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The following analyses was done using the dataset "Alle studies Clean for SPPS use v2.xlsx", sent on 21.03.22.

Logistic regression models were computed for every endpoint. Presence of fluid was defined as the dependent variable and the fluid volume determined by the AI as the explanatory variable. ROC curves of the logistic regression models were drawn and the area under the curve (AUC) was calculated. An optimal cutoff point was calculated using the Youden-Index [1]. The fluid volume corresponding to every respective cutoff and the total accuracy, sensitivity and specificity was calculated.

In case of the "Protocol T" and "TREND"-studies the data includes follow-up visits of patients. Logistic regression models were calculated under the assumption that observations are independent. As a sensitivity analysis, the same models were calculated using only the observations of each patient at baseline. Additionally, a 95% confidence interval for the area under the curve (AUC) was calculated by repeatedly sampling one observation of each patients and calculating the AUC of the ROC curve of the resulting model. This was done 1000 times for each instance. The confidence interval of the AUC was then defined as the interval between the 2.5 - and the 97.5 percentile of the obtained AUCs.



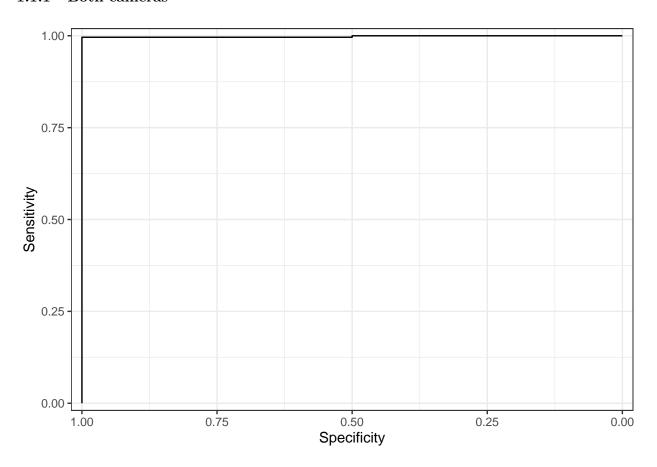
Statistical analysis was done using R, version 3.6.1 or higher.



# 1 Brighter

### $1.1 \quad IRF\_TotalFoV$

#### 1.1.1 Both cameras



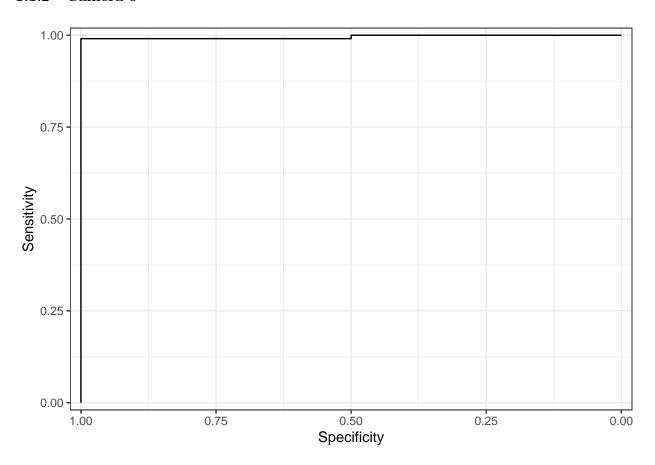
Area under the curve = 0.998

Optimal cutoff for IRF\_TotalFoV = 11.4700

accuracy	specificity	sensitivity
0.996	1	0.996



#### 1.1.2 Camera 0



Area under the curve = 0.995

Optimal cutoff for IRF\_TotalFoV = 12.6310

accuracy	specificity	sensitivity
0.991	1	0.991



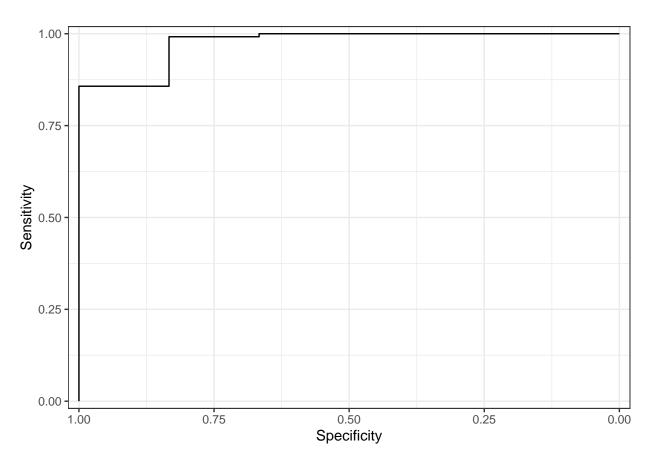
#### 1.1.3 Camera 1

Kann kein Modell rechnen, da nur ein Level an Anwesenheit von Flüssigkeit



## 1.2 IRF\_CMM

#### 1.2.1 Both cameras

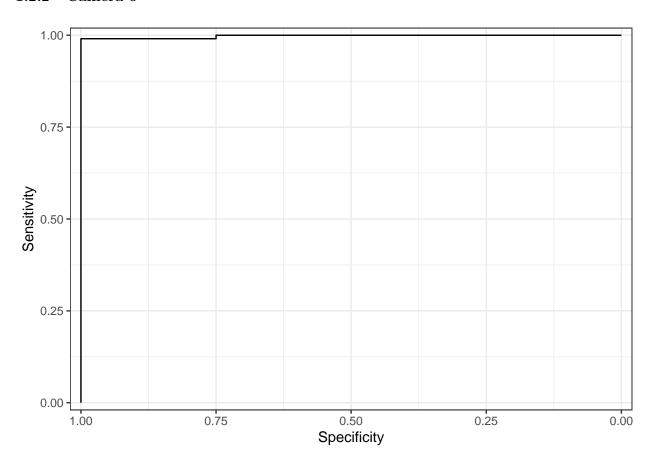


Area under the curve = 0.975

accuracy	specificity	sensitivity
0.861	1	0.857



### 1.2.2 Camera 0

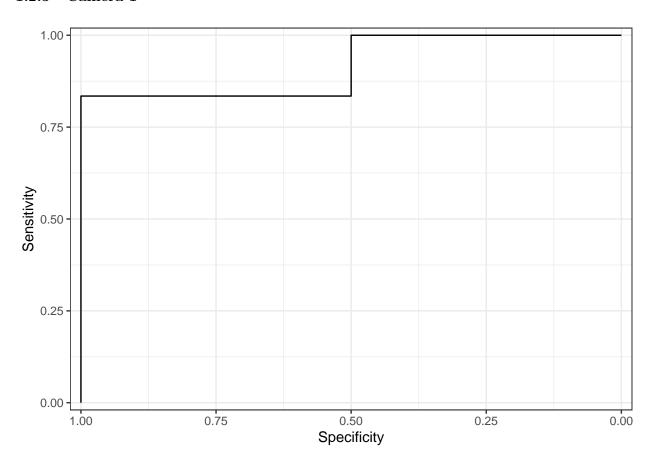


Area under the curve = 0.998

accuracy	specificity	sensitivity
0.991	1	0.991



### 1.2.3 Camera 1



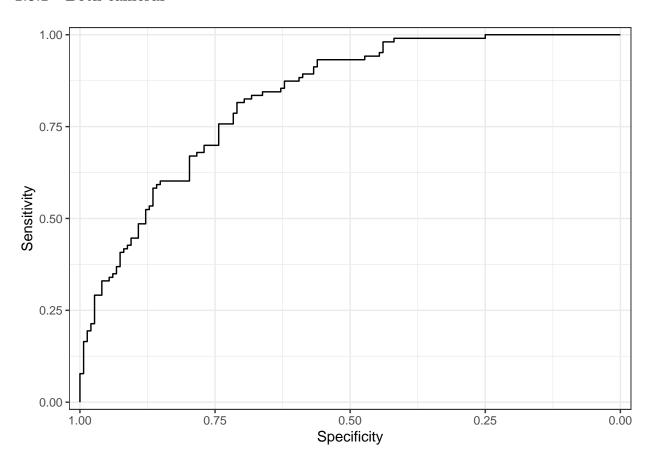
Area under the curve = 0.917

accuracy	specificity	sensitivity
0.837	1	0.835



## $1.3 \quad SRF\_TotalFoV$

#### 1.3.1 Both cameras



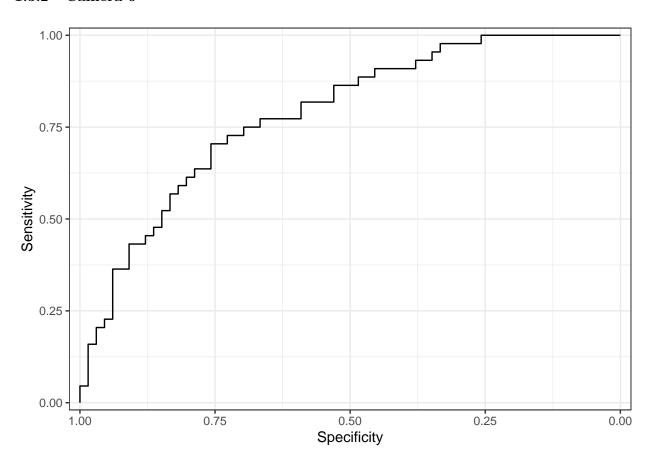
Area under the curve = 0.830

Optimal cutoff for SRF\_TotalFoV = 28.5880

accuracy	specificity	sensitivity
0.753	0.709	0.816



### 1.3.2 Camera 0



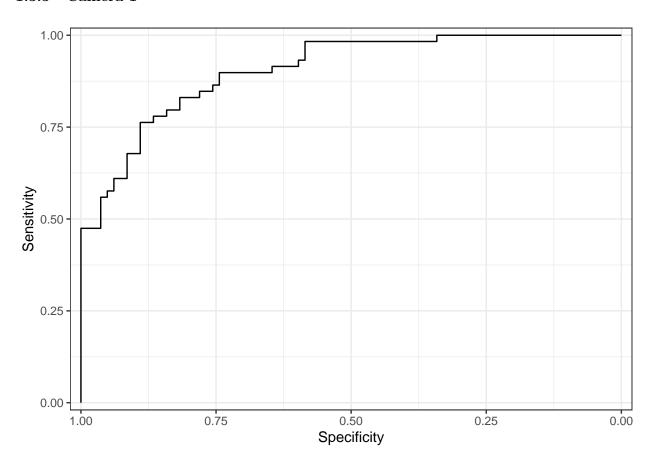
Area under the curve = 0.785

Optimal cutoff for SRF\_TotalFoV = 176.3380

accuracy	specificity	sensitivity
0.736	0.758	0.705



### 1.3.3 Camera 1



Area under the curve = 0.906

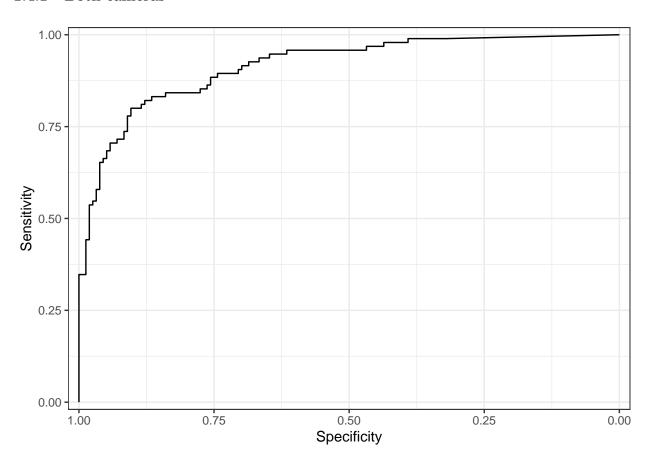
Optimal cutoff for SRF\_TotalFoV = 28.5880

accuracy	specificity	sensitivity
0.837	0.89	0.763



## 1.4 SRF\_CMM

#### 1.4.1 Both cameras

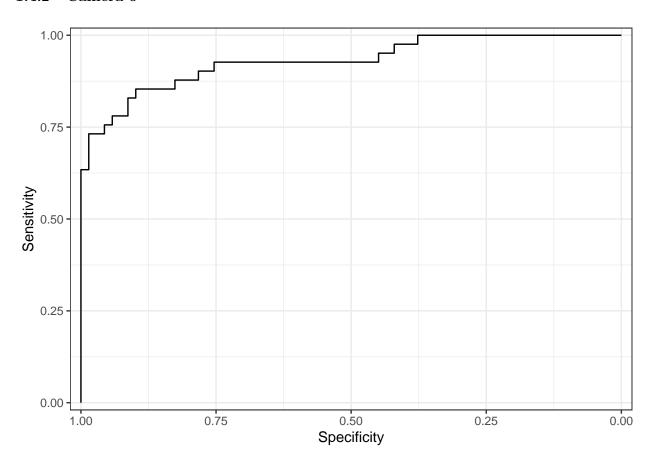


Area under the curve = 0.916

accuracy	specificity	sensitivity
0.865	0.904	0.8



### 1.4.2 Camera 0

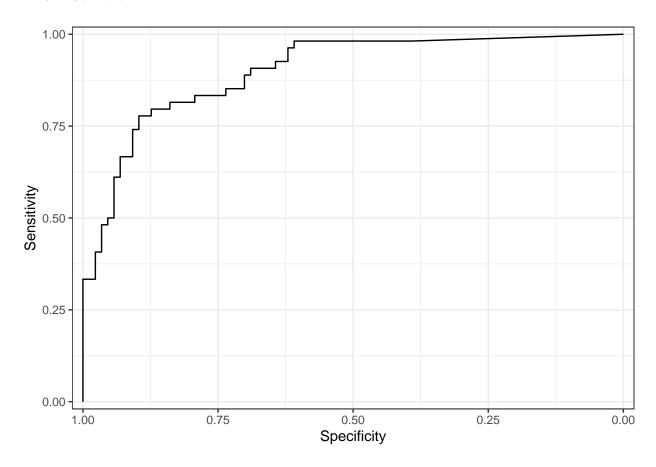


Area under the curve = 0.931

accuracy	specificity	sensitivity
0.882	0.899	0.854



### 1.4.3 Camera 1



Area under the curve = 0.900

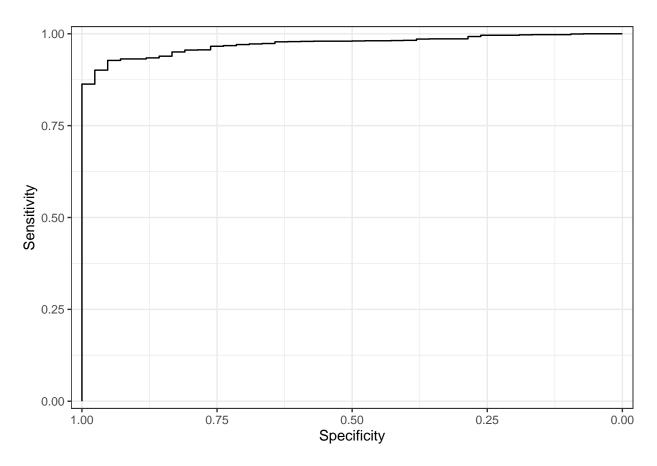
accuracy	specificity	sensitivity
0.851	0.897	0.778



## 2 Protocol T

### 2.1 IRF\_TotalFoV

#### 2.1.1 Both cameras



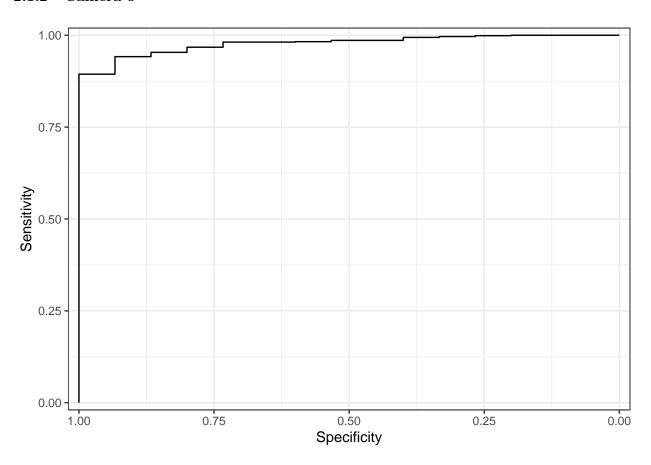
Area under the curve = 0.972~95% CI for AUC: [0.963;~0.984]

Optimal cutoff for IRF\_TotalFoV = 10.3240

accuracy	specificity	sensitivity
0.928	0.952	0.928



#### 2.1.2 Camera 0

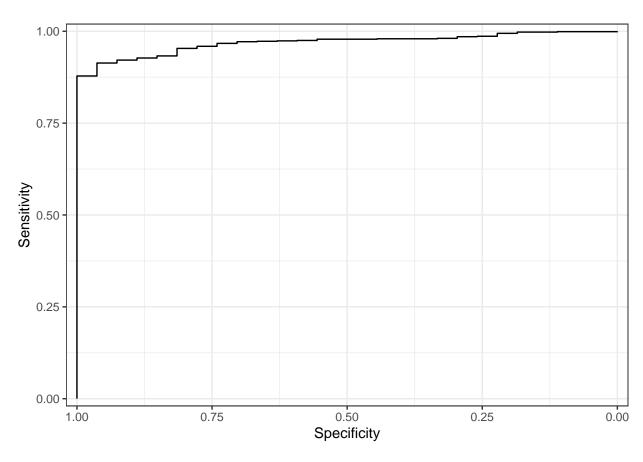


Area under the curve = 0.978 95% CI for AUC: [0.962; 0.995] Optimal cutoff for IRF\_TotalFoV = 21.6910

accuracy	specificity	sensitivity
0.896	1	0.894



#### **2.1.3** Camera 1



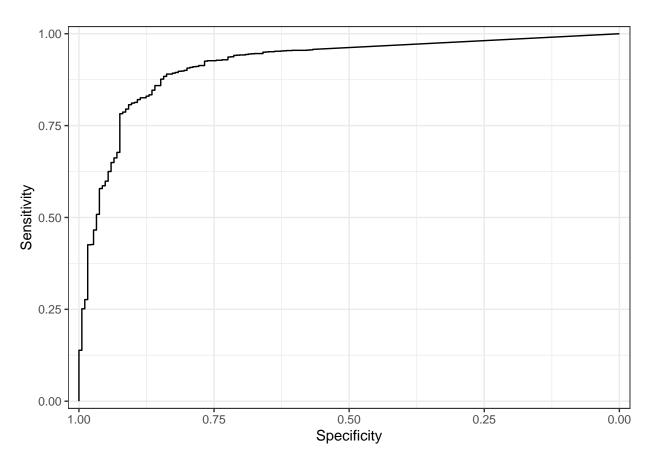
Area under the curve = 0.969 95% CI for AUC: [0.953; 0.980] Optimal cutoff for IRF\_TotalFoV = 14.8370

accuracy	specificity	sensitivity
0.882	1	0.878



## 2.2 IRF\_CMM

#### 2.2.1 Both cameras

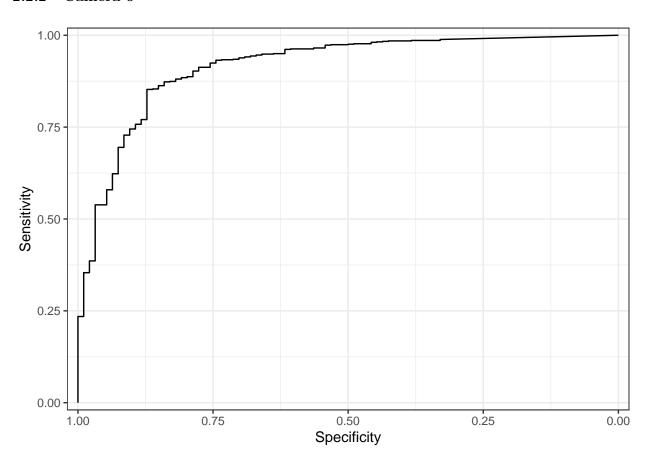


Area under the curve = 0.917 95% CI for AUC: [0.886; 0.934]

accuracy	specificity	sensitivity
0.885	0.838	0.89



## 2.2.2 Camera 0

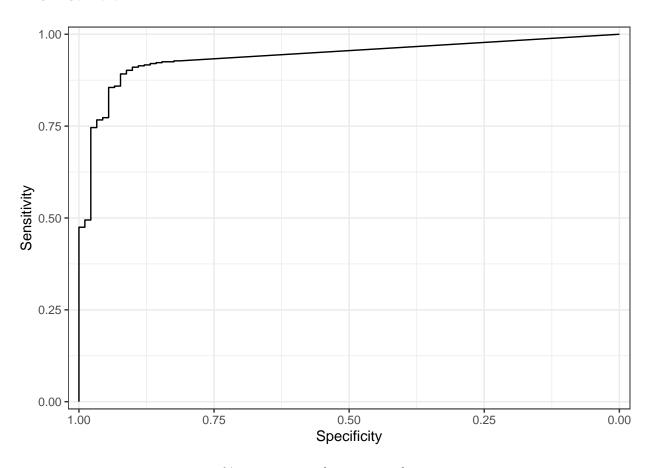


Area under the curve = 0.915 95% CI for AUC: [0.871; 0.942]

accuracy	specificity	sensitivity
0.855	0.872	0.853



### **2.2.3** Camera 1



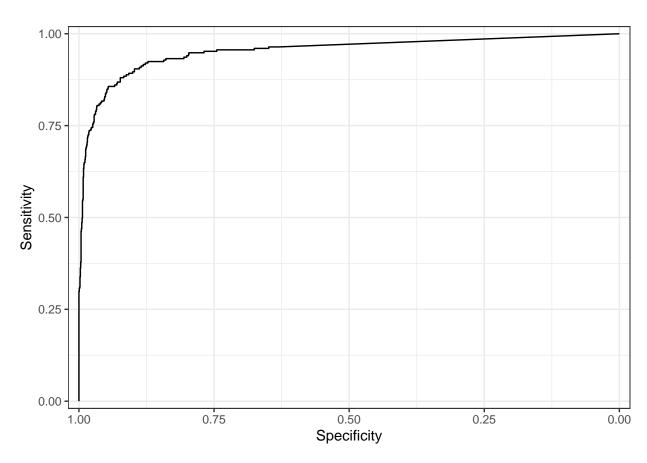
Area under the curve = 0.939 95% CI for AUC: [0.917; 0.963]

accuracy	specificity	sensitivity
0.895	0.923	0.892



## 2.3 SRF\_CMM

#### 2.3.1 Both cameras

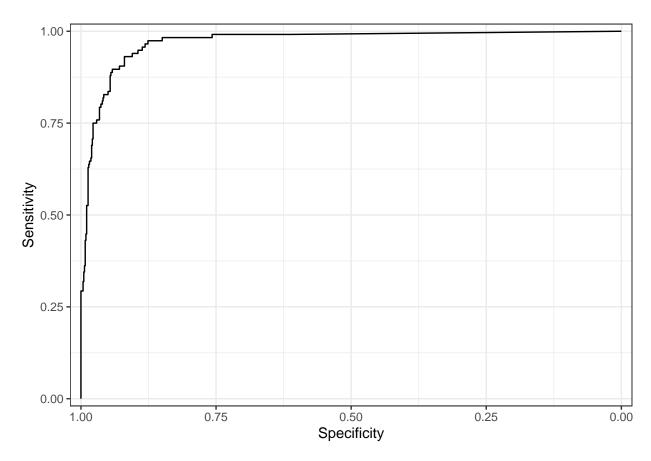


Area under the curve = 0.952 95% CI for AUC: [0.935; 0.972]

accuracy	specificity	sensitivity
0.917	0.923	0.88



#### 2.3.2 Camera 0

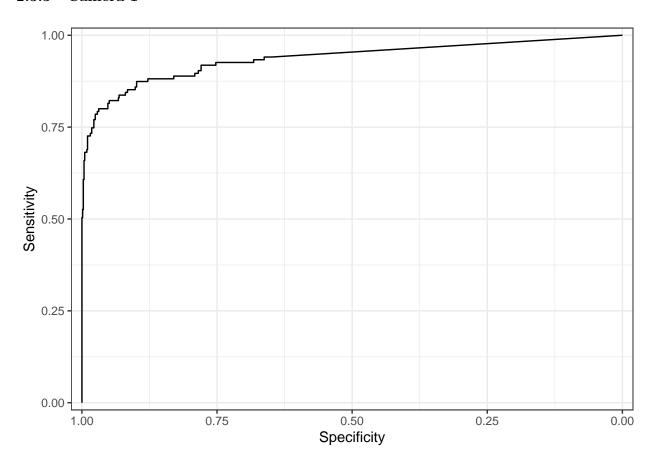


Area under the curve = 0.971 95% CI for AUC: [0.959; 0.988] Optimal cutoff for SRF\_CMM = 1.2810

accuracy	specificity	sensitivity
0.921	0.92	0.931



#### 2.3.3 Camera 1



Area under the curve = 0.936 95% CI for AUC: [0.902; 0.965]

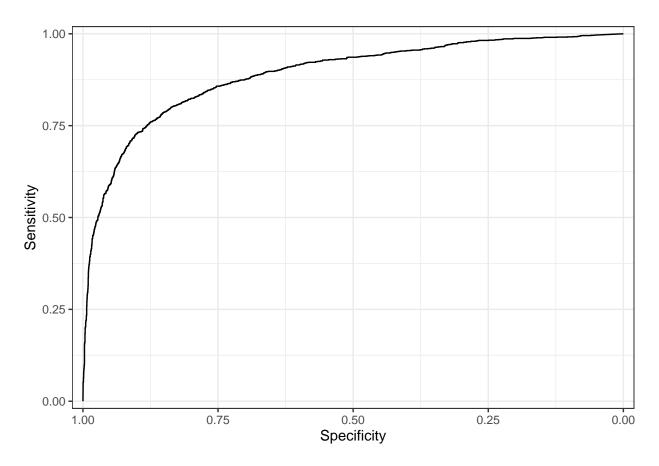
accuracy	specificity	sensitivity
0.895	0.899	0.874



## 3 Trend T

### 3.1 IRF\_TotalFoV

#### 3.1.1 Both cameras



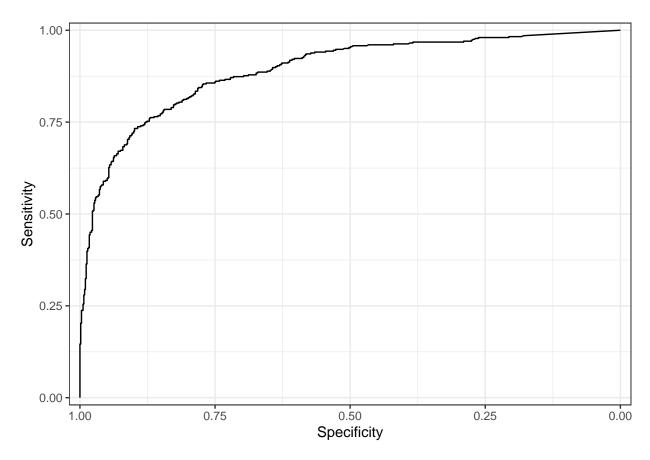
Area under the curve = 0.889~95% CI for AUC: [0.868;~0.914]

Optimal cutoff for IRF\_TotalFoV = 3.1450

accuracy	specificity	sensitivity
0.829	0.852	0.785



#### 3.1.2 Camera 0



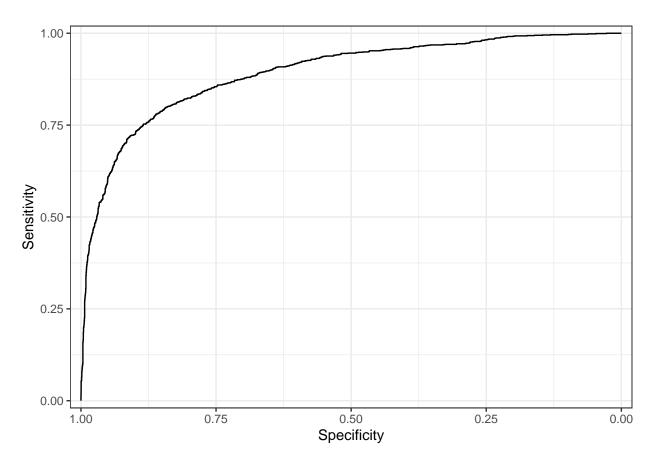
Area under the curve = 0.891 95% CI for AUC: [0.840; 0.931]

Optimal cutoff for IRF\_TotalFoV = 4.6150

accuracy	specificity	sensitivity
0.83	0.87	0.762



#### **3.1.3** Camera 1



Area under the curve = 0.892 95% CI for AUC: [0.867; 0.921]

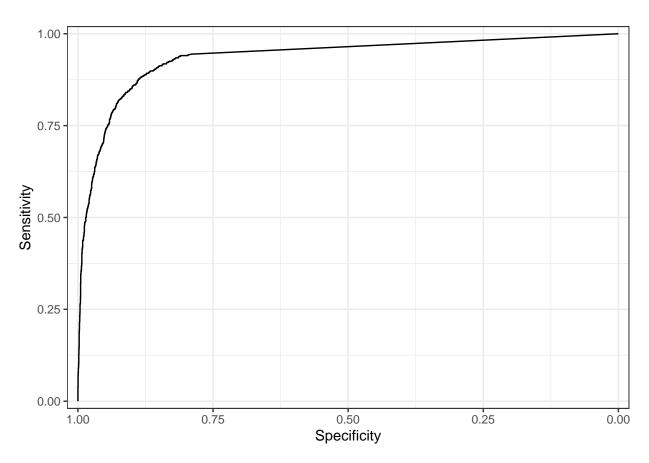
Optimal cutoff for IRF\_TotalFoV = 3.1450

accuracy	specificity	sensitivity
0.834	0.861	0.78



## 3.2 IRF\_CMM

#### 3.2.1 Both cameras

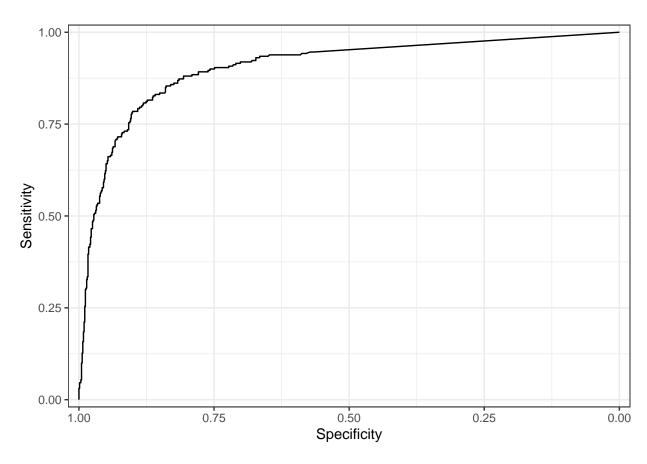


Area under the curve = 0.936 95% CI for AUC: [0.906; 0.954]

accuracy	specificity	sensitivity
0.884	0.884	0.881



#### 3.2.2 Camera 0

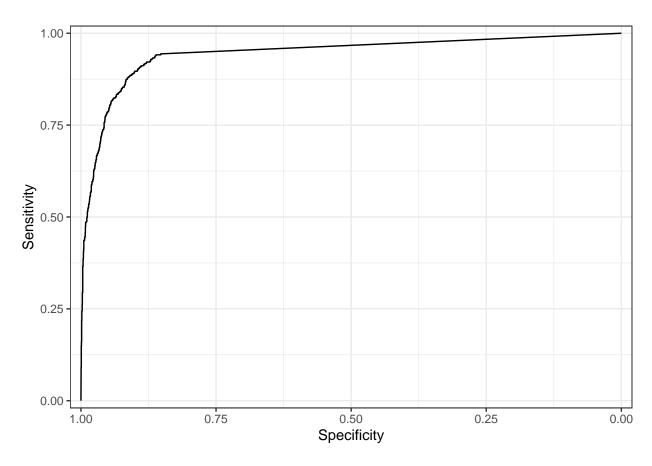


Area under the curve = 0.905 95% CI for AUC: [0.854; 0.955]

accuracy	specificity	sensitivity
0.842	0.839	0.854



#### **3.2.3** Camera 1



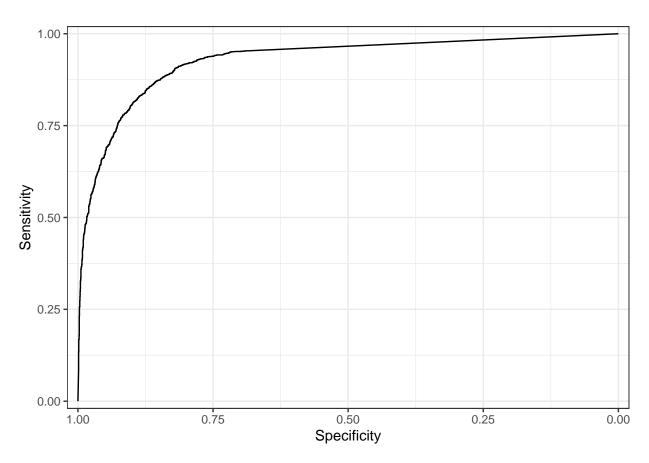
Area under the curve = 0.945 95% CI for AUC: [0.912; 0.965]

accuracy	specificity	sensitivity
0.876	0.861	0.941



## 3.3 IRF\_MM3

#### 3.3.1 Both cameras

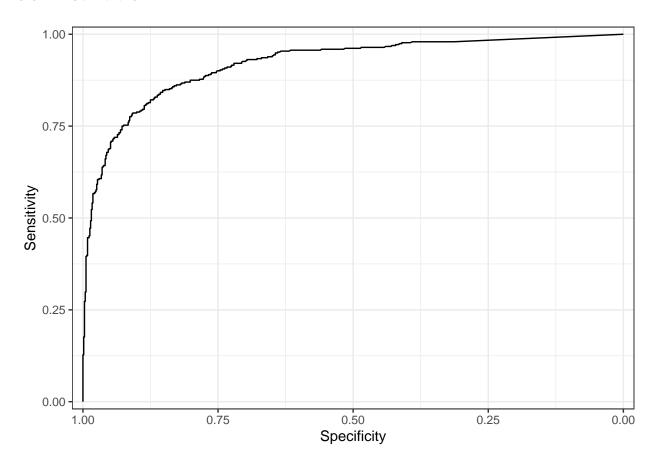


Area under the curve = 0.928 95% CI for AUC: [0.910; 0.946]

accuracy	specificity	sensitivity
0.86	0.855	0.872



#### 3.3.2 Camera 0

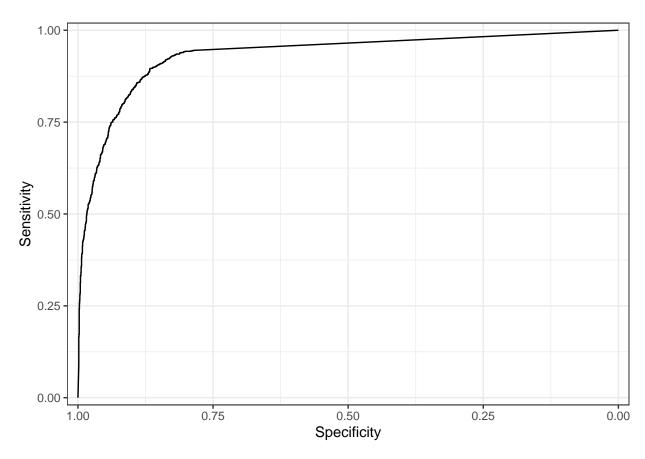


Area under the curve = 0.920 95% CI for AUC: [0.880; 0.957]

accuracy	specificity	sensitivity
0.851	0.852	0.847



#### **3.3.3** Camera 1



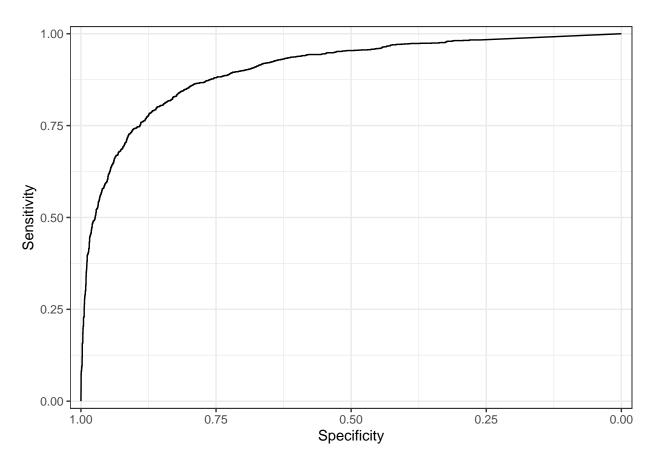
Area under the curve = 0.933 95% CI for AUC: [0.912; 0.954]

accuracy	specificity	sensitivity
0.876	0.866	0.896



## $3.4 \quad IRF\_MM6$

#### 3.4.1 Both cameras

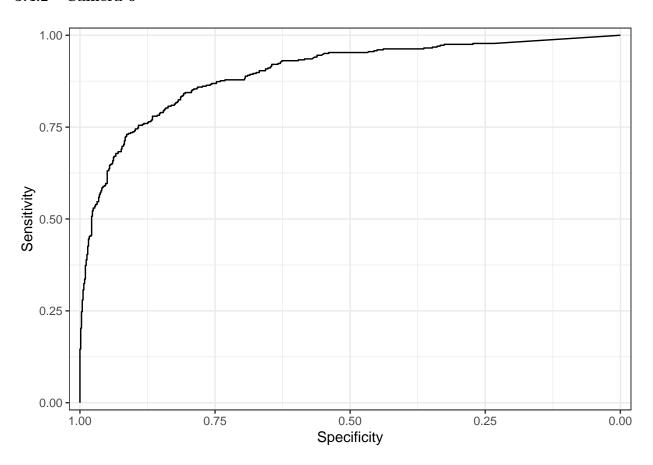


Area under the curve = 0.903 95% CI for AUC: [0.882; 0.925]

accuracy	specificity	sensitivity
0.839	0.859	0.801



#### 3.4.2 Camera 0

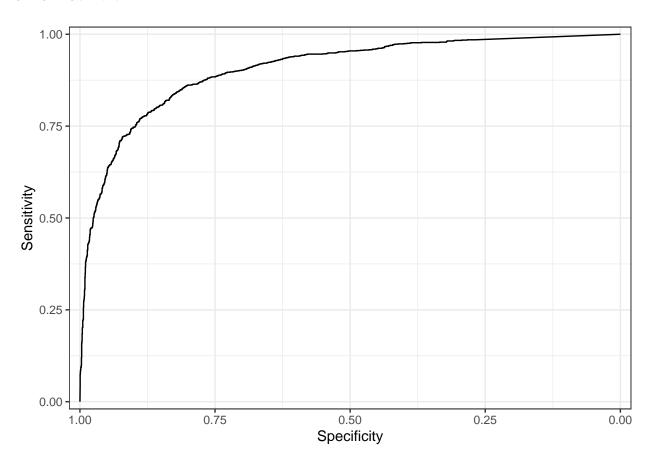


Area under the curve = 0.898 95% CI for AUC: [0.851; 0.939]

accuracy	specificity	sensitivity
0.82	0.808	0.842



#### **3.4.3** Camera 1



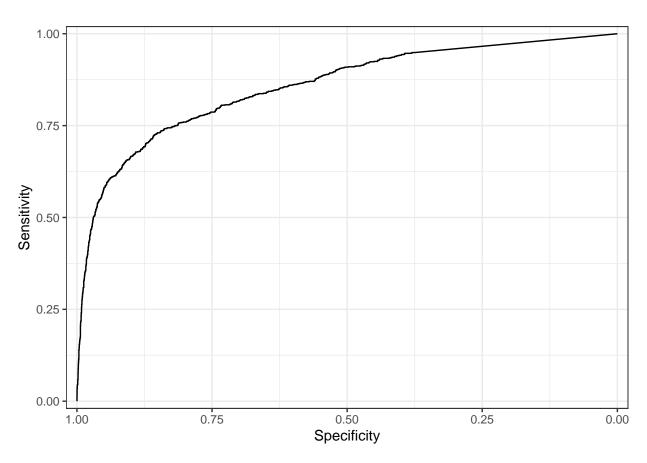
Area under the curve = 0.905 95% CI for AUC: [0.883; 0.931]

accuracy	specificity	sensitivity
0.831	0.828	0.835



### 3.5 IRF\_Perifovea

#### 3.5.1 Both cameras



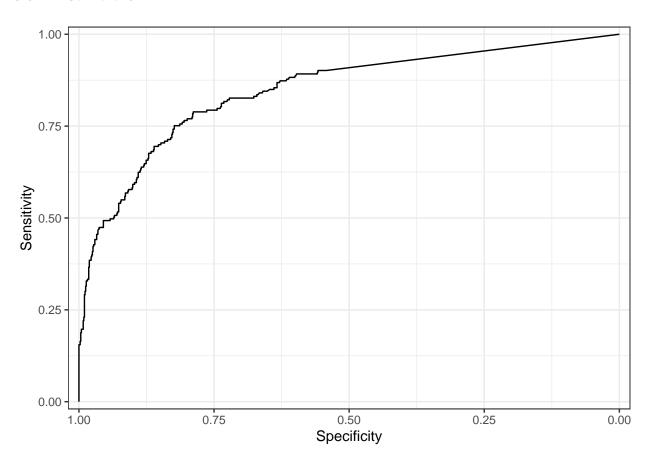
Area under the curve = 0.856 95% CI for AUC: [0.828; 0.894]

Optimal cutoff for IRF\_Perifovea = 1.1030

accuracy	specificity	sensitivity
0.831	0.857	0.725



#### 3.5.2 Camera 0



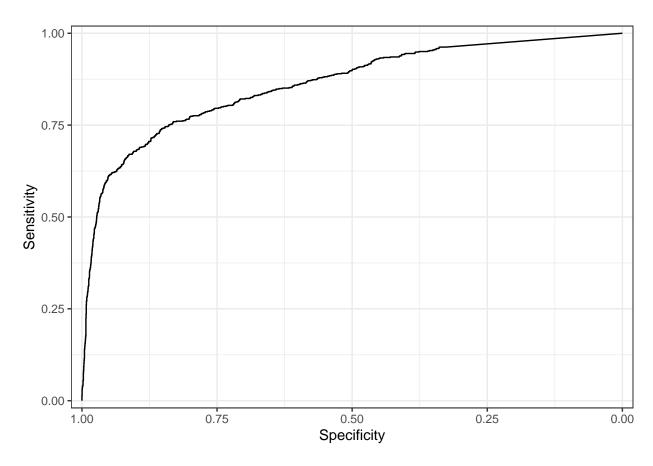
Area under the curve = 0.847 95% CI for AUC: [0.808; 0.922]

Optimal cutoff for IRF\_Perifovea = 0.3830

accuracy	specificity	sensitivity
0.789	0.788	0.789



#### **3.5.3** Camera 1



Area under the curve = 0.861 95% CI for AUC: [0.828; 0.899]

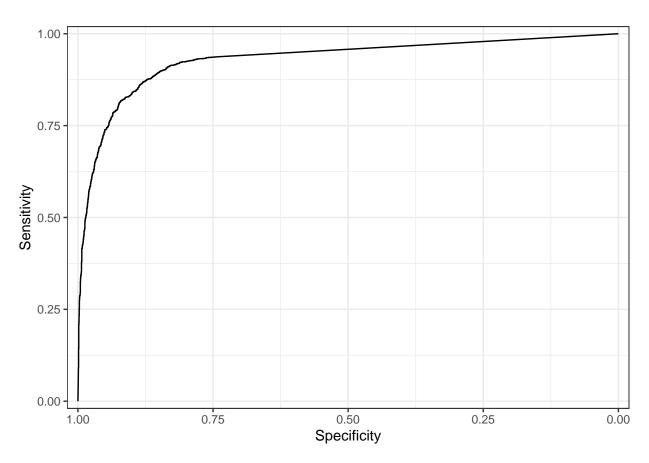
Optimal cutoff for IRF\_Perifovea = 1.1030

accuracy	specificity	sensitivity	
0.83	0.852	0.741	



## 3.6 IRF\_Parafovea

#### 3.6.1 Both cameras



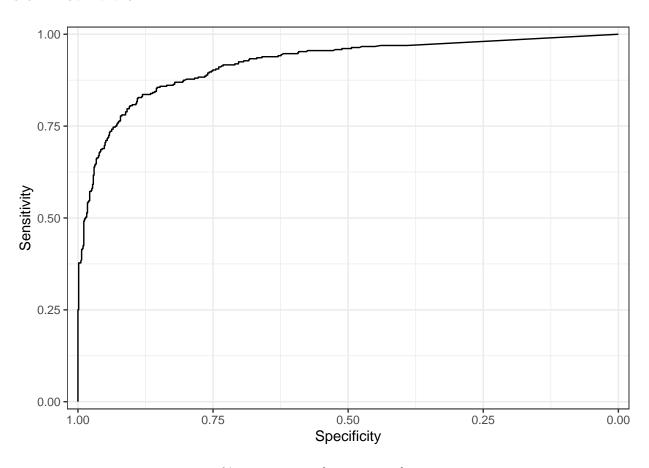
Area under the curve = 0.930~95% CI for AUC: [0.912;~0.949]

Optimal cutoff for IRF\_Parafovea = 0.3620

accuracy	specificity	sensitivity	
0.877	0.88	0.869	



#### 3.6.2 Camera 0



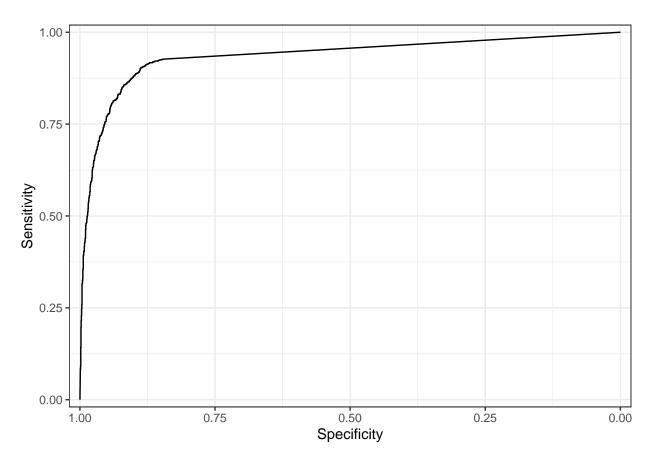
Area under the curve = 0.921 95% CI for AUC: [0.886; 0.963]

Optimal cutoff for IRF\_Parafovea = 1.1180

accuracy	specificity	sensitivity	
0.866	0.881	0.836	



#### 3.6.3 Camera 1



Area under the curve = 0.935 95% CI for AUC: [0.916; 0.958]

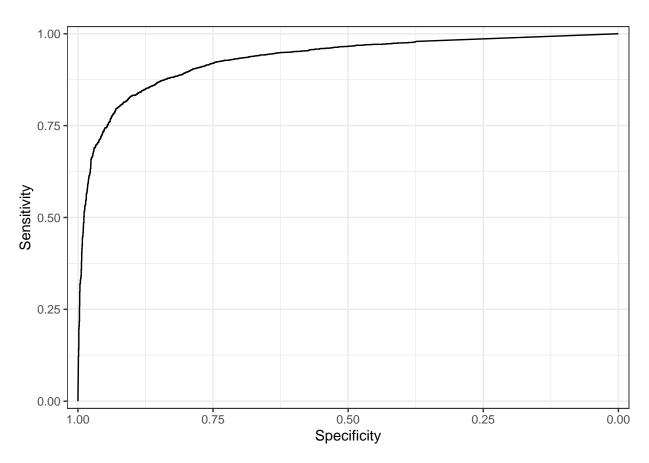
Optimal cutoff for IRF\_Parafovea = 0.1330

accuracy	specificity	sensitivity	
0.892	0.887	0.904	



## 3.7 SRF\_TotalFoV

#### 3.7.1 Both cameras



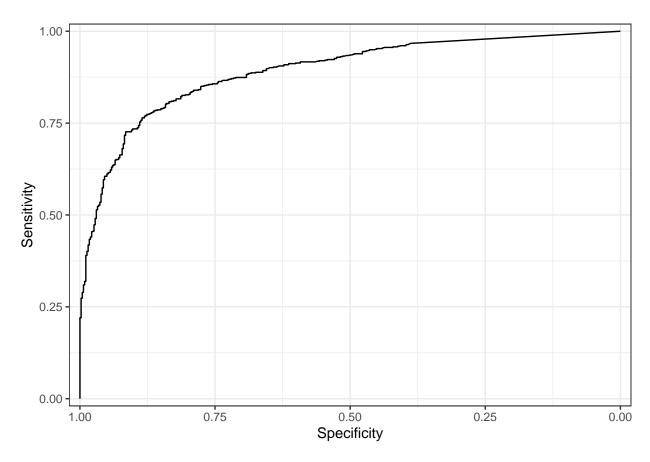
Area under the curve = 0.930 95% CI for AUC: [0.915; 0.948]

Optimal cutoff for SRF\_TotalFoV = 4.8390

accuracy	specificity	sensitivity	
0.867	0.902	0.83	



### 3.7.2 Camera 0

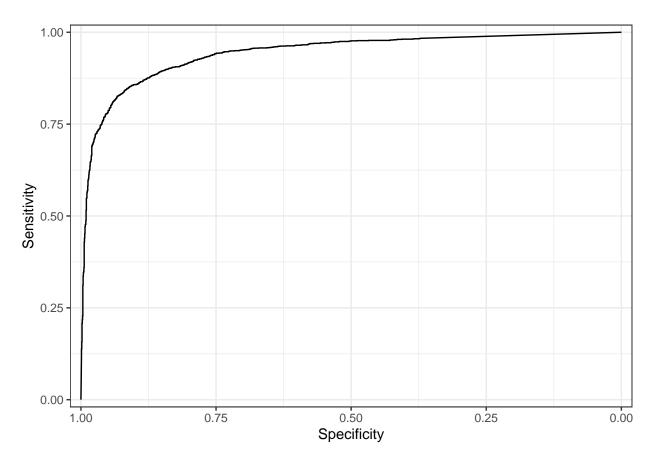


Area under the curve = 0.891 95% CI for AUC: [0.856; 0.934] Optimal cutoff for SRF\_TotalFoV = 3.8380

accuracy	specificity	sensitivity	
0.817	0.876	0.774	



### **3.7.3** Camera 1



Area under the curve = 0.943~95% CI for AUC: [0.926;~0.961]

Optimal cutoff for SRF\_TotalFoV = 5.0950

accuracy	specificity	sensitivity	
0.883	0.91	0.852	



# 4 Descriptive statistics

Study	Fluid Type	Localisation	Fluid yes $(n(\%))$	Fluid no (n(%))	Mean volume AI if fluid present (median(IQR))	Mean volume AI if no fluid present $(median(IQR))$
BRIGHTER	IRF	CMM	245 (97.61)	6 (2.39)	106.08 (62.21-161.93)	0.06 (0.01-1.31)
BRIGHTER	IRF	TotalFoV	249 (99.20)	2 (0.80)	410.62 (208.38-689.50)	4.29 (2.25-6.34)
BRIGHTER	SRF	$_{\rm CMM}$	95 (37.85)	156 (62.15)	36.04 (11.10-68.51)	0.34 (0.00-3.90)
BRIGHTER	SRF	TotalFoV	103 (41.04)	148 (58.96)	162.06 (42.93-516.86)	6.92 (0.73-50.05)
Protocol T	IRF	$_{\rm CMM}$	1595 (89.61)	185 (10.39)	39.66 (9.98-98.34)	0.00 (0.00-0.38)
Protocol T	IRF	TotalFoV	1738 (97.64)	42 (2.36)	177.54 (51.38-485.68)	3.46 (1.62-5.04)
Protocol T	SRF	$_{\rm CMM}$	251 (14.10)	1529 (85.90)	13.14 (4.15-46.39)	0.00 (0.00-0.13)
TREND	IRF	$_{\rm CMM}$	977 (20.16)	3869 (79.84)	8.59 (1.80-34.60)	0.00 (0.00-0.00)
TREND	IRF	MM3	1597 (32.96)	3249 (67.04)	11.62 (2.24-63.27)	0.00 (0.00-0.11)
TREND	IRF	MM6	1663 (34.32)	3183 (65.68)	14.62 (2.73-76.07)	0.27 (0.00-0.98)
TREND	IRF	Parafovea	1507 (31.10)	3339 (68.90)	9.49 (1.43-46.18)	0.00 (0.00-0.00)
TREND	IRF	Perifovea	957 (19.76)	3887 (80.24)	5.21 (0.89-29.54)	0.10 (0.00-0.62)
TREND	IRF	TotalFoV	1663 (34.32)	3183 (65.68)	15.42 (3.75-78.41)	1.04 (0.41-2.07)
TREND	SRF	TotalFoV	2394 (49.38)	2454 (50.62)	68.21 (10.75-272.29)	0.07 (0.00-0.87)

# 5 References

[1] YOUDEN, William J. Index for rating diagnostic tests. Cancer, 1950, 3. Jg., Nr. 1, S. 32-35.