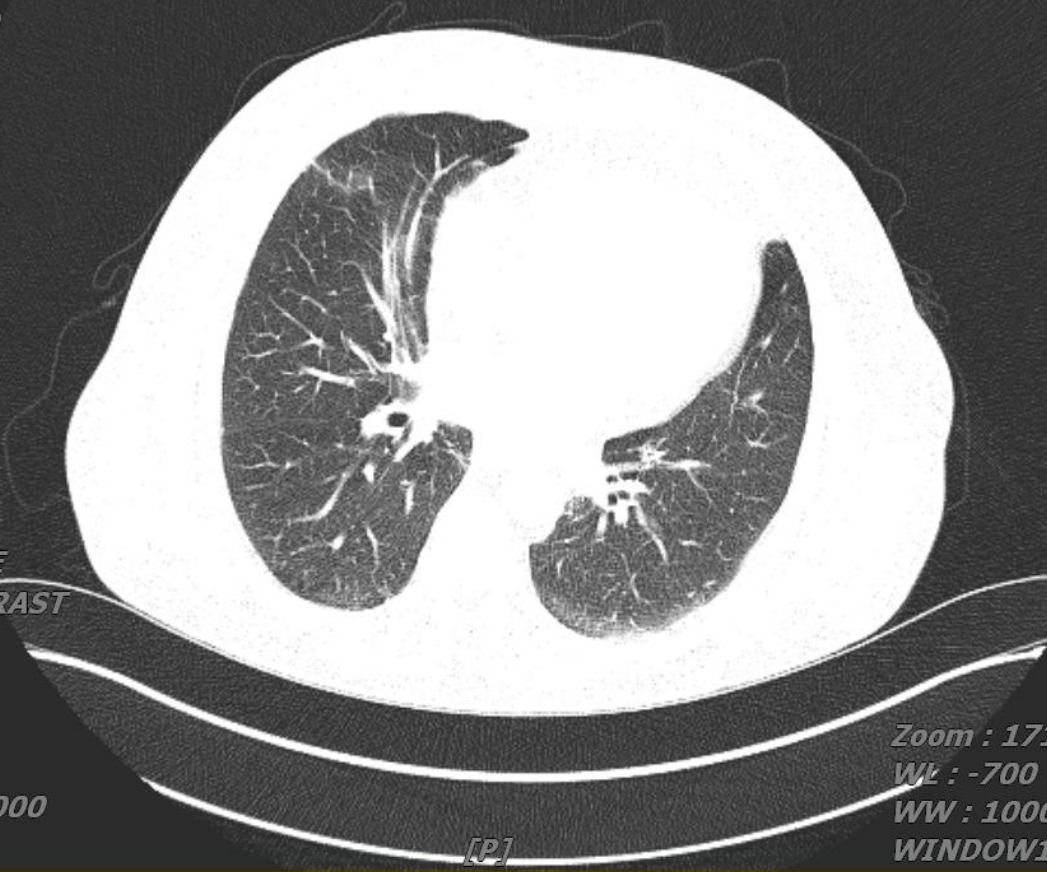
OMNIPAQUE
POST CONTRAST

TI 500 ms

kV:120.000000

mAs:77

Acc:A164



Male

COPD 35 Pk yr
history

Recurrent
exacerbations

HRCT by me ?
Bronchiectasis..

2012 “no
bronchiectasis
seen”..

Zoom : 171

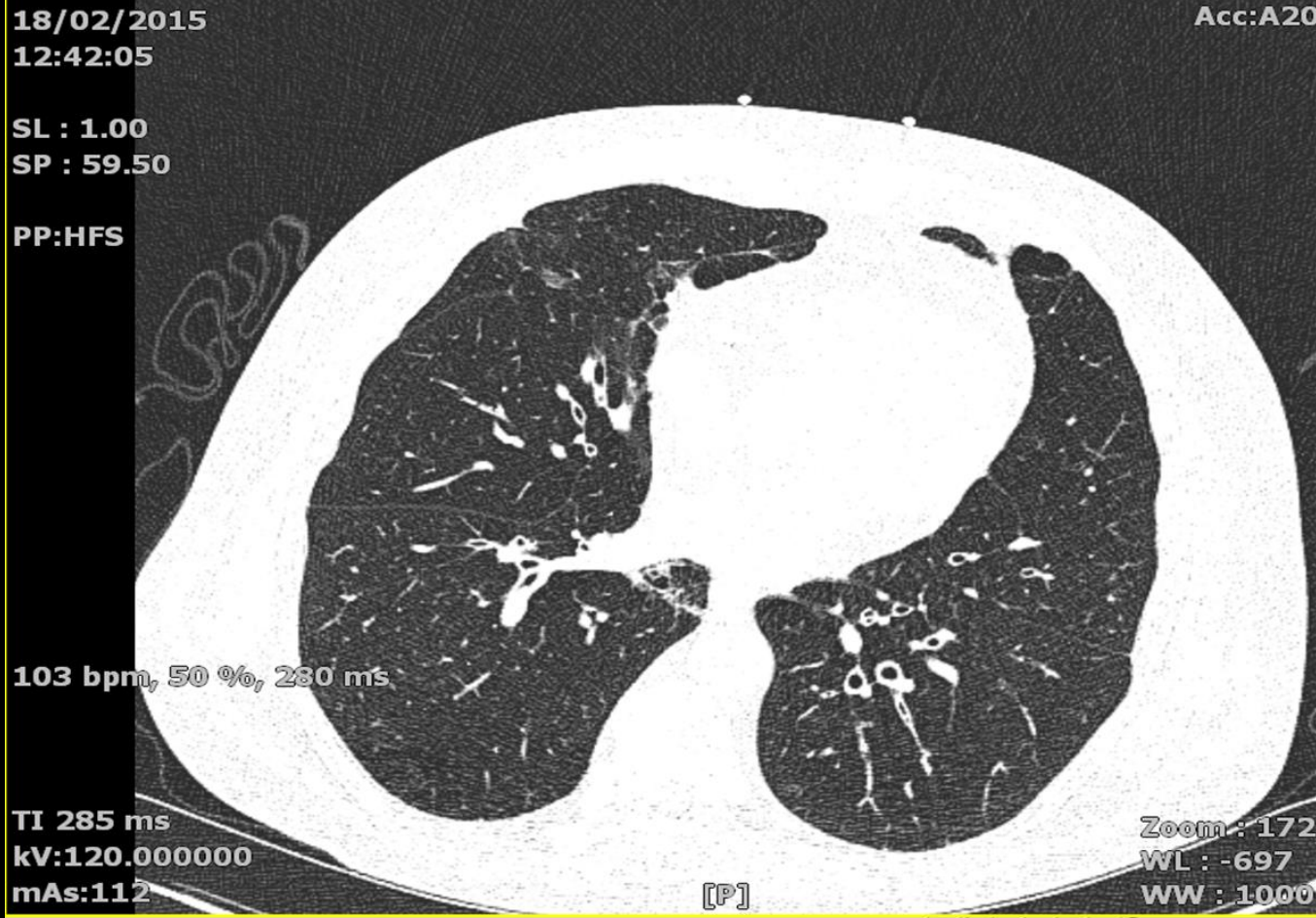
Wk : -700

WW : 1000

WINDOW1

[P]

Case 2: 3 yrs later- BCOS 2015



Male

COPD 35 Pk yr history

Further exacerbations

HRCT by me ?
Bronchiectasis..
Symptoms worse than 2102

“Bilateral multilobar bronchiectasis”..

Case 3: ? COPD associated bronchiectasis

28/01/2015
17:27:44

Acc:A199

SL : 1.00
SP : 0.50

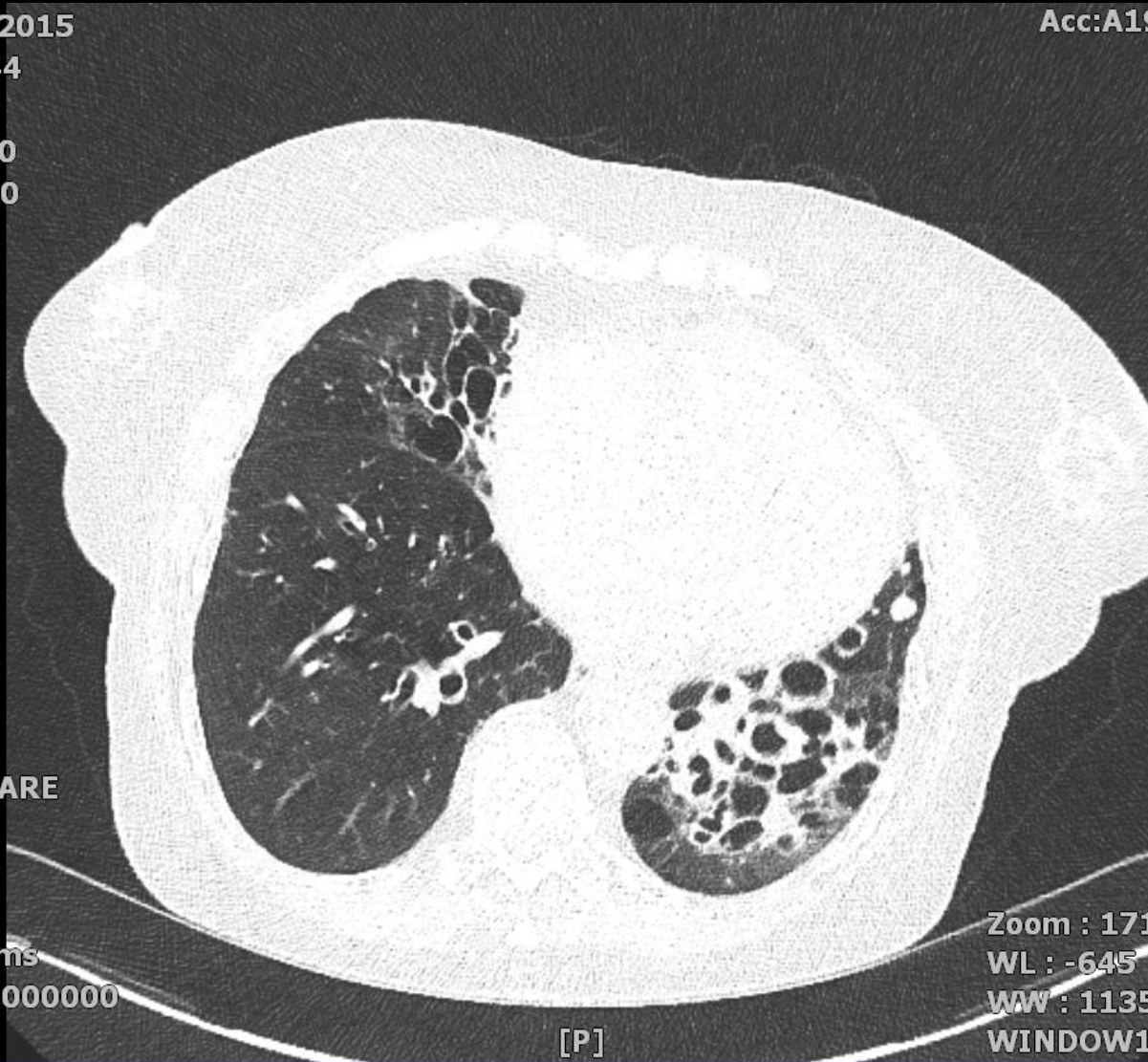
PP:HFS

Female

40 pack
years

Usually
culture
negative

FEV1



X-CARE

TI 285 ms
kV:100.000000
mAs:68

Zoom : 171.
WL : -645
WW : 1135
WINDOW1

[P]

Case 4: "COPD"- ? BCOS

14:12:52

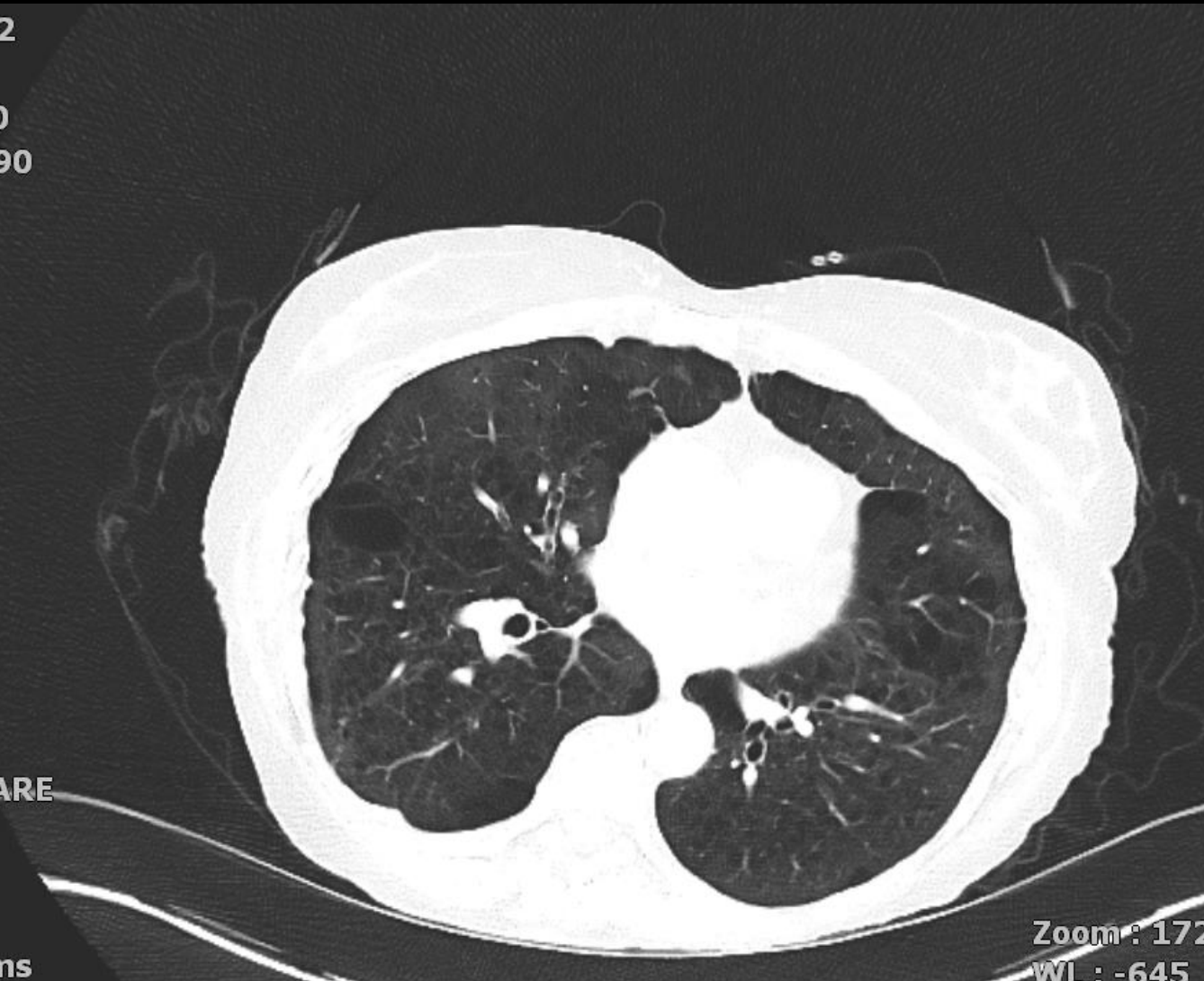
SL : 3.00

SP : 75.90

PP:HFS

X-CARE

TI 285 ms



Zoom : 172.

WL : -645

Prev LVRS
surgery for
advanced
Emphysema

Hx of
recurrent
AE-COPD

Baseline tests as per BTS broncheuictasis guidance

- Hypogammaglobulinaemia ; Immunology review Late diagnosis of CVID
- Now on long term Ivlg
- Likely CVID and COPD mixed

Case 5: BCOS

23/03/2011

15:52:15

SL : 3.00

SP : -222.00

PP:HFS

Acc:AN0006!



TI 500 ms

kV:120.000000

mAs:100

Zoom : 172.

WL : -700

WW : 1000

WINDOW1

- 2011
- 8 Exacerbations per year-
- Referred to COPD clinic
- FEV1 25% pred
- Gentamicin nebulised therapy and physio started after BCOS diagnosed
- 2015 4
- exacerbations per yr and no hospitalisations
- FEV1 30% predicted....

What we don't know...

- What predicts BCOS in COPD (Pseudomonas in sputum)
- Does treating BCOS aggressively reduce admissions or mortality?
 - Is there a genetic locus predicting BCOS (eg MMP1, etc etc)
- Do anti-inflammatory therapies for COPD help or worsen BCOS?
 - ICS, PDE4 inhibitors roles all unclear

Suggested references

- COPD-related bronchiectasis; independent impact on disease course and outcomes. Gatheral T, Kumar N, Sansom B, Lai D, Nair A, Vlahos I, Baker EH. COPD. 2014 Dec;11(6):605-14.
- Bronchiectasis, Exacerbation Indices, and Inflammation in Chronic Obstructive Pulmonary Disease Patel et al Am J Respir Crit Care Med Vol 170. pp 400–407, 2004
- Mortality in non-cystic fibrosis bronchiectasis: a prospective cohort analysis Goeminne et al Respir Med. 2014 Feb;108(2):287-96.
- Pseudomonas aeruginosa isolates in severe chronic obstructive pulmonary disease: characterization and risk factors Gallego et al BMC Pulm Med. 2014; 14: 103.
- Characterisation of COPD heterogeneity in the ECLIPSE cohort. Agusti A1, Respir Res. 2010 Sep 10;11:122. doi: 10.1186/1465-9921-11-122.

	GOLD II		GOLD III			GOLD IV		Comparing			
	Females (n = 380)	Males (n = 574)	p value	Females (n = 293)	Males (n = 618)	p value	Females (n = 77)	Males (n = 219)	p value	GOLD stage within females	GOLD stage within males
Clinical Data											
Age (years)	63.0 ± 7.1	63.8 ± 7.3	0.043	62.6 ± 6.8	64.2 ± 7.0	< 0.001	60.7 ± 6.8	63.0 ± 7.0	0.012	0.034	0.075
Number of exacerbations ^a	0.8 ± 1.2	0.5 ± 0.9	< 0.001	1.2 ± 1.4	0.9 ± 1.3	0.005	1.5 ± 1.6	1.1 ± 1.4	0.044	< 0.001	< 0.001
Imaging											
Emphysema (%)	11.2 ± 9.5	12.7 ± 9.5	0.002	20.1 ± 11.7	20.0 ± 11.5	0.876	27.1 ± 13.7	28.6 ± 12.1	0.435	< 0.001	< 0.001
Bronchiectasis (%)	< 1	2	0.057	3	6	0.044	9	7	0.468	< 0.001	0.003