Supplemental File 1

Guilliams et al. AJNR 2021: MRI Protocol Specifics

Scanner	TRIO	TRIO	TRIO
Head coil	32-channel	32-channel	32-channel
Sequence	T1-MPRAGE	TOF-MRA	T2-SPACE
Mode	3D	3D	3D
Orientation	Sagittal	Axial	Axial
Resolution (mm)	1.0 x 1.0 x 1.0	0.57 x 0.57 x 0.69	0.53 x 0.53 x 0.50
TE (ms)	2.94	3.59	132
TR (ms)	1800	20	1000
Flip angle (deg)	8	18	120
Other			

Scanner	TRIO	TRIO
Head coil	32-channel	32-channel
Sequence	PC-CBF	pCASL
Mode	2D	3D
Orientation	Axial	Axial
Resolution (mm)	0.7 x 0.7 x 5.0	3.0 x 3.0 x 5.0
TE (ms)	4.06	12
TR (ms)	107.2	3780
Flip angle (deg)	25	90
Other	Level = C2-C3 VENC = 120 cm/s 10 averages	Labeling Duration = 2000ms Postlabeling delay = 1500ms

Scanner	PrismaFit	PrismaFit	PrismaFit
Head coil	32-channel	32-channel	32-channel
Sequence	TOF-MRA	pCASL	T1-MPRAGE
Mode	3D	3D	3D
Orientation	Axial	Axial	Sagittal
Resolution (mm)	0.57 x 0.57 x 0.69	3.0 x 3.0 x 5.0	1.0 x 1.0 x 1.0
TE (ms)	3.59	12	2.94
TR (ms)	21	3810	1810
Flip angle (deg)	18	90	8
Other		Labeling Duration = 2000ms Postlabeling delay = 1500ms	

Supplemental File 2:

Code for Statistical Analysis

```
# Circle of Willis in Children and Adults Final Analysis
#
# Last Updated: 2021 June 14
# Code checked with Kristin Guilliams and Michael Binkley

library(ggplot2)
library(grid)
library(reshape)
library(randomForest)
library(glmnet)
library(plotly)
library(diptest)
library(Rtsne)
library(raster)
library(ggseg)
library(tsne)


setwd("C:/Users/Manu/Documents/Lifespan Brain Vasculature/Final Data")
rawdata = t(read.csv("MasterDataNov19.csv", stringsAsFactors = FALSE))
dim(rawdata)
mdata = as.data.frame(rawdata[2:67,], stringsAsFactors = FALSE)
names(mdata) = rawdata[1,]
dim(mdata)
names(mdata)
rm(rawdata)
mdata[,1] = as.numeric(mdata[,1])
for (n in 4:464){
  mdata[,n] = as.numeric(mdata[,n])
}
mdata$wholebrain.FQ = apply(cbind(mdata$LICA.FQ, mdata$RICA.FQ,
mdata$Lvert.FQ, mdata$Rvert.FQ),1,
                            function(x) sum(x,na.rm=TRUE))
mdata$wholebrain.FQ[which(mdata$wholebrain.FQ==0)] = NA
mdata$wholebrain.FQ
cbind(mdata$wholebrain.FQ,mdata$LICA.FQ,mdata$RICA.FQ,mdata$Lvert.FQ,m
data$Rvert.FQ)

cor.test(mdata$wholebrain.CBF,mdata$wholebrain.CBFs)
# Smoothing (CBFs) lowers the CBF estimates. Best to use the
unsmoothed data.

mean(as.numeric(mdata$Age[which(as.numeric(mdata$Age)<19)]))
mean(as.numeric(mdata$Age[which(as.numeric(mdata$Age)>18)]))
table(mdata$Sex[which(as.numeric(mdata$Age)<19)])
table(mdata$Sex[which(as.numeric(mdata$Age)>18)])

plot(mdata$wholebrain.CBF,mdata$wholebrain.FQ)
```

```
mdata$brainvolume =
mdata$cerebralvolume+mdata$brainstem+mdata$cerebellum.L.Vol+mdata$cere
bellum.R.Vol
# Units for flow quant whole brain is in mL/sec
# Note that whole brain CBF based on ASL is in terms of mL/min/100g
brain tissue

# Compare whole brain blood flow based on FQ vs ASL
plot(mdata$wholebrain.FQ*60,
     mdata$wholebrain.CBF*(mdata$brainvolume)/100000,
     xlim = c(0,1600),ylim=c(0,1600),
     xlab = "Phase contrast MRI", ylab = "ASL")
points(cbind(seq(0,1600,1),seq(0,1600,1)),type="l")
cor.test(mdata$wholebrain.FQ*60,
         mdata$wholebrain.CBF*(mdata$brainvolume)/100000)
FQASL = cbind(mdata$wholebrain.FQ*60,
              mdata$wholebrain.CBF*(mdata$brainvolume)/100000)
FQASL = FQASL[which(!is.na(FQASL[,1])),]
FQASL = FQASL[which(!is.na(FQASL[,2])),]
summary(glm(FQASL[,2]~FQASL[,1]))
0.9588+0.1065*1.96; 0.9588-0.1065*1.96;

# Next step is to start looking at the vessel diameters
names(mdata)[1:3] # Age, Sex, noise
names(mdata)[4:55] # TOF data (first 4 are basilar and ACOM, next 8:31
are LTOF, next 32:55 are RTOF)
names(mdata)[56:83] # T2 data (56,57 = Bd and ACOM, 58:70 = C7-SCA.L,
71:83 = C7-SCA.R)

# Make a matrix of vessel diameters for MDS
vessels.TOF = mdata[,4:55]
# Simplify and prepare by taking out the heavy NA sections
names(vessels.TOF)
vessels.TOF = vessels.TOF[,-c(17,18,22,24,25,41,42,46,48,49)]
names(vessels.TOF)
vessels.Age = mdata$Age
vessels.Sex = mdata$Sex
rownames(vessels.TOF)

# Remove those with missing data, significant MRA noise
mdata$MRAnoise[c(14,23,25,59,63)]
vessels.TOF[c(14,23,25,59,63),]
vessels.TOF = vessels.TOF[-c(14,23,25,59,63),]
vessels.Age = vessels.Age[-c(14,23,25,59,63)]
vessels.Sex = vessels.Sex[-c(14,23,25,59,63)]

# Set TOF-MRA NA's to 0, as these reflect non-visualized vessel
segments (none affect CoW)
vessels.TOF[which(is.na(vessels.TOF),arr.ind=TRUE)] = 0   # affects
only 9 vessels, all AICA and PICA, felt to be absent
mdata$P2.L.T2[which(mdata$P2.L.T2==0)]=NA
```

```
# Define circle of Willis

# The idea is that there are 7 components: A1.L, A1.R, ACOM, PCOM.L,
PCOM.R, P1.L, and P1.R
mean(mdata$A1.L.TOF,na.rm=TRUE)
mean(mdata$A1.R.TOF,na.rm=TRUE)
mean(mdata$PCOM.L.TOF,na.rm=TRUE)
mean(mdata$PCOM.R.TOF,na.rm=TRUE)
mean(mdata$P1.L.TOF,na.rm=TRUE)
mean(mdata$P1.R.TOF,na.rm=TRUE)
mean(mdata$ACOM.TOF,na.rm=TRUE)

# Create CoW matrix
names(vessels.TOF)[c(13,32,12,31,17,36,4)]
CoW.TOF = vessels.TOF[,c(13,32,12,31,17,36,4)]
names(CoW.TOF)

CoW.area = pi*(CoW.TOF[,1]/2)^2 + pi*(CoW.TOF[,2]/2)^2 +
pi*(CoW.TOF[,3]/2)^2 +
  pi*(CoW.TOF[,4]/2)^2 + pi*(CoW.TOF[,5]/2)^2 + pi*(CoW.TOF[,6]/2)^2 +
  pi*(CoW.TOF[,7]/2)^2

cbind(vessels.Age,rowMeans(CoW.TOF))
cor.test(vessels.Age,rowMeans(CoW.TOF))
t.test(rowMeans(CoW.TOF)[which(vessels.Age<19)],rowMeans(CoW.TOF)[whic
h(vessels.Age>18)])
t.test(CoW.area[which(vessels.Age<19)],CoW.area[which(vessels.Age>18)]
)

mean(CoW.area[which(vessels.Age<19)])
sd(CoW.area[which(vessels.Age<19)])
mean(CoW.area[which(vessels.Age<19)])+(sd(CoW.area[which(vessels.Age<1
9)])/sqrt(19))*1.96
mean(CoW.area[which(vessels.Age<19)])-
(sd(CoW.area[which(vessels.Age<19)])/sqrt(19))*1.96
mean(CoW.area[which(vessels.Age>18)])
sd(CoW.area[which(vessels.Age>18)])
mean(CoW.area[which(vessels.Age>18)])+(sd(CoW.area[which(vessels.Age>1
8)])/sqrt(42))*1.96
mean(CoW.area[which(vessels.Age>18)])-
(sd(CoW.area[which(vessels.Age>18)])/sqrt(42))*1.96

boxplot(CoW.area[which(vessels.Age<19)],CoW.area[which(vessels.Age>18)
],
        xlab="Children vs Adults",ylab="CoW.area",outline=FALSE)
points(jitter(c(rep(1,19),rep(2,42))),

c(CoW.area[which(vessels.Age<19)],CoW.area[which(vessels.Age>18)]),
       col="blue",pch=19)

apply(vessels.TOF[which(vessels.Age<19),],2,mean)
apply(vessels.TOF[which(vessels.Age<19),],2,sd)
```

```
apply(vessels.TOF[which(vessels.Age>18),],2,mean)
apply(vessels.TOF[which(vessels.Age>18),],2,sd)

# Create CoW.di
CoW.norm.TOF = CoW.TOF
for (n in 1:61){
  CoW.norm.TOF[n,] = CoW.TOF[n,]/mean(as.numeric(CoW.TOF[n,]))
}
colMeans(CoW.norm.TOF)
cor(cbind(vessels.Age,CoW.norm.TOF))

# PCOM has reciprocal unilateral relationship with P1 (-0.67 L, -0.70
R)
# ACOM has a stronger reciprocal relationship with the right A1 (-0.04
L, -0.52 R)

rbind(CoW.norm.TOF[1,],colMeans(CoW.norm.TOF))
CoW.DI = vector('numeric',61)
CoW.means = colMeans(CoW.norm.TOF)
for (n in 1:61){
  CoW.DI[n] = (CoW.norm.TOF[n,1]-CoW.means[1])^2+
    (CoW.norm.TOF[n,2]-CoW.means[2])^2+
    (CoW.norm.TOF[n,3]-CoW.means[3])^2+
    (CoW.norm.TOF[n,4]-CoW.means[4])^2+
    (CoW.norm.TOF[n,5]-CoW.means[5])^2+
    (CoW.norm.TOF[n,6]-CoW.means[6])^2+
    (CoW.norm.TOF[n,7]-CoW.means[7])^2
  CoW.DI[n] = sqrt(CoW.DI[n])
}

plot(vessels.Age,CoW.DI)
cor.test(vessels.Age,CoW.DI)

mean(CoW.DI[which(vessels.Age<19)])
sd(CoW.DI[which(vessels.Age<19)])
mean(CoW.DI[which(vessels.Age<19)])+(sd(CoW.DI[which(vessels.Age<19)])
/sqrt(19))*1.96
mean(CoW.DI[which(vessels.Age<19)])-
(sd(CoW.DI[which(vessels.Age<19)])/sqrt(19))*1.96
mean(CoW.DI[which(vessels.Age>18)])
sd(CoW.DI[which(vessels.Age>18)])
mean(CoW.DI[which(vessels.Age>18)])+(sd(CoW.DI[which(vessels.Age>18)])
/sqrt(42))*1.96
mean(CoW.DI[which(vessels.Age>18)])-
(sd(CoW.DI[which(vessels.Age>18)])/sqrt(42))*1.96

t.test(CoW.DI[which(vessels.Age<19)],CoW.DI[which(vessels.Age>18)])
wilcox.test(CoW.DI[which(vessels.Age<19)],CoW.DI[which(vessels.Age>18)
])


boxplot(CoW.DI[which(vessels.Age<19)],CoW.DI[which(vessels.Age>18)],
```

```
        xlab="Children vs Adults",ylab="CoW.di",outline=FALSE)
points(jitter(c(rep(1,19),rep(2,42))),
       c(CoW.DI[which(vessels.Age<19)],CoW.DI[which(vessels.Age>18)]),
       col="blue",pch=19)

# Confirm with T2-SPACE data
vessels.T2 = mdata[,56:83]
names(vessels.T2)
CoW.T2 = vessels.T2[,c(6,19,5,18,12,25,2)]
CoW.T2 = CoW.T2[-c(14,23,25,38,59,60,61,62,63,64,65,66),]
vessels.Age.T2 = mdata$Age[-c(14,23,25,38,59,60,61,62,63,64,65,66)]
# Set all other NA's to 0
CoW.T2[which(is.na(CoW.T2),arr.ind=TRUE)] = 0 #No NA's, code left in
to be c/w TOF above

CoW.T2.area = pi*(CoW.T2[,1]/2)^2 + pi*(CoW.T2[,2]/2)^2 +
pi*(CoW.T2[,3]/2)^2 +
  pi*(CoW.T2[,4]/2)^2 + pi*(CoW.T2[,5]/2)^2 + pi*(CoW.T2[,6]/2)^2 +
  pi*(CoW.T2[,7]/2)^2


CoW.norm.T2 = CoW.T2
cor.test(vessels.Age.T2,rowMeans(CoW.T2))
t.test(rowMeans(CoW.T2)[which(vessels.Age.T2<19)],rowMeans(CoW.T2)[whi
ch(vessels.Age.T2>18)],alternative=c("greater"))
t.test(CoW.T2.area[which(vessels.Age.T2<19)],CoW.T2.area[which(vessels
.Age.T2>18)],alternative=c("greater"))
length(which(vessels.Age.T2<19)); length(which(vessels.Age.T2>18))
mean(CoW.T2.area[which(vessels.Age.T2<19)])+sd(CoW.T2.area[which(vesse
ls.Age.T2<19)])/sqrt(15)*1.96
mean(CoW.T2.area[which(vessels.Age.T2<19)])-
sd(CoW.T2.area[which(vessels.Age.T2<19)])/sqrt(15)*1.96
mean(CoW.T2.area[which(vessels.Age.T2>18)])+sd(CoW.T2.area[which(vesse
ls.Age.T2>18)])/sqrt(39)*1.96
mean(CoW.T2.area[which(vessels.Age.T2>18)])-
sd(CoW.T2.area[which(vessels.Age.T2>18)])/sqrt(39)*1.96

(16.60751-14.23182)/14.23182
# Confirms results with T2-SPACE

for (n in 1:54){
  CoW.norm.T2[n,] = CoW.T2[n,]/mean(as.numeric(CoW.T2[n,]))
}
colMeans(CoW.norm.T2)
cor(cbind(vessels.Age.T2,CoW.norm.T2))

# PCOM has reciprocal unilateral relationship with P1 bilaterally (-
0.66 L, -0.68 R)
# ACOM has a stronger reciprocal relationship with the right A1 (-0.07
L, -0.51 R)

rbind(CoW.norm.T2[1,],colMeans(CoW.norm.T2))
```

```
CoW.DI.T2 = vector('numeric',54)
CoW.means.T2 = colMeans(CoW.norm.T2)
for (n in 1:54){
  CoW.DI.T2[n] = (CoW.norm.T2[n,1]-CoW.means.T2[1])^2+
    (CoW.norm.T2[n,2]-CoW.means.T2[2])^2+
    (CoW.norm.T2[n,3]-CoW.means.T2[3])^2+
    (CoW.norm.T2[n,4]-CoW.means.T2[4])^2+
    (CoW.norm.T2[n,5]-CoW.means.T2[5])^2+
    (CoW.norm.T2[n,6]-CoW.means.T2[6])^2+
    (CoW.norm.T2[n,7]-CoW.means.T2[7])^2
  CoW.DI.T2[n] = sqrt(CoW.DI.T2[n])
}

mean(CoW.DI.T2[which(vessels.Age.T2<19)])
mean(CoW.DI.T2[which(vessels.Age.T2>18)])
t.test(CoW.DI.T2[which(vessels.Age.T2<19)],CoW.DI.T2[which(vessels.Age
.T2>18)], alternative=c("less"))

mean(CoW.DI.T2[which(vessels.Age.T2<19)])+sd(CoW.DI.T2[which(vessels.A
ge.T2<19)])/sqrt(15)*1.96
mean(CoW.DI.T2[which(vessels.Age.T2<19)])-
sd(CoW.DI.T2[which(vessels.Age.T2<19)])/sqrt(15)*1.96
mean(CoW.DI.T2[which(vessels.Age.T2>18)])+sd(CoW.DI.T2[which(vessels.A
ge.T2>18)])/sqrt(39)*1.96
mean(CoW.DI.T2[which(vessels.Age.T2>18)])-
sd(CoW.DI.T2[which(vessels.Age.T2>18)])/sqrt(39)*1.96

hist(CoW.DI.T2[which(vessels.Age.T2<19)])
hist(CoW.DI.T2[which(vessels.Age.T2>18)])
wilcox.test(CoW.DI.T2[which(vessels.Age.T2<19)],CoW.DI.T2[which(vessel
s.Age.T2>18)], alternative=c("less"), conf.int=TRUE)

# So all key results are confirmed with separately acquired T2 SPACE
data


# Look at (L-R) asymmetry index
# Measure distance between L and R A1, P1, and PCOM
CoW.AI.TOF = sqrt(
  (CoW.norm.TOF[,1]-CoW.norm.TOF[,2])^2 +
    (CoW.norm.TOF[,3]-CoW.norm.TOF[,4])^2 +
    (CoW.norm.TOF[,5]-CoW.norm.TOF[,6])^2
)
t.test(CoW.AI.TOF[which(vessels.Age<19)],CoW.AI.TOF[which(vessels.Age>
18)])
# CoW is more left-right asymmetric in adults

# Look at anatomic and functional 'completeness'

which(CoW.TOF[which(vessels.Age<19),]==0,arr.ind=TRUE)
length(which(vessels.Age<19))*7
5/133
```

```
# So 5 undetectable out of 133 segments (3.8%) in children
5/19
# So 26.3% with 'incomplete' CoW

which(CoW.TOF[which(vessels.Age>18),]==0,arr.ind=TRUE)
dim(table(which(CoW.TOF[which(vessels.Age>18),]==0,arr.ind=TRUE)[,1]))
# Number of adults with missing segments
length(table(which(CoW.TOF[which(vessels.Age>18),]==0,arr.ind=TRUE)[,1
]))
dim(which(CoW.TOF[which(vessels.Age>18),]==0,arr.ind=TRUE))
length(which(vessels.Age>18))*7
dim(CoW.TOF[which(vessels.Age>18),])
31/294
23/42
# So 54.8% with 'incomplete' CoW

fisher.test(cbind(c(5,133),c(31,294)))
# So significant at p=0.036 (OR 0.36, CI: 0.11-0.96)

# Check reliability data
irrdata =
read.csv("VesselReliability.csv",header=FALSE,stringsAsFactors =
FALSE)
names(irrdata)
which(mdata$Age==4 & mdata$Sex=="F")
cbind(t(mdata[57,8:20]),irrdata[5:17,3])

# Now match vessels and check intrarater reliability
cbind(irrdata[5:72,1],irrdata[73:140,1])
# It all matches
library(irr)
icc.intra = vector('numeric',15)
for(n in 1:15){
  icc.intra[n] =
icc(cbind(as.numeric(irrdata[5:72,n+1]),as.numeric(irrdata[73:140,n+1]
)))$value
}
icc(cbind(as.numeric(unlist(irrdata[5:72,2:16])),as.numeric(unlist(irr
data[73:140,2:16]))))
min(icc.intra)
max(icc.intra)
median(icc.intra)
mean(icc.intra)
# ICC is high for intra-rater reliability across subjects: 0.96 (0.89-
0.98)
cor.test(icc.intra,as.numeric(irrdata[1,2:16]))
# So no age relationship
# Also look for error and whether it relates to size
error.intra = matrix(NA,68,15)
for(n in 1:15){
  error.intra[,n]=as.numeric(irrdata[73:140,n+1])-
as.numeric(irrdata[5:72,n+1])
```

```
}
hist(error.intra)
median(error.intra)
mean(error.intra)
sd(error.intra)
mean(abs(error.intra))
# Mean absolute deviation was 0.216 mm (about half the resolution)
# Minimal difference in error with different values
# To summarize: ICC was 0.96 without relation to age
# Mean absolute deviation was 0.22 mm (about half the resolution)
# No intra rater bias (0 mm median and 0.02 mm mean)

# Now test interrater
# Remove 17, 37, 56, 67, 153, 173, 192, 203
irr.inter = irrdata[c(-17,-37,-56,-67,-153,-173,-192,-203),]
irr.inter1 = irr.inter[c(5:68),]
irr.inter2 = irr.inter[c(137:200),]
cbind(irr.inter1[,1],irr.inter2[,1])
# Ok, they match
icc.inter = vector('numeric',15)
icc(cbind(as.numeric(unlist(irr.inter1[1:64,2:16])),as.numeric(unlist(
irr.inter2[1:64,2:16]))))
for(n in 1:15){
  icc.inter[n] =
icc(cbind(as.numeric(irr.inter1[1:64,n+1]),as.numeric(irr.inter2[1:64,
n+1])))$value
}
icc.inter
min(icc.inter)
max(icc.inter)
mean(icc.inter)
# ICC mean was 0.86 across the subjects
cor.test(icc.inter,as.numeric(irrdata[1,2:16]))
# No significant correlation with age
# Now check for errors and bias

error.inter = matrix(NA,64,15)
error.inter.full = mean(as.numeric(unlist(irr.inter1[1:64,2:16]))-
as.numeric(unlist(irr.inter2[1:64,2:16])),na.rm=TRUE)
for(n in 1:15){
  error.inter[,n]=as.numeric(irr.inter1[1:64,n+1])-
as.numeric(irr.inter2[1:64,n+1])
}
hist(error.inter)
median(error.inter,na.rm=TRUE)
mean(error.inter,na.rm=TRUE)
sd(error.inter,na.rm=TRUE)
mean(abs(error.inter),na.rm=TRUE)
# Mean absolute deviation here is 0.53, but there is also a bias of -
0.49 mm

# If we correct for this, then what do we get?
```

```
mean(abs(error.inter-mean(error.inter,na.rm=TRUE)),na.rm=TRUE)
# Thus, accounting for the -0.49 mm bias, one gets a 0.31 mm MAD

cor.test(as.numeric(as.matrix(irr.inter1[1:64,2:16])),as.numeric(abs(e
rror.inter-mean(error.inter,na.rm=TRUE)),na.rm=TRUE))
# No correlation with size

# So bottom line: high intra- and inter-rater reliability (0.96 and
0.86, respectively)
# For intra-rater: 0.02 mm bias, 0.22 mm MAD
# For inter-rater: 0.49 mm bias, 0.31 mm MAD (after correcting for the
bias)

# Comparison with atlas (Sci Data 2019)
# Radii: ICA ~1.7, M1 ~1.1, BA ~1.3
mean(c(mdata$C7.L.TOF,mdata$C7.R.TOF),na.rm=TRUE)/2
mean(c(mdata$M1.L.TOF,mdata$M1.R.TOF),na.rm=TRUE)/2
mean(c(mdata$Bm.TOF),na.rm=TRUE)/2
mean(c(mdata$C7.L.T2,mdata$C7.R.T2),na.rm=TRUE)/2
mean(c(mdata$M1.L.T2,mdata$M1.R.T2),na.rm=TRUE)/2
mean(c(mdata$Bd.T2),na.rm=TRUE)/2
# Fairly consistent, though M1 and BA a bit higher in this study
(likely due to children)

# How does CoW.area and CoW.di compare to CBF?
cor.test(CoW.area,CoW.DI)
CoW.CBF = mdata$wholebrain.CBF[-c(14,23,25,59,63)]
cor.test(CoW.area,CoW.CBF)
plot(CoW.CBF,CoW.area)
cor.test(CoW.DI,CoW.CBF)
plot(CoW.CBF,CoW.DI)

cor.test(CoW.CBF,vessels.Age)

t.test((mdata$wholebrain.CBF*mdata$brainvolume/100000)[mdata$Age<19],
       (mdata$wholebrain.CBF*mdata$brainvolume/100000)[mdata$Age>18])

mean((mdata$wholebrain.CBF*mdata$brainvolume/100000)[mdata$Age<19],na.
rm=TRUE)
sd((mdata$wholebrain.CBF*mdata$brainvolume/100000)[mdata$Age<19],na.rm
=TRUE)
length(which(!is.na((mdata$wholebrain.CBF*mdata$brainvolume/100000)[md
ata$Age<19])))
mean((mdata$wholebrain.CBF*mdata$brainvolume/100000)[mdata$Age>18],na.
rm=TRUE)
sd((mdata$wholebrain.CBF*mdata$brainvolume/100000)[mdata$Age>18],na.rm
=TRUE)
length(which(!is.na((mdata$wholebrain.CBF*mdata$brainvolume/100000)[md
ata$Age>18])))

mean((mdata$brainvolume/1000000)[mdata$Age<19],na.rm=TRUE)
sd((mdata$brainvolume/1000000)[mdata$Age<19],na.rm=TRUE)
```

```
length(which(!is.na((mdata$brainvolume/1000000)[mdata$Age<19])))
mean((mdata$brainvolume/1000000)[mdata$Age>18],na.rm=TRUE)
sd((mdata$brainvolume/1000000)[mdata$Age>18],na.rm=TRUE)
length(which(!is.na((mdata$brainvolume/1000000)[mdata$Age>18])))


# whole brain CBF in children is ~1.1 L/min vs 0.7 L/min in adults
mean((mdata$wholebrain.CBF*mdata$brainvolume/100000)[mdata$Age<19],na.
rm=TRUE)/

mean((mdata$wholebrain.CBF*mdata$brainvolume/100000)[mdata$Age>18],na.
rm=TRUE)
# whole brain CBF is 59% higher in children
mean(CoW.area[vessels.Age<19])/mean(CoW.area[vessels.Age>18])
# CoW area is ~56% higher in children

# Does PCOM+P1 asymmetry correlate with occipital lobe CBF asymmetry?
PCOM.AI = vessels.TOF$PCOM.L.TOF-vessels.TOF$PCOM.R.TOF
RPCA.CBF =
mdata$cuneus.R.CBF*mdata$cuneus.R.Vol+mdata$pericalcarine.R.CBF*mdata$
pericalcarine.R.Vol+
  mdata$lateraloccipital.R.CBF*mdata$lateraloccipital.R.Vol
LPCA.CBF =
mdata$cuneus.L.CBF*mdata$cuneus.L.Vol+mdata$pericalcarine.L.CBF*mdata$
pericalcarine.L.Vol+
  mdata$lateraloccipital.L.CBF*mdata$lateraloccipital.L.Vol
PCA.AI = LPCA.CBF/RPCA.CBF
PCA.AI = PCA.AI[-c(14,23,25,59,63)]
cor.test(PCOM.AI,PCA.AI)
cor.test(abs(PCOM.AI),PCA.AI)
# Interesting--There is a modest correlation, suggesting L-R asymmetry
correlation

# Does A1 asymmetry correlate with ACA CBF?
A1.AI = vessels.TOF$A1.L.TOF-vessels.TOF$A1.R.TOF
RACA.CBF =
mdata$rostralanteriorcingulate.R.CBF*mdata$rostralanteriorcingulate.R.
Vol+

mdata$caudalanteriorcingulate.R.CBF*mdata$caudalanteriorcingulate.R.Vo
l+
  mdata$medialorbitofrontal.R.CBF*mdata$medialorbitofrontal.R.Vol+
  mdata$superiorfrontal.R.CBF*mdata$superiorfrontal.R.Vol
LACA.CBF =
mdata$rostralanteriorcingulate.L.CBF*mdata$rostralanteriorcingulate.L.
Vol+

mdata$caudalanteriorcingulate.L.CBF*mdata$caudalanteriorcingulate.L.Vo
l+
  mdata$medialorbitofrontal.L.CBF*mdata$medialorbitofrontal.L.Vol+
  mdata$superiorfrontal.L.CBF*mdata$superiorfrontal.L.Vol
ACA.AI = LACA.CBF/RACA.CBF
```

```
ACA.AI = ACA.AI[-c(14,23,25,59,63)]
cor.test(A1.AI,ACA.AI)
# A1 asymmetry does not correlate with ACA CBF asymmetry

# Finally check antero-posterior asymmetry correlation
CoW.API =
(vessels.TOF$PCOM.L.TOF+vessels.TOF$PCOM.R.TOF+vessels.TOF$P1.L.TOF+ve
ssels.TOF$P1.R.TOF)/
  (vessels.TOF$A1.L.TOF+vessels.TOF$A1.R.TOF)
hist(CoW.API)
CBF.API = (LPCA.CBF+RPCA.CBF)/(LACA.CBF+RACA.CBF)
CBF.API = CBF.API[-c(14,23,25,59,63)]
cor.test(CBF.API, CoW.API)
# So no significant correlation here also

# Figures for the paper

# Figure 3: CoW.area in children vs adults, CoW.di in children vs
adults
boxplot(CoW.area[which(vessels.Age<19)],CoW.area[which(vessels.Age>18)
],
        ylab="Total CoW cross-sectional area",
names=c("Children","Adults"),

outline=FALSE,col=c("orange","skyblue"),cex.axis=1.5,cex.lab=1.5)
points(jitter(c(rep(1,19),rep(2,42))),

c(CoW.area[which(vessels.Age<19)],CoW.area[which(vessels.Age>18)]),
       col="black",pch=19,cex=1.3)

boxplot(CoW.DI[which(vessels.Age<19)],CoW.DI[which(vessels.Age>18)],
        ylab="CoW deviation index", names=c("Children","Adults"),

outline=FALSE,col=c("orange","skyblue"),cex.axis=1.5,cex.lab=1.5)
points(jitter(c(rep(1,19),rep(2,42))),
       c(CoW.DI[which(vessels.Age<19)],CoW.DI[which(vessels.Age>18)]),
       col="black",pch=19,cex=1.3)

# Figure 4: CBF change over time overlapped with CoW.area change over
time
par(mar = c(5, 5, 3, 5))
col1 = "blue"
col2 = "red"
cexaxis = 1.5
plot(vessels.Age,CoW.area,type="p",ylab="",
     xlab="",cex=1,col=col1,cex.axis=cexaxis)
points(seq(4,70,1),predict(loess(CoW.area~vessels.Age,span=1),seq(4,70
,1)),type="l",col=col1,lwd=3,lty=5)
mtext("Age (years)",side=1,line=3,cex=cexaxis)
axis(side=2,col=col1,col.axis=col1,col.lab=col1,cex.axis=cexaxis)
mtext("Total CoW cross-sectional area (sq-
mm)",side=2,line=3,col=col1,cex=cexaxis)
```

```
par(new=TRUE)
plot(vessels.Age,CoW.CBF,type="p",xaxt="n",yaxt="n",ylab="",xlab="",co
l=col2,cex=1)
points(seq(4,70,1),predict(loess(CoW.CBF~vessels.Age,span=1),seq(4,70,
1)),type="l",col=col2,lwd=3,lty=5)
axis(side=4,col=col2,col.axis=col2,col.lab=col2,cex.axis=cexaxis)
mtext("Whole brain CBF (mL/100g/min)", side = 4, line = 3,
col=col2,cex=cexaxis)
legend("topright", c("CoW-area", "CBF"),
       col = c(col1, col2), lty = c(5, 5),lwd=3)
```