pbr28 test-retest

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Contents

| Aims | 1 |
|---|-----------------|
| Libraries CRAN libraries | 2 |
| Demographic Data tidying the demographic data | 3 |
| TACs and Blood Data | 3 |
| Creating logan_tstar Plotting logan_tstar | |
| Define functions for fitting the models | 10 |
| Fit kinetic models Plot 2tcm | 10 10 |
| new plot 2tcm Plot ma1 | |
| Test-retest trt preparation | |
| Interregional Correlation | 2 6 |
| | 29 |

Aims

The aim of this assignment is to analyze the PK11195 data in kinfitr

Libraries

CRAN libraries

installing packages

```
install.packages("stringr")
install.packages("corrplot")
```

```
install.packages("grid")
install.packages("gridExtra")
install.packages("RColorBrewer")
install.packages("psych")
install.packages("readxl")
install.packages("pracma")
install.packages("lme4")
install.packages("rjags")
install.packages("knitr")
install.packages("corrplot")
install.packages("corrplot")
install.packages("kableExtra")
install.packages("tidyverse")
```

First, the libraries for the analysis and plotting are loaded.

```
library(stringr)
library(corrplot)
library(grid)
library(gridExtra)
library(RColorBrewer)
library(psych)
library(readxl)
library(pracma)
library(jracma)
library(ime4)
library(complot)
library(corrplot)
library(corrplot)
library(kableExtra)
library(tidyverse)
```

Non-CRAN libraries

The libraries above can be installed from CRAN. Those which cannot are installed as follows:

```
install.packages("devtools") # If you do not already have devtools
devtools::install_github("mathesong/kinfitr")
devtools::install_github("mathesong/granviller")
devtools::install_github("mvuorre/vmisc")
devtools::install_github("mathesong/kipettools")
devtools::install_github("mathesong/relfeas")
```

Loading Non_CRAN libraries and setting theme

```
library(kinfitr)
library(vmisc)
library(kipettools)
library(granviller)
library(relfeas)
library(pander)

theme_set(theme_light())
```

Creating folders using "initProjectFolder()"

```
initProjectFolder()
```

Demographic Data

Here, the demographic data is loaded in.

```
demog <- read_excel('DerivedData/TrT_chemistry_demograph.xlsx')</pre>
```

tidying the demographic data

TACs and Blood Data

First, we must read in the TAC and blood data. It should be noted that the blood data is already dispersion corrected, and the plasma data is already metabolite corrected, thus the plasma fraction is set to 100% in the input data frame. It should also be noted that we set all negative values of both blood and plasma radioactivity concentrations to zero.

```
tacdata <- read_csv("DerivedData/tacdata.csv") %>%
  group_by(PET) %>%
  nest(.key = 'tacdata')
blooddata <- read_csv("DerivedData/blooddata.csv") %>%
mutate(Cbl.disp.corr = ifelse(Cbl.disp.corr < 0, 0, Cbl.disp.corr),</pre>
Cpl..metabcorr. = ifelse(Cpl..metabcorr. < 0, 0, Cpl..metabcorr.)) %>%
  group by (PET) %>%
  nest(.key='blooddata') %>%
  mutate(input = map(blooddata, ~blood_interp(
            t_blood = .x$ABSS.sec/60, blood=.x$Cbl.disp.corr,
            t_plasma=.x$ABSS.sec/60, plasma=.x$Cpl..metabcorr.,
             t parentfrac = 1, parentfrac=1 ) ))
tacs <- inner_join(tacdata, blooddata) %>%
separate(PET, c("Subjname", "PETNo"), sep='_', remove = F, convert=T)
tacs <- tacs %>%
  inner_join(demog) %>%
  arrange (PET)
saveRDS(tacs, 'DerivedData/tacs.rds')
```

#Read tacs.rds and create delay fit and inputshift

Here, the delay and blood bolume fraction are fitted using the whole brain ROI using 2TCM.

```
tacs <- readRDS('DerivedData/tacs.rds')
tacs <- tacs %>%
```

New weights with kinfitr::weights create

```
#Creating start and end times and
#removing the old weights, so that there is no mix-up later on

# tacdata <- names(tacs$tacdata[[1]])

tacs <- tacs %>%
    unnest(tacdata, .drop = F) %>%
    select(-Weights)

# New weights

tacs$Weights <- weights_create(t_start = tacs$StartTime/60, t_end = (tacs$StartTime + tacs$Duration)/60
#Nest

tacs <- tacs %>%
    nest(-(PET:Times), .key = 'tacdata')
```

Summary Statistics again

Below are presented some summary statistics of the demographic data. What's up with kurtosis?

```
tacs %>%
  select(Age, InjectedRadioactivity = injRad) %>%
  describe() %>%
  pandoc.table(digits=3, caption = "Summary Statistics", split.tables=Inf)
```

creating logan_tstar

```
logantstar <- function(tacdata, input, inpshift) {
  Logan_tstar(t_tac = tacdata$Times/60, input = input, lowroi = tacdata$FC, medroi = tacdata$CBL, hig
}

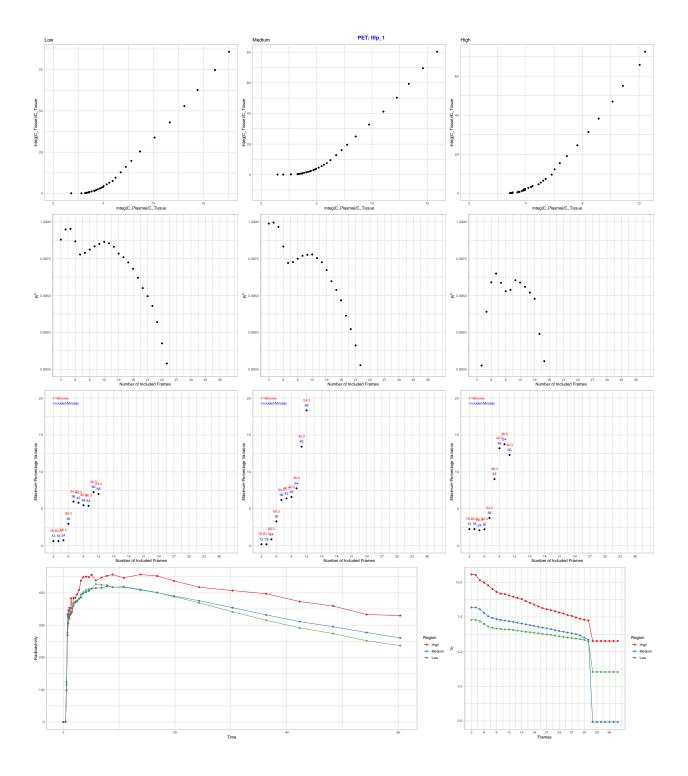
tacs <- tacs %>%
  group_by(Subjname, PETNo) %>%
  mutate(logan_tstar = pmap(list(tacdata, input, inpshift), logantstar))

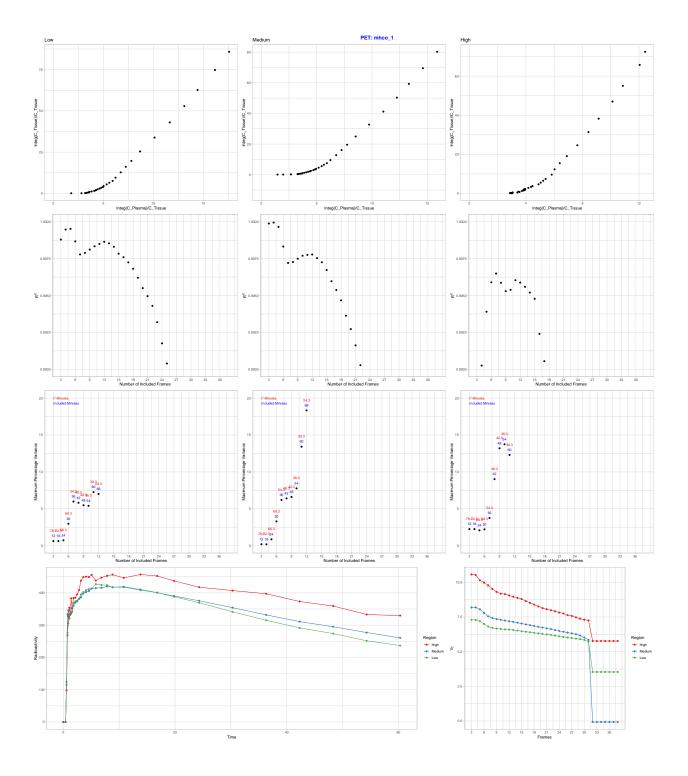
#Rearrangement of the Data into Long Format
tacs_long <- tacs %>%
  unnest(tacdata, .drop = FALSE) %>%
  select(-Weights)
```

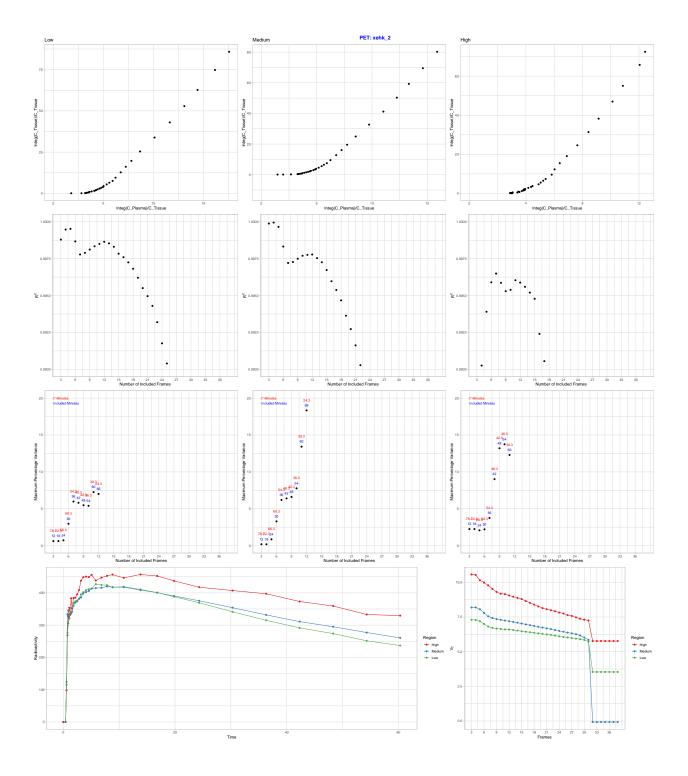
```
tacs_long$weights = weights_create(t_start = tacs_long$StartTime/60, t_end = (tacs_long$StartTime + tac
tacs_long <- tacs_long %>%
gather(Region, TAC, -(PET:Times), -(StartTime:weights)) %>%
group_by(PET, Subjname, PETNo, Region) %>%
nest(-(blooddata:logan_tstar), .key = 'tacdata')

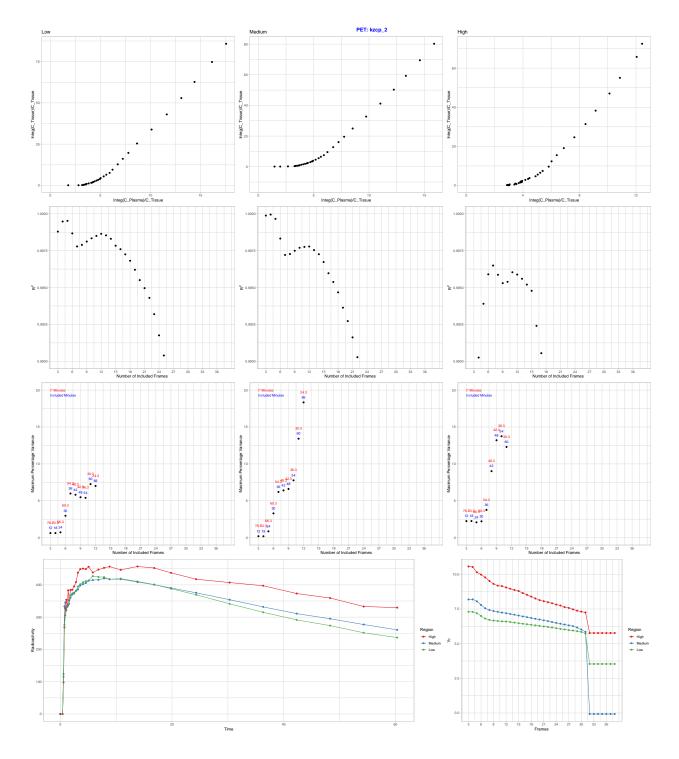
tacs_long <- tacs %>%
    select(PET, Subjname, PETNo, blooddata:logan_tstar) %>%
    inner_join(tacs_long, by = c("PET", "Subjname", "PETNo"))
```

Plotting logan_tstar









All 4 tstar plots on a single page

Note: I would like to have the "draw_figure_label" be drawn a bit above the first PET, but that does not seem to be happening. Should I just skip it? I Placed the plots in a single column because it was a little hard distinguishing where one ands and another begins in a 2×2 format. Perhaps one could put borders and then the 2×2 would work better?

```
plot_grid(plotlist = tstar_fits$logan_tstar, ncol = 2, nrow = 1, labels = paste('PET:',tstar_fits$PET),
    draw_figure_label("t*", position = "top", fontface = "bold", size = 32, colour = "red")
```

Define functions for fitting the models

Fit kinetic models

```
set.seed(123)

tacs_long <- tacs_long %>%

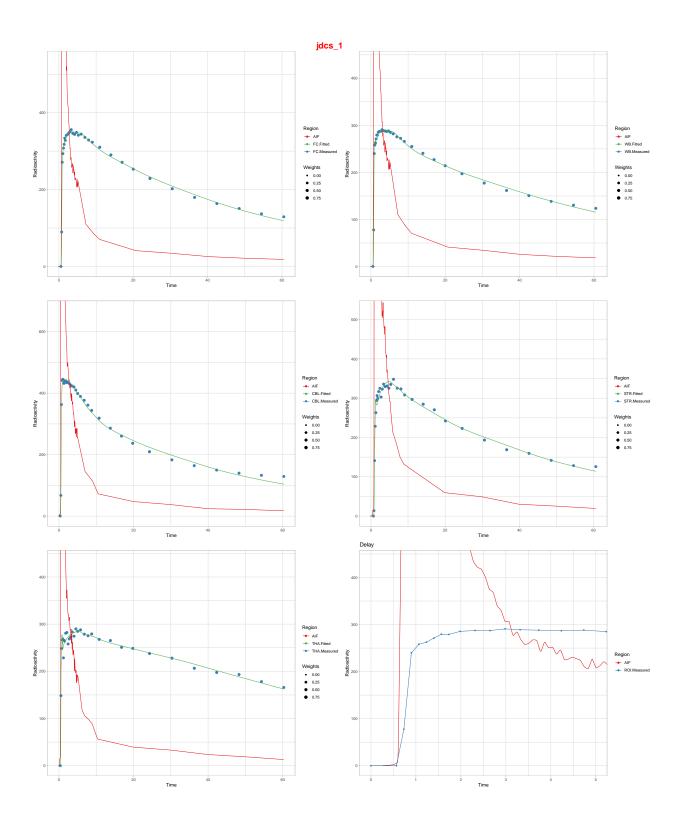
# 2TCM using fitted vB and delay
mutate(fit_2tcm= pmap(list(tacdata, input, delayFit), fit2tcm)) %>%
mutate(Vt_2tcm = map_dbl(fit_2tcm, c('par', 'Vt'))) %>%

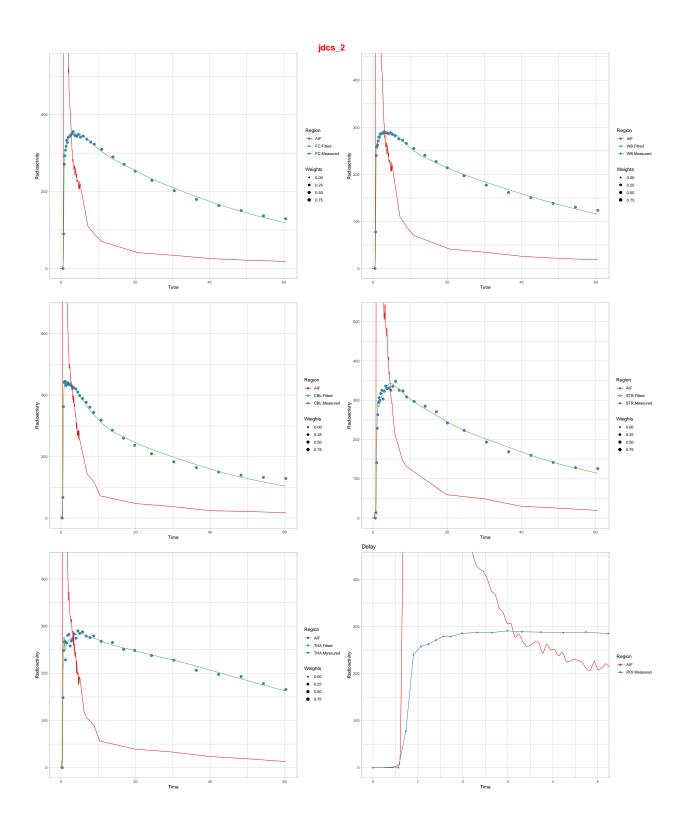
# MA1
mutate(fit_ma1 = pmap(list(tacdata, input, delayFit), fitma1)) %>%
mutate(Vt_ma1 = map_dbl(fit_ma1, c('par', 'Vt'))) %>%

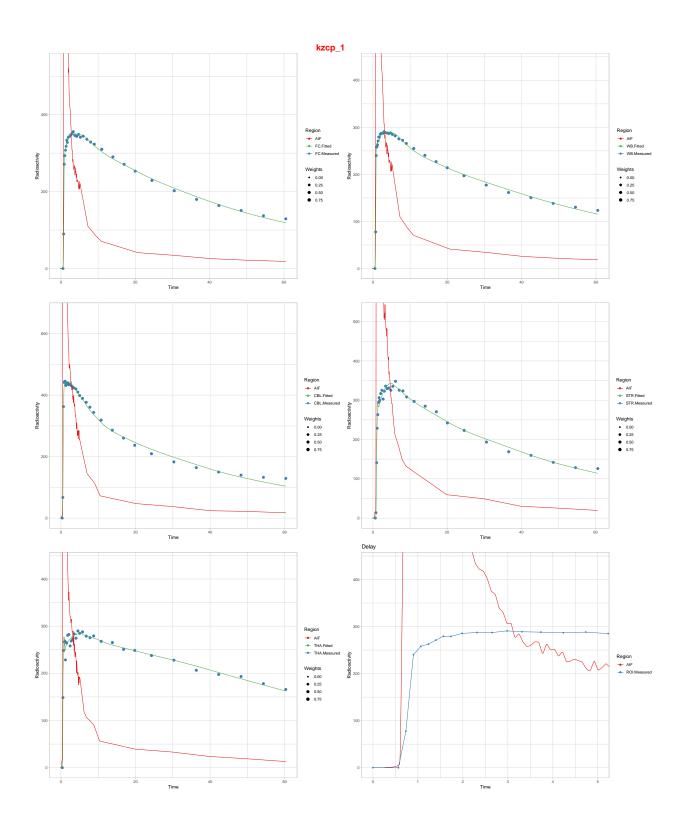
#Loganplot
mutate(Loganfit = pmap(list(tacdata, input, delayFit), fit_Logan)) %>%
mutate(Vt_Logan = map_dbl(Loganfit, c("par", "Vt")))
```

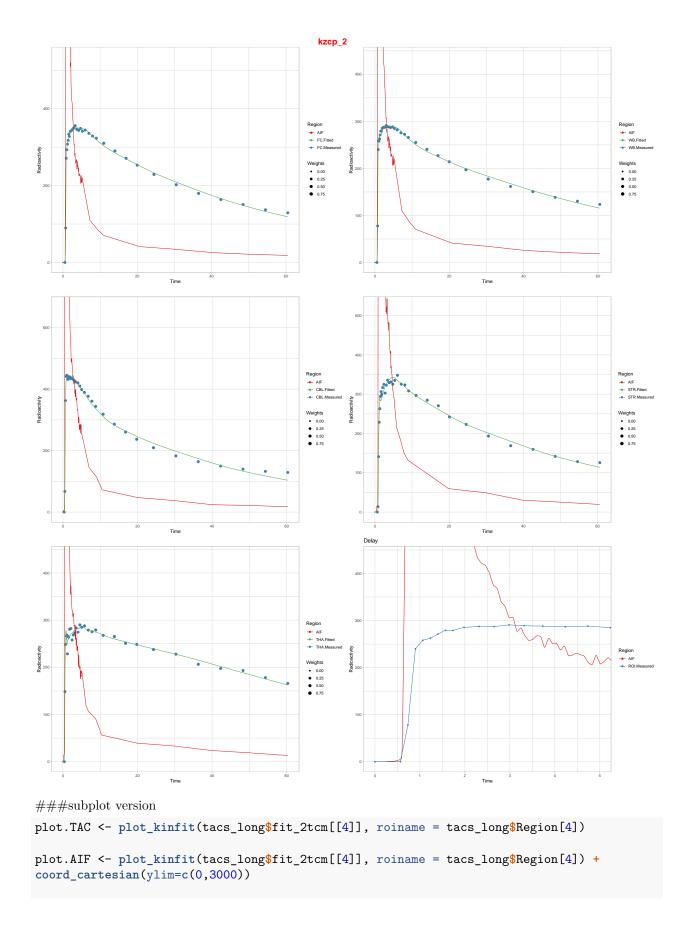
#Plot kinetic models

Plot 2tcm







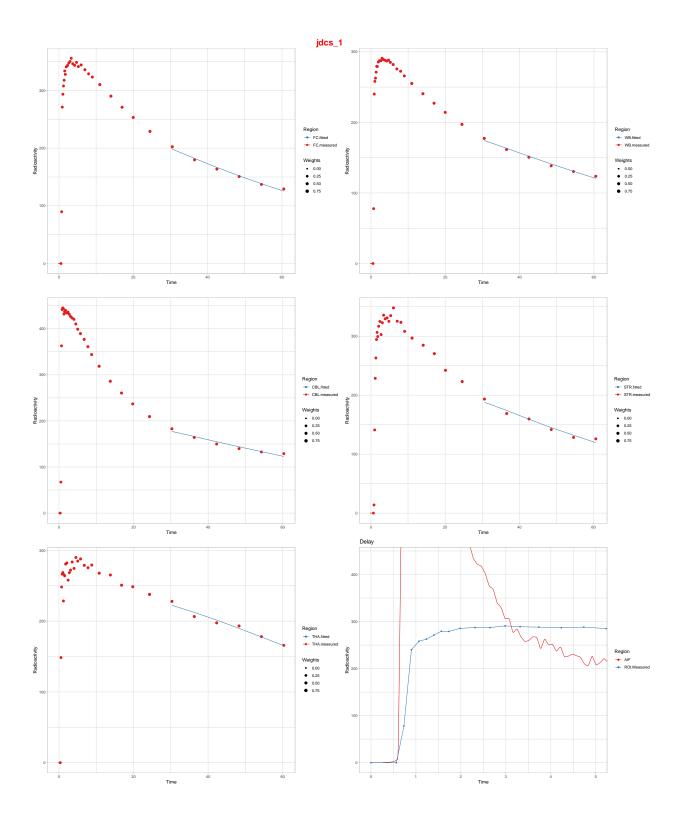


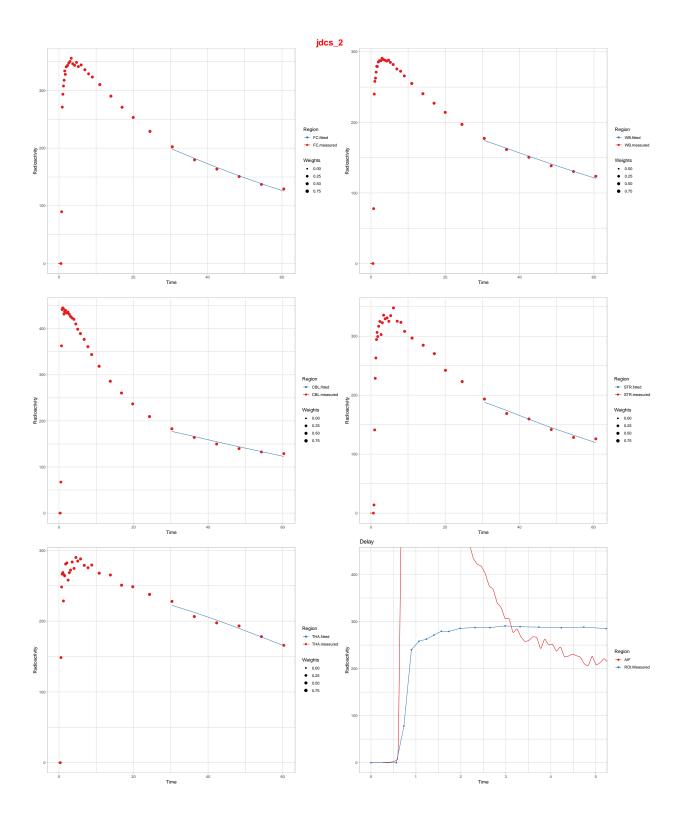
new plot 2tcm

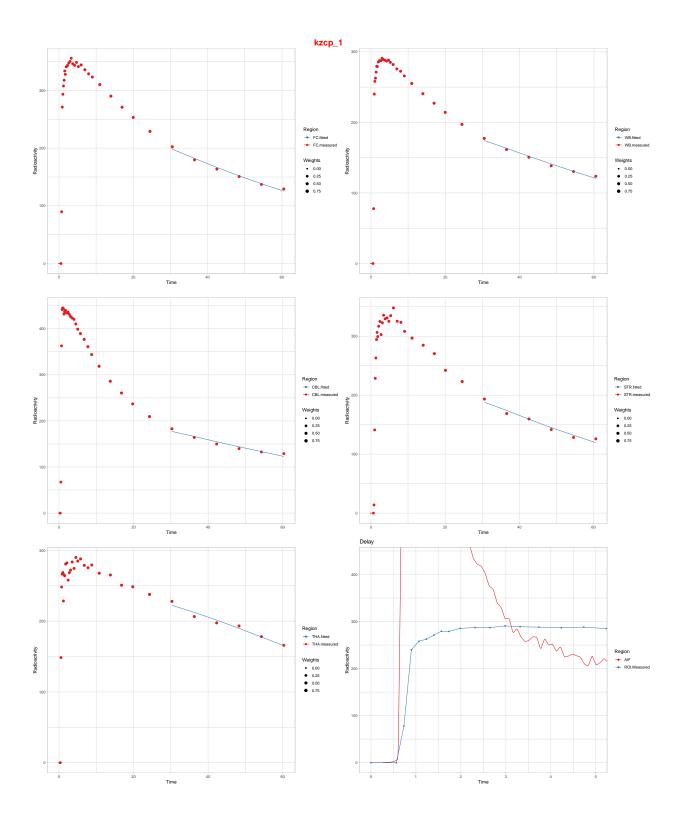
```
k <- tacs_long %>%
  group_by(PET, Region) %>%
  mutate(twotcm = map(fit_2tcm, c("tacs"))) %>%
  select(PET, Region, twotcm) %>%
  filter(Region %in% c('FC', 'WB', 'STR', 'CBL')) %>%
  unnest()

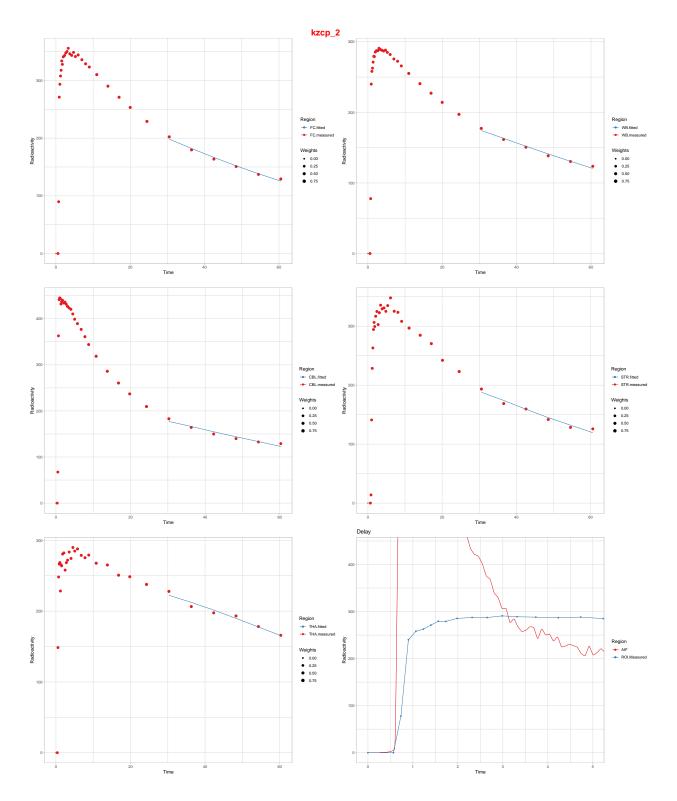
ggplot(k, aes(x=Time, y=Target, color = Region)) +
  geom_point() + geom_line(aes(y=Target_fitted, color = Region)) +
  facet_wrap(~ PET , ncol=2)
```

Plot ma1



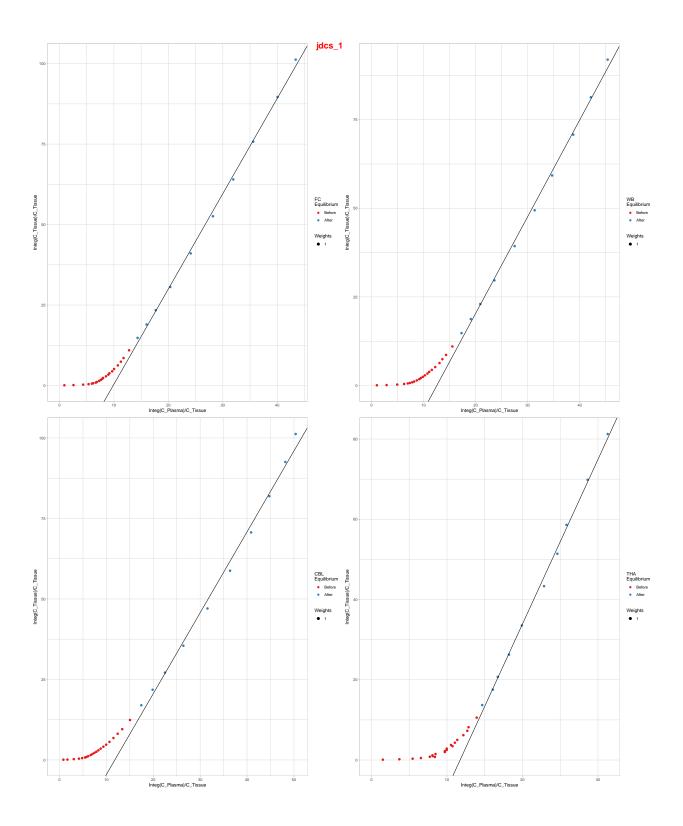


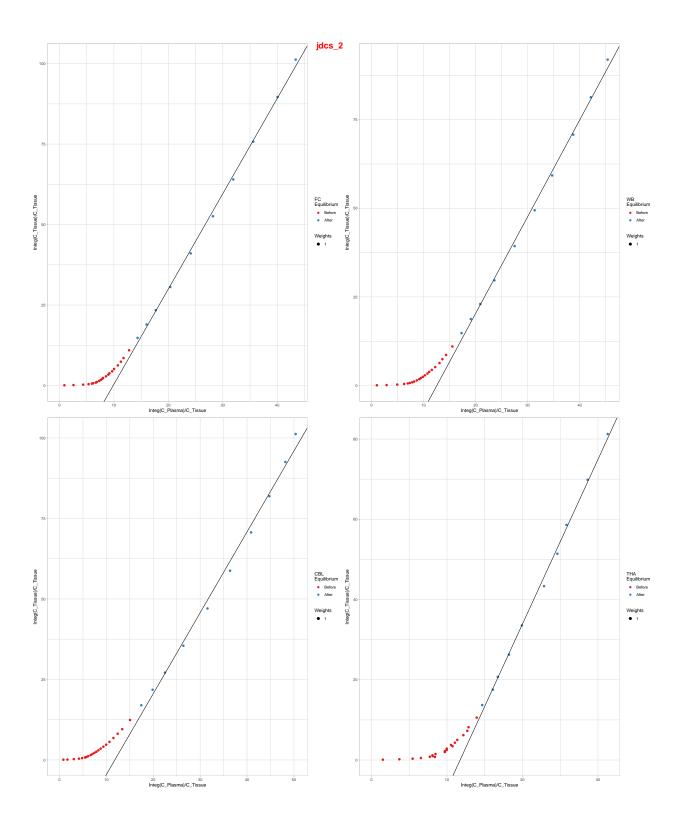


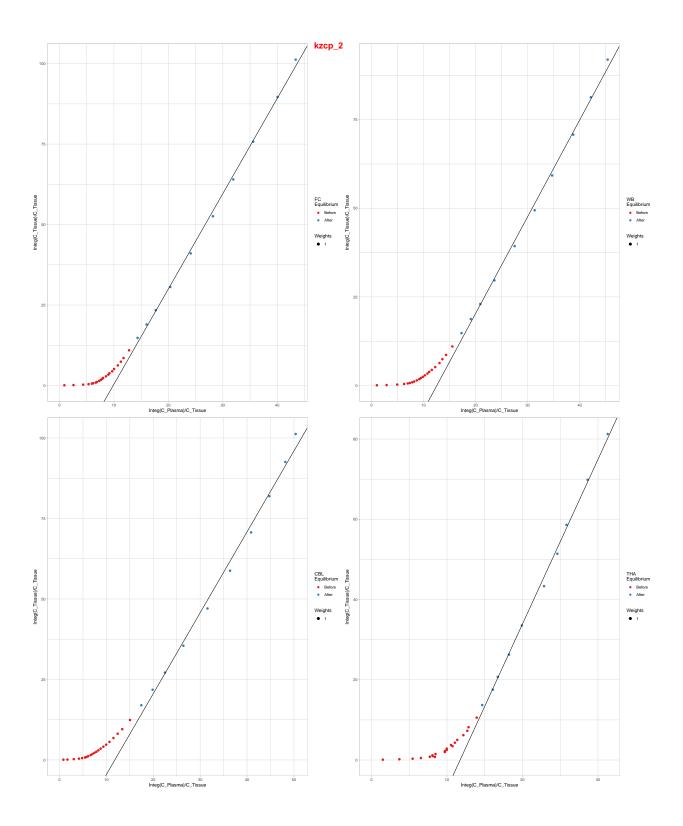


Plot Loganplot

```
plot_Logan <- tacs_long %>%
  filter(PET == PETs[5:8]) %>%
  group_by(PET, Region) %>%
```







Test-retest

trt preparation

```
trt_check <- tacs_long %>%
  select(Subjname, PETNo, Region, Vt_ma1, Vt_2tcm, Vt_Logan) %>%
  gather(Measure, Value, -Subjname, -PETNo, -Region) %>%
  group_by(Region, Measure) %>%
  nest(.key = "data")

saveRDS(tacs_long, 'DerivedData/raw_kinfit_pbr28.rds')
```

trt results

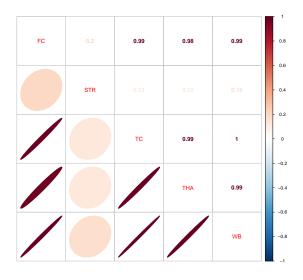
| Region | mean | sd | cov | skew | kurtosis | icc | icc 1 | icc u | wscv |
|--------|-------|--------|-------|-------|----------|-------|--------|-------|-------|
| | | | | | | | | | |
| FC | 3.131 | 1.499 | 0.479 | 1.243 | 0.977 | 0.913 | 0.736 | 0.974 | 0.145 |
| TC | 3.157 | 1.544 | 0.489 | 1.311 | 1.342 | 0.927 | 0.777 | 0.978 | 0.135 |
| STR | 3.026 | 1.465 | 0.484 | 1.220 | 0.982 | 0.906 | 0.720 | 0.972 | 0.151 |
| THA | 4.050 | 2.239 | 0.553 | 1.204 | 0.831 | 0.905 | 0.715 | 0.971 | 0.174 |
| WB | 3.050 | 1.469 | 0.481 | 1.301 | 1.192 | 0.905 | 0.715 | 0.971 | 0.152 |
| CBL | 3.355 | 1.680 | 0.501 | 1.352 | 1.367 | 0.922 | 0.759 | 0.977 | 0.143 |
| FC | 3.083 | 1.496 | 0.485 | 0.922 | 0.214 | 0.899 | 0.699 | 0.969 | 0.158 |
| TC | 3.028 | 1.517 | 0.501 | 1.053 | 0.659 | 0.917 | 0.750 | 0.975 | 0.147 |
| STR | 8.798 | 27.297 | 3.102 | 4.266 | 17.026 | 0.010 | -0.545 | 0.560 | 3.087 |
| THA | 3.907 | 2.196 | 0.562 | 1.067 | 0.401 | 0.910 | 0.728 | 0.973 | 0.173 |
| WB | 2.919 | 1.437 | 0.492 | 1.031 | 0.455 | 0.902 | 0.707 | 0.970 | 0.158 |
| CBL | 3.054 | 1.631 | 0.534 | 1.227 | 0.926 | 0.909 | 0.716 | 0.973 | 0.165 |
| FC | 2.940 | 1.471 | 0.501 | 1.173 | 0.827 | 0.917 | 0.741 | 0.975 | 0.147 |
| TC | 2.933 | 1.480 | 0.505 | 1.259 | 1.198 | 0.922 | 0.756 | 0.977 | 0.144 |
| STR | 2.816 | 1.426 | 0.506 | 1.156 | 0.830 | 0.906 | 0.719 | 0.972 | 0.158 |
| THA | 3.794 | 2.062 | 0.544 | 1.182 | 0.781 | 0.907 | 0.722 | 0.972 | 0.169 |
| WB | 2.822 | 1.401 | 0.497 | 1.254 | 1.098 | 0.907 | 0.718 | 0.972 | 0.155 |
| CBL | 3.103 | 1.603 | 0.517 | 1.321 | 1.290 | 0.915 | 0.736 | 0.975 | 0.154 |

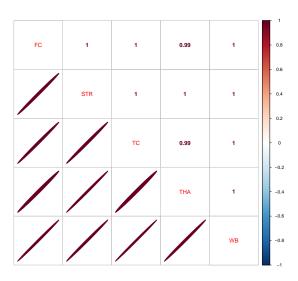
Interregional Correlation

Here the interregional correlations for V_{T} are assessed

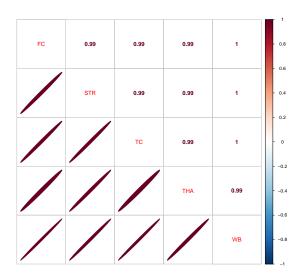
```
Vt_2TCM <- tacs_long %>%
  ungroup() %>%
  select(PET, Region, Vt_2tcm) %>%
  spread(Region, Vt_2tcm)
Vt_MA1 <- tacs_long %>%
  ungroup() %>%
  select(PET, Region, Vt ma1) %>%
  spread(Region, Vt_ma1)
Vt_logan <- tacs_long %>%
  ungroup() %>%
  select(PET, Region, Vt_Logan) %>%
  spread(Region, Vt_Logan)
col2 <- colorRampPalette(rev(c("#67001F", "#B2182B", "#D6604D", "#F4A582", "#FDDBC7",
                           "#FFFFFF", "#D1E5F0", "#92C5DE", "#4393C3", "#2166AC", "#053061")))
par(mfrow=c(2,2))
Vt_2TCM %>%
  select(FC:WB) %>%
  cor() %>%
  corrplot.mixed(lower='ellipse', upper='number',
                 lower.col = col2(200), upper.col = col2(200), diag='n',
                 number.digits = 2, title=expression(Vt_2TCM ~ Correlations),
                 mar=c(0,0,1,0))
Vt_logan %>%
  select(FC:WB) %>%
  cor() %>%
  corrplot.mixed(lower='ellipse', upper='number',
                 lower.col = col2(200), upper.col = col2(200), diag='n',
                 number.digits = 2, title=expression(Vt_logan ~ Correlations),
                 mar=c(0,0,1,0))
Vt_MA1 %>%
  select(FC:WB) %>%
  cor() %>%
  corrplot.mixed(lower='ellipse', upper='number',
                 lower.col = col2(200), upper.col = col2(200), diag='n',
                 number.digits = 2, title=expression(Vt_MA1 ~ Correlations),
                 mar=c(0,0,1,0))
```

Vt_2TCM Correlations Vt_logan Correlations





Vt_MA1 Correlations



#Corrplot between measures for a single region

```
compare <- tacs_long %>%
  ungroup() %>%
  select(PET, Region, Vt_2tcm, Vt_Logan ,Vt_ma1 ) %>%
  filter(Region %in% c('FC', 'WB', 'STR', 'THA'))

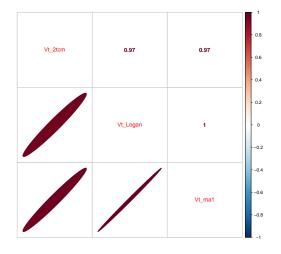
par(mfrow=c(2,2))

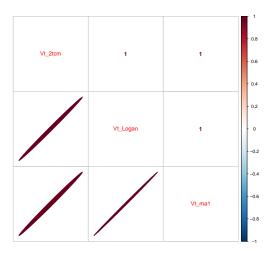
compare %>%
  filter(Region == "FC") %>%
  select(Vt_2tcm:Vt_ma1) %>%
  cor() %>%
  corrplot.mixed(lower='ellipse', upper='number',
```

```
lower.col = col2(200), upper.col = col2(200), diag='n',
                 number.digits = 2, title=expression(Model ~ Correlations ~ Region: FC),
                 mar=c(0,0,1,0)
compare %>%
  filter(Region == "THA") %>%
  select(Vt_2tcm:Vt_ma1) %>%
  cor() %>%
  corrplot.mixed(lower='ellipse', upper='number',
                 lower.col = col2(200), upper.col = col2(200), diag='n',
                 number.digits = 2, title=expression(Model ~ Correlations ~ Region: OC), mar=c(0,0,1,0)
compare %>%
  filter(Region == "STR") %>%
  select(Vt_2tcm:Vt_ma1) %>%
  cor() %>%
  corrplot.mixed(lower='ellipse', upper='number',
                 lower.col = col2(200), upper.col = col2(200), diag='n',
                 number.digits = 2, title=expression(Model ~ Correlations ~ Region: STR),
                 mar=c(0,0,1,0))
compare %>%
 filter(Region == "WB") %>%
  select(Vt_2tcm:Vt_ma1) %>%
  cor() %>%
  corrplot.mixed(lower='ellipse', upper='number',
                 lower.col = col2(200), upper.col = col2(200), diag='n',
                 number.digits = 2, title=expression(Model ~ Correlations ~ Region: WB),
                 mar=c(0,0,1,0)
```



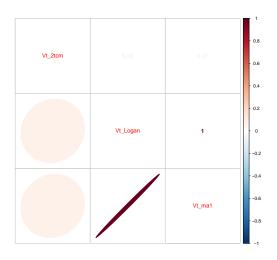
Model Correlations Region : OC

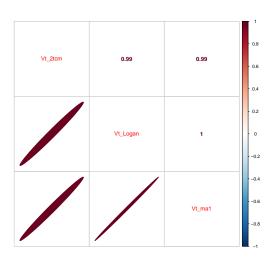




Model Correlations Region : STR

Model Correlations Region : WB





Vt corellation

R-squared

```
trtdata <- tacs_long %>%
    select(PET, Subjname, PETNo, Region, Vt_2tcm, Vt_Logan ,Vt_ma1) %>%
    gather(Measure, Value, -(PET:Region)) %>%
    spread(Region, Value)

trtdata <- trtdata %>%
    gather(Region, Value, -(PET:Measure)) %>%
    unite(Outcome, Measure, Region) %>%
    spread(Outcome, Value)
```

```
corout <- trtdata %>%
  gather(Measure, Binding, -(PET:PETNo), -Vt_2tcm_WB) %>%
  group_by(Measure) %>%
  summarise('R^2^'=cor(Binding, Vt_2tcm_WB)^2) %>%
  arrange(Measure) %>%
  ungroup() %>%
  mutate(Measure = str_replace(string=Measure, pattern='_', replacement='~')) %>%
  mutate(Measure = str_replace(string=Measure, pattern='FC', replacement='FC~')) %>%
  mutate(Measure = str_replace(string=Measure, pattern='CBL', replacement='CBL~')) %>%
  mutate(Measure = str_replace(string=Measure, pattern='ACC', replacement='ACC')) %>%
  mutate(Measure = str_replace(string=Measure, pattern='INS', replacement='INS')) %>%
  mutate(Measure = str_replace(string=Measure, pattern='THA', replacement='THA')) %>%
  mutate(Measure = str_replace(string=Measure, pattern='WB', replacement='WB')) %>%
  mutate(Measure = str_replace(string=Measure, pattern='0C', replacement='0C~')) %>%
  mutate(Measure = str_replace(string=Measure, pattern='WM', replacement='WM~')) %>%
  mutate(Measure = str_replace(string=Measure, pattern='GM', replacement='GM~')) %>%
  mutate(Measure = str_replace(string=Measure, pattern='STR', replacement='STR~'))
kable(corout, digits=2, caption="Correlations with BP_srtm~WB~")
```

 $\left\{ \text{table} \right\} [t]$

\caption{Correlations with BP_srtm_{WB}}

| Measure | R^2^ |
|---------------|------|
| Vt~2tcm_CBL~ | 0.97 |
| Vt~2tcm_FC~ | 0.98 |
| Vt~2tcm_STR~ | 0.03 |
| Vt~2tcm_TC | 0.99 |
| Vt~2tcm_THA~ | 0.98 |
| Vt~Logan_CBL~ | 0.96 |
| Vt~Logan_FC~ | 0.97 |
| Vt~Logan_STR~ | 0.98 |
| Vt~Logan_TC | 0.97 |
| Vt~Logan_THA~ | 0.98 |
| Vt~Logan_WB~ | 0.97 |
| Vt~ma1_CBL~ | 0.95 |
| Vt~ma1_FC~ | 0.97 |
| Vt~ma1_STR~ | 0.98 |
| Vt~ma1_TC | 0.97 |
| Vt~ma1_THA~ | 0.97 |
| Vt~ma1_WB~ | 0.98 |

 \end{table}

#Plot of the change between PETNo = 1 and PETNo = 2.

```
trtdata <- trtdata %>%
  gather(Region, Value, -(PET:PETNo)) %>%
  separate(col = "Region", into = c("outcome", "Measure", "Region"), sep = '_')%>% unite(outcome, outcom ungroup()

trt_2tcm <- trtdata %>%
  filter(outcome == 'Vt_2tcm')
```

