Literature Search Strategies

Electronic Database Searches

The following databases have been searched for relevant information:

ClinicalTrials.gov (through April 2005)
Cochrane Database of Systematic Reviews (through 2005, Issue 2)
Cochrane Registry of Clinical Trials (CENTRAL) (through 2005, Issue 2)
Cochrane Review Methodology Database (through 2005, Issue 2)
Controlled Trials.com (searched April 7, 2005)
CRISP (2004-2005)
Database of Reviews of Effectiveness (Cochrane Library) (through 2005, Issue 2)
ECRI Health Devices Alerts (1977 through April 2005)
ECRI Health Devices Sourcebase (through April 2005)
ECRI Healthcare Standards (1975 through April 2005)
ECRI International Health Technology Assessment Database (IHTA) (through April 2005)
ECRI Library Catalog (through April 2005)
ECRI TARGET (through April 2005)
Embase (1985 through March 31, 2005)
PubMed (includes MEDLINE, HealthSTAR and CancerLit) (Q1-Q2 1985 through May 23, 2005; Q3 1999 through May 23, 2005)
U.S. Centers for Medicare & Medicaid Services (CMS) Web site (through April 2005)

Search Strategies

The search strategies employed a number of freetext keywords as well as controlled vocabulary terms including (but not limited to) the following concepts.

Medical Subject Headings (MeSH) and Keywords

Conventions:
[mh] = MeSH heading
[majr] = MeSH heading designated as major topic
[pt]= Publication Type (PubMed)
[sb] = Subset of PubMed database (PreMEDLINE, Systematic, OldMEDLINE)
[sh] = MeSH subheading (qualifiers used in conjunction with MeSH headings)
[tiab] = keyword in title or abstract
[tw] = Text word
/de = controlled vocabulary heading in Dialog syntax (MeSH, Emtree, PsycINFO)

Topic-Specific
Adverse effects[sh]
Breast neoplasms[mh]
Breast cancer!/de
Breast carcinoma!/de
Breast diseases[mh]
Complications[sh]
Contrast media[mh]
Diagnostic imaging/de
Diagnostic use[sh]

Early diagnosis/de
Echogra*
Echomammogr*
Echomammography/de
Electromagnetic fields[mh]
FDG*
Fluorodeoxyglucose F 18[mh]
"Gamma camera"
Gammagraph*
Magnetic resonance imaging[mh]
"Magnet strength"
Miraluma
Methoxy isobutyl isonitrile technetium TC-99/de
Noninvasive
"Non-invasive"
Nuclear magnetic resonance imaging/de
Nuclear medicine
Organotechnetium compounds/du[mh]
PET[ti]
Positron emission tomography
Pulse sequence
Radionuclide
Radionuclide imaging[sh]
Radiopharmaceuticals[mh]
Radiotracer*
Scintimammogr*
Scintimammography/de
Sestamibi*
Sonogr*
Sonomammogr*
SPECT
Spectrometry, gamma[mh]
Spectrometry, x-ray emission[mh]
SPET
Static
Technetium Tc 99m Sestamibi/du[mh]
Tetrofosmin
Tomography, emission-computed[mh]
Ultrason*
Ultrasonography[sh]
Ultrasonography, mammary[mh]
Ultrasound

Diagnosis
Accuracy
Diagnos*
Di[sh]
Diagnostic accuracy/de
Diagnostic value/de
False negative
False positive
Gold standard
Likelihood
Precision
Predictive value of tests[mh]
"Receiver operating characteristic"
ROC
Sensitivity
Sensitivity and specificity[mh]
specificity
true negative
true positive

Other
Acredit*
Ambulatory
Artifact*
Artefact*
Attenuat*
Boundar*
Calibration[mh]
Clinical competence
Data acquisition
Delineat*
Diagnostic errors[mh]
Differentiat*
Discomfort*
Dynamic range
"Effective dose"
Epidemiology
Equipment design[mh:noexp]
Equipment failure[mh:noexp]
Equipment failure analysis[mh]
Equipment reuse[mh]
Equipment safety[mh]
"Exam time"
Experience
facility
"Field of view"
Focal zone
"Foreign bodies"

"Free-standing"
"Free standing"
"Gain setting"
Hazard*
Human error
Human factors
"Iatrogenic air"
Intraobserver[tiab]
"Intra-observer"[tiab]
Interobserver[tiab]
"Inter-observer"[tiab]
Interpret*[tiab]
"Kappa"
Learning curve
Medical errors[mh]
Mobile
"Observer bias"
"Observer variability"
Observer variation[mh]
Occupational exposure[mh]
Operator error
Outcome
Pain
Patient satisfaction[mh]
Radiation dosage[mh]
Radiation monitoring[mh]
Radiometry[mh]
Reader*[tiab]
"Reader concordance"
Reverberat*
"Review time"
Safe*
Scintillation counting[mh]
Shadow*
"Speckle reduction"
Surgicenter*
Tertiary
Timing
User error
Visuali*
Whole-body counting[mh]

Guidelines:
"Clinical pathway"
Consensus[pt]
Guideline[pt]
Guideline*[ti]
"Policy statement"
"Position paper"
"Position statement"
Practice guidelines[mh]
"Practice parameter"
Standard*[ti]
Standards[sh]
"White paper"

Meta-analyses/Systematic Reviews:
Meta-analysis
Meta-analysis[mh]
Meta-analysis[pt]
"Systematic Review"
(evidence base* OR methodol* OR systematic* OR quantitative* OR studies OR overview*) AND review[pt]

Randomized Controlled Trials:
Crossover*
Cross-over*
Double-blind method[mh]
"Latin square"
Placebo*
Placebos[mh]
Random*[ti]
Random allocation[mh]
Randomized controlled trial[pt]
Randomized controlled trials[mh]
Single-blind method[mh]
((singl*[tw] OR doubl*[tw] OR trebl*[tw] OR tripl*[tw]) AND (mask* OR blind* OR sham* OR dummy)

<u>Publication types</u>

PubMed Search Strategy

1/1/99 – 5/23/05

Parallel strategies were developed to search Embase and the Cochrane libraries

Limited to English language, human population

Set Number	Concept	Search Statement
1	Breast Cancer	Breast neoplasms[mh] OR breast diseases[mh]
2	Diagnosis	#1 AND (diagnosis OR diagnose OR diagnostic OR di[sh] OR "gold standard" OR "ROC" OR "receiver operating characteristic" OR sensitivity and specificity[mh] OR likelihood OR "false positive" OR "false negative" OR "true positive" OR "true negative" OR "predictive value" OR accuracy OR precision)
3	Noninvasive Technique	#2 AND (noninvasive OR non-invasive)
4	Ultrasonography	#2 AND (ultrasonography[sh] OR ultrasonography, mammary[mh] OR echogra* OR echomammogr* OR sonogr* OR sonomammogr*OR ultrasound OR ultrason*)
5	MRI	#2 AND (magnetic resonance imaging[mh] OR "magnet strength" OR miraluma OR pulse sequence OR MR OR MRI OR magnet strength OR nuclear magnetic resonance OR NMR)
6	PET	#2 AND (FDG* OR fluorodeoxyglucose F 18[mh] OR PET[ti] OR organotechnetium compounds/du[mh] OR positron emission tomography OR sestamibi OR technetium Tc 99m Sestamibi/du[mh] OR tomography, emission-computed[mh] OR tetrofosmin)
7	Nuclear Medicine	#2 AND (gamma camera OR gammagraph* OR nuclear medicine OR radionuclide OR radionuclide imaging[sh] OR radiotracer* OR radiopharmaceuticals[mh] OR scintimammogr* OR spectrometry, gamma[mh])
8	SPECT	#2 AND (spectrometry, x-ray emission[mh] OR SPET OR SPECT)
9	Combine sets	#3 OR #4 OR #5 OR #6 OR #7 OR #8
10	Interpretation/quality of test results	#9 AND (artifact* OR artifact* OR attenuate* OR boundar* OR calibration[mh] OR data acquisition OR delineat* OR differentiate* OR dynamic range OR "exam time" OR "field of view" OR "focal zone" OR "foreign bodies" OR "gain setting" OR intraobserver[tiab] OR "intra-observer"[tiab] OR interobserver[tiab] OR "inter-observer"[tiab] OR interpret* OR kappa OR "observer bias" OR "observer variability" OR observer variation[mh] OR reader*[tiab] OR "reader concordance" OR reverberat* OR shadow* OR "speckle reduction" OR visuali*)
11	Operator experience	#9 AND (Accredit* OR Clinical competence[mh] OR experience OR "learning curve" OR "review time")
12	Adverse events	#9 AND (diagnostic errors[mh] OR discomfort* OR "effective dose" OR hazard* OR iatrogenic OR medical errors[mh] OR occupational exposure[mh] OR pain OR patient satisfaction[mh] OR radiation dosage[mh] OR radiation monitoring[mh] OR radiometry[mh] OR safe* OR scintillation counting[mh] OR whole body counting[mh])
13	Human factors	#9 AND (human error OR human factors OR operator error OR timing OR user error)
14	Equipment	#9 AND (equipment design[mh:noexp] OR equipment failure[mh:noexp] OR equipment failure analysis[mh] OR equipment reuse[mh] OR equipment safety[mh])
15	Location	#9 AND (ambulatory OR facility OR "free-standing" OR "free standing" OR mobile OR surgicenter* OR tertiary OR
16	RCTs	(randomized controlled trials[mh] OR random allocation[mh] OR randomized controlled trial[pt] OR double-blind method[mh] OR single-blind method[mh] OR "single-dummy" OR "double-dummy" OR placebo* OR random*[ti] OR crossover OR "cross-over" OR ((singl*[tw] OR doubl*[tw] OR trebl*[tw] OR tripl*[tw]) AND (mask*[tw] OR blind*[tw])) OR "latin square")

Appendix A. Literature Search Strategies (continued)

Set Number	Concept	Search Statement
17	Systematic Reviews	(systematic[sb] OR meta-analysis OR meta-analysis[pt] OR ((evidence base* OR methodol* OR systematic* OR quantitativ* OR studies OR overview*) AND review[pt]))
18	Limit publication types	NOT (letter[pt] OR editorial[pt] OR news[pt] OR comment[pt] OR case reports[pt] OR review[pt])
19	Limit to human	AND (humans[mh] OR preMEDLINE[sb] OR publisher[sb])

Study Quality and Strength of Evidence Evaluation

Quality Assessment Tool for Diagnostic Studies

1. Were the patients enrolled consecutively?
2. Were the patient inclusion/exclusion criteria applied consistently to all patients?
3. Was the study prospective?
4. Did the study avoid a case-control design?
5. Was the funding for this study derived from a source that does not have a financial interest in its results?
6. Did the study compare the diagnostic of interest to a valid reference standard?
7. Was the reference standard an accepted "gold standard"?
8. Did the study account for inter-scorer/reader differences?
9. Were readers of the diagnostic test of interest blinded to the results of the reference standard?
10. Were readers of the reference standard blinded to the results of the diagnostic test of interest?
11. Were the readers of the diagnostic test of interest blinded to all other clinical information?
12. Were the readers of the reference standard blinded to all other clinical information?
13. Were patients assessed by the reference standard regardless of the test's results?
14. If the study reported data for a single diagnostic threshold, was the threshold chosen *a priori*?
15. Were the study results unaffected by intervening treatments or disease progression/regression?
16. Were at least 85% of enrolled patients accounted for?
    Were the authors conclusions, as stated in the abstract or the article's discussion section, supported by the data presented in the article's results section?
17. Was the report of the study free from unresolvable internal discrepancies?

Strength and Stability of Evidence Algorithm

The algorithm developed by ECRI is shown in

Figure 23 and briefly described below.
The algorithm begins with a "General Section" that serves three purposes; (1) to exclude studies of very low quality, (2) to determine whether an evidence base is potentially conclusive by determining whether the aggregate evidence has sufficient statistical power, and (3) to direct the user to either a high, moderate or low quality arm of the algorithm, based on the aggregate quality of the evidence base.

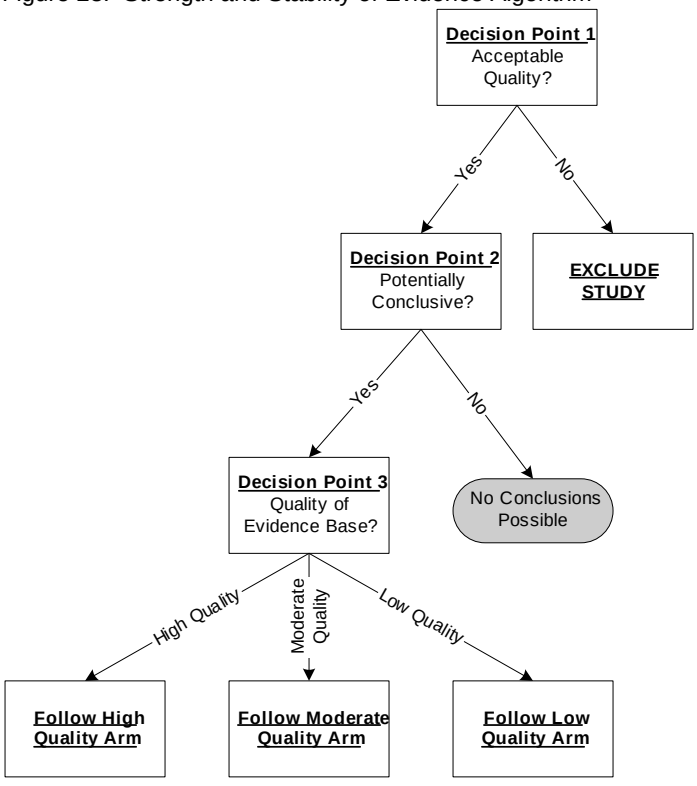
The pathway for high quality evidence bases (see next page of the figure) illustrates the division of the algorithm into a top part that addresses quantitative questions (How well does it work?) and a bottom part that addresses qualitative questions (Does it work?). When an evidence base is comprised of only a small number of studies, the user is routed directly into the qualitative part of the algorithm because quantitative conclusions are not possible. Special rules

apply to these small evidence bases, and these rules account for whether a mega-trial is among the available studies and whether the size of the observed effect is extremely large.

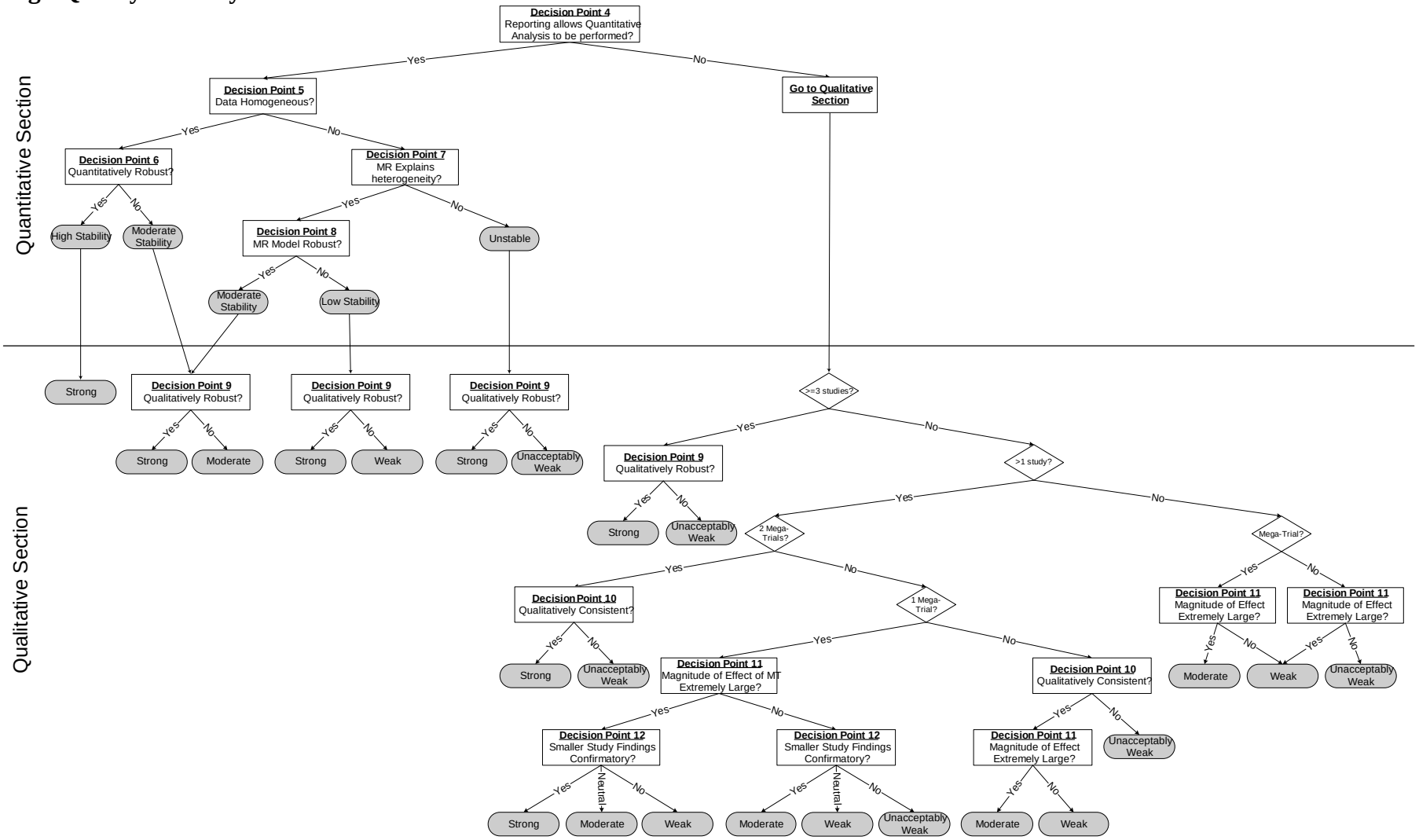
The quantitative section takes into account statistical heterogeneity, robustness (sensitivity analysis and cumulative meta-analysis) and meta-regression to produce a rating of the stability of the estimate. When there is heterogeneity or lack of robustness of the summary estimate, the user is directed through the quantitative section and to the qualitative section. In the quantitative section, there is another test of robustness. This latter robustness test is one of determining whether all (or a certain percentage) of results lead to the same conclusion. To illustrate the difference between quantitative and qualitative robustness, consider a hypothetical meta-analysis that contains k studies, all of which find very large and statistically significant odds ratios. Now assume that there is statistically significant heterogeneity among these results that cannot be explained by meta-regression. Hence, no summary estimate is possible, so the user is directed to the qualitative part of the algorithm. Because all of the studies in the meta-analysis found the technology to be effective, a qualitative conclusion (i.e., "It works") is still possible. The algorithm produces a final rating of the strength of evidence for the qualititative conclusion.

Two other points are worth mentioning. First, it is not possible to obtain a highly stable estimate when meta-regression is used to explain heterogeneity. This is because meta-regression is hypothesis generating, not hypothesis testing. Second, the moderate and low quality algorithm pathways are analogous to the high quality pathway except that the stability and strength of evidence is reduced.

Figure 23. Strength and Stability of Evidence Algorithm

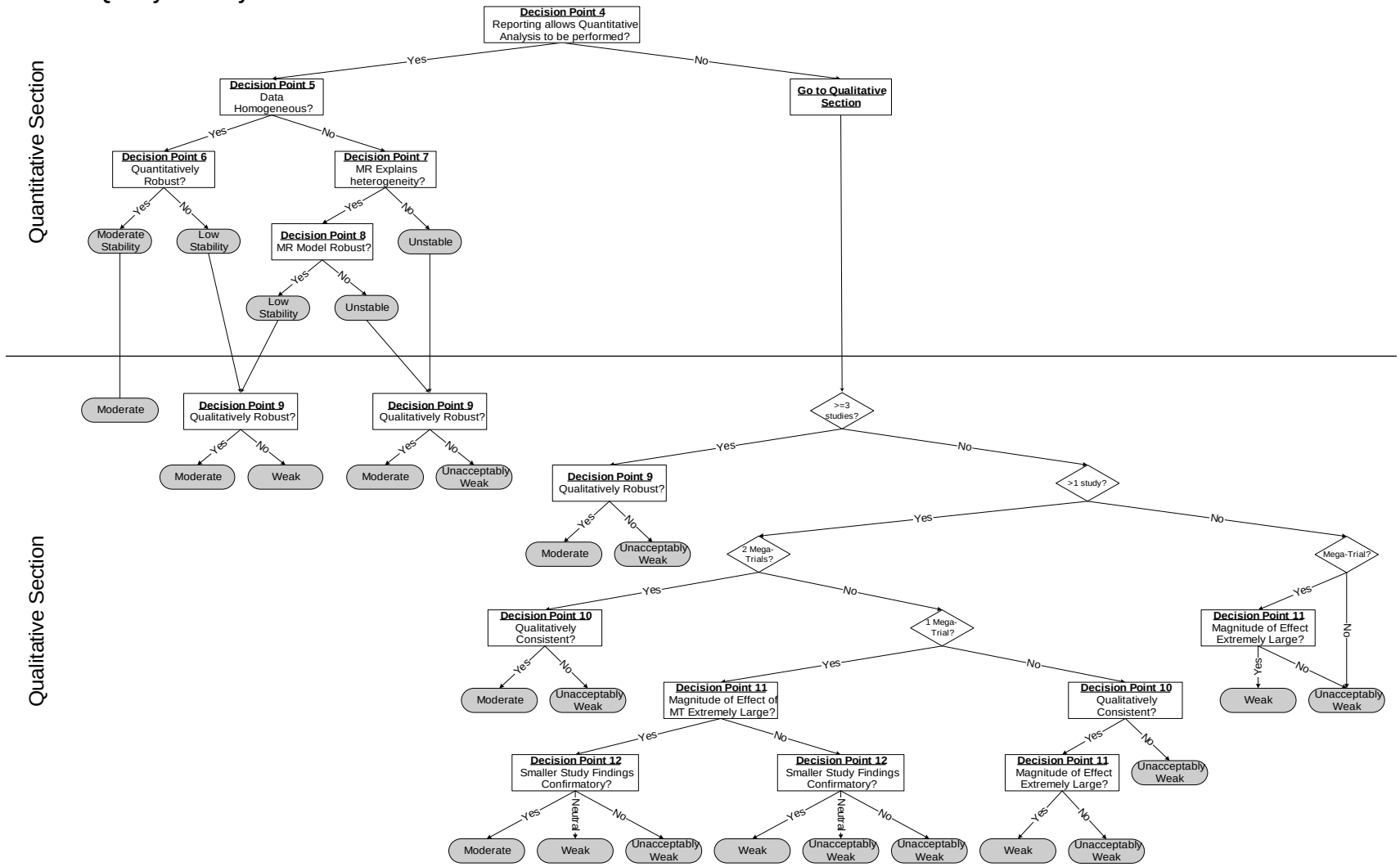


High Quality Pathway



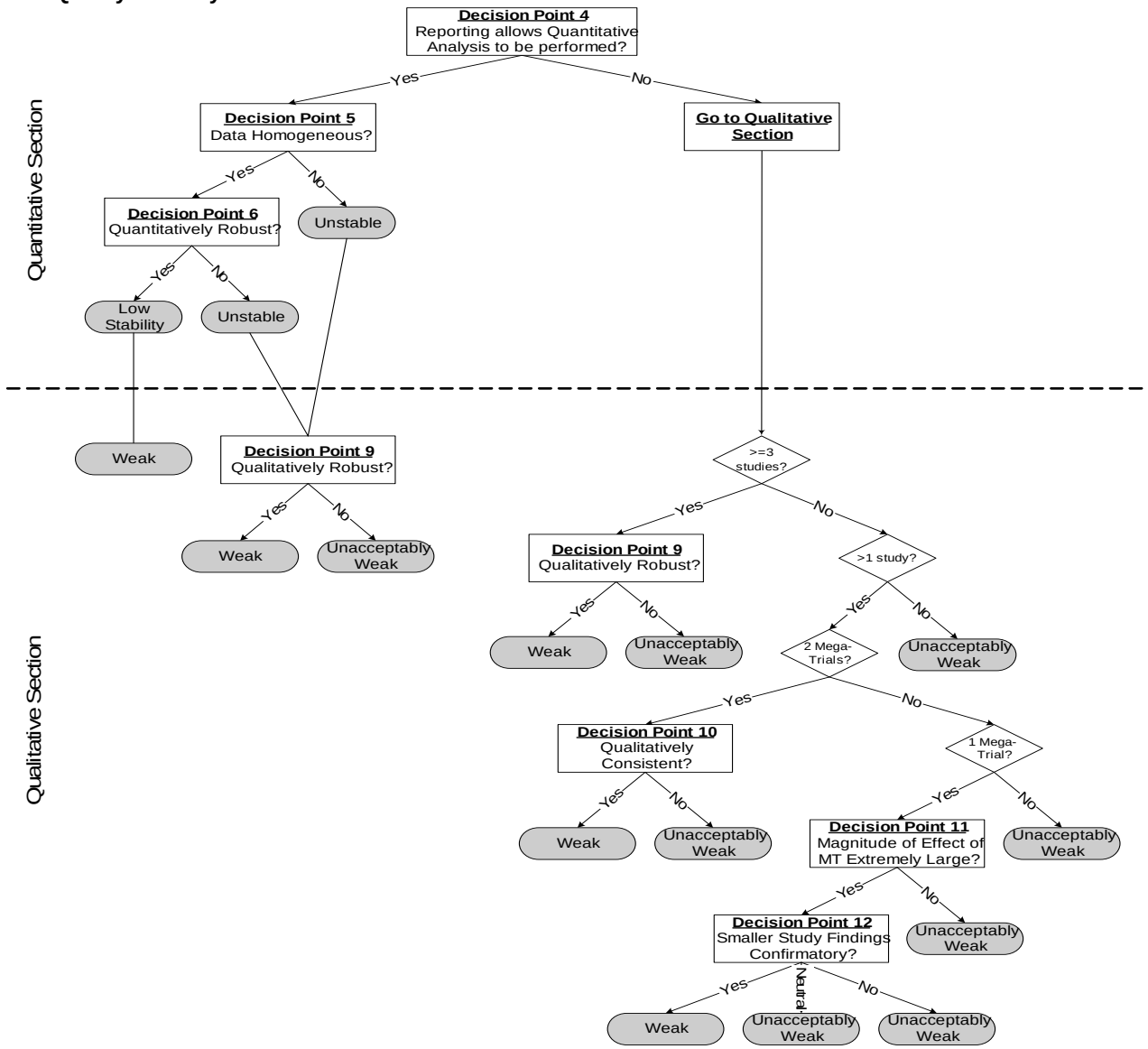
Appendix B. Study Quality and Strength of Evidence Evaluation (continued)

Moderate Quality Pathway



Appendix B. Study Quality and Strength of Evidence Evaluation (continued)

Low Quality Pathway



List of Studies Excluded from Questions 1 and 2

Table 22. Studies of PET that Did Not Meet the Inclusion Criteria

Study	Reason
Adler et al. 1993[210]	Report of the same study published in greater detail in Crowe et al.[53]
Avril et al. 1997[211]	Did not report any of the outcomes of interest.
Avril et al. 1996[212]	Patients enrolled were of a mixed population, and data from the population of interest were not reported separately.
Avril et al. 2000[213]	Update, with additional patients, of Avril et al.[213], which reports that it studied a mixed population of patients (some patients had a history of breast cancer).
Buck et al. 2002[214]	Did not report any of the outcomes of interest.
Danforth et al. 2002[215]	Did not study the population of interest. Enrolled only patients with confirmed breast cancer.
Fujiwara et al. 1999[216]	Did not study the population of interest. Enrolled patients with various types of cancer to look for metastatic lesions. Less than 10 patients.
Inoue et al. 2004[217]	Did not study the population of interest. Enrolled only patients with confirmed breast cancer.
Levine et al. 2003[61]	Did not study the technology of interest-- experimental methods.
Murthy et al. 2000[218]	Did not study the technology of interest-- experimental methods.
Nieweg et al. 1993[219]	Did not study the population of interest. Enrolled only patients with confirmed breast cancer.
Noh et al. 1998[220]	Fewer than 85% were evaluated by biopsy.
Pietrzyk et al. 1995[221]	Did not report any of the outcomes of interest.
Scheidhauer et al. 1996[222]	Confounded. Results of the PET exam were used to change or direct the surgical procedure for some of the patients, increasing the chances that the biopsy results matched the PET results.
Smyczek-Gargya et al. 2004[223]	Did not study the population of interest. Enrolled only patients with confirmed breast cancer.
Yutani et al. 1999[67]	Did not report any of the outcomes of interest.

Table 23. Studies of Scintimammography that Did Not Meet the Inclusion Criteria

Study	Reason
Arslan et al. 1999[224]	Fewer than 85% were evaluated by biopsy.
Aziz et al. 1999[225]	Case-control design
Becherer et al. 1997[226]	Fewer than 85% were evaluated by biopsy.
Buscombe et al. 2001[227]	Retrospective review of patient data.
Buscombe et al. 1997[228]	Reports that not all patients were evaluated by biopsy, but does not report how many were.
Clifford et al. 1996[229]	Fewer than 85% were evaluated by biopsy.
Cwikla et al. 1998[230]	Reports that not all patients were evaluated by biopsy, but does not report how many were.
Danielsson et al. 2003[231]	Did not study the population of interest. Enrolled only patients with confirmed breast cancer.
Dunnwald et al. 1997[232]	Fewer than 85% were evaluated by biopsy.
Farias-Jimenez et al. 2002[233]	Retrospective review of patient data.
Fleming 2002[234]	Did not study the technology of interest-- experimental methods.
Fleming 2002[235]	Did not study the technology of interest-- experimental methods.
Horne et al. 1999[236]	Fewer than 85% were evaluated by biopsy.
Horne et al. 2001[237]	Reports that not all patients were evaluated by biopsy, but does not report how many were.
Howarth et al. 1999[238]	Fatally confounded. Results of the SC exam were used to change or direct the surgical procedure for some of the patients, increasing the chances that the biopsy results matched the SC results.
Howarth et al. 1999[239]	Patients enrolled were of a mixed population, and data from the population of interest were not reported separately.
Iraniha et al. 1999[240]	Reports that not all patients were evaluated by biopsy, but does not report how many were.
Khalkhali et al. 1995[241]	Fewer than 85% were evaluated by biopsy.
Khalkhali et al. 1995[242]	Fewer than 85% were evaluated by biopsy.
Khalkhali et al. 1994[243]	Fewer than 85% were evaluated by biopsy.
Khalkhali et al. 1997[244]	This is a summary of data published in full in Iraniha et al.[240]
Kim et al. 2004[245]	Fewer than 85% were evaluated by biopsy.
Lumachi et al. 1999[246]	Retrospective review of patient data.
Lumachi et al. 2001[247]	Retrospective review of patient data. Appears to be reporting a subgroup analysis of data already reported in Lumachi et al.[248]
Lumachi et al. 2002[249]	Retrospective review of patient data. Appears to be reporting a subgroup analysis of data already reported in Lumachi et al.[250]
Massardo et al. 2002[251]	This is part of a study published in full in Alonso et al.[103]
Maurer et al. 1995[252]	Did not study the technology of interest-- experimental methods.
Myslivecek et al. 2004[253]	Fewer than 85% were evaluated by biopsy.
Nishiyama et al. 2001[254]	Did not study the population of interest. Enrolled only patients with confirmed breast cancer.
Palmedo et al. 1998[255]	Patients enrolled were of a mixed population, and data from the population of interest were not reported separately.
Papantoniou et al. 2002[256]	Did not study the population of interest. Enrolled only patients with confirmed breast cancer.
Polan et al. 2001[257]	Only patients positive by SC were biopsied.
Prats et al. 1999[258]	Retrospective review of patient data.
Ren et al. 2002[259]	Case-control design
Sampalis et al. 2001[260]	This is an interim report of a study that was published in full in Sampalis[260]
Scopinaro et al. 1999[261]	Fewer than 85% were evaluated by biopsy.
Sillar et al. 1997[262]	Fatally confounded. Results of the SC exam were used to change or direct the surgical procedure for some of the patients, increasing the chances that the biopsy results

Appendix C. List of Studies Excluded from Questions 1 and 2 (continued)

Study	Reason
	matched the SC results.
Taillefer et al. 1995[263]	Patients enrolled were of a mixed population, and data from the population of interest were not reported separately.
Tiling et al. 1998[264]	Fewer than 85% were evaluated by biopsy.
Tiling et al. 2005[265]	Fewer than 85% were evaluated by biopsy.
Tolmos et al. 1998[266]	Retrospective review of patient data.
Tolmos et al. 1998[266]	Retrospective review of patient data.
Vargas et al. 2001[267]	Retrospective review of patient data.
Yildiz et al. 2001[118]	Fewer than 85% were evaluated by biopsy.

SC = scintimammography

Appendix C. List of Studies Excluded from Questions 1 and 2 (continued)

Table 24. Studies of MRI that Did Not Meet the Inclusion Criteria

Study	Reason
Barbacioru et al. 2003[268]	Meeting abstract. Not a full-length peer-reviewed publication.
Baum et al. 2002[269]	Fewer than 85% of patients were evaluated with biopsy.
Baum et al. 2002[270]	Patients enrolled were of a mixed population, and data from the population of interest were not reported separately.
Boetes et al. 2004[271]	Retrospective review of patient data.
Bone et al. 2003[272]	Retrospective review of patient data. Does not report any of the outcomes of interest. Did not study the population of interest. Only patients with confirmed breast cancer were enrolled.
Carriero et al. 2002[273]	Did not study the technology of interest-- experimental methods.
Choi et al. 2002[274]	Fewer than 85% of patients were evaluated with biopsy.
Fenlon et al. 1997[275]	Patients enrolled were of a mixed population, and data from the population of interest were not reported separately.
Furman et al. 2003[276]	Retrospective review of patient data.
Gibbs et al. 2004[277]	Retrospective review of patient data.
Gibis et al. 1999[278]	Not published in English.
Guo et al. 2002[279]	Did not study the population of interest. Only patients with confirmed breast lesions were enrolled.
Heywang-Kobrunner et al. 2001[167]	Confounded. For some patients, results of the histology were used to direct and change the readings of the MRI images.
Jacobs et al. 2003[280]	Does not report any of the outcomes of interest.
Jacobs et al. 2003[281]	Retrospective review of patient data.
Kaiser 1985[282]	Does not report any of the outcomes of interest. Did not use a contrast agent.
Kelcz et al. 2002[165]	Fatally confounded. Results of the MRI exam were used to change, direct, or repeat the biopsy procedure for some of the patients, increasing the chances that the biopsy results matched the MRI results.
Khatri et al. 2001[283]	Does not report any of the outcomes of interest.
Kim et al. 2001[284]	Retrospective review of patient data. Did not study the population of interest. Only patients with confirmed invasive breast cancer were enrolled.
Kramer et al. 1998[285]	Fatally confounded. Results of the MRI exam were used to change, direct, or repeat the biopsy procedure for some of the patients, increasing the chances that the biopsy results matched the MRI results.
Lee et al. 2003[286]	Did not study the population of interest. Only patients with confirmed breast cancer were enrolled.
Lucht et al. 2001[287]	Did not study the technology of interest-- experimental methods.
Nagashima et al. 2002[288]	Did not study the population of interest. Only patients with confirmed breast cancer were enrolled.
Nakahara et al. 2002[289]	Did not study the population of interest. Only patients with confirmed breast cancer were enrolled.
Obenauer et al. 2002[290]	Did not study the population of interest. Patients were enrolled only after a breast lesion was detected by MRI.
Reinikainen et al. 2002[291]	Does not report any of the results of interest.
Rigauts et al. 1993[292]	Study enrolled only five patients from the population of interest.
Schelfout et al. 2004[293]	Fatally confounded. Results of the MRI exam were used to change, direct, or repeat the biopsy procedure for some of the patients, increasing the chances that the biopsy results matched the MRI results.
Schelfout et al. 2004[294]	Retrospective review of patient data.
Shahar et al. 2002[295]	Did not study the technology of interest-- experimental methods.
Siegmann et al. 2002[208]	Does not report any of the results of interest. A quarter of the enrolled patients had previously had cancer, and their data were not reported separately.
Slanetz et al. 2002[296]	Did not study the population of interest. Only patients with confirmed breast cancer were enrolled.
Szabo et al. 2003[297]	Did not study the population of interest. Only patients with confirmed invasive breast cancer were reported on.
Szabo et al. 2004[164]	Did not study the technology of interest-- experimental methods.

Appendix C. List of Studies Excluded from Questions 1 and 2 (continued)

Study	Reason
Teifke et al. 2002[298]	Only data from patients referred for surgery or biopsy were reported. Results of the MRI exam may have influenced the decision to refer for surgery/biopsy.
Trecate et al. 2002[299]	Patients enrolled were of a mixed population, and data from the population of interest were not reported separately.
Tuncbilek 2003[300]	Does not report any of the results of interest.
Van Goethem et al. 2004[301]	Fatally confounded. Results of the MRI exam were used to change, direct, or repeat the biopsy procedure for some of the patients, increasing the chances that the biopsy results matched the MRI results.
Wedegartner et al. 2001[302]	Does not report any of the results of interest.
White et al. 2002[303]	Does not report any of the results of interest.
Wiberg et al. 2003[304]	Does not report any of the results of interest.
Yeh et al. 2003[305]	Retrospective review of patient data.
Zuiani et al. 2002[306]	Retrospective review of patient data.

Appendix C. List of Studies Excluded from Questions 1 and 2 (continued)

Table 25. Studies of Ultrasound that Did Not Meet the Inclusion Criteria

Study	Reason
Allen et al. 2001[307]	Did not report any of the outcomes of interest.
Arger et al. 2001[308]	Did not study the population of interest. Only enrolled patients with prior positive findings by ultrasound.
Baker and Soo 2002[309]	Retrospective review of patient data. Does not report any of the outcomes of interest.
Baker et al. 1999[200]	Retrospective review of patient data.
Beeckman et al. 1991[310]	Did not report any of the outcomes of interest.
Bhatti et al. 2001[311]	Did not study the population of interest. Only enrolled patients with prior positive findings by ultrasound.
Bosch et al. 2003[312]	Did not study the population of interest. Enrolled only patients with confirmed breast cancer.
Brittenden et al. 1995[313]	Did not study the technology of interest-- experimental methods.
Britton and Coulden 1990[314]	Fewer than 85% were evaluated by biopsy.
Buadu et al. 1997[315]	Did not study the technology of interest-- experimental methods.
Carson et al. 1997[316]	Did not study the technology of interest-- experimental methods.
Caruso et al. 2002[317]	Did not study the technology of interest-- experimental methods.
Chandawarkar and Shinde 1997[318]	Did not study the population of interest. Enrolled only patients with confirmed breast cancer.
Chao et al. 1999[319]	Did not study the technology of interest-- experimental methods.
Chen et al. 2003[320]	Did not study the population of interest-- screening study of women with dense breasts.
Chen et al. 2002[321]	Did not study the technology of interest-- experimental methods.
Chen et al. 2003[322]	Retrospective review of patient data.
Choi et al. 2000[323]	Retrospective review of patient data.
Ciatto et al. 1994[324]	Fewer than 85% were evaluated by biopsy.
Cilotti et al. 1997[325]	Fewer than 85% were evaluated by biopsy, and results of the ultrasound exam influenced the decision to perform biopsy.
Cimitan et al. 1995[326]	Did not study the population of interest. An unspecified number of patients were only enrolled because of prior positive findings by ultrasound.
Cosgrove et al. 1993[327]	Fewer than 85% were evaluated by biopsy.
Cosmacini 1990[328]	Fewer than 85% were evaluated by biopsy.
Debniak et al. 2004[329]	Did not study the technology of interest-- experimental methods.
Delorme et al. 1998[330]	Retrospective review of patient data.
Dixon et al. 1992[331]	Case-control design.
Dock 1993[332]	Did not study the technology of interest-- experimental methods.
Drukker et al. 2003[333]	Did not study the technology of interest-- experimental methods.
Edde 1994[334]	Fewer than 85% were evaluated by biopsy.
Edgar 1995[335]	Retrospective review of patient data.
Eltahir et al. 1999[336]	Retrospective review of patient data.
Finlay et al. 1994[337]	Retrospective review of patient data.
Flobbe et al. 2003[188]	Fewer than 85% were evaluated by biopsy, and results of the ultrasound exam influenced the decision to perform biopsy.
Forsberg et al. 2004[338]	Did not study the technology of interest-- experimental methods.

Appendix C. List of Studies Excluded from Questions 1 and 2 (continued)

Study	Reason
Foxcroft et al. 2004[339]	Retrospective case-control design.
Fung and Jackson 1990[340]	Did not study the population of interest-- screening study of women with dense breasts.
Garra et al. 1993[341]	Retrospective review of patient data.
Gefan et al. 2003[342]	Did not report any of the outcomes of interest.
Germer et al. 2002[343]	Did not report any of the outcomes of interest.
Giuseppetti et al. 1998[344]	Did not study the population of interest. Only enrolled patients with prior positive findings by ultrasound.
Golshan et al. 2003[345]	Retrospective review of patient data.
Golub et al. 1993[346]	Did not study the technology of interest-- experimental methods.
Graf et al. 2004[347]	Retrospective review of patient data.
Hieken et al. 2001[348]	Did not study the population of interest. Enrolled only patients with confirmed breast cancer.
Hieken et al. 1998[349]	Fewer than 85% were evaluated by biopsy.
Hollerweger et al. 1997[350]	Did not study the population of interest. Only enrolled patients with prior positive findings by ultrasound.
Houssami et al. 2003[351]	Case-control design.
Huang et al. 1999[352]	Did not study the population of interest. Only enrolled patients with prior positive findings by ultrasound.
Huber et al. 1998[353]	Did not study the technology of interest-- experimental methods.
Huber et al. 1994[354]	Did not study the technology of interest-- experimental methods.
Jackson et al. 1986[355]	Fewer than 85% were evaluated by biopsy.
Joo et al. 2004[356]	Did not study the technology of interest-- experimental methods.
Kaiser et al. 2002[357]	Retrospective review of patient data.
Kaplan et al. 2001[358]	Did not study the population of interest-- screening study of women with dense breasts.
Kedar et al. 1995[359]	Did not study the technology of interest-- experimental methods.
Kimme-Smith et al. 1988[360]	Fewer than 85% were evaluated by biopsy.
Kolb et al. 2002[361]	Did not study the population of interest-- screening study of women with dense breasts.
Kolb et al. 1998[362]	Did not study the population of interest-- screening study of women with dense breasts.
Kolb et al. 1997[363]	Meeting abstract. Not a full-length peer-reviewed publication.
Kook et al. 2003[364]	Did not study the population of interest. Only enrolled patients with prior positive findings by ultrasound.
Kook et al. 1999[365]	Retrospective review of patient data.
Krestan et al. 2002[366]	Case-control design.
Kuupers et al. 1994[367]	Did not study the population of interest. Only enrolled patients with prior positive findings by ultrasound.
Lam et al. 2004[368]	Retrospective review of patient data.
Leconte et al. 2003[369]	Retrospective review of patient data.
Lee et al. 1995[370]	Did not study the population of interest. Only enrolled patients with prior positive findings by ultrasound.
Lee et al. 1996[371]	Only data from patients referred for surgery or biopsy were reported. Number of patients initially enrolled in the study is not reported. Results of the ultrasound exam may have influenced the decision to refer for surgery/biopsy.
Leung et al. 2002[372]	Retrospective review of patient data.

Appendix C. List of Studies Excluded from Questions 1 and 2 (continued)

Study	Reason
Lister et al. 1998[373]	Did not study the population of interest. Only enrolled patients with confirmed benign lesions.
Louie et al. 2003[374]	Did not report any of the outcomes of interest.
Madjar et al. 1995[375]	Did not report any of the outcomes of interest.
Madjar et al. 1997[376]	Did not report any of the outcomes of interest.
Madjar et al. 1994[377]	Did not study the technology of interest-- experimental methods.
Madjar et al. 1991[378]	Did not study the technology of interest-- experimental methods.
Madjar et al. 2000[379]	Did not study the technology of interest-- experimental methods.
Marini et al. 2003[380]	Fewer than 85% were evaluated by biopsy.
Martinez et al. 2003[381]	Did not study the technology of interest-- experimental methods.
Medl et al. 1994[382]	Did not study the technology of interest-- experimental methods.
Mesaki et al. 2003[383]	Fewer than 85% were evaluated by biopsy.
Milz et al. 2001[384]	Did not study the technology of interest-- experimental methods.
Moss et al. 1999[385]	Retrospective review of patient data.
Murad and Bari 2004[203]	Retrospective review of patient data.
Obwegeser et al. 1999[386]	Not a full-length peer-reviewed publication.
Ohlinger et al. 2004[387]	Did not report any of the outcomes of interest.
Ozdemir et al. 2004[388]	Did not study the population of interest. Only enrolled patients with prior positive findings by ultrasound.
Ozdemir et al. 2004[389]	Did not study the population of interest. Only enrolled patients with prior positive findings by ultrasound.
Ozdemir et al. 2001[390]	Did not study the technology of interest-- experimental methods.
Ozdemir et al. 1997[391]	Only data from patients referred for surgery or biopsy were reported. Number of patients initially enrolled in the study is not reported. Results of the ultrasound exam may have influenced the decision to refer for surgery/biopsy.
Pamilo et al. 1991[392]	Does not describe what reference standard was used.
Park et al. 2003[393]	Did not study the population of interest. Enrolled only patients with confirmed breast cancer.
Peters-Engl et al. 1998[394]	Did not study the population of interest. Enrolled only patients with confirmed breast cancer.
Peters-Engl et al. 1994[395]	Did not study the technology of interest-- experimental methods.
Pillsbury et al. 2005[396]	Retrospective review of patient data.
Pinero et al. 2003[397]	Did not study the technology of interest-- experimental methods.
Pritt et al. 2004[398]	Retrospective review of patient data.
Puglisi et al. 2003[399]	Pooled the results of US and mammography into a single diagnosis.
Rahbar et al. 1999[202]	Retrospective review of patient data.
Ramlau and Sledzikowski 1993[400]	Did not study the technology of interest-- experimental methods.
Ranieri et al. 1997[401]	Fewer than 85% were evaluated by biopsy.

Appendix C. List of Studies Excluded from Questions 1 and 2 (continued)

Study	Reason
Raza and Baum 1997[402]	Only data from patients referred for surgery or biopsy were reported. Number of patients initially enrolled in the study is not reported. Results of the ultrasound exam may have influenced the decision to refer for surgery/biopsy.
Reinikainen et al. 2001[403]	Did not study the population of interest. Only enrolled patients with prior positive findings by ultrasound.
Richter 1995[404]	Did not study the technology of interest-- experimental methods.
Richter 1996[405]	Did not study the technology of interest-- experimental methods.
Richter and Heywang-Kobrunner 1995[406]	Did not study the technology of interest-- experimental methods.
Richter and Kobrunner 1995[407]	Did not study the technology of interest-- experimental methods.
Richter et al. 1997[408]	Did not study the technology of interest-- experimental methods.
Rosen and Soo 2001[409]	Fewer than 85% were evaluated by biopsy.
Rubin et al. 2001[410]	Retrospective review of patient data.
Saarenmaa et al. 2001[411]	Did not study the population of interest. Enrolled only patients with confirmed breast cancer.
Sahin-Akyar and Sumer 1996[412]	Did not study the population of interest. Only enrolled patients with prior positive findings by ultrasound.
Saitoh et al. 1994[413]	Only data from patients referred for surgery or biopsy were reported. Number of patients initially enrolled in the study is not reported. Results of the ultrasound exam may have influenced the decision to refer for surgery/biopsy.
Schelling et al. 1997[414]	Did not report any of the outcomes of interest.
Schroeder et al. 1999[415]	Fewer than 85% were evaluated by biopsy.
Schutze et al. 1998[416]	Fewer than 85% were evaluated by biopsy, and results of the ultrasound exam influenced the decision to perform biopsy.
Sehgal et al. 2004[417]	Retrospective review of patient data.
Selinko et al. 2004[418]	Retrospective review of patient data.
Seo et al. 2002[419]	Fewer than 85% were evaluated by biopsy.
Shetty et al. 2003[420]	Fewer than 85% were evaluated by biopsy.
Shimamoto et al. 1998[206]	Retrospective review of patient data.
Skaane 1999[421]	Did not study the population of interest. Enrolled only patients with confirmed breast cancer.
Skaane 1999[186]	Retrospective review of patient data.
Skaane and Sauer 1999[422]	Retrospective review of patient data.
Skaane et al. 1997[204]	Retrospective review of patient data.
Skanne and Skjorten 1999[423]	Retrospective review of patient data.
Skanne et al. 1999[424]	Retrospective review of patient data.
Snelling et al. 2004[425]	Did not study the population of interest. Enrolled only patients with confirmed breast cancer.
Spreafico et al. 1994[426]	Did not study the population of interest. Only enrolled patients with a palpable mass that was not visible on ultrasound.
Stavros et al. 1995[427]	Did not study the population of interest. Some patients were only enrolled because of prior positive findings by ultrasound. Only reported data for patients with solid, visible lesions on ultrasound. Unknown how many patients were originally examined.
Steinberg et al. 2001[428]	Did not study the technology of interest-- experimental methods.

Appendix C. List of Studies Excluded from Questions 1 and 2 (continued)

Study	Reason
Szopinski et al. 2003[429]	Did not study the technology of interest-- experimental methods.
Tavassoli et al. 1997[430]	Does not describe what reference standard was used.
Taylor et al. 2002[431]	Pooled the results of US and mammography into a single diagnosis.
Tohnosu et al. 1993[432]	Did not study the population of interest. Enrolled only patients with confirmed breast cancer.
Vetto et al. 1996[433]	Fewer than 85% were evaluated by biopsy.
Wang et al. 2002[434]	Did not study the population of interest-- screening study of women with dense breasts.
Whitehouse et al. 2001[435]	Fewer than 85% were evaluated by biopsy.
Whitehouse et al. 2001[436]	Meeting abstract. Not a full-length peer-reviewed publication.
Wilkens et al. 1998[437]	Did not study the population of interest. An unspecified number of patients were only enrolled because of prior positive findings by ultrasound.
Wright et al. 1998[438]	Does not describe what reference standard was used.
Yang and Metreweli 1996[439]	Did not report any of the outcomes of interest.
Yang and Tse 2004[440]	Retrospective review of patient data.
Yang et al. 1997[441]	Did not report any of the outcomes of interest.
Yang et al. 2001[442]	Did not study the technology of interest-- experimental methods.
Yang et al. 1996[443]	Fewer than 85% were evaluated by biopsy.
Youssefzadeh et al. 1996[444]	Did not study the technology of interest-- experimental methods.
Zonderland et al. 1999[445]	Fewer than 85% were evaluated by biopsy, and results of the ultrasound exam influenced the decision to perform biopsy.

Appendix C. List of Studies Excluded from Questions 1 and 2 (continued)

Table 26. Studies of Multiple Imaging Technologies that Did Not Meet the Inclusion Criteria

Study	Reason
Bagni et al. 2003[446]	Fewer than 85% evaluated by biopsy.
Berg et al. 2004[447]	Did not study the population of interest. Enrolled only patients with confirmed breast cancer.
Boetes et al. 1995[448]	Patients enrolled were of a mixed population, and data from the population of interest were not reported separately.
Hardy et al. 1990[449]	Fewer than 85% evaluated by biopsy.
Hata et al. 2004[450]	Did not study the population of interest. Enrolled only patients with confirmed breast cancer.
Hlawatsch et al. 2002[451]	Patients enrolled were of a mixed population, and data from the population of interest were not reported separately.
Klaus et al. 2000[127]	Did not study the population of interest. Only enrolled patients with prior positive findings by ultrasound.
Leinsinger et al. 2001[452]	Patients enrolled were of a mixed population, and data from the population of interest were not reported separately.
Liang et al. 2003[453]	Did not report any of the outcomes of interest.
Malur et al. 2001[454]	Retrospective review of patient data.
Muller-Schimpfle et al. 1997[455]	Retrospective review of patient data.
Rieber et al. 2002[456]	Fatally confounded. Results of the imaging exams were used to change or direct the surgical procedure for some of the patients, increasing the chances that the biopsy results matched the PET results.
Sommer et al. 1997[457]	Duplicate publication of data reported in Tiling et al.[95]
Tiling et al. 1998[458]	Retrospective review of patient data.
Wang et al. 2002[459]	Did not study the population of interest-- screening study of women with dense breasts.
Yang et al. 1997[460]	Did not study the population of interest. Enrolled only patients with confirmed breast cancer.

Peer Reviewers

David Atkins, M.D.
Agency for Healthcare Research and Quality

Robyn Birdwell, M.D.
Brigham & Women's Hospital

Christie R. Eheman, Ph.D.
Centers for Disease Control and Prevention

Mark Helfand, M.D.
Agency for Healthcare Research and Quality

Maria C. Hinestrosa
National Breast Cancer Coalition

Peter I. Juhn
Johnson & Johnson

Robert Rosenberg, M.D.
University of New Mexico Health Sciences Center

Evidence Tables

Diagnostic Test Characteristics

No diagnostic test is perfect. Studies of diagnostic test performance compare test results on a group of patients, some of whom have the disease and some of whom do not. Each patient undergoes the experimental test as well as a second "gold standard" reference test to determine "true" disease status. The relationship between the diagnostic test results and disease status is described using diagnostic test characteristics. It is important that the "gold standard" test is very accurate in measuring "true" disease status, or else the performance of the experimental diagnostic test will be poorly estimated.

Sensitivity and specificity

The results of the experimental and "gold standard" test and their relationship are commonly presented as 2X2 tables (see Table 27). From the 2X2 table, sensitivity and specificity are readily calculated:

$$\text{Sensitivity} = TP/(TP+F)$$
$$\text{Specificity} = TN/(FP+TN)$$

Table 27. Example of a 2X2 Table

		Disease	
		Present	Absent
Test Results	Positive	True positives (TP)	False positives (FP)
	Negative	False negatives (FN)	True negatives (TN)

Predictive values and likelihood ratios

To make sense of a diagnostic investigation, a clinician needs to be able to make an inference regarding the probability that a patient has the disease in question according to the result obtained from the test. Sensitivity and specificity do not directly provide this information. The predictive values and likelihood ratios can also be directly calculated from a 2X2 table:

$$\text{Positive predictive value} = TP/(TP+FP)$$
$$\text{Negative predictive value} = TN/(FN+TN)$$
$$\text{Positive likelihood ratio} = (TP/(TP+FN))/(FP/(FP+TN))$$
$$\text{Negative likelihood ratio} = (FN/(TP+FN))/(TN/(FP+TN))$$

Predictive values describe the probabilities that positive or negative results are correct for an individual patient. However, predictive values depend on the prevalence of disease in the population. A study that enrolled a patient population with a disease prevalence of 70% may report a positive predictive value of 80%. If a clinician tests a patient from a population with a disease prevalence of 70%, and the test comes back positive, the clinician knows the patient has an 80% chance of having the disease in question. However, if the patient comes from a

population with a disease prevalence of 20%, the clinician cannot apply the results of the study directly to this patient.

Likelihood ratios are independent of prevalence and can be directly applied in the clinic to update an individual's estimated chances of disease according to their test result using Bayes' theorem. Clinicians may be familiar with simple nonograms that allow a direct visualization of post-test chances of disease given a positive or negative test result, without the need to go through the tedious calculations of Bayes' theorem.

Studies of Positron Emisson Tomography (PET) Scanning

Table 28. Included Studies of PET Scanning

Study	N patients	Quality score	PET parameters	Tracer FDG parameters	Patients	Age	% 65 or older	% Female	% Post-menopausal	% Black
Hienisch et al. 2003[56]	36	7.4	Whole-body scanner, patient prone, 70 minutes after tracer	120 to 180 MBq, fast of 12 hours or longer	Women with suspicious breast lesions detected by physical exam, mammography, and/or ultrasound, scheduled for biopsy, referred when there was time on the scanners. Pregnant women were excluded.	Mean 48.3 Range 25 to 77	Not reported	100%	Not reported	Not reported
Walter et al. 2003[57]	44	7.9	Whole-body scanner, patient prone, 40 to 60 minutes after tracer	300 to 370 MBq, fast of 12 hours or longer	Patients referred to the clinic for biopsy of suspicious lesions on the basis of mammography, ultrasound, or physical examination. Referred patients were chosen randomly from 550 possible patients to fill restricted scanner time.	Mean 52 Range 21 to 77	Not reported	Not reported	Not reported	Not reported
Brix et al. 2001[52]	14	8.3	Whole-body scanner, patient prone, 60 minutes after tracer	138 to 248 MBq, fast of 6 hours or longer	Women with suspicious breast lesions detected by physical exam, mammography, and/or ultrasound, scheduled for biopsy, referred when there was time on the scanners. Women with lesions smaller than 10 mm, elevated blood glucose, younger than age 18, pregnant, or had metal implants were excluded.	Mean 49 Range 35 to 66	Not reported	100%	Not reported	Not reported
Yutani et al. 2000[55]	40	7.9	Whole-body scanner, patient supine, 60 minutes after tracer	370 MBq, fast of 4 hours or longer	Patients with suspicious lesions (detected by mammography, ultrasound, or physical exam) scheduled for excisional biopsy.	Mean 51 Range 25 to 86	15%	100%	Not reported	Not reported

Appendix E. Evidence Tables (continued)

Study	N patients	Quality score	PET parameters	Tracer FDG parameters	Patients	Age	% 65 or older	% Female	% Post-menopausal	% Black
Yutani et al. 1999[54]	30	8.8	Whole-body scanner, patient supine, 60 minutes after tracer; and gamma camera, patient supine, 3 hours after tracer	370 MBq, fast of 4 hours or longer	Women referred to the clinic because of suspicion of breast cancer after mammography and physical examination, selected randomly from 84 possible patients on the basis of availability of PET.	Mean 50.9 Median 49 Range 32 to 78	20%	100%	Not reported	Not reported
Palmedo et al. 1997[58]	20	7.9	Whole-body scanner, patient prone, 45 to 60 minutes after tracer	370 MBq, fast overnight	Patients with suspicious lesions (detected by mammography or physical exam) scheduled for excisional biopsy.	Mean 58.4 Range 28 to 84	Not reported	100%	Not reported	Not reported
Holle et al. 1996[51]	50	7.9	Gamma camera, patient prone, 50 minutes after tracer	500 to 1,000 MBq, fast overnight	Women with breast lesions of unknown histology, identified by mammography or ultrasound, who presented when there was time on the scanner.	Mean 57 Range 20 to 82	38%	100%	Not reported	Not reported
Crowe et al. 1994[53]	28	7.5	Whole-body scanner, 40 minutes after tracer	200 uCi/kg body mass, fast 4 hours or longer	Patients attending the clinic who had a breast lesion 1 cm or greater in diameter, detected by palpation, mammography, or both, which, in the opinion of the surgeon, required definitive pathological diagnosis. Pregnant or diabetic women were excluded.	Mean 55 Range 35 to 79	Not reported	92.90%	53.60%	35.70%
Tse et al. 1992[59]	14	7.9	Whole-body scanner, 40 minutes after tracer	10 mCi, fast length not reported	Women with a history of a mammographic abnormality or palpable breast mass, who were candidates for surgical resection.	Not reported	Not reported	100%	Not reported	Not reported

PET = positron emission tomography
FDG = 18-fluorodeoxyglucose

Appendix E. Evidence Tables (continued)

Table 29. Quality Assessment of Studies of PET

Question	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	score
Study	consecutive	consistent	prospective	Case control	funding	valid reference	gold standard	interreader	blinding	blinding	blinding	blinding	full testing	threshold	intervening	attrition	conclusions	discrepancy	standardized
Hienisch et al. 2003[56]	r	y	y	y	r	y	y	r	y	r	n	r	y	y	y	y	y	y	7.4
Walter et al. 2003[57]	y	y	y	y	r	y	y	r	y	r	r	r	y	y	y	y	y	y	7.9
Brix et al. 2001[52]	y	y	y	y	r	y	y	r	y	r	y	r	y	y	y	y	y	y	8.3
Yutani et al. 2000[54]	y	y	y	y	r	y	y	r	y	r	r	r	y	y	y	y	y	y	7.9
Yutani et al. 1999[55]	y	y	y	y	r	y	y	y	y	r	y	r	y	y	y	y	y	y	8.8
Palmedo et al. 1997[58]	r	y	y	y	r	y	y	r	y	r	y	r	y	y	y	y	y	y	7.9
Holle et al. 1996[51]	r	y	y	y	r	y	y	r	y	r	y	r	y	y	y	y	y	y	7.9
Crowe et al. 1994[53]	r	y	y	y	r	y	y	r	y	r	y	r	y	r	y	y	y	y	7.5
Tse et al. 1992[59]	r	y	y	y	y	y	y	r	y	r	y	r	y	r	y	y	y	y	7.9

y = yes
n = no
r = not reported

Table 30. Diagnostic Test Characteristics of PET

Study	N lesions	Type of scanner	Patient subgroup	Prevalence	True positive	False negative	False positive	True negative	Sensitivity (95% CI)	Specificity (95% CI)	Positive predictive value (95% CI)	Negative predictive value (95% CI)	Positive likelihood ratio (95% CI)	Negative likelihood ratio (95% CI)
Hienisch et al. 2003[56]	40	Whole-body	All	62.5%	17	8	4	11	68.0% (48.4% to 82.7%)	73.3% (48.0% to 88.9%)	81.0% (59.9% to 92.1%)	57.9% (36.3 to 76.7)	2.55 (1.95 to 3.34)	0.44 (0.23 to 0.83)
Walter et al. 2003[57]	42	Whole-body	All	45.2%	12	7	2	21	63.2% (41.0% to 80.7%)	91.3% (73.0% to 97.4%)	85.7% (59.8% to 95.7%)	75.0% (56.6 to 87.2)	7.26 (5.15 to 10.24)	0.40 (0.22 to 0.74)
Brix et al. 2001[52]	13	Whole-body	Lesions 1.0 cm or larger	69.2%	8	1	2	2	88.9% (56.2% to 97.6%)	50.0% (15.4% to 84.6%)	80.0% (48.9% to 94.0%)	66.7% (21.0% to 93.3%)	1.78 (1.41 to 2.24)	0.22 (0.03 to 1.80)
Yutani et al. 2000[55]	40	Whole-body	All	95.0%	30	8	0	2	78.9% (63.6% to 88.8%)	100.0% (34.0% to 99.3%)	100.0% (88.4% to 99.9%)	20.0% (6.0% to 51.1%)	4.69 (3.98 to 5.54)	0.26 (0.12 to 0.57)
	30	Whole-body	BIRADS 5	93.3%	26	2	0	2	92.9% (77.1% to 97.9%)	100.0% (34.0% to 99.3%)	100.0% (86.8% to 99.9%)	50.0% (15.4% to 84.6%)	5.48 (4.90 to 6.13)	0.10 (0.03 to 0.38)
	29	Whole-body	Lesion 1.5 cm or larger	96.6%	27	1	0	1	96.4% (82.0% to 99.2%)	100.0% (20.8% to 99.2%)	100.0% (87.2% to 99.9%)	50.0% (10.0% to 90.0%)	3.79 (3.48 to 4.13)	0.07 (0.01 to 0.40)
	37	Whole-body	Palpable lesion	97.3%	29	7	0	1	80.6% (64.9% to 90.1%)	100.0% (20.8% to 99.2%)	100.0% (88.0% to 99.9%)	12.5% (2.6% to 47.4%)	3.19 (2.71 to 3.75)	0.27 (0.10 to 0.75)
	34	Whole-body	Younger than 65	94.1%	25	7	0	2	78.1% (61.2% to 88.8%)	100.0% (34.0% to 99.3%)	100.0% (86.3% to 99.9%)	22.2% (6.7% to 47.74%)	4.64 (3.85 to 5.58)	0.27 (0.12 to 0.61)
Yutani et al. 1999[54]	30	Whole-body	All	86.7%	26	0	2	2	100.0% (86.8% to 99.9%)	50.0% (15.4% to 84.6%)	92.9% (77.1% to 97.9%)	100.0% (34.0% to 99.3%)	1.96 (1.86 to 2.07)	0.04 (0.00 to 0.66)
	19	Whole-body	BIRADS 5	94.7%	18	0	0	1	100.0% (82.0% to 99.8%)	100.0% (20.8% to 99.2%)	100.0% (82.0% to 99.8%)	100.0% (20.8% to 99.2%)	3.89 (3.62 to 4.19)	0.04 (0.00 to 0.61)
	29	Whole-body	Palpable lesion	89.7%	26	0	2	1	100.0% (86.8% to 99.9%)	33.3% (6.7% to 79.0%)	92.9% (77.1% to 97.9%)	100.0% (20.8% to 99.2%)	1.57 (1.49 to 1.65)	0.05 (0.00 to 1.02)
	24	Whole-body	Younger than 65	83.3%	20	0	2	2	100.0% (83.5% to 99.8%)	50.0% (15.4% to 84.6%)	90.9% (72.0% to 97.3%)	100.0% (34.0% to 99.3%)	1.95 (1.83 to 2.09)	0.05 (0.00 to 0.84)

Appendix E. Evidence Tables (continued)

Study	N lesions	Type of scanner	Patient subgroup	Prevalence	True positive	False negative	False positive	True negative	Sensitivity (95% CI)	Specificity (95% CI)	Positive predictive value (95% CI)	Negative predictive value (95% CI)	Positive likelihood ratio (95% CI)	Negative likelihood ratio (95% CI)
	30	Gamma camera	All	86.7%	22	4	2	2	84.6% (66.3% to 93.7%)	50.0% (15.4% to 84.6%)	91.7% (73.9% to 97.5%)	33.3% (10.1% to 69.9%)	1.69 (1.44 to 1.99)	0.31 (0.08 to 1.17)
	19	Gamma camera	BIRADS 5	94.7%	16	2	0	1	88.9% (67.0% to 96.7%)	100.0% (20.8% to 99.2%)	100.0% (80.2% to 99.8%)	33.3% (6.7% to 79.0%)	3.47 (2.92 to 4.14)	0.18 (0.04 to 0.72)
	29	Gamma camera	Palpable lesion	89.7%	22	4	2	1	84.6% (66.3% to 93.7%)	33.3% (6.7% to 79.0%)	91.7% (73.9% to 97.5%)	20.0% (4.1% to 62.6%)	1.27 (1.08 to 1.50)	0.46 (0.07 to 2.90)
	24	Gamma camera	Younger than 65	83.3%	18	2	2	2	90.0% (69.7% to 97.0%)	50.0% (15.4% to 84.6%)	90.0% (69.7% to 97.0%)	50.0% (15.4% to 84.6%)	1.80 (1.56 to 2.08)	0.20 (0.04 to 1.03)
Palmedo et al. 1997[58]	20	Whole-body	All	65.0%	12	1	1	6	92.3% (66.4% to 98.3%)	85.7% (48.4% to 97.0%)	92.3% (66.4% to 98.3%)	85.7% (48.4% to 97.0%)	6.46 (5.52 to 7.56)	0.09 (0.01 to 0.60)
Holle et al. 1996[51]	50	Gamma camera	All	54.0%	18	9	4	19	66.7% (47.8% to 81.2%)	82.6% (62.7% to 92.8%)	81.8% (61.3% to 92.5%)	67.9% (49.3% to 82.0%)	3.83 (2.94 to 5.01)	0.40 (0.23 to 0.71)
	31	Gamma camera	Younger than 65	32.3%	8	2	4	17	80.0% (48.9% to 94.0%)	81.0% (59.9% to 92.1%)	66.7% (39.0% to 86.0%)	89.5% (68.4% to 96.8%)	4.20 (3.08 to 5.73)	0.25 (0.07 to 0.87)
	19	Gamma camera	65 or older	89.5%	10	7	0	2	58.8% (36.0% to 78.3%)	100.0% (34.0% to 99.3%)	100.0% (71.7% to 99.7%)	22.2% (6.7% to 54.9%)	3.50 (2.37 to 5.17)	0.50 (0.24 to 1.05)
Crowe et al. 1994[53]	37	Whole-body	Lesions 1.0 cm or larger	62.2%	23	0	0	10	100.0% (85.3% to 99.9%)	100.0% (71.7% to 99.7%)	100.0% (85.3% to 99.9%)	100.0% (71.7% to 99.7%)	21.54 (20.32 to 22.84)	0.02 (0.00 to 0.34)
	24	Whole-body	Palpable lesions 1.0 cm or larger	79.2%	19	0	0	5	100.0% (82.8% to 99.8%)	100.0% (56.0% to 99.6%)	100.0% (82.8% to 99.8%)	100.0% (56.0% to 99.6%)	11.70 (10.91 to 12.55)	0.03 (0.00 to 0.43)
	18	Whole-body	BIRADS 3, lesions 1.0 cm or larger	44.4%	8	0	0	10	100.0% (67.0% to 99.7%)	100.0% (71.7% to 99.7%)	100.0% (67.0% to 99.7%)	100.0% (71.7% to 99.7%)	20.78 (17.73 to 24.35)	0.06 (0.00 to 0.86)

Appendix E. Evidence Tables (continued)

Study	N lesions	Type of scanner	Patient subgroup	Prevalence	True positive	False negative	False positive	True negative	Sensitivity (95% CI)	Specificity (95% CI)	Positive predictive value (95% CI)	Negative predictive value (95% CI)	Positive likelihood ratio (95% CI)	Negative likelihood ratio (95% CI)
	14	Whole-body	BIRADS 4-5, lesions 1.0 cm or larger	100.0%	14	0	0	0	100.0% (78.0% to 99.8%)	Could not calculate	100.0% (78.0% to 99.8%)	Could not calculate	1.93 (1.76 to 2.12)	0.07 (0.00 to 1.91)
Tse et al. 1992[59]	14	Whole-body	All	71.4%	8	2	0	4	80.0% (48.9% to 94.0%)	100.0% (50.5% to 99.5%)	100.0% (67.0% to 99.7%)	66.7% (30.1% to 89.9%)	7.73 (5.61 to 10.65)	0.25 (0.08 to 0.78)

Table 31. Meta-analysis of Studies of PET for Suspicious Breast Lesions

Study	N lesions	Quality score	Sensitivity (95% CI)	Specificity (95% CI)	Positive predictive value (95% CI)	Negative predictive value (95% CI)	Positive likelihood ratio (95% CI)	Negative likelihood ratio (95% CI)
Hienisch et al. 2003[56]	40	7.4	68.0% (48.4% to 82.7%)	73.3% (48.0% to 88.9%)	81.0% (59.9% to 92.1%)	57.9% (36.3% to 76.7%)	2.55 (1.95 to 3.34)	0.44 (0.23 to 0.83)
Walter et al. 2003[57]	42	7.9	63.2% (41.0% to 80.7%)	91.3% (73.0% to 97.4%)	85.7% (59.8% to 95.7%)	75.0% (56.6% to 87.2%)	7.26 (5.15 to 10.24)	0.40 (0.22 to 0.74)
Yutani et al. 2000[55]	40	7.9	78.9% (63.6% to 88.8%)	100.0% (34.0% to 99.3%)	100.0% (88.4% to 99.9%)	20.0% (6.0% to 51.1%)	4.69 (3.98 to 5.54)	0.26 (0.12 to 0.57)
Yutani et al. 1999[54]	30	8.8	100.0% (86.8% to 99.9%)	50.0% (15.4% to 84.6%)	92.9% (77.1% to 97.9%)	100.0% (34.0% to 99.3%)	1.96 (1.86 to 2.07)	0.04 (0.00 to 0.66)
Palmedo et al. 1997[58]	20	7.9	92.3% (66.4% to 98.3%)	85.7% (48.4% to 97.0%)	92.3% (66.4% to 98.3%)	85.7% (48.4% to 97.0%)	6.46 (5.52 to 7.56)	0.09 (0.01 to 0.60)
Tse et al. 1992[59]	14	7.9	80.0% (48.9% to 94.0%)	100.0% (50.5% to 99.5%)	100.0% (67.0% to 99.7%)	66.7% (30.1% to 89.9%)	7.73 (5.61 to 10.65)	0.25 (0.08 to 0.78)
6 studies	186 lesions	Median 7.9 Moderate	At mean threshold 82.2%	At mean threshold 78.3% At 95% sensitivity 46.7%	At mean threshold 90.0% At 95% sensitivity 80.9%	At mean threshold 64.8% At 95% sensitivity 79.7%	Heterogeneous, no summary estimate calculated	0.33 (0.24 to 0.46)

Heterogeneity tests	Cumulative meta-analysis: last three studies				
	New study	D 95% CI	Within 5% limits?	-LHR 95% CI	Within 5% limits?
D I^2 = 0.0% Q = 3.37 p of Q = 0.64287	Yutani et al. 1999[54]	2.62 to 3.01	No	0.25 to 0.52	No
+lnLHR I^2 = 73.1% Q = 364.0 p of Q = 0.00000001	Palmedo et al. 1997[58]	2.78 to 3.10	No	0.24 to 0.49	No
-lnLHR I^2 = 12.3% Q = 5.70 p of Q = 0.3363	Tse et al. 1992[59]	2.88 to 3.17	Yes	0.24 to 0.46	No

	5% limits 2.88 to 3.18	Not stable	5% limits 0.31 to 0.35	Not stable	

D = ln of diagnostic odds ratio
-LHR = negative likelihood ratio
-lnLHR- ln of negative likelihood ratio
+lnLHR = ln of positive likelihood ratio

Studies of Scintimammography

Table 32. Included Studies of Scintimammography

Study	N patients	Quality score	Scintimammography parameters	Patients	Age (Range)	% 65 or older	% Female	% Post-menopausal	Ethnic makeup
Bekis et al. 2004[111]	35	8.3	Planar, patient prone, 15 minutes after 740 MBq tracer, 256X256	Women with suspicious non-palpable lesions detected by mammography.	Mean 51 (35 to 72)	Not reported	100%	Not reported	Not reported
Fondrinier et al. 2004[113]	41	7.2	Planar, patient prone, 5-10 minutes after 740 MBq tracer, 256X256	Women with non-palpable microcalcifications, detected by mammography, that warranted biopsy.	Not reported	Not reported	100%	Not reported	Not reported
Bone et al. 2003[461]	90	8.2	Planar, patient prone and supine, 10 minutes after 700 MBq tracer, 256X256	Patients scheduled for surgery after physical exam, mammography, and fine needle aspiration.	Mean 54 (33 to 81)	Not reported	Not reported	Not reported	Not reported
Krishnaiah et al. 2003[89]	95	7.4	Planar, patient prone, 740 to 1,100 MBq tracer	Patients presenting with palpable lesions and/or abnormal mammograms who were scheduled for biopsy. Pregnant women were excluded.	Median 44 (28 to 86)	Not reported	99%	Not reported	Not reported
Maunda et al. 2003[462]	38	7.8	Planar, patient prone, 5 and 60 minutes after 740 to 1110 MBq tracer, 256X256	Nonpregnant woman with a palpable breast lesion that was indeterminate on mammography (BIRADS 1-3). Women who had previous surgery for a breast lesion or prior chemotherapy or radiotherapy to the breast were excluded.	Median 28 (22 to 38)	0%	100%	Not reported	100% African
Sampalis et al. 2003[82]	1734	6.0	Planar, patient prone, 5 minutes after 740 to 1,100 MBq tracer, 128X128	No inclusion criteria were reported. Pregnant women and patients younger than 18 were excluded.	Mean 56 (19 to 94)	Not reported	100%	40%	Not reported
Sanidas et al. 2003[100]	32	8.3	Planar, patient prone, 15 minutes after 740 MBq tracer, 256X256	Women with clinically and mammographically suspected breast cancer.	Mean 56 (36 to 86)	Not reported	100%	50%	Not reported
Wilczek et al. 2003[88]	96	8.6	Planar, patient prone, 10 minutes after 700 MBq tracer, 256X256	Age 30 years or older, scheduled for breast surgery.	Mean 54.4 (34 to 82)	Not reported	Not reported	Not reported	Not reported

Appendix E. Evidence Tables (continued)

Study	N patients	Quality score	Scintimammography parameters	Patients	Age (Range)	% 65 or older	% Female	% Post-menopausal	Ethnic makeup
Brem et al. 2002[463]	50	8.6	Planar, patient prone, 5 to 10 minutes after 925 MBq tracer	All nonpregnant patients who were 18 years or older, with a palpable lesion with no mammographic correlate; or a possible multicentric tumor as seen by mammography or ultrasound; or asymmetric breast tissue shown on mammography, with no corresponding clinical or sonographic findings.	Mean 53 (30 to 80)	Not reported	Not reported	Not reported	Not reported
Khalkhali et al. 2002[83]	554	8.3	Planar, patient prone, 5 minutes after 740 to 1,100 MBq tracer, 128X128	Women scheduled for biopsy after mammography and/or physical examination.	Mean 52.2	20.3%	100%	61.6%	69.3% White 15.0% Hispanic 14.2% Black 1.5% Asian
Leidenius et al. 2002[97]	46	7.9	Planar, patient prone, 20 minutes after 740 MBq tracer, 128X128	Consecutive patients referred to the hospital because of abnormal findings in clinical breast examination, mammography, or ultrasonography.	Median 58 (46 to 76)	Not reported	Not reported	Not reported	Not reported
Aguilar et al. 2001[110]	36	8.2	Planar, patient prone, 10 minutes after 740 to 925 MBq tracer	All patients with nonpalpable lesions of the breast referred consecutively from a screening campaign.	(50 to 64)	Not reported	Not reported	94.4%	Not reported
Alonso et al. 2001[103]	238	7.9	Planar, patient prone, 10 minutes after 740 to 1,100 MBq tracer, 256X256	Woman with a palpable breast lesion. Patients were excluded for pregnancy, previous surgery for a palpable breast lesion in the affected breast, or prior chemotherapy or radiation treatment to the affected breast.	Median 50 (19 to 84)	Not reported	100%	52%	Not reported
Gutfilen et al. 2001[101]	32	6.9	Planar, patient prone, 15 minutes after 370 MBq tracer	Women with breast masses. Patients were excluded if they were pregnant, nursing, or had a history of prior breast surgery, or prior chemotherapy/radiotherapy to the breast.	(17 to 79)	Not reported	100%	Not reported	Not reported

Appendix E. Evidence Tables (continued)

Study	N patients	Quality score	Scintimammography parameters	Patients	Age (Range)	% 65 or older	% Female	% Post-menopausal	Ethnic makeup
Imbriaco et al. 2001[98]	49	7.6	Planar, patient prone and supine, 10 minutes after 555 MBq tracer, 256X256	Patients with a suspicious breast lesion detected either by physical examination or by mammography and ultrasound. Patients were excluded if they were pregnant or lactating; younger than 18 years of age; or had a history of previous breast cancer.	Mean 49 (20 to 72)	8.1%	Not reported	Not reported	Not reported
Koukouraki et al. 2001[91]	86	7.5	Planar, patient prone, 15 minutes after 740 MBq tracer, 256X256	Women with palpable lumps or women with negative physical examination and abnormal findings on mammography.	(25 to 78)	Not reported	100%	60.3%	Not reported
Lumachi et al. 2001[248]	134	7.5	SPECT or planar, patient prone, 10 minutes after 750 MBq tracer	Women with breast masses 2 cm or less in diameter who had been selected for open breast biopsy.	Median 52 (32 to 78)	Not reported	100%	Not reported	Not reported
Lumachi et al. 2001[250]	239	7.5	SPECT or planar, patient prone, 10 minutes after 750 MBq tracer	Women with breast lesions who had been selected for breast biopsy on the basis of mammography findings and/or fine needle aspiration cytology.	Median 55 (32 to 87)	Not reported	100%	66.5%	Not reported
Papantoniou et al. 2001[99]	41	7.9	Planar, patient prone, 10 to 20 minutes after 740 to 925 MBq tracer, 256X256	Women, older than 21 years of age, presence of a suspicious breast lesion detected by palpation or mammography, recommended for biopsy. Patients with a history of previous breast cancer, previous mastectomy, a medically unstable condition due to severe arrhythmias, heart failure, or recent surgery were excluded, as were pregnant women.	Mean 55	Not reported	100%	Not reported	Not reported
Chen et al. 2000[108]	35	8.8	Planar, patient prone and supine, 10 to 20 minutes after 740 MBq tracer	Women with suspicious breast lesions on clinical examination.	Mean 47.3 (27 to 80)	Not reported	100%	Not reported	100% Asian

Appendix E. Evidence Tables (continued)

Study	N patients	Quality score	Scintimammography parameters	Patients	Age (Range)	% 65 or older	% Female	% Post-menopausal	Ethnic makeup
Yutani et al. 2000[55]	40	8.8	SPECT, patient supine, 5 minutes after 740 MBq tracer, 64X64	Patients with suspicious lesions (detected by mammography, ultrasound, or physical exam) scheduled for excisional biopsy.	Mean 51 (25 to 86)	15%	100%	Not reported	Not reported
Danielsson et al. 1999[87]	96	8.6	Planar, patient prone, 10 minutes after 700 MBq tracer, 256X256	Age 30 years or older, scheduled for breast surgery.	Mean 54.4 (34 to 82)	Not reported	Not reported	Not reported	Not reported
Danielsson et al. 1999[464]	26[a]	8.6	SPECT, patient supine, 40 minutes after 700 MBq tracer, 128X128	Age 30 years or older, scheduled for breast surgery.	Mean 57 (35 to 82)	Not reported	Not reported	Not reported	Not reported
Obwegeser et al. 1999[90]	101	7.4	SPECT, patient prone, immediately after 555 to 650 MBq tracer, 128X128; also planar, patient supine, 5 minutes after 555 to 560 MBq tracer	Women aged 40 or older selected for surgery by the outpatient breast unit. Pregnant women were excluded.	Not reported	Not reported	100%	Not reported	Not reported
Tofani et al. 1999[85]	300	8.3	Planar, patient prone and supine, 10 minutes after 740 MBq tracer, 256X256	Women with suspicious breast masses on mammography or physical examination scheduled for surgery.	Mean 51.7 (27 to 78)	Not reported	100%	56.3%	Not reported
De Vincentis et al. 1998[465]	18	7.9	Planar, patient prone, 60 minutes after 740 MBq tracer, 128X128	Patients with breast masses detected by examination, including mammography.	Mean 71	100%	Not reported	Not reported	Not reported
Mekhmandarov et al. 1998[86]	140	8.8	Planar, patient prone and supine, 10 to 20 minutes after 740 MBq tracer, 256X256	Patients with a clinically palpable mass in the breast and/or suspicious mammographic finding.	Mean 61.4 (29 to 87)	Not reported	99%	Not reported	Not reported
Uriarte et al. 1998[466]	78	7.9	Planar, patient prone, 10 minutes after 740 MBq tracer	Women scheduled for biopsy after mammography.	(35 to 81)	Not reported	100%	Not reported	Not reported
Alonso et al. 1997[467]	18	7.2	Planar, patient prone, 5 minutes after 740 MBq tracer, 256X256	Women with clinical suspicion of breast cancer and nonconclusive mammographic findings.	Not reported	Not reported	100%	Not reported	Not reported
Ambrus et al. 1997[104]	51	7.5	Planar, patient prone and supine, 5 minutes after 900 MBq tracer, 256X256	Women with a palpable breast lesion, scheduled for surgery.	Mean 55 (19 to 77)	33%	100%	Not reported	Not reported
Carril et al. 1997[109]	41	7.9	Planar, patient prone, 10 minutes after 740 MBq tracer	Women with non-palpable breast lesions, detected by mammography, that warranted biopsy.	(35 to 81)	Not reported	100%	Not reported	Not reported

Appendix E. Evidence Tables (continued)

Study	N patients	Quality score	Scintimammography parameters	Patients	Age (Range)	% 65 or older	% Female	% Post-menopausal	Ethnic makeup
Chen et al. 1997[94]	61	8.3	Planar, patient prone, 10 minutes after 740 MBq tracer	Patients referred for a suspicious breast lesion after clinical examination.	Mean 48.8	Not reported	98%	Not reported	100% Asian
Palmedo et al. 1997[58]	20	7.9	Planar and SPECT, patient prone, immediately to 10 minutes after 740 MBq tracer, 256X256	Patients with suspicious lesions (detected by mammography or physical exam) scheduled for excisional biopsy.	Mean 58.4 (28 to 84)	Not reported	100%	Not reported	Not reported
Schillaci et al. 1997[92]	63	8.8	Planar, patient prone and supine, immediately after 370 MBq tracer, 128X128; and SPECT, patient supine, immediately after 370 MBq tracer, 64X64	Female patients with suspicious lesions on mammography.	Mean 57	Not reported	100%	Not reported	Not reported
Scopinaro et al. 1997[84]	420	8.3	Planar, patient prone, 60 to 120 minutes after 740 MBq tracer	Patients with a focal lesion or microcalcification detected on mammography. Patients were excluded if breasts were too dense to get an accurate mammography reading, and patients with advanced cancers were also excluded.	Mean 52 (26 to 79)	Not reported	Not reported	Not reported	Not reported
Scopinaro et al. 1997[468]	85	8.3	Planar, patient prone, 60 minutes after 740 MBq tracer, 128X128	Patients with mammographic results suspicious or highly suspicious (BIRADS 4-5), scheduled for biopsy or surgery.	Mean 53 (30 to 72)	Not reported	Not reported	Not reported	Not reported
Tiling et al. 1997[95]	56	8.3	Planar, patient prone, 5 minutes after 740 MBq tracer, 256X256	Women with abnormal findings on mammography and/or physical examination who were scheduled for surgery.	Mean 53 (22 to 80)	Not reported	100%	Not reported	Not reported
Tiling et al. 1997[469]	82	7.9	Planar, patient prone, 5 minutes after 740 MBq tracer, 256X256	Women with indeterminate mammograms and/or physical exams.	Mean 50 (22 to 80)	Not reported	100%	46.4%	Not reported
Maffioli et al. 1996[112]	24	7.5	Planar, patient prone, 30 to 40 minutes after 740 MBq tracer, 256X256	Non-palpable suspicious lesions detected on mammography.	Mean 49.8 (39 to 67)	8.3%	100%	Not reported	Not reported

Appendix E. Evidence Tables (continued)

Study	N patients	Quality score	Scintimammography parameters	Patients	Age (Range)	% 65 or older	% Female	% Post-menopausal	Ethnic makeup
Palmedo et al. 1996[96]	56	7.9	SPECT and planar, patient prone, 5 to 30 minutes after 740 MBq tracer, 256X256	Women with a suspicious lesion detected by physical examination or by mammography. Patients with prior or concurrent breast cancer were excluded.	Mean 58 (22 to 81)	Not reported	100%	Not reported	Not reported
Palmedo et al. 1996[106,107]	68	8.3	SPECT and planar, patient prone, 5 to 30 minutes after 740 MBq tracer, 256X256 (planar), 64X64 (SPECT)	Women with suspicious lesions detected by physical examination or mammography.	Mean 54 (22 to 81)	Not reported	100%	Not reported	Not reported
Villanueva-Meyer et al. 1996[93]	66	8.6	Planar, patient prone, 15 minutes after 740 MBq tracer	19 years or older, with a mammographic abnormality, and a candidate for surgical biopsy. Pregnant women and women with severe medical conditions were excluded.	Mean 52 (35 to 80)	Not reported	100%	66.6%	Not reported
Yuen-Green et al. 1996[102]	18	7.9	Planar, patient prone, 5 minutes after 740 MBq tracer, 128X128	Women with either a palpable breast mass and/or an abnormal mammograph for which biopsies were recommended.	Mean 53.9	Not reported	100%	Not reported	Not reported
Burak et al. 1994[105]	41	7.9	Planar, 10 minutes after 720 MBq tracer	Women with palpable breast masses.	Mean 51 (29 to 73)	9.7%	100%	Not reported	Not reported

a. These patients were also included in Danielsson et al. 1999[87]

Appendix E. Evidence Tables (continued)

Table 33. Quality Assessment of Studies of Scintimammography

Question	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	score
Study	consecutive	consistent	prospective	Case control	funding	valid reference	gold standard	interreader	blinding	blinding	blinding	blinding	full testing	threshold	intervening	attrition	conclusions	discrepancy	standardized
Bekis et al. 2004[111]	r	y	y	y	r	y	y	y	y	r	y	r	y	y	y	y	y	y	8.3
Fondrinier et al. 2004[113]	r	y	y	y	r	y	y	n	y	r	n	r	y	y	y	y	y	y	7.2
Bone et al. 2003[461]	y	y	y	y	r	y	y	n	y	r	y	r	y	y	y	y	y	y	8.2
Krishnaiah et al. 2003[89]	r	y	y	y	r	y	y	n	y	r	r	r	y	y	y	y	y	y	7.4
Maunda et al. 2003[462]	r	y	y	y	n	y	y	y	y	r	r	r	y	y	y	y	y	y	7.8
Sampalis et al. 2003[82]	r	y	y	y	r	y	y	r	y	r	r	r	y	r	y	n	y	n	6.0
Sandidas et al. 2003[100]	r	y	y	y	r	y	y	y	y	r	y	r	y	y	y	y	y	y	8.3
Wilczek et al. 2003[88]	y	y	y	y	y	y	y	n	y	r	y	r	y	y	y	y	y	y	8.6
Brem et al. 2002[463]	y	y	y	y	n	y	y	y	y	r	y	r	y	y	y	y	y	y	8.6
Khalkhali et al. 2002[83]	r	y	y	y	r	y	y	y	y	r	y	r	y	y	y	y	y	y	8.3
Leidenius et al. 2002[97]	y	y	y	y	r	y	y	r	y	r	r	r	y	y	y	y	y	y	7.9
Aguilar et al. 2001[110]	y	y	y	y	r	y	y	n	y	r	y	r	y	y	y	y	y	y	8.2
Alonso et al. 2001[467]	r	y	y	y	r	y	y	y	y	r	y	r	y	y	y	r	y	y	7.9
Gutfilen et al. 2001[101]	r	y	y	y	r	y	y	r	y	r	r	r	y	y	y	n	y	y	6.9
Imbriaco et al. 2001[98]	y	y	y	y	r	y	y	n	y	r	n	r	y	y	y	y	y	y	7.6
Koukouraki et al. 2001[91]	r	r	y	y	r	y	y	r	y	r	y	r	y	y	y	y	y	y	7.5
Lumachi et al. 2001[248]	r	y	y	y	r	y	y	r	y	r	r	r	y	y	y	y	y	y	7.5
Lumachi et al. 2001[250]	r	y	y	y	r	y	y	r	y	r	r	r	y	y	y	y	y	y	7.5

Appendix E. Evidence Tables (continued)

Question	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	score
Study	consecutive	consistent	prospective	Case control	funding	valid reference	gold standard	interreader	blinding	blinding	blinding	blinding	full testing	threshold	intervening	attrition	conclusions	discrepancy	standardized
Papantoniou et al. 2001[99]	r	y	y	y	r	y	y	y	y	r	r	r	y	y	y	y	y	y	7.9
Chen et al. 2000[108]	y	y	y	y	r	y	y	y	y	r	y	r	y	y	y	y	y	y	8.8
Yutani et al. 2000[55]	y	y	y	y	r	y	y	y	y	r	y	r	y	y	y	y	y	y	8.8
Danielsson et al. 1999[87]	y	y	y	y	y	y	y	n	y	r	y	r	y	y	y	y	y	y	8.6
Danielsson et al. 1999[464]	y	y	y	y	y	y	y	n	y	r	y	r	y	y	y	y	y	y	8.6
Obwegeser et al. 1999[90]	r	n	y	y	r	y	y	y	y	r	r	r	y	y	y	y	y	y	7.4
Tofani et al. 1999[85]	y	y	y	y	r	y	y	r	y	r	y	r	y	y	y	y	y	y	8.3
De Vincentis et al. 1998[465]	r	y	y	y	r	y	y	r	y	r	y	r	y	y	y	y	y	y	7.9
Mekhmandarov et al. 1998[86]	y	y	y	y	r	y	y	y	y	r	y	r	y	y	y	y	y	y	8.8
Uriarte et al. 1998[466]	r	y	y	y	r	y	y	y	y	r	r	r	y	y	y	y	y	y	7.9
Alonso et al. 1997[103]	r	y	y	y	n	y	y	y	y	r	y	r	y	r	y	n	y	y	7.2
Ambrus et al. 1997[104]	r	y	y	y	r	y	y	r	y	r	r	r	y	y	y	y	y	y	7.5
Carril et al. 1997[109]	r	y	y	y	r	y	y	y	y	r	r	r	y	y	y	y	y	y	7.9
Chen et al. 1997[94]	y	y	y	y	r	y	y	r	y	r	y	r	y	y	y	y	y	y	8.3
Palmedo et al. 1997[58]	r	y	y	y	r	y	y	r	y	r	y	r	y	y	y	y	y	y	7.9
Schillaci et al. 1997[92]	r	y	y	y	y	y	y	y	y	r	y	r	y	y	y	y	y	y	8.8
Scopinaro et al. 1997[84]	r	y	y	y	y	y	y	y	y	r	y	r	y	y	y	r	y	y	8.3
Scopinaro et al. 1997[468]	r	y	y	y	y	y	y	y	y	r	y	r	y	r	y	y	y	y	8.3
Tiling et al. 1997[95]	r	y	y	y	r	y	y	y	y	r	y	r	y	y	y	y	y	y	8.3
Tiling et al. 1997[469]	r	y	y	y	r	y	y	r	y	r	y	r	y	y	y	y	y	y	7.9

Appendix E. Evidence Tables (continued)

Question	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	score
Study	consecutive	consistent	prospective	Case control	funding	valid reference	gold standard	interreader	blinding	blinding	blinding	blinding	full testing	threshold	intervening	attrition	conclusions	discrepancy	standardized
Maffioli et al. 1996[112]	y	y	y	y	r	y	y	r	y	r	r	r	y	r	y	y	y	y	7.5
Palmedo et al. 1996[96]	r	y	y	y	r	y	y	r	y	r	y	r	y	y	y	y	y	y	7.9
Palmedo et al. 1996[106] and [107]	r	y	y	y	r	y	y	y	y	r	y	r	y	y	y	y	y	y	8.3
Villanueva-Meyer et al. 1996[93]	y	y	y	y	n	y	y	y	y	r	y	r	y	y	y	y	y	y	8.6
Yuen-Green et al. 1996[102]	r	y	y	y	r	y	y	y	y	r	y	r	y	r	y	y	y	y	7.9
Burak et al. 1994[105]	r	y	y	y	r	y	y	y	y	r	r	r	y	y	y	y	y	y	7.9

y = yes
n = no
r = not reported

Table 34. Diagnostic Test Characteristics of Scintimammography

Study	N lesions	Patient subgroup	Prevalence	True positive	False negative	False positive	True negative	Sensitivity (95% CI)	Specificity (95% CI)	Positive predictive value (95% CI)	Negative predictive value (95% CI)	Positive likelihood ratio (95% CI)	Negative likelihood ratio (95% CI)
Planar Imaging													
Bekis et al. 2004[111]	35	Non-palpable lesions	37.1%	11	2	4	18	84.6% (57.6% to 95.4%)	81.8% (61.3% to 92.5%)	73.3% (48.0% to 88.9%)	90.0% (69.7% to 97.0%)	4.65 (3.69 to 5.87)	0.19 (0.05 to 0.68)
	13	Non-palpable lesions, with micro-calcifications	46.2%	4	2	0	7	66.7% (30.1% to 89.9%)	100.0% (64.0% to 99.6%)	100.0% (50.5% to 99.5%)	77.8% (45.1% to 93.3%)	10.29 (5.92 to 17.87)	0.38 (0.14 to 1.05)
Fondrinier et al. 2004[113]	45	Non-palpable lesions, with micro-calcifications	53.3%	14	10	4	17	58.3% (38.8% to 75.4%)	81.0% (59.9% to 92.1%)	77.8% (54.7% to 90.8%)	63.0% (44.2% to 78.4%)	3.06 (2.18 to 4.29)	0.51 (0.31 to 0.86)
	13	Non-palpable lesions, with micro-calcifications, larger than 10 mm	66.6%	6.8	1.86	1.24	3.1	78.5% (45.2% to 93.8%)	71.4% (28.9% to 93.4%)	84.6% (49.8% to 96.4%)	62.5% (24.8% to 89.1%)	2.75 (1.94 to 3.89)	0.30 (0.07 to 1.23)
	32	Non-palpable lesions, with micro-calcifications, 10 mm or smaller	36.4%	2.91	8.73	2.91	17.41	25.0% (9.0% to 53.7%)	85.7% (64.7% to 94.9%)	50.0% (18.7% to 81.3%)	66.6% (47.4% to 81.4%)	1.75 (0.65 to 4.72)	0.88 (0.60 to 1.28)

Study	N lesions	Patient subgroup	Prevalence	True positive	False negative	False positive	True negative	Sensitivity (95% CI)	Specificity (95% CI)	Positive predictive value (95% CI)	Negative predictive value (95% CI)	Positive likelihood ratio (95% CI)	Negative likelihood ratio (95% CI)
Bone et al. 2003[461]	111	Positive by FNA	71.2%	65	14	8	24	82.3% (72.4% to 89.1%)	75.0% (57.8% to 86.6%)	89.0% (79.8% to 94.3%)	63.2% (47.3% to 76.5%)	3.29 (2.97 to 3.65)	0.24 (0.14 to 0.40)
	40	Positive by FNA, 10 mm or smaller	50.0%	10	10	3	17	50.0% (30.0% to 70.0%)	85.0% (63.8% to 94.6%)	76.9% (49.6% to 91.6%)	63.0% (44.2% to 78.4%)	3.33 (2.15 to 5.17)	0.59 (0.37 to 0.95)
	71	Positive by FNA, larger than 10 mm	83.1%	55	4	5	7	93.2% (83.7% to 97.2%)	58.3% (32.0% to 80.5%)	91.7% (81.8% to 96.3%)	63.6% (35.4% to 84.6%)	2.24 (2.09 to 2.40)	0.12 (0.04 to 0.34)
Krishnaiah et al. 2003[89]	104	All	23.1%	20	4	14	66	83.3% (64.0% to 93.1%)	82.5% (72.7% to 89.2%)	58.8% (42.2% to 73.6%)	94.3% (86.1% to 97.7%)	4.76 (3.98 to 5.69)	0.20 (0.08 to 0.50)
	59	Palpable lesions	27.1%	14	2	9	34	87.5% (63.7% to 96.3%)	79.1% (64.7% to 88.5%)	60.9% (40.8% to 77.7%)	94.4% (81.7% to 98.3%)	4.18 (3.47 to 5.03)	0.16 (0.04 to 0.58)
	45	Non-palpable lesions	17.8%	6	2	5	32	75.0% (40.8% to 92.5%)	86.5% (71.9% to 94.0%)	54.5% (28.1% to 78.6%)	94.1% (80.7% to 98.2%)	5.55 (3.72 to 8.28)	0.29 (0.09 to 0.97)
Maunda et al. 2003[462]	38	Palpable lesion that scored BIRADS 1 to 3 on mammo-graphy	5.3%	2	0	0	36	100.0% (34.0% to 99.3%)	100.0% (90.1% to 99.9%)	100.0% (34.0% to 99.3%)	100.0% (90.1% to 99.9%)	61.67 (37.18 to 102.29)	0.17 (0.01 to 2.12)
Sampalis et al. 2003[82]	1243	All	16.2%	186	15	136	906	92.5% (88.0% to 95.4%)	86.9% (84.8% to 88.9%)	57.8% (52.3% to 63.0%)	98.4% (97.3% to 99.0%)	7.09 (6.82 to 7.37)	0.09 (0.05 to 0.14)
	696	BIRADS 1 or 2	1.9%	10	3	84	599	76.9% (49.6% to 91.6%)	87.7% (85.0% to 89.9%)	10.6% (5.9% to 18.5%)	99.5% (98.5% to 99.8%)	6.25 (4.64 to 8.42)	0.26 (0.10 to 0.71)
	348	BIRADS 3 or 4	21.3%	65	9	24	250	87.8% (78.4% to 93.4%)	91.2% (87.3% to 94.0%)	73.0% (63.0% to 81.1%)	96.5% (93.5% to 98.1%)	10.03 (9.21 to 10.92)	0.13 (0.07 to 0.25)

Study	N lesions	Patient subgroup	Prevalence	True positive	False negative	False positive	True negative	Sensitivity (95% CI)	Specificity (95% CI)	Positive predictive value (95% CI)	Negative predictive value (95% CI)	Positive likelihood ratio (95% CI)	Negative likelihood ratio (95% CI)
	199	BIRADS 5	57.3%	111	3	28	57	97.4% (92.5% to 99.1%)	67.1% (56.5% to 76.1%)	79.9% (72.4% to 85.6%)	95.0% (86.2% to 98.2%)	2.96 (2.87 to 3.05)	0.04 (0.01 to 0.12)
Sanidas et al. 2003[100]	33	All	86.1%	28	3	1	4	90.3% (74.9% to 96.5%)	80.0% (37.4% to 95.9%)	96.6% (82.6% to 99.2%)	57.1% (25.2% to 83.9%)	4.52 (4.02 to 5.07)	0.12 (0.04 to 0.39)
Wilczek et al. 2003[88]	119	All	69.7%	71	12	9	27	85.5% (76.3% to 91.5%)	75.0% (58.9% to 86.1%)	88.8% (79.9% to 93.9%)	69.2% (53.5% to 81.3%)	3.42 (3.13 to 3.74)	0.19 (0.11 to 0.34)
	65	Palpable lesions	70.8%	42	4	7	12	91.3% (79.5% to 96.5%)	63.2% (41.0% to 80.7%)	85.7% (73.2% to 92.8%)	75.0% (50.4% to 89.6%)	2.48 (2.27 to 2.71)	0.14 (0.05 to 0.37)
	54	Non-palpable lesions	68.5%	29	8	2	15	78.4% (62.7% to 88.5%)	88.2% (65.4% to 96.5%)	93.5% (79.1% to 98.1%)	65.2% (44.9% to 81.1%)	6.66 (5.62 to 7.89)	0.25 (0.13 to 0.46)
Brem et al. 2002[463]	58	Palpable and BIRADS 1, or non-palpable and BIRADS 4 or 5	48.3%	18	10	2	28	64.3% (45.8% to 79.2%)	93.3% (78.5% to 98.0%)	90.0% (69.7% to 97.0%)	73.7% (57.9% to 84.9%)	9.64 (7.32 to 12.71)	0.38 (0.23 to 0.63)
Khalkhali et al. 2002[83]	580	All	39.9%	153	61	67	255	71.5% (65.1% to 77.1%)	79.2% (74.4% to 83.3%)	69.5% (63.2% to 75.2%)	80.7% (76.0% to 84.7%)	3.44 (3.16 to 3.74)	0.36 (0.29 to 0.45)
	276	Dense breast tissue	38.6%	69	29	34	122	70.4% (60.7% to 78.5%)	78.2% (71.1% to 83.9%)	67.0% (57.4% to 75.3%)	80.8% (73.7% to 86.3%)	3.23 (2.84 to 3.67)	0.38 (0.28 to 0.52)
	304	Fatty breast tissue	41.1%	84	32	33	133	72.4% (63.6% to 79.7%)	80.1% (73.4% to 85.5%)	71.8% (63.0% to 79.1%)	80.6% (73.9% to 85.9%)	3.64 (3.26 to 4.08)	0.34 (0.25 to 0.47)
Leidenius et al. 2002[97]	49	All	63.3%	24	7	7	11	77.4% (60.1% to 88.5%)	61.1% (38.6% to 79.6%)	77.4% (60.1% to 88.5%)	61.1% (38.6% to 79.6%)	1.99 (1.65 to 2.41)	0.37 (0.17 to 0.78)
Aguilar et al. 2001[110]	37	Non-palpable lesions	51.4%	15	4	5	13	78.9% (56.5% to 91.3%)	72.2% (49.1% to 87.3%)	75.0% (53.0% to 88.6%)	76.5% (52.6% to 90.2%)	2.84 (2.25 to 3.58)	0.29 (0.12 to 0.73)

Appendix E. Evidence Tables (continued)

Study	N lesions	Patient subgroup	Prevalence	True positive	False negative	False positive	True negative	Sensitivity (95% CI)	Specificity (95% CI)	Positive predictive value (95% CI)	Negative predictive value (95% CI)	Positive likelihood ratio (95% CI)	Negative likelihood ratio (95% CI)
Alonso et al. 2001[103]	245	Palpable lesions	77.1%	157	32	13	43	83.1% (77.1% to 87.7%)	76.8% (64.2% to 85.8%)	92.4% (87.3% to 95.4%)	57.3% (46.0% to 67.9%)	3.58 (3.36 to 3.82)	0.22 (0.16 to 0.31)
Gutfilen et al. 2001[101]	30	All	76.7%	22	1	4	3	95.7% (78.7% to 99.0%)	42.9% (16.1% to 74.8%)	84.6% (66.3% to 93.7%)	75.0% (30.1% to 94.9%)	1.67 (1.53 to 1.83)	0.10 (0.01 to 0.83)
	22	Younger than 65	72.7%	15	1	4	2	93.8% (71.4% to 98.6%)	33.3% (10.1% to 69.9%)	78.9% (56.5% to 91.3%)	66.7% (21.0% to 93.3%)	1.41 (1.24 to 1.60)	0.19 (0.02 to 1.71)
	23	Lesions larger than 10 mm	87.0%	20	0	2	1	100.0% (83.5% to 99.8%)	33.3% (6.7% to 79.0%)	90.9% (72.0% to 97.3%)	100.0% (20.8% to 99.2%)	1.56 (1.46 to 1.67)	0.06 (0.00 to 1.30)
	27	Palpable lesions	85.2%	22	1	2	2	95.7% (78.7% to 99.0%)	50.0% (15.4% to 84.6%)	91.7% (73.9% to 97.5%)	66.7% (21.0% to 93.3%)	1.91 (1.75 to 2.09)	0.09 (0.01 to 0.75)
Imbriaco et al. 2001[98]	49	All	52.0%	21	5	3	21	80.8% (62.0% to 91.3%)	87.5% (68.8% to 95.5%)	87.5% (68.8% to 95.5%)	80.8% (62.0% to 91.3%)	6.46 (5.36 to 7.79)	0.22 (0.10 to 0.49)
	45	Younger than 65	54.3%	20	5	3	18	80.0% (60.7% to 91.0%)	85.7% (65.2% to 94.8%)	87.0% (67.7% to 95.3%)	78.3% (58.0% to 90.2%)	5.60 (4.60 to 6.81)	0.23 (0.10 to 0.52)
	23	Lesions 10 mm or smaller	39.1%	6	3	1	13	66.7% (35.4% to 87.7%)	92.9% (68.2% to 98.5%)	85.7% (48.4% to 97.0%)	81.3% (56.8% to 93.2%)	9.33 (5.88 to 14.81)	0.36 (0.14 to 0.91)
	26	Lesions larger than 10 mm	61.5%	14	2	2	8	87.5% (63.7% to 96.3%)	80.0% (48.9% to 94.0%)	87.5% (63.7% to 96.3%)	80.0% (48.9% to 94.0%)	4.38 (3.64 to 5.27)	0.16 (0.04 to 0.59)
Koukouraki et al. 2001[91]	86	All	74.1%	80	6	5	25	93.0% (85.5% to 96.7%)	83.3% (66.3% to 92.5%)	94.1% (86.9% to 97.4%)	80.6% (63.6% to 90.7%)	5.58 (5.27 to 5.91)	0.08 (0.04 to 0.18)
	78	Palpable lesions	85.9%	63	4	3	8	94.0% (85.5% to 97.6%)	72.7% (43.4% to 90.0%)	95.5% (87.4% to 98.4%)	66.7% (39.0% to 86.0%)	3.45 (3.25 to 3.66)	0.08 (0.03 to 0.23)
	38	Non-palpable lesions	50.0%	17	2	2	17	89.5% (68.4% to 96.8%)	89.5% (68.4% to 96.8%)	89.5% (68.4% to 96.8%)	89.5% (68.4% to 96.8%)	8.50 (7.29 to 9.92)	0.12 (0.03 to 0.44)

Study	N lesions	Patient subgroup	Prevalence	True positive	False negative	False positive	True negative	Sensitivity (95% CI)	Specificity (95% CI)	Positive predictive value (95% CI)	Negative predictive value (95% CI)	Positive likelihood ratio (95% CI)	Negative likelihood ratio (95% CI)
Papantoniou et al. 2001[99]	41	All	63.4%	23	3	1	14	88.5% (70.8% to 95.8%)	93.3% (69.9% to 98.6%)	95.8% (79.5% to 99.1%)	82.4% (58.8% to 93.6%)	13.27 (11.55 to 15.25)	0.12 (0.04 to 0.36)
Chen et al. 2000[108]	38	Palpable lesions	51.4%	14	4	2	15	77.8% (54.7% to 90.8%)	88.2% (65.4% to 96.5%)	87.5% (63.7% to 96.3%)	78.9% (56.5% to 91.3%)	6.61 (5.16 to 8.46)	0.25 (0.10 to 0.61)
Danielsson et al. 1999[87]	121	All	71.1%	72	14	9	26	83.7% (74.5% to 90.0%)	74.3% (57.9% to 85.7%)	88.9% (80.1% to 94.0%)	65.0% (49.5% to 77.8%)	3.26 (2.97 to 3.57)	0.22 (0.13 to 0.37)
Obwegeser et al. 1999[90]	103[a]	All	54.4%	26	30	6	41	46.4% (34.0% to 59.3%)	87.2% (74.7% to 93.9%)	81.3% (64.6% to 91.0%)	57.7% (46.1% to 68.5%)	3.64 (2.75 to 4.82)	0.61 (0.47 to 0.80)
Tofani et al. 1999[85]	300	All	72.7%	194	24	14	68	89.0% (84.1% to 92.5%)	82.9% (73.3% to 89.5%)	93.3% (89.0% to 95.9%)	73.9% (64.1% to 81.8%)	5.21 (4.97 to 5.46)	0.13 (0.09 to 0.20)
	43	Lesion 1 cm or smaller	67.4%	14	15	0	14	48.3% (31.4% to 65.5%)	100.0% (78.0% to 99.8%)	100.0% (78.0% to 99.8%)	48.3% (31.4% to 65.5%)	14.50 (10.02 to 20.99)	0.53 (0.37 to 0.77)
	257	Lesion larger than 1 cm	73.5%	180	9	14	54	95.2% (91.2% to 97.4%)	79.4% (68.3% to 87.3%)	92.8% (88.2% to 95.6%)	85.7% (74.9% to 92.2%)	4.63 (4.48 to 4.78)	0.06 (0.03 to 0.11)
	140	Post-meno-pausal	78.6%	103	7	4	26	93.6% (87.4% to 96.8%)	86.7% (70.2% to 94.5%)	96.3% (90.7% to 98.5%)	78.8% (62.2% to 89.2%)	7.02 (6.69 to 7.37)	0.07 (0.04 to 0.15)
	117	Pre-meno-pausal	67.5%	77	2	10	28	97.5% (91.1% to 99.2%)	73.7% (57.9% to 84.9%)	88.5% (80.1% to 93.6%)	93.3% (78.5% to 98.0%)	3.70 (3.57 to 3.84)	0.03 (0.01 to 0.14)
De Vincentis et al. 1998[465]	18	65 or older	88.9%	11	5	0	2	68.8% (44.4% to 85.6%)	100.0% (34.0% to 99.3%)	100.0% (73.6% to 99.7%)	28.6% (8.6% to 64.1%)	4.06 (2.92 to 5.64)	0.39 (0.17 to 0.91)
Mekhmandarov et al. 1998[86]	140	All	60.7%	71	14	8	47	83.5% (74.2% to 89.9%)	85.5% (73.8% to 92.4%)	89.9% (81.2% to 94.7%)	77.0% (65.0% to 85.7%)	5.74 (5.23 to 6.31)	0.19 (0.12 to 0.31)
	85	Palpable	71.8%	58	3	6	18	95.1% (86.4% to 98.2%)	75.0% (55.0% to 87.8%)	90.6% (80.9% to 95.5%)	85.7% (65.2% to 94.8%)	3.80 (3.59 to 4.03)	0.07 (0.02 to 0.20)

Study	N lesions	Patient subgroup	Prevalence	True positive	False negative	False positive	True negative	Sensitivity (95% CI)	Specificity (95% CI)	Positive predictive value (95% CI)	Negative predictive value (95% CI)	Positive likelihood ratio (95% CI)	Negative likelihood ratio (95% CI)
	55	Non-palpable	43.6%	13	11	2	29	54.2% (35.1% to 72.0%)	93.5% (79.1% to 98.1%)	86.7% (61.9% to 96.0%)	72.5% (57.1% to 83.8%)	8.40 (5.81 to 12.13)	0.49 (0.31 to 0.76)
	31	Lesion 1 to 1.5 cm	74.2%	18	5	2	6	78.3% (58.0% to 90.2%)	75.0% (40.8% to 92.5%)	90.0% (69.7% to 97.0%)	54.5% (28.1% to 78.6%)	3.13 (2.52 to 3.88)	0.29 (0.12 to 0.69)
	58	Lesion 1.5 cm or larger	100.0%	52	6	0	0	89.7% (79.1% to 95.1%)	#DIV/0!	100.0% (92.9% to 99.9%)	0.0% (0.4% to 39.6%)	1.78 (1.63 to 1.95)	0.22 (0.03 to 1.78)
Uriarte et al. 1998[466]	78	BIRADS 3 to 5	52.6%	38	3	19	18	92.7% (80.4% to 97.4%)	48.6% (33.5% to 64.1%)	66.7% (53.7% to 77.5%)	85.7% (65.2% to 94.8%)	1.80 (1.66 to 1.97)	0.15 (0.05 to 0.47)
	28	BIRADS 5	85.7%	22	2	0	4	91.7% (73.9% to 97.5%)	100.0% (50.5% to 99.5%)	100.0% (84.8% to 99.8%)	66.7% (30.1% to 89.9%)	9.00 (7.90 to 10.26)	0.11 (0.03 to 0.37)
	30	BIRADS 4	43.3%	12	1	8	9	92.3% (66.4% to 98.3%)	52.9% (31.0% to 73.7%)	60.0% (38.7% to 78.0%)	90.0% (59.3% to 97.9%)	1.96 (1.68 to 2.29)	0.15 (0.02 to 1.01)
	20	BIRADS 3	20.0%	4	0	11	5	100.0% (50.5% to 99.5%)	31.3% (14.4% to 55.6%)	26.7% (11.1% to 52.0%)	100.0% (56.0% to 99.6%)	1.33 (0.99 to 1.78)	0.31 (0.02 to 4.68)
Alonso et al. 1997[467]	18	Clinically suspicious lesions with non-conclusive mammo-graphy findings	55.6%	8	2	2	6	80.0% (48.9% to 94.0%)	75.0% (40.8% to 92.5%)	80.0% (48.9% to 94.0%)	75.0% (40.8% to 92.5%)	3.20 (2.35 to 4.36)	0.27 (0.07 to 0.98)
Ambrus et al. 1997[104]	51	Palpable lesions	78.4%	20	20	1	10	50.0% (35.2% to 64.8%)	90.9% (61.9% to 98.1%)	95.2% (77.0% to 99.0%)	33.3% (19.3% to 51.3%)	5.50 4.03 to 7.50)	0.55 (0.38 to 0.79)
	17	Palpable lesions, 65 or older	94.1%	8	8	0	1	50.0% (28.1% to 71.9%)	100.0% (20.8% to 99.2%)	100.0% (67.0% to 99.7%)	11.1% (2.4% to 43.8%)	2.00 (1.24 to 3.22)	0.67 (0.26 to 1.69)

Appendix E. Evidence Tables (continued)

Study	N lesions	Patient subgroup	Prevalence	True positive	False negative	False positive	True negative	Sensitivity (95% CI)	Specificity (95% CI)	Positive predictive value (95% CI)	Negative predictive value (95% CI)	Positive likelihood ratio (95% CI)	Negative likelihood ratio (95% CI)
	33	Palpable lesions, younger than 65	72.7%	12	12	1	8	50.0% (31.5% to 68.5%)	88.9% (56.2% to 97.6%)	92.3% (66.4% to 98.3%)	40.0% (22.0% to 61.3%)	4.50 (3.02 to 6.71)	0.56 (0.35 to 0.89)
Carril et al. 1997[109]	41	Non-palpable lesions	53.7%	19	3	8	11	86.4% (66.5% to 95.1%)	57.9% (36.3% to 76.7%)	70.4% (51.5% to 84.0%)	78.6% (52.3% to 92.2%)	2.05 (1.74 to 2.42)	0.24 (0.08 to 0.72)
	17	Non-palpable lesions, BIRADS 5	94.1%	14	2	0	1	87.5% (63.7% to 96.3%)	100.0% (20.8% to 99.2%)	100.0% (78.0% to 99.8%)	33.3% (6.7% to 79.0%)	3.41 (2.80 to 4.16)	0.20 (0.05 to 0.79)
	15	Non-palpable lesions, BIRADS 4	26.7%	3	1	4	7	75.0% (30.1% to 94.9%)	63.6% (35.4% to 84.6%)	42.9% (16.1% to 74.8%)	87.5% (52.6% to 97.4%)	2.06 (1.17 to 3.63)	0.39 (0.07 to 2.27)
Chen et al. 1997[94]	63	All	50.8%	25	7	3	28	78.1% (61.2% to 88.8%)	90.3% (74.9% to 96.5%)	89.3% (72.6% to 96.1%)	80.0% (64.0% to 89.8%)	8.07 (6.72 to 9.70)	0.24 (0.12 to 0.47)
Palmedo et al. 1997[58]	20[b]	All	65.0%	12	1	1	6	92.3% (66.4% to 98.3%)	85.7% (48.4% to 97.0%)	92.3% (66.4% to 98.3%)	85.7% (48.4% to 97.0%)	6.46 (5.52 to 7.56)	0.09 (0.01 to 0.60)
Schillaci et al. 1997[92]	66[c]	All	63.6%	36	6	2	22	85.7% (72.0% to 93.2%)	91.7% (73.9% to 97.5%)	94.7% (82.5% to 98.4%)	78.6% (60.4% to 89.6%)	10.29 (9.09 to 11.64)	0.16 (0.07 to 0.33)
Scopinaro et al. 1997[84]	449	All	79.1%	301	54	9	85	84.8% (80.7% to 88.1%)	90.4% (82.7% to 94.8%)	97.1% (94.5% to 98.4%)	61.2% (52.8% to 68.8%)	8.86 (8.47 to 9.25)	0.17 (0.13 to 0.22)
	283	Palpable lesions	79.5%	219	6	6	52	97.3% (94.3% to 98.7%)	89.7% (79.1% to 95.1%)	97.3% (94.3% to 98.7%)	89.7% (79.1% to 95.1%)	9.41 (9.21 to 9.61)	0.03 (0.01 to 0.07)
	166	Non-palpable lesions	78.3%	81	49	3	33	62.3% (53.7% to 70.2%)	91.7% (78.0% to 97.0%)	96.4% (89.9% to 98.7%)	40.2% (30.3% to 51.1%)	7.48 (6.54 to 8.55)	0.41 (0.32 to 0.52)
Scopinaro et al. 1997[468]	91	BIRADS 4 or 5	57.1%	43	9	4	35	82.7% (70.2% to 90.5%)	89.7% (76.3% to 95.8%)	91.5% (79.9% to 96.5%)	79.5% (65.4% to 88.7%)	8.06 (7.12 to 9.13)	0.19 (0.11 to 0.35)

Study	N lesions	Patient subgroup	Prevalence	True positive	False negative	False positive	True negative	Sensitivity (95% CI)	Specificity (95% CI)	Positive predictive value (95% CI)	Negative predictive value (95% CI)	Positive likelihood ratio (95% CI)	Negative likelihood ratio (95% CI)
Tiling et al. 1997[95]	56	All	58.9%	29	4	4	19	87.9% (72.5% to 95.0%)	82.6% (62.7% to 92.8%)	87.9% (72.5% to 95.0%)	82.6% (62.7% to 92.8%)	5.05 (4.45 to 5.74)	0.15 (0.06 to 0.37)
Tiling et al. 1997[469]	82	Indeter-minate mammo-grams and/or physical findings	35.4%	23	6	16	37	79.3% (61.5% to 90.0%)	69.8% (56.4% to 80.4%)	59.0% (43.4% to 72.9%)	86.0% (72.6% to 93.3%)	2.63 (2.18 to 3.16)	0.30 (0.14 to 0.62)
Maffioli et al. 1996[112]	24	Non-palpable	58.3%	7	7	1	9	50.0% (26.9% to 73.1%)	90.0% (59.3% to 97.9%)	87.5% (52.6% to 97.4%)	56.3% (33.2% to 76.8%)	5.00 (2.96 to 8.44)	0.56 (0.32 to 0.98)
	22	Non-palpable, younger than 65 years	59.1%	7	6	1	8	53.8% (29.2% to 76.7%)	88.9% (56.2% to 97.6%)	87.5% (52.6% to 97.4%)	57.1% (32.6% to 78.5%)	4.85 (2.93 to 8.02)	0.52 (0.28 to 0.98)
	21	Non-palpable, micro-calcifica-tions	61.9%	7	6	1	7	53.8% (29.2% to 76.7%)	87.5% (52.6% to 97.4%)	87.5% (52.6% to 97.4%)	53.8% (29.2% to 76.7%)	4.31 (2.60 to 7.13)	0.53 (0.28 to 1.00)
Palmedo et al. 1996[106,107]	54[d]	All	44.4%	21	3	4	26	87.5% (68.8% to 95.5%)	86.7% (70.2% to 94.5%)	84.0% (65.2% to 93.4%)	89.7% (73.4% to 96.3%)	6.56 (5.64 to 7.63)	0.14 (0.05 to 0.42)
	14[d]	Non-palpable	28.6%	1	3	0	10	25.0% (5.1% to 69.9%)	100.0% (71.7% to 99.7%)	100.0% (20.8% to 99.2%)	76.9% (49.6% to 91.6%)	6.60 (1.73 to 25.18)	0.73 (0.41 to 1.32)
	40[d]	Palpable	51.3%	20	0	4	15	100.0% (83.5% to 99.8%)	78.9% (56.5% to 91.3%)	83.3% (64.0% to 93.1%)	100.0% (79.2% to 99.8%)	4.34 (4.06 to 4.64)	0.03 (0.00 to 0.48)
Villanueva-Meyer et al. 1996[93]	66	All	53.0%	29	6	2	29	82.9% (67.2% to 91.8%)	93.5% (79.1% to 98.1%)	93.5% (79.1% to 98.1%)	82.9% (67.2% to 91.8%)	12.84 (11.05 to 14.93)	0.18 (0.09 to 0.38)
Yuen-Green et al. 1996[102]	21	All	28.6%	5	1	1	14	83.3% (43.5% to 96.5%)	93.3% (69.9% to 98.6%)	83.3% (43.5% to 96.5%)	93.3% (69.9% to 98.6%)	12.50 (8.74 to 17.88)	0.18 (0.03 to 1.07)

Appendix E. Evidence Tables (continued)

Study	N lesions	Patient subgroup	Prevalence	True positive	False negative	False positive	True negative	Sensitivity (95% CI)	Specificity (95% CI)	Positive predictive value (95% CI)	Negative predictive value (95% CI)	Positive likelihood ratio (95% CI)	Negative likelihood ratio (95% CI)
Burak et al. 1994[105]	41	Palpable lesions	65.9%	24	3	2	12	88.9% (71.8% to 96.0%)	85.7% (59.8% to 95.7%)	92.3% (75.6% to 97.7%)	80.0% (54.7% to 92.7%)	6.22 (5.45 to 7.11)	0.13 (0.04 to 0.38)
	37	Palpable lesions, younger than 65	62.2%	20	3	2	12	87.0% (67.7% to 95.3%)	85.7% (59.8% to 95.7%)	90.9% (72.0% to 97.3%)	80.0% (54.7% to 92.7%)	6.09 (5.20 to 7.13)	0.15 (0.05 to 0.45)
SPECT imaging													
Yutani et al. 2000[55]	40	All	95.0%	29	9	1	1	76.3% (60.7% to 86.9%)	50.0% (10.0% to 90.0%)	96.7% (83.1% to 99.3%)	10.0% (2.1% to 40.7%)	1.53 (1.28 to 1.82)	0.47 (0.11 to 2.12)
	34	Younger than 65	94.1%	25	7	1	1	78.1% (61.2% to 88.8%)	50.0% (10.0% to 90.0%)	96.2% (80.8% to 99.2%)	12.5% (2.6% to 47.4%)	1.56 (1.30 to 1.88)	0.44 (0.09 to 2.03)
	29	Lesion 1.5 cm or larger	96.6%	24	4	1	0	85.7% (68.4% to 94.1%)	0.0% (0.8% to 79.2%)	96.0% (80.2% to 99.1%)	0.0% (0.5% to 49.5%)	1.13 (0.96 to 1.32)	0.62 (0.05 to 7.92)
	37	Palpable lesion	97.3%	27	9	1	0	75.0% (58.9% to 86.1%)	0.0% (0.8% to 79.2%)	96.4% (82.0% to 99.2%)	0.0% (0.3% to 30.5%)	0.99 (0.82 to 1.20)	1.03 (0.09 to 12.05)
	30	BIRADS 5	93.3%	24	4	1	1	85.7% (68.4% to 94.1%)	50.0% (10.0% to 90.0%)	96.0% (80.2% to 99.1%)	20.0% (4.1% to 62.6%)	1.71 (1.47 to 1.99)	0.29 (0.05 to 1.50)
Danielsson et al. 1999[464]	34	All	67.6%	14	9	4	7	60.9% (40.8% to 77.7%)	63.6% (35.4% to 84.6%)	77.8% (54.7% to 90.8%)	43.8% (23.2% to 66.8%)	1.67 (1.21 to 2.32)	0.61 (0.31 to 1.21)
Obwegeser et al. 1999[90]	103[a]	All	54.4%	39	17	10	37	69.6% (56.6% to 80.0%)	78.7% (65.0% to 87.9%)	79.6% (66.3% to 88.4%)	68.5% (55.2% to 79.3%)	3.27 (2.75 to 3.89)	0.39 (0.25 to 0.59)
Palmedo et al. 1997[58]	20[b]	All	65.0%	12	1	2	5	92.3% (66.4% to 98.3%)	71.4% (35.9% to 91.4%)	85.7% (59.8% to 95.7%)	83.3% (43.5% to 96.5%)	3.23 (2.76 to 3.78)	0.11 (0.02 to 0.75)
Schillaci et al. 1997[92]	66[c]	All	63.6%	39	3	3	21	92.9% (80.8% to 97.4%)	87.5% (68.8% to 95.5%)	92.9% (80.8% to 97.4%)	87.5% (68.8% to 95.5%)	7.43 (6.83 to 8.08)	0.08 (0.03 to 0.25)
Palmedo et al. 1996[106,107]	54[d]	All	44.4%	20	4	5	25	83.3% (64.0% to 93.1%)	83.3% (66.3% to 92.5%)	80.0% (60.7% to 91.0%)	86.2% (69.3% to 94.3%)	5.00 (4.18 to 5.98)	0.20 (0.08 to 0.50)

Study	N lesions	Patient subgroup	Prevalence	True positive	False negative	False positive	True negative	Sensitivity (95% CI)	Specificity (95% CI)	Positive predictive value (95% CI)	Negative predictive value (95% CI)	Positive likelihood ratio (95% CI)	Negative likelihood ratio (95% CI)
	14[d]	Non-palpable	28.6%	0	4	1	9	0.0% (0.5% to 49.5%)	90.0% (59.3% to 97.9%)	0.0% (0.8% to 79.2%)	69.2% (42.3% to 87.1%)	0.73 (0.05 to 10.17)	1.04 (0.72 to 1.52)
	40[d]	Palpable	51.3%	20	0	4	15	100.0% (83.5% to 99.8%)	78.9% (56.5% to 91.3%)	83.3% (64.0% to 93.1%)	100.0% (79.2% to 99.8%)	4.34 (4.06 to 4.64)	0.03 (0.00 to 0.48)
Data from planar and SPECT imaging combined													
Lumachi et al. 2001[248]	134	Lesions 2 cm or less in diameter	79.9%	87	20	2	25	81.3% (72.8% to 87.5%)	92.6% (76.4% to 97.8%)	97.8% (92.1% to 99.3%)	55.6% (41.2% to 69.0%)	10.98 (10.02 to 12.02)	0.20 (0.13 to 0.30)
	51	Lesions 1 cm or less in diameter	62.7%	25	7	1	18	78.1% (61.2% to 88.8%)	94.7% (75.1% to 98.8%)	96.2% (80.8% to 99.2%)	72.0% (52.4% to 85.6%)	14.84 (12.36 to 17.83)	0.23 (0.12 to 0.45)
Lumachi et al. 2001[250]	239	All	86.6%	182	25	2	30	87.9% (82.8% to 91.7%)	93.8% (79.7% to 98.1%)	98.9% (96.1% to 99.7%)	54.5% (41.5% to 66.9%)	14.07 (13.37 to 14.80)	0.13 (0.09 to 0.19)
Palmedo et al. 1996[96]	56	All	48.2%	23	4	10	19	85.2% (67.4% to 93.9%)	65.5% (47.3% to 80.0%)	69.7% (52.6% to 82.5%)	82.6% (62.7% to 92.8%)	2.47 (2.11 to 2.89)	0.23 (0.09 to 0.58)
	43	Palpable	51.2%	20	2	8	13	90.9% (72.0% to 97.3%)	61.9% (40.9% to 79.1%)	71.4% (52.9% to 84.6%)	86.7% (61.9% to 96.0%)	2.39 (2.09 to 2.72)	0.15 (0.04 to 0.57)
	13	Non-palpable	38.5%	3	2	2	6	60.0% (23.3% to 87.9%)	75.0% (40.8% to 92.5%)	60.0% (23.3% to 87.9%)	75.0% (40.8% to 92.5%)	2.40 (1.17 to 4.91)	0.53 (0.17 to 1.68)
Palmedo et al. 1996[106,107]	68[d]	All	42.6%	24	5	7	32	82.8% (65.3% to 92.3%)	82.1% (67.2% to 90.9%)	77.4% (60.1% to 88.5%)	86.5% (71.9% to 94.0%)	4.61 (3.91 to 5.44)	0.21 (0.09 to 0.47)

FNA = fine needle aspiration

a. The same patients studied by both SPECT and planar imaging.

b. The same patients studied by both SPECT and planar imaging.

c. The same patients studied by both SPECT and planar imaging.

d. The same patients studied by both SPECT and planar imaging.

Table 35. Meta-analysis of Studies of Scintimammography for Suspicious Breast Lesions

Study	N lesions	Quality score	Sensitivity (95% CI)	Specificity (95% CI)	Positive predictive value (95% CI)	Negative predictive value (95% CI)	Positive likelihood ratio (95% CI)	Negative likelihood ratio (95% CI)
Sampalis et al. 2003[82]	1,243	6	92.5% (88.0% to 95.4%)	86.9% (84.8% to 88.9%)	57.8% (52.3% to 63.0%)	98.4% (97.3% to 99.0%)	7.09 (6.82 to 7.37)	0.09 (0.05 to 0.14)
Khalkhali et al. 2002[83]	580	8.3	71.5% (65.1% to 77.1%)	79.2% (74.4% to 83.3%)	69.5% (63.2% to 75.2%)	80.7% (76.0% to 84.7%)	3.44 (3.16 to 3.74)	0.36 (0.29 to 0.45)
Scopinaro et al. 1997[84]	449	8.3	84.8% (80.7% to 88.1%)	90.4% (82.7% to 94.8%)	97.1% (94.5% to 98.4%)	61.2% (52.8% to 68.8%)	8.86 (8.47 to 9.25)	0.17 (0.13 to 0.22)
Tofani et al. 1999[85]	300	8.3	89.0% (84.1% to 92.5%)	82.9% (73.3% to 89.5%)	93.3% (89.0% to 95.9%)	73.9% (64.1% to 81.8%)	5.21 (4.97 to 5.46)	0.13 (0.09 to 0.20)
Mekhmandarov et al. 1998[86]	140	8.8	83.5% (74.2% to 89.9%)	85.5% (73.8% to 92.4%)	89.9% (81.2% to 94.7%)	77.0% (65.0% to 85.7%)	5.74 (5.23 to 6.31)	0.19 (0.12 to 0.31)
Danielsson et al. 1999[87]	121	8.6	83.7% (74.5% to 90.0%)	74.3% (57.9% to 85.7%)	88.9% (80.1% to 94.0%)	65.0% (49.5% to 77.8%)	3.26 (2.97 to 3.57)	0.22 (0.13 to 0.37)
Wilczek et al. 2003[88]	119	8.6	85.5% (76.3% to 91.5%)	75.0% (58.9% to 86.1%)	88.8% (79.9% to 93.9%)	69.2% (53.5% to 81.3%)	3.42 (3.13 to 3.74)	0.19 (0.11 to 0.34)
Krishnaiah et al. 2003[89]	104	7.4	83.3% (64.0% to 93.1%)	82.5% (72.7% to 89.2%)	58.8% (42.2% to 73.6%)	94.3% (86.1% to 97.7%)	4.76 (3.98 to 5.69)	0.20 (0.08 to 0.50)
Obwegeser et al. 1999[90]	103	7.4	46.4% (34.0% to 59.3%)	87.2% (74.7% to 93.9%)	81.3% (64.6% to 91.0%)	57.7% (46.1% to 68.5%)	3.64 (2.75 to 4.82)	0.61 (0.47 to 0.80)
Koukouraki et al. 2001[91]	86	7.5	93.0% (85.5% to 96.7%)	83.3% (66.3% to 92.5%)	94.1% (86.9% to 97.4%)	80.6% (63.6% to 90.7%)	5.58 (5.27 to 5.91)	0.08 (0.04 to 0.18)
Schillaci et al. 1997[92]	66	8.8	85.7% (72.0% to 93.2%)	91.7% (73.9% to 97.5%)	94.7% (82.5% to 98.4%)	78.6% (60.4% to 89.6%)	10.29 (9.09 to 11.64)	0.16 (0.07 to 0.33)
Villanueva-Meyer et al. 1996[93]	66	8.6	82.9% (67.2% to 91.8%)	93.5% (79.1% to 98.1%)	93.5% (79.1% to 98.1%)	82.9% (67.2% to 91.8%)	12.84 (11.05 to 14.93)	0.18 (0.09 to 0.38)
Chen et al. 1997[94]	63	8.1	78.1% (61.2% to 88.8%)	90.3% (74.9% to 96.5%)	89.3% (72.6% to 96.1%)	80.0% (64.0% to 89.8%)	8.07 (6.72 to 9.70)	0.24 (0.12 to 0.47)

Appendix E. Evidence Tables (continued)

Study	N lesions	Quality score	Sensitivity (95% CI)	Specificity (95% CI)	Positive predictive value (95% CI)	Negative predictive value (95% CI)	Positive likelihood ratio (95% CI)	Negative likelihood ratio (95% CI)
Tiling et al. 1997[95]	56	8.3	87.9% (72.5% to 95.0%)	82.6% (62.7% to 92.8%)	87.9% (72.5% to 95.0%)	82.6% (62.7% to 92.8%)	5.05 (4.45 to 5.74)	0.15 (0.06 to 0.37)
Palmedo et al. 1996[96]	54	7.9	87.5% (68.8% to 95.5%)	86.7% (70.2% to 94.5%)	84.0% (65.2% to 93.4%)	89.7% (73.4% to 96.3%)	6.56 (5.64 to 7.63)	0.14 (0.05 to 0.42)
Leidenius et al. 2002[97]	49	7.9	77.4% (60.1% to 88.5%)	61.1% (38.6% to 79.6%)	77.4% (60.1% to 88.5%)	61.1% (38.6% to 79.6%)	1.99 (1.65 to 2.41)	0.37 (0.17 to 0.78)
Imbriaco et al. 2001[98]	49	7.6	80.8% (62.0% to 91.3%)	87.5% (68.8% to 95.5%)	87.5% (68.8% to 95.5%)	80.8% (62.0% to 91.3%)	6.46 (5.36 to 7.79)	0.22 (0.10 to 0.49)
Papantoniou et al. 2001[99]	41	7.9	88.5% (70.8% to 95.8%)	93.3% (69.9% to 98.6%)	95.8% (79.5% to 99.1%)	82.4% (58.8% to 93.6%)	13.27 (11.55 to 15.25)	0.12 (0.04 to 0.36)
Sanidas et al. 2003[100]	33	8.3	90.3% (74.9% to 96.5%)	80.0% (37.4% to 95.9%)	96.6% (82.6% to 99.2%)	57.1% (25.2% to 83.9%)	4.52 (4.02 to 5.07)	0.12 (0.04 to 0.39)
Gutfilen et al. 2001[101]	30	6.9	95.7% (78.7% to 99.0%)	42.9% (16.1% to 74.8%)	84.6% (66.3% to 93.7%)	75.0% (30.1% to 94.9%)	1.67 (1.53 to 1.83)	0.10 (0.01 to 0.83)
Yuen-Green et al. 1996[102]	21	7.9	83.3% (43.5% to 96.5%)	93.3% (69.9% to 98.6%)	83.3% (43.5% to 96.5%)	93.3% (69.9% to 98.6%)	12.50 (8.74 to 17.88)	0.18 (0.03 to 1.07)
Palmedo et al. 1997[58]	20	7.9	92.3% (66.4% to 98.3%)	85.7% (48.4% to 97.0%)	92.3% (66.4% to 98.3%)	85.7% (48.4% to 97.0%)	6.46 (5.52 to 7.56)	0.09 (0.01 to 0.60)
22 studies	3,793 lesions	Median 8.0 Moderate	Heterogeneous, no summary estimates calculated.					
Heterogeneity tests of D			I^2 = 69% Q = 67.23 p of Q = 0.0000000009					

D= ln of the diagnostic odds ratio

Table 36. Meta-regression of Studies of Scintimammography for Suspicious Breast Lesions

Study	D	Standard error of D	Year of publication	Quality score	Size of study	Prevalence of disease %	S	Tracer	Time elapsed
Sampalis et al. 2003[82]	4.38	2.09	2003	6	1243	16.17%	0.59	740 to 1,100	5
Khalkhali et al. 2002[83]	2.25	1.50	2002	8.3	580	39.93%	-0.42	740 to 1,100	5
Scopinaro et al. 1997[84]	3.91	1.98	1997	8.3	449	79.06%	-0.49	740	90
Tofani et al. 1999[85]	3.62	1.90	1999	8.3	300	72.67%	0.52	740	10
Mekhmandarov et al. 1998[86]	3.32	1.82	1998	8.8	140	60.71%	-0.13	740	15
Danielsson et al. 1999[87]	2.64	1.62	1999	8.6	121	71.07%	0.58	700	10
Wilczek et al. 2003[88]	2.81	1.68	2003	8.6	119	69.75%	0.68	700	10
Krishnaiah et al. 2003[89]	3.04	1.74	2003	7.4	104	23.08%	-0.01	740 to 1,100	1
Obwegeser et al. 1999[90]	1.71	1.31	1999	7.4	103	54.37%	-1.99	555 to 650	1
Koukouraki et al. 2001[91]	4.05	2.01	2001	7.5	86	74.14%	0.98	740	15
Schillaci et al. 1997[92]	3.92	1.98	1997	8.8	66	63.64%	-0.47	370	1
Villanueva-Meyer et al. 1996[93]	3.98	2.00	1996	8.6	66	53.03%	-0.96	740	15
Chen et al. 1997[94]	3.32	1.82	1997	8.1	63	50.79%	-0.87	740	10
Tiling et al. 1997[95]	3.35	1.83	1997	8.3	56	58.93%	0.41	740	5
Palmedo et al. 1996[96]	3.59	1.89	1996	7.9	54	44.44%	0.04	740	17
Leidenius et al. 2002[97]	1.61	1.27	2002	7.9	49	63.27%	0.76	740 to 1,100	20
Imbriaco et al. 2001[98]	3.18	1.78	2001	7.6	49	52.00%	-0.45	555	10
Papantoniou et al. 2001[99]	4.17	2.04	2001	7.9	41	63.41%	-0.36	740 to 925	15
Sanidas et al. 2003[100]	3.20	1.79	2003	8.3	33	86.11%	1.00	740	15

Appendix E. Evidence Tables (continued)

Study	D	Standard error of D	Year of publication	Quality score	Size of study	Prevalence of disease %	S	Tracer	Time elapsed
Gutfilen et al. 2001[101]	2.46	1.57	2001	6.9	30	76.67%	2.96	370	15
Yuen-Green et al. 1996[102]	3.57	1.89	1996	7.9	21	28.57%	-0.97	740	5
Palmedo et al. 1997[58]	3.59	1.89	1997	7.9	20	65.00%	0.65	740	5
p value			0.167	0.745	0.428	0.781	0.951	0.433 to 0.518	0.442
No model could be fitted with these variables that explained the heterogeneity.									

D = ln of diagnostic odds ratio
SE = standard error
S= ln of measure of threshold

Table 37. Meta-analysis of Studies of Scintimammography for Palpable Lesions

Study	N lesions	Quality score	Sensitivity (95% CI)	Specificity (95% CI)	Positive predictive value (95% CI)	Negative predictive value (95% CI)	Positive likelihood ratio (95% CI)	Negative likelihood ratio (95% CI)
Scopinaro et al. 1997[84]	283	8.3	97.3% (94.3% to 98.7%)	89.7% (79.1% to 95.1%)	97.3% (94.3% to 98.7%)	89.7% (79.1% to 95.1%)	9.41 (9.21 to 9.61)	0.03 (0.01 to 0.07)
Alonso et al. 2001[103]	245	7.9	83.1% (77.1% to 87.7%)	76.8% (64.2% to 85.8%)	92.4% (87.3% to 95.4%)	57.3% (46.0% to 67.9%)	3.58 (3.36 to 3.82)	0.22 (0.16 to 0.31)
Mekhmandarov et al. 1998[86]	85	8.8	95.1% (86.4% to 98.2%)	75.0% (55.0% to 87.8%)	90.6% (80.9% to 95.5%)	85.7% (65.2% to 94.8%)	3.80 (3.59 to 4.03)	0.07 (0.02 to 0.20)
Koukouraki et al. 2001[91]	78	7.5	94.0% (85.5% to 97.6%)	72.7% (43.4% to 90.0%)	95.5% (87.4% to 98.4%)	66.7% (39.0% to 86.0%)	3.45 (3.25 to 3.66)	0.08 (0.03 to 0.23)
Wilczek et al. 2003[88]	65	8.6	91.3% (79.5% to 96.5%)	63.2% (41.0% to 80.7%)	85.7% (73.2% to 92.8%)	75.0% (50.4% to 89.6%)	2.48 (2.27 to 2.71)	0.14 (0.05 to 0.37)
Krishnaiah et al. 2003[89]	59	7.4	87.5% (63.7% to 96.3%)	79.1% (64.7% to 88.5%)	60.9% (40.8% to 77.7%)	94.4% (81.7% to 98.3%)	4.18 (3.47 to 5.03)	0.16 (0.04 to 0.58)
Ambrus et al. 1997[104]	51	7.5	50.0% (35.2% to 64.8%)	90.9% (61.9% to 98.1%)	95.2% (77.0% to 99.0%)	33.3% (19.3% to 51.3%)	5.50 (4.03 to 7.50)	0.55 (0.38 to 0.79)
Burak et al. 1994[105]	41	7.9	88.9% (71.8% to 96.0%)	85.7% (59.8% to 95.7%)	92.3% (75.6% to 97.7%)	80.0% (54.7% to 92.7%)	6.22 (5.45 to 7.11)	0.13 (0.04 to 0.38)
Palmedo et al. 1996[106,107]	40	7.9	100.0% (83.5% to 99.8%)	78.9% (56.5% to 91.3%)	83.3% (64.0% to 93.1%)	100.0% (79.2% to 99.8%)	4.34 (4.06 to 4.64)	0.03 (0.00 to 0.48)
Chen et al. 2000[108]	38	8.8	77.8% (54.7% to 90.8%)	88.2% (65.4% to 96.5%)	87.5% (63.7% to 96.3%)	78.9% (56.5% to 91.3%)	6.61 (5.16 to 8.46)	0.25 (0.10 to 0.61)
Gutfilen et al. 2001[101]	27	6.9	95.7% (78.7% to 99.0%)	50.0% (15.4% to 84.6%)	91.7% (73.9% to 97.5%)	66.7% (21.0% to 93.3%)	1.91 (1.75 to 2.09)	0.09 (0.01 to 0.75)
11 studies	1,012 lesions	Median 7.9 Moderate	Heterogeneous, no summary estimates calculated.					
Heterogeneity tests of D			I^2 = 57% Q = 23.46 p of Q = 0.00916					

D = ln of the diagnostic odds ratio

Table 38. Meta-regression of Studies of Scintimammography for Palpable Lesions

Study	D	Standard error of D	Year of publication	Quality score	Size of study	Prevalence of disease %	S	Tracer	Time elapsed
Scopinaro et al. 1997[84]	5.61	0.58	1997	8.30	283	79.51%	1.43	740	90
Alonso et al. 2001[103]	2.75	0.37	2001	7.90	245	77.14%	0.41	740 to 1100	10
Mekhmandarov et al. 1998[86]	3.86	0.71	1998	8.80	85	71.76%	1.77	740	15
Koukouraki et al. 2001[91]	3.53	0.80	2001	7.50	78	85.90%	1.76	740	15
Wilczek et al. 2003[88]	2.76	0.68	2003	8.60	65	70.77%	1.73	700	10
Krishnaiah et al. 2003[89]	3.05	0.78	2003	7.40	59	27.12%	0.47	740 to 1100	1
Ambrus et al. 1997[104]	1.95	0.93	1997	7.50	51	78.43%	-1.95	900	5
Burak et al. 1994[105]	3.56	0.90	1994	7.90	41	65.85%	0.34	720	10
Palmedo et al. 1996[106,107]	4.95	1.53	1996	7.90	40	51.28%	2.48	740	18
Chen et al. 2000[108]	2.99	0.87	2000	8.80	38	51.43%	-0.65	740	15
Gutfilen et al. 2001[101]	2.71	1.23	2001	6.90	27	85.19%	2.71	370	15
p value			0.1910	0.4640	0.1770	0.809	0.177	0.422 to 0.961	0.0040
D = 2.81 + 0.033 time elapsed, p = 0.0040 95% confidence intervals: constant (2.18 to 3.43), coefficient (0.012 to 0.054)									

D = ln of diagnostic odds ratio
SE = standard error
S = ln of measure of threshold

Table 39. Meta-analysis of Studies of Scintimammography for Non-palpable Lesions

Study	N lesions	Quality score	Sensitivity (95% CI)	Specificity (95% CI)	Positive predictive value (95% CI)	Negative predictive value (95% CI)	Positive likelihood ratio (95% CI)	Negative likelihood ratio (95% CI)
Scopinaro et al. 1997[84]	166	8.3	62.3% (53.7% to 70.2%)	91.7% (78.0% to 97.0%)	96.4% (89.9% to 98.7%)	40.2% (30.3% to 51.1%)	7.48 (6.54 to 8.55)	0.41 (0.32 to 0.52)
Mekhmandarove et al. 1998[86]	55	8.8	54.2% (35.1% to 72.0%)	93.5% (79.1% to 98.1%)	86.7% (61.9% to 96.0%)	72.5% (57.1% to 83.8%)	8.40 (5.81 to 12.13)	0.49 (0.31 to 0.76)
Wilczek et al. 2003[88]	54	8.6	78.4% (62.7% to 88.5%)	88.2% (65.4% to 96.5%)	93.5% (79.1% to 98.1%)	65.2% (44.9% to 81.1%)	6.66 (5.62 to 7.89)	0.25 (0.13 to 0.46)
Krishnaiah et al. 2003[89]	45	7.4	75.0% (40.8% to 92.5%)	86.5% (71.9% to 94.0%)	54.5% (28.1% to 78.6%)	94.1% (80.7% to 98.2%)	5.55 (3.72 to 8.28)	0.29 (0.09 to 0.97)
Carril et al. 1997[109]	41	7.9	86.4% (66.5% to 95.1%)	57.9% (36.3% to 76.7%)	70.4% (51.5% to 84.0%)	78.6% (52.3% to 92.2%)	2.05 (1.74 to 2.42)	0.24 (0.08 to 0.72)
Koukouraki et al. 2001[91]	38	7.5	89.5% (68.4% to 96.8%)	89.5% (68.4% to 96.8%)	89.5% (68.4% to 96.8%)	89.5% (68.4% to 96.8%)	8.50 (7.29 to 9.92)	0.12 (0.03 to 0.44)
Aguilar et al. 2001[110]	37	8.2	78.9% (56.5% to 91.3%)	72.2% (49.1% to 87.3%)	75.0% (53.0% to 88.6%)	76.5% (52.6% to 90.2%)	2.84 (2.25 to 3.58)	0.29 (0.12 to 0.73)
Bekis et al. 2004[111]	35	8.3	84.6% (57.6% to 95.4%)	81.8% (61.3% to 92.5%)	73.3% (48.0% to 88.9%)	90.0% (69.7% to 97.0%)	4.65 (3.69 to 5.87)	0.19 (0.05 to 0.68)
Maffioli et al. 1996[112]	24	7.5	50.0% (26.9% to 73.1%)	90.0% (59.3% to 97.9%)	87.5% (52.6% to 97.4%)	56.3% (33.2% to 76.8%)	5.00 (2.96 to 8.44)	0.56 (0.32 to 0.98)
Palmedo et al. 1996[106,107]	14	8.3	25.0% (5.1% to 69.9%)	100.0% (71.7% to 99.7%)	100.0% (20.8% to 99.2%)	76.9% (49.6% to 91.6%)	6.60 (1.73 to 25.18)	0.73 (0.41 to 1.32)
10 studies	509 lesions	Median 8.3 Moderate	At mean threshold 68.7%	At mean threshold 84.8% At 95% sensitivity 39.2%	At mean threshold 85.7% At 95% sensitivity 67.4%	At mean threshold 67.2% At 95% sensitivity 54.1%	Heterogeneous, no summary estimate calculated	0.41 (0.34 to 0.49)

Heterogeneity tests	Cumulative meta-analysis, last three studies				
D		D		-LHR	Within 5% limits?
I^2 = 0%	New study	95% CI	Within 5% limits?	95% CI	
Q = 4.03	Bekis et al. 2004[111]	2.60 to 2.48	Yes	0.31 to 0.45	No
p of Q = 0.90925					
-LHR	Maffioli et al. 1996[112]	2.60 to 2.49	Yes	0.32 to 0.47	No
I^2 = 38.5%					
Q = 14.6					
p of Q = 0.10165					
+LHR	Palmedo et al. 1996[106,107]	2.57 to 2.47	Yes	0.34 to 0.49	No
I^2 = 57.2%					
Q = 229.1					
p of Q = 0.0000001					

		5% limits 2.68 to 2.42	Robust	5% limits 0.39 to 0.43	Not robust

D = ln of diagnostic odds ratio
-LHR = negative likelihood ratio
-lnLHR = ln of negative likelihood ratio
+lnLHR = ln of positive likelihood ratio

Table 40. Meta-analysis of Studies of Scintimammography for Non-palpable Lesions with Microcalcifications

Study	N lesions	Quality score	Sensitivity (95% CI)	Specificity (95% CI)	Positive predictive value (95% CI)	Negative predictive value (95% CI)	Positive likelihood ratio (95% CI)	Negative likelihood ratio (95% CI)
Fondrinier et al. 2004[113]	45	7.2	58.3% (38.8% to 75.4%)	81.0% (59.9% to 92.1%)	77.8% (54.7% to 90.8%)	63.0% (44.2% to 78.4%)	3.06 (2.18 to 4.29)	0.51 (0.31 to 0.86)
Maffioli et al. 1996[112]	21	7.5	53.8% (29.2% to 76.7%)	87.5% (52.6% to 97.4%)	87.5% (52.6% to 97.4%)	53.8% (29.2% to 76.7%)	4.31 (2.60 to 7.13)	0.53 (0.28 to 1.00)
Bekis et al. 2004[111]	13	8.3	66.7% (30.1% to 89.9%)	100.0% (64.0% to 99.6%)	100.0% (50.5% to 99.5%)	77.8% (45.1% to 93.3%)	10.29 (5.92 to 17.87)	0.38 (0.14 to 1.05)
3 studies	79 lesions	Median 7.5 Moderate	58.1% (43.3% to 72.9%)	86.1% (74.8% to 97.4%)	83.3% (72.2% to 94.5%)	63.3% (47.6% to 79.0%)	4.27 (3.47 to 5.26)	0.50 (0.32 to 0.78)

Heterogeneity tests	Cumulative meta-analysis, last three studies						
D I^2 = 0% Q = 0.83 p of Q = 0.66001	New study	Sensitivity 95% CI	Within 5% limits?	Specificity 95% CI	Within 5% limits?	pLHR 95% CI	nLHR 95% CI	Within 5% limits?
	Fondrinier et al. 2004[113]	38.6% to 78.1%	No	64.2% to 97.7%	No	2.2 to 4.2	0.27 to 0.97	No
-LHR I^2 = 0% Q = 0.317 p of Q = 0.8535	Maffioli et al. 1996[112]	40.8% to 72.7%	No	69.0% to 96.5%	No	2.6 to 4.4	0.32 to 0.86	No
+LHR I^2 = 0% Q = 13.45 p of Q = 1.000	Bekis et al. 2004[111]	43.4% to 72.9%	No	74.8% to 97.4%	No	3.5 to 5.3	0.32 to 0.78	No
		5% limits 55.5% to 61.0%	Not robust	5% limits 81.8% to 90.4%	Not robust	5% limits 4.1 to 4.5	5% limits 0.48 to 0.53	Not robust

Appendix E. Evidence Tables (continued)

Table 41. Meta-analysis of Studies of Scintimammography for Lesions Larger than 10 mm

Study	N lesions	Quality score	Sensitivity (95% CI)	Specificity (95% CI)	Positive predictive value (95% CI)	Negative predictive value (95% CI)	Positive likelihood ratio (95% CI)	Negative likelihood ratio (95% CI)
Tofani et al. 1999[85]	257	8.3	95.2% (91.2% to 97.4%)	79.4% (68.3% to 87.3%)	92.8% (88.2% to 95.6%)	85.7% (74.9% to 92.2%)	4.63 (4.48 to 4.78)	0.06 (0.03 to 0.11)
Imbriaco et al. 2001[98]	26	7.6	87.5% (63.7% to 96.3%)	80.0% (48.9% to 94.0%)	87.5% (63.7% to 96.3%)	80.0% (48.9% to 94.0%)	4.38 (3.64 to 5.27)	0.16 (0.04 to 0.59)
Gutfilen et al. 2001[101]	23	6.9	100.0% (83.5% to 99.8%)	33.3% (6.7% to 79.0%)	90.9% (72.0% to 97.3%)	100.0% (20.8% to 99.2%)	1.56 (1.46 to 1.67)	0.06 (0.00 to 1.30)
3 studies	306 lesions	Median 7.6 Moderate	95.1% (92.2% to 97.9%)	77.8% (68.7% to 86.8%)	92.2% (88.7% to 95.7%)	85.1% (77.4% to 92.9%)	Heterogeneous, no summary estimate calculated	0.07 (0.05 to 0.10)

Heterogeneity tests	Cumulative meta-analysis, last three studies						
D I^2 = 0% Q = 1.62 p of Q = 0.445	New study	Sensitivity 95% CI	Within 5% limits?	Specificity 95% CI	Within 5% limits?	nLHR 95% CI	Within 5% limits?
	Tofani et al. 1999[85]	92.2 to 98.3	Yes	69.8 to 89.0	No	0.04 to 0.09	No
-LHR I^2 = 0% Q = 1.61 p of Q = 0.447	Imbriaco et al. 2001[98]	91.5 to 97.7	Yes	70.5 to 88.4	No	0.05 to 0.10	No
+LHR I^2 = 88.2% Q = 829 p of Q = 0.0000000001	Gutfilen et al. 2001[101]	92.3 to 97.9	Yes	68.7 to 86.8	No	0.05 to 0.10	No
		5% limits 90.3 to 99.4	Robust	5% limits 73.9 to 81.7	Not robust	5% limits 0.067 to 0.074	Not robust

Table 42. Analysis of Studies of Scintimammography: SPECT vs. Planar Imaging

Study	N lesions	Quality score	False negatives on SPECT	False negatives on planar	Odds ratio (95% CI)	p value of difference	Conclusion
Obwegeser et al. 1999[90]	103	7.4	17	30	0.48 (0.25 to 0.94)	0.0327	SPECT better
Schillaci et al. 1997[92]	66	8.8	3	6	0.48 (0.11 to 2.0)	0.309	No statistically significant difference
Palmedo et al. 1996[106,107]	54	7.9	4	3	1.36 (0.29 to 6.36)	0.697	No statistically significant difference
Palmedo et al. 1997[58]	20	8.3	1	1	1.00 (0.058 to 17.12)	1.00	No statistically significant difference
4 studies	243 lesions	Median 8.1 Moderate					Not qualitatively robust No conclusion

Studies of MRI

Table 43. Included Studies of MRI

Study	N patients	Quality score	MRI parameters	Contrast agent	Patients	Mean age (range)	% 65 or older	% Female	Demographics
Bluemke et al. 2004[130]	1,004	7.8	1.5T T2 3D fat suppressed 3/20/4.5/45[a]	0.1 mmol/kg gadolinium chelate	Age 18 to 80 years, referred for breast biopsy due to abnormal mammogram (BIRADS 4 or 5), or a suspicious clinical or sonographic finding. Patients were excluded if pregnant or had a history of breast cancer.	53.2 (NR)	NR	NR	76% White 16.6% Black 38.4% Family history 36.2% Premenopausal
Huang et al. 2004[139]	50	7.1	1.5T T1 3D spoiled gradient-recalled echo 5/9/3.8/30[a]	0.1 mmol/kg gadodiamide	Referred for breast biopsy due to a finding of BIRADS 4 or 5 on screening mammography.	NR	NR	NR	NR
Bone et al. 2003[461]	97	8.2	1.5T T1 3D fast low angle shot 2.2/12/5/25[a] Patient prone	0.1 mmol/kg gadopenetate dimeglumine	Patients scheduled for surgery after physical exam, mammography, and fine needle aspiration.	54 (33 to 81)	NR	NR	NR
Hienisch et al. 2003[56]	36	7.2	T2 Dynamic 3D FFE sequence, fat suppressed 2.2/12/6/30[a] Patient prone	0.2 mmol/kg gadopenetate dimeglumine	Women with suspicious breast lesions detected by physical exam, mammography, and/or ultrasound, scheduled for biopsy, referred when there was time on the scanners. Pregnant women were excluded.	48.4 (25 to 77)	NR	100%	NR
Knopp et al. 2003[138]	47	8.3	1.5, 1.0, or 0.5T T1 3D spoiled gradient-recalled echo, no fat suppression 3/13/NR/10 to 35[a] Patient prone	0.1 mmol/kg gadopenetate dimeglumine	At least 18 years old, and had a mammographic examination within the previous 30 days that revealed an abnormality highly suspected of cancer so that the patient was highly likely to undergo either core or excisional biopsy. Pregnant or lactating patients were excluded.	54.9 (42 to 67)	NR	NR	NR

Appendix E. Evidence Tables (continued)

Study	N patients	Quality score	MRI parameters	Contrast agent	Patients	Mean age (range)	% 65 or older	% Female	Demographics
Walter et al. 2003[57]	44	7.9	1.5 or 1.0T T1 3D gradient echo 4/11/6.9/35[a] Patient prone	0.1 mmol/kg gadolinium-DTPA	Patients referred to the clinic for biopsy of suspicious lesions on the basis of mammography, ultrasound, or physical examination. Referred patients were chosen randomly from 550 possible patients to fill restricted scanner time.	52 (21 to 77)	NR	NR	NR
Del Maschio et al. 2002[135]	215	6.5	1.5 or 1.0T 3D gradient echo NR/NR/NR/NR[a]	0.1 mmol/kg gadoteridol	Patients with microcalcification foci identified by mammography as BIRADS 3-5, and scheduled for biopsy or surgery. Patients who were pregnant, lactating, or in severe kidney failure were excluded.	NR	NR	NR	NR
Wiberg et al. 2002[470]	97	7.6	1.5T T1 3D fast low angle shot 2.2/12/5/25[a] Patient prone	0.2 mmol/kg gadopentetate dimeglumine	Referred for breast biopsy after evaluation by physical exam, mammography, and fine needle aspiration/cytology.	54 (33 to 81)	NR	NR	NR
Brix et al. 2001[52]	14	8.3	1.5T 3D fast low angle shot 4/12/5/35[a] Patient prone	0.1 mmol/kg gadopenetate dimeglumine	Women with suspicious breast lesions detected by physical exam, mammography, and/or ultrasound, scheduled for biopsy, referred when there was time on the scanners. Patients with lesions smaller than 10 mm, elevated blood glucose, younger than 18 years of age, or pregnant were excluded.	49 (35 to 66)	NR	100%	NR
Cecil et al. 2001[134]	38	7.2	1.5T T2 3D fast spoiled gradient recalled echo, fat saturated, fat suppressed 2-3/9.3/2.2/4[a]	0.1 mmol/kg gadopenetate dimeglumine	Patients with either a palpable mass or abnormal mammographic findings.	49.8 (18 to 85)	NR	NR	NR
Imbriaco et al. 2001[98]	49	7.6	0.5T 3D gradient echo Patient prone	0.1 mmol/kg gadopenetate dimeglumine	Patients with a suspicious breast lesion detected either by physical examination or by mammography and ultrasound. Patients younger than 18 years of age, pregnant, lactating, or with a previous history of breast cancer were excluded.	49 (20 to 72)	8.1%	NR	NR

Appendix E. Evidence Tables (continued)

Study	N patients	Quality score	MRI parameters	Contrast agent	Patients	Mean age (range)	% 65 or older	% Female	Demographics
Malich et al. 2001[137]	94	7.9	1.5T T1 2D fast field echo 4/97/5/80[a] Patient prone	0.1 mmol/kg gadopenetate dimeglumine	Patients being evaluated for mammographic abnormalities.	NR	NR	NR	NR
Nakahara et al. 2001[136]	40	7.9	0.5T 3D spoiled gradient-recalled echo, fat saturated 1.5/60/9/45[a] Patient prone	0.1 mmol/kg gadopenetate dimeglumine	All patients who had significant microcalcifications detected by mammography between October 1994 and July 1998 who were sent for biopsy.	49.5 (27 to 76)	NR	NR	NR
Tiling et al. 1997[469]	82	8.3	1.5T 3D fast low angle shot NR/40/14/50[a] Patient prone	0.1 mmol/kg gadopenetate dimeglumine	Women with indeterminate mammograms and/or physical exams.	50 (22 to 80)	NR	NR	NR
Tiling et al. 1997[95]	56	7.4	1.5T T1 3D fast low angle shot NR/40/14/50[a] Patient prone	0.1 mmol/kg gadopenetate dimeglumine	Women with abnormal findings on mammography and/or physical examination who were scheduled for surgery.	53 (22 to 80)	NR	100%	46.4% White
Heiberg et al. 1996[131]	56	6.4	1.5T T1 and T2, 3D fast spoiled gradient recalled echo 3-4/10.6/2.2/20[a] Patient prone	0.1 mmol/kg gadopenetate dimeglumine	Patients scheduled for biopsy for a mammographic or palpable breast mass. First few patients enrolled had a minimal lesion size requirement, but this criterion was dropped later in the study.	NR (25 to 83)	NR	NR	NR
Obdeijn et al. 1996[132]	54	7.9	1.5T T1 Gradient echo scan with 2-D FLASH, not fat saturated, fat suppressed 4/290/5/NR[a] Patient prone	0.1 mmol/kg gadopenetate dimeglumine	Patients with clinically and/or mammographically suspicious breast lesions, who had been scheduled for surgery.	NR	NR	NR	NR

Appendix E. Evidence Tables (continued)

Study	N patients	Quality score	MRI parameters	Contrast agent	Patients	Mean age (range)	% 65 or older	% Female	Demographics
Palmedo et al. 1996[96]	56	7.9	1.5T T1 3D gradient echo 5/NR/NR/NR[a] Patient prone	0.2 mmol/kg gadopenetate dimeglumine	Women with a suspicious lesion detected by physical examination or by mammography. Patients with a prior or concurrent history of breast cancer were excluded.	58 (22 to 81)	NR	100%	NR
Hachiya et al. 1991[133]	52	7.5	0.5T T1 Gradient echo NR/50/14/50[a] Patient prone	0.1 mmol/kg gadolinium-DTPA	Patients with clinically palpable lesions.	NR (35 to 79)	NR	98.10%	NR

a. slice thickness mm/time to repetition ms/time to echo ms/flip angle degrees
NR = not reported

Table 44. Quality Assessment of Studies of MRI

Question	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	score
Study	consecutive	consistent	prospective	case control	funding	valid reference	gold standard	interreader	blinding	blinding	blinding	blinding	full testing	threshold	intervening	attrition	conclusions	discrepancy	standardized
Bluemke et al. 2004[130]	r	y	y	y	y	y	y	n	y	r	r	r	y	y	y	y	y	y	7.8
Huang et al. 2004[139]	r	y	y	y	r	y	y	r	y	r	r	r	y	r	y	y	y	y	7.1
Bone et al. 2003[461]	y	y	y	y	r	y	y	n	y	r	y	r	y	y	y	y	y	y	8.2
Hienisch et al. 2003[56]	r	y	y	y	r	y	y	n	y	r	n	r	y	y	y	y	y	y	7.2
Knopp et al. 2003[138]	y	y	y	y	r	y	y	r	y	r	y	r	y	y	y	y	y	y	8.3
Walter et al. 2003[57]	y	y	y	y	r	y	y	r	y	r	r	r	y	y	y	y	y	y	7.9
Del Maschio et al. 2002[135]	r	y	y	y	r	y	y	r	y	r	r	r	y	r	y	n	y	y	6.5
Wiberg et al. 2002[470]	y	y	y	y	r	y	y	n	y	r	n	r	y	y	y	y	y	y	7.6
Brix et al. 2001[52]	y	y	y	y	r	y	y	r	y	r	y	r	y	y	y	y	y	y	8.3
Cecil et al. 2001[134]	r	n	y	y	y	y	y	r	y	r	n	r	y	y	y	y	y	y	7.2
Imbriaco et al. 2001[98]	y	y	y	y	r	y	y	n	y	r	n	r	y	y	y	y	y	y	7.6
Malich et al. 2001[137]	y	y	y	y	r	y	y	r	y	r	r	r	y	y	y	y	y	y	7.9
Nakahara et al. 2001[136]	y	y	y	y	r	y	y	r	y	r	r	r	y	y	y	y	y	y	7.9
Tiling et al. 1997[95]	r	y	y	y	r	y	y	y	y	r	y	r	y	y	y	y	y	y	8.3
Tiling et al. 1997[469]	r	y	y	y	r	y	y	r	y	r	y	r	y	y	y	n	y	y	7.4
Heiberg et al. 1996[131]	r	n	y	y	n	y	y	r	y	r	r	r	y	r	y	y	y	y	6.4
Obdeijn et al. 1996[132]	r	y	y	y	r	y	y	r	y	r	y	r	y	y	y	y	y	y	7.9
Palmedo et al. 1996[96]	r	y	y	y	r	y	y	r	y	r	y	r	y	y	y	y	y	y	7.9
Hachiya et al. 1991[133]	r	y	y	y	r	y	y	y	y	r	r	r	y	r	y	y	y	y	7.5

y = yes
n = no
r = not reported

Table 45. Diagnostic Test Characteristics of MRI

Study	N lesions	Patient subgroup	Prevalence	True positive	False negative	False positive	True negative	Sensitivity (95% CI)	Specificity (95% CI)	Positive predictive value (95% CI)	Negative predictive value (95% CI)	Positive likelihood ratio (95% CI)	Negative likelihood ratio (95% CI)
Bluemke et al. 2004[130]	821	All	49.3	356.27	48.12	135.81	280.79	88.1% (84.6% to 91.1%)	67.4% (62.7% to 71.9%)	72.4% (68.2% to 76.3%)	85.4% (81.1% to 89.0%)	2.70 (2.61 to 2.80)	0.18 (0.13 to 0.23)
	346	Premeno-pausal	41.7	123.07	21.04	68.04	133.85	85.4% (78.6% to 90.7%)	66.3% (59.4% to 71.2%)	64.4% (57.2% to 71.2%)	86.5% (80.0% to 91.4%)	2.53 (2.37 to 2.71)	0.22 (0.15 to 0.33)
	474	Post meno-pausal	54.9	233.01	27.05	68.04	145.91	89.6% (85.3% to 93.0%)	68.2% (61.5% to 74.4%)	77.4% (72.3% to 82.0%)	84.4% (78.1% to 89.5%)	2.82 (2.70 to 2.94)	0.15 (0.11 to 0.22)
	345	Palpable lesions	61.7	194.03	18.96	50.96	81.06	91.1% (86.4% to 94.5%)	61.4% (52.5% to 69.7%)	79.2% (73.6% to 84.1%)	81.0% (71.9% to 88.2%)	2.36 (2.26 to 2.46)	0.14 (0.09 to 0.23)
	474	Non-palpable lesions	40.3	161.93	29.02	84.91	198.13	84.8% (78.9% to 89.6%)	70.0% (64.3% to 75.2%)	65.6% (59.3% to 71.5%)	87.2% (82.2% to 91.3%)	2.83 (2.66 to 3.00)	0.22 (0.15 to 0.31)
	300	Micro-calcifica-tions	42.3	106.01	20.95	42.05	130.99	83.5% (75.8% to 89.5%)	75.7% (68.6% to 81.9%)	71.6% (63.6% to 78.7%)	86.2% (79.7% to 91.2%)	3.44 (3.18 to 3.71)	0.22 (0.15 to 0.33)
	470	No micro-calcifica-tions	54.6	231.85	24.9	84.02	129.23	90.3% (86.0% to 93.6%)	60.6% (53.7% to 67.2%)	73.4% (68.2% to 78.2%)	83.8% (77.0% to 89.2%)	2.29 (2.20 to 2.39)	0.16 (0.11 to 0.24)
	170	First degree relatives with history of breast cancer	55.3	81.09	12.98	23.01	52.92	86.2% (77.5% to 92.4%)	69.7% (58.1% to 79.8%)	77.9% (68.7% to 85.4%)	80.3% (68.7% to 89.1%)	2.84 (2.62 to 3.08)	0.20 (0.12 to 0.34)
	145	Other relatives with history of breast cancer	45.7	59.7	6.63	31.86	46.81	90.9% (81.3% to 96.6%)	59.5% (47.9% to 70.4%)	65.2% (54.6% to 74.9%)	88.7% (77.0% to 95.7%)	2.22 (2.05 to 2.41)	0.17 (0.08 to 0.35)

Study	N lesions	Patient subgroup	Prevalence	True positive	False negative	False positive	True negative	Sensitivity (95% CI)	Specificity (95% CI)	Positive predictive value (95% CI)	Negative predictive value (95% CI)	Positive likelihood ratio (95% CI)	Negative likelihood ratio (95% CI)
	496	No relatives with history of breast cancer	48.9	214.77	27.91	79.03	174.28	88.5% (83.8% to 92.2%)	68.8% (62.7% to 74.4%)	73.1% (67.7% to 78.1%)	86.1% (80.6% to 90.6%)	2.84 (2.71 to 2.97)	0.17 (0.12 to 0.24)
	79	Dense breast tissue	46.8	32.01	5	17.01	24.99	86.5% (71.2% to 95.5%)	59.5% (43.3% to 74.4%)	65.3% (50.4% to 78.3%)	83.3% (65.3% to 94.4%)	2.14 (1.88 to 2.43)	0.23 (0.10 to 0.53)
	106	Mostly fatty breast tissue	50.9	48.98	5.02	25.01	26.99	90.7% (79.7% to 96.9%)	51.9% (37.6% to 66.0%)	66.2% (54.3% to 76.6%)	84.4% (67.2% to 94.7%)	1.89 (1.73 to 2.05)	0.18 (0.07 to 0.43)
Huang et al. 2004[139]	50	BIRADS 4 or 5	36.0	18	0	12	20	100.0% (82.0% to 99.8%)	62.5% (45.2% to 77.0%)	60.0% (42.3% to 75.3%)	100.0% (83.5% to 99.8%)	2.57 (2.39 to 2.77)	0.04 (0.00 to 0.66)
Bone et al. 2003[461]	111	Positive on FNA	71.2	74	5	17	15	93.7% (85.9% to 97.2%)	46.9% (30.9% to 63.5%)	81.3% (72.1% to 87.9%)	75.0% (53.0% to 88.6%)	1.76 (1.66 to 1.87)	0.14 (0.05 to 0.34)
	40	Lesions ≤10 mm, positive on FNA	50.0	15	5	11	9	75.0% (53.0% to 88.6%)	45.0% (25.9% to 65.8%)	57.7% (39.0% to 74.4%)	64.3% (38.8% to 83.5%)	1.36 (1.06 to 1.76)	0.56 (0.23 to 1.37)
	71	Lesions >10 mm, positive by FNA	83.1	59	0	6	6	100.0% (93.7% to 99.9%)	50.0% (25.5% to 74.5%)	90.8% (81.2% to 95.6%)	100.0% (60.4% to 99.6%)	1.98 (1.94 to 2.03)	0.02 (0.00 to 0.28)
Hienisch et al. 2003[56]	40	All	62.5	23	2	4	11	92.0% (74.8% to 97.6%)	73.3% (48.0% to 88.9%)	85.2% (67.4% to 93.9%)	84.6% (57.6% to 95.4%)	3.45 (3.07 to 3.87)	0.11 (0.03 to 0.43)
Knopp et al. 2003[138]	61	BIRADS 4-5	78.7	34	14	3	10	70.8% (56.8% to 81.7%)	76.9% (49.6% to 91.6%)	91.9% (78.5% to 97.1%)	41.7% (24.6% to 61.2%)	3.07 (2.56 to 3.68)	0.38 (0.22 to 0.65)
Walter et al. 2003[57]	42	All	45.2	17	2	6	17	89.5% (68.4% to 96.8%)	73.9% (53.4% to 87.3%)	73.9% (53.4% to 87.3%)	89.5% (68.4% to 96.8%)	3.43 (2.94 to 4.00)	0.14 (0.04 to 0.54)

Appendix E. Evidence Tables (continued)

Study	N lesions	Patient subgroup	Prevalence	True positive	False negative	False positive	True negative	Sensitivity (95% CI)	Specificity (95% CI)	Positive predictive value (95% CI)	Negative predictive value (95% CI)	Positive likelihood ratio (95% CI)	Negative likelihood ratio (95% CI)
Del Maschio et al. 2002[135]	134	Micro-calcifica-tions	66.0	77	10	16	32	88.5% (80.1% to 93.6%)	66.7% (52.5% to 78.3%)	82.8% (73.8% to 89.1%)	76.2% (61.4% to 86.4%)	2.66 (2.46 to 2.86)	0.17 (0.09 to 0.32)
Wiberg et al. 2002[470]	114	Positive by FNA	71.9	77	5	17	15	93.9% (86.4% to 97.3%)	46.9% (30.9% to 63.5%)	81.9% (72.9% to 88.3%)	75.0% (53.0% to 88.6%)	1.77 (1.67 to 1.87)	0.13 (0.05 to 0.33)
	32	Postiive by FNA, dense breast tissue	56.3	17	1	9	5	94.4% (73.9% to 98.8%)	35.7% (16.5% to 61.2%)	65.4% (46.2% to 80.5%)	83.3% (43.5% to 96.5%)	1.47 (1.31 to 1.64)	0.16 (0.02 to 1.18)
Brix et al. 2001[52]	13	Lesions >10 mm	69.2	8	1	2	2	88.9% (56.2% to 97.6%)	50.0% (15.4% to 84.6%)	80.0% (48.9% to 94.0%)	66.7% (21.0% to 93.3%)	1.78 (1.41 to 2.24)	0.22 (0.03 to 1.80)
Cecil et al. 2001[134]	38	All	60.5	21	2	3	12	91.3% (73.0% to 97.4%)	80.0% (54.7% to 92.7%)	87.5% (68.8% to 95.5%)	85.7% (59.8% to 95.7%)	4.57 (4.02 to 5.18)	0.11 (0.03 to 0.42)
	32	Younger than age 65	59.4	19	0	3	10	100.0% (82.8% to 99.8%)	76.9% (49.6% to 91.6%)	86.4% (66.5% to 95.1%)	100.0% (71.7% to 99.7%)	3.90 (3.64 to 4.18)	0.03 (0.00 to 0.52)
Imbriaco et al. 2001[98]	49	All	51.0	24	1	6	18	96.0% (80.2% to 99.1%)	75.0% (55.0% to 87.8%)	80.0% (62.6% to 90.4%)	94.7% (75.1% to 98.8%)	3.84 (3.54 to 4.16)	0.05 (0.01 to 0.37)
	45	Younger than age 65	53.3	23	1	6	15	95.8% (79.5% to 99.1%)	71.4% (50.0% to 86.0%)	79.3% (61.5% to 90.0%)	93.8% (71.4% to 98.6%)	3.35 (3.09 to 3.65)	0.06 (0.01 to 0.40)
	23	Lesions ≤10 mm	39.1	9	0	3	11	100.0% (69.5% to 99.7%)	78.6% (52.3% to 92.2%)	75.0% (46.7% to 90.8%)	100.0% (73.6% to 99.7%)	4.07 (3.53 to 4.69)	0.07 (0.00 to 0.99)
	26	Lesions >10 mm	61.5	15	1	3	7	93.8% (71.4% to 98.6%)	70.0% (39.6% to 88.9%)	83.3% (60.6% to 93.9%)	87.5% (52.6% to 97.4%)	3.13 (2.75 to 3.55)	0.09 (0.01 to 0.62)
Malich et al. 2001[137]	90	BIRADS 4-5	50.0	53	1	7	29	98.1% (90.1% to 99.6%)	80.6% (64.9% to 90.1%)	88.3% (77.7% to 94.1%)	96.7% (83.1% to 99.3%)	5.05 (4.87 to 5.24)	0.02 (0.00 to 0.16)

Study	N lesions	Patient subgroup	Prevalence	True positive	False negative	False positive	True negative	Sensitivity (95% CI)	Specificity (95% CI)	Positive predictive value (95% CI)	Negative predictive value (95% CI)	Positive likelihood ratio (95% CI)	Negative likelihood ratio (95% CI)
Nakahara et al. 2001[136]	40	Micro-calcifica-tions	60.0	18	2	1	19	90.0% (69.7% to 97.0%)	95.0% (76.1% to 98.9%)	94.7% (75.1% to 98.8%)	90.5% (70.9% to 97.1%)	18.00 (15.55 to 20.83)	0.11 (0.03 to 0.39)
Tiling et al. 1997[469]	68	Indeter-minate mammo-gram or physical exam	36.8	14	11	9	34	56.0% (37.1% to 73.3%)	79.1% (64.7% to 88.5%)	60.9% (40.8% to 77.7%)	75.6% (61.3% to 85.7%)	2.68 (1.89 to 3.79)	0.56 (0.35 to 0.89)
Tiling et al. 1997[95]	56	All	58.9	30	3	11	12	90.9% (76.3% to 96.7%)	52.2% (33.0% to 70.7%)	73.2% (58.0% to 84.2%)	80.0% (54.7% to 92.7%)	1.90 (1.71 to 2.12)	0.17 (0.06 to 0.55)
Heiberg et al. 1996[131]	81	All	25.9	21	0	16	44	100.0% (84.2% to 99.8%)	73.3% (60.9% to 82.8%)	56.8% (40.9% to 71.3%)	100.0% (91.8% to 99.9%)	3.61 (3.39 to 3.85)	0.03 (0.00 to 0.48)
Obdeijn et al. 1996[132]	54	All	61.1	30	3	7	14	90.9% (76.3% to 96.7%)	66.7% (45.3% to 82.7%)	81.1% (65.7% to 90.4%)	82.4% (58.8% to 93.6%)	2.73 (2.45 to 3.04)	0.14 (0.04 to 0.42)
Palmedo et al. 1996[96]	56	All	48.2	25	2	23	6	92.6% (76.4% to 97.8%)	20.7% (10.0% to 38.5%)	52.1% (38.3% to 65.5%)	75.0% (40.8% to 92.5%)	1.17 (1.05 to 1.30)	0.36 (0.08 to 1.62)
	43	Palpable lesions	51.2	20	2	18	3	90.9% (72.0% to 97.3%)	14.3% (5.2% to 34.8%)	52.6% (37.3% to 67.5%)	60.0% (23.3% to 87.9%)	1.06 (0.93 to 1.21)	0.64 (0.12 to 3.44)
	13	Non-palpable lesions	38.5	5	0	4	4	100.0% (56.0% to 99.6%)	50.0% (21.7% to 78.3%)	55.6% (26.8% to 80.9%)	100.0% (50.5% to 99.5%)	1.83 (1.44 to 2.33)	0.17 (0.01 to 2.56)
Hachiya et al. 1991[133]	52	All	73.1	36	2	0	14	94.7% (82.5% to 98.4%)	100.0% (78.0% to 99.8%)	100.0% (90.1% to 99.9%)	87.5% (63.7% to 96.3%)	28.08 (25.86 to 30.48)	0.07 (0.02 to 0.22)

FNA = fine needle aspiration

Appendix E. Evidence Tables (continued)

Table 46. Meta-analysis of Studies of MRI for Suspicious Breast Lesions

Study	N lesions	Quality score	Sensitivity (95% CI)	Specificity (95% CI)	Positive predictive value (95% CI)	Negative predictive value (95% CI)	Positive likelihood ratio (95% CI)	Negative likelihood ratio (95% CI)
Bluemke et al. 2004[130]	821	7.8	88.1% (84.6% to 91.1%)	67.4% (62.7% to 71.9%)	72.4% (68.2% to 76.3%)	85.4% (81.1% to 89.0%)	2.70 (2.61 to 2.80)	0.18 (0.13 to 0.23)
Heiberg et al. 1996[131]	81	6.4	100.0% (84.2% to 99.8%)	73.3% (60.9% to 82.8%)	56.8% (40.9% to 71.3%)	100.0% (91.8% to 99.9%)	3.61 (3.39 to 3.85)	0.03 (0.00 to 0.48)
Tiling et al. 1997[95]	56	7.4	90.9% (76.3% to 96.7%)	52.2% (33.0% to 70.7%)	73.2% (58.0% to 84.2%)	80.0% (54.7% to 92.7%)	1.90 (1.71 to 2.12)	0.17 (0.06 to 0.55)
Palmedo et al. 1996[96]	56	7.9	92.6% (76.4% to 97.8%)	20.7% (10.0% to 38.5%)	52.1% (38.3% to 65.5%)	75.0% (40.8% to 92.5%)	1.17 (1.05 to 1.30)	0.36 (0.08 to 1.62)
Obdeijn et al. 1996[132]	54	7.9	90.9% (76.3% to 96.7%)	66.7% (45.3% to 82.7%)	81.1% (65.7% to 90.4%)	82.4% (58.8% to 93.6%)	2.73 (2.45 to 3.04)	0.14 (0.04 to 0.42)
Hachiya et al. 1991[133]	52	7.5	94.7% (82.5% to 98.4%)	100.0% (78.0% to 99.8%)	100.0% (90.1% to 99.9%)	87.5% (63.7% to 96.3%)	28.08 (25.86 to 30.48)	0.07 (0.02 to 0.22)
Imbracio et al. 2001[98]	49	7.6	96.0% (80.2% to 99.1%)	75.0% (55.0% to 87.8%)	80.0% (62.6% to 90.4%)	94.7% (75.1% to 98.8%)	3.84 (3.54 to 4.16)	0.05 (0.01 to 0.37)
Walter et al. 2003[57]	42	7.9	89.5% (68.4% to 96.8%)	73.9% (53.4% to 87.3%)	73.9% (53.4% to 87.3%)	89.5% (68.4% to 96.8%)	3.43 (2.94 to 4.00)	0.14 (0.04 to 0.54)
Hienisch et al. 2003[56]	40	7.2	92.0% (74.8% to 97.6%)	73.3% (48.0% to 88.9%)	85.2% (67.4% to 93.9%)	84.6% (57.6% to 95.4%)	3.45 (3.07 to 3.87)	0.11 (0.03 to 0.43)
Cecil et al. 2001[134]	38	7.2	91.3% (73.0% to 97.4%)	80.0% (54.7% to 92.7%)	87.5% (68.8% to 95.5%)	85.7% (59.8% to 95.7%)	4.57 (4.02 to 5.18)	0.11 (0.03 to 0.42)
10 studies	1,289 lesions	Median 7.6 Moderate	At mean threshold 92.5%	At mean threshold 72.4% At 95% sensitivity 62.8%	At mean threshold 77.2% At 95% sensitivity 72.1%	At mean threshold 90.5% At 95% sensitivity 92.5%	Heterogeneous, no summary estimate calculated	0.16 (0.13 to 0.19)

Heterogeneity tests	Cumulative meta-analysis (last three studies)				
D I^2 = 34% Q = 13.56 p of Q = 0.13877	New study	D 95% CI	Within 5% limits?	-LHR 95% CI	Within 5% limits?
	Walter et al. 2003[57]	2.84 to 2.88	Yes	0.14 to 0.20	No
+lnLHR I^2 = 97.0% Q = 3240 p of Q = 0.00000001	Hienisch et al. 2003[56]	2.86 to 2.90	Yes	0.14 to 0.19	No

-lnLHR I^2 = 0% Q = 7.0 p of Q = 0.63717	Cecil et al. 2001[134]	2.88 to 2.92	Yes	0.13 to 0.19	No
		5% limits 2.76 to 3.04	Stable	5% limits 0.15 to 0.17	Not stable

D = ln of diagnostic odds ratio

Table 47. Meta-analysis of Studies of MRI for Lesions with Microcalcifications

Study	N lesions	Quality score	Sensitivity (95% CI)	Specificity (95% CI)	Positive predictive value (95% CI)	Negative predictive value (95% CI)	Positive likelihood ratio (95% CI)	Negative likelihood ratio (95% CI)
Bluemke et al. 2004[130]	300	7.8	83.5% (75.8% to 89.5%)	75.7% (68.6% to 81.9%)	71.6% (63.6% to 78.7%)	86.2% (79.7% to 91.2%)	3.44 (3.18 to 3.71)	0.22 (0.15 to 0.33)
Del Maschio et al. 2002[135]	134	6.5	88.5% (80.1% to 93.6%)	66.7% (52.5% to 78.3%)	82.8% (73.8% to 89.1%)	76.2% (61.4% to 86.4%)	2.66 (2.46 to 2.86)	0.17 (0.09 to 0.32)
Nakahara et al. 2001[136]	40	7.9	90.0% (69.7% to 97.0%)	95.0% (76.1% to 98.9%)	94.7% (75.1% to 98.8%)	90.5% (70.9% to 97.1%)	18.00 (15.55 to 20.83)	0.11 (0.03 to 0.39)
3 studies	474 lesions	median 7.8 Moderate	Summary estimate 85.9% (81.5% to 90.4%)	Summary estimate 75.5% (70.1% to 80.9%)	Summary estimate 77.3% (71.9% to 82.7%)	Summary estimate 84.7% (80.1% to 89.2%)	Heterogeneous, no summary estimate calculated	Summary estimate 0.20 (0.15 to 0.25)

Heterogeneity tests	Cumulative meta-analysis						
D I^2 = 28% Q = 2.79 p of Q = 0.24747	New study	Sensitivity 95% CI	Within 5% limits?	Specificity 95% CI	Within 5% limits?	-LHR 95%CI	Within 5% limits?
	Bluemke et al. 2004[130]	77.0 to 90.0	No	69.3 to 82.1	No	0.16 to 0.33	No
+lnLHR I^2 = 81.43% Q = 527.6 p of Q = 0.00000001	Del Maschio et al. 2002[135]	80.8 to 90.2	No	67.9 to 79.5	No	0.16 to 0.27	No
-lnLHR I^2 = 0.0% Q = 1.29 p of Q = 0.524526	Nakahara et al. 2001[136]	81.5 to 90.4	No	70.1 to 80.9	No	0.15 to 0.25	No
		5% limits 81.6 to 90.2	Not stable	5% limits 71.7 to 79.3	Not stable	5% limits 0.19 to 0.21	Not stable

D = ln diagnostic odds ratio
+lnLHR = ln of positive likelihood ratio
-lnLHR = ln of negative likelihood ratio

Table 48. Meta-analysis of Studies of MRI for Lesions of BIRADS 4 or 5

Study	N lesions	Quality score	Sensitivity (95% CI)	Specificity (95% CI)	Positive predictive value (95% CI)	Negative predictive value (95% CI)	Positive likelihood ratio (95% CI)	Negative likelihood ratio (95% CI)
Malich et al. 2001[137]	90	7.9	98.1% (90.1% to 99.6%)	80.6% (64.9% to 90.1%)	88.3% (77.7% to 94.1%)	96.7% (83.1% to 99.3%)	5.05 (4.87 to 5.24)	0.02 (0.00 to 0.16)
Knopp et al. 2003[138]	61	8.3	70.8% (56.8% to 81.7%)	76.9% (49.6% to 91.6%)	91.9% (78.5% to 97.1%)	41.7% (24.6% to 61.2%)	3.07 (2.56 to 3.68)	0.38 (0.22 to 0.65)
Huange et al. 2004[139]	50	7.1	100.0% (82.0% to 99.8%)	62.5% (45.2% to 77.0%)	60.0% (42.3% to 75.3%)	100.0% (83.5% to 99.8%)	2.57 (2.39 to 2.77)	0.04 (0.00 to 0.66)
3 studies	201 lesions	Median 7.9 Moderate	Heterogeneous, no summary estimates calculated.					
Heterogeneity tests			**D** I^2 = 70% Q = 7.12 p of Q = 0.02843				**+lnLHR** I^2 = 63.97% Q = 271.98 p of Q = 0.00000001	**-lnLHR** I^2 = 78.6% Q = 9.36 p of Q = 0.00927

D = ln diagnostic odds ratio
+lnLHR = ln of positive likelihood ratio
-lnLHR = ln of negative likelihood ratio

Studies of Ultrasound

Table 49. Included Studies of Ultrasound

Study	N patients	Quality score	US parameters	Patients	Age	% 65 or older	% Female
Chen et al. 2004[191]	1,203	6.9	Aloka SSD-2000 or SSD-5500, 7.5 or 10 MHz linear array	Women with palpable breast lesions	Range 14 to 83	Not reported	100%
Meyberg-Solomayer et al. 2004[189]	65	7.4	HDI 3000 or Voluson 730, 5 to 12 MHz or 5 to 10 MHz linear array	Women with breast lesions	Mean 54 Range 16 to 96	Not reported	100%
Malich et al. 2001[137]	94	7.9	HDI 5000, 7.5 to 10 MHz	Patients being evaluated for mammographic abnormalities	Not reported	Not reported	Not reported
Chao et al. 1999[190]	3,050	7.5	Aloka SSD-2000 or SSD-5500, 7.5 MHz linear array	Patients with solid breast lesions	Mean 38.7 Range 14 to 86	Not reported	Not reported
Perre et al. 1994[192]	380	7.4	Toshiba SSA-270-A or Technicare Autosector IV, 7.5 MHz linear array	Women with palpable breast lesions	Median 49.3 Range 13.7 to 98.8	Not reported	100%
McNicholas et al. 1993[194]	203	7.8	Acuson 128, 7 MHz	Women with palpable breast lesions	Mean 42 Range 17 to 82	Not reported	100%
Hachiya et al. 1991[133]	52	7.1	Hitachi EUB, 7.5 MHz	Patients with palpable lesions	Range 35 to 79	Not reported	98.10%
van Oord et al. 1991[193]	305	7.2	Diasonic DR F 400, 10 MHz	Women with palpable breast lesions	Mean 48 Range 18 to 88	Not reported	100%

Appendix E. Evidence Tables (continued)

Table 50. Quality Assessment of Studies of Ultrasound

Question	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	score
Study	consecutive	consistent	prospective	Case control	funding	valid reference	gold standard	interreader	blinding	blinding	blinding	blinding	full testing	threshold	intervening	attrition	conclusions	discrepancy	standardized
Chen et al. 2004[191]	r	y	y	y	r	y	y	n	y	r	r	r	y	r	y	y	y	y	6.9
Meyberg-Solomayer et al. 2004[189]	r	y	y	y	r	y	y	n	y	r	r	r	y	y	y	y	y	y	7.4
Malich et al. 2001[137]	y	y	y	y	r	y	y	r	y	r	r	r	y	y	y	y	y	y	7.9
Chao et al. 1999[190]	r	y	y	y	r	y	y	r	y	r	r	r	y	y	y	y	y	y	7.5
Perre et al. 1994[192]	r	y	y	y	r	y	y	n	y	r	r	r	y	y	y	y	y	y	7.4
McNicholas et al. 1993[194]	y	y	y	y	r	y	y	n	y	r	r	r	y	y	y	y	y	y	7.8
Hachiya et al. 1991[133]	r	y	y	y	r	y	y	y	r	r	r	r	y	r	y	y	y	y	7.1
van Oord et al. 1991[193]	r	y	y	y	r	y	y	n	y	r	y	r	y	y	y	n	y	y	7.2

y = yes
n = no
r = not reported

Table 51. Diagnostic Test Characteristics of Ultrasound

Study	N lesions	Patient subgroup	Prevalence	True positive	False negative	False positive	True negative	Sensitivity (95% CI)	Specificity (95% CI)	Positive predictive value (95% CI)	Negative predictive value (95% CI)	Positive likelihood ratio (95% CI)	Negative likelihood ratio (95% CI)
Chen et al. 2004[191]	1,203	Palpable lesions	32.5%	310	81	87	725	79.3% (75.0% to 83.0%)	89.3% (87.0% to 91.2%)	78.1% (73.8% to 81.9%)	90% (87.7% to 91.8%)	7.4 (7.1 to 7.8)	0.23 (0.19 to 0.28)
	135	Palpable lesion 1 cm or smaller	28.9%	17	22	11	85	43.6% (29.4% to 59.0%)	88.5% (80.5% to 93.4%)	60.7% (42.4% to 76.3%)	79.4% (70.7% to 85.9%)	3.8 (2.7 to 5.4)	0.64 (0.48 to 0.85)
	567	Palpable lesion 1.1 to 2 cm	27.5%	114	42	35	376	73.1% (65.6% to 79.4%)	91.5% (88.4% to 93.8%)	76.5% (69.0% to 82.6%)	90% (86.7% to 92.5%)	8.6 (7.8 to 9.5)	0.29 (0.23 to 0.38)
	501	Palpable lesion larger than 2 cm	39.1%	179	17	41	264	91.3% (86.5% to 94.5%)	86.6% (82.3% to 90.0%)	81.4% (75.7% to 86.0%)	94% (90.5% to 96.2%)	6.8 (6.5 to 7.1)	0.10 (0.06 to 0.16)
Meyberg-Solomayer et al. 2004[189]	65	All	64.6%	42	0	10	13	100.0% (91.4% to 99.9%)	56.5% (36.8% to 74.3%)	80.8% (68.0% to 89.1%)	100.0% (76.7% to 99.8%)	2.3 (2.2 to 2.3)	0.02 (0.00 to 0.33)
Malich et al. 2001[137]	100	All	62.0%	48	14	4	34	77.4% (65.5% to 86.0%)	89.5% (75.7% to 95.7%)	92.3% (81.7% to 96.9%)	70.8% (56.8% to 81.7%)	7.4 (6.4 to 8.4)	0.25 (0.16 to 0.41)
Chao et al. 1999[190]	3,093	All	23.7%	631	102	800	1560	86.1% (83.4% to 88.4%)	66.1% (64.2% to 68.0%)	44.1% (41.5% to 46.7%)	93.9% (92.6% to 94.9%)	2.5 (2.5 to 2.6)	0.21 (0.18 to 0.25)
Perre et al. 1994[192]	400	Palpable lesions	43.5%	170	4	15	211	97.7% (94.2% to 99.1%)	93.4% (89.3% to 95.9%)	91.9% (87.0% to 95.0%)	98.1% (95.3% to 99.2%)	14.7 (14.4 to 15.1)	0.02 (0.01 to 0.06)
McNicholas et al. 1993[194]	203	Palpable lesions	26.6%	48	6	19	130	88.9% (77.7% to 94.7%)	87.2% (80.9% to 91.6%)	71.6% (59.9% to 81.0%)	95.6% (90.7% to 97.9%)	7.0 (6.3 to 7.7)	0.13 (0.06 to 0.27)
Hachiya et al. 1991[133]	52	Palpable lesions	73.1%	37	1	0	14	97.4% (86.3% to 99.4%)	100.0% (78.0% to 99.8%)	100.0% (90.3% to 99.9%)	93.3% (69.9% to 98.6%)	28.9 (27.1 to 30.7)	0.04 (0.01 to 0.19)
van Oord et al. 1991[193]	232	Palpable lesions	32.8%	75	1	51	105	98.7% (92.8% to 99.7%)	67.3% (59.6% to 74.2%)	59.5% (50.8% to 67.7%)	99.1% (94.8% to 99.8%)	3.0 (2.9 to 3.1)	0.02 (0.00 to 0.14)

Table 52. Meta-analysis of Studies of Ultrasound for Suspicious Breast Lesions

Study	N lesions	Quality score	Sensitivity (95% CI)	Specificity (95% CI)	Positive predictive value (95% CI)	Negative predictive value (95% CI)	Positive likelihood ratio (95% CI)	Negative likelihood ratio (95% CI)
Meyberg-Solomayer et al. 2004[189]	65	7.4	100.0% (91.4% to 99.9%)	56.5% (36.8% to 74.3%)	80.8% (68.0% to 89.1%)	100.0% (76.7% to 99.8%)	2.3 (2.2 to 2.3)	0.02 (0.00 to 0.33)
Malich et al. 2001[137]	100	7.9	77.4% (65.5% to 86.0%)	89.5% (75.7% to 95.7%)	92.3% (81.7% to 96.9%)	70.8% (56.8% to 81.7%)	7.4 (6.4 to 8.4)	0.25 (0.16 to 0.41)
Chao et al. 1999[190]	3,093	7.5	86.1% (83.4% to 88.4%)	66.1% (64.2% to 68.0%)	44.1% (41.5% to 46.7%)	93.9% (92.6% to 94.9%)	2.5 (2.5 to 2.6)	0.21 (0.18 to 0.25)
3 studies	3,258 lesions	Median 7.6 Moderate	Summary estimate 86.1% (83.8% to 88.5%)	Summary estimate 66.4% (64.5% to 68.2%)	Summary estimate 47.0% (43.6% to 50.4%)	Summary estimate 93.3% (92.3% to 94.2%)	Heterogeneous, no summary estimate calculated	Summary estimate 0.21 (0.24 to 0.19)

Heterogeneity tests	Cumulative meta-analysis						
D I^2 = 47% Q = 3.78 p of Q = 0.15109	New study	Sensitivity 95% CI	Within 5% limits?	Specificity 95% CI	Within 5% limits?	-LHR 95% CI	Within 5% limits?
	Chao et al. 1999[190]	83.6 to 88.6	Yes	64.2 to 68.0	Yes	0.18 to 0.24	No
+lnLHR I^2 = 65.7% Q = 285.56 p of Q = 0.00000001	Malich et al. 2001[137]	83.0 to 87.9	Yes	64.6 to 68.4	Yes	0.19 to 0.25	No
-lnLHR I^2 = 37.8% Q = 3.22 p of Q = 0.200	Meyberg-Solomayer et al. 2004[189]	83.8 to 88.5	Yes	64.5 to 68.3	Yes	0.19 to 0.24	No
		5% limits 81.8 to 90.4	Stable	5% limits 63.1 to 69.7	Stable	5% limits 0.20 to 0.23	Not stable

D = ln diagnostic odds ratio
+lnLHR = ln of positive likelihood ratio
-lnLHR = ln of negative likelihood ratio

Table 53. Meta-analysis of Studies of Ultrasound for Palpable Lesions

Study	N lesions	Quality score	Sensitivity (95% CI)	Specificity (95% CI)	Positive predictive value (95% CI)	Negative predictive value (95% CI)	Positive likelihood ratio (95% CI)	Negative likelihood ratio (95% CI)
Chen et al. 2004[191]	1,203	6.9	79.3% (75.0% to 83.0%)	89.3% (87.0% to 91.2%)	78.1% (73.8% to 81.9%)	90% (87.7% to 91.8%)	7.4 (7.1 to 7.8)	0.23 (0.19 to 0.28)
Perre et al. 1994[192]	400	7.4	97.7% (94.2% to 99.1%)	93.4% (89.3% to 95.9%)	91.9% (87.0% to 95.0%)	98.1% (95.3% to 99.2%)	14.7 (14.4 to 15.1)	0.02 (0.01 to 0.06)
van Oord et al. 1991[193]	232	7.2	98.7% (92.8% to 99.7%)	67.3% (59.6% to 74.2%)	59.5% (50.8% to 67.7%)	99.1% (94.8% to 99.8%)	3.0 (2.9 to 3.1)	0.02 (0.00 to 0.14)
McNicholas et al. 1993[194]	203	7.8	88.9% (77.7% to 94.7%)	87.2% (80.9% to 91.6%)	71.6% (59.9% to 81.0%)	95.6% (90.7% to 97.9%)	7.0 (6.3 to 7.7)	0.13 (0.06 to 0.27)
Hachiya et al. 1991[133]	52	7.1	97.4% (86.3% to 99.4%)	100.0% (78.0% to 99.8%)	100.0% (90.3% to 99.9%)	93.3% (69.9% to 98.6%)	28.9 (27.1 to 30.7)	0.04 (0.01 to 0.19)
5 studies	2,090 lesions	Median 7.2 Moderate	Heterogeneous, no summary estimate calculated					
Heterogeneity tests D				I^2 = 90% Q = 28.22 p of Q = 0.000011				

Appendix E. Evidence Tables (continued)

Table 54. Meta-regression of Studies of Ultrasound for Palpable Lesions

Study	D	Standard error of D	Year of publication	Quality score	Size of study	Number of operators	Open or core biopsy	Patients lost %	Accounted for interreader reliablility	Prevalence of disease %	S
Chen et al. 2004[191]	3.5	0.168	2004	6.9	1203	1	1 (Either)	0	0 (No)	32.5	-0.77764
Perre et al. 1994[192]	6.3	0.531	1994	7.4	380	1	2 (Open only)	0	0 (No)	43.5	1.021273
van Oord et al. 1991[193]	4.6	0.965	1991	7.2	305	1	0 (Not reported)	23.9	0 (No)	32.8	3.201538
McNicholas et al. 1993[194]	3.9	0.483	1993	7.8	203	1	1 (Either)	0	0 (No)	26.6	0.108803
Hachiya et al. 1991[133]	6.6	1.662	1991	7.1	52	2	1 (Either)	0	1 (Yes)	73.1	-0.14842
p value			0.412	0.934	0.428	0.602	0.503	1.0	0.601	0.173	0.685

D = ln of diagnostic odds ratio
SE = standard error
S = ln of measure of thresholdform

Negative Predictive Value Analysis

Table 55. Negative Predictive Values Adjusted to 20% Prevalence

Threshold Sensitivity	PET all lesions		SC nonpalpable lesions		MRI all lesions		US all lesions	
	Specificity	NPV	Specificity	NPV	Specificity	NPV	Specificity	NPV
95% from SROC	46.7	97.4	39.2	96.9	62.8	98.0	NA	NA
90% from SROC	65.0	96.3	58.0	95.9	NA	NA	NA	NA
85% from SROC	75.0	95.2	67.0	94.7	84.0	95.7	NA	NA
80% from SROC	NA	NA	75.0	93.8	88.0	94.6	NA	NA
70% from SROC	87.0	92.1	NA	NA	93.0	92.5	NA	NA
60% from SROC	93.0	90.3	88.0	89.8	95.0	90.5	NA	NA
50% from SROC	94.0	88.3	93.0	88.2	96.0	88.5	NA	NA
Mean from SROC	Sensitivity 82.2% Specificity 78.3%	94.6	Sensitivity 68.7% Specificity 84.8%	91.6	Sensitivity 92.5% Specificity 72.4%	97.5	Sensitivity 86.1 Specificity 66.4	95.0
At Mean threshold: from summary negative likelihood ratio (95% confidence interval)	Sensitivity 82.2% Specificity 78.3%	92.4 (89.7 to 94.3)	Sensitivity 68.7% Specificity 84.8%	90.7 (89.1 to 92.2)	Sensitivity 92.5% Specificity 72.4%	96.2 (95.5 to 96.9)	Sensitivity 86.1 Specificity 66.4	95.0 (94.3 to 95.5)

Mean threshold is the average threshold used by the actual studies. It is the threshold that the test will most likely be used at in the clinical setting.
The 95% confidence intervals for results derived from the SROC cannot be calculated due to technical difficulties, but it should not be assumed that the numbers are precide estimates; an range of error around each number does exist.
NA= not calculated. See the mean threshold instead for results close to this threshold.