

TABLE E-1 Characteristics of the Included Studies

Study	Year	Author	Design	Patients demographics	Reference test(s)
Al Sheikh et al. ³⁸	1985	TC	Prospective	n = 21, Gender not described Ages: 32-65 yrs.	Culture or CFU
Esterhai et al. ³⁶	1985	TC	Retrospective	n = 24, (M = 14, F = 10) Ages: 13 – 76 yrs ^a	Culture
Esterhai et al. ³⁷	1987	TC	Prospective	n = 20, (M = 14, F = 6) Ages: 19 – 61 yrs	Culture
Wukich et al. ¹²	1987	SC	Retrospective	n = 26, Gender and age unclear for subset	Culture
Schauwecker ⁶	1989	TC	Retrospective	n = 193, Gender and age unclear for subset	Culture
Mason et al. ³⁵	1989	TC	Retrospective	n = 14, Gender and age not described	Culture
Seabold et al. ³³	1989	TC	Prospective	n = 49, (M = 37, F = 12) Ages: 19 – 75 yrs	Culture
Whalen et al. ³¹	1991	TC	Retrospective	n = 12, Gender unclear for subset Ages: 33 – 68 yrs	Culture
Palestro et al. ³⁴	1991	TC	Retrospective	n = 15, (M = 10, F = 5) Ages: 31 – 83 yrs	Culture
Sciuk et al. ²⁸	1991	TC	Prospective	n = 17, (M = 10, F = 7) Ages: 21 – 79 yrs	Culture or histology
Williamson et al. ²⁹	1991	TC	Prospective	n = 16, Gender and age unclear for subset	Culture
El Esper et al. ³²	1992	TC	Retrospective	n = 27, Gender and age unclear for subset	Culture or CFU
Flivik et al. ³⁰	1993	TC	Retrospective	n = 10, (M = 7, F = 3) Ages: 16 –73 yrs ^a	Culture
Nepola et al. ²⁶	1993	TC	Retrospective	n = 96, (M = 68, F = 28) Ages: 11-75 yrs ^a	Culture
Devillers et al. ²⁵	1995	TC	Retrospective	n = 24, Gender and age not described	Culture or CFU
Krznaric et al. ²⁷	1996	TC	Retrospective	n = 55, (M = 32, F = 23) Ages: 18 – 85 yrs	Culture or histology or CFU
Kaim et al. ²²	1997	TC	Retrospective	n = 24, (M = 17, F = 7) Ages: 21 – 83 yrs	Culture or CFU
Nijhof et al. ²³	1997	TC	Retrospective	n = 36, Gender and age unclear for subset	Culture or histology or CFU
Guhlmann et al. ²⁴	1998	TC	Prospective	n = 51, (M = 39, F = 12) Ages: 22 – 81 yrs	Culture or CFU
Kaim et al. ²¹	2000	TC	Retrospective	n = 18, (M = 13, F = 5) Ages: 27 – 65 yrs	Culture or histology or CFU
De Winter et al. ¹⁹	2001	TC	Prospective	n = 60, (M = 28, F = 32) Ages: 13 – 75 yrs ^a	Culture or CFU
Meller et al. ²⁰	2002	TC	Prospective	n = 30, (M = 14, F = 16) Ages: 24 – 72 yrs	Culture
Schiesser et al. ¹⁸	2003	TC	Prospective	n = 22, (M = 16, F = 6) Ages: 18 – 86 yrs	Culture or CFU

TC: Tertiary care; SC: Secondary Care; M: male; F: female; CFU: clinical follow-up.

^aNumber of patients under the age of 18 yrs was negligible for 2x2 contingency table.

TABLE E-2A Criteria List Used to Assess the Methodological Quality of the Studies

Criteria of Validity		Positive Score
A.	Internal study validity	
A1.	Valid reference test	Histology, culture, clinical follow-up of >6 months
A2.	Blind measurement of reference test(s) without knowledge of index test(s)	
A3.	Blind measurement of index test(s) without knowledge of reference test(s)	
A4.	Avoidance of verification bias	Assessment of reference test independent of index test(s) results
A5.	Index test(s) interpreted independently of all clinical information	Mentioned in publication
A6.	Prospective study	Mentioned in publication
B.	External study validity	
B1.	Spectrum of diseases	Localization of disease described; central and/or peripheral
B2.	Demographic information	Age and sex given
B3.	Inclusion criteria described	Mentioned in publication
B4.	Exclusion criteria described	Mentioned in publication
B5.	Avoidance of selection bias	Consecutive series of patients
B6.	Standardized execution of index test(s)	Described technical aspects of index test(s)
C.	Reproducibility described	Mentioned in publication

TABLE E-2B Methodological Quality Assessment of the Diagnostic Studies Included

Study	Year	Index Test	Internal Validity						External Validity						C
			A1	A2	A3	A4	A5	A6	B1	B2	B3	B4	B5	B6	
Al Sheikh et al. ³⁸	1985	R / LS / BS / Ga / BS-LS / BS-Ga	+	+	-	-	+	+	-	+	-	-	+	+	-
Esterhai et al. ³⁶	1985	BS / BS-Ga	+	+	+	+	+	-	+	+	-	-	-	+	-
Esterhai et al. ³⁷	1987	LS	+	+	-	+	+	+	+	+	-	+	-	+	+
Wukich et al. ¹²	1987	LS	+	+	-	+	+	-	+	+	-	+	-	+	+
Schauwecker ⁶	1989	BS-LS	+	-	-	+	-	-	+	+	-	+	-	+	-
Mason et al. ³⁵	1989	MRI	+	+	+	-	+	-	+	+	+	+	+	+	+
Seabold et al. ³³	1989	LS / BS-LS / BS-Ga	+	+	-	+	+	+	+	+	+	+	-	+	-
Whalen et al. ³¹	1991	LS / BS / MRI / CT / R	+	-	-	-	-	-	+	+	+	+	+	-	-
Palestro et al. ³⁴	1991	LS	+	-	-	-	-	-	+	+	-	+	+	+	-
Sciuk et al. ²⁸	1991	LS / BS	+	+	+	+	-	+	+	-	+	+	+	+	-
Williamson et al. ²⁹	1991	LS / BS / MRI	+	+	-	-	+	+	-	+	+	-	-	+	-
El Esper et al. ³²	1992	LS	+	-	-	-	+	-	+	+	-	+	-	-	-
Flivik et al. ³⁰	1993	LS	+	+	-	-	-	-	+	+	-	+	-	+	+
Nepola et al. ²⁶	1993	BS-LS	+	+	+	+	+	-	+	+	+	+	-	+	-
Devillers et al. ²⁵	1995	LS	+	+	+	-	+	-	+	-	-	-	-	+	-
Krznaric et al. ²⁷	1996	BS-LS	+	+	+	-	+	-	+	+	-	+	-	+	-
Kaim et al. ²²	1997	BS / BS-LS	+	+	+	-	+	-	+	+	-	+	-	+	+
Nijhof et al. ²³	1997	BS	+	+	+	-	+	-	-	+	-	-	-	+	-
Guhlmann et al. ²⁴	1998	LS / FDG-PET	+	+	-	-	+	+	+	+	-	+	-	+	+
Kaim et al. ²¹	2000	MRI	+	+	-	-	+	-	+	+	-	+	-	+	+
De Winter et al. ¹⁹	2001	FDG-PET	+	+	+	-	+	+	+	+	-	+	-	+	+
Meller et al. ²⁰	2002	MRI / LS / FDG-PET	+	+	-	-	-	+	+	+	-	+	+	-	-
Schiesser et al. ¹⁸	2003	FDG-PET	+	+	-	-	+	+	+	+	+	+	-	+	+

A-criteria for internal validity; B-criteria for external validity; C-criterion for reproducibility; +: positive score; -: negative score; R: radiographs; LS: leukocyte scintigraphy; BS: bone scintigraphy; Ga: Gallium scintigraphy; FDG-PET: fluorodeoxyglucose-positron emission tomography

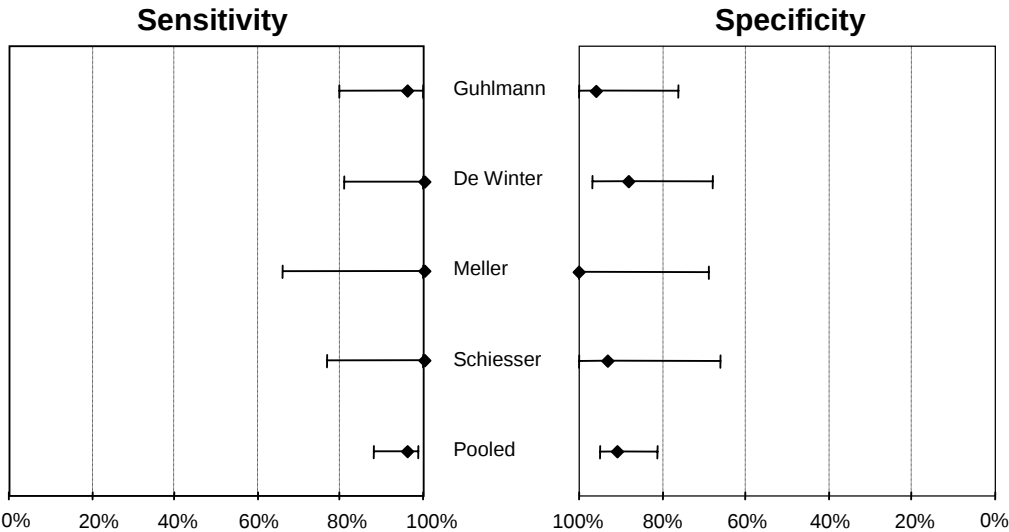
Fig. E-1

Electronic Appendix.

Search string used for identifying studies on diagnostic imaging in chronic osteomyelitis

((((Infection OR infect OR infections OR infektion OR infected OR inflammation OR inflamed OR inflammatory OR infectious OR infectieus OR infectious) **AND** (Bone and bones OR oss OR osseous OR osseus OR osteo OR tibia OR tibiae OR tibial OR crural OR cruris OR spine OR spines OR vertebral OR vertebra OR vertebrae OR femur OR femura OR humerus OR skeleton OR Skeletal OR skellet)) **OR** (Osteomyelitis OR osteitis OR periostitis OR myelitis OR spondylitis OR spondylodiscitis OR spondylodiskitis OR discitis OR diskitis)) **AND** ((Imaging OR 2fluoro-2deoxyglucose OR 2-18f-fluoro-2-deoxy-d-glucose OR fluoro-2-deoxy-d-glucose OR f-18dg OR 18fdg OR 18fluorodeoxyglucose OR fdg\$ OR deoxy-glucose OR fluorodeoxyglucose OR deoxyglucose OR fluoro-d-glucose OR fluorodeoxyglucose OR fluorine-18) **OR** (radiography OR radiographic OR X-ray OR X-rays OR X-radiography OR radiography OR X-ray\$ OR fluoroscopy OR rontgen OR radiographs OR radio\$) **OR** (Chemical Shift Imaging OR MR Tomography OR MRI Scans OR MRI, Functional OR NMR Imaging OR NMR Tomography OR Tomography, NMR OR Tomography, Proton Spin OR fMRI OR Imaging, Chemical Shift OR Proton Spin Tomography OR Tomography, MR OR Zeugmatography OR MRI OR magnetic resonance tomography OR magnetic resonance imaging OR MR imaging OR MRT OR MR) **OR** (Electron Beam Tomography OR Computerized Tomography, X Ray OR CT X Ray OR Tomodensitometry OR Electron Beam Computed Tomography OR Cine-CT OR CT OR Computer tomography) **OR** (bone scintigraphy OR tc-phosphonates OR tc-mdp OR 99m-tc-mdp OR phosphate bone scan OR bone scan OR 99mtc-mdp OR mdp OR 99m-tc-methylene OR 99m-mdp-tc OR 99m-hdp-tc OR 99m-hmdp-tc OR 99mtc-hdp OR 99mtc-hmdp OR tc-99m-hdp OR ga-67 OR ga-67 citrate OR gallium-67 OR ga67 OR 67gallium OR 67ga OR 99mtc OR 99m-tc) **OR** (In-111 wbc OR Indium 111 wbc OR In-111 OR 111-indium OR 111indium-wbc OR 111in-wbc OR indium-labeled-leucocytes OR indium-labeled-leukocytes OR indium-labeled-leucocyte OR indium-labeled-leukocyte OR labeled-leucocyte OR labeled-leukocyte OR leukocyte scintigraphy OR leucocyte scintigraphy OR Leukocyte scans OR Leucocyte scans OR indium-111-leukocyte OR indium111-leucocytes OR indium111-leukocytes OR in111 leucocyte OR leukoscan OR 99m-tc-wbc OR 99m-technetium-wbc OR tc99m-wbc OR tc99m-leukocyte OR 99mTc hexamethylpropyleneamine oxime OR 99m-tc-hmpao OR 99tc-hmpao OR tc99m-hmpao OR tc-99m-hmpao OR technetium-99m-hmpao OR 99m-Technetium-hexamethylpropyleneamine oxime OR Tc-99m-hexamethylpropyleneamine oxime OR wbc-HMPAO OR tc-hmpao OR technetium-hmpao OR hexamethylpropyleneamine oxime OR hmpao))

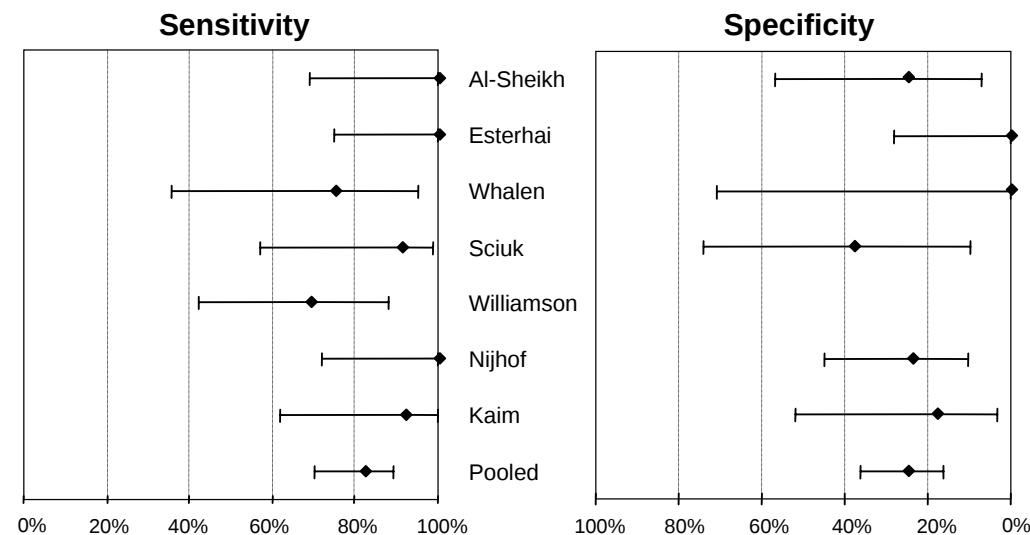
Fig. E-2. Diagnostic accuracy of FDG-PET for detection of COM



Study	Year	Disease		Sensitivity	95% CI	Specificity	95% CI
		+	-				
Guhlmann	1998	28	23	0.96	0.80 – 1.00	0.96	0.76 – 1.00
De Winter	2001	18	25	1.00	0.81 – 1.00	0.88	0.68 – 0.97
Meller	2002	9	10	1.00	0.66 – 1.00	1.00	0.69 – 1.00
Schiesser	2003	14	15	1.00	0.77 – 1.00	0.93	0.66 – 1.00
Total		69	73				
Pooled estimate				0.96	0.88 – 0.99	0.91	0.81 – 0.95

COM: chronic osteomyelitis; +: positive; -: negative; 95% CI: 95% confidence interval; FDG-PET: fluorodeoxyglucose positron emission tomography.

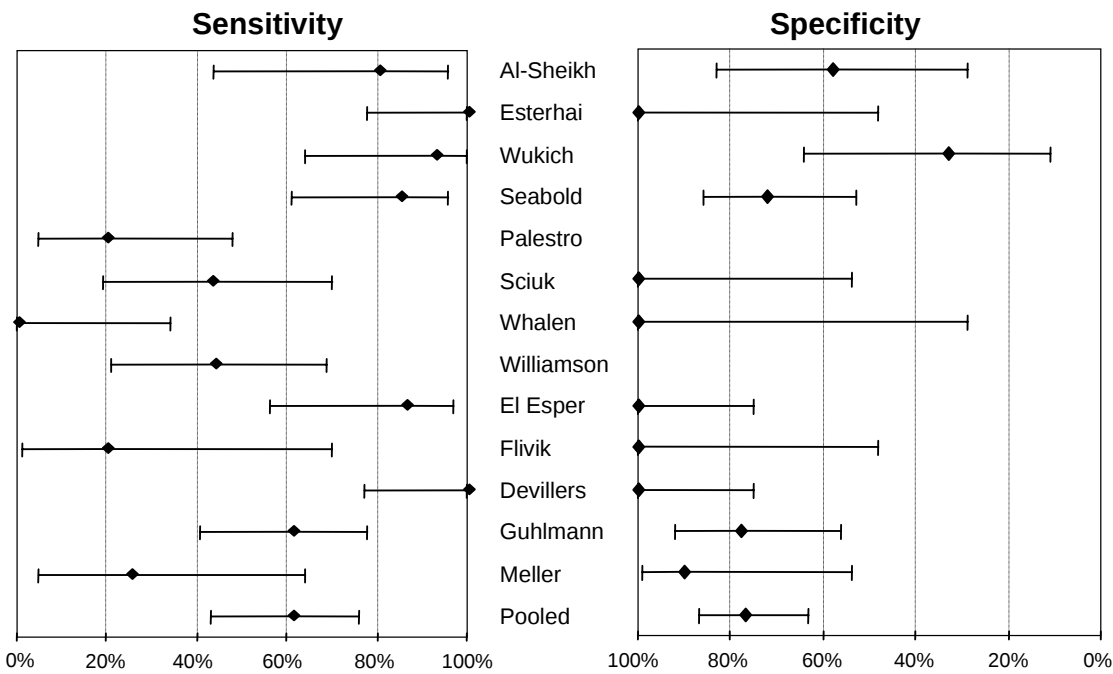
Fig. E-3. Diagnostic accuracy of BS for detection of COM



Study	Year	Disease		Sensitivity	95% CI	Specificity	95% CI
		+	-				
Al Sheikh	1985	10	12	1.00	0.69 – 1.00	0.25	0.07 – 0.57
Esterhai	1985	13	11	1.00	0.75 – 1.00	0.00	0.00 – 0.28
Whalen	1991	8	3	0.75	0.36 – 0.95	0.00	0.00 – 0.71
Sciuk	1991	11	8	0.91	0.57 – 0.99	0.38	0.10 – 0.74
Williamson [†]	1991	16	0	0.69	0.42 – 0.88	x	x
Nijhof	1997	11	25	1.00	0.72 – 1.00	0.24	0.10 – 0.45
Kaim	1997	13	11	0.92	0.62 – 1.00	0.18	0.03 – 0.52
Total		82	70				
Pooled estimate				0.82	0.70 – 0.89	0.25	0.16 – 0.36

BS: bone scintigraphy; COM: chronic osteomyelitis; +: positive; -: negative; 95% CI: 95% confidence interval; [†]: study excluded for specificity.

Fig. E-4. Diagnostic accuracy of LS for detection of COM

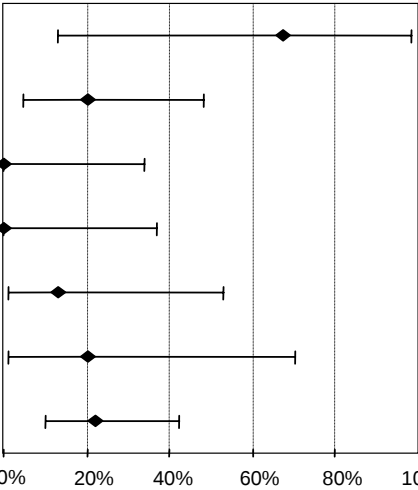


Study	Year	Disease		Sensitivity	95% CI	Specificity	95% CI
		+	-				
Al Sheikh	1985	10	12	0.80	0.44 – 0.96	0.58	0.29 – 0.83
Esterhai	1987	15	5	1.00	0.78 – 1.00	1.00	0.48 – 1.00
Wukich	1987	14	12	0.93	0.64 – 1.00	0.33	0.11 – 0.64
Seabold	1989	20	29	0.85	0.61 – 0.96	0.72	0.53 – 0.86
Palestro [†]	1991	15	0	0.20	0.05 – 0.48	x	x
Sciuk	1991	14	6	0.43	0.19 – 0.70	1.00	0.54 – 1.00
Whalen	1991	9	3	0.00	0.00 – 0.34	1.00	0.29 – 0.99
Williamson [†]	1991	16	0	0.44	0.21 – 0.69	x	x
El Esper	1992	14	13	0.86	0.56 – 0.97	1.00	0.75 – 1.00
Flivik	1993	5	5	0.20	0.01 – 0.70	1.00	0.48 – 1.00
Devillers	1995	14	13	1.00	0.77 – 1.00	1.00	0.75 – 1.00
Guhlmann	1998	28	23	0.61	0.41 – 0.78	0.78	0.56 – 0.92
Meller	2002	8	10	0.25	0.05 – 0.64	0.90	0.54 – 0.99
Total		182	131				
Pooled estimate				0.61	0.43 – 0.76	0.77	0.63 – 0.87

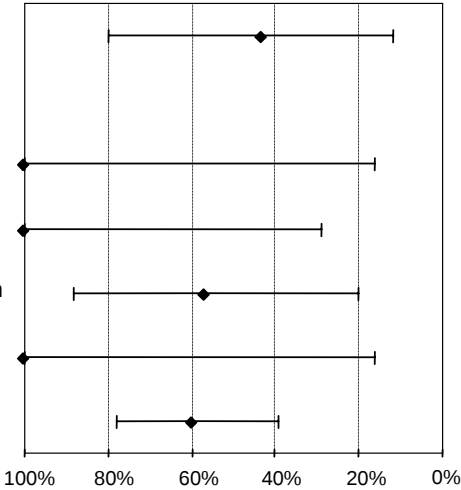
LS: leukocyte scintigraphy; COM: chronic osteomyelitis; +: positive; -: negative; 95% CI: 95% confidence interval; [†]: study excluded for specificity.

Fig. E-5. Diagnostic accuracy of LS for detection of COM in axial skeleton

Sensitivity



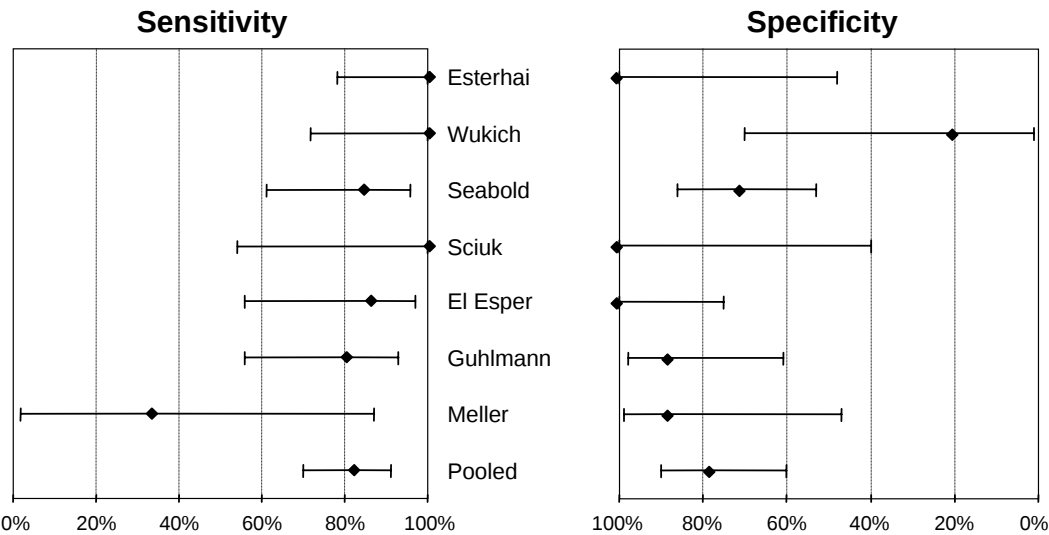
Specificity



Study	Year	Disease		Sensitivity	95% CI	Specificity	95% CI
		+	-				
Wukich	1987	3	7	0.67	0.13 – 0.98	0.43	0.12 – 0.80
Palestro	1991	15	0	0.20	0.05 – 0.48	x	X
Whalen	1991	9	3	0.00	0.00 – 0.34	1.00	0.29 – 1.00
Sciuk	1991	8	2	0.00	0.00 – 0.37	1.00	0.16 – 1.00
Guhlmann	1998	8	7	0.13	0.01 – 0.53	0.57	0.20 – 0.88
Meller	2002	5	2	0.20	0.01 – 0.70	1.00	0.16 – 1.00
Total		48	21				
Pooled estimate				0.21	0.11 – 0.38	0.60	0.39 – 0.78

LS: leukocyte scintigraphy; COM: chronic osteomyelitis; +: positive; -: negative; 95% CI: 95% confidence interval; †: study excluded for specificity.

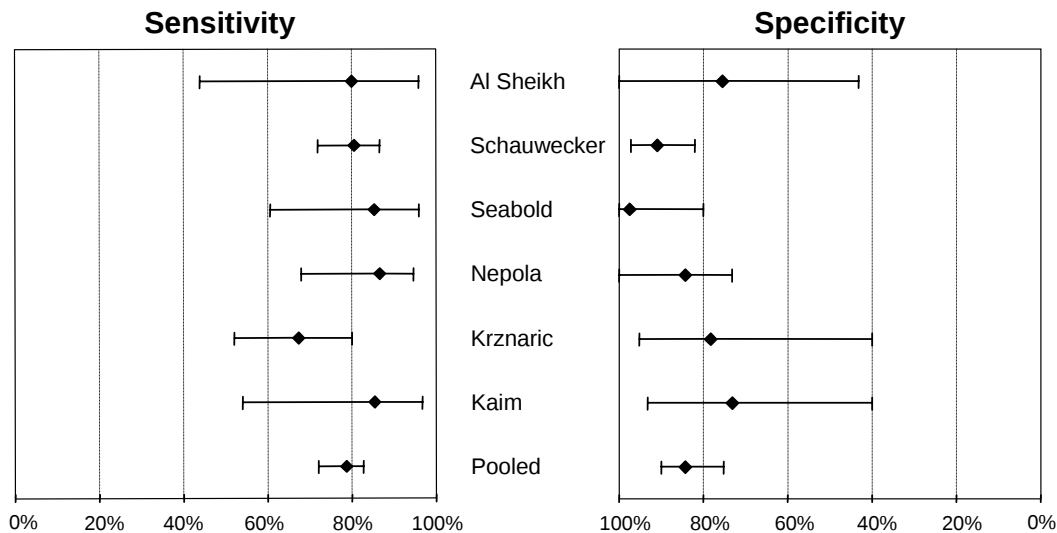
Fig. E-6. Diagnostic accuracy of LS for detection of COM in peripheral skeleton



Study	Year	Disease		Sensitivity	95% CI	Specificity	95% CI
		+	-				
Esterhai	1987	15	5	1.00	0.78 – 1.00	1.00	0.48 – 1.00
Wukich	1987	11	5	1.00	0.72 – 1.00	0.20	0.01 – 0.70
Seabold	1989	20	29	0.85	0.61 – 0.96	0.72	0.53 – 0.86
Sciuk	1991	6	4	1.00	0.54 – 1.00	1.00	0.40 – 1.00
El Esper	1992	14	13	0.86	0.56 – 0.97	1.00	0.75 – 1.00
Guhlmann	1998	20	16	0.80	0.56 – 0.93	0.88	0.61 – 0.98
Meller	2002	3	8	0.33	0.02 – 0.87	0.88	0.47 – 0.99
Total		89	80				
Pooled estimate				0.84	0.72 – 0.91	0.80	0.61 – 0.91

LS: leukocyte scintigraphy; COM: chronic osteomyelitis; +: positive; -: negative; 95% CI: 95% confidence interval.

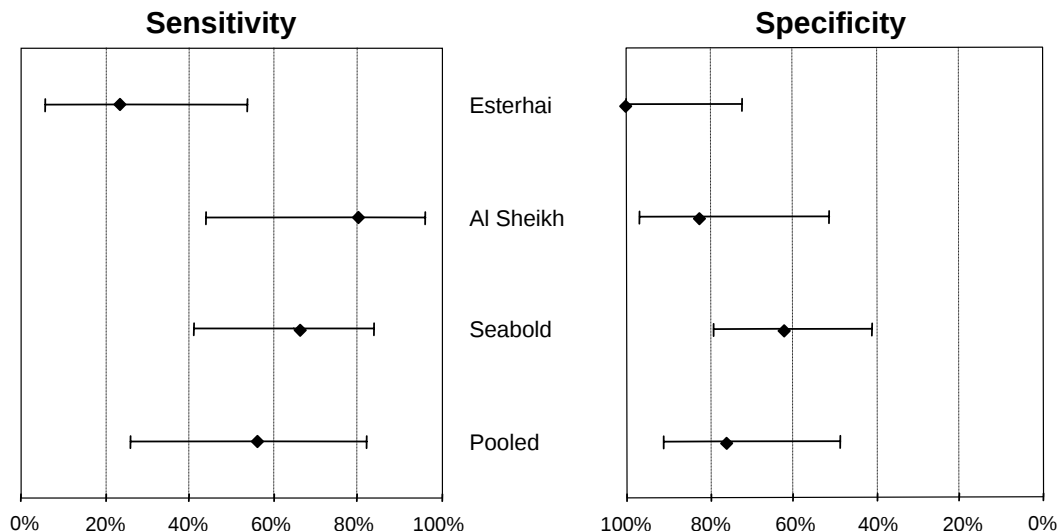
Fig. E-7. Diagnostic accuracy of combined BS-LS for detection of COM



Study	Year	Disease		Sensitivity	95% CI	Specificity	95% CI
		+	-				
Al Sheikh	1985	10	12	0.80	0.44 – 0.96	0.75	0.43 – 0.93
Schauwecker	1989	112	81	0.80	0.72 – 0.87	0.91	0.82 – 0.96
Seabold	1989	20	29	0.85	0.61 – 0.96	0.97	0.80 – 1.00
Nepola	1993	29	70	0.86	0.68 – 0.95	0.84	0.73 – 0.91
Krznaric	1996	46	9	0.67	0.52 – 0.80	0.78	0.40 – 0.96
Kaim	1997	13	11	0.85	0.54 – 0.97	0.73	0.40 – 0.93
Total		230	212				
Pooled estimate				0.78	0.72 – 0.83	0.84	0.75 – 0.90

BS-LS: bone and leukocyte scintigraphy; COM: chronic osteomyelitis; +: positive; -: negative; 95% CI: 95% confidence interval.

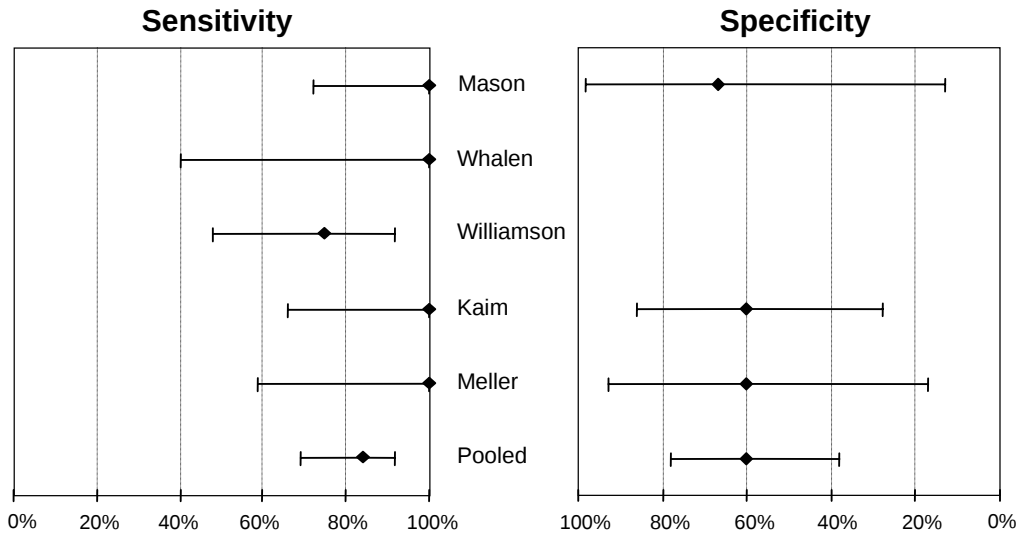
Fig. E-8. Diagnostic accuracy of combined BS-Ga for detection of COM



Study	Year	Disease		Sensitivity	95% CI	Specificity	95% CI
		+	-				
Esterhai	1985	13	11	0.23	0.06 – 0.54	1.00	0.72 – 1.00
Al Sheikh	1985	10	12	0.80	0.44 – 0.96	0.83	0.51 – 0.97
Seabold	1989	20	26	0.65	0.41 – 0.84	0.62	0.41 – 0.79
Total		43	49				
Pooled estimate				0.56	0.26 – 0.82	0.76	0.49 – 0.91

BS-Ga: bone and gallium scintigraphy; COM: chronic osteomyelitis; +: positive; -: negative; 95% CI: 95% confidence interval.

Fig. E-9. Diagnostic accuracy of MRI for detection of COM



Study	Year	Disease		Sensitivity	95% CI	Specificity	95% CI
		+	-				
Mason	1989	11	3	1.00	0.72 – 1.00	0.67	0.13 – 0.98
Whalen [†]	1991	4	0	1.00	0.40 – 1.00	x	X
Williamson [†]	1991	16	0	0.75	0.48 – 0.92	x	X
Kaim	2000	9	10	1.00	0.66 – 1.00	0.60	0.28 – 0.86
Meller	2002	7	5	1.00	0.59 – 1.00	0.60	0.17 – 0.93
Total		47	18				
Pooled estimate				0.84	0.69 – 0.92	0.60	0.38 – 0.78

MRI: magnetic resonance imaging; COM: chronic osteomyelitis; +: positive; -: negative; 95% CI: 95% confidence interval; [†]: study excluded for specificity.