SCH23390

$Jonathan\ Tjerkaski$

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Aims

The aim of this assignment is to analyze the AZ10419369 data in kinfitr

Libraries

CRAN libraries

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

```
library(tidyverse)
library(stringr)
library(corrplot)
library(grid)
library(gridExtra)
library(RColorBrewer)
library(psych)
library(readxl)
library(pracma)
library(jags)
library(xingt)
library(xingt)
library(cowplot)
library(corrplot)
library(viridis)
```

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)

theme_set(theme_light())
```

Creating folders using "initProjectFolder()"

```
initProjectFolder()
```

Extracting kinfitresults

```
paste0("../RawData/", .x))))
saveRDS(tactibble, '../DerivedData/tactibble.rds')
```

Tidying data.

New weights with kinfitr::weights_create

Fitting and plotting MRTM1 multiple times for regions FC and WB

Fitting MRTM2 to each region of each individual

First, let's select some specific regions. Note: I duplicated the CBL region column into "CBL" and "Ref". One of them is used to make the reference tissue models when nested in tacdata whereas the other is used for plotting in the new "all regions per PET +facet wrap by PET" - plot. However, the srtm fitting gave me an error when I did this

```
regions <- c("STR" = "FSLSSTR", "FC" = "FSLSFC", "WB", "WM", "GM", "OC" = "FSLSOC", "insula" = "FSLSINS
             "THA" = "FSLSTHA", "TC" = "FSLSTC")
tacs <- tacs %>%
  select(tacdata, Subjname, PETNo, k2prime_MRTM1, logan_tstar) %>%
  mutate(tacdata = map(tacdata, ~select(.x, regions, times, weights)))
#Long data. By gathering the regions into a single region collumn we can group_by region and then itera
tacs_long <- tacs %>%
  unnest(tacdata, .drop = FALSE) %>%
  gather(key = Region, value = TAC, -times, -weights,
         -Subjname, -PETNo, -k2prime_MRTM1, -CBL, -logan_tstar) %>%
  group_by(Subjname, PETNo, Region, k2prime_MRTM1) %>%
  nest(.key = "tacdata") %>%
  mutate(PET = paste(Subjname, PETNo, sep=' '))
#Fitting MRTM2 using the K2_prime values obtained for the striatum through the MRTM1 fitting earlier. n
tacs_long <- tacs_long %>%
  group_by(Subjname, PETNo, Region) %>%
  mutate(MRTM2fit = map2(tacdata, k2prime_MRTM1,
                         ~mrtm2(t_tac=.x$times, reftac = .x$CBL,
                               roitac = .x$TAC, k2prime = .y,
                               weights = .x$weights)),
         bp_MRTM2 = map_dbl(MRTM2fit, c("par", "bp")))
```

Plotting fitted MRTM2 model

And now, let's take a look at the BP_{ND} values. We'll want to divide them by ROI I think.

```
ggplot(tacs_long, aes(x=bp_MRTM2, fill=Region)) +
  geom_histogram(colour="black") +
  facet_wrap(~Region, scales="free") +
  guides(fill=FALSE)
```

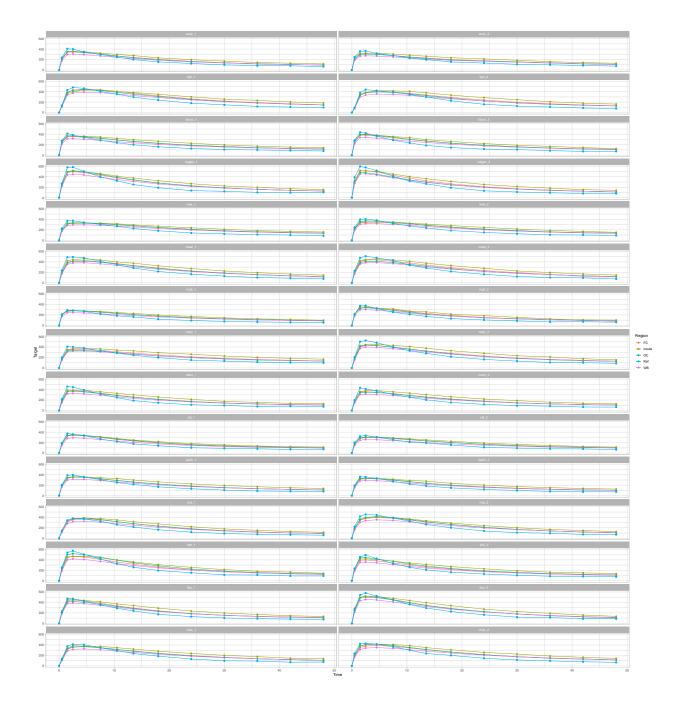
Plot MRTM2 tacs

Labels for regions are wrong. My intention is to have one plot per region for each PET in the same grid. Currently, all labels for the regions are the same for each individual.

new plot MRTM2

```
MRTM2 <- tacs_long %>%
  group_by(PET, Region) %>%
  mutate(mrtm2fits = map(MRTM2fit, c("tacs"))) %>%
  select(PET, Region, mrtm2fits) %>%
  filter(Region %in% c('FC', 'WB', 'insula', 'OC')) %>%
  unnest()

ggplot() +
  geom_point(data = MRTM2, aes(x=Time, y=Target, color = Region)) + geom_line(data = MRTM2, aes(x = Tim facet_wrap(~ PET , ncol=2))
```

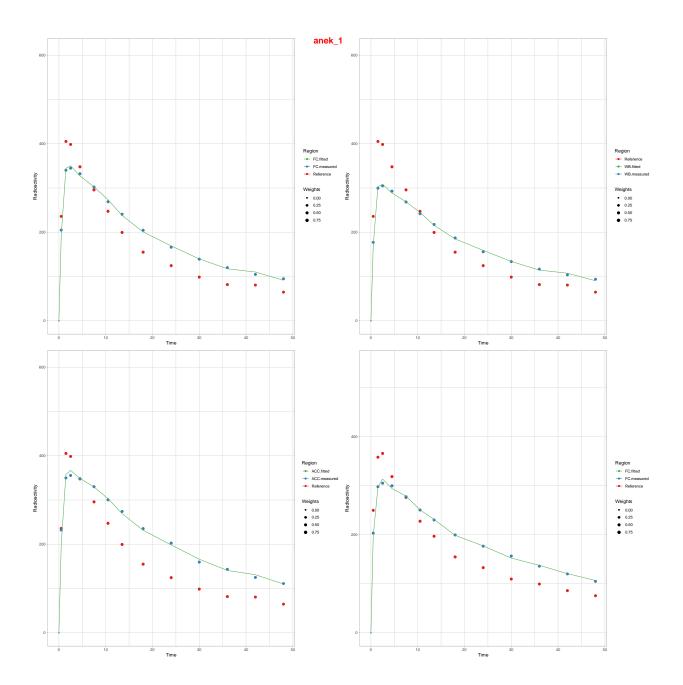


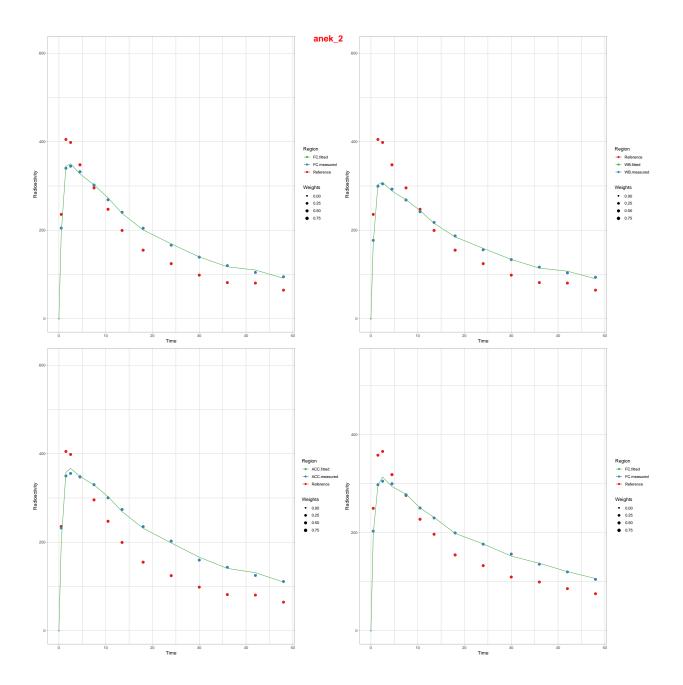
Fitting kintetic model srtm

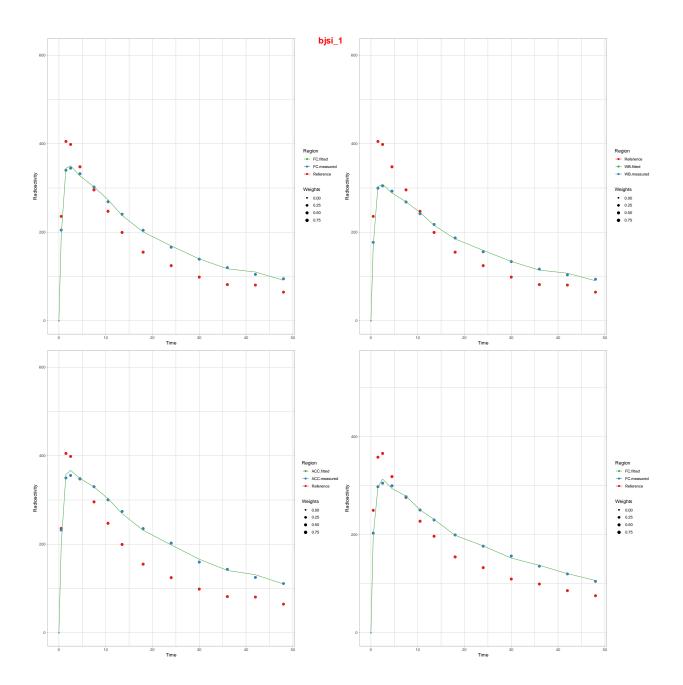
```
## cooks.distance.influence.merMod lme4
## dfbeta.influence.merMod lme4
## dfbetas.influence.merMod lme4
```

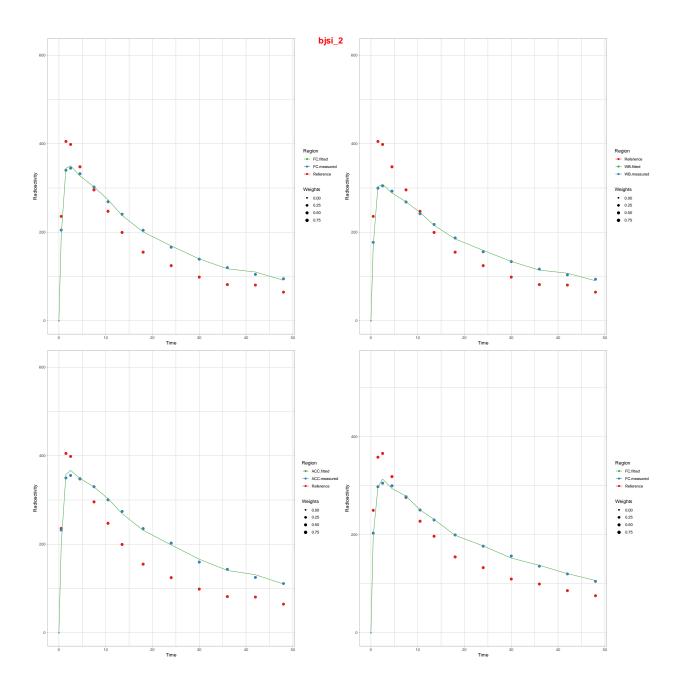
Plotting Kinetic Model srtm

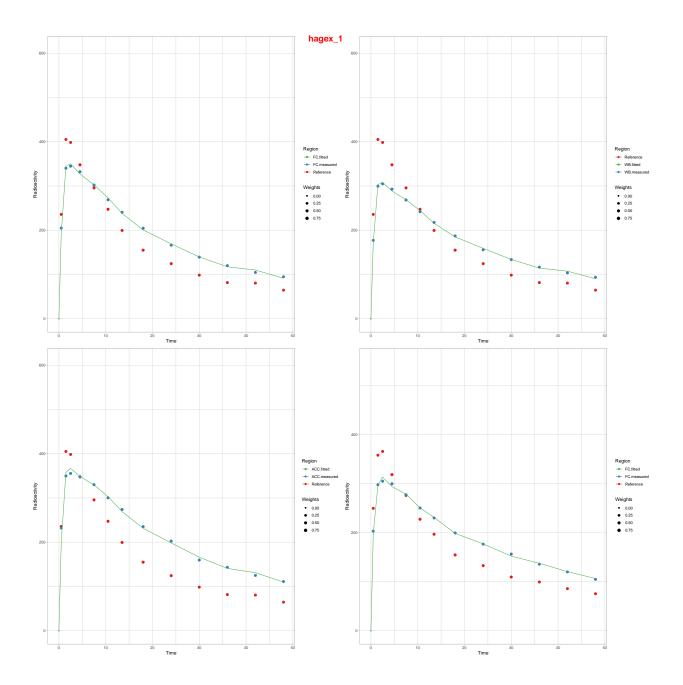
Note: Labels are not quite at the same location for each PET, still unsolved.

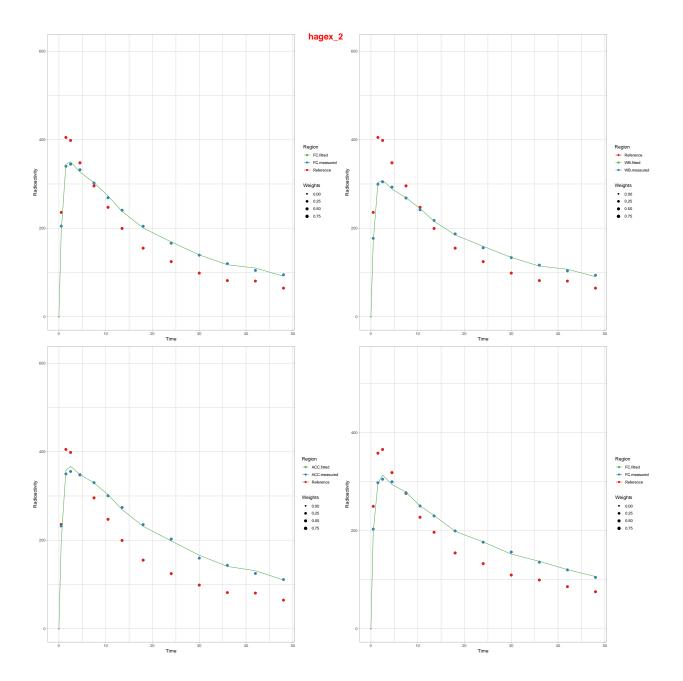


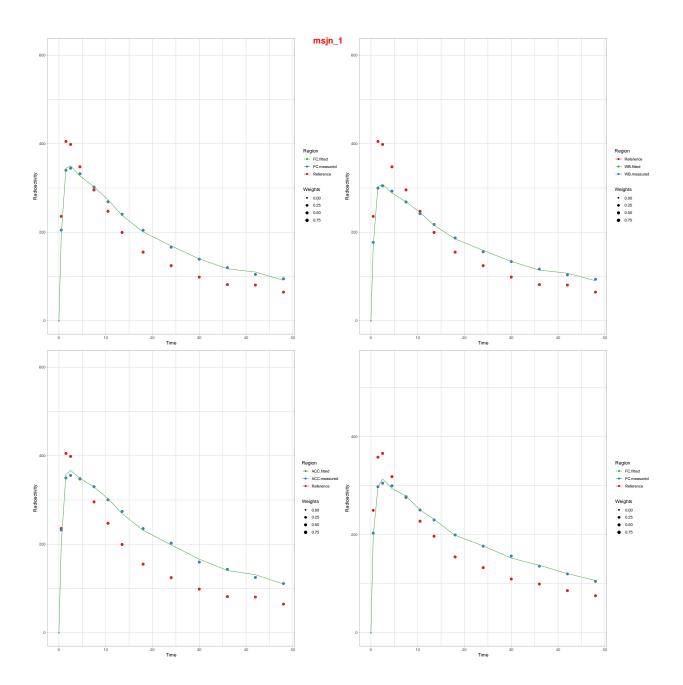


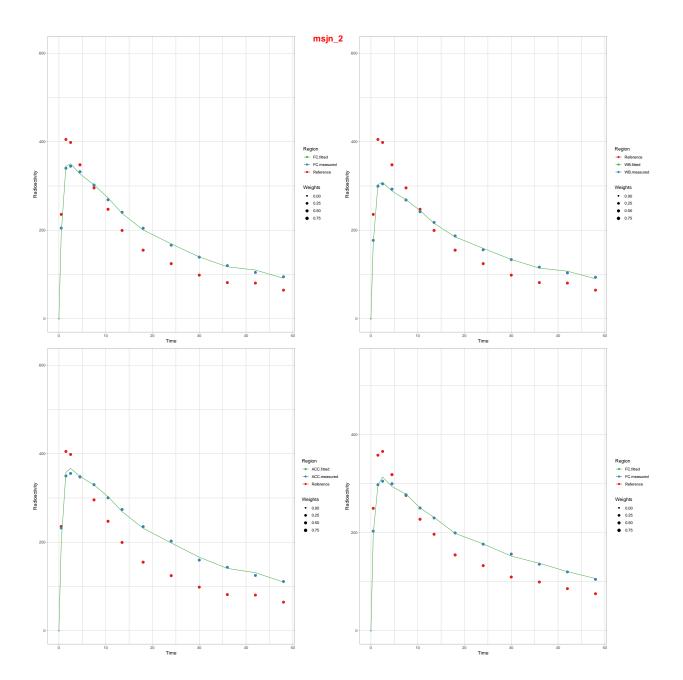


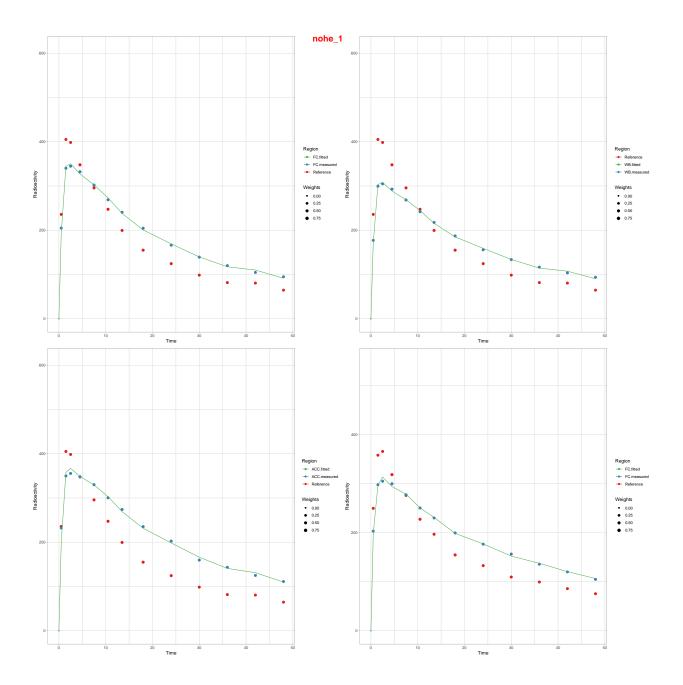


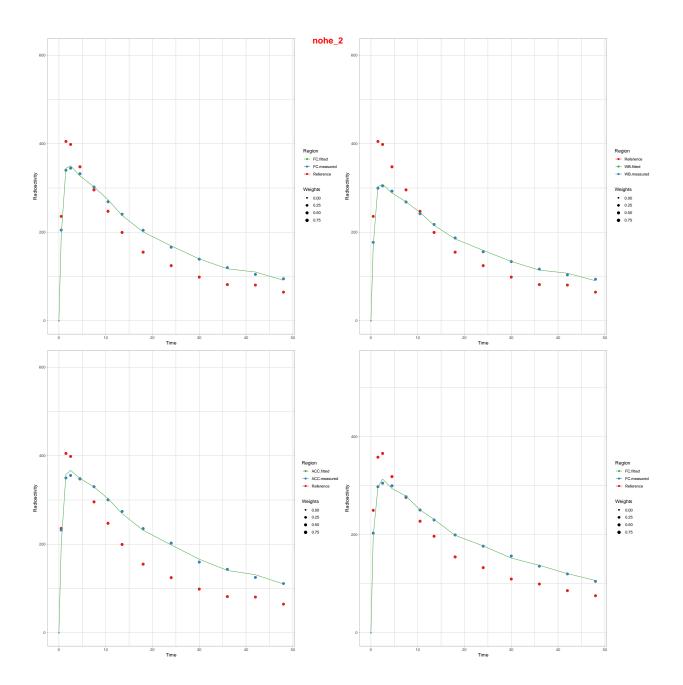


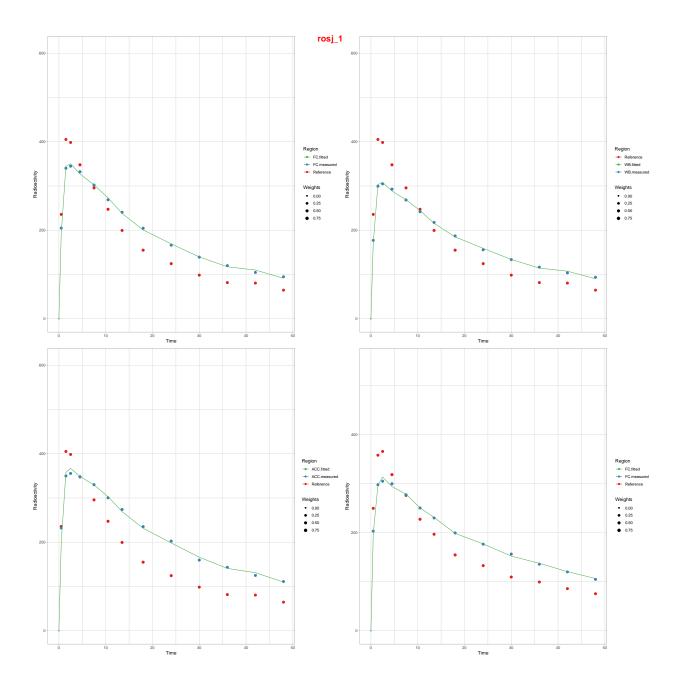


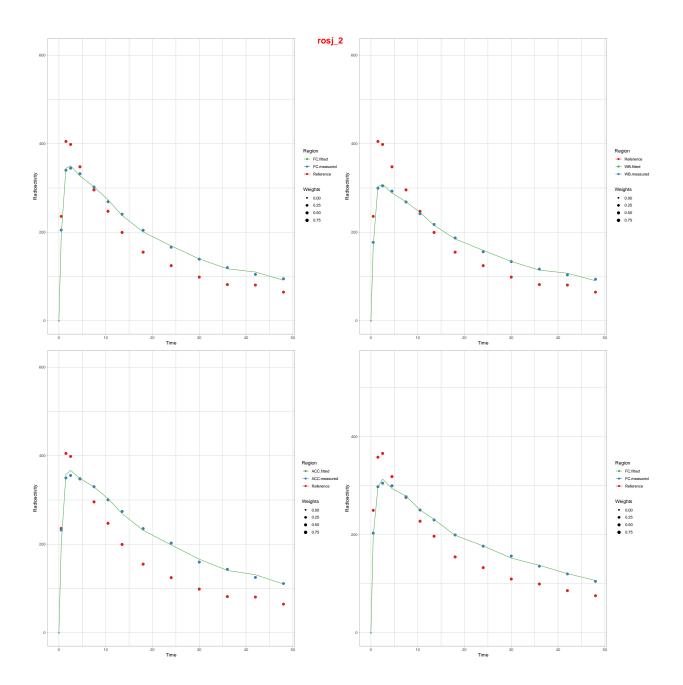


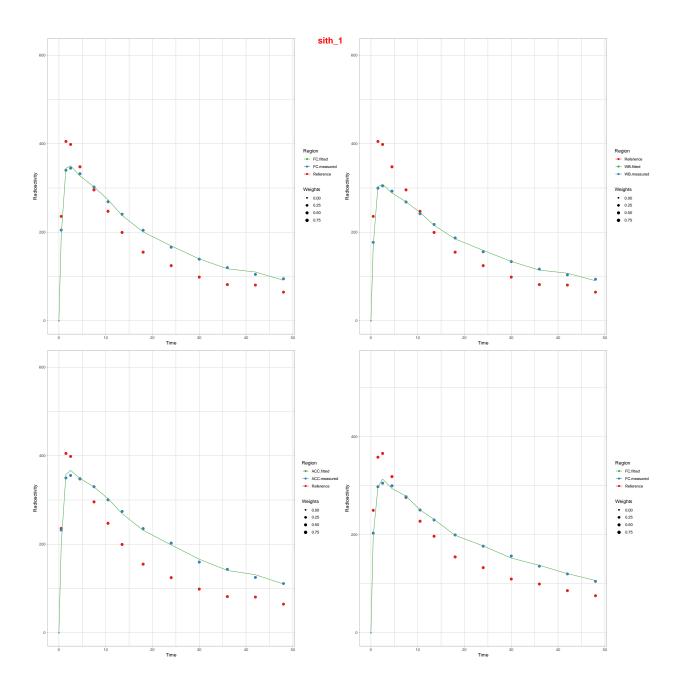


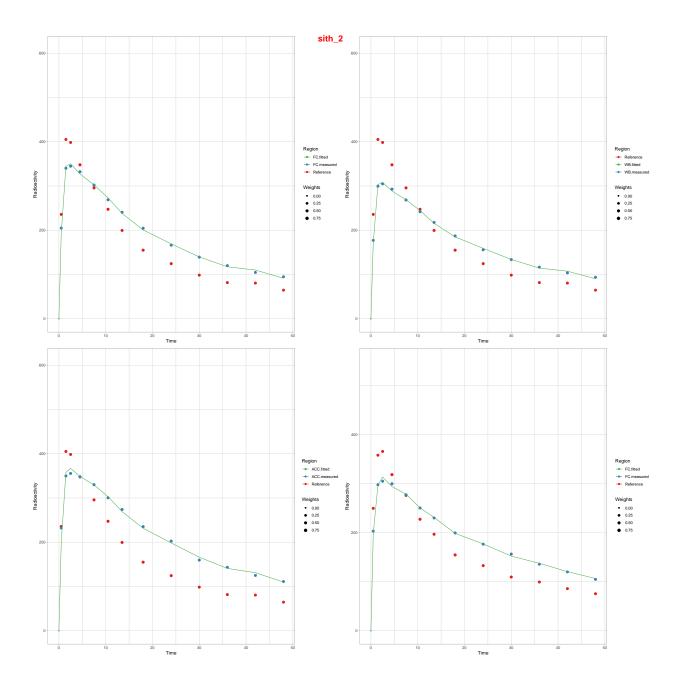


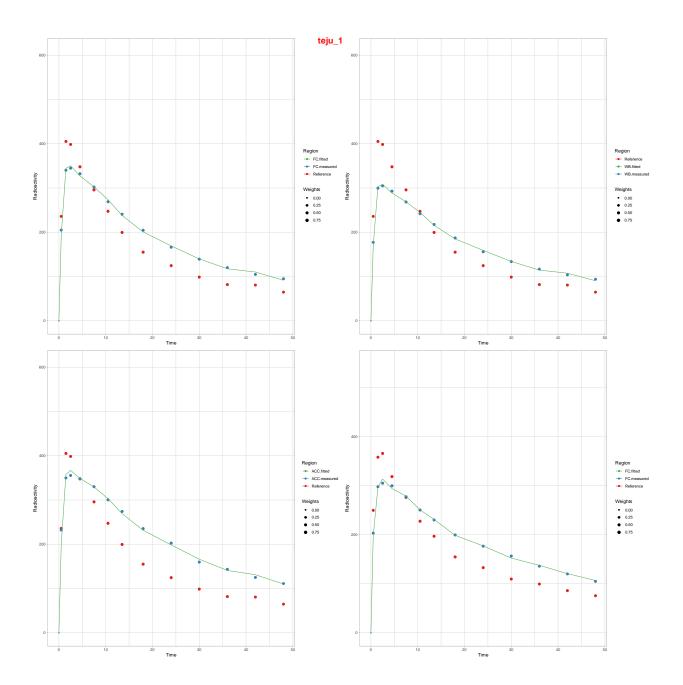


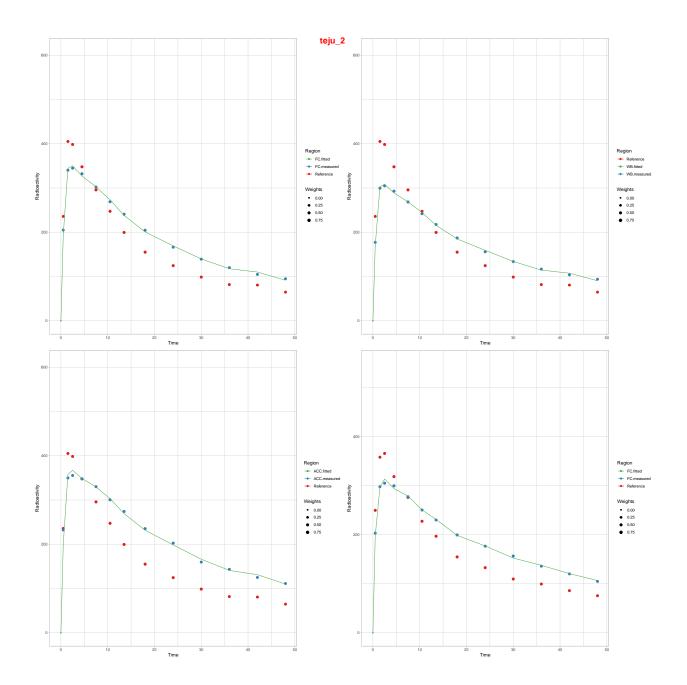












new plot srtm

```
Srtm <- tacs_long %>%
  group_by(PET, Region) %>%
  mutate(srtmtacs = map(srtmfit, c("tacs"))) %>%
  select(PET, Region, srtmtacs) %>%
  filter(Region %in% c('FC', 'WB', 'insula', 'OC')) %>%
  unnest()

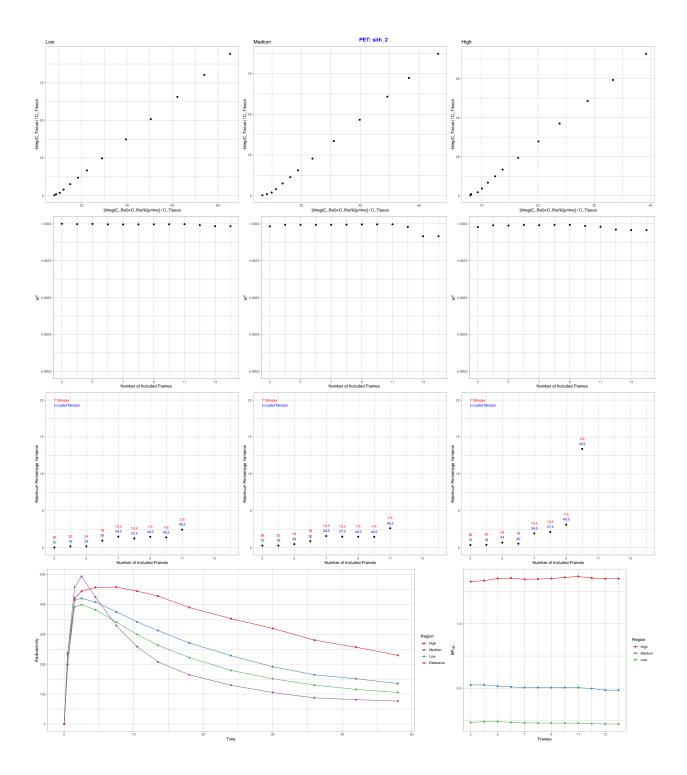
ggplot() +
  geom_point(data = Srtm, aes(x=Time, y=Target, color = Region)) + geom_line(data = Srtm, aes(x = Time, facet_wrap(~ PET , ncol=2))
```

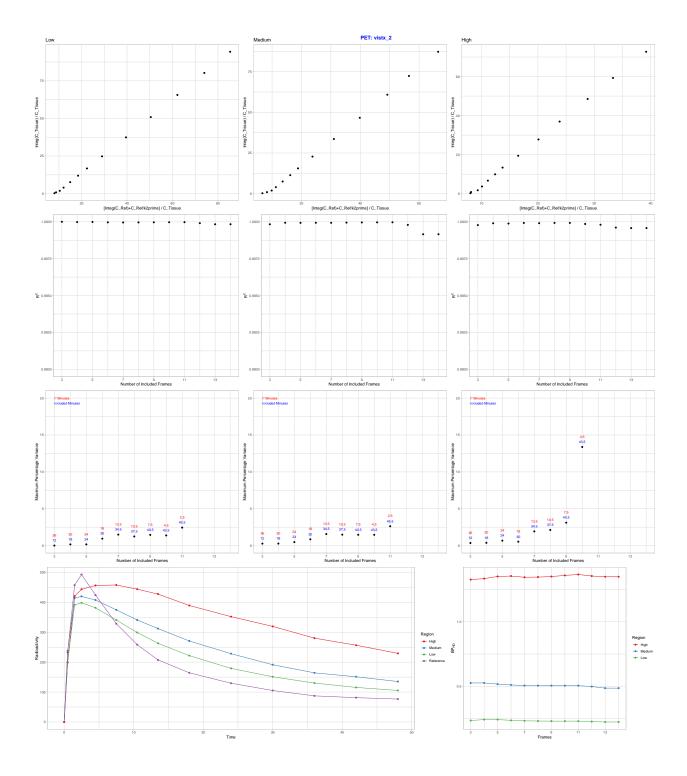
plot logan tstar

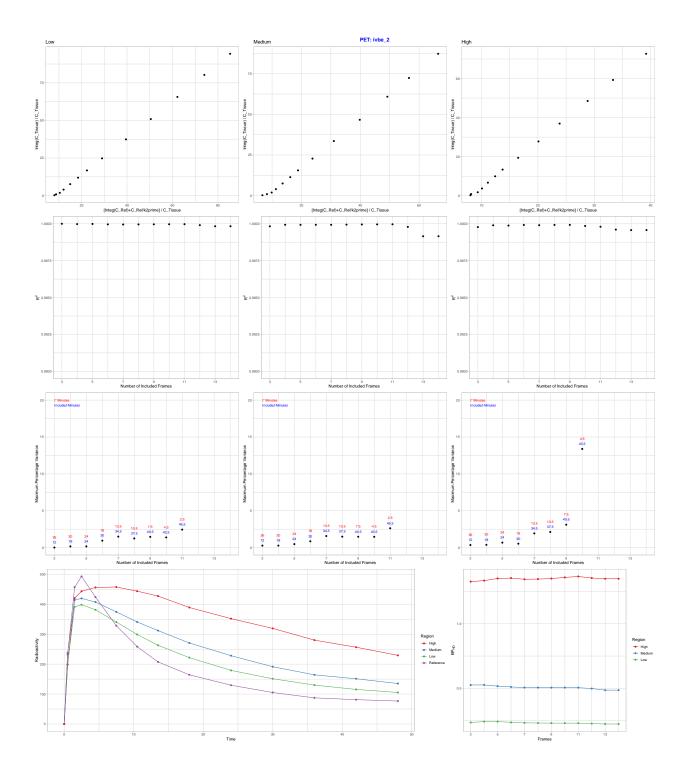
Trouble with label, it is at the same level as the medium, high and low ROI labels. Tried moving label with vjust = 0.5. It works, sort of. the label moves up, half of it dissapears and part of the plots at the bottom dissapear. Solution?? Addition: in the end I did manage to get the label up a bit without harming the graph, vjust = 0.97 was the lowest vjust value I could make. I temporarilly changed the color of the label to distinguish easier. Looks a little unprofessional, though. I tried with draw_labels or draw-figure_labels and didn't see any improvement. Also, I tried getting all the subjects into the same pane by making ncol = 2 and nrow = 3 or making sample_n(size = 4) and ncol and nrow = 2. It just got really messy. Also, initially I thought I could skip "print", but that is not possible. you get no error without print, but no graphs either. I thought I got no graph because of eval = FALSE, but that was an incorrect assumption.

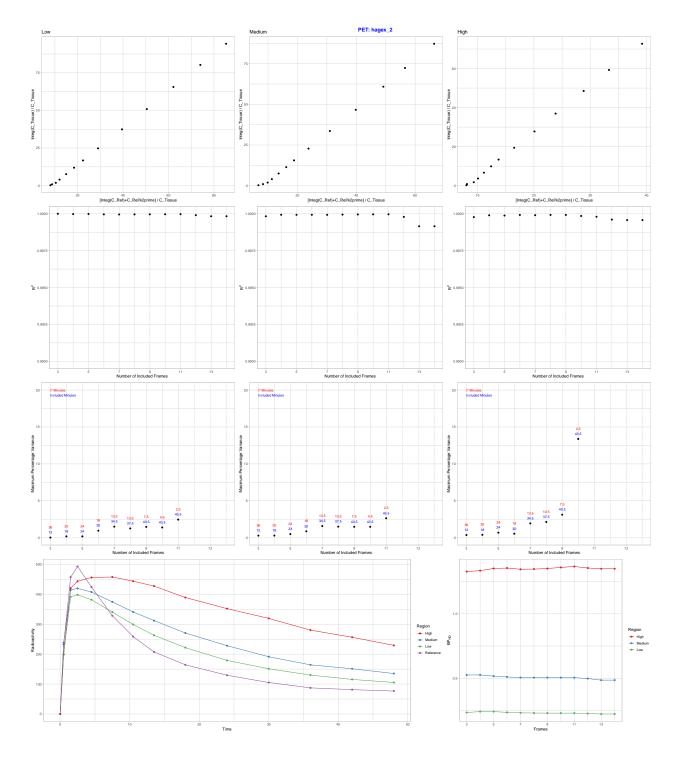
```
tstar_fits <- tacs_long %>%
  ungroup() %>%
  select(tacdata, PET) %>%
  unnest() %>%
  select(PET, logan_tstar) %>%
  select(PET, logan_tstar) %>%
  sample_n(size = 4, replace = F)

walk2(list(tstar_fits$logan_tstar), tstar_fits$PET,
  ~print(plot_grid(plotlist = .x, ncol = 1, nrow = 1, labels = paste('PET:',.y), label_x = 0.5, label_x
```









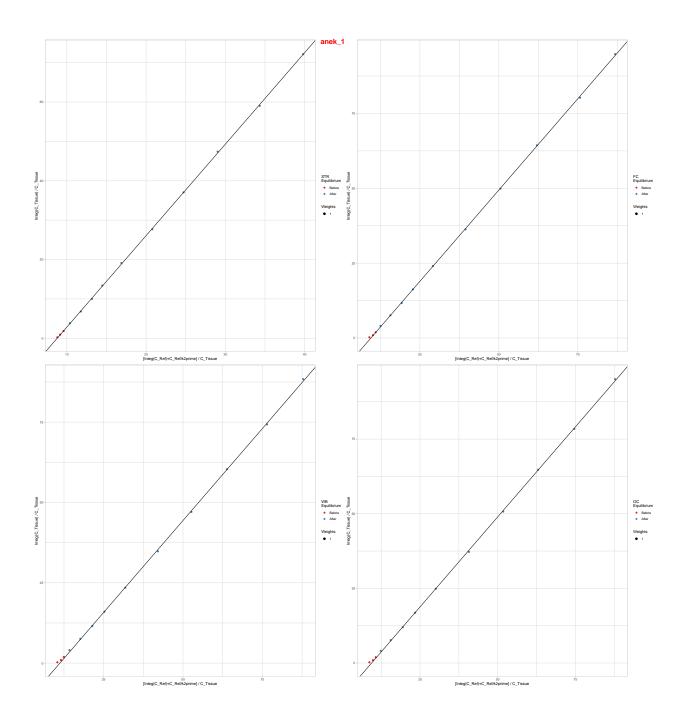
All 4 tstar plots on a single page

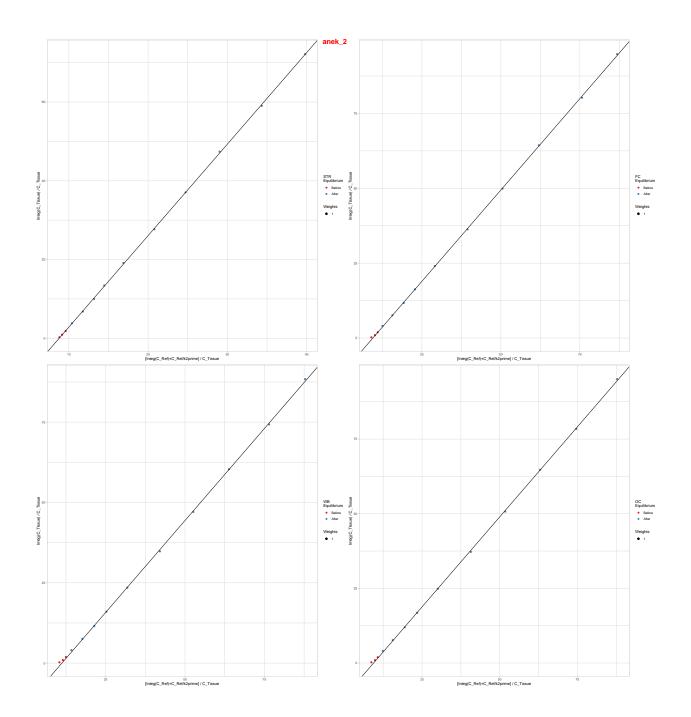
Note: I would like to have the "draw_figure_label" be drawn a bit above the first PET, but that does not seem to be happening. Should I just skip it? I Placed the plots in a single column because it was a little hard distinguishing where one ands and another begins in a 2×2 format. Perhaps one could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

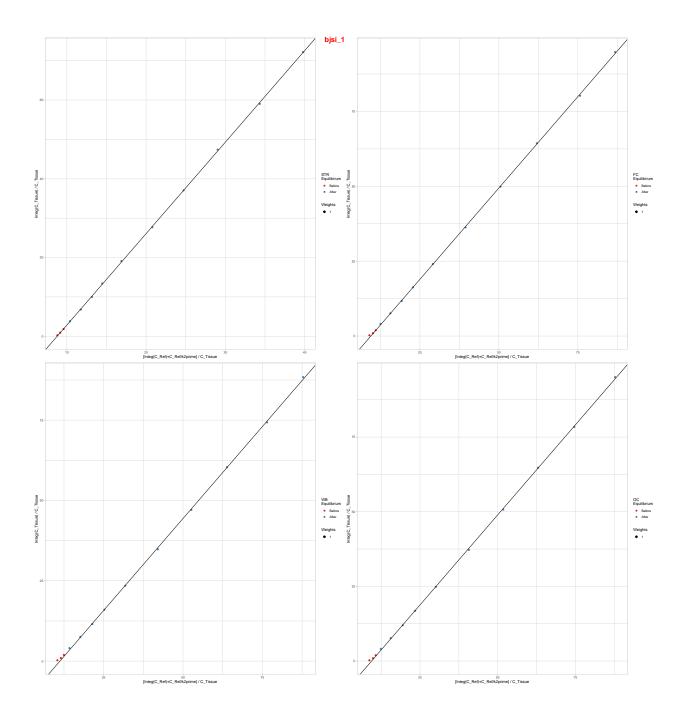
```
plot_grid(plotlist = tstar_fits$logan_tstar, ncol = 1, nrow = 4, labels = paste('PET:',tstar_fits$PET),
    #draw_figure_label("t*", position = "top", fontface = "bold", size = 32, colour = "red")
```

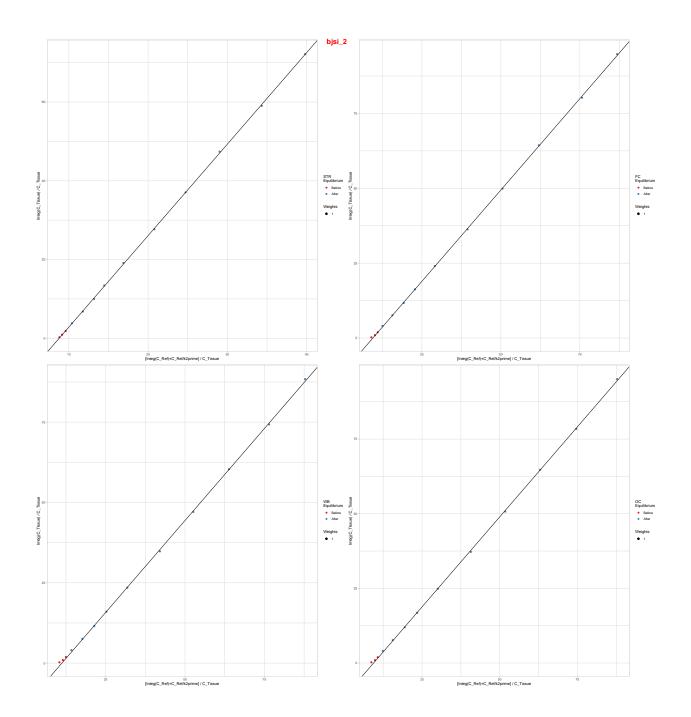
#Fitting and plotting Kinetic Model refLogan

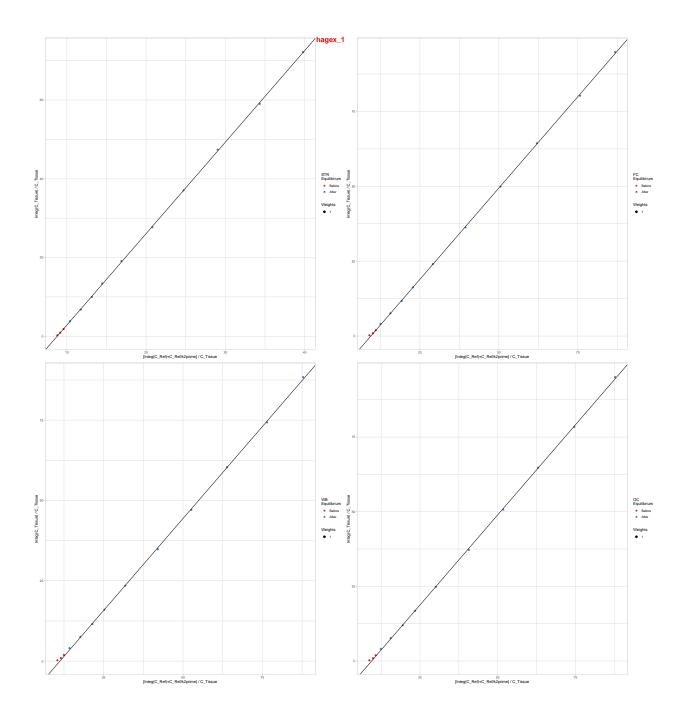
Plot refLogan

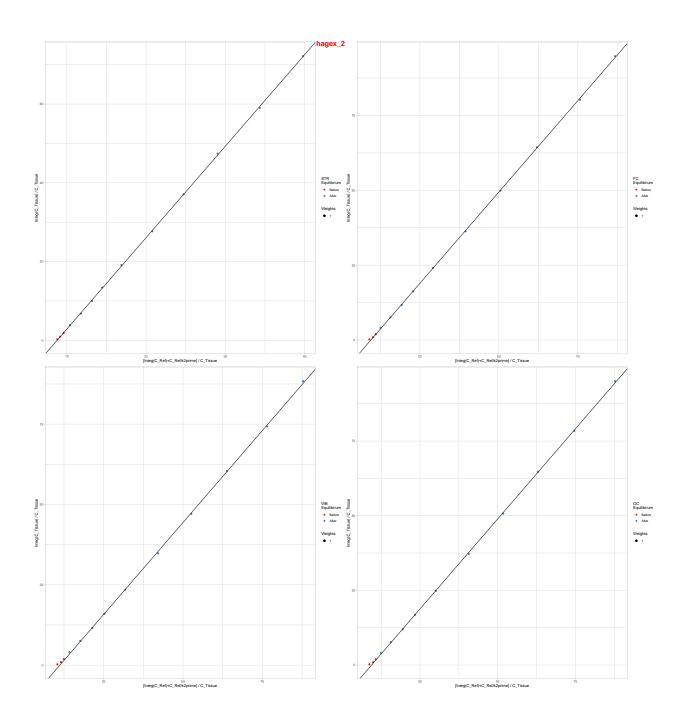


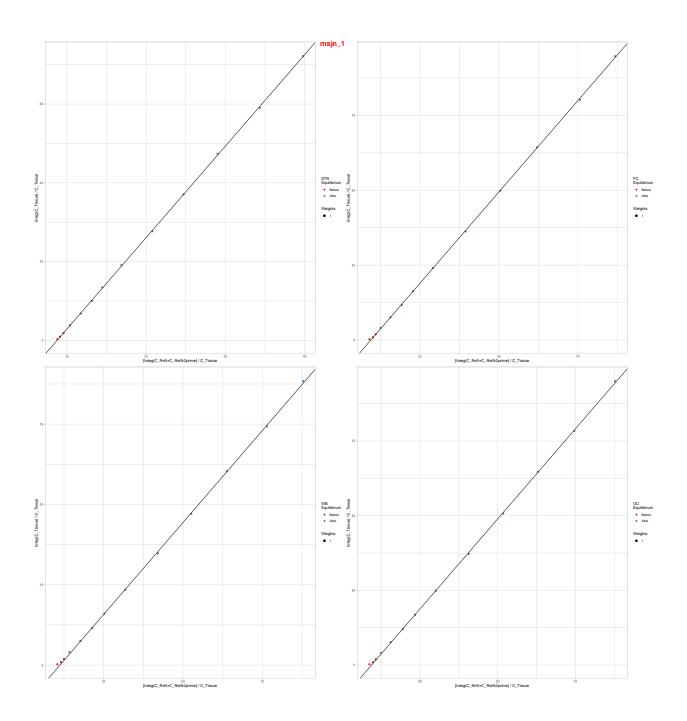


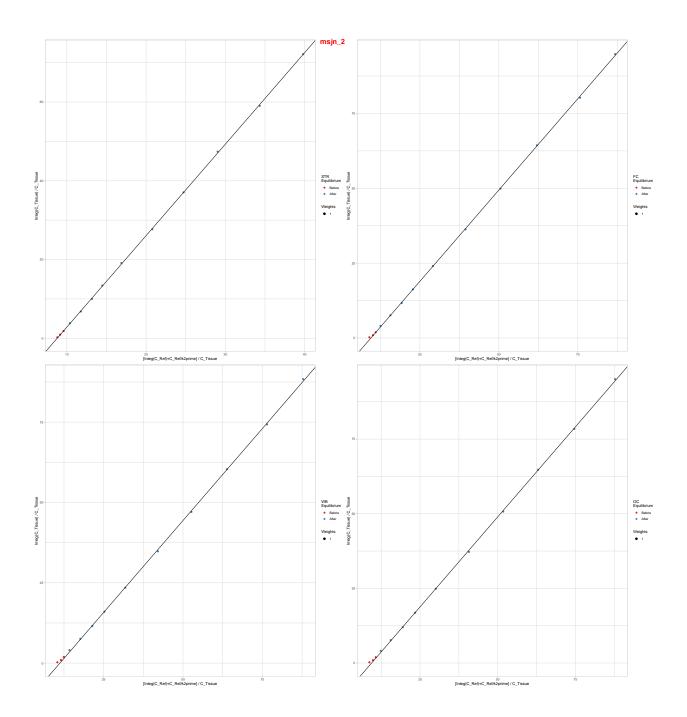


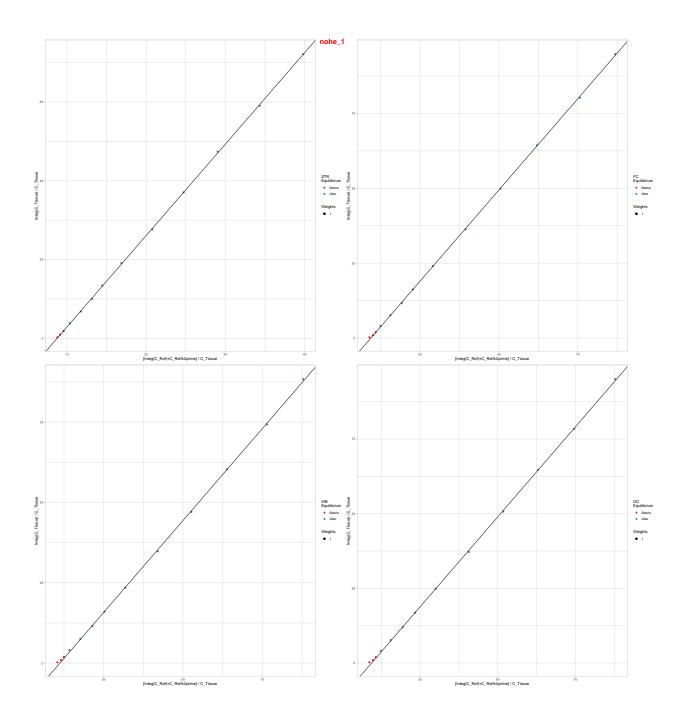


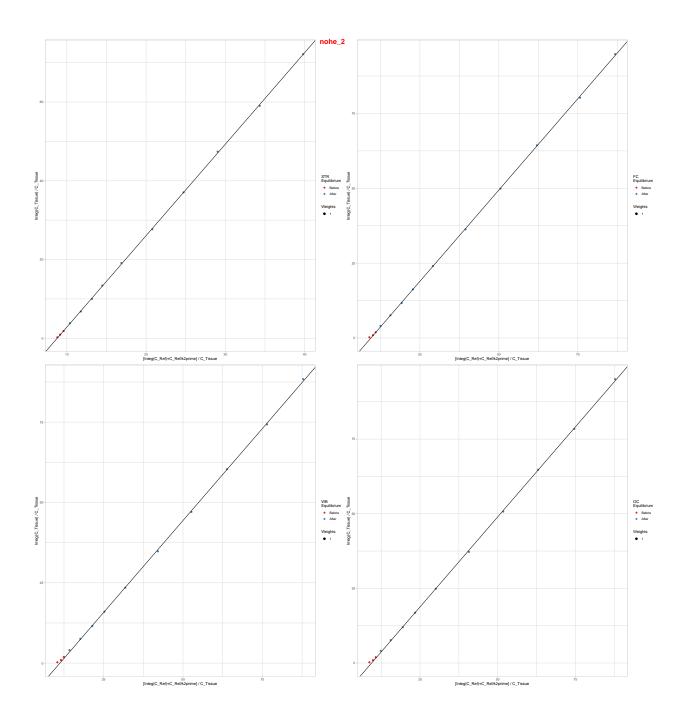


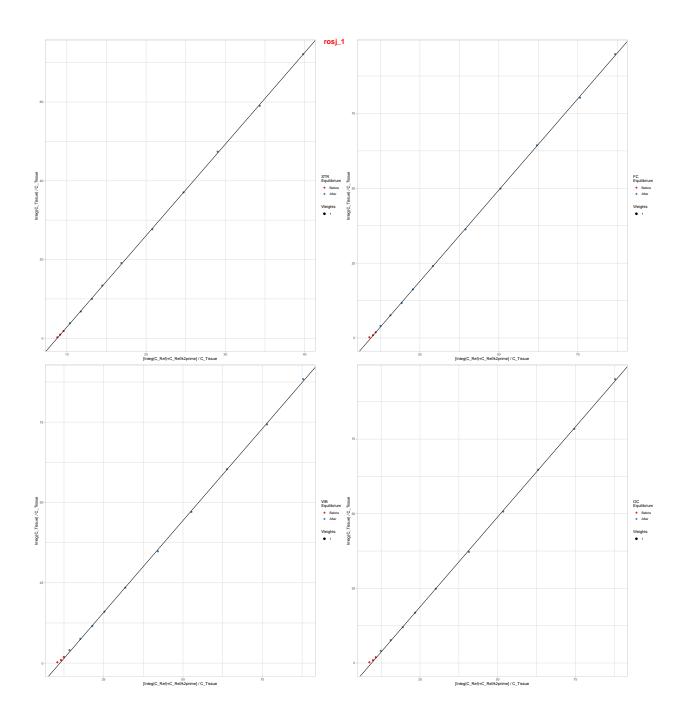


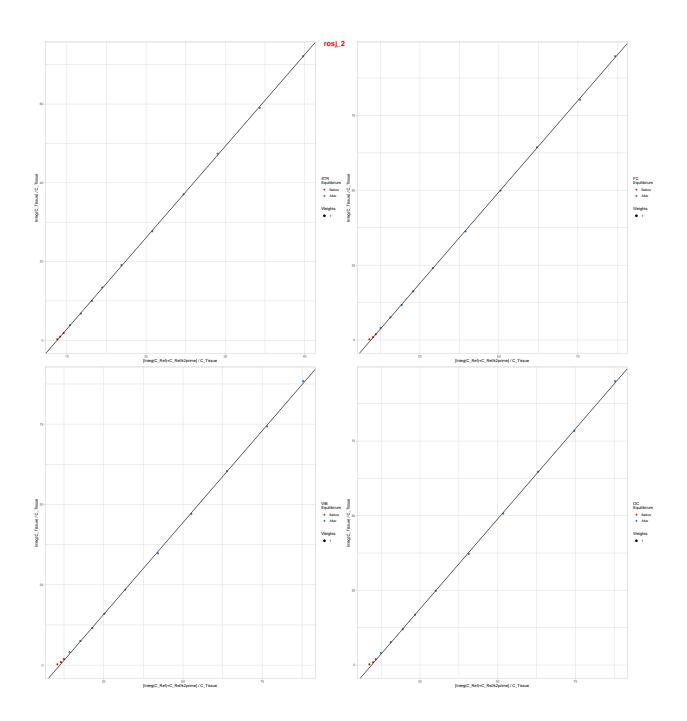


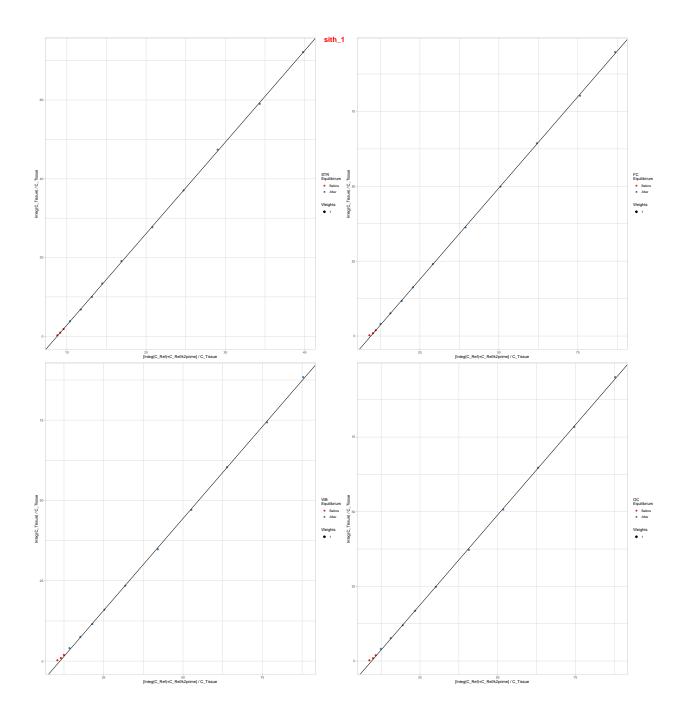


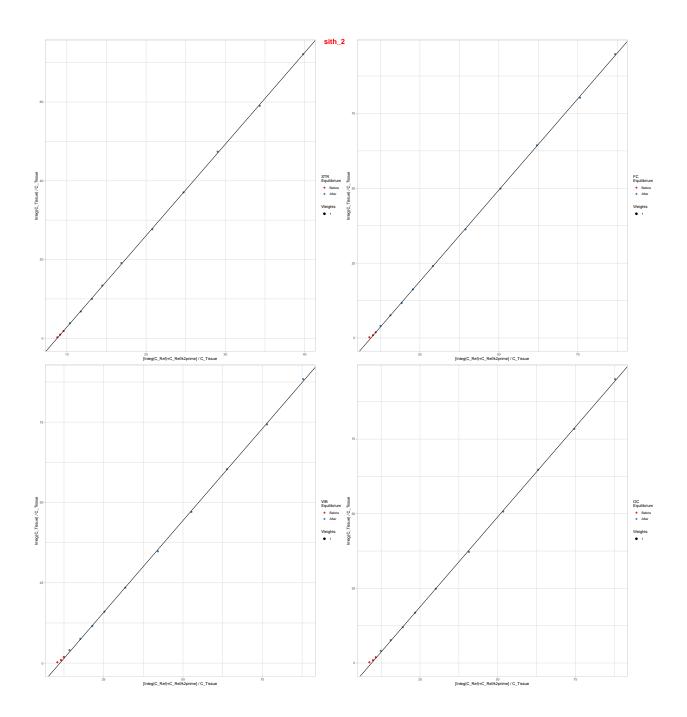


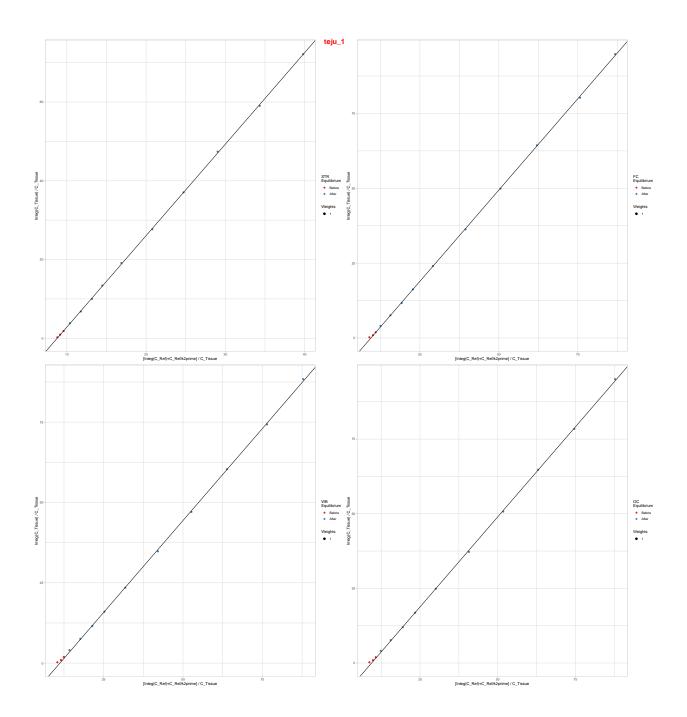


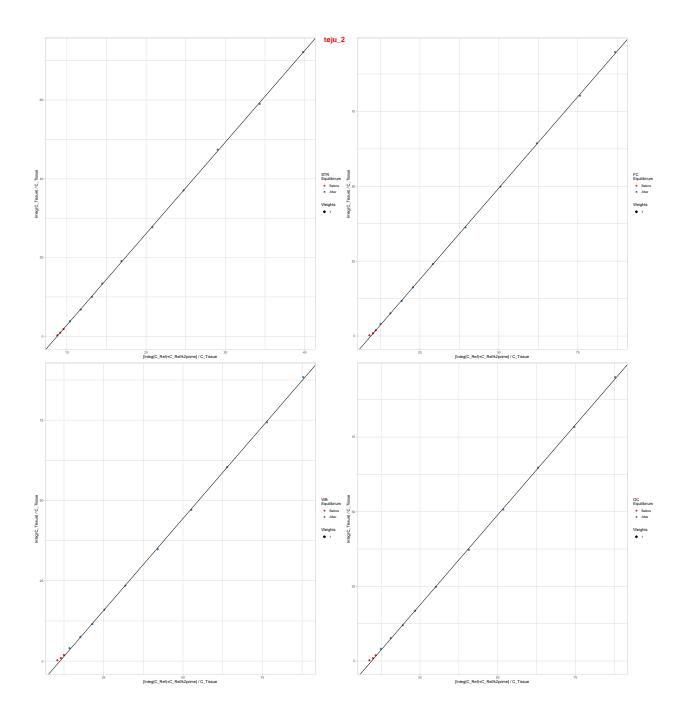












Test-retest

```
trt_check <- tacs_long %>%
  select(Subjname, PETNo, Region, bp_MRTM2, bp_srtm, bp_refLogan) %>%
  gather(Measure, Value, -Subjname, -PETNo, -Region) %>%
  group_by(Region, Measure) %>%
  nest(.key = "data")

# saveRDS(tacs_long,'../DerivedData/raw_kinfit_SCH23390.rds')
```

Making the trt_table

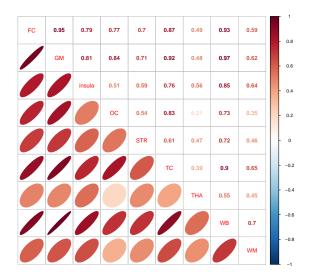
Region	Measure	mean	sd	cov	skew	kurtosis	icc	icc_l	icc_u	wscv	sdd	absvar
STR	bp_MRTM2	1.488	0.165	0.111	-0.307	-0.593	0.831	0.579	0.939	0.046	0.190	0.049
FC	bp_MRTM2	0.274	0.047	0.172	0.183	-0.346	0.581	0.132	0.835	0.112	0.085	0.129
WB	bp_MRTM2	0.195	0.038	0.196	0.248	-0.460	0.494	0.008	0.794	0.141	0.076	0.166
WM	bp_MRTM2	-0.107	0.051	-0.477	0.403	-1.318	0.862	0.648	0.951	-0.180	0.053	-0.302
GM	bp_MRTM2	0.253	0.040	0.158	0.210	-0.211	0.451	-0.047	0.773	0.118	0.083	0.136
OC	bp_MRTM2	0.268	0.061	0.227	0.064	-0.727	0.535	0.084	0.811	0.158	0.117	0.167
insula	bp_MRTM2	0.491	0.053	0.107	-0.004	-1.199	0.294	-0.228	0.689	0.091	0.123	0.102
Putamen	bp_MRTM2	1.591	0.136	0.086	-0.327	0.052	0.787	0.486	0.922	0.040	0.177	0.049
ACC	bp_MRTM2	0.459	0.052	0.113	0.218	-1.083	0.259	-0.265	0.668	0.097	0.124	0.111
THA	bp_MRTM2	0.074	0.062	0.844	0.090	-0.279	0.490	0.003	0.792	0.608	0.124	-24.441
TC	bp_MRTM2	0.363	0.054	0.150	0.145	-0.557	0.564	0.119	0.826	0.100	0.101	0.117
STR	bp_srtm	1.492	0.166	0.111	-0.313	-0.601	0.830	0.576	0.939	0.046	0.192	0.050
FC	bp_srtm	0.289	0.050	0.174	0.583	0.464	0.510	0.030	0.802	0.123	0.098	0.137
WB	bp_srtm	0.234	0.043	0.183	0.664	0.546	0.371	-0.144	0.731	0.146	0.095	0.167
WM	bp_srtm	-0.022	0.054	-2.495	0.357	-0.391	0.611	0.177	0.849	-1.573	0.094	1.895
GM	bp_srtm	0.283	0.045	0.158	0.728	1.167	0.349	-0.169	0.719	0.128	0.101	0.144
OC	bp_srtm	0.295	0.063	0.215	0.657	0.832	0.429	-0.053	0.758	0.165	0.135	0.149
insula	bp_srtm	0.525	0.055	0.105	0.021	-1.104	0.201	-0.322	0.633	0.094	0.136	0.103
Putamen	bp_srtm	1.593	0.137	0.086	-0.285	0.055	0.780	0.473	0.919	0.041	0.181	0.049
ACC	bp_srtm	0.486	0.054	0.111	0.394	-0.721	0.253	-0.271	0.665	0.096	0.130	0.110
THA	bp_srtm	0.087	0.063	0.726	-0.031	-0.228	0.392	-0.119	0.742	0.570	0.138	1.244
TC	bp_srtm	0.384	0.056	0.147	0.446	-0.006	0.417	-0.072	0.753	0.114	0.121	0.127
STR	$bp_refLogan$	1.485	0.168	0.113	-0.365	-0.596	0.825	0.566	0.937	0.048	0.198	0.053
FC	$bp_refLogan$	0.280	0.048	0.172	0.330	-0.045	0.550	0.086	0.821	0.116	0.090	0.131
WB	$bp_refLogan$	0.212	0.039	0.186	0.393	-0.072	0.446	-0.053	0.770	0.139	0.082	0.162
WM	$bp_refLogan$	-0.083	0.050	-0.600	0.379	-1.254	0.859	0.641	0.950	-0.229	0.053	-0.278
GM	$bp_refLogan$	0.266	0.041	0.155	0.383	0.249	0.416	-0.091	0.755	0.120	0.088	0.137
OC	$bp_refLogan$	0.280	0.061	0.218	0.243	-0.381	0.515	0.056	0.802	0.155	0.120	0.161
insula	$bp_refLogan$	0.503	0.054	0.106	-0.032	-1.178	0.241	-0.283	0.658	0.093	0.130	0.103
Putamen	$bp_refLogan$	1.586	0.138	0.087	-0.355	-0.003	0.784	0.480	0.921	0.041	0.181	0.049
ACC	$bp_refLogan$	0.468	0.052	0.111	0.287	-0.884	0.233	-0.291	0.653	0.098	0.127	0.109
THA	$bp_refLogan$	0.079	0.062	0.791	0.081	-0.241	0.456	-0.041	0.775	0.589	0.129	2.130
TC	bp_refLogan	0.371	0.055	0.149	0.248	-0.336	0.508	0.040	0.799	0.106	0.109	0.122

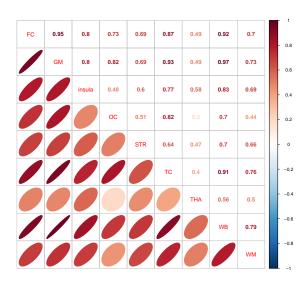
Interregional Correlation

Here the interregional correlations BP are assessed

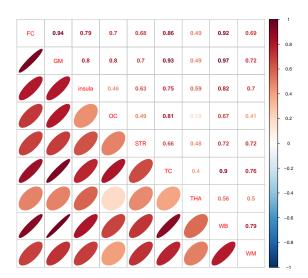
```
bp_srtm <- tacs_long %>%
  select(PET, Region, bp_srtm) %>%
  spread(Region, bp_srtm)
bp_mrtm2 <- tacs_long %>%
  select(PET, Region, bp_MRTM2) %>%
  spread(Region, bp_MRTM2)
bp_logan <- tacs_long %>%
  select(PET, Region, bp_refLogan) %>%
  spread(Region, bp_refLogan)
col2 <- colorRampPalette(rev(c("#67001F", "#B2182B", "#D6604D", "#F4A582", "#FDDBC7",</pre>
                           "#FFFFFF", "#D1E5F0", "#92C5DE", "#4393C3", "#2166AC", "#053061")))
par(mfrow=c(2,2))
bp_srtm %>%
  select(FC:WM, - Putamen) %>%
  cor() %>%
  corrplot.mixed(lower='ellipse', upper='number',
                 lower.col = col2(200), upper.col = col2(200), diag='n',
                 number.digits = 2, title=expression(bp_srtm ~ Correlations),
                 mar=c(0,0,1,0))
bp_logan %>%
  select(FC:WM, - Putamen) %>%
  cor() %>%
  corrplot.mixed(lower='ellipse', upper='number',
                 lower.col = col2(200), upper.col = col2(200), diag='n',
                 number.digits = 2, title=expression(bp_logan ~ Correlations),
                 mar=c(0,0,1,0)
bp_mrtm2 %>%
  select(FC:WM, - Putamen) %>%
  cor() %>%
  corrplot.mixed(lower='ellipse', upper='number',
                 lower.col = col2(200), upper.col = col2(200), diag='n',
                 number.digits = 2, title=expression(bp_MRTM2 ~ Correlations),
                 mar=c(0,0,1,0)
```

bp_srtm Correlations bp_logan Correlations





bp_MRTM2 Correlations

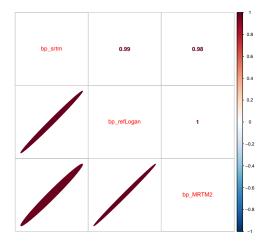


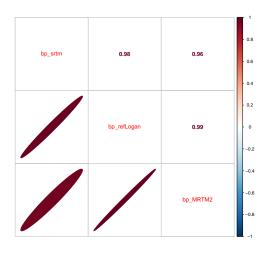
 $\# \mbox{Corrplot}$ between measures for a single region

```
number.digits = 2, title=expression(Model ~ Correlations ~ Region: FC),
                 mar=c(0,0,1,0)
compare %>%
  filter(Region == "OC") %>%
  select(bp_srtm:bp_MRTM2) %>%
  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 == "insula") %>%
  select(bp_srtm:bp_MRTM2) %>%
  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: insula),
                 mar=c(0,0,1,0))
compare %>%
 filter(Region == "WB") %>%
  select(bp_srtm:bp_MRTM2) %>%
  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)
```



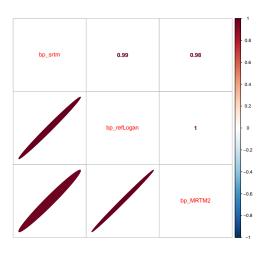
Model Correlations Region : OC

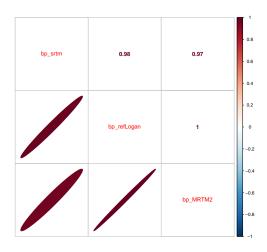




Model Correlations Region : insula

Model Correlations Region : WB





bp corellation

R-squared

```
trtdata <- tacs_long %>%
  select(PET, Subjname, PETNo, Region, bp_refLogan, bp_srtm, bp_MRTM2) %>%
  gather(Measure, Value, -(PET:Region)) %>%
  spread(Region, Value)

trtdata <- trtdata %>%
  select( -(c(STR, OC, insula))) %>%
  gather(Region, Value, -(PET:Measure)) %>%
  unite(Outcome, Measure, Region) %>%
```

```
corout <- trtdata %>%
  gather(Measure, Binding, -(PET:PETNo), -bp_srtm_WB) %>%
  group_by(Measure) %>%
  summarise('R^2^'=cor(Binding, bp_srtm_WB)^2) %>%
  arrange(Measure) %>%
  ungroup() %>%
  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='WB', replacement='WB-')) %>%
  mutate(Measure = str_replace(string=Measure, pattern='OC', replacement='UB-')) %>%
  mutate(Measure = str_replace(string=Measure, pattern='OC', replacement='OC-')) %>%
  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-")
```

Table 2: Correlations with BP_srtm_{WB}

Measure	R^2
bp~MRTM2_ACC	0.46
bp_{MRTM2_FC}	0.78
bp_{MRTM2_GM}	0.86
bp~MRTM2_Putamen	0.48
bp~MRTM2_TC	0.76
bp~MRTM2_THA	0.26
bp_{MRTM2_WB}	0.94
bp _{MRTM2_WM}	0.69
bp~refLogan_ACC	0.49
$\mathrm{bp_{refLogan_FC}}$	0.82
$\mathrm{bp_{refLogan_GM}}$	0.90
bp~refLogan_Putamen	0.47
bp~refLogan_TC	0.78
bp~refLogan_THA	0.29
$\mathrm{bp_{refLogan}}_{\mathrm{WB}}$	0.96
$\mathrm{bp_{refLogan}_WM}$	0.67
bp~srtm_ACC	0.52
$\mathrm{bp}_{\mathrm{srtm_FC}}$	0.86
$\mathrm{bp}_{\mathrm{srtm_GM}}^{\mathrm{-}}$	0.95
bp~srtm_Putamen	0.48
bp~srtm_TC	0.80
bp~srtm_THA	0.31
$\mathrm{bp}_{\mathrm{srtm}}$	0.49

#Plot of the change between PETNo = 1 and PETNo = 2. error bars for the wscv probably mean nothing as there is just a single value, but looks nice?

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

