External validation of the computerized analysis of TRUS of the prostate with the system ANNA/C-TRUS: a potential role of Artificial Intelligence for improving prostate cancer detection

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Research Article

Keywords: Prostate cancer, Imaging, Ultrasound, TRUS, Transrectal, artificial intelligence, diagnosis ANNA/C-TRUS Biopsy

Posted Date: March 7th, 2022

DOI: <https://doi.org/10.21203/rs.3.rs-1121880/v1>

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Abstract

PURPOSE:

Prostate cancer (PCa) imaging has been revolutionized by the introduction of multi-parametric Magnetic Resonance Imaging (mpMRI). Transrectal ultrasound (TRUS) has always been considered a low-performance modality. To overcome this, a computerized artificial neural network analysis (ANNA/C-TRUS) of the TRUS based on an artificial intelligence (AI) analysis has been proposed. Our aim was to evaluate the diagnostic performance of the ANNA/C-TRUS system and its ability to improve conventional TRUS in PCa diagnosis.

METHODS

We retrospectively analyzed data from 64 patients with PCa and scheduled for radical prostatectomy who underwent TRUS followed by ANNA/C-TRUS analysis before the procedure. The results of ANNA/C-TRUS analysis with whole mount sections from final pathology.

RESULTS

On a per-sectors analysis, sensitivity, specificity, negative predictive value (NPV), positive predictive value (PPV) and accuracy were 62%, 81%, 80%, 64% and 78% respectively. The values for the detection of clinically significant prostate cancer were 69%, 77%, 88%, 50% and 75%. The diagnostic values for high grade tumours were 70%, 74%, 91%, 41% and 74%, respectively. Cancer volume (≤ 0.5 or greater) did not influence the diagnostic performance of the ANNA/C-TRUS system.

CONCLUSIONS

ANNA/C-TRUS represents a promising diagnostic tool and application of AI for PCa diagnosis. It improves the ability of conventional TRUS to diagnose prostate cancer, preserving its simplicity and availability. Since it is an AI system, it does not hold the inter-observer variability nor a learning curve. Multicenter biopsy-based studies with the inclusion of an adequate number of patients are needed to confirm these results.

Introduction And Background

Over the last 10 years, prostate cancer (PCa) imaging and diagnosis have been revolutionized by the introduction of new techniques and technologies such as multi-parametric Magnetic Resonance Imaging (mpMRI) and targeted biopsy. Nowadays, according to the current guidelines, an mpMRI of the prostate should be performed before any prostate biopsy [1]. Nevertheless, transrectal ultrasound (TRUS) guided prostate biopsy remains the standard of care, by combining systematic and targeted biopsy cores in one intervention, when a suspicious lesion on MRI is present [1]. It is well known that conventional gray-scale TRUS of the prostate has a poor diagnostic performance due to its lack of specificity, lack of standardized criteria for detection of PCa, and due to its learning curve and operator dependency.

Moreover, the echogenicity and appearance of the prostatic lesions in gray-scale TRUS is very variable and heterogeneous, increasing the difficulties with this imaging tool. In general, TRUS can detect and visualize only between 11 to 35% of cancer lesions in the prostate [2]. To overcome these limitations, a computerized artificial neural network analysis (ANNA/C-TRUS) of the prostate TRUS images was developed for the detection of PCa. This imaging modality seems to have several advantages arising from its TRUS-based nature, which gives the advantages of short procedure duration and associated low-costs, allowing for potential widespread use in the urological field. Moreover, compared to other similar imaging techniques, it has a commercially available platform that gives the possibility of being used with any available TRUS scanner without the need for any additional equipment or instrumentation [3, 4]. On the other hand, till date, no prospective trials have been made to evaluate the efficacy and performance of the ANNA/C-TRUS system. Conversely, mpMRI has been extensively studied and its superiority compared to the systemic TRUS-guided biopsy pathway has clearly been shown in several trials [5, 6]. Nevertheless, the mpMRI pathway is still limited due its higher costs, its lack of availability, and the need for expertise and experienced uro-radiologists to achieve high-quality images and reports.

The aim of our study was to externally validate the diagnostic performance of the ANNA/C-TRUS system and to explore its ability in PCa detection in our office-based cohort of patients.

Materials And Methods

The study was reported according to the Standards for Reporting of Diagnostic Accuracy (STARD) criteria. Data were retrospectively analyzed between March 2017 and April 2018. In total, 64 patients with biopsy-proven PCa and scheduled for robot-assisted radical prostatectomy (RARP) underwent a TRUS exam of the prostate followed by an ANNA/C-TRUS system analysis before the procedure. The TRUS exam was performed by a single operator (JW) equipped with a Prius Ultrasound scanner (Hitachi medical, Tokyo, Japan) and a Hitachi C41L47RP transrectal probe using default settings for TRUS.

The computerized ANNA/C-TRUS system analysis of the TRUS images was performed in a multicenter setup as follows. According to a standardized protocol, provided by the center of system origin, axial images were taken at 5-mm intervals, beginning at the prostate apex (designated level 00) and proceeding up to the seminal vesicles. Each image was labelled to indicate its level in 5mm steps above the apex. All images of transrectal ultrasound were stored digitally on computer memory and transmitted online from an internet platform to the analysis center using a Java-based web client. The ANNA/C-TRUS algorithms were applied to evaluate the information of the ultrasound images. The detailed methodology was published elsewhere by *Loch et al.* [3]. The data acquired with the computerized analysis were then displayed in a way that tumour-suspicious areas were marked by superimposed red color on the original static image (Fig. 1), where dark red areas mean high risk of PCa and lighter red and yellow areas a lower risk of PCa. Absence of any color coding means absence of PCa suspicion. After the analysis made by the commercially available online platform of ANNA/C-TRUS (ANNA/C-TRUS GmbH, Flensburg, Deutschland), the color-coded images were transmitted back to our center. A lesion was considered suspicious if the color coding was also found at a level above and/or below the level of interest. This rule

was applied to assure detection of higher volume PCa lesions and to increase the specificity by avoiding overcalling lesions and with this avoiding false positives. For validation purposes each prostate was partitioned into 6 sectors (left, right and base, middle gland, and apex) for a total of 384 sectors evaluated. Suspicious zones were filed depending on their localization. The PCa index lesion was defined as the biggest visible lesion and was filed depending on the localization. In the case of an index lesion extending into two or several neighbouring sectors, each sector was considered to contain the index lesion. Radical prostatectomy specimen was considered the reference test. Pathological analysis was performed by a dedicated uro-pathologist (JTP). Prostatectomy specimens were processed according to the Stanford protocol (3-5 mm intervals whole mount transverse sections). All PCa lesions were filed identified and filed according to the 6-sector scheme also used for the ANNA/C-TRUS images. The PCa index lesion was defined as the biggest lesion with the highest grade according to the ISUP grade groups. In the case of an index lesion extending into two or several neighbouring sectors, each sector was considered to contain the index lesion. Moreover, for each lesion the cancer volume and the ISUP grade group were recorded. Cancer volume was categorized into $\geq 0.5\text{cc}$, and $\geq 1.0\text{cc}$, clinically significant PCa (csPCa) was defined as the presence of Gleason pattern 4 or 5 (ISUP GG ≥ 2) or a volume $>0.5\text{cc}$. High-grade PCa lesions were defined as the presence of Gleason pattern 4 or 5 (ISUP GG ≥ 2).

We thereafter compared the sectors containing suspicious lesions based on the ANNA/C-TRUS analysis with the sectors containing cancer lesions based on the pathology results of the final specimen (Fig. 2). Preoperative and postoperative results regarding the identification of the index lesion were then compared and further the sensitivity, specificity, negative and positive predictive values, and accuracy were calculated. For each comparison, 2×2 contingency tables were used to present the results and calculate the diagnostic accuracy estimates. The unit of assessment for our 2×2 contingency table for assessment of accuracy was one sector. Comparisons of the proportions were done by the χ^2 test. The statistical analysis was done with SPSS 25 (SPSS Inc., Chicago, IL, The USA).

Results

The patient's baseline demographics and pathological characteristics are reported in Table 1. A total of 64 men were examined with the ANNA/C-TRUS system before surgery. The diagnostic values of the ANNA/C-TRUS system in the detection of PCa analyzing all lesions, are reported in Table 2a. We found a sensitivity, specificity, negative predictive value (NPV), positive predictive value (PPV) and accuracy of respectively 62%, 81%, 80%, 64% and 78%.

Table 1
Demographic, baseline and histopathologic characteristics
variables of patients (N=64)

All patients (N=64)	
Age (years)	
Median (IQR)	63 (60-69)
Preoperative PSA (ng/ml)	
Median (range) (IQR)	6,60 (5,5-9,8)
Pathological stage [N. (%)]	
pT2a	3 (4,7%)
pT2b	4 (6,3%)
pT2c	39 (60,9%)
pT3a	11 (17,2%)
pT3b	7 (10,9%)
Pathological Gleason score [N. (%)]	
3+3	16 (25%)
3+4	26 (40,6%)
3+5	1 (1,6%)
4+3	16 (25%)
4+5	4 (6,3%)
5+4	1 (1,6%)
Pathological ISUP grade [N. (%)]	
1	16 (25%)
2	26 (40,6%)
3	15 (23,4%)
4	2 (3,1%)
5	5 (7,8%)
Pathological N stage [N. (%)]	
pN0	38 (59,4%)
pN1	5 (7,8%)

pNX	All patients (N=64)
	21 (32,8%)
IQR: interquartile range	

Table 2a: Diagnostic performance and accuracy of ANNA/C – TRUS for detection of prostate cancer in all prostate sectors

Sensitivity (%)	62%
Specificity (%)	81%
NPV (%)	80%
PPV (%)	64%
Accuracy (%)	78%

Table 2b: Diagnostic performance and accuracy of ANNA/C – TRUS for detection of prostate cancer index lesions

Sensitivity (%)	
	60%
Specificity (%)	87%
NPV (%)	88%
PPV (%)	58%
Accuracy (%)	81%

Table 2c: Diagnostic performance and accuracy of ANNA/C – TRUS for detection of clinically significant prostate cancer lesions (defined as ISUP grade group >2)

Sensitivity (%)	69%
Specificity (%)	77%
NPV (%)	88%
PPV (%)	50%
Accuracy (%)	75%

Table 2d: Diagnostic performance and accuracy of ANNA/C – TRUS for detection of high-grade prostate cancer lesions (defined as presence of Gleason score 4 or 5)

Sensitivity (%)	70%
Specificity (%)	74%
NPV (%)	91%
PPV (%)	41%
Accuracy (%)	74%

NPV: negative predictive value, PPV: positive predictive value

The ability to detect the PCa index lesions is reported in Table 2b. For PCa index lesion detection, the ANNA/C-TURS system showed a sensitivity and a NPV of 60% and 88%, a specificity and a PPV of 87% and 58%, and an accuracy of 81%, respectively.

For the detection of csPCa, values of sensitivity and NPV were 69% and 88% respectively, and the specificity, PPV and an accuracy of 77%, 50% and 75%, respectively (Table 2c). When addressing high-grade lesions, sensitivity and NPV were 70% and 91% respectively, while the specificity, PPV and accuracy were 74%, 41% and 74%, respectively (Table 2d).

According to the cancer volume, ANNA/C-TRUS showed no variations in terms of diagnostic performance. Sensitivity and NPV for lesions with a volume of at least 0.5 cc were 69% and 88% respectively. Similarly, for lesions with a volume ≥ 1.0 cc sensitivity and NPV were 69% and 90% respectively. However the specificity, PPV and accuracy showed the same tendencies as reported in Supplementary Table 3 and Supplementary Table 4.

Discussion

The role of conventional TRUS imaging in PCa diagnosis is currently limited to the guidance of the biopsy needle inside of the prostate to retrieve systematic cores or to target a suspect area previously identified by mpMRI [1]. This limited use of gray-scale TRUS is due to its poor diagnostic performance in the detection of PCa that has been extensively studied in the past with an estimated sensitivity and

specificity of approximately 40% and 50% [7]. Since the introduction of ultrasound (US) scanners in clinical practice, around 30 years ago [8, 9], different tools and technologies have been proposed to overcome this problem. Among these advancements, some involve the use of advanced US modalities (such as Color/Power-Doppler US, Contrast-Enhanced US, Elastography and Micro-ultrasound), whilst others introduce a different way of processing the subvisual information that is already available inside the US image either analyzing the raw data of the tissue characteristics (Histoscanning) or using algorithms and Artificial Intelligence (AI) such as the Artificial Neural Network Analysis (ANNA) which is the object of our study.

The use of AI is constantly gaining more interest in healthcare, motivating numerous applications being proposed for several diseases and pathologies [10–12]. The ANNA approach is one of the AI approaches available, defined as a form of machine learning, composed of adaptative computational statistical models (designed to mimic a biological nervous system) which is able to recognize complex patterns in data and can predict outcomes after being trained with datasets including input and known output (or outcome) data [10, 11]. These methods have shown promising results in improving and automating the ability to diagnose, characterize, and assess the severity of PCa by interpolating clinical or image-based information. For these reasons, one of the earliest applications of ANNA was used to improve the diagnostic accuracy of the TRUS of the prostate. Loch *et al.* in a study with 61 patients used an ANNA system trained with 289 pathological confirmed digitalized images of TRUS showing a sensitivity of 79% and a specificity of 99%. [3]. Ronco and Fernandez used an ANNA system combining fourteen TRUS variables (including length, diameter, prostate and central zone volume, echoic level, volume, the major and minor diameter of the pathological area and presence or absence of calcifications) with clinical parameters (such as age, PSA level and PSA density) of 442 cases showing a PPV, NPV and accuracy of 82%, 97% and 83% respectively [12]. Tokas *et al.* reported results from a study with 71 patients with 12-year follow-up performed with serial ANNA/C-TRUS imaging and repeated prostate biopsy with only six targeted cores. They showed several findings: first, 97% of patients were correctly diagnosed either harbouring PCa or being without the disease. Second, during the follow-up, patients underwent several biopsy sessions but performed with targeted cores only, which allowed for less invasive procedures with no need for local anaesthesia and no decrease in diagnostic performance. Last but not least, thanks to the help of internal landmarks and the Ultrasound Computed Tomography (US-CT), which allows correlating sections on a mm level and record image changes over time (ANNA 2.0). This imaging method showed to be able to monitor patients safely as no csPCa was diagnosed after 12 years of follow-up in those patients with a non-suspicious ANNA/C-TRUS analysis [13].

With the introduction of mpMRI into the armamentarium of PCa imaging, a comparison between mpMRI and the ANNA/C-TRUS system in terms of diagnostic performance for PCa detection is warranted.

Recently, Harland *et al.* published results from 202 patients using the ANNA/C-TRUS system combined with robotic US-CT and mpMRI. In 44 patients the results were then compared with whole-mount sections of radical prostatectomy specimens. In this study they showed that the use of a robotic registration of TRUS images can help to overcome the problem of the operator dependency of the US techniques,

allowing for a reassessment of the findings by different readers similar to what is done in mpMRI. Moreover, ANNA/C-TRUS detected PCa in 30 out of the 44 patients (68%) for whom prostatectomy specimen was available for comparison. The detection rate increased to 80% in combination with conventional gray-scale ultrasound [14].

Looking at the evidence coming from high-quality trials such as from the PROMIS trial, the values of sensitivity, specificity, NPV and PPV for MRI were reported to be 93%, 41%, 89% and 55% respectively (for csPCa defined as Gleason score $\geq 4+3$ or cancer core length ≥ 6 mm). It is important to highlight that in the PROMIS trial, MRI images were reported by specifically trained radiologists. This detailed reduced substantially the inter-reader variability, which is well documented limitation of mpMRI in the literature and may limit the reproducibility of the PROMIS results beyond expert and academic MRI centers [5, 15, 16]. Conversely, ANNA/C-TRUS being based on an AI analysis of subvisual information of the gray-scale TRUS image, can overcome limitations such as learning curve, inter-observer variability and need for expertise. It is interesting to notice how AI has also been applied to MRI in several studies, mainly to better differentiate and score the aggressiveness of PCa lesions, confirming the enormous attention and interest that nowadays AI has gained in the medical field [17–19].

Looking at the costs of imaging modalities for PCa diagnosis, TRUS and its variants appears to compare favorable. In fact, the average cost of an ultrasound scanner is around €100.000; whilst the cost for additional software and technologies which allow performing elastography, Doppler or contrast-enhanced ultrasound, is in the order of a few thousand dollars more. This total amount is still considered to be ten times less than the economic burden of an MRI scanner. The economic aspect is also at the base of the limited availability and access to MRI scans which, as mentioned above, require also additional expertise (radiologists, technicians, etc.) [20]. On the other hand, TRUS is much more readily available, can be performed in-office by urologists and, thanks to technological advancements such as ANNA/C-TRUS, are associated with a more favorable learning curve and need less specific expertise. In fact, especially in the multicenter setup (C-TRUS-MS), which was the modality used in our study, ANNA/C-TRUS appears to be an accessible system, relatively less expensive, and user-friendly. This AI system, in its multicenter setup, allows urologists to perform TRUS utilizing any US scanner available, send images via any internet platform for analysis and receive, also via internet, results with valid and enriched information about a prostate harboring PCa or not. [21].

Strunk *et al.* [22], in a targeted biopsy-based study with 20 patients, proposed a combination between ANNA/C-TRUS and mpMRI. In this study, it was suggested that combining the two methods could improve PCa detection. Moreover, all patients with PCa were detected by the ANNA/C-TRUS, whilst MRI-target biopsy missed cancers in 3 patients (27%). These results, even though coming from an era in which standardization with PIRADS-score v.2 was not yet available and from a small sample size, highlights the possible difficulties encountered when transferring mpMRI information to US imaging for the purpose of targeting MRI lesions. This problem is, indeed, not yet solved even with the last modern software of fusion imaging due to the intrinsic differences in these two imaging modalities.

Conclusion

The ANNA/C-TRUS system represents a promising diagnostic modality and application of AI in the field of prostate cancer imaging. As confirmed by the values of the diagnostic performance, it can improve the cancer detection ability of conventional TRUS by maintaining and highlighting the advantages of this method such as the ease of use and the availability. The ANNA/C-TRUS system allows to remove inter-observer variability and reduce the learning curve. Nevertheless, multicenter biopsy-based studies with the inclusion of an adequate number of patients need to be done to confirm these results, ideally comparing head-to-head with mpMRI pathways.

Declarations

Conflict of interest

JW declares the following conflicts of interest: Hitachi, Supersonic, ANNA/C-TRUS, 3D-Biopsy, Exact imaging. ANNA/C-TRUS provided image data analysis for research purposes for this study. All other authors declare that they have no conflict of interest.

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Author Disclosure Statement

No competing financial interests exist.

Authors contribution:

VL: Protocol, Data collection or management, Data analysis, Manuscript writing. BK: project development, Data analysis. GP: Data collection, Manuscript editing. NB: Data collection, Manuscript editing. AP: Data collection. JTP: Manuscript review. SB: Coordination, Manuscript review. NN: Coordination. GM: Coordination. NS: Coordination, Manuscript editing. EM: Coordination. ODC: Coordination. GG: Manuscript editing. JW: Protocol/project development, Data analysis, Manuscript concept, Coordination

References

1. Mottet N, Cornford P, van den Burgh RCN, Briers E et al. EAU guidelines on prostate cancer. Updated 2021. Available online: <https://uroweb.org/guideline/prostate-cancer/>
2. Beemsterboer PM, Kranse R, de Koning HJ, Habbema JD, Schröder FH (1999) Changing role of 3 screening modalities in the Euro- pean randomized study of screening for prostate cancer (Rotterdam). Int J Cancer 84:437–441. [https://doi.org/10.1002/\(SICI\)1097-0215\(19990820\)84:4<437::AID-IJC19>3.0.CO;2-S](https://doi.org/10.1002/(SICI)1097-0215(19990820)84:4<437::AID-IJC19>3.0.CO;2-S)

3. Loch T, Leuschner I, Genberg C, Weichert-Jacobsen K, Küppers F, Yfantis E, Evans M, Tsarev V, Stöckle M. Artificial neural network analysis (ANNA) of prostatic transrectal ultrasound. *Prostate*. 1999 May 15;39(3):198-204. [https://doi.org/10.1002/\(SICI\)1097-0045\(19990515\)39:3<198::AID-PROS8>3.0.CO;2-X](https://doi.org/10.1002/(SICI)1097-0045(19990515)39:3<198::AID-PROS8>3.0.CO;2-X)
4. Loch T, Leuschner I, Genberg C, Weichert-Jacobsen K, Küppers F, Retz M, Lehmann J, Yfantis E, Evans M, Tsarev V, Stöckle M. Weiterentwicklung des transrektalen Ultraschalls. Artifizielle neuronale Netzwerkanalyse (ANNA) in der Erkennung und Stadieneinteilung des Prostatakarzinoms [Improvement of transrectal ultrasound. Artificial neural network analysis (ANNA) in detection and staging of prostatic carcinoma]. *Urologe A*. 2000 Jul;39(4):341-7. German. <https://doi.org/10.1007/s001200050367>
5. Ahmed HU, El-Shater Bosaily A, Brown LC, Gabe R, Kaplan R, Parmar MK, Collaco-Moraes Y, Ward K, Hindley RG, Freeman A, Kirkham AP, Oldroyd R, Parker C, Emberton M; PROMIS study group. Diagnostic accuracy of multi-parametric MRI and TRUS biopsy in prostate cancer (PROMIS): a paired validating confirmatory study. 2017 Feb 25;389(10071):815-822. [https://doi.org/10.1016/S0140-6736\(16\)32401-1](https://doi.org/10.1016/S0140-6736(16)32401-1)
6. Kasivisvanathan V, Rannikko AS, Borghi M, Panebianco V, Mynderse LA, Vaarala MH, Briganti A, Budäus L, Hellawell G, Hindley RG, Roobol MJ, Eggener S, Ghei M, Villers A, Bladou F, Villeirs GM, Viridi J, Boxler S, Robert G, Singh PB, Venderink W, Hadaschik BA, Ruffion A, Hu JC, Margolis D, Crouzet S, Klotz L, Taneja SS, Pinto P, Gill I, Allen C, Giganti F, Freeman A, Morris S, Punwani S, Williams NR, Brew-Graves C, Deeks J, Takwoingi Y, Emberton M, Moore CM; PRECISION Study Group Collaborators. MRI-Targeted or Standard Biopsy for Prostate-Cancer Diagnosis. *N Engl J Med*. 2018 May 10;378(19):1767-1777. doi: <https://doi.org/10.1056/NEJMoa1801993>
7. Correas JM, Halpern EJ, Barr RG, Ghai S, Walz J, Bodard S, Dariane C, de la Rosette J. Advanced ultrasound in the diagnosis of prostate cancer. *World J Urol*. 2021 Mar;39(3):661-676. <https://doi.org/10.1007/s00345-020-03193-0>
8. Mansfield P, Maudsley AA. Medical imaging by NMR. *Br J Radiol*. 1977 Mar;50(591):188-94. <https://doi.org/10.1259/0007-1285-50-591-188>
9. Dussik KT. The ultrasonic field as a medical tool. *Am J Phys Med* 1954;33:5-20. PMID: 13124475.
10. Van Booven DJ, Kuchakulla M, Pai R, Frech FS, Ramasahayam R, Reddy P, Parmar M, Ramasamy R, Arora H. A Systematic Review of Artificial Intelligence in Prostate Cancer. *Res Rep Urol*. 2021 Jan 22;13:31-39. <https://doi.org/10.2147/RRU.S268596>
11. Hu X, Cammann H, Meyer HA, Miller K, Jung K, Stephan C. Artificial neural networks and prostate cancer-tools for diagnosis and management. *Nat Rev Urol*. 2013 Mar;10(3):174-82. <https://doi.org/10.1038/nrurol.2013.9>
12. Ronco AL, Fernández R. Improving ultrasonographic diagnosis of prostate cancer with neural networks. *Ultrasound Med Biol*. 1999 Jun;25(5):729-33. [https://doi.org/10.1016/S0301-5629\(99\)00011-3](https://doi.org/10.1016/S0301-5629(99)00011-3)

13. Tokas T, Grabski B, Paul U, Bäurle L, Loch T. A 12-year follow-up of ANNA/C-TRUS image-targeted biopsies in patients suspicious for prostate cancer. *World J Urol.* 2018 May;36(5):699-704. doi: <https://doi.org/10.1007/s00345-017-2160-z>
14. Harland N, Russo GI, Kaufmann S, Amend B, Rausch S, Erne E, Scharpf M, Nikolaou K, Stenzl A, Bedke J, Kruck S. Robotic Transrectal Computed Tomographic Ultrasound with Artificial Neural Network Analysis: First Validation and Comparison with MRI-Guided Biopsies and Radical Prostatectomy. *Urol Int.* 2022;106(1):90-96. doi: 10.1159/000517674.
15. Müller S, Lilleaasen G, Sand TE, Løfsgaard L, Estop-Garanto M, Helgø D, Sund P, Mygland V. Poor reproducibility of PIRADS score in two multiparametric MRIs before biopsy in men with elevated PSA. *World J Urol.* 2018 May;36(5):687-691. <https://doi.org/10.1007/s00345-018-2252-4>
16. Sonn GA, Fan RE, Ghanouni P, Wang NN, Brooks JD, Loening AM, Daniel BL, To'o KJ, Thong AE, Leppert JT. Prostate Magnetic Resonance Imaging Interpretation Varies Substantially Across Radiologists. *Eur Urol Focus.* 2019 Jul;5(4):592-599. <https://doi.org/10.1016/j.euf.2017.11.010>
17. Fehr D, Veeraraghavan H, Wibmer A, Gondo T, Matsumoto K, Vargas HA, Sala E, Hricak H, Deasy JO. Automatic classification of prostate cancer Gleason scores from multiparametric magnetic resonance images. *Proc Natl Acad Sci U S A.* 2015 Nov 17;112(46):E6265-73. <https://doi.org/10.1073/pnas.1505935112>
18. Antonelli M, Johnston EW, Dikaio N, Cheung KK, Sidhu HS, Appayya MB, Giganti F, Simmons LAM, Freeman A, Allen C, Ahmed HU, Atkinson D, Ourselin S, Punwani S. Machine learning classifiers can predict Gleason pattern 4 prostate cancer with greater accuracy than experienced radiologists. *Eur Radiol.* 2019 Sep;29(9):4754-4764. <https://doi.org/10.1007/s00330-019-06244-2>
19. Toivonen J, Montoya Perez I, Movahedi P, Merisaari H, Pesola M, Taimen P, Boström PJ, Pohjankukka J, Kiviniemi A, Pahikkala T, Aronen HJ, Jambor I. Radiomics and machine learning of multisequence multiparametric prostate MRI: Towards improved non-invasive prostate cancer characterization. *PLoS One.* 2019 Jul 8;14(7):e0217702. <https://doi.org/10.1371/journal.pone.0217702>
20. Grey ADR, Connor MJ, Tam J, Loch T. Can transrectal prostate ultrasound compete with multiparametric MRI in the detection of clinically significant prostate cancer? *Transl Androl Urol.* 2020 Jun;9(3):1492-1500. doi: 10.21037/tau.2020.02.26.
21. Grabski B, Bäurle L, Loch A, Wefer B, Paul U, Loch T. Computerized transrectal ultrasound of the prostate in a multicenter setup (C-TRUS-MS): detection of cancer after multiple negative systematic random and in primary biopsies. *World J Urol.* 2011 Oct;29(5):573-9. <https://doi.org/10.1007/s00345-011-0713-0>
22. Strunk T, Decker G, Willinek W, Mueller SC, Rogenhofer S. Combination of C-TRUS with multiparametric MRI: potential for improving detection of prostate cancer. *World J Urol.* 2014 Apr;32(2):335-9. <https://doi.org/10.1007/s00345-012-0924-z>

Figures

Figure 1

Prostate image after analysis with ANNA/C-TRUS, tumor-suspicious areas are marked by superimposed red color on the original static image

Figure 2

Comparison between final specimen (left) and ANNA/C-TRUS analysis (right)

Supplementary Files

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