TITLE:

Evaluating persistent biases and quality issues in inter-modality image translation studies for neuroradiology: a systematic review

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Supplementary methods

There are several tools available for evaluating the quality of research studies. For this work, we considered how relevant the tool was for AI and medical imaging, as well as how common the tool was in similar systematic reviews. We considered three tools for our work, CLAIM, QUADAS-2, and PROBAST.
CLAIM is designed for AI studies and imaging studies, so it was included in this work.
QUADAS-2 was found to have significant overlap with PROBAST, our determination of overlapping criteria is shown below. PROBAST was developed more recently and has a more thorough explanation document, as well as deeper analysis of the model analysis, so we chose to use it for our study rather than QUADAS.

Overlap between QUADAS-2 and PROBAST criteria:

QUADAS-2 criteria	**Overlapping PROBAST criteria**
1.1	1.1
1.2	1.1
1.3	1.2
2.1	3.5 - not relevant for image translation
2.2	4.7 - not relevant for image translation
3.1	Domain 2: Applicability
3.2	2.2 - not relevant for AI
4.1	3.6 - relevant for time-sensitive analyses
4.2	2.1 - not relevant for AI
4.3	2.1 - not relevant for AI
4.4	4.3 - not relevant for AI

CLAIM:

Overview:
In general, the approach from Sivanesan, et al. will be followed.
CLAIM is designed specifically for AI studies in medical imaging, so the questions should be relevant to the studies included in this review.
It should be noted that CLAIM is designed based on the STARD criteria for diagnostic studies. Many image-to-image translation models are designed for attenuation correction, radiotherapy planning, MRI-only protocols, and other purposes unrelated to classification tasks. Thus, questions such as CLAIM 14 and 15 are difficult to judge since the work generates an image rather than annotations or a diagnosis. Without image annotations, there is no need for annotation evaluations, so questions 16-18 are not applicable to those studies.

See also supplementary table 1 for detailed judging criteria.

PROBAST

Overview:
PROBAST was extensively designed to evaluate prognostic or diagnostic studies where the patients are provided a treatment and their outcomes are recorded. This is vastly different from AI development research where it is unethical to alter the outcome of a patient until the AI model has been approved by the appropriate regulatory agency. However, several questions posed are relevant to nearly all studies, and these can help differentiate the methods of the researchers.

Thus, a modified PROBAST was used to evaluate if the methods or datasets used in these studies showed risks of bias. Questions were omitted if they are not relevant to AI models or to image generation studies. Below are the criteria all studies were judged using. See also supplementary table 2.

Domain 1. Participants

Question 1.1: Domain 1 examines if the enrolled patients were appropriate for the study. Several aspects of the traditional PROBAST are not applicable to image translation, For our work we considered if the included participants were collected consistently and that there weren't any obvious exclusions that would have gifted the authors a cleaner dataset at the expense of population representation.

Most studies utilized a publicly available dataset. While these are encouraged in AI research, many are not ideal for medical research.[1-5] It is common to curate data for AI research in a way that alters the demographic and disease ratios,[1, 2, 4-6] or so that only the cleanest examples of only the target disease are included. However, real patient data can show many conditions at the same time and there may be artifacts from movement or differences in equipment. Further, curated data may have a set prevalence—so the model has enough training data—which may differ wildly from actual population prevalence. This means the model looks great using the training data, but can only perform this well when given images within that prevalence and that rank of image quality. So, the use of public datasets is a source of concern if the target population does not match that of the current study.

Question 1.2: though the inclusion and exclusion criteria are relevant to establish any changes to the prevalence ratio, this information is not explicitly stated in most studies. The importance of including clear inclusion and exclusion criteria is two-fold. If certain images have been excluded such that misrepresents the typical image quality[4] or the disease or demographic prevalence in the population,[7] the resultant model will have poor performance on real images.[2, 4, 8-14] Conversely, it is reasonable to exclude images from AI model development if they may lead to spurious correlations.[2, 15] Studies which clearly stated their exclusion criteria were rated as low risk of bias.[16]

Domain 2. Predictors

This domain is meant to identify human biases (such as knowing the answer before performing the assessment) and bias introduced by using different means to identify or collect the predictors.

In our work, we consider the features of the input image as the predictors, and the output translated image as the outcome. However, the predictors are not being "assessed" in a traditional sense, an AI is identifying the features, then mathematically manipulating them according to rules it made up. Therefore, this entire domain is unlikely to have any bias and was excluded.

Domain 3. Outcome

This domain is designed to identify bias caused by inappropriately defining or assessing the outcome. In our case, the outcome is the generation of the translated image rather than a diagnosis or prognosis. So, again, this domain was excluded.

Questions 3.1 and 3.2 of this domain ask if the person collecting the outcome data did so knowing how much data and in what format it should be collected. Again, this is not applicable to AI studies since the model always outputs the outcome (translated image) according to its algorithm. Similarly, questions 3.4 and 3.6 are not applicable for AI studies.

Questions 3.3 and 3.5 are inappropriate for image translation studies because the outcome is completely dependent on the predictors. In cases where the translated image is used as part of a diagnostic test, question 3 may be applicable, but we have excluded it for the purpose of this review.

Domain 4. Analysis

Domain 4 is designed to assess if the final data was evaluated appropriately to form the resultant model performance measurement. For example, did enough patients have the outcome to create an adequate sample size? Did the researchers utilize p-hacking techniques such as altering the category definitions to fit the results? This domain is the most complex, but also the most relevant to AI model development studies.

Question 4.1 asks if the sample size was appropriate. This question is relevant to AI model development as small test datasets are not sufficient to prove generalizability[5, 17] or expose any biases or overfitting[18, 19] that happened during training. There is no standard for either the required number of individuals or the included number of images for multi-section modalities such as MRI. PROBAST recognizes that the necessary number of patients for machine learning studies differs based on model type and purpose, but recommends validation on a test set including more than 100 individuals. Studies with fewer than 100 patients in the test dataset were regarded as at high risk of bias.

A question for future studies is "Is it acceptable to test on thousands of images from one patient and assume similar results will be produced for other patients?" Particularly for MRI and CT models, there may be very few patients, but thousands of images. It is not yet possible to prove this question, so, we considered the number of patients to be the main determinant here.

Question 4.2 is not appropriate for image translation works and was excluded.
Question 4.3 and 4.4 are not appropriate for AI studies.
Question 4.5 is not appropriate for AI studies since the algorithm is not subject to this problem.
Question 4.6 is not relevant for image translation studies and was excluded.
Question 4.7 addresses model calibration. This is usually calculated for AI models using AUC, the c-index, or sensitivity and specificity, which are not applicable to image translation studies

Question 4.8 asks if the model optimism caused by insufficient data was addressed. PROBAST explicitly states that splitting a single dataset into training and test datasets is not adequate; the authors must test on an external dataset. An external test set shows if the model is robust to typical image variance[2, 14] and may expose learned biases which can be addressed with further model training. Studies with no external testing data were marked as high risk of bias.

Question 4.9 is not relevant for AI models.

Adherence evaluation

Statistical tests for CLAIM:
In general, the approach from Sivanesan, et al. will be followed.

"Yes" and "N/A" are scored as 1 point, while "No" is 0 points.

The Shapiro-Wilks test was used to confirm normal distribution of CLAIM adherence scores, the two-sample t test was used to compare means and the Wilcoxon rank-sum test was used to compare median scores between manuscripts published in medically-focused vs engineering-focused journals. Fisher's exact test was used to compare medically-focused versus engineering-focused studies.

Statistical tests for PROBAST:

Each of the 5 possible responses is given a score. As shown in the table below, questions are given zero points for a "no" answer, one point for a "probably no" answer, two points for an "unclear" answer, three points for a "probably yes" answer and four points for a "yes" answer. This gives a total possible total score of 16 for the four questions. We can then use this score to rank studies based on the extent of bias rather than the classification of at risk of bias or not.

Study adheres to the PROBAST criteria	Points
Yes	4
Probably Yes	3
Unclear	2
Probably No	1
No	0

The Shapiro-Wilks test was used to confirm normal distribution of PROBAST adherence scores, the two-sample t test was used to compare means and the Wilcoxon rank-sum test was used to compare median scores between manuscripts published in medically-focused vs engineering-focused publications. Fisher's exact test was used to compare medically-focused versus engineering-focused studies.

Statistical significance is defined as $P < .05$.

Search criteria:

We chose our search criteria based on the most commonly used terms and their variants. These terms were based on our inclusion criteria: radiological imaging, image translation using AI.
In the case of IEEE, since there was no filter to ensure medically related studies were returned, we added exclusion criteria to filter out unrelated topics.

Scopus

8/2/2023
(TITLE-ABS-KEY (radiology) OR TITLE-ABS-KEY (radiography) OR TITLE-ABS-KEY (radiograph) OR TITLE-ABS-KEY (computed tomography) OR TITLE-ABS-KEY (CT) OR TITLE-ABS-KEY (MRI) OR TITLE-ABS-KEY (magnetic resonance) OR TITLE-ABS-KEY (positron emission tomography) OR TITLE-ABS-KEY (PET) OR TITLE-ABS-KEY (x-ray))
AND (TITLE-ABS-KEY (pix2pix) OR TITLE-ABS-KEY ("image translation") OR TITLE-ABS-KEY ("generative adversarial network") OR TITLE-ABS-KEY ("generative network") OR TITLE-ABS-KEY ("GAN") OR TITLE-ABS-KEY (" cycleGAN ") OR TITLE-ABS-KEY (" image synthesis ") OR TITLE-ABS-KEY (" image generation ") OR TITLE-ABS-KEY (" image-to-image "))
AND (LIMIT-TO (SUBJAREA , "MEDI"))

IEEE Xplore

8/9
2015 - present
NOT (("Full Text Only":"transducer") OR ("Full Text Only":"face recognition") OR ("Full Text Only":"automotive") OR ("Full Text Only":"defect detect") OR ("Full Text Only":"automobile") OR ("Full Text Only":"transportation") OR ("Full Text Only":"radar") OR("Full Text Only":"baggage inspection") OR ("Full Text Only":"sonar") OR ("Full Text Only":"remote sensing") OR ("Full Text Only":"suspicious object") OR ("Full Text Only":"addiction") OR ("Full Text Only":"welding") OR ("Full Text Only":"Fourier") OR ("Full Text Only":"solder") OR ("Full Text Only":"antenna") OR ("Full Text Only":"pollution") OR ("Full Text Only":"mobile communication") OR ("Full Text Only":"security") OR ("Full Text Only":"forgery") OR ("Full Text Only":"forensic"))

AND (("Full Text Only":"magnetic resonance") OR ("Full Text Only":"positron emission tomography") OR ("Full Text Only":"computed tomography") OR ("Full Text Only":"PET") OR ("Full Text Only":"MRI") OR ("Full Text Only":"CT") OR ("Full Text Only":"radiograph") OR ("Full Text Only":"x-ray") OR ("Full Text Only":"radiography")) AND (("Full Text Only":"deep learning") OR ("Full Text Only":"AI") OR ("Full Text Only":"artificial intelligence")) AND (("Full Text Only":"image translation") OR ("Full Text Only":"GAN") OR ("Full Text Only":"generative adversarial network") OR ("Full Text Only":"cycleGAN") OR ("Full Text Only":"pix2pix") OR ("Full Text Only":"image generation") OR ("Full Text Only":"image-to-image") OR ("Full Text Only":"image synthesis"))

Pubmed

12/18/2023 1015 results
("Pix2Pix"[All Fields] OR "conditional gan"[All Fields] OR "cGAN"[All Fields] OR "image-to-image"[All Fields] OR "image-to-image"[All Fields] OR "image translation"[All Fields] OR "image synthesis"[All Fields] OR "synthesized image"[All Fields] OR "generative adversarial network"[All Fields] OR "GAN"[All Fields]) AND ("radiology"[All Fields] OR "radiograph"[All Fields] OR "x-ray"[All Fields] OR "radiography"[All Fields] OR "positron emission tomography"[All Fields] OR "PET"[All Fields] OR "MR"[All Fields] OR "magnetic resonance"[All Fields] OR "CT"[All Fields] OR "computed tomography"[All Fields])
AND ("artificial intelligence"[All Fields] OR "AI"[All Fields] OR "machine learning"[All Fields] OR "deep learning"[All Fields]) AND 2010/01/01:2024/12/31[Date - Publication]

R code for Shapiro-Wilk normality test

```
> shapiroResults <- shapiro.test(shapiroInputData)
> cat("Shapiro-Wilk Test:\n")
> cat("Test Statistic =", shapiroResults$statistic, "\n")
> cat("P-value =", shapiroResults$p.value, "\n")
```

R code for determining Fisher's statistic

For CLAIM tables

	Medically focused	Engineering focused
Y		
N		

```
# Load the readxl package if not already loaded
if (!requireNamespace("readxl", quietly = TRUE)) {
  install.packages("readxl")
  library(readxl)
}

# Specify the directory path where your .xlsx files are located
folder_path <- "/Users/Desktop/"

# List all .xlsx files in the specified folder
xlsx_files <- list.files(path = folder_path, pattern = ".xlsx", full.names = TRUE)

# Create an empty list to store the matrices
matrices <- list()

# Loop through the .xlsx files and read them into matrices
for (file in xlsx_files) {
  # Read the .xlsx file into a data frame
  data <- read_excel(file)

  # Convert the data frame to a matrix
  data_matrix <- as.matrix(data)

  # Assign a name to the matrix (e.g., based on the file name)
  matrix_name <- sub(".xlsx", "", basename(file))

  # Store the matrix in the list
  matrices[[matrix_name]] <- data_matrix
}

# You now have a list of matrices, where each matrix corresponds to a .xlsx file.
# You can access them using matrices[[1]], matrices[[2]], etc.

for (i in 1:length(matrices)) {
  result <- fisher.test(matrices [[i]])
  results_list[[i]] <- result
}
```

```
# Specify the directory and filename where you want to save the CSV file
output_file <- "/Users/Desktop/results.csv"

# Write the results_list to a CSV file
write.csv(do.call(rbind, results_list), file = output_file, row.names = FALSE)
```

for PROBAST tables:

	Medically focused	Engineering focused
Y or PY		
U, PN, or N		

```
#Import table for each question (four times in this work)
> library(readxl)
> Table <- ("Users/Desktop/Table.xlsx")

#Add row names
> rownames(Table) = c("Yes", "Probably Yes", "Unclear", "Probably No", "No")

# Convert table to matrix
> Matrix1 <- as.matrix(Table)

#Perform Fisher’s Exact test
> fisher.test(Matrix1,,simulate.p.value = TRUE)

        Fisher's Exact Test for Count Data with simulated p-value (based on 2000 replicates)
```

Supplementary results

Analysis results:
Shapiro-Wilk normality test using all data:

CLAIM adherence:
Test Statistic = 0.9758616
P-value = .05841379
The data is normally distributed

Probast adherence
Test Statistic = 0.7777314
P-value < .000001
The data is not normally distributed

Shapiro-Wilk normality test using studies from medically-focused journals

CLAIM adherence:
Test Statistic = 0.9608678
P-value = .04048373
The data is not normally distributed

Probast adherence
Test Statistic = 0.7363182
P-value < .000001
The data is not normally distributed

Shapiro-Wilk normality test using studies from engineering-focused journals

CLAIM adherence:
Test Statistic = 0.937612
P-value = .03507005
The data is not normally distributed

Probast adherence
Test Statistic = 0.8972887
P-value = .0021388
The data is not normally distributed

Supplementary Tables

Supplementary table 1. CLAIM criteria as used in this study

Title/ Abstract	1	Is AI, GAN, or deep learning mentioned in the title, abstract, or keywords? (main text only)
	2	Is there a rational order to the abstract? (main text only)
Introduction	3	Is background and rationale for the work described? (main text only)
	4	Is the purpose of the work described? (main text only)
Methods	5	Do the authors explicitly state that data was prospectively or retrospectively collected? (main text only)
	6	Is some study goal described in the introduction or methods? (main text only)
	7	Is the source of the data described? (main text or supplement)
	8	Do the authors detail which data was eligible, including where it is from and when the exams occurred? (main text or supplement)
	9	If the authors perform preprocessing of the data, is it described? (main text or supplement)
	10	Are data subsets used in the study? This refers to preprocessing subsets, not training/validation (main text or supplement)
	11	Do the authors define the data using terms common for indexing? (main text or supplement)
	12	Do the authors state that and how data was deidentified or anonymized? (main text or supplement)
	13	Do the authors state how missing data was handled? (main text or supplement)
	14	Typically the Ground Truth is the target imaging modality. Do the authors state enough details for replication? (ie: T1 MRI rather than MRI) (main text or supplement)
	15	N/A if image translation only. Do the authors give reason for this Ground Truth if there are variations within the modality? (ie: manual versus computer-assisted segmentation or T1 MRI rather than T2 MRI) (main text or supplement)
	16	N/A if image translation only. For segmentation works, are the annotators qualifications listed? (main text or supplement)
	17	N/A if image translation only. For segmentation works, are the segmentation tools described? (main text or supplement)
	18	N/A if image translation only. For segmentation works, was the variability described? (main text or supplement)
	19	Do the authors justify the size of the dataset with sample size calculations anywhere in the text? (main text or supplement)
	20	Are the training/test dataset partitions described in either patient numbers or proportions? (main text or supplement)
	21	Do the authors state that the above partitions were on a patient/image/ etc basis? (main text or supplement)
	22	Is the model described in enough detail that an AI researcher could replicate it? Best is with a figure. (main text or supplement)
	23	Are the software libraries (python, etc) listed? (main text or supplement)
	24	Is model parameter initialization described? (main text or supplement)
	25	Are training details described? Especially hyperparameters and any augmentation used. (main text or supplement)
	26	Did the authors describe when to stop training? Describing the loss functions is sufficient. If multiple models were developed, how was the best model chosen? (main text or supplement)
	27	N/A if no ensembling is apparent. If ensembling applied, was the method described? (main text or supplement)
	28	Do the authors state the metrics they will use in the methods section? ("No" if you have to guess the metrics by looking at the table.) (main text only)

	29	Do the authors state how they measured significance (if numerical values were used)? This can be significance when using p-value or confidence range. (main text or supplement)
	30	Was there evaluation of robustness of the model? Or were results shown for all participants? ie: violin plots, geometrical accuracy plots. (main text or supplement)
	31	Do the authors provide saliency maps, uncertainty maps, or error maps for model explainability? (main text or supplement)
	32	Was there an external test dataset? Can be geographic or temporal. (main text only)
Results	33	Is there a diagram detailing the inclusion and exclusion of participants? (main text or supplement)
	34	Are relevant demographics presented for each partition? (main text or supplement)
	35	Are the performance metrics described in #28 presented? (main text only)
	36	Are confidence intervals for the performance metrics given? (main text or supplement)
	37	Is there any evaluation of failed or improperly classified or segmented cases? (main text or supplement)
Discussion	38	Are limitations explicitly provided? (main text only)
	39	Do the authors discuss how this model is clinically valuable? (main text only)
Other information	40	Was the study registered? (main text or supplement)
	41	If there is a separate protocol, is the website or supplementary file described? N/A if no additional information provided (main text only)
	42	Are funding sources revealed? (main text only)

Supplementary table 2. PROBAST criteria as used in this study

Domain 1		
	1.1	Was internal data used or a public dataset? Were there consistent collection methods? Was there a data collection protocol? Was the dataset size determined based on reaching statistical significance? Was the data collection setting described? Were collection dates described? Was this a convenience, consecutive, or random sample? Was the disease/normal distribution consistent with the population at that facility? Were dataset demographics listed? (at least sex) Was the disease/normal distribution consistent with the population at that facility? Were reader/annotator qualifications described? (if applicable) Was any pre-processing performed? (including cropping and resizing) Was data anonymized? Were there methods for handling missing data?
	1.2	Were inclusion or exclusion criteria appropriate?
Domain 2		Not appropriate for AI
Domain 3		Not appropriate for image translation
Domain 4		
	4.1	Were there enough patients in the test set? (>100)
	4.2	Not appropriate for image translation
	4.3	Not appropriate for image translation
	4.4	Not appropriate for image translation
	4.5	Not appropriate for AI
	4.6	Not appropriate for Image translation
	4.7	Were calibration and discrimination assessed?
	4.8	Did the authors consider and compensate for model optimism? Especially by use of an external test.
	4.9	Not appropriate for AI

Supplementary table 3. Included studies

First author	Publication year	Translation direction	Clinical purpose	Purpose category	Source journal type
Abu-Srhan A[20]	2021	bidirectional MRI-CT	Treatment	Radiotherapy planning	Medicine
Amini Amirkolaee H[21]	2022	bidirectional MRI-CT	No specific clinical purpose	Image translation	Medicine
Amini Amirkolaee H[22]	2022	bidirectional MR-CT, bidirectional PET-CT	No specific clinical purpose	Image translation	Engineering
Anaya E[23]	2020	MRI-CT	Diagnosis	Attenuation correction	Engineering
Arabi H[24]	2019	MRI-CT	Diagnosis	Attenuation correction	Medicine
Armanious K[25]	2019	PET-CT	Diagnosis	Attenuation correction	Engineering
Armanious K[26]	2020	PET-CT	Diagnosis	Attenuation correction	Medicine
Bazangani F[27]	2022	PET-MR	No specific clinical purpose	Image translation	Engineering
Bharti V[28]	2023	bidirectional MRI-CT	Treatment	Radiotherapy planning	Medicine
Blanc-Durand P[29]	2019	MRI-CT	Diagnosis	Attenuation correction	Medicine
Bourbonne V[30]	2021	MRI-CT	Treatment	Radiotherapy planning + dose calculations	Medicine
Cao G[31]	2021	MRI-CT	Treatment	Radiotherapy planning	Engineering
Chen X[32]	2022	MRI-CT	Segmentation	Segmentation	Engineering
Choi H[33]	2018	PET-MR	Diagnosis	Amyloid burden quantification	Medicine
Dinkla AM[34]	2018	MRI-CT	Treatment	Radiotherapy planning + dose calculations	Medicine
Dovletov G[35]	2022	MRI-CT	Treatment	Radiotherapy planning	Engineering
Emami H[36]	2020	MRI-CT	Treatment	Radiotherapy planning	Engineering
Emami H[37]	2018	MRI-CT	Treatment	Radiotherapy planning	Medicine
Estakhraji SIZ[38]	2023	MRI-CT	Treatment	Radiotherapy planning	Medicine
Feng E[39]	2022	CT-MRI	Segmentation	Stroke lesion identification	Medicine
Garzon G[40]	2022	CT-MRI	Segmentation	Stroke lesion identification	Engineering
Gholamiankhah F[41]	2022	MRI-CT	Treatment	Radiotherapy planning	Medicine
Gong K[19]	2018	MRI-CT	Diagnosis	Attenuation correction	Medicine
Gong K[42]	2021	MRI-CT	Diagnosis	Attenuation correction	Medicine
Gu X[43]	2023	CT-MRI	Treatment	Radiotherapy planning	Medicine
Gu Y[44]	2021	MRI-CT	Treatment	Radiotherapy planning	Engineering
Gupta D[45]	2019	MRI-CT	Treatment	Radiotherapy planning + dose calculations	Medicine
Gutierrez A[46]	2022	bidirectional MRI-CT	Segmentation	Stroke lesion identification	Medicine
Han R[47]	2022	MRI-CT	Registration	Registration	Engineering
Han R[48]	2021	MRI-CT	Registration	Registration	Engineering
Han X[49]	2017	MRI-CT	Treatment	Radiotherapy planning	Medicine
Hashimoto F[50]	2021	PET-CT	Diagnosis	Attenuation correction	Medicine

First author	Publication year	Translation direction	Clinical purpose	Purpose category	Source journal type
Hu S[51]	2022	MRI-PET	Diagnosis	Alzheimer's classification	Engineering
Hu S[52]	2019	MRI-PET	Diagnosis	Diagnosis	Engineering
Huo Y[53]	2019	CT-MRI	Segmentation	Segmentation	Engineering
Hussein R[54]	2022	MRI-PET	Diagnosis	Diagnosis of several diseases	Engineering
Jabbarpour A[55]	2022	MRI-CT	Treatment	Radiotherapy planning + dose calculations	Medicine
Jang H[56]	2018	MRI-CT	Diagnosis	Attenuation correction	Medicine
Jiao J[57]	2020	US-MRI	Diagnosis	Diagnosis	Engineering
Jin C B[58]	2019	CT-MRI	Treatment	Radiotherapy planning	Engineering
Jin C B[59]	2018	CT-MRI	Treatment	Radiotherapy planning	Engineering
Kazemifar S[60]	2020	MRI-CT	Treatment	Radiotherapy planning + dose calculations	Medicine
Kazemifar S[61]	2019	MRI-CT	Treatment	Radiotherapy planning + dose calculations	Medicine
Kearney V[62]	2019	MRI-CT	Treatment	Radiotherapy planning	Medicine
Kläser K[63]	2021	MRI-CT	Diagnosis	Attenuation correction	Medicine
Kläser K[64]	2021	MRI-CT	Treatment	Radiotherapy planning	Medicine
Koh H[65]	2022	MRI-CT	Treatment	Therapy planning	Medicine
Koike Y[66]	2019	MRI-CT	Treatment	Radiotherapy planning + dose calculations	Medicine
Ladefoged CN[67]	2019	MRI-CT	Diagnosis	Attenuation correction	Medicine
Lan H[68]	2021	MRI-PET	Diagnosis	Diagnosis	Medicine
Lei Y[69]	2019	MRI-CT	Treatment	Radiotherapy planning	Engineering
Lei Y[70]	2019	MRI-CT	Treatment	Radiotherapy planning	Medicine
Li G[71]	2019	MRI-CT	Treatment	Radiotherapy planning	Engineering
Li W[72]	2020	CT-MRI	Treatment	Radiotherapy planning	Medicine
Li Y[73]	2020	MRI-CT	Treatment	Radiotherapy planning	Engineering
Li Y[74]	2020	bidirectional MRI-CT	No specific clinical purpose	Image translation	Medicine
Liu F[75]	2018	MRI-CT	Diagnosis	Attenuation correction	Medicine
Liu F[76]	2019	MRI-CT	Treatment	Radiotherapy planning + dose calculations	Medicine
Liu H[77]	2021	MRI-PET	Diagnosis	Amyloid burden quantification	Medicine
Liu H[78]	2020	MRI-PET	Diagnosis	Amyloid burden quantification	Engineering
Liu M[79]	2022	CT-MRI	Treatment	Radiotherapy planning	Engineering
Liu X[80]	2021	MRI-CT	Treatment	Radiotherapy planning + dose calculations	Medicine
Maspero M[81]	2020	MRI-CT	Treatment	Radiotherapy planning + dose calculations	Medicine
Nehra R[82]	2021	MRI-CT	Treatment	Radiotherapy planning	Engineering
Neppl S[83]	2019	MRI-CT	Treatment	Radiotherapy planning + dose calculations	Medicine
Nie D[84]	2017	MRI-CT	Treatment	Radiotherapy planning	Medicine
Nie D[85]	2018	MRI-CT	Treatment	Radiotherapy planning	Engineering

First author	Publication year	Translation direction	Clinical purpose	Purpose category	Source journal type
Nijskens L[86]	2023	MRI-CT	Treatment	Radiotherapy planning + dose calculations	Medicine
Pan Y[87]	2018	MRI-PET	Diagnosis	Alzheimer's classification	Medicine
Prokopenko D[88]	2019	MRI-CT	Treatment	Radiotherapy planning	Engineering
Qin J[89]	2022	MRI-PET	Prognosis	MRI-only Glioma management	Medicine
Ranjan A[90]	2021	MRI-CT	Treatment	Radiotherapy planning	Medicine
Reinhold JC[91]	2020	CT-MRI	No specific clinical purpose	Image translation	Engineering
Reinhold JC[92]	2020	CT-MRI	Segmentation	Segmentation	Engineering
Rubin J[93]	2019	CT-MRI	Segmentation	Stroke lesion identification	Engineering
Sanaat A[94]	2021	MRI-CT	No specific clinical purpose	Image translation	Medicine
Shafai-Erfani G[95]	2019	MRI-CT	Treatment	Radiotherapy planning + dose calculations	Medicine
Singh M[96]	2021	MRI-CT	Treatment	Radiotherapy planning	Engineering
Soltanpour M[97]	2023	CT-MRI	Segmentation	Stroke lesion identification	Engineering
Spuhler KD[98]	2019	MRI-PET	Diagnosis	Attenuation correction	Medicine
Stimpel B[99]	2019	MRI-Xray	Treatment	Interventional imaging	Engineering
Sun B[100]	2022	MRI-CT	Treatment	Radiotherapy planning	Medicine
Sun H[101]	2019	MRI-PET	Diagnosis	Diagnosis	Engineering
Takamiya K[102]	2023	MRI-CT	Treatment	Radiotherapy planning	Engineering
Takita H[103]	2023	MRI-PET	Diagnosis, Prognosis	Diagnosis, Prognosis of glioma	Medicine
Tang B[12]	2020	MRI-CT	Treatment	Radiotherapy planning + dose calculations	Medicine
Tao L[104]	2020	MRI-CT	Diagnosis	Attenuation correction	Medicine
Wang C[105]	2021	MRI-CT	Treatment	Radiotherapy planning + dose calculations	Medicine
Wang C[106]	2022	MRI-CT	Treatment	Radiotherapy planning + dose calculations	Medicine
Wang CC[107]	2022	MRI-CT	Treatment	Radiotherapy planning	Medicine
Wang J[108]	2022	MRI-CT	Treatment	Radiotherapy planning	Medicine
Wang J[109]	2022	MRI-CT	Treatment	Radiotherapy planning + dose calculations	Medicine
Wang J[110]	2021	MRI-CT	Treatment	Radiotherapy planning	Engineering
Wang J[111]	2023	bidirectional MRI-CT	No specific clinical purpose	Image translation	Medicine
Wei W[112]	2019	MRI-PET	Diagnosis	MRI-only MS classification	Medicine
Wolterink J[113]	2017	MRI-CT	Treatment	Radiotherapy planning	Medicine
Xiang L[114]	2018	MRI-CT	Treatment	Radiotherapy planning	Medicine
Xu R[115]	2022	MRI-CT	Treatment	Radiotherapy planning	Engineering
Yang H[116]	2020	MRI-CT	Registration	Registration	Medicine
Yang H[117]	2020	MRI-CT	Treatment	Radiotherapy planning	Engineering
Zhang J[118]	2022	MRI-PET	Diagnosis	Alzheimer's classification	Medicine

First author	Publication year	Translation direction	Clinical purpose	Purpose category	Source journal type
Zhao S[119]	2022	MRI-CT	Treatment	Radiotherapy planning + dose calculations	Medicine

Supplementary table 4. Timing of imaging pairs for model training

First author	Clinical purpose	Purpose category	Database name	Case-cohort, consecutive, or case-control sample	Timing between source image and ground truth image
Abu-Srhan A[20]	Treatment	Radiotherapy planning	Han (2017), pooled with internal data	random, unknown	Unclear
Amini Amirkolaee H[22]	No specific clinical purpose	Image translation	Han (2017)	random	Unclear
Amini Amirkolaee H[22]	No specific clinical purpose	Image translation	Han (2017)	random	Unclear
Anaya E[23]	Diagnosis	Attenuation correction	internal	cohort	Unclear
Arabi H[24]	Diagnosis	Attenuation correction	internal	cohort	Unclear
Armanious K[25]	Diagnosis	Attenuation correction	internal	consecutive	Unclear
Armanious K[26]	Diagnosis	Attenuation correction	internal	cohort	joint PET/CT scanner (SOMATOM mCT)
Bazangani F[27]	No specific clinical purpose	Image translation	ADNI (10/11/2020)	controls taken from database	less than 1 year
Bharti V[28]	Treatment	Radiotherapy planning	Al-Kadi (2021)	cohort	N/A
Blanc-Durand P[29]	Diagnosis	Attenuation correction	manufacturer's dataset, internal	consecutive	Unclear
Bourbonne V[30]	Treatment	Radiotherapy planning	internal	cohort	less than 14 days
Cao G[31]	Treatment	Radiotherapy planning	internal	cohort	N/A
Chen X[32]	Segmentati on	Segmentation	CQ500, ADNI	cohort	Unclear
Choi H[33]	Diagnosis	Amyloid burden quantificatio n	ADNI	cohort	Unclear
Dinkla AM[34]	Treatment	Radiotherapy planning	internal	cohort	Unclear
Dovletov G[35]	Treatment	Radiotherapy planning	RIRE	cohort	Unclear
Emami H[36]	Treatment	Radiotherapy planning	internal	cohort	Unclear
Emami H[37]	Treatment	Radiotherapy planning	internal	cohort	Unclear
Estakhraji SIZ[38]	Treatment	Radiotherapy planning	internal	cohort	within 48 hours
Feng E[39]	Segmentati on	Stroke lesion identification	ISLES2018	stroke cohort	within 3 hours
Garzon G[40]	Segmentati on	Stroke lesion identification	ISLES2017 & ISLES2018 for training, testing on iDBMRXFDG	unclear, unclear, healthy cohort	unpaired training, same day for iDBMRXFDG
Gholamiank hah F[41]	Treatment	Radiotherapy planning	internal	cohort	Unclear
Gong K[19]	Diagnosis	Attenuation correction	internal	healthy cohort	Unclear
Gong K[42]	Diagnosis	Attenuation correction	internal	healthy cohort	Unclear
Gu X[43]	Treatment	Radiotherapy planning	internal	cohort	within 2 weeks

First author	Clinical purpose	Purpose category	Database name	Case-cohort, consecutive, or case-control sample	Timing between source image and ground truth image
Gu Y[44]	Treatment	Radiotherapy planning	https://brainweb.bic.mni.mcgill.ca/	cohort	Unclear (all synthetic data)
Gupta D[45]	Treatment	Radiotherapy planning	internal	cohort	Unclear
Gutierrez A[46]	Segmentation	Stroke lesion identification	pooled ESCAPE trial, the I-KNOW study, the INTERRSeCT study, and local datasets from the University Medical Center, Hamburg-Eppendorf	RCT, cohort, cohort, unclear	2-7 days after symptoms (follow-up imaging), unclear
Han R[48]	Registration	Registration	internal	cohort	same day
Han R[47]	Registration	Registration	internal	cohort	same day
Han X[49]	Treatment	Radiotherapy planning	internal (this is the Han dataset source paper)	random	Unclear
Hashimoto F[50]	Diagnosis	Attenuation correction	internal	cohort	Unclear
Hu S[52]	Diagnosis	Diagnosis	ADNI	cohort	Unclear
Hu S[51]	Diagnosis	Alzheimer's classification	ADNI, OASIS-3 for test	cohort	Unclear
Huo Y[53]	Segmentation	Segmentation	OASIS	cohort	N/A
Hussein R[54]	Diagnosis	Diagnosis of several diseases	internal	case-control	simultaneously
Jabbarpour A[55]	Treatment	Radiotherapy planning	internal	cohort	N/A
Jang H[56]	Diagnosis	Attenuation correction	internal	cohort	same day
Jiao J[57]	Diagnosis	Diagnosis	MRI from CRL fetal brain atlas, US from INTERGROWTH-21st project	convenience	N/A
Jin C B[58]	Treatment	Radiotherapy planning	internal	cohort	Unclear
Jin C B[59]	Treatment	Radiotherapy planning	internal	cohort	Unclear
Kazemifar S[60]	Treatment	Radiotherapy planning	internal	random, cohort	Unclear
Kazemifar S[61]	Treatment	Radiotherapy planning	internal	cohort	Unclear
Kearney V[62]	Treatment	Radiotherapy planning	internal	cohort	Unclear
Kläser K[63]	Diagnosis	Attenuation correction	internal	cohort	immediately after
Kläser K[64]	Treatment	Radiotherapy planning	internal	cohort	same day
Koh H[65]	Treatment	Therapy planning	internal	cohort	Unclear
Koike Y[66]	Treatment	Radiotherapy planning	TCIA	cohort	Unclear
Ladefoged CN[67]	Diagnosis	Attenuation correction	internal	cohort	less than 8 months
Lan H[68]	Diagnosis	Diagnosis	ADNI	random	Unclear
Lei Y[70]	Treatment	Radiotherapy planning	internal	cohort	Unclear
Lei Y[69]	Treatment	Radiotherapy planning	internal	cohort	Unclear

First author	Clinical purpose	Purpose category	Database name	Case-cohort, consecutive, or case-control sample	Timing between source image and ground truth image
Li G[71]	Treatment	Radiotherapy planning	internal	cohort	Unclear
Li W[72]	Treatment	Radiotherapy planning	internal	unclear	Unclear
Li Y[73]	Treatment	Radiotherapy planning	internal	cohort	Unclear
Li Y[74]	No specific clinical purpose	Image translation	internal	cohort	Unclear
Liu F[75]	Diagnosis	Attenuation correction	internal	stroke cohort	same day
Liu F[76]	Treatment	Radiotherapy planning	internal	stroke cohort for training, cancer cohort for testing	same day
Liu H[78]	Diagnosis	Amyloid burden quantificatio n	internal	cohort	simultaneously
Liu H[77]	Diagnosis	Amyloid burden quantificatio n	internal	cohort	simultaneously
Liu M[79]	Treatment	Radiotherapy planning	SZSPH dataset	unclear	Unclear
Liu X[80]	Treatment	Radiotherapy planning	internal	cohort	Unclear
Maspero M[81]	Treatment	Radiotherapy planning	internal	cohort	within 35 days, but one outlayer at 521 days
Nehra R[82]	Treatment	Radiotherapy planning	ADNI	cohort	N/A
Neppl S[83]	Treatment	Radiotherapy planning	internal	cohort	Unclear
Nie D[84]	Treatment	Radiotherapy planning	ADNI	cohort	Unclear
Nie D[85]	Treatment	Radiotherapy planning	ADNI	cohort	Unclear
Nijskens L[86]	Treatment	Radiotherapy planning	internal	cohort	within 1.5 months
Pan Y[87]	Diagnosis	Alzheimer's classification	ADNI-1 and ADNI-2	cohort	Unclear
Prokopenko D[88]	Treatment	Radiotherapy planning	TCIA CPTAC, Head-and-neck cancer dataset, internal (internal split for train and test)	cohort	N/A
Qin J[89]	Prognosis	MRI-only Glioma management	TCIA ACRIN-FMISO-Brain	cohort	1-7 days
Ranjan A[90]	Treatment	Radiotherapy planning	Atlas project	cohort	1-5 days
Reinhold JC[91]	No specific clinical purpose	Image translation	internal	healthy cohort	Unclear
Reinhold JC[92]	Segmentati on	Segmentation	internal	healthy cohort	Unclear
Rubin J[93]	Segmentati on	Stroke lesion identification	ISLES2018	stroke cohort	within 3 hours
Sanaat A[94]	No specific clinical purpose	Image translation	internal	cohort	Unclear

First author	Clinical purpose	Purpose category	Database name	Case-cohort, consecutive, or case-control sample	Timing between source image and ground truth image
Shafai-Erfani G[95]	Treatment	Radiotherapy planning	internal	cohort	Unclear
Singh M[96]	Treatment	Radiotherapy planning	internal	cohort	Unclear
Soltanpour M[97]	Segmentation	Stroke lesion identification	internal	cohort	Unclear
Spuhler KD[98]	Diagnosis	Attenuation correction	internal	cohort	Unclear
Stimpel B[99]	Treatment	Interventional imaging	internal	cohort	Unclear
Sun B[100]	Treatment	Radiotherapy planning	ABCs MICCAI 2020 challenge dataset	cohort	N/A
Sun H[101]	Diagnosis	Diagnosis	ADNI	cohort	similar dates
Takamiya K[102]	Treatment	Radiotherapy planning	internal	cohort	Unclear
Takita H[103]	Diagnosis, Prognosis	Diagnosis, Prognosis of glioma	internal, TCIA	cohort	within 1 month
Tang B[12]	Treatment	Radiotherapy planning	internal	cohort	same day
Tao L[104]	Diagnosis	Attenuation correction	internal	cohort	Unclear
Wang C[105]	Treatment	Radiotherapy planning	internal	cohort	same day for initial CT, 3 days or less for replanning CT
Wang C[106]	Treatment	Radiotherapy planning	internal	cohort	same day for initial CT, 3 days or less for replanning CT
Wang CC[107]	Treatment	Radiotherapy planning	internal	cohort	Unclear
Wang J[108]	Treatment	Radiotherapy planning	internal	cohort	less than 2 days
Wang J[109]	Treatment	Radiotherapy planning	internal	cohort	N/A
Wang J[110]	Treatment	Radiotherapy planning	internal	cohort	less than one month
Wang J[111]	No specific clinical purpose	Image translation	Han (2017)	selected cohort of 1/3 of dataset	Unclear
Wei W[112]	Diagnosis	MRI-only MS classification	internal	age-matched case-control	Unclear
Wolterink J[113]	Treatment	Radiotherapy planning	internal	cohort	same day
Xiang L[114]	Treatment	Radiotherapy planning	ADNI	cohort	Unclear
Xu R[115]	Treatment	Radiotherapy planning	internal	cohort	N/A
Yang H[116]	Registration	Registration	internal	healthy cohort	Unclear
Yang H[117]	Treatment	Radiotherapy planning	internal	cohort	Unclear
Zhang J[118]	Diagnosis	Alzheimer’s classification	ADNI	cohort	Unclear
Zhao S[119]	Treatment	Radiotherapy planning	internal, model pre-trained on RIRE	cohort	within 1 week

Supplementary table 5. CLAIM adherence per clinical purpose

Clinical purpose	Medicine		Engineering	
	N	CLAIM score	N	CLAIM score
Diagnosis	19	75%	8	69%
Prognosis	2	74%	0	
Registration	1	67%	2	75%
Segmentation	2	69%	6	58%
Treatment	37	73%	19	63%
No specific clinical purpose	4	70%	3	65%

N: number of studies.

Supplementary table 6. CLAIM adherence per criteria excluding conference publications

		Medically-focused Journal publications (N=61)				Engineering-focused Journal publications (N=11)				P-value
	Criteria	Yes	No	N/A	% adherence	Yes	No	N/A	% adherence	
TITLE / ABSTRACT	1	60	1	0	98%	9	2	0	82%	0.0590
	2	61	0	0	100%	11	0	0	100%	1.0000
INTRO-DUCTION	3	61	0	0	100%	11	0	0	100%	1.0000
	4	61	0	0	100%	11	0	0	100%	1.0000
METHODS	5	19	42	0	31%	0	11	0	0%	**0.0307**
	6	61	0	0	100%	11	0	0	100%	1.0000
	7	61	0	0	100%	10	1	0	91%	0.1528
	8	20	41	0	33%	0	11	0	0%	**0.0279**
	9	55	6	0	90%	9	2	0	82%	0.5990
	10	10	0	51	100%	0	0	11	100%	1.0000
	11	60	1	0	98%	10	1	0	91%	0.2840
	12	5	56	0	8%	0	11	0	0%	1.0000
	13	4	57	0	7%	0	11	0	0%	1.0000
	14	61	0	0	100%	11	0	0	100%	1.0000
	15	8	0	53	100%	0	0	11	100%	1.0000
	16	3	6	52	90%	0	0	11	100%	0.5812
	17	7	2	52	97%	0	0	11	100%	1.0000
	18	1	8	52	87%	0	0	11	100%	0.3439
	19	1	60	0	2%	0	11	0	0%	1.0000
	20	59	1	1	98%	10	1	0	91%	0.2840
	21	53	7	1	89%	8	3	0	73%	0.1740
	22	60	1	0	98%	11	0	0	100%	1.0000
	23	48	13	0	79%	7	4	0	64%	0.2754
	24	29	32	0	48%	8	3	0	73%	0.1909
	25	53	7	1	89%	11	0	0	100%	0.5854
	26	58	3	1	95%	11	0	0	100%	1.0000
	27	0	0	61	100%	0	0	11	100%	1.0000
	28	58	3	0	95%	11	0	0	100%	1.0000
	29	36	25	0	59%	3	8	0	27%	0.0972
	30	25	36	0	41%	3	8	0	27%	0.5108
	31	43	18	0	70%	8	3	0	73%	1.0000
	32	6	55	0	10%	0	11	0	0%	0.5812
RESULTS	33	2	59	0	3%	0	11	0	0%	1.0000
	34	21	40	0	34%	0	11	0	0%	**0.0269**
	35	61	0	0	100%	11	0	0	100%	1.0000
	36	6	1	54	98%	0	0	11	100%	1.0000
	37	19	42	0	31%	1	10	0	9%	0.2704
DISCUSSION	38	33	28	0	54%	4	7	0	36%	0.3378
	39	57	4	0	93%	9	2	0	82%	0.2258
OTHER	40	2	4	55	93%	0	1	10	91%	0.5748
	41	26	0	35	100%	4	0	7	100%	1.0000
	42	47	14	0	77%	10	1	0	91%	0.4387

Bold indicates significance.

Supplementary table 7. CLAIM adherence per purpose group

	Medicine		Engineering	
Purpose group	N	CLAIM score	N	CLAIM score
Alzheimer’s classification	2	0.655	2	0.750
Attenuation correction	12	0.752	2	0.655
CT-based radiotherapy planning	0		3	0.667
MRI-only Glioma management	2	0.762	0	
MRI-only MS classification	1	0.833	0	
MRI-only radiotherapy planning	34	0.737	15	0.627
Other	10	0.712	8	0.667
Registration	1	0.667	2	0.750
Segmentation	0		3	0.659
Stroke lesion identification	2	0.690	3	0.508

N: number of studies. MS: Multiple sclerosis

Supplementary table 8. PROBAST adherence results per question

PROBAST question	% Yes or Probably Yes (low risk of bias) Medically-focused (N=64)	Engineering-focused (N=38)	P-value
1.1	100%	87%	**0.006**
1.2	28%	13%	0.0919
4.1	11%	5%	0.4781
4.8	13%	3%	0.1482

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