



Koninklijke Marine



Pulmonale zuurstoftoxiciteit

Eerste resultaten
promotieonderzoek

LTZ 20C (AR) T.T. Wingelaar
Duikerarts-KM
Promovendus AMC (pulmonale zuurstoftoxiciteit)

Duikmedisch Centrum
Rijkszee- en Marinehaven
Postbus 10000
1780 CA Den Helder
088 951 0480



Disclosure belangen spreker

- Duikerarts bij de Koninklijke Marine
- Bestuurslid Nederlandse Onderwatersport Bond (NOB)
- Potentiele belangenverstrengeling: geen.
- Geen relevante relaties met bedrijven.



Zuurstooftoxiciteit

- Cerebraal / pulmonaal
- Onderzoeksopzet
- Eerste resultaten







Pathofysiologie

- Auto oxidatie van NO tot ROS ($\cdot\text{O}_2$, $\cdot\text{OH}$, ONOO^-)
- ROS \rightarrow Angiotensine-II vaatwand \rightarrow vasoconstrictie
- *Breaking point?*
- eNOS en nNOS \rightarrow NO \rightarrow vasodilatatie



Breaking point

- Waarschijnlijk uitputting van scavenger system
 - Rol van SOD en catalase (mn in hippocampus)?
 - Modulatie NMDA en NNA beschermt
- Daling CBF is meetbaar enkele seconden voor insult.
- Herstel van 'tolerantie' bij 15 min $PO_2 < 1.3$



Risicofactoren

- $PO_2 > 1.4$ Hoger geeft sneller klachten
- Exposure Air-brakes, He, N₂
- Stijging CO₂ Sport, hypoventilatie
- Voedingsstatus Muizen, ketogeen dieet?
- Medicatie Cinnarizine wls niet



Predictiemodel

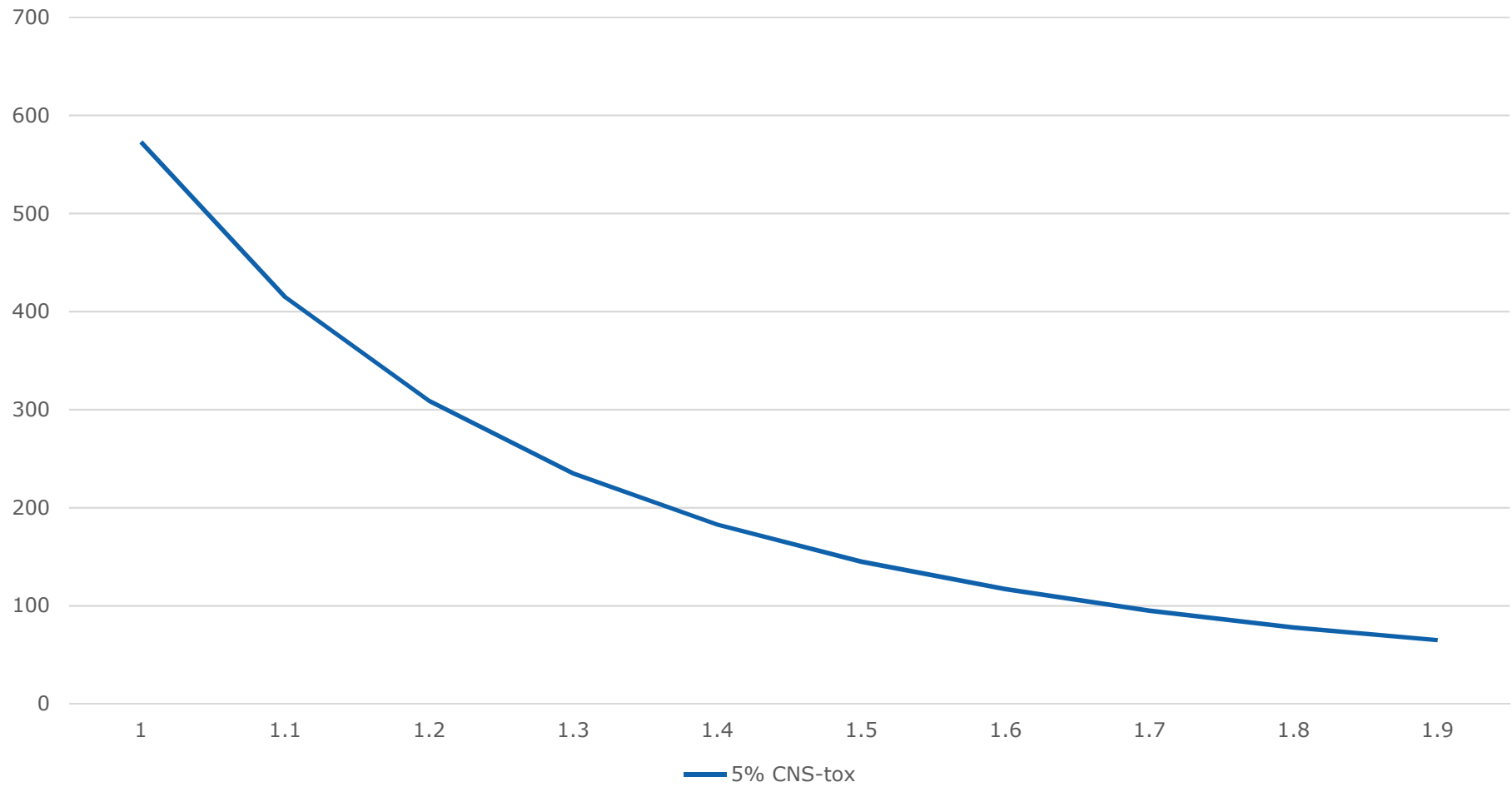
- Incidentie geschat op $\sim 3.5\%$ van de CCR duiken.

$$Z = \frac{\ln(t) - 9.63 + 3.38 \times \ln(\text{PO}_2)}{2.02}$$

- Er is altijd risico, welk risico accepteert je?
 - Behalve bij $\text{PO}_2 < 1.3$
 - Denken we...



Max exposure (min) per PO2 (ATA)





Verder lezen?

MINI REVIEW ARTICLE

Front. Psychol., 25 July 2017 | <https://doi.org/10.3389/fpsyg.2017.01263>



military diving, especially within the domain of the Special Operations Forces (SOF), is one of the most extreme forms of diving. Depending on the task, this type of diving demands different equipment, procedures and training and, therefore, it is totally unlike commercial or civilian diving. For SOF divers, range and endurance, high mobility and stealth, are of utmost importance. To facilitate



Pulmonale zuurstoftoxiciteit

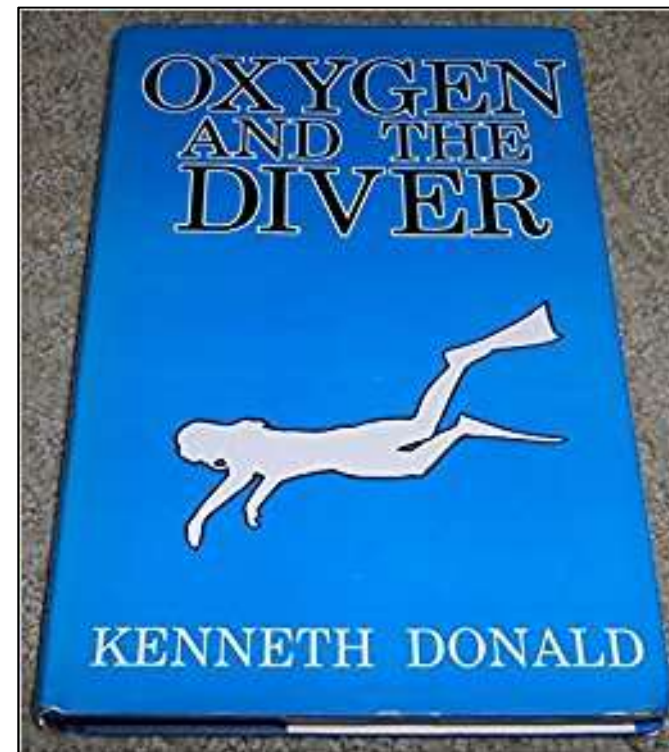
Irritatie luchtwegen

Hoesten

Retrosternale pijn

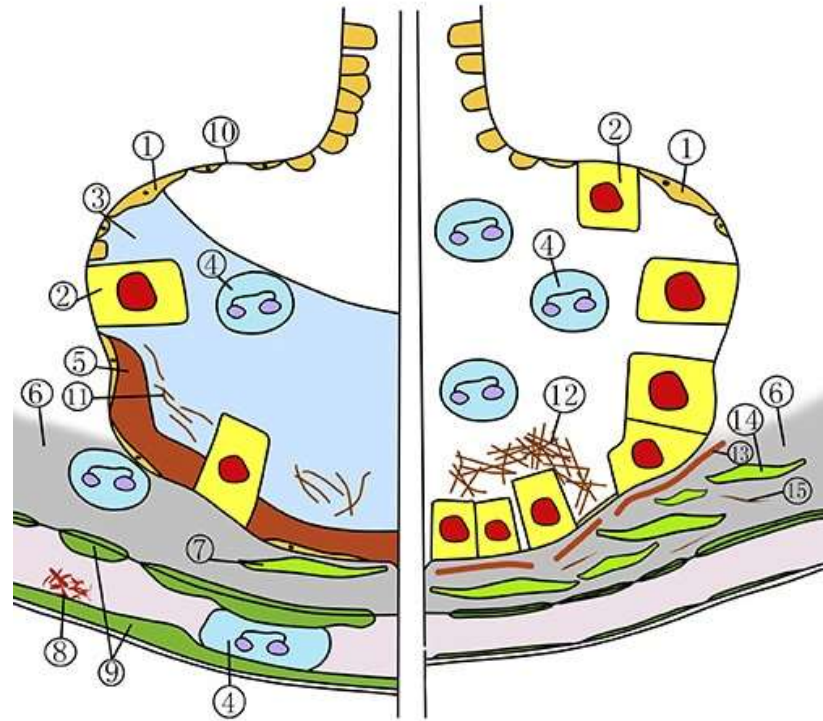
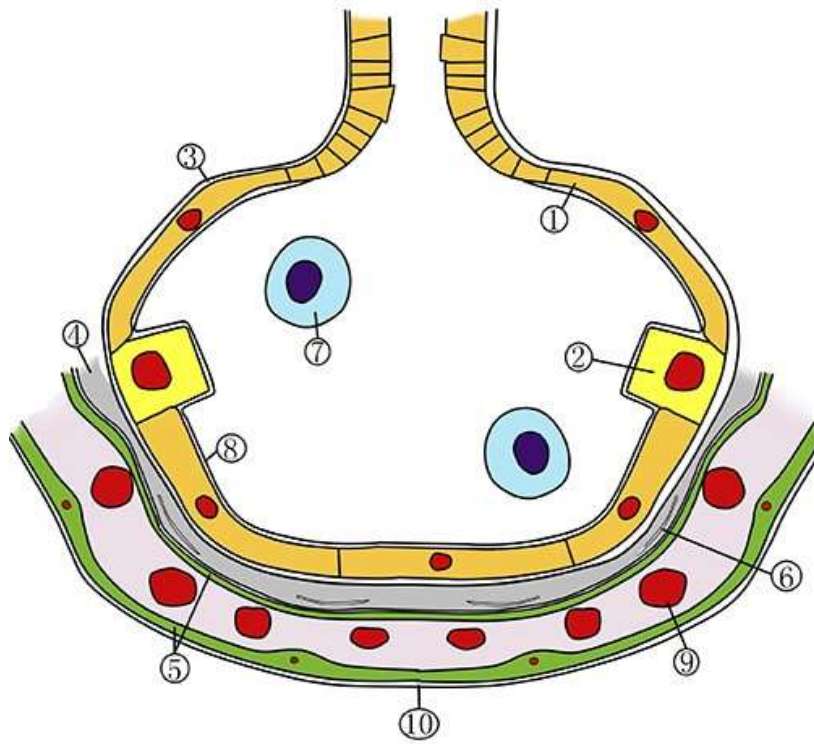
Afname mucusklaring

Daling longfunctie





Pathofysiologie





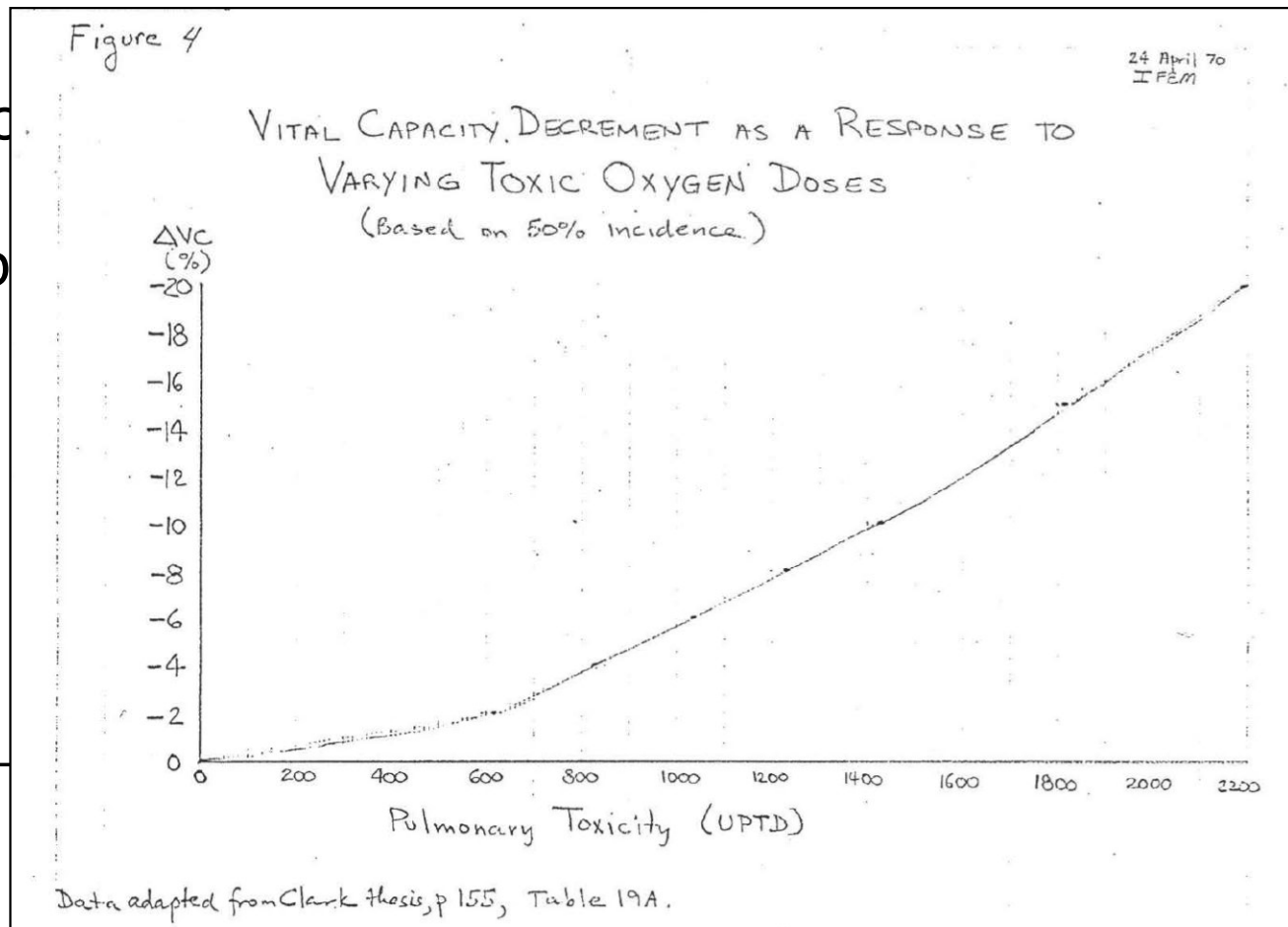
Risicofactoren

Geen idee! :)



Predictiemodel

- Indic
- Op b

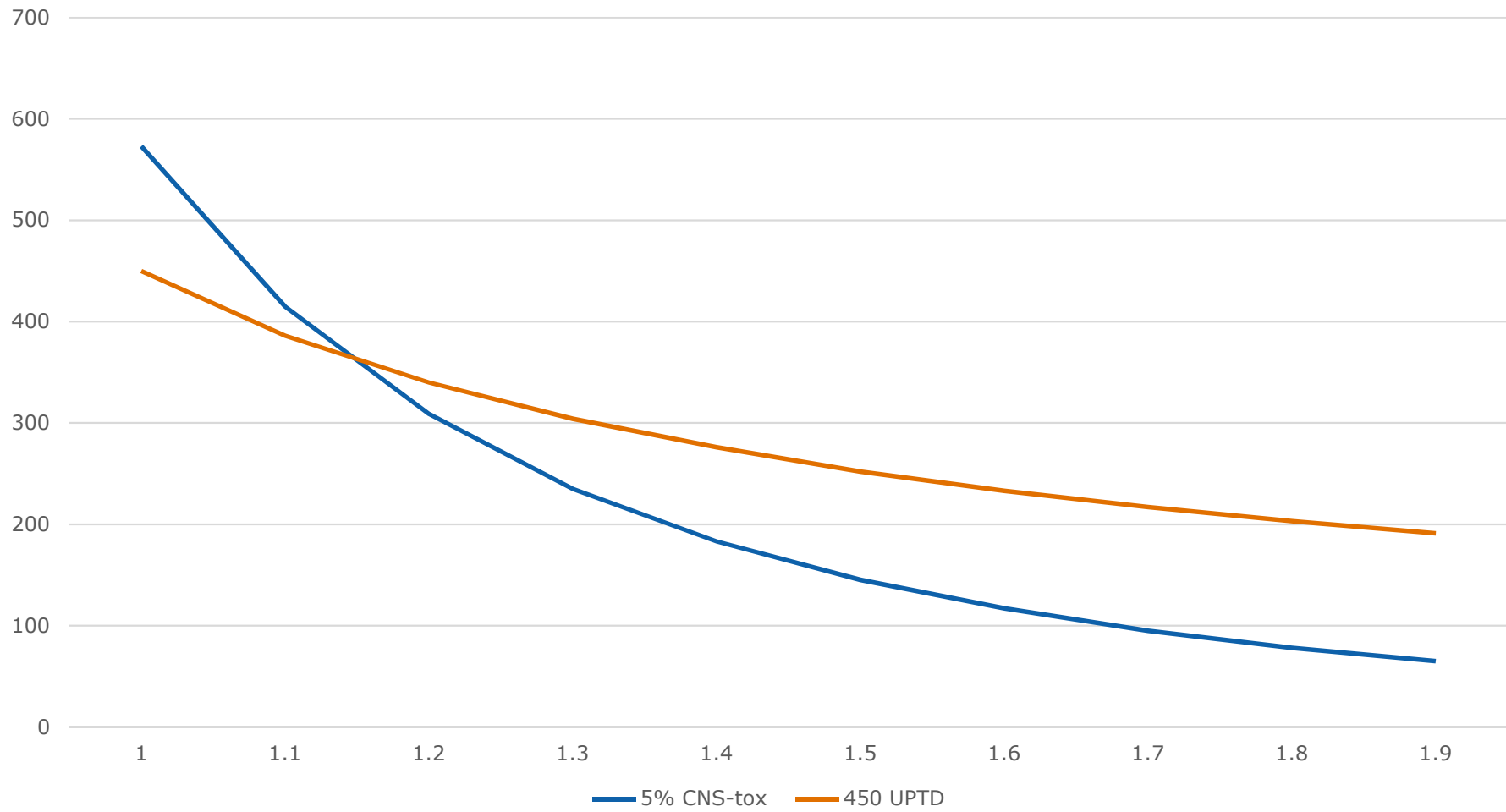


• ΔVC

n-uren)



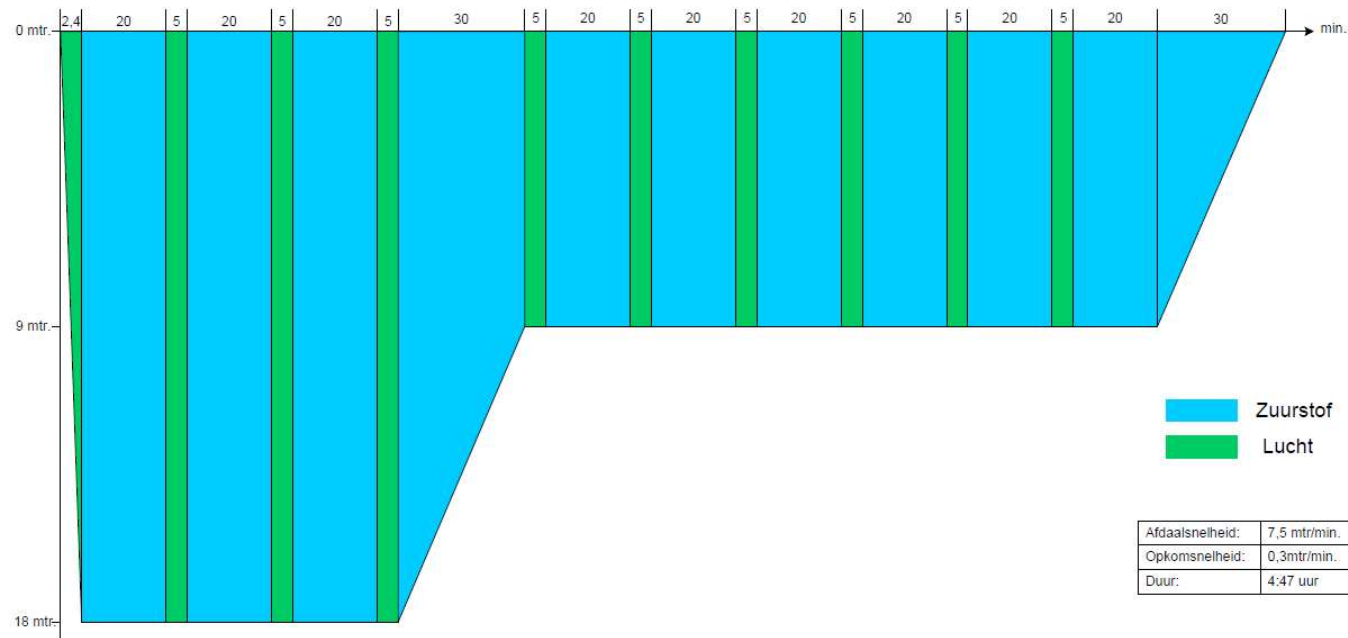
Max exposure (min) per PO2 (ATA)





Veilig, toch?

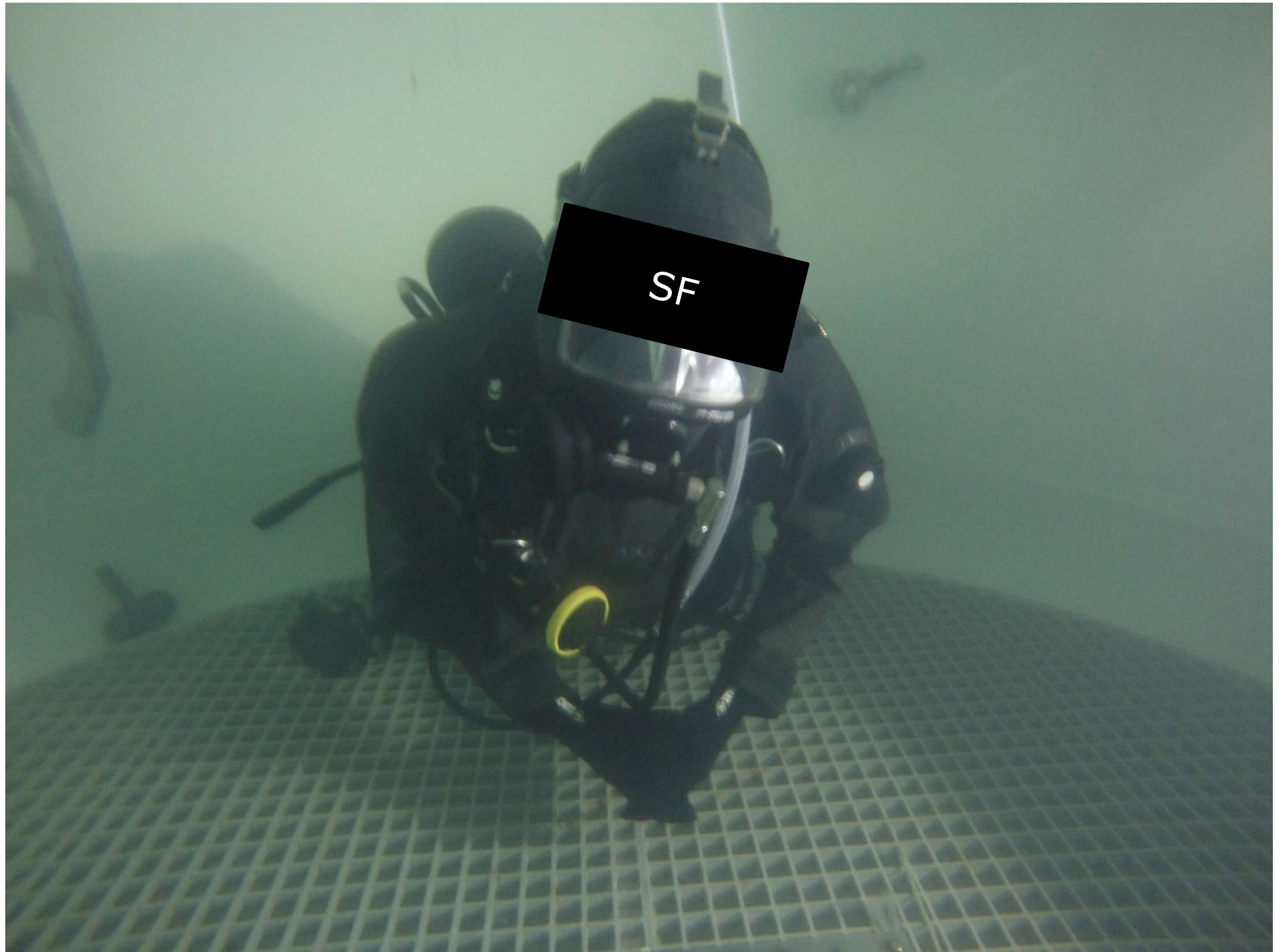
- VKM 007 deel 1:
 - 450 UPTD/dag en max 2250 UPTD/week





Onderzoek feb/mrt 2018

- Twee duiken van 1 uur op 9 MSW
 - Duik A, zuurstof
 - Duik B, lucht
- Zes HBO-tracks van 90 minuten op 15 MSW
 - Altijd zuurstof
- Nadien meting van uitgeademde lucht



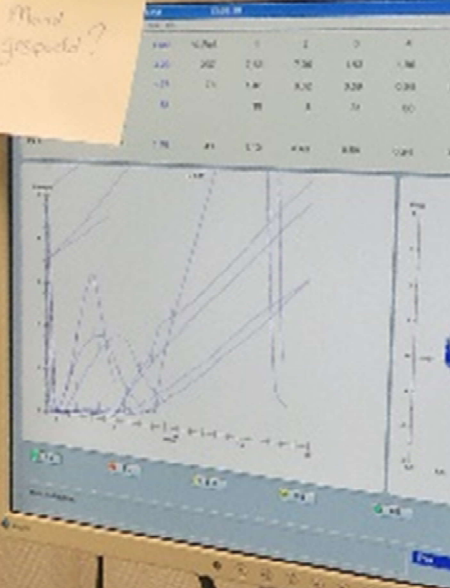
SF





SF

How good?

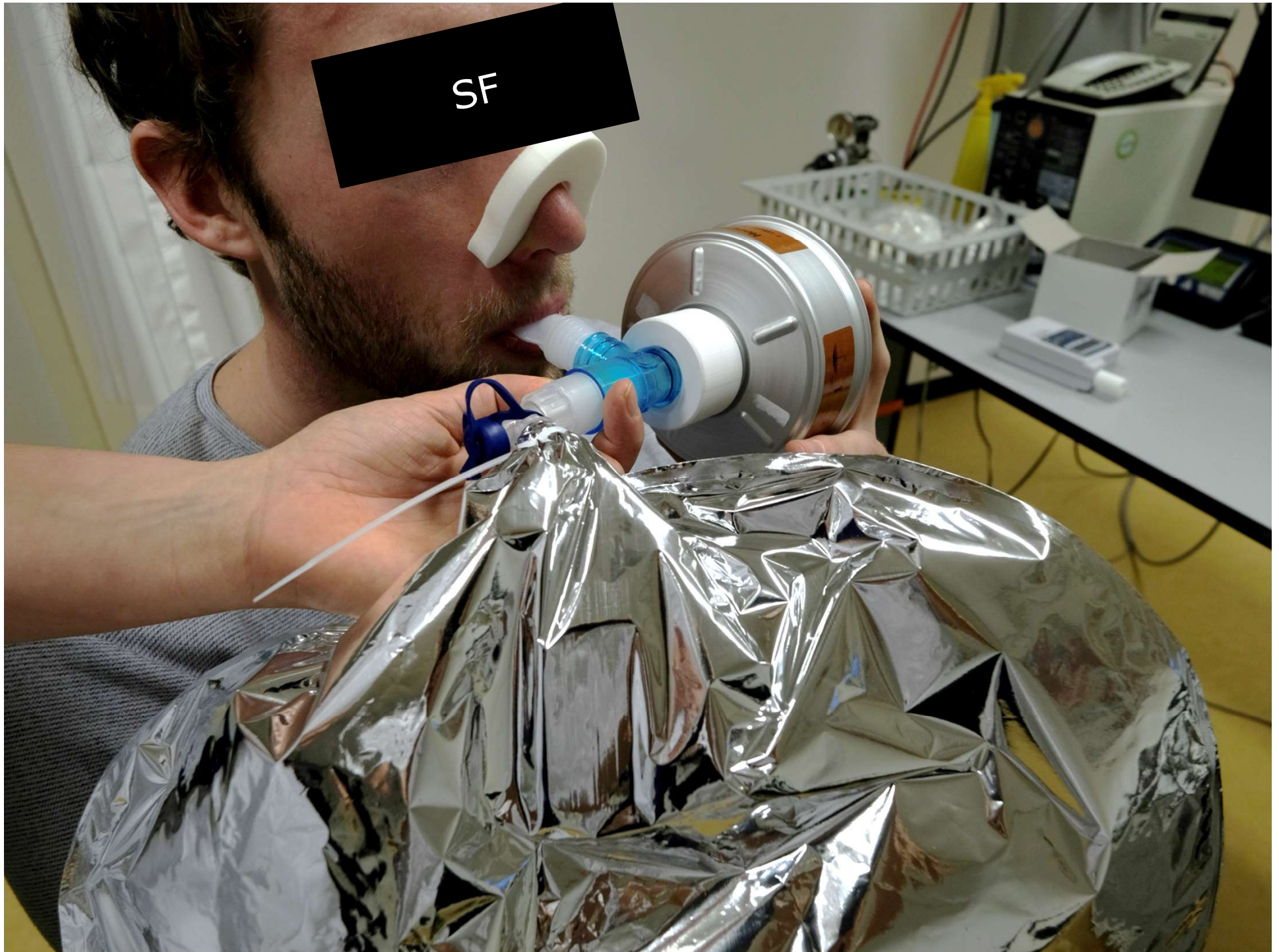


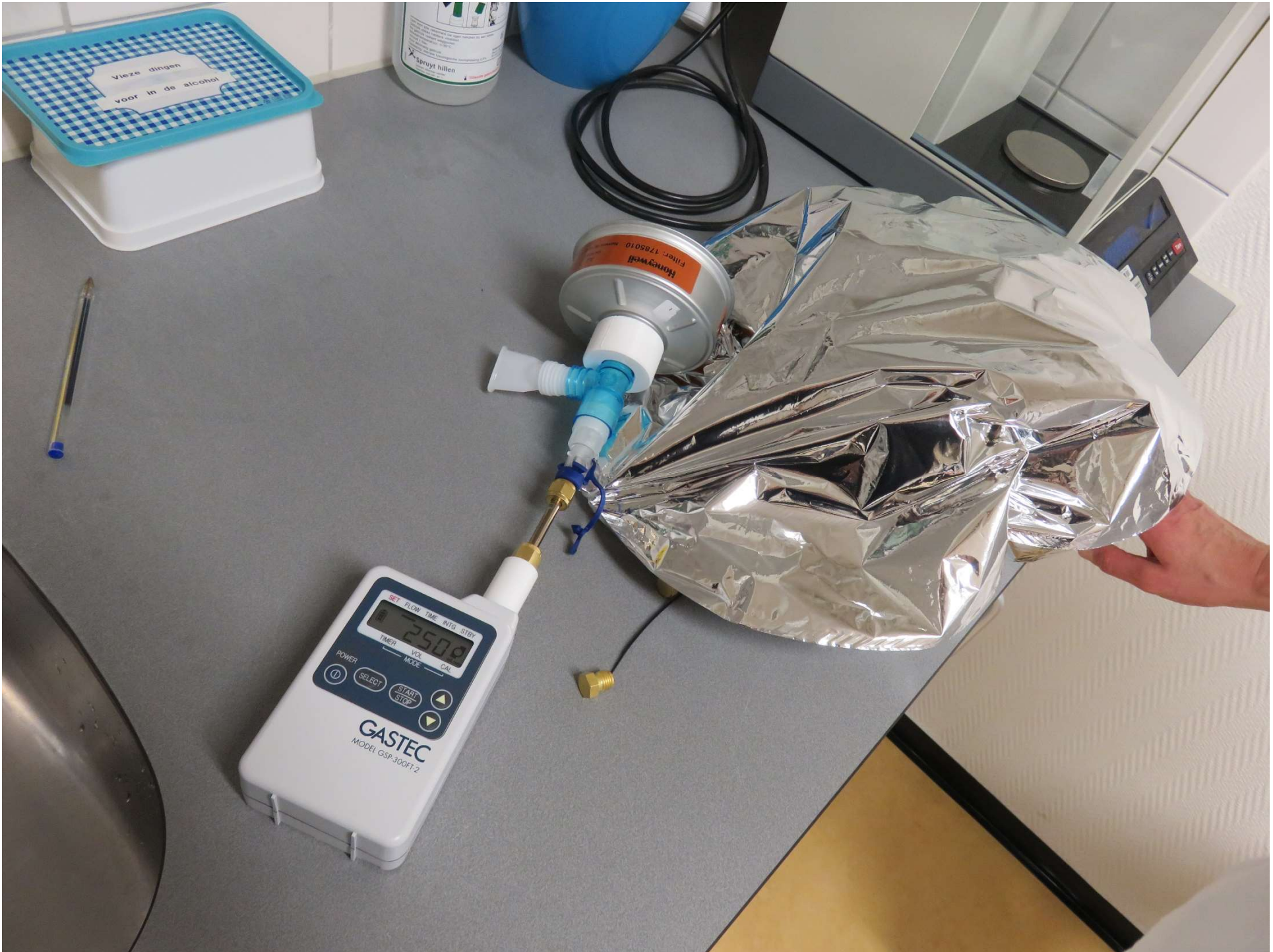
Handwritten notes and forms on the desk, including a yellow sticky note with the text "How good?" and various printed forms with handwritten entries.





SF



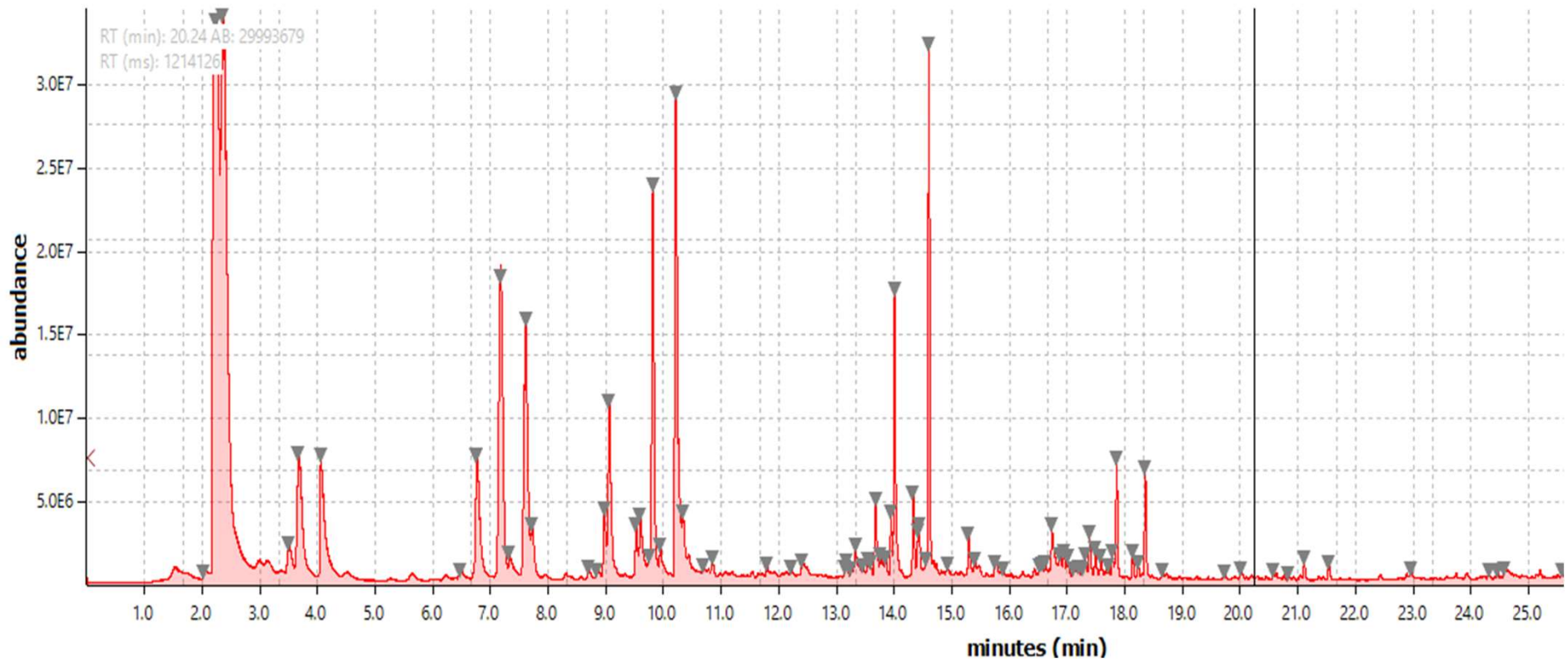








Gas chromatografie / massa spectroscopie





RStudio interface showing R code execution and results.

```

9 # Missing sample of subject 18w08, meetdag 1, visit 2 (tubeID: #010318_1053228) due to failed sampling)
10
11 # Batch correction
12 plot(GCMS_data[,10]) # before batch correction
13 batch = GCMS_data$Measurement_date
14 combat_optimize_peakdata = ComBat(dat=t(GCMS_data[,c(1:3796)]), batch=batch, par.prior=TRUE, prior.plots=FALSE)
15 GCMS_data[,1:3796]=t(combat_optimize_peakdata)
16 plot(GCMS_data[,10]) # after batch correction
17
18 # Sorting data
19 GCMS_data$PID # subject identification
20 GCMS_data$Visit # visit number || 1. Baseline 2. ½h post 3. 1h post 4. 2h post 5. 3h post 6. 4h post
21 GCMS_data$Meetdag # 1 = oxygen 2 = air
22 GCMS_data_sorted=GCMS_data[order(GCMS_data$Meetdag, GCMS_data$Visit, GCMS_data$PID),]
23 GCMS_data_sorted[,c(3800:3802)]
24
25 # Explore data using univariate paired tests
26 m1=which(GCMS_data_sorted$Visit==6 & GCMS_data_sorted$Meetdag==1)
27 m2=which(GCMS_data_sorted$Visit==6 & GCMS_data_sorted$Meetdag==2)
28
29 if(length(m1) > length(m2)){
30   remain=which(GCMS_data_sorted$PID[m1] %in% GCMS_data_sorted$PID[m2])
31   m1=m1[remain]
32 }
33
34 if(length(m2) > length(m1)){
35   remain=which(GCMS_data_sorted$PID[m2] %in% GCMS_data_sorted$PID[m1])
36   m2=m2[remain]
37 }
38
39 p_value=rep(1,3796)
40 for(i in 1:3796){
41   p_value[i]=wilcox.test(GCMS_data_sorted[m1,i] , GCMS_data_sorted[m2,i], paired = TRUE)$p.value
42 }
43 hist(p_value, breaks = 20)
44
45 colnames(GCMS_data_sorted)[which(p_value<0.05)]
46 p_value[which(p_value<0.05)]
47
33:1 (Top Level) R Script

```

Environment History Connections

Global Environment

Data

combat_optimi...	Large matrix (527644 elements, 4.2 ...
GCMS_data	139 obs. of 3802 variables
GCMS_data_sor...	139 obs. of 3809 variables
LMM.aov	List of 4
sig_fragments	62 obs. of 3 variables
sig_fragments...	12 obs. of 43 variables
sorting_matrix	3796 obs. of 3 variables
SumA	12 obs. of 7 variables
SumB	12 obs. of 7 variables
SumC	12 obs. of 7 variables
SumD	12 obs. of 7 variables
SumE	12 obs. of 7 variables
SumF	12 obs. of 7 variables
SumG	12 obs. of 7 variables
SumZ	12 obs. of 7 variables

Values

batch	int [1:139] 10318 10318 10318 10318 1...
dump	62L
i	43L
m1	int [1:11] 60 61 62 63 64 65 66 67 68...

Files Plots Packages Help Viewer

Zoom Export

GCMS_data[,10]

Index

```

~/Promotie/Onderzoeksmat/15 - Statistics/15.2 Raw Datasets/
> hist(p_value, breaks = 20)
> colnames(GCMS_data_sorted)[which(p_value<0.05)]
[1] "x39.271" "x41.592" "x42.592" "x43.995" "x44.945" "x44.598" "x50.412" "x53.592" "x54.899" "x56.41
1" "x56.592" "x57.411" "x57.592" "x66.103"
[15] "x67.591" "x67.576" "x67.321" "x69.592" "x70.794" "x70.411" "x70.592" "x71.411" "x71.592" "x72.41
0" "x74.544" "x75.827" "x85.592" "x86.592"
[29] "x87.880" "x88.826" "x93.1302" "x96.1084" "x99.534" "x100.411" "x111.1031" "x112.843" "x113.1620" "x114.5
92" "x115.844" "x115.547" "x115.964" "x115.592"
[43] "x126.798" "x131.2" "x133.798" "x150.413" "x151.803" "x154.1147" "x156.1140" "x160.1380" "x163.1141" "x165.8
94" "x166.226" "x167.225" "x167.413" "x168.991"
[57] "x174.136" "x181.1031" "x188.995" "x192.811" "x195.1030" "x198.210" "x200.817" "x201.995" "x201.608" "x201.8
17" "x203.995" "x204.817" "x208.1877" "x215.136"
[71] "x225.844" "x228.413" "x229.995" "x229.818" "x229.1975" "x232.136" "x235.408" "x240.136" "x241.259" "x242.2
59" "x246.1975" "x248.136" "x250.342" "x254.342"
[85] "x254.816" "x256.162" "x260.853" "x264.136" "x264.259" "x269.862" "x274.817" "x274.136" "x284.343" "x297.2
59" "x300.259"

```



Geïdentificeerde stoffen

2-4-Dimethylhexaan

Cyclohexaan

3-(1,1-dimethylethoxy)methyl]heptaan

3-Methylnonaan

Nonanal

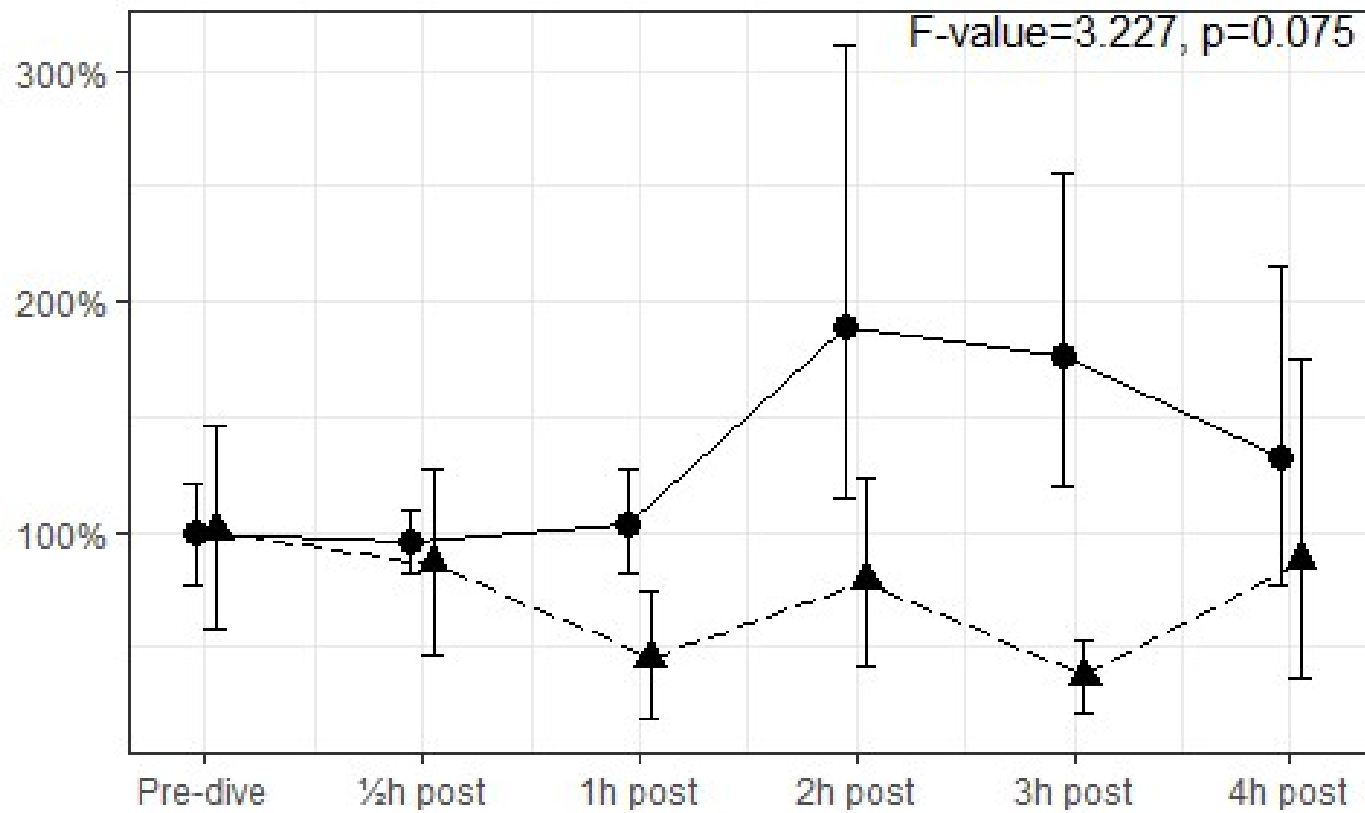
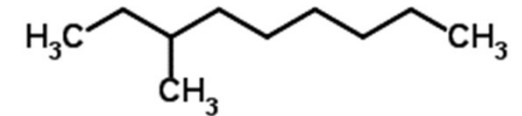
Decaan

Decanal



b. 3-Methylnonane

Typical fragments (mz): 41, 43, 55, 56, 57 and 71

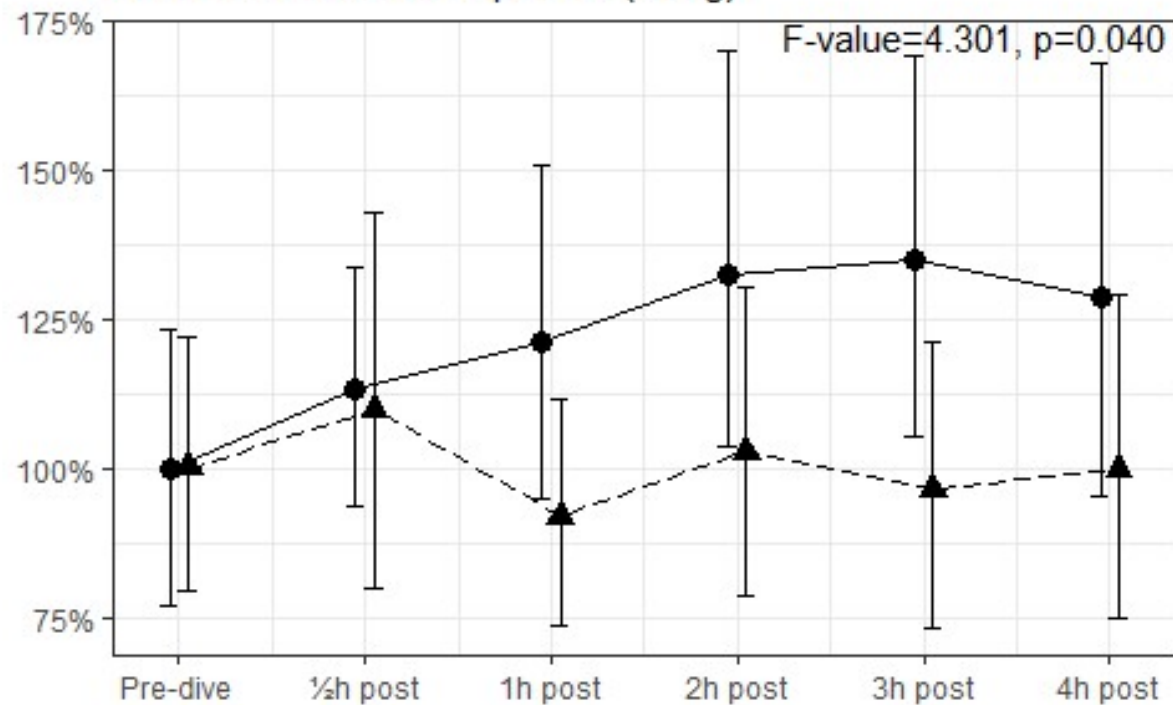




Alle gevonden stoffen gecombineerd

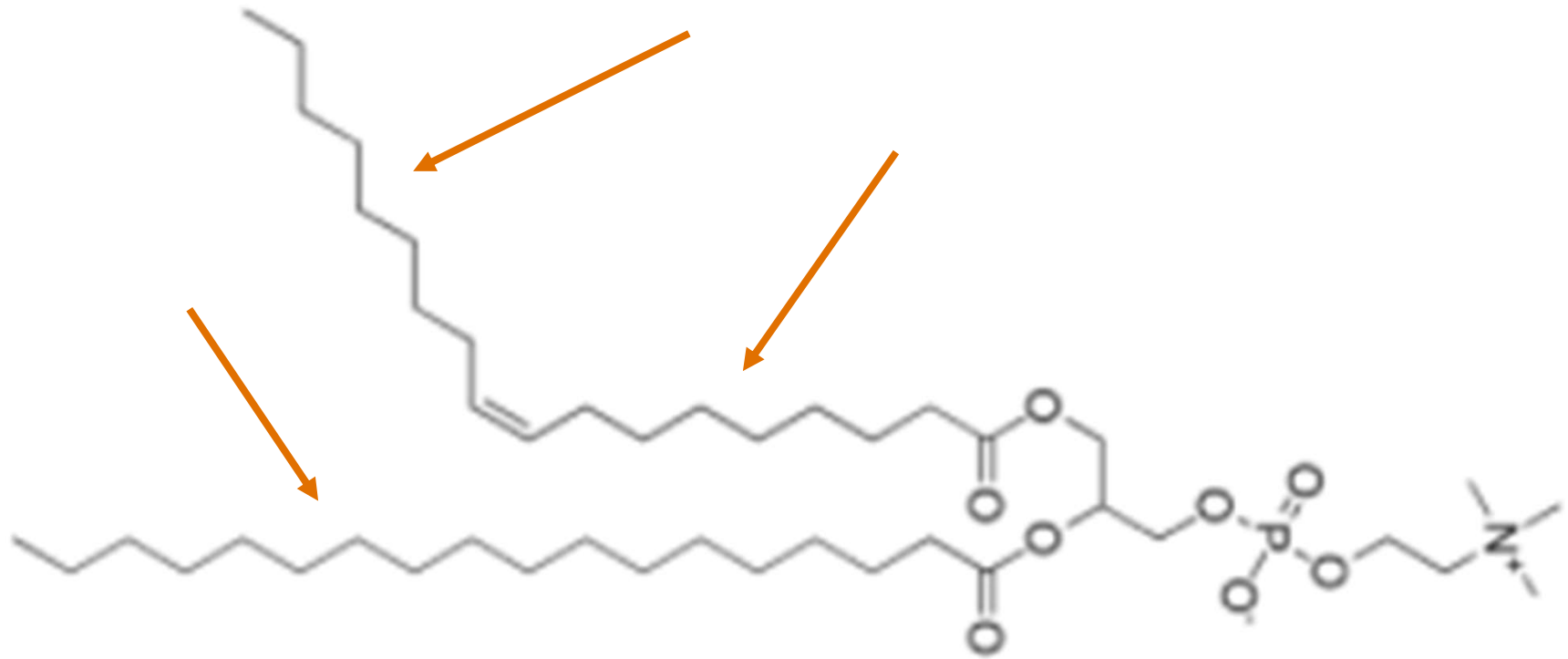
h. Combined VOC profile*

All aforementioned compounds (a to g)



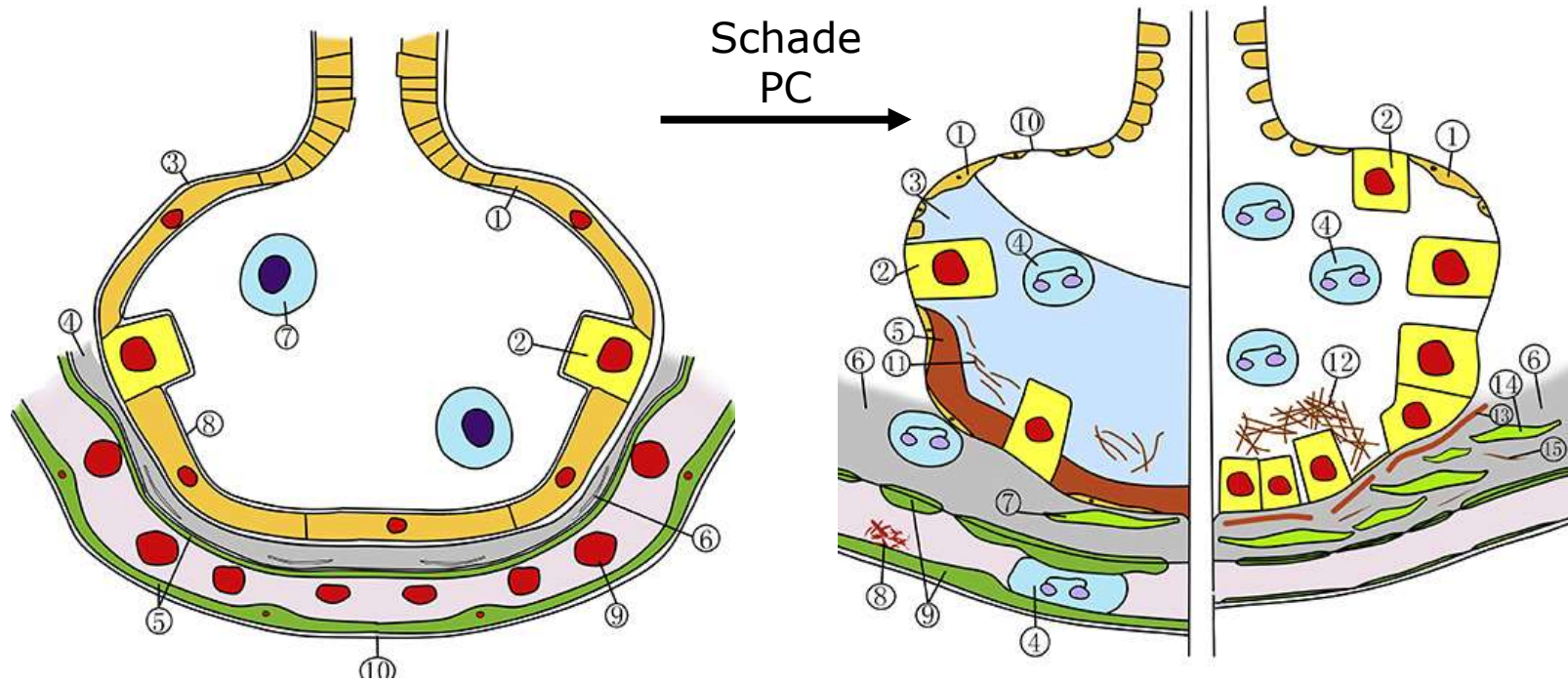


Phosphatidylcholine (PC)





Pulmonale zuurstoftoxiciteit





What's on the horizon?

- Data 'droge tracks'
- Vergelijking eNose met GCMS
- Veldmetingen met MARSOF (okt/nov 2018)