APPENDIX

F

Studies of Transrectal Ultrasound for Prostate Cancer Screening and Early Detection

APPENDIX F: STUDIES OF TRANSRECTAL ULTRASOUND FOR PROSTATE CANCER SCREENING AND EARLY DETECTION: RESEARCH DESIGN AND FINDINGS

Author	Biases and methodologic weaknesses[a]	Setting	Time frame (years)	Number patients (N)	Age (Y) range (mean)	Criteria for positive TRUS	Biopsy method	Proportion BPH	TRUS lesion-Diameter (cm) Range (mean)	Overall detection yield (%)[b]	Proportion detected cancers clinically localized (%)	Positive predictive value[c] (clinically localized)	Proportion detected cancer pathologically localized (%)
Carter et al. (1989)	1,2,3,7	Retrospective All patients with abnormal DRE who got TRUS before surg for known cancer 1 lobe.	—	59 highly selected	not provided	peripheral hypoechoic in contralateral lobe	en bloc surgical specimen	Not specified.	0.5-4.5 cm (1.7 mean)	25/59 patient cancer in other lobe	NA Sensitivity 13/25 (52%) Specificity 23/34 (68%)	13/24 (66%)	NA Sensitivity 10/20 (50%) if diameter 0.5-2.0 cm
Coffield et al. (1992)	1,2,3,7	Consecutive autopsy no history prostate cancer; all non-suspicious DRE within 1 year	—	63 (7 others excluded, insufficient information)	37-87 (64)	Broad, any echo suggesting space occupying lesion	en bloc autopsy	Not specified.	diameter not specified, volume range .009-6.3 ml (1.62 ml mean)	19/63 cancer (30%)	Sensitivity 6/19 (32%) for hypoechoic Specificity 7/44 (39%) for hypoechoic	6/33 (18%) overall Half TRUS isoechoic	Surgical state not specified Proportion extracapsular not given. Histologic grade distribution not given.
Cooner et al. (1990)	1,2,3,4,6,7,8	Urology continuity clinic (42% new) work-up bias no patient with suspected PC referral bias	—	1807 varying levels of symptoms	50-89	Peripheral hypoechoic	TRUS, DRE no blind biopsy 46% biopsied	Not specified.	Not provided volume range 0.5-41 ml (mean 2.2) if DRE neg. 0.5-5.5 (1.2)	263/1807 (14.6%) all cancers; 136/1807 (7.5%) clinically localized	136/242 (56%)	263/835 (31%) all cancer	43/60 (72%) only 23% detected cancer surgically staged
Cooner et al. (1988)	1,2,3,4,6,7,8	Urology Continuity Clinic referral bias	1 time	255 (all benign DRE)	50-89	Peripheral hypoechoic (≥ 5 mm)	TRUS 43% biopsied	Not specified.	5-6 mm diameter lowest, no data (all lesions/Prostate Cancer in peripheral)	incomplete clinical staging 28/225 (12.4%)	—	28/96 (29%) overall cancer	8/28 got surgical staging (7/8 pathologically localized)
Dahnert (1986)	1,2,3,7	Known cancer (presurgery)	—	52	47-73 (61)	Hypoechoic 5.0 mHz	en bloc surgery specimens	85% pathologically evident	—	NA	100% (preselected for surgery)	NA, Sensitivity 64% (Unilateral) 81% (Bilateral)	NA, 24/52 (46%) upstaged to extracapsular at surgery
Devonac et al. (1990)	1,2,3,4,6,7,8	Urology Symptomatic (most BPH prospective)	1 time	666	Not provided	Peripheral hypoechoic (no size threshold) 7.0 or 7.5 mHz 226/666 (34%) abnormal TRUS	TRUS or DRE Imply all abnormal TRUS biopsied	Not specified	—	45/666 (6.7%) (34/45 detected DRE[c])	24/45 (53%)	24/225 (11%) 45/246 (19%) all cancer	unknown (no data on histologic grade)

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Author	Biases and methodologic weaknesses[a]	Setting	Time frame (years)	Number patients (N)	Age (Y) range (mean)	Criteria for positive TRUS	Biopsy method	Proportion BPH	TRUS lesion Diameter (cm) Range (mean)	Overall detection yield (%)[b]	Proportion detected cancers clinically localized (%)	Positive predictive value[c] (clinically localized)	Proportion detected cancer pathologically localized (%)
Drago et al. (1992)	1,2,3,5,6,7,8	Urology unknown prostate disease-not true screening population	Serial 4.5 year annual follow-up	1940 recruitment not well described	55-70 (64)	Hypoechoic 352/1940 (18%) abnormal test	TRUS guided abnormal DRE PSA alone in 2% of biopsies	Not specified	—	70/1940 (3.6%)	Not specified for TRUS detected, overall 64/79 cancers (81%) in study clinically localized when discovered by any method.	70/352 (20%) all cancers	—
Guinan et al. (1987)	1,2,3	Inpatient Urology Service Comparative study of 5 studies, including TRUS, PSA. All symptomatic selection bias Not generalizable to office-based population	1 time	280	68 (mean)	3.5 mHz scanner not specified 3 "independent" reviewers 84/280 (30%) had TRUS 37/84 (44%) TRUS positive	All patients biopsied	129/280 (46%) on pathology biopsy spec.	—	78/280 (28%) overall prevalence of TRUS received 22/84 (26%) cancers	—	NA 22/37 (59%) Sensitivity = 22/31 (71%) Specificity = 38/53 (72%)	—
Gustafsson et al. (1992)	6,8	Swedish screening population-based randomly selected	1 time	2,400 eligible 1,780 recruited (74%)	55-70	Any hypoechoic area (non cyst) or asymmetry	TRUS guided and/or DRE guided if PSA > 10 blind bx (21% biopsied)	Not specified.	—	58/1780 (3.3%)	34/58 (59%)	34/244 (14%) 58/244 (24%) all cancer	—
Hammerer et al. (1992)	1,2,3,7,8	Urology all cancers at other site no prostate symptoms	—	73	54-70 (65)	Hypoechoic	TRUS, DRE and systematic 100% biopsied	Not specified.	—	17/73 (23%) cancers (13/17 TRUS[c]) (15/17 DRE[c])	Not specified (implied all clinically localized)	13/30 (43%) overall; if DRE 1/14 (7%)	Not provided.
Lee et al. (1988)[d]	1,2,3,6	Screening invitational/ referral	1 time	784 Half normal DRE < 1 yr.	60-86 (65)	Peripheral hypoechoic > 5 mm 64/784 (8%) TRUS abnormal	DRE or TRUS (2-fold greater # biopsies for TRUS DX cases than DRE 10%	Not specified.	0.7-3.0 (1.3)	20/784 (2.6) 20/22 cancers TRUS[c]	Unknown for TRUS alone 17/22 (77%) overall DRE and TRUS.	Unknown 20/64 (31%) for all cancers by TRUS.	16/22 (73%)

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Mettlin et al. (1991)	2,3,6,7,8	Screening invitation	1st year of serial study	2425	55-70 (63)	Peripheral hypoechoic > 0.5 cm	TRUS, DRE few if PSA elevated 14% biopsied)	135/330 biopsied (41%)	10/50 < 1.0 cm 40/50 > 1.0 cm	44/2425 (1.8%) for TRUS 44/57 detected ca. for TRUS[b]	unknown for clinical loc. for TRUS only 39/51 (76%) stage A,B for available data	44/290 (15%) all cancer. if < 1.0 cm 6/135 (7%); if ≥ 1.0 cm 30/136 (22%)	Unknown for TRUS only 21/31 (68%) overall study for available data
Naito, 1988	1,2,3,4,7	see Appendix C	1 time	109	35-89 (70)	Proposed by Japanese Urological Association including disarranged forms, asymmetry, discontinuity in capsule, irregular echogenicity of parenchyma (especially hypoechoic). Do not specificity if discrete hypoechoic included 46/109 (42%) Abnormal	All patients biopsied but technique not detailed		Not provided.	28/109 (25.6%)	Not specified.	28/46 (61%) 'sensitivity' = 28/32 (88%) 'specificity' = 59/77 (77%)	Not specified.
Nesbitt et al. (1989)	1,2,3,4,6,7,8	Urology Not pure screening	1 time	240 asymptomatic self-selected or referral for unrelated problem	55-70	Peripheral anechoic hypoechoic 5.5 or 7.0 mHz scan	TRUS, DRE (unclear if PSA influenced) 19% biopsied	Not specified.	1.0-1.5 approximate only	19/240 (7.9%)	17/19 (89%) (11/19 DRE[b])	17/45 (38%)	15/19 (79%)
Norming et al. (1991)	6,8	Swedish Population Screening (75% compliance)	1 time	1,788	50-70	Hypoechoic Asymmetry (no size) 246/1788 (14%) TRUS abnormal	TRUS, DRE or PSA > 10 365/1788 (20%) biopsied overall proportion of TRUS abn. biopsied not specified	Not specified.	—	62/1788 (3.5%)	Not specified for TRUS alone overall 26/62 cancers T1 or T2A.	Not specified 56/246 (23%) all cancers.	Unknown (no surgical staging).

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Author	Biases and methodologic weaknesses[a]	Setting	Time frame (years)	Number patients (N)	Age (Y) range (mean)	Criteria for positive TRUS	Biopsy method	Proportion BPH	TRUS lesion Diameter (cm) Range (mean)	Overall detection yield (%)[b]	Proportion detected cancers clinically localized (%)	Positive predictive value[c] (clinically localized)	Proportion detected cancer pathologically localized (%)
Palken et al. (1991)	1,2,3,5,6,8	Urology invitational referral	1 time	315	50-86	2 classes "high" suspicious "low"	DRE, TRUS systematic if negative first time 28 biopsied	Not specified.	—	14/315 (4.4%)	Unknown 14/23 (61%) cancers TRUS[b].	Unknown 14/52 (27%) all cancers.	—
Perrin et al. (1989)	1,2,3,4,6,7,8	Screening invitation	1 time	666 (602 DRE)		Hypoechoic	TRUS	Not specified.	—	11/666 (1.7%)	—	11/162 (6.8%) all cancers	—
Perrin et al. (1992)	1,2,3,4,6,7,8	French urology referral population	1 time	481	(67)	Not specified.	'Abnormal' TRUS and/or abnormal DRE[e]	—	—	83/481 (17%)	24/83 (29%)	8/233 (3%) 65/233 (28%) all cancers	—
Ragde et al. (1989)	1,2,3,4,6,7,8	Radiology screening invitational	1 time	1,051	over 50	Hypoechoic	TRUS (some DRE pos. not biopsied)	Not specified.	—	50/1051 (4.8%) all cancers	—	50/138 (36%) all cancers	—
Rifkin (1988)	1,2,3,4,6,7,8	Radiology prospective referral population	1 time "all comers" to USG clinic since 1986	329 heteroge-nous none with known PC include symptom-atic "mild" Abn DRE (180)	45-91 (64)	Peripheral hypoechoic Used 5, 6.5, or 7.5 mHz scanner 80/329 (24%) abn. TRUS	TRUS or DRE 79/329 (24%) biopsied only 56/180 "mild DRE" Abnormal were biopsied	Not specified.	0.5-1.5	5.2% (17/329)	—	Unknown, overall 17/79 (22%) all can-cers	—
Shinohara et al. (1989)	1,2,3,7,8	Preopera-tive TRUS known clinically localized cancer (pre-sur-gery TRUS)	—	70	48-78 (63)	Hypoechoic (42) Hyperechoic (1) Isoechoic (27)	en bloc surgical specimen	Not specified.	Smallest lesion seen by TRUS (hypoechoic) 4.5 mm (actual tumor size)	Overall 42/70 (60%) hypoecho-ic abnor-mal 3/17 (18%) cancers were < 1.0 cm were hypoecho-ic 40/52 (77%) cancers > 1.0 cm were hypo-echoic	NA	9/25 (36%) cancers with DRE normal had hypo-echoic abn. 34/45 (79%) cancer with DRE pos itive were hypo-echoic	

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Simak (1993)	1,2,3,7	Prospective Urology Clinic Consecutive patients with nonsuspicious DRE who received TRUS and PSA prior to TURP	1 time	288 All scheduled for TURP for BPH	55-84 (68)	Hypoechoic (near capsule) 32/288 (11%) TRUS Abnormal	TRUS-guided (no apparent systematic)		Not provided Histologic grade: Moderate (6) Poor (8)	14/288 (4.9%) by TRUS total of 46/288 (16%) cancers at TURP 1/231 patients with PSA < 7 had TRUS detected cancer (0.4% yield)	13/14 (93%) total 45/46 cancers at TURP were clinically localized	14/32 (44%) [13/32 (41%)] for 13/14 TRUS detected cancers, PSA > 7 57/288 (20%) PSA > 7	12/14 (86%) Overall, post TURP 44/46 (96%) were pathologically localized of 32 cancers missed by TRUS, 7 stage A_2 25 stage A_1
Terris et al. (1991)	1,2,3,7	Preoperative Cystoprostatectomy for Bladder cancer	—	51 (no known prostate cancer)	31-79 (64)	Hypoechoic	en bloc surgical specimen	Not specified.	volume .001-5.3 ml (0.8 mL mean)	NA, 15/51 (29%) prevalence prostate cancer	8/17 (47%) both clinical and pathologically localized	overall sensitivity 53% specificity 75%	Peripheral zone sens. = 70% spec. = 81% PV+ = 64% Transition sens. = 20% spec. = 64% PV+ = 17%
Watanabe et al. (1991)	2,3,4,6,7,8	Japanese mass screening	1 time	7235 asymptomatic	> 55	Hypoechoic	TRUS guided (small minority of patients got DRE)	—	—	48/7235 (0.7%)	25/48 (52%)	not provided	—

[a] Legend for study biases/methodologic weaknesses: 1) Not population-based/community setting, 2) Selection/referral bias, 3) Non-randomly sampled study group, 4) Explicit inclusion/exclusion criteria not provided, 5) Abnormal test criterion and type and TRUS equipment (e.g., 3.5, 5.0, 7.5 mHz) not described, 6) Incomplete application of appropriate reference (gold) standard work-up bias, 7) Lack of proper blinding in test interpretation, 8. Failure to account completely for all enrolled subjects (including biopsy of all abnormal tests and reporting of clinical and pathologic staging information). For each listed study the presence or absence of one or more of these methodologic deficiencies is denoted with the corresponding number (above). Further grading of the degree to which these biases/deficiencies are present was not performed.

[b] Detection yield = number of patients prostate cancer detected/number patients screened (for TRUS only).

[c] Positive predictive value = proportion of patients with abnormal test (TRUS) who have clinically localized prostate cancer.

[d] Potential bias against DRE comparison (with TRUS); solo men had "normal" DRE within 1 year prior.

[e] This study has significant weaknesses both in terms of potential selection and work-up bias as well as sloppy presentation of data and apparent contradictions. For example, patients are said to have received biopsy only if DRE or TRUS was abnormal (criterion for each not specified), but 16 of the 83 cancers detected were both DRE and TRUS negative. PSA testing was not used to also select patients for biopsy, nor was a systematic biopsy applied according to the brief selection. Nor was it clearly stated that all "test positive" patients actually received a biopsy. Only 8/135 (6%) patients with a normal DRE but an abnormal TRUS had prostate cancer detected. Of the 24 Stage T1-T2 (A,B) cancers found among the 83 overall detected, 16 of these patients (66%) had both normal DRE and TRUS.

KEY: NA = not applicable.