Supplemental Materials

Using deep learning to predict temporomandibular joint disc perforation based on magnetic resonance imaging

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1. Loading the dataset

1.1. Loading the raw data

```
Sys.setlocale("LC_ALL", "English")
```

```
## [1] "LC_COLLATE=English_United States.1252;LC_CTYPE=English_United Stat
es.1252;LC_MONETARY=English_United States.1252;LC_NUMERIC=C;LC_TIME=Englis
h_United States.1252"
```

```
tmj <- read.csv("D:/Perforation_ML3.csv", sep=",", header=TRUE)
```

1.2. Checking the first 6 rows of the dataset 'tmj'

```
head(tmj)
```

```
##   Group Age Disc_Shape BMS JS Condyle_Fossa
## 1     0  24          3   1  2            0
## 2     1  53          5   1  2            0
## 3     0  21          1   1  2            0
## 4     0  71          1   1  1            0
## 5     0  23          4   1  2            0
## 6     1  64          5   1  3            0
```

1.3. Checking the structure of the dataset 'tmj'

```
str(tmj)
```

```
## 'data.frame':    299 obs. of  6 variables:
##  $ Group       : int  0 1 0 0 0 1 1 1 0 1 ...
##  $ Age         : int  24 53 21 71 23 64 54 70 58 43 ...
##  $ Disc_Shape   : int  3 5 1 1 4 5 5 5 5 5 ...
##  $ BMS         : int  1 1 1 1 1 1 2 1 1 1 ...
##  $ JS          : int  2 2 2 1 2 3 2 3 2 3 ...
##  $ Condyle_Fossa: int  0 0 0 0 0 0 0 0 1 1 ...
```

1.4. Changing column names

```
colnames(tmj)=c("Group","age","ds","bms","joint","bone")
```

1.5. Converting categorical variables into factors (currently integers)

```
tmj$ds <- as.factor(tmj$ds)
tmj$bms <- as.factor(tmj$bms)
tmj$joint <- as.factor(tmj$joint)
tmj$bone <- as.factor(tmj$bone)
str(tmj)
```

```
## 'data.frame':    299 obs. of  6 variables:
##  $ Group: int  0 1 0 0 0 1 1 1 0 1 ...
##  $ age  : int  24 53 21 71 23 64 54 70 58 43 ...
##  $ ds   : Factor w/ 5 levels "1","2","3","4",..: 3 5 1 1 4 5 5 5 5 5 ...
##  $ bms  : Factor w/ 2 levels "1","2": 1 1 1 1 1 1 2 1 1 1 ...
##  $ joint: Factor w/ 4 levels "1","2","3","4": 2 2 2 1 2 3 2 3 2 3 ...
##  $ bone : Factor w/ 2 levels "0","1": 1 1 1 1 1 1 1 1 2 2 ...
```

2. Data Preprocessing

2.1. Converting variables into numerical values for neural network

```
tmj$Group<-as.numeric(tmj$Group)
tmj$age<-as.numeric(tmj$age)
tmj$dsN<-as.numeric(tmj$ds)
tmj$bmsN<- as.numeric(tmj$bms)
tmj$jointN<-as.numeric(tmj$joint)
tmj$boneN<-as.numeric(tmj$bone)
```

2.2. Scale

```
tmj$ageS <- scale(tmj$age)
tmj$dsNS <- scale(tmj$dsN)
tmj$bmsNS <- scale(tmj$bmsN)
tmj$jointNS <- scale(tmj$jointN)
tmj$boneNS <- scale(tmj$boneN)
```

2.3. Partition of the data set into 80% training and 20% testing set

```
set.seed(180801)
ind <-sample(1:nrow(tmj),nrow(tmj)*0.8)
train <-tmj[ind,]
test <-tmj[-ind,]
```

3. Random forest (RF)

3.1. Load package “randomForest”

```
require(randomForest)

## Loading required package: randomForest

## randomForest 4.6-14

## Type rfNews() to see new features/changes/bug fixes.
```

3.2. Build model & predict

```
tmj.rf<-randomForest(as.factor(Group) ~ age + ds + bms + joint + bone,
                     train, importance=TRUE)
tmj.rf.prob <- predict(tmj.rf, type = "prob", newdata=test)
```

3.3. Looking inside the RF model

```
tmj.rf

##
## Call:
```

```
##  randomForest(formula = as.factor(Group) ~ age + ds + bms + joint +
bone, data = train, importance = TRUE)
##                Type of random forest: classification
##                      Number of trees: 500
## No. of variables tried at each split: 2
##
##         OOB estimate of  error rate: 19.67%
## Confusion matrix:
##     0  1 class.error
## 0 113 22   0.1629630
## 1  25 79   0.2403846
```

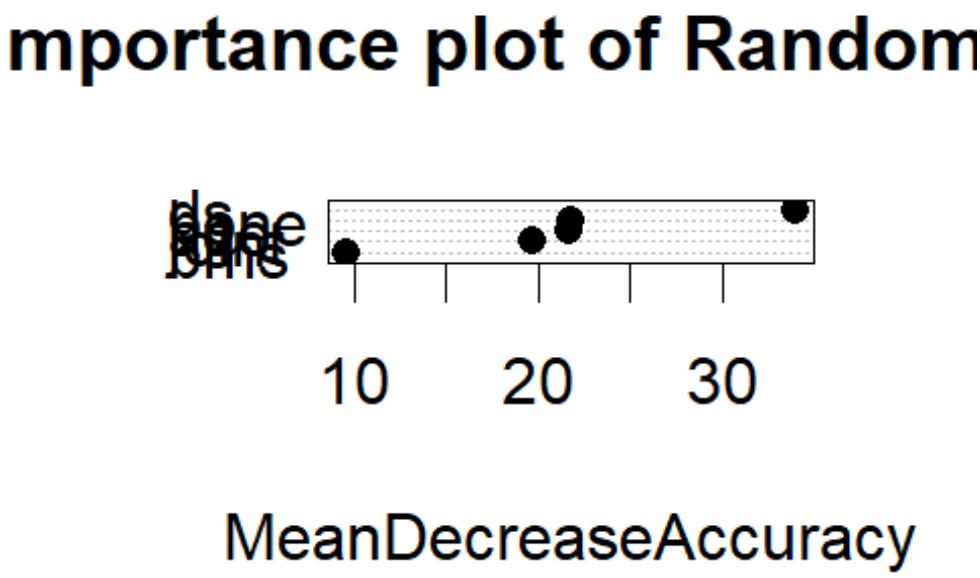
- this model has 500 trees

3.4. Importance of variables

```
importance(tmj.rf)

##              0        1 MeanDecreaseAccuracy MeanDecreaseGini
## age   18.65502 13.875118           21.638490        28.69686
## ds    31.44433 19.952991           33.977186        27.01476
## bms   15.91349 -3.670312            9.518296         5.29825
## joint 20.00317  8.646952           19.718832        10.92813
## bone  25.99064  5.026209           21.722192        11.70334
```

3.5. Importance plot

```
#png(filename = "importance.png", width =2000, height=2000, units="px", res
=300)
varImpPlot(tmj.rf, type=1, cex=2.0, pch=16, pt.cex=2, main="Variable import
ance plot of Random forest model")
```



- type1= mean decrease in accuracy
- type2= mean decrease in node impurity

3.6. Export into .eps format

```
setEPS()
postscript("var importance plot.eps")
varImpPlot(tmj.rf, type=1, cex=2.0, pch=16, pt.cex=2, main="Variable import
ance plot of Random forest model")
```

4. Deep learning with keras

4.1. Loading libraries

```
#devtools::install_github("rstudio/tensorflow")
#install_tensorflow()
library(tensorflow)
library(keras)

## Warning: package 'keras' was built under R version 3.5.1

use_condaenv("tf-keras")
use_session_with_seed(617)

## Set session seed to 617 (disabled GPU, CPU parallelism)

library(yardstick)

## Loading required package: broom

## Warning: package 'broom' was built under R version 3.5.1

require(tidyquant)

## Loading required package: tidyquant

## Loading required package: lubridate

##
## Attaching package: 'lubridate'

## The following object is masked from 'package:base':
##
##     date

## Loading required package: PerformanceAnalytics

## Loading required package: xts

## Loading required package: zoo

##
## Attaching package: 'zoo'
```

```
## The following objects are masked from 'package:base':
##
##     as.Date, as.Date.numeric

##
## Attaching package: 'PerformanceAnalytics'

## The following object is masked from 'package:graphics':
##
##     legend

## Loading required package: quantmod

## Loading required package: TTR

## Version 0.4-0 included new data defaults. See ?getSymbols.

## Loading required package: tidyverse

## -- Attaching packages --------------------------------------- tidyverse
 1.2.1 --

## v ggplot2 3.0.0     v purrr   0.2.4
## v tibble  1.4.2     v dplyr   0.7.6
## v tidyr   0.8.0     v stringr 1.3.0
## v readr   1.1.1     v forcats 0.3.0

## Warning: package 'ggplot2' was built under R version 3.5.1

## Warning: package 'dplyr' was built under R version 3.5.1

## -- Conflicts ------------------------------------------ tidyverse_conf
licts() --
## x lubridate::as.difftime() masks base::as.difftime()
## x dplyr::combine()         masks randomForest::combine()
## x lubridate::date()        masks base::date()
## x dplyr::filter()          masks stats::filter()
## x dplyr::first()           masks xts::first()
## x lubridate::intersect()   masks base::intersect()
## x dplyr::lag()             masks stats::lag()
## x dplyr::last()            masks xts::last()
## x ggplot2::margin()        masks randomForest::margin()
## x lubridate::setdiff()     masks base::setdiff()
## x readr::spec()            masks yardstick::spec()
## x lubridate::union()       masks base::union()

library(caret)

## Loading required package: lattice

##
## Attaching package: 'caret'

## The following object is masked from 'package:purrr':
##
##     lift
```

```
## The following objects are masked from 'package:yardstick':
##
##     mnLogLoss, precision, recall

## The following object is masked from 'package:tensorflow':
##
##     train

np<-import("numpy")
```

4.2. trainging and test sets for keras

```
keras_train <- subset(train, select=c(ageS, dsNS,bmsNS, jointNS, boneNS, Gr
oup))
keras_test <- subset(test, select=c(ageS, dsNS,bmsNS, jointNS, boneNS, Grou
p))
```

4.3. Predictor variable for the training and testing set

```
X_train <- keras_train[,-6]
X_test <- keras_test[,-6]
```

4.4. Target Variable for training and testing set

```
y_train <- keras_train[,6]
y_test <- keras_test[,6]
```

4.5. Multi-Layer Perceptron

```
model_keras <- keras_model_sequential()
model2 <- model_keras %>%
  layer_dense(units = 32, kernel_initializer = "uniform", activation = "rel
u",
              input_shape = ncol(X_train)) %>%
  layer_dropout(rate = 0.1) %>%

  layer_dense(units = 16, kernel_initializer = "uniform", activation = "rel
u") %>%
  layer_dropout(rate = 0.1) %>%
  layer_dense(units = 1, kernel_initializer = "uniform", activation = "sigm
oid")
```

4.6. Compile

```
compile2 <- model_keras %>%
  compile(optimizer = "rmsprop", loss = "binary_crossentropy", metrics = c
("accuracy"))

compile2

## Model
## _____
____
## Layer (type)                 Output Shape              Param #
## =====================================================================
====
## dense_1 (Dense)              (None, 32)                192
## _____
____
```

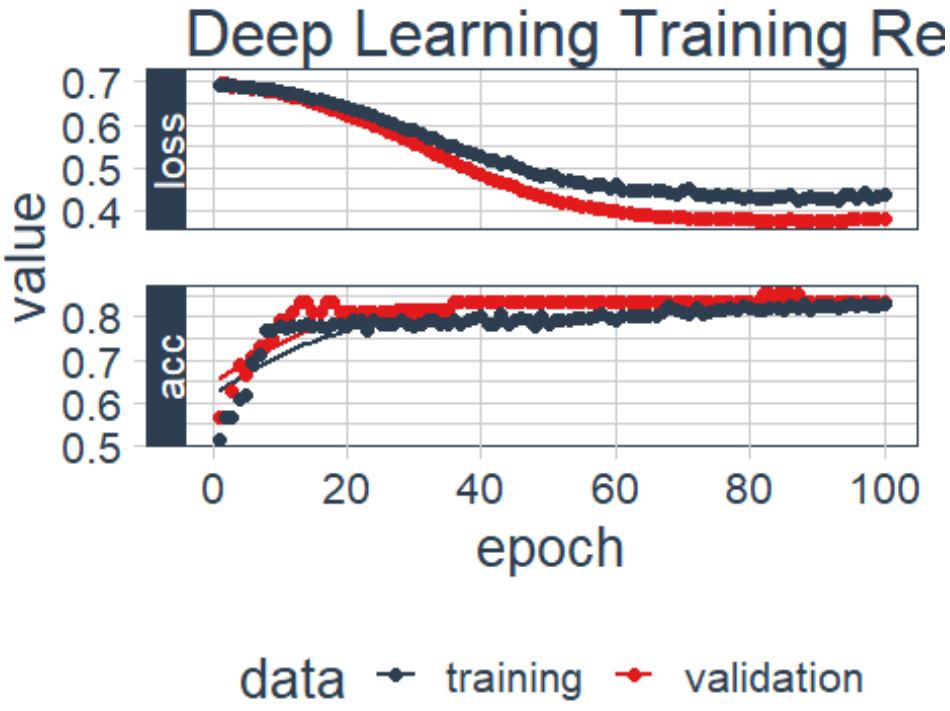
```
## dropout_1 (Dropout)              (None, 32)                    0
## _____
____
## dense_2 (Dense)                  (None, 16)                    528
## _____
____
## dropout_2 (Dropout)              (None, 16)                    0
## _____
____
## dense_3 (Dense)                  (None, 1)                     17
## ================================================================
====
## Total params: 737
## Trainable params: 737
## Non-trainable params: 0
## _____
____
```

4.7. Fit the model to the training Data

```
kemodel <- fit(object = model2, x = as.matrix(X_train),
               y = y_train, batch_size = 100, epochs = 100,
               validation_split = 0.2, silent=TRUE)
```

4.8. Plotting the training / validation history of our Keras's Model

```
#png(filename = "learning.png", width =2400, height=3000, units="px", res=3
00)
plot(kemodel) + theme_tq(base_size=20) +
  scale_color_tq() +
  scale_fill_tq() +
  geom_point(size=2) +
  labs(title = "Deep Learning Training Result")
```



4.8.1. *Export into .eps format*

```
setEPS()
postscript("learning loss red and black.eps")
plot(kemodel) + theme_tq(base_size=20) +
  scale_color_tq() +
  scale_fill_tq() +
  geom_point(size=2) +
  labs(title = "Deep Learning Training Result")
```

4.9. Performance

4.9.1. *Predicted class*

```
pred_class <- predict_classes(object = model2,
                              x = as.matrix(X_test)) %>%  as.vector()
```

4.9.2. *Predicted class probability*

```
pred_prob <- predict_proba(object = model2,
                           x = as.matrix(X_test)) %>%  as.vector()
```

4.9.3. *Format test data and prediction*

```
predict_value <- tibble(truth = as.factor(y_test) %>% fct_recode(Yes = "1",
 No = "0"),
                        estimate = as.factor(pred_class) %>% fct_recode(Yes =
 "1", No = "0"),
                        pred_prob = pred_prob)

print(predict_value)

## # A tibble: 60 x 3
##    truth estimate pred_prob
```

```
##    <fct> <fct>       <dbl>
##  1 No    No         0.134
##  2 No    No         0.233
##  3 Yes   Yes        0.866
##  4 No    No         0.0583
##  5 Yes   Yes        0.854
##  6 No    No         0.340
##  7 Yes   No         0.242
##  8 Yes   Yes        0.591
##  9 Yes   Yes        0.505
## 10 No    No         0.105
## # ... with 50 more rows
```

4.9.4. Confusion table

```
predict_value %>% conf_mat(truth, estimate)
```

```
##          Truth
## Prediction No Yes
##        No  30   3
##        Yes  3  24
```

4.9.5. Accuracy

```
predict_value %>% metrics(truth, estimate)
```

```
## # A tibble: 1 x 1
##   accuracy
##      <dbl>
## 1      0.9
```

4.9.6. AUC of ROC

```
predict_value %>% roc_auc(truth,pred_prob)
```

```
## [1] 0.9399551
```

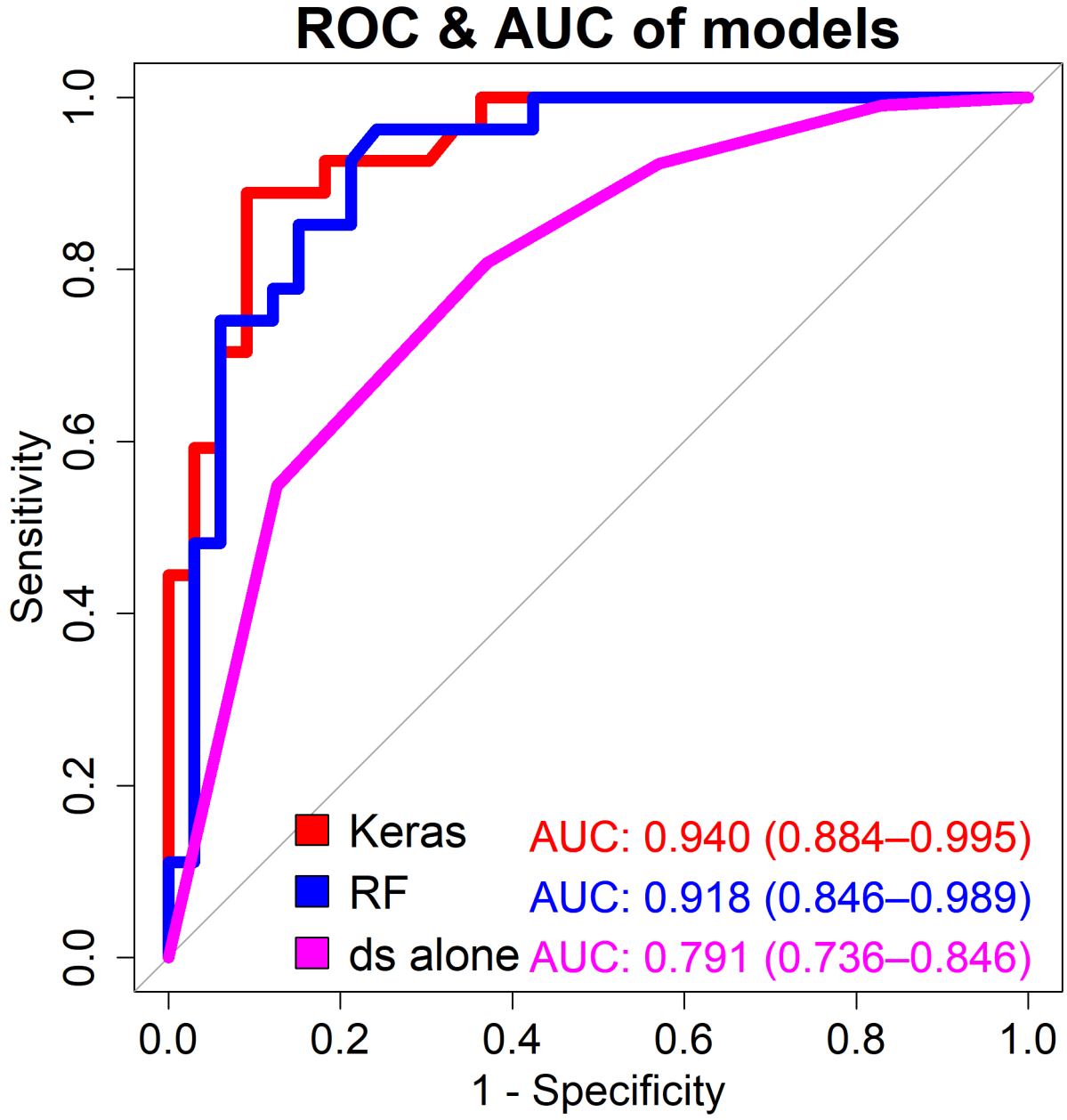
5. Plotting ROC with AUC of all Machine Learning models + single predictors

```
library(pROC)
```

```
## Type 'citation("pROC")' for a citation.

##
## Attaching package: 'pROC'

## The following objects are masked from 'package:stats':
##
##     cov, smooth, var
```

```
#setEPS()
#postscript("ROC of models.eps")
#png(filename = "ROC.png", width = 2000, height=2000, units="px", res=300)


# keras Neural Network
```

```
roc.keras = roc(test[,'Group'], pred_prob, ci=TRUE)
plot(roc.keras, print.auc=TRUE, print.auc.cex=1.5, col='red', lwd=7,
     cex.axis=1.5, cex.lab=1.5, cex.main=2.0,
     print.auc.x= 0.58, print.auc.y = .16,
     main="ROC & AUC of models", legacy.axes=TRUE)

# RandomForest
roc.rf = roc(test[,'Group'],tmj.rf.prob[,2], ci=TRUE)
plot(roc.rf,  print.auc=TRUE, print.auc.cex=1.5, col='blue', lwd=7,
     print.auc.x= 0.58, print.auc.y = .09, add = TRUE, legacy.axes=TRUE)

# disc space alone
roc.ds=roc(form=train$Group~train$dsN, ci=TRUE)
plot(roc.ds, print.auc=TRUE, print.auc.cex=1.5, col='magenta1',lwd=7,
     print.auc.x= 0.58, print.auc.y = .020, add=TRUE, legacy.axes=TRUE)


legend(0.9, 0.22, c('Keras','RF', 'ds alone'),
       cex=1.6,x.intersp = 0.5, y.intersp = 1.0, bty = 'n',
       c('red', 'blue', 'magenta1'), xjust=0)
```



5.1. Testing if the differences between models are statistically significant

```
roc.test(roc.keras, roc.rf, alternative = "greater" )

##
##  DeLong's test for two correlated ROC curves
##
## data:  roc.keras and roc.rf
## Z = 0.92665, p-value = 0.1771
## alternative hypothesis: true difference in AUC is greater than 0
## sample estimates:
## AUC of roc1 AUC of roc2
##   0.9399551   0.9175084

roc.test(roc.keras, roc.ds, alternative = "greater" )
```

```
##
##  DeLong's test for two ROC curves
##
## data:  roc.keras and roc.ds
## D = 3.7413, df = 187.12, p-value = 0.0001217
## alternative hypothesis: true difference in AUC is greater than 0
## sample estimates:
## AUC of roc1 AUC of roc2
##   0.9399551   0.7908832
```

```
roc.test(roc.rf, roc.ds, alternative = "greater" )
```

```
##
##  DeLong's test for two ROC curves
##
## data:  roc.rf and roc.ds
## D = 2.7399, df = 136.39, p-value = 0.003484
## alternative hypothesis: true difference in AUC is greater than 0
## sample estimates:
## AUC of roc1 AUC of roc2
##   0.9175084   0.7908832
```

6. Sensitivity, Specificity at Optimal cutpoints for each model

* Optimal cutpoint

- "youden": Youden's J statistic (Youden, 1950) is employed. The optimal cut-off is the threshold that maximizes the distance to the identity (diagonal) line. Can be shortened to "y". The optimality criterion is: max(sensitivities + specificities)

- "closest.topleft": The optimal threshold is the point closest to the top-left part of the plot with perfect sensitivity or specificity. Can be shortened to "c" or "t". The optimality criterion is: min((1 - sensitivities)^2 + (1- specificities)^2)

6.1. keras model

```
coords(roc.keras, x="best", input="threshold", best.method="youden")
```

```
##   threshold specificity sensitivity
##   0.4863707   0.9090909   0.8888889
```

```
coords(roc.keras, x="best", input="threshold", best.method="closest.toplef
t")
```

```
##   threshold specificity sensitivity
##   0.4863707   0.9090909   0.8888889
```

6.2. RF model

```
coords(roc.rf, x="best", input="threshold", best.method="youden")
```

```
##   threshold specificity sensitivity
##   0.1730000   0.7575758   0.9629630
```

```
coords(roc.rf, x="best", input="threshold", best.method="closest.topleft")
```

```
##   threshold specificity sensitivity
##   0.3960000   0.8484848   0.8518519
```

6.3. ds alone

```
coords(roc.ds, x="best", input="threshold", best.method="youden")
```

```
##   threshold specificity sensitivity
##   3.5000000   0.6296296   0.8076923
```

```
coords(roc.ds, x="best", input="threshold", best.method="closest.topleft")
```

```
##   threshold specificity sensitivity
##   3.5000000   0.6296296   0.8076923
```

7. Testing with imaginary data

```
imag.data<- read.csv("D:/tmj_keras_ex2.csv", sep=",", header=TRUE)
str(imag.data)
```

```
## 'data.frame':    1 obs. of  6 variables:
##  $ age  : int 65
##  $ ds   : int 3
##  $ bms  : int 2
##  $ joint: int 4
##  $ bone : int 1
##  $ perf : int 0
```

7.1. Scale imaginary data to the scale of previous dataset

```
imag.data$ageS <- scale(imag.data$age, attr(tmj$ageS, "scaled:center"), att
r(tmj$ageS, "scaled:scale"))
imag.data$dsNS <- scale(imag.data$ds, attr(tmj$dsNS, "scaled:center"), attr
(tmj$dsNS, "scaled:scale"))
imag.data$bmsNS <- scale(imag.data$bms, attr(tmj$bmsNS, "scaled:center"), a
ttr(tmj$bmsNS, "scaled:scale"))
imag.data$jointNS <- scale(imag.data$joint, attr(tmj$jointNS, "scaled:cent
er"), attr(tmj$jointNS, "scaled:scale"))
imag.data$boneNS <- scale(imag.data$bone, attr(tmj$boneNS, "scaled:center
"), attr(tmj$boneNS, "scaled:scale"))
imag.data<-subset(imag.data, select=c(ageS, dsNS, bmsNS, jointNS, boneNS, p
erf))
str(imag.data)
```

```
## 'data.frame':    1 obs. of  6 variables:
##  $ ageS   : num [1, 1] 2.87
##  $ dsNS   : num [1, 1] -0.342
##  $ bmsNS  : num [1, 1] 1.99
##  $ jointNS: num [1, 1] 2.73
##  $ boneNS : num [1, 1] -0.588
##  $ perf   : int 0
```

7.2. Predictor & Target variable for the imaginary data set

```
X_test <- imag.data[,-6]
y_test <- imag.data[,6]
```

7.3. Predicted class

```
pred_class_imag <- predict_classes(object = model2,
                                   x = as.matrix(X_test)) %>%  as.vector()
```

7.4. Predicted class probability

```
pred_prob_imag <- predict_proba(object = model2,
                                x = as.matrix(X_test)) %>%  as.vector()
```

7.5. format test data and prediction

```
predict_value_imag <- tibble(Dummy = as.factor(y_test) %>% fct_recode(Yes =
 "1", No = "0"),
                             estimate = as.factor(pred_class_imag) %>% fct_recode
(Yes = "1", No = "0"),
                             pred_prob = pred_prob_imag)

## Warning: Unknown levels in `f`: 1

## Warning: Unknown levels in `f`: 0

print(predict_value_imag)

## # A tibble: 1 x 3
##   Dummy estimate pred_prob
##   <fct> <fct>        <dbl>
## 1 No    Yes          0.939
```

–> high probability of having disc perforation