Appendices

Appendix 1. Pubmed Search Syntax

#1 biopsy [All fields]
#2 biopsies [All fields]
#3 biops* [All fields]
#4 biopsy [MeSH terms]
#5 pathology [All fields]
#6 aspiration [All fields]

#7 OR #1-6

#8 mri [All fields]
#9 mpmri [All fields]
#10 magnetic resonance imaging [All fields]
#11 multiparametric magnetic resonance imaging [All fields]
#12 mri [MeSH terms]

#13 OR #8-12

#14 prostate [All fields]
#15 prostate [MeSH terms]
#16 prostatic [All fields]
#17 prostat* [All fields]

#18 OR #14-#17

#19 "micro ultrasound" [All fields]
#20 "micro US" [All fields]
#21 mUS [All fields]
#22 29Mhz [All fields]
#23 "29 Mhz" [All fields]
#24 “29 Megahertz” [All fields]
#25 EXACTVU [All fields]
#26 "high resolution"

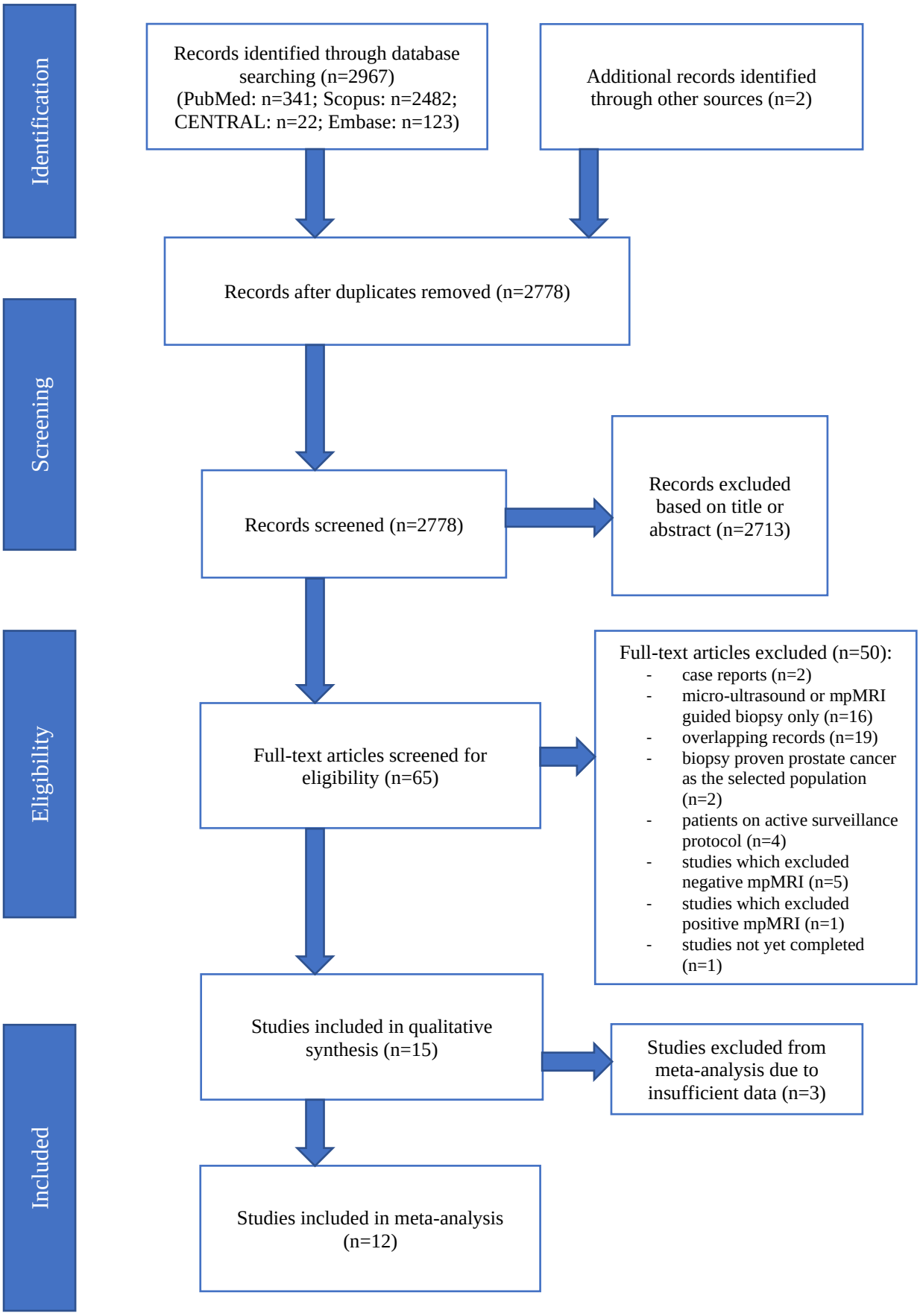
#27 OR #19-#26

#22 #7 AND #13 AND #18 AND #27

Appendix 2. Pubmed Search String

((((((((((((("biopsie"[All Fields] OR "biopsy"[MeSH Terms]) OR "biopsy"[All Fields]) OR "biopsied"[All Fields]) OR "biopsies"[All Fields]) OR "biopsy s"[All Fields]) OR "biopsying"[All Fields]) OR "biopsys"[All Fields]) OR "pathology"[MeSH Subheading]) OR "pathology"[All Fields]) OR (((((((("biopsie"[All Fields] OR "biopsy"[MeSH Terms]) OR "biopsy"[All Fields]) OR "biopsied"[All Fields]) OR "biopsies"[All Fields]) OR "biopsy s"[All Fields]) OR "biopsying"[All Fields]) OR "biopsys"[All Fields]) OR "pathology"[MeSH Subheading]) OR "pathology"[All Fields])) OR "biops*"[All Fields]) OR "biopsy"[MeSH Terms]) OR ((((((((((((((((("aspirant"[All Fields] OR "aspirants"[All Fields]) OR "aspirate"[All Fields]) OR "aspirated"[All Fields]) OR "aspirates"[All Fields]) OR "aspirating"[All Fields]) OR "aspiration"[All Fields]) OR "aspirational"[All Fields]) OR "aspirations, psychological"[MeSH Terms]) OR ("aspirations"[All Fields] AND "psychological"[All Fields])) OR "psychological aspirations"[All Fields]) OR "aspirations"[All Fields]) OR "aspirative"[All Fields]) OR "aspirator"[All Fields]) OR "aspirators"[All Fields]) OR "aspire"[All Fields]) OR "aspired"[All Fields]) OR "aspires"[All Fields]) OR "aspiring"[All Fields])) OR (("pathology"[MeSH Terms] OR "pathology"[All Fields]) OR "pathologies"[All Fields]) OR "pathology"[MeSH Subheading])) AND ((((((((((("prostat"[All Fields] OR "prostate"[MeSH Terms]) OR "prostate"[All Fields]) OR "prostates"[All Fields]) OR "prostatic"[All Fields]) OR "prostatism"[MeSH Terms]) OR "prostatism"[All Fields]) OR "prostatitis"[MeSH Terms]) OR "prostatitis"[All Fields]) OR "prostate"[MeSH Terms]) OR (((((((("prostat"[All Fields] OR "prostate"[MeSH Terms]) OR "prostate"[All Fields]) OR "prostates"[All Fields]) OR "prostatic"[All Fields]) OR "prostatism"[MeSH Terms]) OR "prostatism"[All Fields]) OR "prostatitis"[MeSH Terms]) OR "prostatitis"[All Fields])) OR "prostat*"[All Fields]) AND (((((((("micro ultrasound"[All Fields] OR "micro US"[All Fields]) OR "mUS"[All Fields]) OR "29Mhz"[All Fields]) OR "29 Mhz"[All Fields]) OR ("29"[All Fields] OR "megahertz"[All Fields])) OR "EXACTVU"[All Fields]) OR "high resolution"[All Fields])) AND ((((((((((("magnetic resonance imaging"[MeSH Terms] OR ("magnetic"[All Fields] AND "resonance"[All Fields] AND "imaging"[All Fields]) OR "magnetic resonance imaging"[All Fields] OR "mri"[All Fields] OR ("mpmris"[All Fields] OR "multiparametric magnetic resonance imaging"[MeSH Terms] OR ("multiparametric"[All Fields] AND "magnetic"[All Fields] AND "resonance"[All Fields] AND "imaging"[All Fields]) OR "multiparametric magnetic resonance imaging"[All Fields] OR "mpmri"[All Fields]) OR ("magnetic resonance imaging"[MeSH Terms] OR ("magnetic"[All Fields] AND "resonance"[All Fields] AND "imaging"[All Fields]) OR "magnetic resonance imaging"[All Fields]) OR ("multiparametric magnetic resonance imaging"[MeSH Terms] OR ("multiparametric"[All Fields] AND "magnetic"[All Fields] AND "resonance"[All Fields] AND "imaging"[All Fields]) OR "multiparametric magnetic resonance imaging"[All Fields] OR ("multiparametric"[All Fields] AND "mri"[All Fields]) OR "multiparametric mri"[All Fields]) OR ("multiparametric magnetic resonance imaging"[MeSH Terms] OR ("multiparametric"[All Fields] AND "magnetic"[All Fields] AND "resonance"[All Fields] AND "imaging"[All Fields]) OR "multiparametric magnetic resonance imaging"[All Fields]) OR "magnetic resonance imaging"[MeSH Terms])

Appendix 4. Flow diagram for study selection process



Appendix 3. Excluded studies and reason for exclusion

Full-text articles excluded – Case reports (n=2), Micro-Ultrasound or mpMRI Guided Biopsy Only (n=16), Overlapping (n=19), Biopsy Proven Prostate Cancer as Selected Population (n=2), Patients on Active Surveillance Protocol (n=4), Studies Which Excluded Negative mpMRI (n=5), Studies Which Excluded Positive mpMRI (n=1), Studies not yet completed (n=1)

Studies excluded from meta-analysis – Insufficient data (n=3)

Biopsy Proven Prostate Cancer as Selected Population

1) Lorusso V, B K, G P, et al. Comparison Between Micro-Ultrasound and Multiparametric MRI Regarding the Correct Identification of Prostate Cancer Lesions. Clinical genitourinary cancer 2022.
2) Brisbane W, Pensa J, Sisk A, et al. Micro-ultrasound to whole mount image correlation for detection and localization of prostate cancer. *J Urol* 2021; 206: e394.

Insufficient Data

1) Ghai S, Perlis N, Atallah C, et al. Comparison of Micro-US and Multiparametric MRI for Prostate Cancer Detection in Biopsy-Naive Men. Radiology 2022; 0: 212163. DOI: 10.1148/radiol.212163.
2) Socarras ME, Elbers JR, Esposito F, et al. Transperineal Prostate Biopsies using Micro-ultrasound, MRI-guided and Systematic Biopsies (Madrid Protocol), an Update with 482 patients. *J Urol* 2022; 207: e691.
3) Hofbauer S.L. LF, Harland N., Plage H., Reimann M., Hollenbach M., Gusenleitner A., Stenzl A., Schlomm T., Wiemer L., Cash H. A non-inferiority comparative analysis of micro-ultrasonography and MRI-targeted biopsy in men at risk of prostate cancer. 2022; 129.

Studies Not Yet Completed

1) Klotz L, Andriole G, Cash H, et al. Optimization of prostate biopsy - Micro-Ultrasound versus MRI (OPTIMUM): A 3-arm randomized controlled trial evaluating the role of 29MHz micro-ultrasound in guiding prostate biopsy in men with clinical suspicion of prostate cancer. *Contemp Clin Trials* 2022; 112.

Case Reports

1) Ghai S. VdKT. Suspicious findings on micro-ultrasound imaging and early detection of prostate cancer. 2018; 16.
2) Stanton W, Crawford ED, Arangua P, Hoyer G, Werahera PN. Evaluation of the 29 MHz Micro-Ultrasound Imaging for Prostate Cancer Diagnosis and Treatment. Ann. Urol. Nephrol. 2019;

Micro-Ultrasound or mpMRI Guided Biopsy Only

1) Hailemariam M, Kelly D and Langston J. A comparison of Mri fusion biopsy pi-RADS scoring system to exact VU micro-ultrasound PRI-MUS scoring system in identifying prostate cancer: A single institution retrospective analysis. J Urol 2021; 206: e853-e854.
2) Claros OR, Tourinho-Barbosa RR, Fregeville A, et al. Comparison of Initial Experience with Transrectal Magnetic Resonance Imaging Cognitive Guided Micro-Ultrasound Biopsies versus Established Transperineal Robotic Ultrasound Magnetic Resonance Imaging Fusion Biopsies for Prostate Cancer. *J Urol* 2020; 203: 918-925.
3) Luger F, Gusenleitner A, Kaar J, et al. Does the diagnostic accuracy of micro-ultrasound vary with prostate location? Eur Urol Suppl 2019; 18: e3393.
4) Francesco C, Riccardo S, Eugenio B, et al. Diagnostic accuracy of the novel 29 MHz micro-ultrasound "Exactvutm" for the detection of clinically significant prostate cancer: a prospective single institutional study. J Urol 2019;201(Supplement 4):e1081–e1081.
5) Ghai S, Eure G, Fradet V, et al. Assessing Cancer Risk on Novel 29 MHz Micro- Ultrasound Images of the Prostate: Creation of the Micro-Ultrasound Protocol for Prostate Risk Identification. J Urol 2016;196(2):562–9.
6) Hyndman ME, Pavlovich CP, Eure G, Fradet V, Ghai S. Prospective validation of PRI-MUS, the prostate risk identification using micro-ultrasound protocol for real- time detection of prostate cancer using high resolution micro-ultrasound imaging. J Urol 2018;199(4):e733- .
7) Lopci E, Lughezzani G, Castello A, et al. PSMA-PET and micro-ultrasound potential in the diagnostic pathway of prostate cancer. Clin Transl Oncol 2020;
8) Luger F, Gusenleitner A, Kaar J, Mayr C, Loidl W. A Prospective Validation of the Diagnostic Accuracy of PRI-MUS for Prostate Cancer Risk Identification. Eur Urol Suppl 2018;17(13):e2763.
9) Luger F, Gusenleitner A, Kaar J, Mayr C, Loidl W. Does 29Mhz Micro-Ultrasound Provide Uniform Diagnostic Accuracy Within and Beyond the Peripheral Zone? Ann. Urol. Nephrol. 2019;
10) Pavlovich C, Hyndman ME, Eure G, Ghai S, Fradet V. A multi-institutional randomized controlled trial comparing novel first generation high-resolution micro- ultrasound with conventional frequency ultrasound for transrectal prostate biopsy. J Urol 2019;201(4):e394- .
11) Pavlovich C, Hyndman ME, Eure G, Ghai S, Fradet V. A multi-institutional randomized controlled trial comparing novel first generation high-resolution micro- ultrasound with conventional frequency ultrasound for transrectal prostate biopsy. Eur Urol Suppl 2019;18(1):e737- .

12) Pavlovich CP, Cornish TC, Mullins JK, et al. High-resolution transrectal ultrasound: Pilot study of a novel technique for imaging clinically localized prostate cancer. Urol Oncol Semin Orig Investig 2014;32(1):34.e27-34.e32.
13) Regis F, Casale P, Persico F, et al. Use of 29-MHz Micro-ultrasound for Local Staging of Prostate Cancer in Patients Scheduled for Radical Prostatectomy: A Feasibility Study. Eur Urol Open Sci 2020;19:20–3.
14) Rohrbach D, Wodlinger B, Wen J, Mamou J, Feleppa E. Machine learning-based lesion detection via quantitative high frequency ultrasound for prostate-cancer imaging using a novel high resolution micro-ultrasound platform. J Urol 2018;199(4):e154- .
15) Rohrbach D, Wodlinger B, Wen J, Mamou J, Feleppa E. High-Frequency Quantitative Ultrasound for Imaging Prostate Cancer Using a Novel Micro-Ultrasound Scanner. Ultrasound Med Biol 2018;44(7):1341–54.
16) Wodlinger B, Ghai S, Eure G, Fradet V, Hyndman E, Mcgrath T PC. Using patient screening data and machine learning algorithms to improve PRI-MUSTM accuracy with micro-ultrasound-based prostate biopsies. Eur Urol Suppl 2016;Conference(12):e1499- e1500.

Overlapping Study Records

1) Maffei D, Paciotti M, Avolio P, et al. Diagnostic accuracy of mpMRI-US fusion and micro-ultrasound guided biopsies for clinically significant prostate cancer detection. Eur Urol 2021; 79: S1303-S1304.
2) Abouassaly R, Klein EA, El-Shefai A, et al. Impact of using 29 MHz high-resolution micro-ultrasound in real-time targeting of transrectal prostate biopsies: initial experience. *World J Urol* 2020; 38: 1201-1206.
3) Astobieta Odriozola A, Sanchez A, De La Cruz I, et al. Initial results comparing 29 MHz micro-ultrasound with multi-parametric MRI for targeted prostate biopsy: Relative sensitivity to clinically significant prostate cancer. *Eur Urol Suppl* 2017; 16: e2616.
4) Lopez L, Rivière J, Pierquet G, et al. Added value of MRI and high-resolution micro-ultrasound targeting of prostate biopsies for suspicion on cancer. *Eur Urol Suppl* 2019; 18: e3394.
5) Abouassaly R, Klein E, El-Shefai A, Stephenson A. Initial Results Comparing Micro- Ultrasound with MRI for Prostate Cancer Detection. Eur Urol Suppl 2018;17(13):e2764.
6) Astobieta Odriozola A, Sanchez A, De La Cruz I, et al. Initial results comparing 29 MHz micro-ultrasound with multi-parametric MRI for targeted prostate biopsy: Relative sensitivity to clinically significant prostate cancer. Eur Urol Suppl 2018;17(2):e901.
7) Bevilacqua G, Maffei D, Paciotti M, et al. Diagnostic performance of micro-ultrasound in a contemporary cohort of patients in active surveillance for localized prostate cancer: A single-institutional experience. Eur Urol Suppl 2019;18(9):e3183-4.
8) Di Cosmo G, Russo A, Lopez L, Gaston R. Added value of MRI and high resolution micro-ultrasound image-based targeting during prostate biopsy on suspicion of prostate cancer. Eur Urol Suppl 2019;18(9):e3341.

9) Eure G, Fanney D, Lin J, Ghai S. Comparison of conventional TRUS, MRI and micro- ultrasound for visualizing prostate cancer in an active surveillance population: A feasibility study. Eur Urol Suppl 2017;16(9):e2614.
10) Klotz L, Woon D. High resolution 29 MHz micro-ultrasound in the diagnosis of primary and recurrent prostate cancer. J Urol 2019;201(Supplement 4).
11) Lughezzani G, Paciotti M, Mondellini G, et al. Comparison between the diagnostic accuracy of high resolution micro-ultrasound versus multiparametric MRI in the detection of prostate cancer: Preliminary results from a single-institutional ongoing prospective trial. Eur Urol Suppl 2018;17(8):179.
12) Lughezzani G, Paciotti M, Mondellini GM, et al. Where Do Micro-Ultrasound and MRI Find Prostate Cancer? A Target Localization Study. Eur Urol Suppl 2018;17(14):e2809.
13) Lughezzani G, Saita A, Lazzeri M, Paciotti M, Maffei D, Lista G, et al. Comparison of the Diagnostic Accuracy of Micro-ultrasound and Magnetic Resonance Imaging/Ultrasound Fusion Targeted Biopsies for the Diagnosis of Clinically Significant Prostate Cancer. Eur Urol Oncol. 2019 May;2(3):329-332.
14) Maffei D, Paciotti M, Lazzeri M, et al. Diagnostic accuracy of targeted prostate biopsies: Results from a prospective trial comparing micro-ultrasound with multiparametric MRI for the detection of prostate cancer. Eur Urol Suppl 2019;18(1):e731.
15) Maffei D, Paciotti M, Lazzeri M, et al. Micro-ultrasound versus multiparametric MRI in the detection of prostate cancer: Results from a prospective single center trial. Eur Urol Suppl 2019;18(11):e3410.
16) Rojas Claros O, Muttin F, Barbosa RRT, et al. Comparison of cancer detection rates in micro-ultrasound biopsies versus robotic ultrasound-magnetic resonance imaging fusion biopsies for prostate cancer. Eur Urol Suppl 2019;18(11):e3503.
17) Salomon G, Lughezzani G, Astobieta A, et al. Risk Stratification for Equivocal PI-RADS Results: Can Micro-Ultrasound Help Determine Which Men to Biopsy? Eur Urol Suppl 2018;17(13):e2765.
18) Staerman F. Can High Resolution Micro-Ultrasound Detect Extra-Prostatic Extension? A New Sonographic Feature. Eur Urol Suppl 2018;17(13):e2762.
19) Wiemer L, Hofbauer S, Heckmann R, et al. Prostate biopsy using micro-ultrasound and fusion biopsy of the prostate: True precision? Eur Urol Suppl 2019;18(11):e3501.

Patients on Active Surveillance Protocol

1) Wiemer L, Hollenbach M, Heckmann R, et al. Evolution of Targeted Prostate Biopsy by Adding Micro-Ultrasound to the Magnetic Resonance Imaging Pathway. Eur Urol Focus 2021; 7: 1292-1299.
2) Staerman F. The utility of 29 MHz high resolution micro-ultrasound and mpMRI in the management of Gleason six prostate cancer with active surveillance. *Eur Urol Suppl* 2019; 18: e3502.
3) Martel P, Tawadros T, Burruni R, et al. The utility of high-frequency micro-ultrasound in performing MRI-ultrasound fusion targeted biopsy. *Eur Urol Suppl* 2019; 18: e3392.
4) Eure G, Fanney D, Lin J, et al. Comparison of conventional transrectal ultrasound, magnetic resonance imaging, and micro-ultrasound for visualizing prostate cancer in an active surveillance population: A feasibility study. *Can Urol Assoc J* 2019; 13: E70-e77. 2018/09/01. DOI: 10.5489/cuaj.5361.

Studies Which Excluded Negative mpMRI

1) Paciotti M, Maffei D, Avolio PP, et al. The Role of Micro-Ultrasound Among Patients with a PIRADS 5 Lesion at Multiparametric Magnetic Resonance Imaging. *J Urol* 2022; 207: e692.
2) Cornud F. LA, Camparo P., Barat M., Dumonceau O., Galiano M., Flam T., Soyer P., Barral M. Post-MRI transrectal micro-ultrasonography of transition zone PI-RADS > 2 lesions for biopsy guidance. 2022.
3) Avolio PP, Lughezzani G, Paciotti M, et al. The use of 29 MHz transrectal micro-ultrasound to stratify the prostate cancer risk in patients with PI-RADS III lesions at multiparametric MRI: A single institutional analysis. *Urol Oncol Semin Orig Invest* 2021; 39: 832.e831-832.e837.
4) Lughezzani G, Maffei D, Saita A, et al. Diagnostic Accuracy of Microultrasound in Patients with a Suspicion of Prostate Cancer at Magnetic Resonance Imaging: A Single-institutional Prospective Study. *Eur Urol Focus* 2020; 7: 1019-1026.
5) Cornud F, Lefevre A, Flam T, et al. MRI-directed high-frequency (29MhZ) TRUS-guided biopsies: initial results of a single-center study. *Eur Radiol* 2020; 30: 4838-4846.

Studies Which Excluded Positive mpMRI

1) Avolio PP, Fasulo V, Saitta C, et al. Assessing the Role of High-Resolution Micro-Ultrasound Among Patients with a Negative Multiparametric MRI and a Persistent Suspicion of Prostate Cancer. *J Urol* 2022; 207: e997-e998.

Appendix 5. Abbreviations

CI – Confident Interval
csPCa – Clinically Significant Prostate Cancer
DRE – Digital Rectal Examination
Micro-US – micro-ultrasound
mpMRI – Multi-Parametric Magnetic Resonance Imaging
NPV – Negative Predictive Value
PCa – Prostate Cancer
PI-RADS - Prostate Imaging–Reporting and Data System
PRI-MUS - Prostate Risk Identification using Micro-Ultrasound
PSA – Prostate Specific Antigen
PPV – Positive Predictive Value
QUADAS-2 - Quality Assessment of Diagnostic Accuracy Studies-2
SBx - Systematic Biopsy
SROC - Summary Receiver Operating Characteristics
TBx – Targeted Biopsy
TRUS – Transrectal Ultrasound