## Supplementary Material

# DEMIST: A deep-learning-based task-specific denoising approach for myocardial perfusion SPECT

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#### S-I. NETWORK ARCHITECTURE

 TABLE S-1

 Network Architecture (Conv. = convolutional, BN = Batch Normalization, ReLU = Rectified Linear Unit, MaxPool = Max Pooling).

Layer	Layer type	Number of filters	Filter size	Stride/Pool size	Input size	Output size
1	Conv.	16	3×3×3	1×1×1	48×48×48×1	48×48×48×16
2	BN + Leaky ReLU	-	-	-	48×48×48×16	48×48×48×16
3	MaxPool	-	-	2×2×2	24×24×24×16	24×24×24×16
4	Conv.	32	3×3×3	1×1×1	24×24×24×16	24×24×24×32
5	BN + Leaky ReLU	-	-	-	24×24×24×32	24×24×24×32
6	MaxPool	-	-	2×2×2	12×12×12×32	12×12×12×32
7	Conv.	64	3×3×3	1×1×1	12×12×12×32	12×12×12×64
8	BN + Leaky ReLU	-	-	-	12×12×12×64	12×12×12×64
9	MaxPool	-	-	2×2×2	12×12×12×64	6×6×6×64
10	Conv.	128	3×3×3	1×1×1	6×6×6×64	6×6×6×128
11	BN + Leaky ReLU	-	-	-	6×6×6×128	6×6×6×128
12	Dropout	-	-	-	6×6×6×128	6×6×6×128
13	Transposed Conv.	64	3×3×3	2×2×2	6×6×6×128	12×12×12×64
14	BN + Leaky ReLU	-	-	-	12×12×12×64	12×12×12×64
15	Add Layer 8	-	-	-	12×12×12×64	12×12×12×64
16	Conv.	64	3×3×3	1×1×1	12×12×12×64	12×12×12×64
17	BN + Leaky ReLU	-	-	-	12×12×12×64	12×12×12×64
18	Transposed Conv.	32	3×3×3	2×2×2	12×12×12×64	24×24×24×32
19	BN + Leaky ReLU	-	-	-	24×24×24×32	24×24×24×32
20	Add Layer 5	-	-	-	24×24×24×32	24×24×24×32
21	Conv.	32	3×3×3	1×1×1	24×24×24×32	24×24×24×32
22	BN + Leaky ReLU	-	-	-	24×24×24×32	24×24×24×32
23	Transposed Conv.	16	3×3×3	2×2×2	24×24×24×32	48×48×48×16
24	BN + Leaky ReLU	-	-	-	48×48×48×16	48×48×48×16
25	Add Layer 2	-	-	-	48×48×48×16	48×48×48×16
26	Conv.	16	3×3×3	1×1×1	48×48×48×16	48×48×48×16
27	BN + Leaky ReLU	-	-	-	48×48×48×16	48×48×48×16
28	Conv	1	1×1×1	1×1×1	48×48×48×1	48×48×48×1
29	BN + Leaky ReLU	-	-	-	48×48×48×1	48×48×48×1

#### S-II. EVALUATION WITH CHANNELIZED MULTI-TEMPLATE OBSERVER

#### A. Background

To assess the robustness of DEMIST method across various channelized model observers, we performed our objective evaluation study using a different channelized model observer, namely a channelized multi-template observer (CMTO). In our population, the defect sizes, severities and locations were all varying. In this case, it has been observed that the channel outputs (vectors) for the entire population may not be multivariate normally distributed [1], thus limiting the applicability of the widely known Hotelling observer. However, the channel outputs for sub-ensembles of patient data grouped based on defect type may have multivariate normal distributions [2]. For this case, a CMTO was developed and evaluated in the context of MPI SPECT [2]. The CMTO applies the Hotelling template to the channel outputs and adds a constant term to compute test statistics for each sub-ensemble, and calculates a single global area under the ROC curve (AUC) using the pooled test statistics from all the sub-ensembles. The observer yields the maximal AUC when shifting the distributions of Hotelling observer test statistics by a different constant for each sub-ensemble is allowed [2]. The channels chosen for this observer were also the rotationally symmetric frequency channels, as in the CHO study. Also, the clinical task for this observer was detecting perfusion defects where the defect location was known.

#### B. Generation of test statistic

We followed the same procedure as described in Sec. III-C of the manuscript to obtain channel vectors. For each subensemble, the channel vectors of defect-present and defectabsent population were used to learn the template using a leave-one-out approach. The collection of test statistic from each sub-ensemble were then pooled [2] and were used to perform the ROC analysis.

#### C. Results

Fig. S-1 shows the AUC values obtained with the low-dose protocol, TADL method, DEMIST method and normal-dose protocol. We observed that at all dose levels, the DEMIST method yielded a significant improvement (p < 0.05) in performance on detection task compared to the low-dose protocol as well as the TADL method. The TADL method generally did not improve performance compared to the low-dose protocol.

Figs. S-2 and S-3 show the AUC values obtained for stratified analysis based on sex. We observed that at all dose levels and stratified groups, the DEMIST method yielded a significant improvement (p < 0.05) in performance on detection task compared to the low-dose protocol and TADL method. Again, we observed that the TADL method generally did not improve performance significantly compared to the low-dose protocol.

Figs. S-4 and S-5 show the AUC values obtained for stratified analysis based on defect extent and severity, respectively. Similar to previous results, we observed that at all dose levels and stratified groups, the DEMIST method yielded a significant improvement (p < 0.05) in performance on detection task compared to low-dose protocol and TADL method. Again, the TADL method generally did not improve performance significantly compared to the low-dose protocol.

Fig. S-6 shows the AUC values obtained for stratified analysis based on scanner type. We observed that at all dose levels, for both NaI and CZT scanners, the DEMIST method yielded a significant improvement (p < 0.05) in performance on detection task compared to low-dose protocol and TADL method. The TADL method generally did not improve performance significantly compared to the low-dose protocol.



Fig. S-1. AUC values obtained for the normal and low-dose images, the images denoised using the proposed DEMIST approach and TADL approach at various dose levels with CMTO. Error bars denote 95% confidence intervals.



Fig. S-2. AUC values for male patients obtained for the different approaches and at various dose levels using CMTO. Error bars denote 95% confidence intervals.



Fig. S-3. AUC values obtained for the different approaches and at various dose levels with female patients using CMTO. Error bars denote 95% confidence intervals.



Fig. S-4. AUC values obtained using CMTO for the various approaches as a function of different defect extents with (a) 6.25%, (b) 12.5% and (c) 25% dose levels. Error bars denote 95% confidence intervals.



Fig. S-5. AUC values obtained using CMTO for the various approaches as a function of different defect severities with (a) 6.25%, (b) 12.5% and (c) 25% dose levels. Error bars denote 95% confidence intervals.



Fig. S-6. AUC values obtained using CMTO for the various approaches for (a) NaI and (b) CZT scanner at various dose levels. Error bars denote 95% confidence intervals.

### S-III. CORRECTED P-VALUES OF DELONG'S TEST FOR AUC COMPARISON BETWEEN TWO METHODS

Analysis type         Stratified group         Observer         Comparisons         6.25%         12.50%         25%           Non-stratified analysis         -         DEMIST VS LD         2.72E-32         8.05E-38         1.44E           Non-stratified analysis         -         DEMIST VS TADL         2.74E-29         1.19E-29         2.08E           Non-stratified analysis         -         DEMIST VS TADL         0.111834         0.840879         0.079           CHO         DEMIST VS TADL         5.87E-11         3.71E-17         6.22E           TADL VS LD         0.014445         1.634715         0.035 (EEEEEEEEEEEEEEEEEEEEEEEEEEEEEEEEEEEE	Analysis type Non-stratified analysis Stratified analysis based on sex	Stratined group       -       Male       Female	CMTO CHO CMTO CHO CMTO CHO	Comparisons DEMIST VS LD DEMIST VS TADL TADL VS LD DEMIST VS TADL TADL VS LD DEMIST VS TADL DEMIST VS LD DEMIST VS LD	6.25% 2.72E-32 2.74E-29 0.111834 8.78E-20 5.87E-11 0.014445 4.43E-07 2.33E-18 0.130437 0.002403 8.25E-10 0.130599 2.59E-49 5.46E-05 6.51E-15 1.51E-18 0.132264 8.02E-11 2.08E-08	12.50% 8.05E-38 1.19E-29 0.840879 5.72E-10 3.71E-17 1.634715 4.39E-18 0.626301 4.71E-05 0.000263 1.255887 1.21E-16 1.04E-05 0.001287 3.47E-07 1.27E-17 0.200286	25% 1.44E-28 2.08E-14 0.079587 2.64E-17 6.22E-08 0.035604 4.8E-09 0.000553 0.607878 7.44E-07 0.018342 0.350955 1.13E-26 3.56E-17 1.792665 2.46E-13 1.94E-08 0.41967 1.04E-25
Non-stratified analysis         -         CMTO         DEMIST VS LD         2.72E-32         8.05E-38         1.44E- 1.9E-29           Non-stratified analysis         -         CMTO         DEMIST VS LD         0.111834         0.840879         0.0792           CHO         DEMIST VS LD         0.878E-20         5.72E-10         2.64E           DEMIST VS LD         0.011445         1.634715         0.22E           TADL VS LD         0.01445         1.634715         0.0079           DEMIST VS LD         2.38E-18         4.39E-18         0.0079           Male         CMTO         DEMIST VS LD         0.11445         1.634715         0.0079           Male         CMTO         DEMIST VS LD         4.43E-07         1.83E-15         4.8E-0           Male         CMTO         DEMIST VS LD         0.130437         0.626301         0.6075           TADL VS LD         0.130437         0.626301         0.0075         0.3059         1.255887         0.3509           Female         CMTO         DEMIST VS LD         0.130437         0.626301         0.6025         1.04E-05         3.56E           TADL VS LD         0.130599         1.255887         0.3506         TADL VS LD         1.51E-18         3.4	Non-stratified analysis	- Male Female	CMTO CHO CMTO CHO CMTO	DEMIST VS LD DEMIST VS TADL TADL VS LD DEMIST VS LD DEMIST VS TADL TADL VS LD DEMIST VS LD	2.72E-32 2.74E-29 0.111834 8.78E-20 5.87E-11 0.014445 4.43E-07 2.33E-18 0.130437 0.002403 8.25E-10 0.130599 2.59E-49 5.46E-05 6.51E-15 1.51E-18 0.132264 8.02E-11 2.08E-08	8.05E-38 1.19E-29 0.840879 5.72E-10 3.71E-17 1.634715 1.83E-15 4.39E-18 0.626301 4.71E-05 0.000263 1.255887 1.21E-16 1.04E-05 0.001287 3.47E-07 1.27E-17 0.200286	1.44E-28 2.08E-14 0.079587 2.64E-17 6.22E-08 0.035604 4.8E-09 0.000553 0.607878 7.44E-07 0.018342 0.350955 1.13E-26 3.56E-17 1.792665 2.46E-13 1.94E-08 0.41967
Non-stratified analysis         -         CMTO         DEMIST VS TADL         2.74E-29         1.19E-29         2.08E           TADL VS LD         0.111834         0.840879         0.0795         DEMIST VS LD         8.78E-20         5.72E-10         2.64E           CHO         DEMIST VS LD         5.78E-20         5.72E-10         2.64E         DEMIST VS LD         0.014445         1.634715         0.0356           Male         CMTO         DEMIST VS LD         4.43E-07         1.83E-15         4.8E-0         0.002403         4.71E-05         7.44E           DEMIST VS LD         0.130437         0.626301         0.6078         0.0002403         4.71E-05         7.44E           DEMIST VS LD         0.130437         0.626301         0.6078         0.0002403         4.71E-05         7.44E           DEMIST VS LD         0.130437         0.626301         0.6078         0.0002403         4.71E-05         7.44E           DEMIST VS LD         0.130437         0.626301         0.6078         0.0002403         4.71E-05         7.44E           DEMIST VS LD         0.130437         0.626301         0.6078         0.002543         0.0183         0.602510         0.00263         0.0183           Female         CMTO	Non-stratified analysis Stratified analysis based on sex	- Male Female	CMTO CHO CMTO CHO CMTO CHO	DEMIST VS TADL TADL VS LD DEMIST VS LD	2.74E-29 0.111834 8.78E-20 5.87E-11 0.014445 4.43E-07 2.33E-18 0.130437 0.002403 8.25E-10 0.130599 2.59E-49 5.46E-05 6.51E-15 1.51E-18 0.132264 8.02E-11 2.08E-08	1.19E-29 0.840879 5.72E-10 3.71E-17 1.634715 1.83E-15 4.39E-18 0.626301 4.71E-05 0.000263 1.255887 1.21E-16 1.04E-05 0.001287 3.47E-07 1.27E-17 0.200286	2.08E-14 0.079587 2.64E-17 6.22E-08 0.035604 4.8E-09 0.000553 0.607878 7.44E-07 0.018342 0.350955 1.13E-26 3.56E-17 1.792665 2.46E-13 1.94E-08 0.41967
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CHO         DEMIST VS LD         3.78E-20         3.74E-10         2.04-10           CHO         DEMIST VS LD         5.78E-11         3.71E-17         6.22E           TADL VS LD         0.014445         1.634715         0.0356           Male         DEMIST VS LD         4.43E-07         1.83E-15         4.8E-0           DEMIST VS LD         0.130437         0.626301         0.6075           TADL VS LD         0.002403         4.71E-05         7.44E           CHO         DEMIST VS TADL         8.25E-10         0.000263         0.0183           TADL VS LD         0.130599         1.255887         0.3050           Female         CMTO         DEMIST VS TADL         5.46E-05         1.04E-05         3.56E-           TADL VS LD         6.51E-15         0.001287         1.7926           DEMIST VS TADL	Stratified analysis based on sex	Female	CHO CMTO CHO CMTO CHO	DEMIST VS LD DEMIST VS LD	5.87E-11 0.014445 4.43E-07 2.33E-18 0.130437 0.002403 8.25E-10 0.130599 2.59E-49 5.46E-05 6.51E-15 1.51E-18 0.132264 8.02E-11 2.08E-08	3.71E-17 3.71E-17 1.634715 1.83E-15 4.39E-18 0.626301 4.71E-05 0.000263 1.255887 1.21E-16 1.04E-05 0.001287 3.47E-07 1.27E-17 0.200286	2.04E-17 6.22E-08 0.035604 4.8E-09 0.000553 0.607878 7.44E-07 0.018342 0.350955 1.13E-26 3.56E-17 1.792665 2.46E-13 1.94E-08 0.41967
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Male         CMTO         DEMIST VS LD         4.01444.3         1.034713         0.0303           Male         CMTO         DEMIST VS LD         4.43E-07         1.83E-15         4.8E-0           Stratified analysis based on sex         CHO         DEMIST VS LD         0.130437         0.626301         0.6075           Female         CHO         DEMIST VS LD         0.130437         0.626301         0.6075           TADL VS LD         0.130599         1.255887         0.3506           Female         CMTO         DEMIST VS LD         0.130599         1.255887         0.3506           Female         CMTO         DEMIST VS LD         2.59E-49         1.21E-16         1.13E-17           Male         CMTO         DEMIST VS LD         2.59E-49         1.21E-16         1.13E-17           Female         CMTO         DEMIST VS LD         1.51E-18         3.47E-07         2.46E-05           TADL VS LD         0.132264         1.27E-17         1.94E-07         2.46E-07         1.04E-07         2.46E-07           CHO         DEMIST VS LD         0.132264         1.27E-17         1.94E-07         2.46E-07         1.04E-07         2.46E-07         1.04E-07         2.46E-07         1.04E-07         2.46E-07	Stratified analysis based on sex	Female	СМТО СНО СМТО СНО	DEMIST VS LD DEMIST VS LD TADL VS LD DEMIST VS LD	4.43E-07 2.33E-18 0.130437 0.002403 8.25E-10 0.130599 2.59E-49 5.46E-05 6.51E-15 1.51E-18 0.132264 8.02E-11 2.08E-08	1.034713 1.83E-15 4.39E-18 0.626301 4.71E-05 0.000263 1.255887 1.21E-16 1.04E-05 0.001287 3.47E-07 1.27E-17 0.200286	4.8E-09 0.000553 0.607878 7.44E-07 0.018342 0.350955 1.13E-26 3.56E-17 1.792665 2.46E-13 1.94E-08 0.41967
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$ \begin{array}{c c c c c c c c c c c c c c c c c c c $	Stratified analysis based on sex	Female	СНО СМТО СНО	TADL VS LD DEMIST VS LD DEMIST VS TADL TADL VS LD DEMIST VS LD DEMIST VS TADL TADL VS LD DEMIST VS TADL TADL VS LD DEMIST VS LD	0.130437 0.002403 8.25E-10 0.130599 2.59E-49 5.46E-05 6.51E-15 1.51E-18 0.132264 8.02E-11 2.08E-08	0.626301 4.71E-05 0.000263 1.255887 1.21E-16 1.04E-05 0.001287 3.47E-07 1.27E-17 0.200286	0.607878 7.44E-07 0.018342 0.350955 1.13E-26 3.56E-17 1.792665 2.46E-13 1.94E-08 0.41967
$ \begin{array}{c c c c c c c c c c c c c c c c c c c $	Stratified analysis based on sex	Female	СНО СМТО СНО	DEMIST VS LD DEMIST VS TADL TADL VS LD DEMIST VS LD DEMIST VS TADL TADL VS LD DEMIST VS TADL TADL VS LD DEMIST VS LD	0.002403 8.25E-10 0.130599 2.59E-49 5.46E-05 6.51E-15 1.51E-18 0.132264 8.02E-11 2.08E-08	4.71E-05 0.000263 1.255887 1.21E-16 1.04E-05 0.001287 3.47E-07 1.27E-17 0.200286	7.44E-07 0.018342 0.350955 1.13E-26 3.56E-17 1.792665 2.46E-13 1.94E-08 0.41967
$ \begin{array}{ c c c c c c c c c c c c c c c c c c c$	Stratified analysis based on sex	Female	СНО СМТО СНО	DEMIST VS TADL TADL VS LD DEMIST VS LD DEMIST VS TADL TADL VS LD DEMIST VS TADL TADL VS LD DEMIST VS LD	8.25E-10 0.130599 2.59E-49 5.46E-05 6.51E-15 1.51E-18 0.132264 8.02E-11 2.08E-08	0.000263 1.255887 1.21E-16 1.04E-05 0.001287 3.47E-07 1.27E-17 0.200286	0.018342 0.350955 1.13E-26 3.56E-17 1.792665 2.46E-13 1.94E-08 0.41967
Stratified analysis based on sex         TADL VS LD         0.130599         1.255887         0.3509           Female         DEMIST VS LD         2.59E-49         1.21E-16         1.13E           DEMIST VS LD         2.59E-49         1.21E-16         1.13E           DEMIST VS LD         2.59E-49         1.21E-16         1.13E           DEMIST VS LD         5.46E-05         1.04E-05         3.56E           TADL VS LD         6.51E-15         0.001287         1.7926           DEMIST VS LD         1.51E-18         3.47E-07         2.46E           CHO         DEMIST VS TADL         0.132264         1.27E-17         1.94E           TADL VS LD         1.012264         1.27E-17         1.94E           TADL VS LD         8.02E-11         0.200286         0.4196           O           30° extent           30° extent         DEMIST VS LD         2.08E-08         4.02E-15         1.04E           30° extent         CMTO         DEMIST VS LD         2.08E-08         4.02E-15         1.04E           30° extent         DEMIST VS LD         1.581237	Stratified analysis based on sex	Female	СМТО	TADL VS LD DEMIST VS LD DEMIST VS TADL TADL VS LD DEMIST VS LD DEMIST VS LD TADL VS LD	0.130599 2.59E-49 5.46E-05 6.51E-15 1.51E-18 0.132264 8.02E-11 2.08E-08	1.255887 1.21E-16 1.04E-05 0.001287 3.47E-07 1.27E-17 0.200286	0.350955 1.13E-26 3.56E-17 1.792665 2.46E-13 1.94E-08 0.41967
$ \begin{array}{ c c c c c c c c c c c c c c c c c c c$	Stratified analysis based on sex	Female	СМТО	DEMIST VS LD DEMIST VS TADL TADL VS LD DEMIST VS LD DEMIST VS TADL TADL VS LD DEMIST VS LD	2.59E-49 5.46E-05 6.51E-15 1.51E-18 0.132264 8.02E-11 2.08E-08	1.21E-16 1.04E-05 0.001287 3.47E-07 1.27E-17 0.200286	1.13E-26 3.56E-17 1.792665 2.46E-13 1.94E-08 0.41967
$ \begin{array}{c c} \mbox{Female} \\ \mbox{Female} \\ \mbox{Sector} \\ \mbox{Female} \\ \mbox{Temale} \\ \mbox{Female} \\ \mbox{Female} \\ \mbox{Female} \\ \mbox{Female} \\ \mbox{CMTO} \\ \mbox{CMTO} \\ \mbox{CMTO} \\ \mbox{DEMIST VS LD} \\ \mbox{CMTO} \\ \mbox{LD} \\ \mbox{Schedule} \\ \mbox{Schedule} \\ \mbox{Schedule} \\ \mbox{CMTO} \\ \mbox{CMTO} \\ \mbox{DEMIST VS LD} \\ \mbox{Schedule} \\ $		Female	СМТО	DEMIST VS LD DEMIST VS TADL TADL VS LD DEMIST VS LD DEMIST VS TADL TADL VS LD DEMIST VS LD	2.59E-49 5.46E-05 6.51E-15 1.51E-18 0.132264 8.02E-11 2.08E-08	1.21E-16 1.04E-05 0.001287 3.47E-07 1.27E-17 0.200286	1.13E-26 3.56E-17 1.792665 2.46E-13 1.94E-08 0.41967
$ \begin{array}{c cccc} \mbox{Female} & \begin{tabular}{ c c c c c c c c c c c c c c c c c c c$		Female	СМТО	DEMIST VS TADL TADL VS LD DEMIST VS LD DEMIST VS TADL TADL VS LD DEMIST VS LD	5.46E-05 6.51E-15 1.51E-18 0.132264 8.02E-11 2.08E-08	1.04E-05 0.001287 3.47E-07 1.27E-17 0.200286	3.56E-17 1.792665 2.46E-13 1.94E-08 0.41967
$\begin{array}{ c c c c c c c c c c c c c c c c c c c$		Female	СНО	TADL VS LD DEMIST VS LD DEMIST VS TADL TADL VS LD DEMIST VS LD	6.51E-15 1.51E-18 0.132264 8.02E-11 2.08E-08	0.001287 3.47E-07 1.27E-17 0.200286	1.792665 2.46E-13 1.94E-08 0.41967
Female         DEMIST VS LD         1.51E-18         3.47E-07         2.46E-           DEMIST VS TADL         0.132264         1.27E-17         1.94E-           TADL VS LD         8.02E-11         0.200286         0.4196           0         DEMIST VS LD         8.02E-11         0.200286         0.4196           30° extent         DEMIST VS LD         2.08E-08         4.02E-15         1.04E-           30° extent         DEMIST VS LD         1.581237         2.56014         0.6066           DEMIST VS LD         1.4E-05         0.025992         1.57E-           CHO         DEMIST VS LD         2.42E-05         0.000472         0.0042			СНО	DEMIST VS LD DEMIST VS TADL TADL VS LD DEMIST VS LD	1.51E-18 0.132264 8.02E-11 2.08E-08	3.47E-07 1.27E-17 0.200286	2.46E-13 1.94E-08 0.41967
CHO         DEMIST VS TADL         0.132264         1.27E-17         1.94E           TADL VS LD         8.02E-11         0.200286         0.4196           0         DEMIST VS LD         8.02E-11         0.200286         0.4196           30° extent         DEMIST VS LD         2.08E-08         4.02E-15         1.04E-           30° extent         DEMIST VS TADL         7.07E-10         5.29E-14         4.73E-           TADL VS LD         1.581237         2.56014         0.6066           DEMIST VS LD         1.4E-05         0.025992         1.57E-           CHO         DEMIST VS TADL         2.42E-05         0.000472         0.0042			СНО	DEMIST VS TADL TADL VS LD	0.132264 8.02E-11 2.08E-08	1.27E-17 0.200286	1.94E-08 0.41967
Office         DEMIST VS LD         8.02E-11         0.200286         0.4196           TADL VS LD         8.02E-11         0.200286         0.4196           TADL VS LD         8.02E-11         0.200286         0.4196           TADL VS LD         2.08E-08         4.02E-15         1.04E-           TADL VS LD         2.08E-08         4.02E-15         1.04E-           TADL VS LD         1.581237         2.56014         0.6066           DEMIST VS LD         1.4E-05         0.025992         1.57E-           CHO         DEMIST VS TADL         2.42E-05         0.000472         0.0042			СМТО	TADL VS LD	8.02E-11 2.08E-08	0.200286	0.41967
30° extent         CMTO         DEMIST VS LD         2.08E-08         4.02E-15         1.04E- 1.04E- 1.04E- 1.04E- 1.04E- 0.0042           30° extent         CMTO         DEMIST VS LD         2.08E-08         4.02E-15         1.04E- 1.04E- 1.04E- 1.04E- 1.04E- 0.0042           30° extent         CMTO         DEMIST VS LD         1.581237         2.56014         0.6666           CHO         DEMIST VS LD         1.4E-05         0.025992         1.57E- 1.57E- 0.000472         0.0042			СМТО	DEMIST VS LD	2.08E-08	0.200200	1.047.00
CMTO         DEMIST VS LD         2.08E-08         4.02E-15         1.04E-           30° extent         CMTO         DEMIST VS TADL         7.07E-10         5.29E-14         4.73E-           TADL VS LD         1.581237         2.56014         0.6066           DEMIST VS TADL         0.025992         1.57E-           CHO         DEMIST VS TADL         2.42E-05         0.000472         0.0042			CMTO	DEMIST VS LD	2.08E-08	4.005.15	1.047.00
CMTO         DEMIST VS LD         2.06E-06         4.02E-15         1.04E-           30° extent         DEMIST VS TADL         7.07E-10         5.29E-14         4.73E-           TADL VS LD         1.581237         2.56014         0.6066           DEMIST VS TADL         1.4E-05         0.025992         1.57E-           CHO         DEMIST VS TADL         2.42E-05         0.000472         0.0042			СМТО		I ∠.U0E-U6	1 / 1/75 14	
30° extent         CMTO         DEMIST VS TADL         7.07E-10         5.29E-14         4.73E- 4.73E-           30° extent         TADL VS LD         1.581237         2.56014         0.6066           DEMIST VS LD         1.4E-05         0.025992         1.57E-           CHO         DEMIST VS TADL         2.42E-05         0.000472         0.0042		1	1 1/11/1	DEMIST VS TADI	7.075 10	4.02E-13	1.04E-09
30° extent         IADL VS LD         1.581237         2.56014         0.6066           DEMIST VS LD         1.4E-05         0.025992         1.57E-           CHO         DEMIST VS TADL         2.42E-05         0.000472         0.0042			CMIO	DEMIST VS TADL	7.07E-10	5.29E-14	4.73E-05
DEMIST VS LD         1.4E-05         0.025992         1.57E-           CHO         DEMIST VS TADL         2.42E-05         0.000472         0.0042		$30^{\circ}$ extent		TADL VS LD	1.581237	2.56014	0.606618
CHO DEMIST VS TADL 2.42E-05 0.000472 0.0042			СНО	DEMIST VS LD	1.4E-05	0.025992	1.57E-06
				DEMIST VS TADL	2.42E-05	0.000472	0.00423
TADL VS LD 1.077156 2.296377 0.3628				TADL VS LD	1.077156	2.296377	0.362862
DEMIST VS LD 1.1E-11 1.08E-15 9.54E-				DEMIST VS LD	1.1E-11	1.08E-15	9.54E-13
CMTO DEMIST VS TADL 1.37E-17 4.72E-15 1.53E-			CMTO	DEMIST VS TADL	1.37E-17	4.72E-15	1.53E-06
Stratified analysis based on defect extent 45° extent TADL VS LD 1.904022 2.836206 1.2464	Stratified analysis based on defect extent	45° extent	СНО	TADL VS LD	1.904022	2.836206	1.246464
Strained analysis based on delect extent         45 extent         DEMIST VS LD         2.75E-09         2.93E-05         0.0002	Stratified analysis based on defect extent	+5 extent		DEMIST VS LD	2.75E-09	2.93E-05	0.000266
CHO DEMIST VS TADL 5.04E-07 4.47E-08 0.0044				DEMIST VS TADL	5.04E-07	4.47E-08	0.004428
TADL VS LD         0.681075         1.96272         2.0551				TADL VS LD	0.681075	1.96272	2.055168
DEMIST VS LD 1.31E-13 4.45E-08 4.55E-				DEMIST VS LD	1.31E-13	4.45E-08	4.55E-08
CMTO DEMIST VS TADL 7.56E-05 0.002286 0.0003			CMTO	DEMIST VS TADL	7.56E-05	0.002286	0.000327
TADL VS LD 0.002466 0.130788 0.2514		(00)		TADL VS LD	0.002466	0.130788	0.251469
60° extent DEMIST VS LD 1.08E-10 2.12E-06 2.58E-		60° extent		DEMIST VS LD	1.08E-10	2.12E-06	2.58E-08
CHO DEMIST VS TADL 0.088839 3.15E-07 0.0016			СНО	DEMIST VS TADL	0.088839	3.15E-07	0.001602
TADL VS LD         0.000753         1.500372         0.0809				TADL VS LD	0.000753	1.500372	0.080946
DEMIST VS LD 1.11E-07 1.21E-07 0.0012				DEMIST VS LD	1.11E-07	1.21E-07	0.001269
CMTO DEMIST VS TADI. 4 07F-07 6 94F-06 0 0002			CMTO	DEMIST VS TADI	4.07E-07	6.94E-06	0.000468
TADI VS ID 078584 1280538 17855			00	TADL VS LD	0.784584	1.289538	1.785861
10% severity DEMIST VS LD 0.000543 0.038628 0.0011		10% severity		DEMIST VS I D	0.000543	0.038628	0.001143
CHO DEMIST VS TADI 0.142011 0.001213 0.0552			СНО	DEMIST VS TADI	0.0000045	0.021213	0.055386
TADE VS IADE 0.142011 0.201213 0.0007			CHO	TADL VS ID	0.142011	2 305017	0.055500
IADL V3 LD 0.340419 2.353917 0.0007				TADL V3 LD	0.540419	2.393917	0.808731
DEMICT VC LD 200E 11 157E 12 272E			CMTO	DEMICT VOLD	1 00E 11	1.56E 12	2 725 10
DEMIST VS LD 2.88E-11 1.50E-13 2.73E-				DEMIST VS LD	2.00E-11	1.30E-13	2.73E-10
CM10 DEMIST VS IADL 2.85E-10 5.92E-11 9.09E-			CMIO	DEMIST VS TADL	2.85E-10	5.92E-11	9.09E-06
Stratified analysis based on defect severity 17.5% severity	Stratified analysis based on defect severity	17.5% severity		TADL VS LD	0.719325	1.793304	0.692793
DEMIST VS LD 2.35E-07 0.000505 9.99E				DEMIST VS LD	2.35E-07	0.000505	9.99E-07
CHO DEMIST VS TADL 0.00026 1.07E-06 0.0016			СНО	DEMIST VS TADL	0.00026	1.0/E-06	0.001629
TADL VS LD 0.312813 2.061603 0.5146				TADL VS LD	0.312813	2.061603	0.514611
DEMIST VS LD 7.94E-16 5.31E-21 1.33E-				DEMIST VS LD	7.94E-16	5.31E-21	1.33E-17
CMTO DEMIST VS TADL 3.04E-14 1.6E-15 3.68E-			CMTO	DEMIST VS TADL	3.04E-14	1.6E-15	3.68E-07
75% severity TADL VS LD 0.542664 1.39266 0.0383		25% soverity		TADL VS LD	0.542664	1.39266	0.038385
DEMIST VS LD 1.58E-12 4.38E-07 6.98E-		2570 Seventy		DEMIST VS LD	1.58E-12	4.38E-07	6.98E-10
CHO DEMIST VS TADL 1.13E-09 3.32E-13 6.31E-			CHO	DEMIST VS TADL	1.13E-09	3.32E-13	6.31E-05
TADL VS LD 0.260334 1.118241 0.3400				TADL VS LD	0.260334	1.118241	0.340011

TABLE S-2 Corrected P-values for various analyses and observers (LD = low-dose protocol)

 TABLE S-3

 Corrected P-values for stratified analysis with scanner types

Analysis type	Stratified group	tified group Observer Comparisons 6.259			Dose levels	
Analysis type	Suamed group			6.25%	12.50%	25%
		СМТО	DEMIST VS LD	1.79E-38	4.33E-37	3.59E-06
			DEMIST VS TADL	1.50E-21	2.24E-21	4.51E-07
	NoI		TADL VS LD	8.97E-05	0.05029	0.428633
	INAL		DEMIST VS LD	1.79E-14	1.59E-08	2.554406 0.057514
		CHO	DEMIST VS TADL	0.00164	0.454727	0.057514
			TADL VS LD	4.93E-06	0.000214	0.066835
Stratified analysis based on scanner						
		СМТО	DEMIST VS LD	6.16E-08	4.68E-06	4.50E-13
			DEMIST VS TADL	1.48E-08	0.00161	3.14E-05
	С7Т		TADL VS LD	2.692152	0.64725	25% 3.59E-06 4.51E-07 0.428633 2.554406 0.057514 0.066835 4.50E-13 3.14E-05 0.018067 1.88E-16 4.20E-05 0.000155
	CZI	СНО	DEMIST VS LD	0.00263	1.830386	1.88E-16
			DEMIST VS TADL	0.000259	5.87E-11	4.20E-05
			TADL VS LD	2.378452	6.44E-06	0.000155

#### S-IV. SPECT SCANNER CONFIGURATION

TABLE S-4 Acquisition and reconstruction parameters of SPECT/CT systems. (LEHR=Low-energy high-resolution, WEHR=Wide-energy High-resolution)

	Scanner			
	GE Discovery NM/CT 670 Pro NaI	GE Discovery NM/CT 670 Pro CZT		
Number of cases in test data	63	51		
Number of cases in train data	102	82		
Number of cases in validation data	12	28		
Collimator type	LEHR	WEHR		
Collimator grid	Parallel hole	Parallel hole		
Detector	NaI	CZT		
Energy resolution at 140 keV (%)	9.8	6.3		
Intrinsic spatial resolution (in mm)	3.9	2.46		
System sensitivity (cps/MBq) at 10 cm	72	85		
Photopeak energy window (in keV)	126-154	126-154		
Reconstruction	OSEM	OSEM		
Subsets	6	6		
Iteration	8	8		
Attenuation correction	CT	CT		

#### S-V. EXAMPLES OF DEFECT SIGNALS



Fig. S-7. Examples of inserted defect using the LV segmented mask with varying extents and locations. The defects are at 50% severity for illustration purpose.



#### S-VI. ROC CURVES OF NON-STRATIFIED AND STRATIFIED ANALYSIS

Fig. S-8. ROC curves for different approaches with (a) 6.25%, (b) 12.5% and (c) 25% dose levels with CHO.



Fig. S-9. ROC curves for male patients with different approaches at (a) 6.25%, (b) 12.5% and (c) 25% dose levels with CHO.



Fig. S-10. ROC curves for female patients with different approaches at (a) 6.25%, (b) 12.5% and (c) 25% dose levels with CHO.



Fig. S-11. ROC curves for 30° defect extent with different approaches at (a) 6.25%, (b) 12.5% and (c) 25% dose levels with CHO.



Fig. S-12. ROC curves for 45° defect extent with different approaches at (a) 6.25%, (b) 12.5% and (c) 25% dose levels with CHO.



Fig. S-13. ROC curves for 60° defect extent with different approaches at (a) 6.25%, (b) 12.5% and (c) 25% dose levels with CHO.



Fig. S-14. ROC curves for 10% defect severity with different approaches at (a) 6.25%, (b) 12.5% and (c) 25% dose levels with CHO.



Fig. S-15. ROC curves for 17.5% defect severity with different approaches at (a) 6.25%, (b) 12.5% and (c) 25% dose levels with CHO.



Fig. S-16. ROC curves for 25% defect severity with different approaches at (a) 6.25%, (b) 12.5% and (c) 25% dose levels with CHO.



Fig. S-17. ROC curves for NaI scanner with different approaches at (a) 6.25%, (b) 12.5% and (c) 25% dose levels with CHO.



Fig. S-18. ROC curves for CZT scanner with different approaches at (a) 6.25%, (b) 12.5% and (c) 25% dose levels with CHO.

### S-VII. EIGENVALUES OF NOISE COVARIANCE MATRIX

TABLE S-5 Eigenvalues of noise covariance matrix for defect type 1 and 2 in Fig. 10 of the manuscript

Defect type	eigenvalue index	DEMIST	TADL	Low dose	Normal dose
	1	9.0339e+04	5.6555e+04	9.8293e+04	5.8214e+04
1	2	895.7745	548.8621	1.7790e+03	565.8395
1	3	16.2792	12.9378	54.3595	45.9154
	4	4.6574	9.1591	38.1404	12.2971
	1	5.4074e+04	3.5064e+04	7.7168e+04	4.0850e+04
2	2	650.7050	665.1538	2.0431e+03	593.1918
2	3	37.1322	42.6869	42.1296	40.4913
	4	6.0972	7.1659	30.5935	23.7583

#### References

- [1] F. E. Elshahaby, M. Ghaly, A. K. Jha, and E. C. Frey, "Factors affecting the normality of channel outputs of channelized model observers: an investigation using realistic myocardial perfusion SPECT images," *J. Med. Imaging*, vol. 3, no. 1, pp. 015 503–015 503, 2016.
- Med. Imaging, vol. 36, no. 4, pp. 917–929, 2016.