Article

Radiomics and deep learning applications for Prostate Cancer classification: A systematic review.

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**Abstract:** Prostate carcinoma (PCa) classification on MRI using radiomics or deep learning approaches has gained much interest, due to the potential application assisting in clinical decision making. **Objective:**To systematically review the literature to answer the following questions: which algorithms are most frequently used for PCa classification? What is the performance of those methods? Which study design factors affect the performance on PCa classification?  Has the performance been evaluated in a clinical setting? **Methods:** The databases Embase and, Cochrane LIbrary, were searched for studies describing machine learning or deep learning classification methods discriminating between significant and non-significant PCa on multi-parametric MRI that performed a validation procedure. We computed the median AUC from overall methods and the interquartile range. **Results:** From 3946 potentially relevant publications, 37 were included. The most frequent algorithm used in the literature for PCa classification are: random forest (23%), logistic regression (16%) and support vector machines (10%). The median AUC was 0.88 (interquartile range: 0.77 - 0.91). The variation between studies and tumor sizes and Gleason grades was considerable, prohibiting a valid comparison between methods. None of the papers described a validation in a prospective clinical setup. **Conclusions:**To enable the inclusion of radiomics models for PCa from research to clinical stage, researchers should focus on doing prospective validation studies. These studies should include comprehensive descriptions of relevant factors for the model development, patient and tumor characteristics, and validation strategy. By doing so, fair comparison of studies might be feasible.

**Keywords:** keyword 1; keyword 2; keyword 3 (List three to ten pertinent keywords specific to the article; yet reasonably common within the subject discipline.)

0. How to Use This Template

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Remove this paragraph and start section numbering with 1. For any questions, please contact the editorial office of the journal or support@mdpi.com.

1. Introduction

To systematically review the literature to answer the following questions: which algorithms are most frequently used for PCa classification? What is the performance of those methods? Which study design factors affect the performance on PCa classification?  Has the performance been evaluated in a clinical setting?

The introduction should briefly place the study in a broad context and highlight why it is important. It should define the purpose of the work and its significance. The current state of the research field should be reviewed carefully and key publications cited. Please highlight controversial and diverging hypotheses when necessary. Finally, briefly mention the main aim of the work and highlight the principal conclusions. As far as possible, please keep the introduction comprehensible to scientists outside your particular field of research. References should be numbered in order of appearance and indicated by a numeral or numerals in square brackets, e.g., [1] or [2,3], or [4–6]. See the end of the document for further details on references.

2. Results

2.1 Search result

The search generated 3946 potentially relevant publications of which 1505 were duplicated findings. From the remaining 2451 publications, 2271 were removed based on title and/or abstract during screening phase, based on eligibility criteria. Afterwards, 180 articles were found eligible for full text reading and retrieved from their respective journals. From all of these, 143 articles were removed based on exclusion criteria. The remaining 37 studies were included for qualitative synthesis. From these, 8 studies reported enough information to perform meta-analysis (quantitative synthesis).

Qualitative syntesis:

This section may be divided by subheadings. It should provide a concise and precise description of the experimental results, their interpretation as well as the experimental conclusions that can be drawn.

2.1. Subsection

2.1.1. Subsubsection

Bulleted lists look like this:

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All figures and tables should be cited in the main text as Figure 1, Table 1, etc.

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| entry 1 | data | data |
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1 Tables may have a footer.

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|  |  |
| --- | --- |
| a = 1, | (1) |

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The text continues here. Proofs must be formatted as follows:

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3. Discussion

Authors should discuss the results and how they can be interpreted in perspective of previous studies and of the working hypotheses. The findings and their implications should be discussed in the broadest context possible. Future research directions may also be highlighted.

4. Materials and Methods

This systematic review was conducted following the recommendations published on the Preferred Reporting Items for Systematic reviews and Meta-analysis for Diagnostic Test Accuracy (PRISMA-DTA) [reference primsa ] statement. The online databases EMBASE and Cochrane Library were consulted to find articles from January 2008 until January 2020 based on our inclusion criteria: primary publications describing clinically significant PCa classification and/or detection on MRI employing radiomics or any AI approach. The search consisted of the following keywords combination: (radiomics OR deep learning OR machine learning OR texture analysis), (classification OR detection OR segmentation) AND (prostate cancer OR prostate carcinoma OR clinical relevant prostate cancer OR clinically significant prostate cancer ) AND (magnetic resonance OR multiparametric magnetic resonance).

On the figure (PRISMA FIGURE) we summarized our SR protocol. After removal of duplicated findings, the screening process was performed individually by two researchers with experience in medical image analysis. The first researcher was 3rd year PhD student and the second reader x years of post-graduate experience. Both researchers went through the titles and abstracts of potentially relevant publications and decide whether include the study or not. Afterwards, disagreement between researchers was solved by consensus and exclusion criteria.

Previous the eligibility phase, researchers performed a full reading training phase, were they discussed the data extraction from 4 randomly selected articles to check criteria agreement and data collection instrument. Following this training phase, articles were removed when meeting the exclusion criteria, which included the following items: not original research, conference abstracts, publications in other language different than English and studies performing only statistical feature comparison (no ML involved). Furthermore, we also excluded studies that only performed healthy tissue vs PCa tumor classification (without any GS prediction) and articles without description of validation of their methods

After performing qualitative analysis on included papers, we performed a meta-analysis with the studies that complies with detailed information such as: clear patient inclusion criteria, patient Gleason score tumors distribution, area under the curve, sensitivity, and specificity. Statistical analysis was conducted using R language for statistical computing. For statistics computation regarding studies with multiples performance outcomes, we used the highest performance metric reported.

5. Conclusions

This section is mandatory, with one or two paragraphs.

6. Patents

This section is not mandatory, but may be added if there are patents resulting from the work reported in this manuscript.

**Supplementary Materials:** The following are available online at www.mdpi.com/xxx/s1, Figure S1: title, Table S1: title, Video S1: title.

**Author Contributions:** For research articles with several authors, a short paragraph specifying their individual contributions must be provided. The following statements should be used “conceptualization, X.X. and Y.Y.; methodology, X.X.; software, X.X.; validation, X.X., Y.Y. and Z.Z.; formal analysis, X.X.; investigation, X.X.; resources, X.X.; data curation, X.X.; writing—original draft preparation, X.X.; writing—review and editing, X.X.; visualization, X.X.; supervision, X.X.; project administration, X.X.; funding acquisition, Y.Y.”, please turn to the [CRediT taxonomy](http://img.mdpi.org/data/contributor-role-instruction.pdf) for the term explanation. Authorship must be limited to those who have contributed substantially to the work reported.

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Appendix A

The appendix is an optional section that can contain details and data supplemental to the main text. For example, explanations of experimental details that would disrupt the flow of the main text, but nonetheless remain crucial to understanding and reproducing the research shown; figures of replicates for experiments of which representative data is shown in the main text can be added here if brief, or as Supplementary data. Mathematical proofs of results not central to the paper can be added as an appendix.

Appendix B

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References

References must be numbered in order of appearance in the text (including citations in tables and legends) and listed individually at the end of the manuscript. We recommend preparing the references with a bibliography software package, such as EndNote, ReferenceManager or Zotero to avoid typing mistakes and duplicated references. Include the digital object identifier (DOI) for all references where available.

Citations and References in Supplementary files are permitted provided that they also appear in the reference list here.

In the text, reference numbers should be placed in square brackets [ ], and placed before the punctuation; for example [1], [1–3] or [1,3]. For embedded citations in the text with pagination, use both parentheses and brackets to indicate the reference number and page numbers; for example [5] (p. 10), or [6] (pp. 101–105).

1. Author 1, A.B.; Author 2, C.D. Title of the article. *Abbreviated Journal Name* **Year**, *Volume*, page range.
2. Author 1, A.; Author 2, B. Title of the chapter. In *Book Title*, 2nd ed.; Editor 1, A., Editor 2, B., Eds.; Publisher: Publisher Location, Country, 2007; Volume 3, pp. 154–196.
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For all Western blot figures, please include densitometry readings/intensity ratio of each band. In addition, please include the whole blot (uncropped blots) showing all the bands with all molecular weight markers on the Western in the Supplemental Materials

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