

## ON-LINE APPENDIX

### On-Line Methods 1: Search Strategy to Identify Publications in MeSH and Emtree Terms

MeSH subject heading search: “glioma”[mesh] AND (“Diagnostic Imaging”[mesh] OR “Magnetic Resonance Spectroscopy”[mesh]) AND (“Brain Neoplasms/pathology”[Mesh] OR “Brain/pathology”[Mesh]).

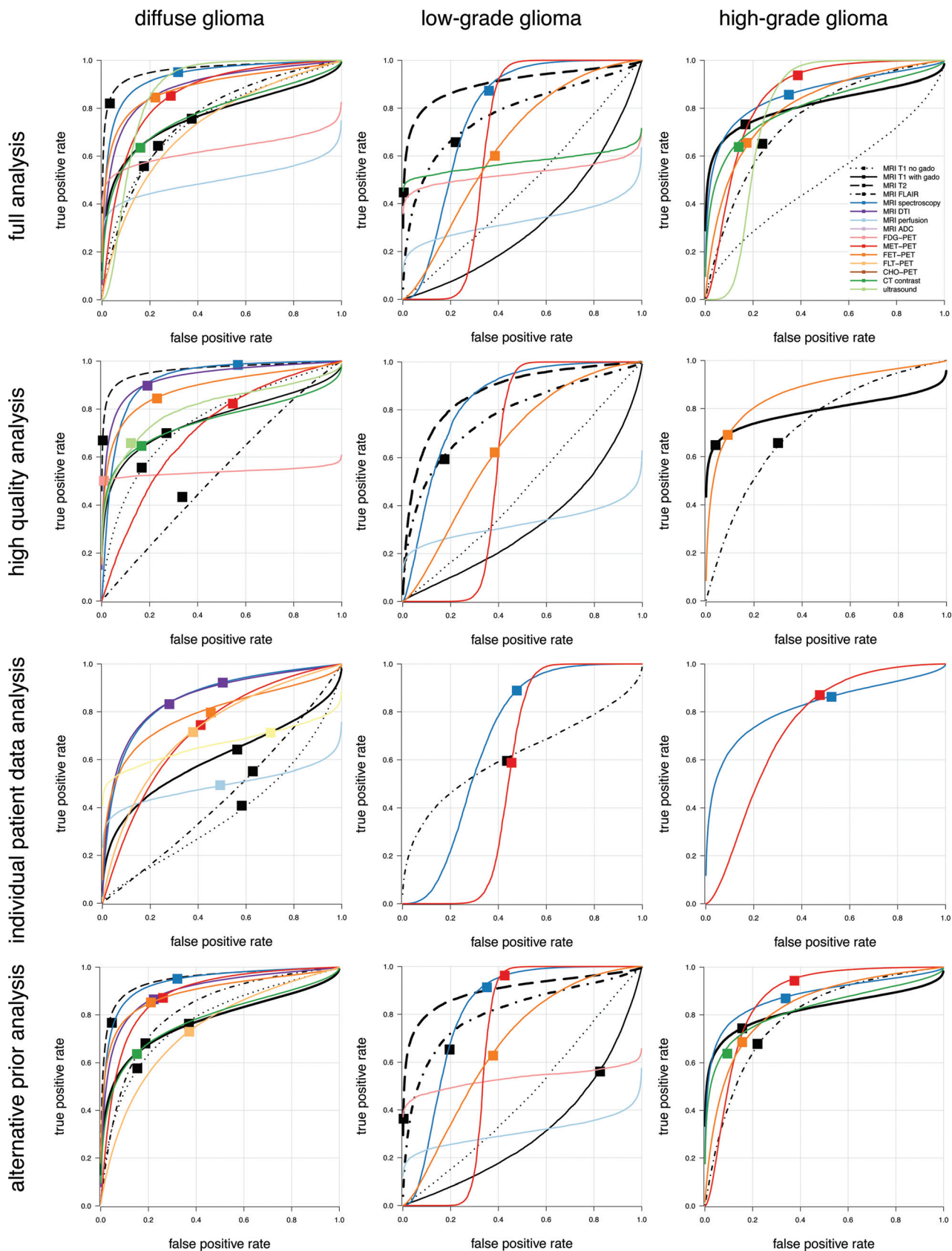
Emtree subject heading search: “glioma” and (“positron emission tomography” or “nuclear magnetic resonance imaging”) and (“pathology” or “histopathology”).

### On-Line Methods 2: Sample Bayesian Code (jags) for Hierarchic Summary ROC Model

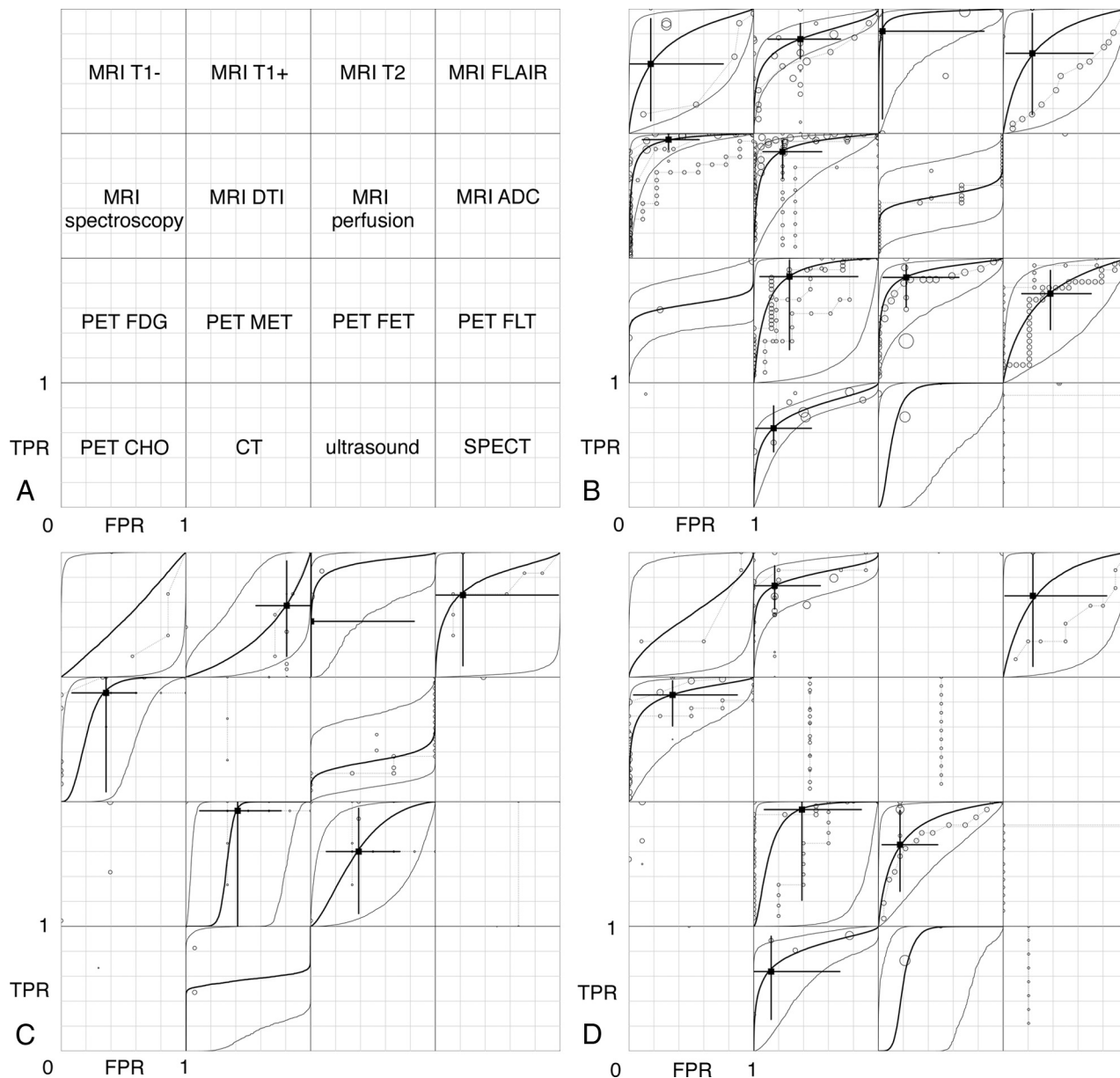
### EXAMPLE DATA

```
# STUDY 1 as use case for 2 × 2 aggregated study data
# STUDY 2 as use case for individual data with 7 ordinal
categories/levels
# N1/2: number of observations
# ncat1/2: number of test categories/levels
# Y1/2: test category level for each observation [1 to ncat]
# D1/2: disease status for each observation [0=non-diseased;
1=diseased]
N1 = 15
ncat1 = 2
Y1 = c(1, 1, 2, 2, 2, 2, 2, 2, 2, 2, 2, 2, 2, 2, 2)
D1 = c(0, 0, 1, 0, 1, 1, 1, 1, 1, 1, 1, 0, 1, 1, 1)
N2 = 52
ncat2 = 7
Y2 = c(1, 2, 2, 2, 2, 2, 3, 3, 3, 3, 3, 3, 3, 3, 4, 4, 4, 4, 4, 4, 4, 4, 4, 4, 4, 4, 4, 4, 4, 4, 5, 5, 5, 5, 5, 5, 5, 5, 5, 5, 5, 6, 6, 6, 6, 6, 6, 7)
D2 = c(1, 0, 0, 0, 1, 1, 0, 1, 1, 1, 1, 1, 1, 0, 0, 0, 0, 0, 0, 0, 1, 1, 1, 1, 1, 1, 1, 1, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 1, 1, 0, 0, 0, 1, 1, 1, 1)
### PRIORS
# example for one neuro-imaging modality, here CT
# b_: beta (scale parameter)
# a_: alpha (accuracy parameter)
# ta_: precision of the accuracy parameter (tau of alpha)
# t_: theta (cut-point parameter)
# tt_: precision of the cut point parameter (tau of theta)
b_CT ~ dnorm(0.0,1.0E-4)T(-10,10)
a_CT ~ dnorm(0.0,1.0E-4)
ta_CT ~ dgamma(0.01,0.01)
t_CT ~ dnorm(0.0,1.0E-4)
tt_CT ~ dgamma(0.01,0.01)
### SUMMARY ESTIMATES
# stpr_: summary true-positive rate
# sfpr_: summary false-positive rate
```

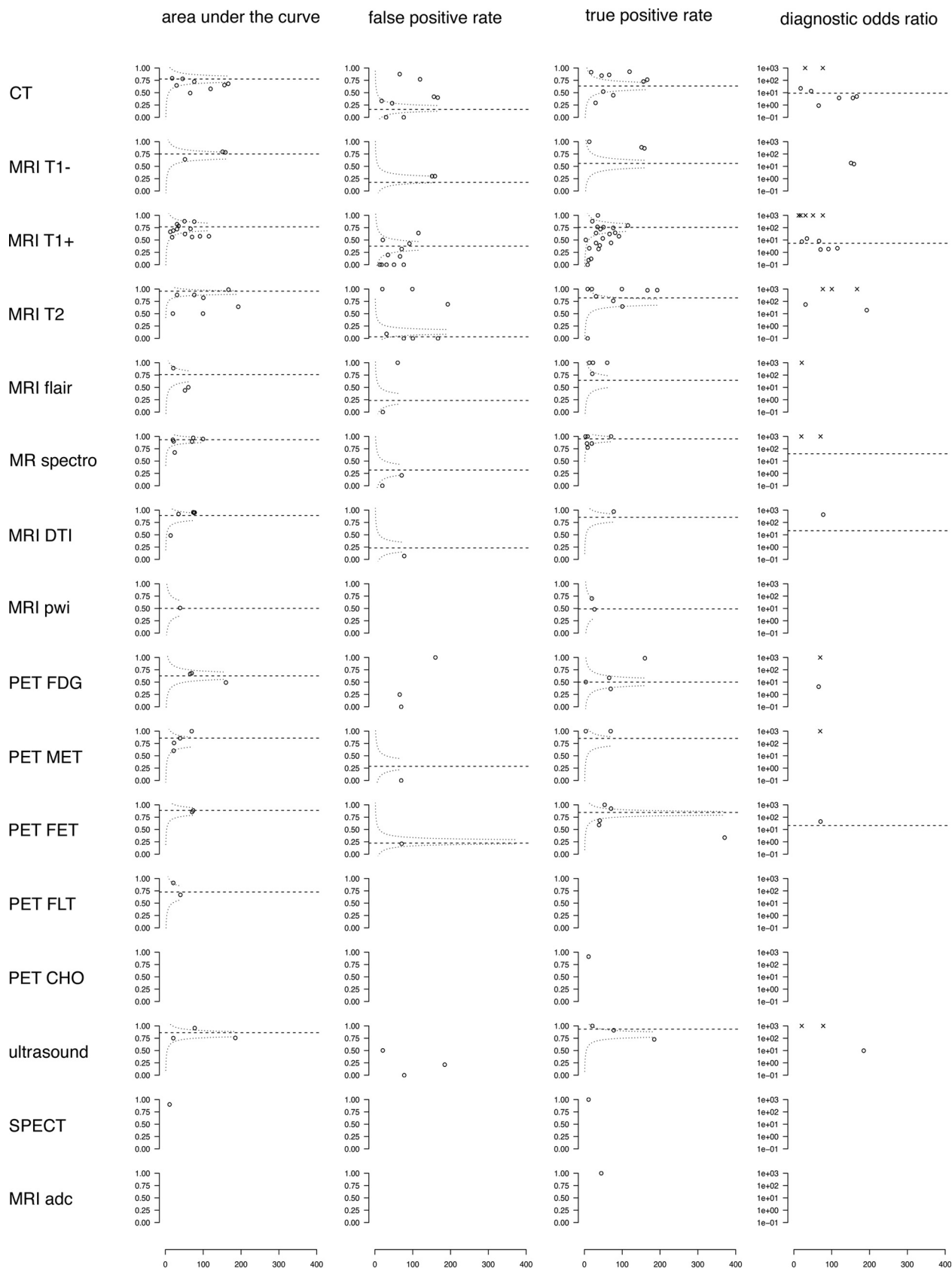
```
# dor_: summary diagnostic odds ratio
# arc_: summary area under the ROC curve
stpr_CT <- 1/(1 + exp(-(t_CT + a_CT/2) * exp(-b_CT/2))))
sfpr_CT <- 1/(1 + exp(-((t_CT - a_CT/2) * exp(b_CT/2))))
dor_CT <- (stpr * (1 - sfpr))/((1 - stpr) * sfpr)
for (i in 1:100) {tfpr[i] <- (i - 1) * 0.01}
for (i in 1:100) {tpr_CT[i] <- 1/(1 + exp(-(a_CT * exp(-b_CT/2) + exp(-b_CT) * log(tfpr[i]/(1-tfpr[i])))))}
tpr_CT[101] <- 1
auc_CT <- 0.01*(tpr_CT[1]/2 + sum(tpr_CT[2:100]) + tpr_CT[101]/2)
### MODEL
#—Study 1— example of aggregated 2 × 2 study data
# model the cumulative probabilities (Q)
for (i in 1:N1) {
  Q1[i] <- 1/(1 + exp(-((theta1 - alpha1 * (D1[i]-0.5)) * exp(-beta1 * (D1[i]-0.5)))))
  # Create P from cumulative P (ie, Q)
  P1[i, 1] <- min(max(Q1[i], 0), 1)
  P1[i, ncat1] <- min(max(1-Q1[i], 0), 1)
  # Discretize P to create Y
  Y1[i] ~ dcat(P1[i, 1: ncat1])
}
# Distribution for alpha1 (accuracy) and beta1 (scale) and theta1 (cut-point/positivity)
beta1 <- b_CT
alpha1 ~ dnorm(a_CT,ta_CT)
theta1 ~ dnorm(t_CT,tt_CT)
#—Study 2— example of multilevel individual data
# model the cumulative probabilities (Q)
for (i in 1:N2) {
  for (j in 1:(ncat2-1)) {Q2[i,j] <- 1/(1 + exp(-((theta2[j] - alpha2 * (D2[i]-0.5)) * exp(-beta2 * (D2[i]-0.5)))))}
  # Create P from cumulative P (ie, Q)
  P2[i,1] <- min(max(Q2[i,1], 0), 1)
  for (r in 2:(ncat2-1)) {P2[i, r] <- Q2[i,r] - Q2[i,(r-1)]}
  P2[i, ncat2] <- min(max(1-Q2[i, ncat2-1], 0), 1)
  # Discretize P to create Y
  Y2[i] ~ dcat(P2[i, 1: ncat2])
}
# Distribution for alpha2 (accuracy) and beta2 (scale) and theta2 (cut-point/positivity)
beta2 <- b_CT
alpha2 ~ dnorm(a_CT,ta_CT)
for(t in 1:6) {theta2_0[t] ~ dnorm(t_CT,tt_CT)}
theta2[1:6] <- sort(theta2_0)
```



**ON-LINE FIG1.** Sensitivity analysis with results from a subset of high-quality studies, individual patient data studies, and alternative vague priors.



**ON-LINE FIG 2.** Summary hierarchic ROC curves of imaging techniques with individual study data. Imaging techniques (A), diffuse glioma studies (B), low-grade glioma studies (C), and high-grade glioma studies (D). Envelopes of 95% CIs for hsROC curves are plotted with *thinner lines*. Operating points for summary false-positive and summary true-positive rates are shown with 95% CIs. The size of *circles* corresponds with study sample size. *Circles* connected by *lines* represent an ROC curve for individual studies based on individual patient data. FLT indicates  $^{18}\text{F}$  fluorothymidine; TPR, true-positive rate; FPR, false-positive rate.



**ON-LINE FIG 3.** Exploration of publication bias plotted by sample size versus outcome measures (area under the curve, false-positive rate, true-positive rate, and diagnostic odds ratio) per imaging technique. Points correspond with individual studies. Crosses indicate diagnostic odds ratios, truncated at 1000. Horizontal dotted lines represent summary estimates of outcome measures. Most imaging modalities have insufficient numbers of studies to evaluate publication bias, but there is an indication that small studies with small areas under the curve or low false-positive rates may be missing for T1-weighted gadolinium-enhanced and T2-weighted imaging.