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Radiomics and machine learning for predicting the consistency of benign tumors of the central nervous system: A systematic review

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ABSTRACT

Purpose: Predicting the consistency of benign central nervous system (CNS) tumors prior to surgery helps to improve surgical outcomes. This review summarizes and analyzes the literature on using radiomics and/or machine learning (ML) for consistency prediction.
Method: The Medical Literature Analysis and Retrieval System Online (MEDLINE) database was screened for studies published in English from January 1st 2000. Data was extracted according to the PRISMA guidelines and quality of the studies was assessed in compliance with the Quality Assessment of Diagnostic Accuracy Studies 2 (QUADAS-2).
Results: Eight publications were included focusing on pituitary macroadenomas (n = 5), pituitary adenomas (n = 1), and meningiomas (n = 2) using a retrospective (n = 6), prospective (n = 1), and unknown (n = 1) study design with a total of 763 patients for the consistency prediction. The studies reported an area under the curve (AUC) of 0.71–0.99 for their respective best performing model regarding the consistency prediction. Of all studies, four articles validated their models internally whereas none validated their models externally. Two articles stated making data available on request with the remaining publications lacking information with regard to data availability.
Conclusions: The research on consistency prediction of CNS tumors is still at an early stage regarding the use of radiomics and different ML techniques. Best-practice procedures regarding radiomics and ML need to be followed more rigorously to facilitate the comparison between publications and, accordingly, the possible implementation into clinical practice in the future.

1. Introduction

The field of radiomics has seen a rapid development over the past years, facilitated - among other reasons - by the more widespread use of machine learning (ML) techniques [1–3]. Radiomics is based on extracting quantitative features from imaging data and leveraging them for the prediction of different endpoints [4].

Tumor consistency, also called texture or firmness, has been reported to affect surgery-related factors of various benign tumors of the central nervous system (CNS) [5–13]. This includes the timing of surgery, the planning of the surgical approach and the extent of resection, as well as the occurrence of intra-operative injuries and post-operative neurological deficits. A radiomics-based ability to predict the tumor texture prior to surgery would be of great clinical value, as it would allow for improved surgical planning [5–13]. The tumor consistency can be defined by a binary grading system (i.e. soft and hard consistency) or a grading system with several sub-categories as e.g. the Zada's consistency grading system for meningiomas according to the continuous spectrum of tumor firmness [14].

In two systematic reviews published in 2016, researchers investigated whether radiological images can predict meningioma consistency [15,16]. Shiroishi et al. observed that conventional magnetic resonance imaging (MRI) was the most studied imaging modality to forecast the meningioma texture [15]. Out of all imaging methods, T2-weighted MRI was recommended to predict meningioma firmness based on the findings by Yao et al. [16]. Yao et al. further concluded that the signal intensity ratios of tumor to the cerebral cortex or the cerebellar peduncle predicted the consistency most robustly and reliably. However, neither of the two reviews mention the terms radiomics or machine learning [15,16].

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The aim of this review is therefore to summarize the literature on the consistency prediction of benign CNS tumors based on radiological imaging with the use of radiomics or ML and to assess the quality of the analyzed publications.

2. Method

This systematic review was executed in accordance with the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) guidelines where applicable [17].

2.1. Literature search

The literature search was conducted on the Medical Literature Analysis and Retrieval System Online (MEDLINE) database using the PubMed interface without prospective registration. The database was searched for reports concurrently including terms associated with ML techniques and benign CNS tumors in the title according to a previous publication by Windisch et al. [18]. The search terms associated with ML techniques included automated, computer aided, computer-aided, computer-aided design (CAD), radiomic, texture analysis, deep learning, machine learning, neural network, and artificial intelligence. The search keys related to benign brain tumors included meningioma, schwannoma, craniopharyngioma, ganglioglioma, gangliogliomas, glomus, pineocytoma, pilocytic, pituitary, and benign brain tumor. The database was last screened on July 4th 2022 for reports published between January 1st 2000 and the last search date. The following query was used: "((automated[title]) OR (computer aided[title]) OR (computer-aided[title]) OR (CAD[title]) OR (radiomic[title]) OR (radiomics [title]) OR (texture analysis[title]) OR (texture analyses[title]) OR (textural analysis[title]) OR (textural analyses[title]) OR (deep learning [title]) OR (machine learning[title]) OR (ML[title]) OR (neural network [title]) OR (NN[title]) OR (artificial intelligence[title]) OR (AI[title])) AND ((meningioma[title]) OR (meningiomas[title]) OR (schwannoma [title]) OR (schwannomas[title]) OR (craniopharyngioma[title]) OR (craniopharyngiomas[title]) OR (ganglioglioma[title]) OR (gangliogliomas[title]) OR (glomus[title]) OR (glomera[title]) OR (pineocytoma [title]) OR (pineocytomas[title]) OR (pilocytic[title]) OR (pituitary [title]) OR (benign brain tumor[title]) OR (benign brain tumors[title]) OR (benign brain tumour[title]) OR (benign brain tumours[title])) AND ("2000/01/01"[Date - Create]: "2022/07/04"[Date - Create])" [18].

2.2. Inclusion criteria

The retrieved articles were screened for publications predicting the consistency of benign tumors of the CNS based on radiological imaging using ML techniques as follows: First, duplicates were excluded. In a next step, the titles and abstracts of all remaining reports were reviewed independently by the authors C.K. and P.W. with a third author (D.R.Z.) acting as a referee in case of discordance. Only articles in English were included. No automated tools were used for the screening of the articles.

2.3. Data extraction

The data was independently extracted and stored in a standardised form by the authors C.K. and P.W. according to the PRISMA guidelines, the Checklist for Artificial Intelligence in Medical Imaging (CLAIM), and radiomics guidance when applicable [17,19,20]. The extracted characteristics were then discussed by the two authors until consensus was reached. The subsequent data was retrieved (additional characteristics were extracted as apparent in Supplementary Table 2):

Study characteristics: authors, publication year, study design, conflict of interest, funding source, code and data availability, inter- and intrarater variability, ground truth.

Clinical characteristics: tumor entity, tumor size.

Data partition: total number of patients, internal and external validation, assignment procedure, cross-validation.

Imaging protocols: machine model and brand, imaging technique and sequence, magnetic field strength, slice thickness, spacing between slices, information regarding the in-plane resolution.

Radiomics and modeling: dimensionality of the region of interest (ROI), segmentation, number of extracted features, modeling.

Key findings.

2.4. Quality assessment

The bias risk and applicability concern of the included studies were assessed in compliance with the Quality Assessment of Diagnostic Accuracy Studies 2 (QUADAS-2) [21]. The QUADAS-2 was adapted to radiomics and machine learning accordingly. The risk of bias was evaluated for the key domains comprising patient selection, radiomics index test, ML index test, reference standard, and flow and timing. For each key domain, signaling questions were used to assess the risk of bias in accordance with the QUADAS-2. Each signaling question was answered as "yes", "no", or "unclear" (in case of insufficient data). Each key domain was rated as "low", "high", or "unclear" risk of bias. The concern of applicability was assessed for the following domains: patient selection, radiomics index test, ML index test, and reference standard. The concern of applicability was judged based on the recorded information for each domain as "low", "high", and "unclear" [21].

The radiomics quality score (RQS) was calculated using https://www.radiomics.world/rqs for each included study to homogeneously evaluate compliance with best practices [20,22]. The RQS was proposed by Lambin et al. to assess publications based on sixteen criteria. Points between minus five and seven are assigned to each item depending on the significance of the respective item. The components include the following: Image protocol quality, multiple segmentations, phantom study, imaging at multiple time points, feature reduction or adjustment for multiple testing, multivariable analysis with non radiomics features, detect and discuss biological correlates, cuf-off analyses, discrimination statistics, calibration statistics, prospective study, validation, comparison to gold standard, potential clinical utility, cost-effectiveness analysis, open science and data [20,22]. For each criteria, the option associated with the lowest score was selected in case of missing information.

All quality assessment steps were performed by C.K. and reviewed by P.W. with D.R.Z. acting as a referee in case of discordance.

3. Results

3.1. Literature search

The database search and selection process is described in the inclusion flow diagram in Fig. 1. 172 publications were obtained by the database search without identifying any duplicates. Thereof, 163 records were excluded during the review process of the titles and abstracts due to the following reasons. Fifty-one studies were excluded due to the prediction of clinical features other than consistency [23–73]. Forty-five articles focused on predicting pathological features [74–118]. One publication investigated the drivers of costs [119]. Twenty-two records studied the tumor detection or segmentation [120–141]. One paper investigated the automatic segmentation and differentiation of cystic and solid tumor components based on MRI and correlated these radiological features with tumor response after Gamma knife surgery [142]. Two studies examined ML for image reconstruction [143,144]. Four publications focused on ML for tissue analysis [145–148]. Three records looked at tumors in animals [149–151]. Twelve articles did not focus on ML techniques [152–163]. Twenty-one studies were reviews, editorials or corrections rather than original reports [164–184]. One publication examined non-CNS-tumor entities [185]. During the assessment of the remaining nine full-text reports, one additional article was excluded due to the respective full-text article being written in a language other than

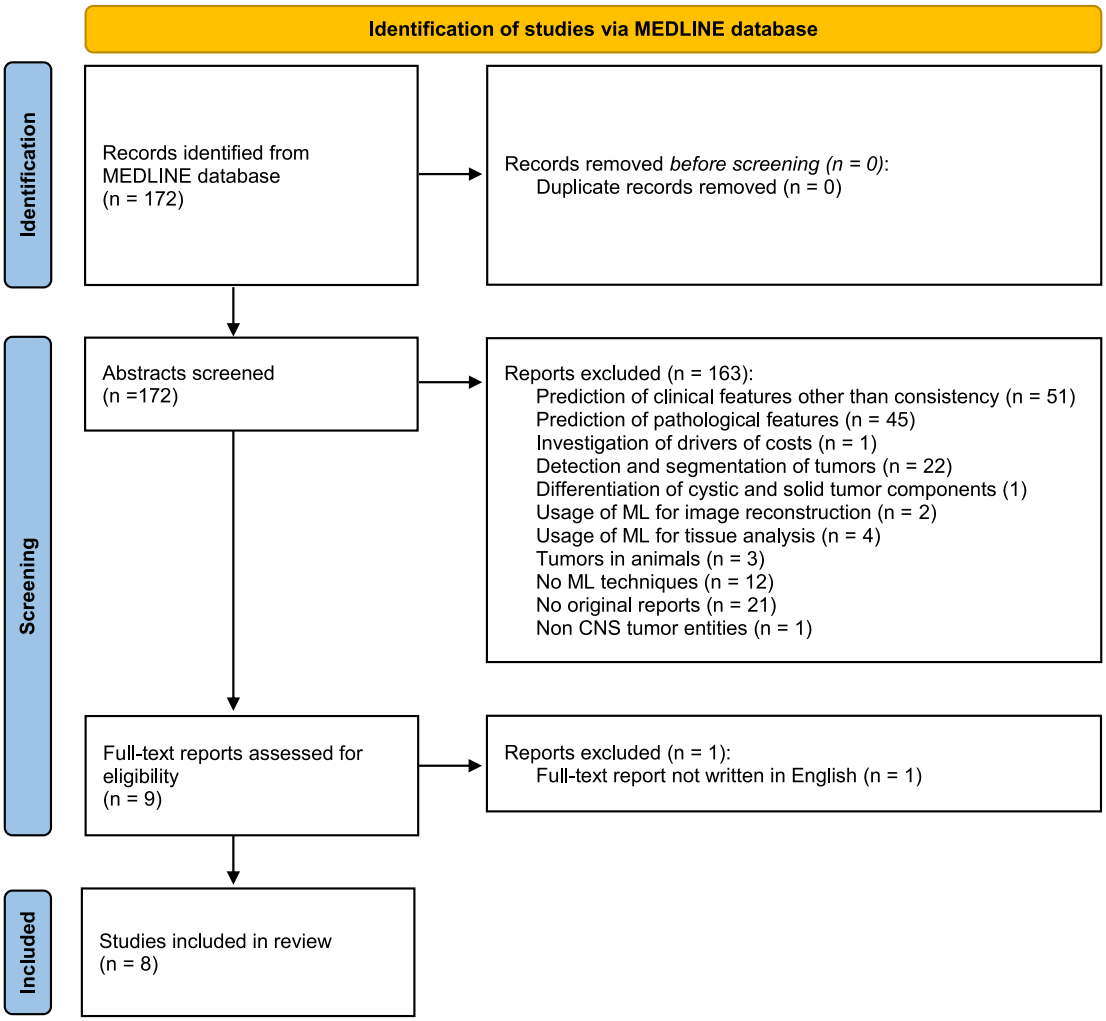

Fig. 1. Inclusion flow diagram. The inclusion flow diagram based on PRISMA 2020.17 From: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:n71. https://doi.org/10.1136/bmj.n71. For more information, visit: https://www.prisma-statement.org/ (accessed on 22 July 2022)17.

English [186]. Ultimately, eight articles were included in this systematic review [187–194]. The Supplementary Table 1 contains a list of all screened articles and the corresponding reasons for exclusion or inclusion coded inline with a previous publication by Windisch et al. [18]. The Supplementary Table 2 includes all gathered characteristics of the studies.

3.2. Characteristics of the included studies

The main characteristics of the included studies are summarized in Table 1 and 2. The papers were published between 2018 and 2022 [187–194]. Thereof, six studies were conducted retrospectively [188–191,193,194], one publication was designed prospectively [192], and one paper did not specify the study design [187]. The studied tumor entities included pituitary macroadenomas (n = 5) [189–193], pituitary adenomas (n = 1) [194], and meningiomas (n = 2) [187,188]. The required tumor size of pituitary macroadenomas was defined as either > 1 cm or ≥ 1 cm [189–193]. Seven studies reported to have no conflict of interest [187–189,191–194] whereas one study did not mention whether there were any conflicts of interest [190]. Four reports did not include a funding statement [188,190,193,194] while two articles reported not receiving any funding [191,192]. Two publications were provided funding by public institutions [187,189]. Six articles did not state data availability [188–193] whereas two reports specified making data available on request [187,194]. For feature extraction, five studies used an open-source software including PyRadiomics [195] (n = 4) [187,189,191,194] and LifEx [196] (n = 1) [188] whereas two articles applied the commercial software Omni Kinetics [190,192]. One publication provided the feature extraction pipeline programmed in MatLab (R2019b) online on GitHub [193]. For feature selection, one study used the open-source software Orange [188,197], another article used SPSS [192], one article used Python [189], and one article applied the Waikato environment [198] for knowledge analysis (Weka) toolkit [191]. The remaining articles neither stated the used software nor provided the programming code used to select the features [187,190,193,194]. For modeling, one publication used SPSS [190] and another article used Python and R [187]. One additional report provided the code written in Python [189]. The residual studies neither specified the used software nor gave access to the programming code used for modeling [188,191–194].

18 to 172 participants were included in each publication [187–194]. Four out of the eight studies validated their models with an internal data set [187,189,193,194]. Thereof, one report assigned the patients randomly to training and validation [193] whereas the remaining studies did not state the assignment procedure [187,189,194]. However, none of the articles validated their models externally, i.e. with a data set from a different institution than the one the data was trained on. Cross-validation was applied in two publications for feature selection

Table 1
Study and clinical characteristics. COI: conflict of interest.

Authors	Year	Entity	Tumor size	Study design	COI	Funding source	Data availability	Code availability
Wan et al.	2021 (issue 2022)	Pituitary macroadenoma	> 1 cm	Retrospective	No	Not mentioned	Not mentioned	Feature extraction: MatLab R2019b (available on github: https://github.com/ccipd/BrIC_Lab)
Rui et al.	2018 (issue: 2019)	Pituitary macroadenoma	> 1 cm	Prospective	No	None	Not mentioned	Feature extraction: in-house software Omni Kinetics (GE healthcare, China), feature selection: SPSS
Wang et al.	2021	Pituitary adenoma	Training (mean +/- SD): 7.9 cm^3 +/- 9.6 cm^3, validation: 7.8 cm^3 +/- 8.7 cm^3	Retrospective	No	Not mentioned	On request	Feature extraction: open-source software PyRadiomics
Cepeda et al.	2020 (issue 2021)	Meningioma	Not mentioned	Retrospective	No	Not mentioned	Not mentioned	Feature extraction: Open-source software LifEx for texture analysis, feature selection: open-source software Orange (university of Ljubjana, Slovenia)
Zeynalova et al.	2019	Pituitary macroadenoma	≥ 1 cm, mean diameter: 2.41 cm (soft: 2.47 cm, hard: 2.24 cm)	Retrospective	No	None	Not mentioned	Feature extraction: open-source software PyRadiomics, feature selection: Waikato environment for knowledge analysis (WEKA) toolkit (amongst others)
Su et al.	2019 (issue 2020)	Pituitary macroadenoma	> 1 cm, max. tumor size: 2.46 cm +/- 0.65 cm (soft: 2.37 cm +/- 0.62 cm, hard: 2.72 cm +/- 0.71 cm)	Retrospective	Not mentioned	Not mentioned	Not mentioned	Feature extraction: in-house software Omnikinetics (GE Healthcare, China), consistency prediction model: SPSS (Chicago, IL; MedCalc for Windows, Mariakerke, Belgium)
Cuocolo et al.	2020	Pituitary macroadenoma	≥ 1 cm (average lesion size: 2.5 cm +/-0.8 cm, range 0.8–4.6 cm)	Retrospective	No	Open access funding provided by Università degli Studi di Napoli Federico II within the CRUI-CARE Agreement	Not mentioned	Feature extraction: open-source software PyRadiomics, feature selection: Python, consistency prediction model: Python (code available)
Zhai et al.	2021	Meningioma	Not mentioned	Not mentioned	No	Joint Construction Project of Medical Science and Technology Planning Project of Henan Province	On request	Feature extraction: open-source software PyRadiomics, consistency prediction model: Python and R software

Table 2
Characteristics of study and data partition. The number of patients refers to the consistency prediction model.

Authors	# of patients[1]	Internal validation	External validation	Assignment procedure	Cross-validation	Inter- and intrarater variability
Wan et al.	156	Yes	No	Random assignment	Yes (modeling: 10-fold cross validation)	Not mentioned
Rui et al.	53	No	No	Not applicable	No	Yes
Wang et al.	Clinical and radiomics model: 170[2]	Yes[2]	No	Not mentioned[3]	Yes (modeling: 10-fold cross validation)	Not mentioned
Cepeda et al.	18	No	No	Not applicable	Yes (modeling: 5-fold cross-validationl)	Not mentioned
Zeynalova et al.	55	No	No	Not applicable	Yes (feature selection: Nested cross-validation approach with 10-fold inner and outer loops, respectively, modeling: 10-fold cross-validation)	Not mentioned
Su et al.	50	No	No	Not applicable	No	Not mentioned
Cuocolo et al.	89	Yes	No	Not mentioned	Yes (feature selection: 5-fold cross-validation)	Interrater variability used to exclude unstable features
Zhai et al.	172	Yes	No	Not mentioned	No	Interrater variability used to exclude unstable features

[1] For the consistency prediction model
[2] The clinical consistency prediction model was validated whereas it is unclear for the radiomics consistency prediction model whether a training and validation data set and 170 patients were included
[3] The 170 patients include part of the first group and the entire second group. It is unclear how the subset of the first group was selected (entire group of 163 patients used for automatic segmentation and feature extraction). Additional 50 patients selected through secondary recruitment as a second group for the training and validation data set.

[189,191] and in three reports for modeling [188,193,194]. One study measured inter- and intrarater variability [192]. Two articles used interrater variability to exclude unstable features [187,189]. The remaining publications did not report inter- or intrarater variability [188,190,191,193,194].

3.3. Ground truth

The definition of the ground truth, i.e. the tumor consistency, can be found for all studies in Table 3. In all publications, the firmness was classified into soft and hard consistency [187–194]. Thereof, one article applied Zada's consistency grading system differentiating between five consistency grades with grade 1 and 2 assigned to soft and grade 3, 4, and 5 characterized as hard texture [14,188]. The tumor consistency was defined based on surgical findings in six articles [187,189,190,192–194] and based on the combination of surgical and histopathological results in one study [191]. Cepeda et al. specified the tumor texture based on intraoperative ultrasound strain elastography (IOUS-E) and surgical outcomes [188]. Specifically, the surgical findings were used to determine the cut-off value of the mean tissue elasticity by randomly selecting a group of patients. The reference value was then used to distinguish between soft and hard tumor firmness for the remaining patients [188].

3.4. Imaging

The imaging protocols of the included studies are summarized in Table 4. MRI machines from different brands were used, including machine models from Siemens, GE Healthcare, and Philips [187–194]. Six articles used one single model from one brand for all patients, respectively [188,190–194]. One report stated the use of two MRI machines from different brands [189] whereas another publication reported the use of three different machine models from the same brand [187]. All studies used some form of magnetic resonance (MR) imaging with varying imaging sequences as follows: T1-weighted (T1) [190,193,194], contrast-enhanced T1-weighted (T1c) [187,190,193,194], T2-weighted (T2) [187,190,193,194], T1-weighted spin echo (T1 SE) [188,192], contrast-enhanced T1-weighted spin echo (T1c SE) [188,192], T2-weighted turbo spin echo (T2 TSE) [188,189,191], turbo spin-echo contrast enhanced T2-weighted 3D sequence using variable flip angles for refocusing (3D-T2c SPACE) [192], fluid attenuated inversion recovery imaging (FLAIR) [187], and readout segmentation of long variable echo-trains diffusion-weighted imaging (RESOLVE DWI) [190]. The magnetic field strength was 3 T in four publications [190,192–194] and 1.5 T in two records [188,191] while one article used two machines with a field strength of 3 T and 1.5 T, respectively [189]. One article did not state the magnetic field strength [187]. Overall, the slice thickness ranged from 1 mm up to 5 mm [187–194]. The spacing between slices was between 0 mm and 6.75 mm [187,189–194] with missing specifications in one study [188]. In three studies, the MR images were resampled to the same resolution [187–189].

3.5. Radiomics and modeling

The radiomics and modeling characteristics are depicted in Table 5. The selected ROI was three-dimensional (3D) in five studies [187,188,190,193,194] and two-dimensional (2D) in three publications [189,191,192]. The ROI was segmented automatically in two reports [188,193] and manually in five articles [187,189–192] while one publication reported both automatic and manual segmentations [194]. 0 to 37 features were extracted in the included studies with some articles extracting a varying number of features for the different investigated models, respectively. A variety of modeling approaches were investigated including random forest [187,188,193,194], (linear) support vector machine [187,188,193,194], different types of logistic regression [187,188,190], other tree-based classifiers [189,194], k neighbors

Table 3
Definition of the ground truth.

Authors	Definition of ground truth	Definition of ground truth (details)
Wan et al.	Surgical	Soft tumor: removable by aspiration and curettage after incision of the dura mater, firm: not removable by aspiration, sometimes required electrocoagulation or sharp segmentation resection. Consistency assessment immediately after surgery by two neurosurgeons
Rui et al.	Surgical	Soft tumor: easily removable by aspiration or curettage, firm tumor: not removable by aspiration or curettage but needing piecemeal resection by a microdissector or tumor forceps. Consistency assessment based on surgical notes and video recordings right after surgery by two neurosurgeons.
Wang et al.	Surgical	Soft: suctioned out using an aspirator, firm: not removable by suctioning out
Cepeda et al.	IOUS-E and surgical	Intraoperative findings of the ultrasound elastography (IOUS-E) as gold standard of stiffness by manual segmentation of five different slices followed by the average of the intensity histograms as the mean tissue elasticity (MTE). Cut-off value of MTE defined based on a regression tree by radomly selecting a group of patients. Reference value of the MTE was established by reviewing the intraoperative videos and assessing the tumor consistency by the opening of the tumor capsule.
Zeynalova et al.	Surgical and histopathological	Surgical findings: soft tumor (easily removable from the opening of the dura through aspiration), hard tumor (not easily removable from the opening of the dura through aspiration), retrospective consistency assessment based on surgical notes and video records by two neurosurgeons. Histopathological examination: mainly by two pathologists blinded to clinical, surgical, and radiological data of the patients. In case of any discrepancy, a third pathologist was involved. In case of a disagreement between the surgical and histopathological findings on consistency, the decision was achieved by consensus.
Su et al.	Surgical	Soft tumors: easily removable through aspiration or curettage, hard tumors: not removable through aspiration and/or curettage and requiring piece-meal resection by use of a microdissector or tumor forceps. Immediate assessment of tumor consistency after surgery by two neurosurgeons.
Cuocolo et al.	Surgical	Soft tumor consistency: easily removable with conventional maneuvers of curettage and suction, fibrous tumor consistency: difficult to remove and thus requiring more complex maneuvers such as extracapsular dissection. Consistency assessment by double-blinding two neurosurgeons based on the lesions' inner surgical features.
Zhai et al.	Surgical	Tumor consistency classification based on surgical videos and operative recordings according to Zada's consistency grading system. Soft: Grade 1 & 2 (completely removable or mainly removable by suction), firm: Grade 3, 4, and 5 (requiring sharp resection, ultrasonic aspiration or with calcified lesions).

Table 4
Characteristics of the imaging protocols. T1: T1-weighted, T1c: contrast-enhanced T1-weighted, T2: T2-weighted, T2c: contrast-enhanced T2-weighted, DWI: diffusion-weighted imaging, FLAIR: fluid attenuated inversion recovery imaging, ADC: apparent diffusion coefficient, 3D-T2c SPACE: turbo spin-echo T2c-weighted 3D sequence using variable flip angles for refocusing, SE: spin echo, TSE: turbo spin echo, RESOLVE-DWI: readout segmentation of long variable echo-trains diffusion-weighted imaging.

Authors	Machine: model & brand	Imaging technique & sequence	Magnetic field strength	Slice thickness	Spacing between slices	Information regarding the in-plane resolution
Wan et al.	MAGNETOM TrioTim (Siemens, Berlin, Germany)	T1, T1c, T2	3 T	3 mm	T1 & T2: 6.5 mm, T1c: 3.3 mm	T1: FOV 220 mm × 220 mm, matrix size 512 × 432; T1c: FOV 220 mm × 220 mm, matrix size: 512 × 512; T2: 220 mm × 220 mm, matrix size: 512 × 432
Rui et al.	Magnetom Verio (Siemens, Germany)	T1 SE, T1c SE, 3D-T2c SPACE	3 T	T1-SE & T1c SE: 2.5 mm, 3D-T2c SPACE: 1 mm	T1 SE & T1c SE: 0 mm, 3D-T2c SPACE: 0 mm	T1 SE: matrix: coronal: 350 × 512, sagittal: 175 × 256, field of view: 224 × 230)
Wang et al.	Discovery MR 750 (GE Healthcare)	T1, T2, T1c	3 T	T1c: 3 mm	T1c: 0.39 mm	T1c: 512 × 512 × 8 pixel
Cepeda et al.	SignaHDxt (GE Healthcare, Milwaukee, Wisconsin, USA)	T1 SE(?), T1c SE, T2 TSE, DWI	1.5 T	T1, T1c SE: 1 mm	Not mentioned	Resampled to 0.5 × 0.5 × 0.5 pixels° (T1 & post-contrasted T1-weighted SE: FOV 220 × 220 mm, matrix: 512 × 512 × 8 pixels; not mentioned for the remaining sequences)
Zeynalova et al.	Magnetom Avanto (Siemens)	T2 TSE	1.5 T	2.5 mm	2.8 mm	0.5–0.8 mm (in-plane pixel size, FOV: 180 mm × 180 mm, matrix size: 224 × 320)
Su et al.	Magnetom Verio Tim (Siemens, Erlangen, Germany)	T1, T1c, T2, RESOLVE-DWI with ADC1000 and ADC2000	3 T	T1, T1c, T2: 2 mm, RESOLVE-DWI: 3 mm	T1, T1c, and T2: not mentioned, RESOLVE-DWI: 0.9 mm	T1 & T1c: FOV: 200 × 200 mm^2, matrix: 320 × T2: FOV 200 × 200 mm^2, matrix 384 × RESOLVE-DWI: FOV 200 &times
Cuocolo et al.	Gyroscan Intera (Philips, Eindhoven, the Nettherlands) and Magnetom Trio (Siemens Medical Solutions, Erlangen, Germany)	T2 TSE	Gyroscan Intera: 1.5 T, Magnetom Trio: 3 T	3 mm	0 mm	Resampled to 2 × 2 × 2 mm isotropic voxels (FOV: 180 × 180 mm/200 × 200 mm, matrix: 288 × 288/384 × 384)
Zhai et al.	Prisma, TrioTim, and Verio (Siemens Healthineers, Erlangen, Germany)	T1c, T2, FLAIR, ADC	Not mentioned	T1c: 5 mm, T2: 5 mm, FLAIR: 5 mm, ADC: 5 mm	T1c: 6.5–6.75 mm, T2: 6.5–6.75 mm, FLAIR: 6.5–6.75 mm, ADC: 6.5–6.75 mm	Resampled to 3 × 3 × 3 mm

Table 5
Radiomics, modeling, and radiomics quality score (RQS). 2D: two-dimensional, 3D: three-dimensional.

Authors	ROI dimensionality	Segmentation	# of extracted features	Modeling	RQS
Wan et al.	3D	Automatic	4–11	Random forest, support vector machine	12/36
Rui et al.	2D	Manual	6	Binary logistic regression	16/36
Wang et al.	3D	Automatic, manual	0–37 features	Linear support vector machine, random forest classifier, extra trees classifier, k neighbors classifier, decision tree classifier, gradient boosting classifier, adaptive boosting classifier, multi-layer perceptron, extreme gradient boosting classifier	12/36
Cepeda et al.	3D	Automatic	3	LASSO (least absolute square shrinkage and select operator) logistic regression, naive Bayes, k neighbors classifier, multi-layer perceptron algorithm (neural network), random forest, and support vector machine	9/36
Zeynalova et al.	2D	Manual	6	Artificial neural network	14/36
Su et al.	3D	Manual	6	Multivariate logistic regression analysis	10/36
Cuocolo et al.	2D	Manual	14	Extra trees classifier	16/36
Zhai et al.	3D	Manual	28	Random forest, k neighbors classifier, support vector machine, logistic regression, adaboost classifier	15/36

classifier [187,188,194], (extreme) gradient boosting classifier [194], adaptive boosting classifier [194], multi-layer perceptron [188,194], naive Bayes [188], and artificial neural network [191].

3.6. Pituitary adenoma

Wang et al. observed that the model using automatic segmentations showed superior performance compared to the one with manual segmentations in terms of the consistency prediction of pituitary adenomas [194]. Their automatic segmentation model achieved the highest area under the curve (AUC) of 0.920 when selecting 27 radiomics features [194].

Wan et al. reported an AUC of 0.9, an accuracy of 97%, a sensitivity of 83% and a specificity of 87% for their best performing model predicting the texture of pituitary macroadenomas. This model combined T1, T1c, and T2 imaging features [193].

Likewise, the firmness of pituitary macroadenomas was predicted with an AUC of 0.99, an accuracy of 93%, a sensitivity of 100% and a specificity of 87% based on T2 images according to Cuocolo et al. [189].

Zeynalova et al. compared a model including radiomics and a machine learning classifier to the evaluation of the signal intensity ratio of T2 TSE images regarding the predictive performance of the texture of pituitary macroadenomas [191]. An AUC of 0.710 and an accuracy of 72.5% were stated for the former whereas an AUC of 0.551 and an accuracy of 74.5% were observed for the latter [191]. The article by Zeynalova et al. was the only one using both surgical and histopathological findings to define the ground truth out of all the reports on pituitary macroadenomas [189–193].

Rui et al. identified three radiomics features each correlated positively and negatively with the consistency of pituitary macroadenomas based on 3D-T2c SPACE [192]. The combination of positively correlated features achieved an AUC of 0.836, a sensitivity of 85.2%, and a specificity of 69.2% while combining the negatively correlated features resulted in an AUC of 0.819, a sensitivity of 88.9%, and a specificity of 61.5% [192].

Su et al. observed a significant difference (i.e. p-value < 0.05) in radiomics parameters based on the apparent diffusion coefficient with b-values b = 1000 s/mm^2 and b = 2000 s/mm^2 in terms of soft and hard pituitary macroadenomas [190]. The performance was superior for ADC (b = 2000 s/mm^2) compared to ADC (b = 1000 s/mm^2) parameters. In contrast, no significant difference was calculated for T2 radiomics parameters. The multivariate logistic regression achieved an AUC of 0.911, sensitivity of 78.4%, and specificity of 92.3% by combining the mean value and the entropy of ADC (b = 2000 s/mm^2) [190].

3.7. Meningioma

Zhai et al. developed and validated a radiomics nomogram predicting the meningioma consistency with an AUC of 0.960 for validation [187]. They determined the ground truth based on surgical findings [187].

The consistency prediction model of Cepeda et al. reported a similar AUC of 0.961 and a classification accuracy and precision of 94% and 95% by using intraoperative findings of the ultrasound elastography combined with surgical findings to define the ground truth [188]. However, Cepeda et al. did not use a previously unseen validation cohort for their model and instead used a 5-fold cross-validation [188].

3.8. Quality assessment

RQSs are depicted in Table 5. Scores of 9 to 16 out of 36 points (i.e. 25.00 to 44.44%) were calculated with none of the publications claiming to follow the RQS criteria [187–194]. The item-by-item scoring of the RQS is included in Supplementary Table 2. The risk of bias and concern of applicability are summarized in Fig. 2A and 2B. On the whole, the risk of bias was assessed as unclear for all articles regarding the patient selection. It was judged as low for three studies and as high for five studies regarding the index test and reference standard, respectively. It was further rated as low for one study, as high for one study, and as unclear for six studies regarding the flow and timing. The concern of applicability was assessed as low for six studies and high for two reports regarding the patient selection. Furthermore, it was judged as low for all articles regarding the index test and reference standard, respectively [187–194].

4. Discussion

The consistency prediction of benign CNS tumors using radiomics and ML is still at an early stage. Eight studies published between 2018 and 2022 were included in this systematic review predicting the consistency of pituitary adenomas, pituitary macroadenomas, and meningiomas [187–194]. 18 to 172 patients were included in the publications,

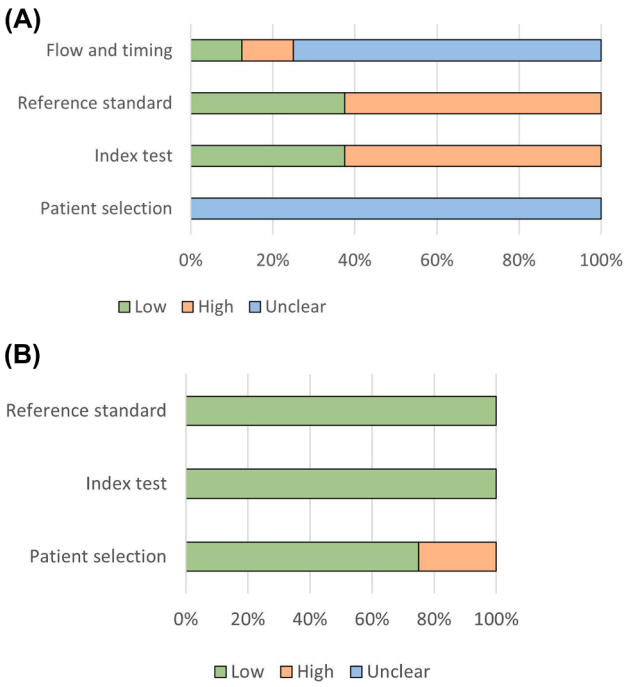

Fig. 2. A: QUADAS-2: Risk of bias. Summary of all included studies regarding the risk of bias based on the Quality Assessment of Diagnostic Accuracy Studies 2 (QUADAS-2).21 B: QUADAS-2: Concern of applicability. Summary of all included studies in terms of the concern of applicability based on the QUADAS-2.21.

respectively. An AUC was reported of up to 0.96 for meningiomas, 0.71 to 0.99 for pituitary macroadenomas, and 0.92 for pituitary adenomas regarding the best radiomics model for consistency prediction of the included publications. However, these values can only be compared and summarized with reservations due to the missing internal validation in case of four studies and accordingly the risk of overfitting. None of the articles validated their models with data from another institution to test for generalizability of their models [187–194].

The limitations of the evidence include that all publications were single-center studies with mostly a retrospective study design conducted with a limited number of patients and partly missing internal validation [187–194]. None of the articles claimed to follow guidelines and checklists specifically for radiomics or artificial intelligence [187–194]. For instance, it is reported in some articles that two physicians determined the ground truth while no other guidelines and checklists were mentioned [189,190,192]. However, two reports stated following guidelines including the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines [188,199] and the standard guidelines for retrospective observational and diagnostic studies as well as MRI studies [193]. The RQSs of 9 to 16 out of 36 possible points indicates that there is room for improvement in terms of the adherence to guidelines [187–194]. Providing standard wordings for writing publications in specific research fields might enhance the adherence to guidelines by lowering the amount of missing specifications and thereby improving the applicability of quality assessments. In a systematic review on the topic of RQS, the overall median RQS was 21.00% (i.e., 7.56 out of 36 points, interquartile range of 11.50) for all included systematic reviews on various topics [200]. There was no significant difference in the median in the subgroup analysis on varying application domains, indicating that there is a general need for improved quality in the field [200].

There seems to be a shift in research from basic models to more sophisticated radiomics models used to predict the consistency of benign CNS tumors according to the findings of this review and the reviews by Shiroishi et al. and Yao et al. published in 2016 [15,16]. Shiroshi et al.

concluded in their review on consistency prediction of meningioma published in 2016 that T2 weighted MR images are a promising, but not yet validated method for consistency prediction [15]. They further reported a lack in publications using more advanced MRI techniques such as DWI [15]. Similarly, Yao et al. came to the conclusion that T2 weighted MR images are suggested to predict the meningioma texture [16]. The included studies in this review used a variety of imaging sequences and applied radiomics for modeling [187–194]. One included publication even directly compared their radiomics model to using the signal intensity ratio of T2 weighted images with the former outperforming the latter in terms of the prediction capacity [191].

Due to the difficulty of consistently executing radiomics studies, the reproduction and replication of the articles' results would be facilitated by providing the imaging protocols, the scans, the segmentations of the volume of interest, feature extraction and selection, and the model [20]. Data sharing was rare with only two publications providing the data on request while the remaining neither provided the data nor mentioned data sharing [187–194]. However, providing the data entails legal and privacy issues such as the risk of utilization for facial feature recognition with a sufficiently high image resolution [20]. Further obstacles to overcome include a lack of human resources or time, differences in the culture or language, the political or academic value of data, reputation hazards, and methods of data recording [20]. Several initiatives have tried to address this issue such as the centralized data approach by CancerLinQ and the distributed data approach by euroCAT [201,202]. Code sharing would be beneficial to better understand the methodology description as e.g. in the case of one included publication with an incomplete description of the feature selection procedure [190]. Furthermore, the use of commercial softwares poses a problem if the code is not provided as in the case of two of the included studies in terms of the feature extraction [190,192].

Limits of this review comprise a restricted number of included studies, a heterogenous characterization of methodologies, and accordingly the absence of a quantitative analysis. Furthermore, the MEDLINE database was the only one screened for this paper, but we consider this limitation to be mitigated by the fact that most publications in the field appear in journals indexed in this database. Strengths of this work include adhering to the PRISMA guidelines, as well as the discussion of the application of CLAIM, and the radiomics guidance.

Our results imply that services for model deployment need to be further developed for future research, policy, and practice. Thereby, reviewers and readers could test these models with their own data. Further multicentric collaborations are required for data handling including the sharing, storing, and curation of data. This would promote prospective studies and facilitate recruiting a sufficient number of patients and thus allowing to not only develop but also validate models to test their generalizability.

5. Conclusion

In conclusion, the included studies reported that some of their implemented models were capable of predicting the consistency of benign CNS tumors based on MR images. Before these models can be used for clinical practice, however, further research is needed with larger, preferably multicentric patient cohorts. This would allow for testing for overfitting and other potential biases of these predictive models and for further investigating the various MRI techniques. Adherence to guidelines is crucial to allow for an easier assessment of potential sources of bias.

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CRediT authorship contribution statement

Carole Koechli: Data curation, Formal analysis, Investigation, Methodology, Project administration, Visualization, Writing – original draft. **Daniel R. Zwahlen:** Investigation, Supervision, Writing – review & editing. **Philippe Schucht:** Supervision, Writing – review & editing. **Paul Windisch:** Conceptualization, Data curation, Formal analysis, Investigation, Project administration, Supervision, Writing – review & editing.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ejrad.2023.110866.

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