

Deep Interactive Segmentation of Medical Images: A Systematic Review and Taxonomy

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APPENDIX A CLICK GUIDANCE SIGNALS

Clicks are defined as 3D or 2D points, i.e., $c_i \in \mathbb{R}^3$ or $c_i \in \mathbb{R}^2$, depending on the dimensions of the input image. We define the set of clicks provided by the annotator as $\mathcal{C} := \{c_1, \dots, c_N\}$, where N is the number of clicks. Examples of click guidance signals are depicted in Fig. 7.

Disks. As disks and Gaussian heatmaps are computed independently for each click, they are defined for a single click c_i over voxels/pixels v in the image volume. Here, σ controls the radius of the disks in Eq. (1).

$$\text{disk}(v, c_i, \sigma) = \begin{cases} 1, & \text{if } \|v - c_i\|_2 \leq \sigma \\ 0, & \text{otherwise} \end{cases} \quad (1)$$

Gaussian Heatmaps apply Gaussian filters centered around each click c_i to create softer edges with an exponential decrease away from the click in Eq. (2).

$$\text{heatmap}(v, c_i, \sigma) = \exp\left(-\frac{\|v - c_i\|_2}{2\sigma^2}\right) \quad (2)$$

Euclidean Distance Transform (EDT) is defined in Eq. (3) as the minimum Euclidean distance between a voxel/pixel v and the set of clicks \mathcal{C} . It is similar to the disk signal in Eq. (1), but instead of filling the sphere with a constant value it computes the distance of each voxel to the closest click point.

$$\text{EDT}(v, \mathcal{C}) = \min_{c_i \in \mathcal{C}} \|v - c_i\|_2 \quad (3)$$

Geodesic Distance Transform (GDT) is defined in Eq. (4) as the shortest geodesic path distance between each voxel in the volume and the closest click in the set \mathcal{C} [181]. The shortest geodesic path in GDT also takes into account intensity

differences between voxels along the path. The shortest path is denoted as Φ in Eq. (4) and can be computed with, e.g., the Fast Marching method [182].

$$\text{GDT}(v, \mathcal{C}) = \min_{c_i \in \mathcal{C}} \Phi(v, c_i) \quad (4)$$

Exponentialized Geodesic distance (exp-GDT) proposed in MIDeepSeg [38] is defined in Eq. (5) as an exponentiation of GDT from Eq. (4):

$$\text{exp-GDT}(v, \mathcal{C}) = 1 - \exp(-\text{GDT}(v, \mathcal{C})) \quad (5)$$

Location Prior (LP), as proposed by Sun et al. [3], incorporates both the Manhattan distance and the information about crossed edges detected by a Canny edge detector [123]. The LP assigns an initial intensity value of 255 to the center voxel, denoted as $c = (c_x, c_y)$, and decreases this value by 1 for each vertical or horizontal step taken. Furthermore, when a step crosses a detected edge the intensity value decreases by an additional 10. LP combines the notion of distance with the presence of edges to provide a comprehensive measure for location estimation.

$$\text{LP}(v) = \left(0, 255 - \sum_{i=c_x}^{v_x} \sum_{j=c_y}^{v_y} \begin{cases} -10 & \text{if Canny}(I)(x_i, y_i) == 1 \text{ and edge_crossed} \\ -1 & \text{otherwise} \end{cases} \right)$$

Attraction Field Weight Map (AF), as introduced in [14], draws inspiration from the attraction field generated by punctual electric charges of opposite values. AF utilizes unitary gradient fields, denoted as $\nabla S_i(v)$, which are centered around two clicks, namely c_1 and c_2 . These gradient fields exhibit higher values between the clicks, indicating their significance for the segmentation process. The hyperparameter $p \in \mathbb{R}$ controls the decay of the vectors' magnitude.

$$\text{AF}(v, c_1, c_2) = \frac{\nabla S_1(v)}{|\nabla S_1(v)|^p} - \frac{\nabla S_2(v)}{|\nabla S_2(v)|^p} \quad (6)$$

$$\nabla S_i(v) = \frac{2(v_x - c_{ix}) + 2(v_y - c_{iy}) + (v_z - c_{iz})}{2\|v - c_i\|} \quad (7)$$

APPENDIX B SCRIBBLE GUIDANCE SIGNALS

Scribbles are defined as 3D or 2D sets of points \mathcal{C} , i.e., $\mathcal{C} := \{c_1, \dots, c_N\}$, where $c_i \in \mathbb{R}^3$ or $c_i \in \mathbb{R}^2$, depending on the dimensions of the input image. In a formal sense, scribbles can be seen as a set of clicks. However, conceptually, scribbles manifest as a diverse array of interactions, encompassing

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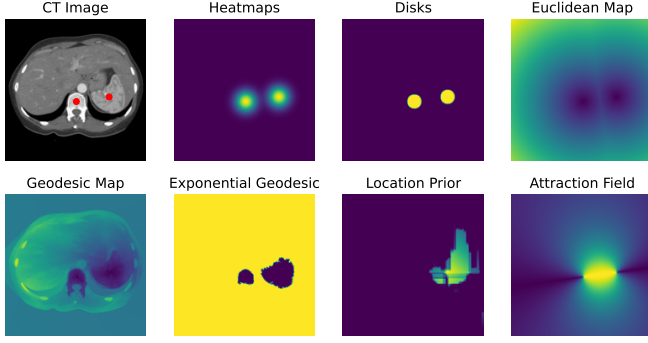


Fig. 7. Examples of click-based guidance signals.

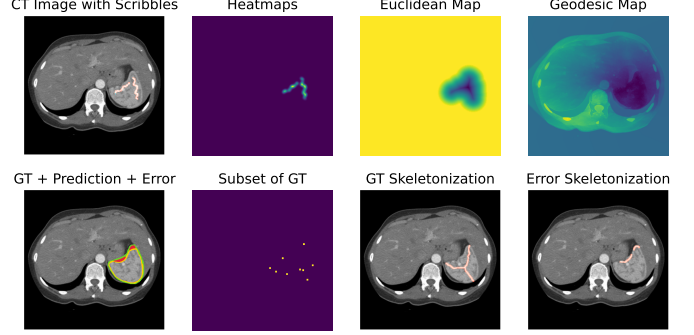


Fig. 8. Examples of scribble-based guidance signals. GT: Ground-truth mask. Bottom left image – green: GT, yellow: model prediction, red: error.

structured actions like deliberate line strokes, spontaneous unstructured marks such as random dabs, or a fusion of both. Examples of scribble guidance signals are shown in Fig. 8.

Gaussian Heatmaps for scribbles are derived from the click heatmaps in Eq. (2) by summing all click heatmaps into one guidance signal, resulting in Eq. (8).

$$\text{heatmap}(v, \mathcal{C}, \sigma) = \sum_{i=0}^N \text{heatmap}(v, c_i, \sigma) \quad (8)$$

The **Euclidean Distance Transform** (EDT) and the **Geodesic Distance Transform** (GDT) do not differ in any way from their click-based versions in Eq. (3) and (4) since those are already defined over a set of points \mathcal{C} .

Subset of Ground-Truth. One way to simulate scribbles with a robot user is to randomly sample a subset of the ground-truth mask \mathcal{M} . As scribbles do not inherently adhere to a specific structure, this typically manifests as a series of random clicks, resembling the illustration in Fig. 8.

$$\mathcal{C} = \{c_i\}_{i=1}^N, \text{ where } x_i \sim \mathcal{M} \text{ and } N \leq |\mathcal{M}| \quad (9)$$

Ground-truth Skeletonization is another way to simulate scribbles with a robot user by representing the morphological structure of the ground-truth mask \mathcal{M} in the scribble \mathcal{C} . The $\text{skeleton}(\cdot)$ in Eq. (10) consists of the 1-pixel wide medial axes of the mask [184]. An example is depicted in Fig. 8.

$$\mathcal{C} = \text{skeleton}(\mathcal{M}) \quad (10)$$

Error Skeletonization is a way to simulate iterative scribbles, which are used to correct the previous prediction with a corrective stroke [27], [33], [53], [54]. The scribbles are computed the same way as in Eq. (10) but over the missegmented region \mathcal{E} instead of the ground-truth mask \mathcal{M} .

$$\mathcal{C} = \text{skeleton}(\mathcal{E}) \quad (11)$$

Ground-truth Scribbles are a guidance signal where the raw scribble set \mathcal{C} provided by a real human annotator is used directly as a representation of the interaction. This is often done to avoid information leaking into neighboring voxels, e.g., through applying a distance transform or a heatmap to the scribbles [75], [91].

APPENDIX C

IMPLICIT SIGNALS AND OTHER GUIDANCE SIGNALS

Implicit signals subtly incorporate interactions into the model’s training or inference, without using structured inputs like spherical heatmaps or skeletonized scribbles. Examples include weights in the loss function based on the distance to clicks/scribbles, or cropping inputs via bounding box interactions to selectively feed to the model. Implicit signals are represented by an *action*, such as loss function *weighting*, or input *cropping*. In contrast, explicit signals are conveyed through a defined *structure*, like Gaussian *heatmaps* or error *skeletons*.

Less common guidance signals encompass vertex polygons and B-splines, employed to outline the segmentation mask boundary [50], [70]. Users can adjust the boundary by manipulating vertices or control points of the spline. Another signal involves leveraging predictions from an auxiliary approach, such as GraphCut [131], which generates pseudolabels added to the input image. Additionally, methods utilizing the Segment Anything Model (SAM) [137] use positional encodings to represent bounding box or click coordinates.

APPENDIX D

PUBLIC DATASETS AND PUBLIC CODE LINKS

APPENDIX E

FULL LIST OF LITERATURE DATABASES AND VENUES IN OUR SEARCH STRATEGY

APPENDIX F

PRISMA 2020 CHECKLIST

Tables VIII, IX, and X show the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 [139] checklist and where we have reported each item in our review. Certain items are marked with “-” since they either do not apply to our review or are excluded due to the technical nature of our study, which diverges from the clinical emphasis of the PRISMA guidelines.

While our review predominantly centers on technical methodology rather than clinical outcomes, we make an effort to adhere to the definition of “synthesis methods” within the PRISMA guidelines as closely as possible. In this review, we define synthesis methods as the systematic analysis and summarization of results from the reviewed studies to draw

TABLE III
PUBLIC DATASETS USED FOR INTERACTIVE SEGMENTATION

Abbreviation	Dataset	Link	Modality	Abbreviation	Link	Modality
D1	ACDC	Link	MRI	D92	TN3K	US
D2	NCI-ISBI-13	Link	MRI	D93	CoronA Artery	Link
D3	Brats15	Link	MRI	D94	TN-SCU	US
D4	Brats18	Link	MRI	D95	Gla5	Link
D5	MM WHS	Link	MRI	D96	CHAI	Microscopy
D6	Brats19	Link	MRI	D97	MonSeg	Link
D7	Brats20	Link	MRI	D98	CPM	Link
D8	PROSTATE12	Link	MRI	D99	NoCack	Link
D9	Multi-Atlas MICCAI12	Link	MRI	D100	CEC	Link
D10	GM-ZIB	Link	MRI	D101	PAP19	Microscopy
D11	SCGMS	Link	MRI	D102	CAMELYON16	Link
D12	ICCVB	Link	MRI	D103	Agnal et al	Link
D13	Duke-Breast-Cancer-MRI	Link	MRI	D104	TSP 2018	Link
D14	WMHSC	Link	MRI	D105	CoeSP	Link
D15	Flyphase	Link	MRI	D106	BACH	Link
D16	GemmaKnife	Link	MRI	D107	NEPTUNE	Link
D17	CC-Tumor	Link	MRI	D108	Habmap HPA	Link
D18	crossMed24	Link	MRI	D109	Habmap Kidney	Link
D19	FeTs	Link	MRI	D110	NeurIPS22	Link
D20	HanSeg	Link	MRI	D111	FBCT	Link
D21	ISLES	Link	MRI	D112	oTEM	Link
D22	Meiningsoma-SEG	Link	MRI	D113	MouseColon	Link
D23	M4M	Link	MRI	D114	EPFL-IM	Link
D24	PI-CAI	Link	MRI	D115	MouseBrain	Link
D25	PP-MI	Link	MRI	D116	Mouse_4T1	Link
D26	Qin-Prostate	Link	MRI	D117	HPC	Link
D27	Qubeq	Link	MRI	D118	MouseBrain_FL	Link
D28	Spine	Link	MRI	D119	TOGA	Link
D29	ATLAS	Link	MRI	D120	CREMI	Link
D30	AtasSeg	Link	MRI	D121	PR2	Link
D31	BrainPDM 2021	Link	MRI	D122	BCN-2000	Link
D32	Isag2019	Link	MRI	D123	UWatefooskin	Link
D33	ISX	Link	MRI	D124	HAM-10000	Link
D34	IC2VB	Link	MRI	D125	MLD	Link
D35	LinScan	Link	MRI	D126	FUSC	Link
D36	MRSpineSeg	Link	MRI	D127	ISIC	Link
D37	ADNI	Link	MRI	D128	SIM-ACR	Link
D38	SKID	Link	MRI	D129	Xray-Chest	Link
D39	DeepLanion	Link	CT	D130	Xray-Hip	Link
D40	RTCV	Link	CT	D131	COVID-19 X-Ray	Link
D41	SegThor	Link	CT	D132	ChestXRay	Link
D42	LITS	Link	CT	D133	Chest X-Ray-Montgomery	Link
D43	Gibson et al	Link	CT	D134	Chest Pneumothora	Link
D44	LIDC-IDRI	Link	CT	D135	COVID Radiography	Link
D45	IBCAD	Link	CT	D136	COVID-Q	Link
D46	FUMPE	Link	CT	D137	JSRT	Link
D47	SnacSeg2019	Link	CT	D138	Lung-CXR	Link
D48	KITS 19	Link	CT	D139	CTD-CESM	Link
D49	Pancreas-CT	Link	CT	D140	Qata-COVID	Link
D50	CTORG	Link	CT	D141	CVC-ClinicalDB	Link
D51	COVID19-CT-Lung	Link	CT	D142	Pro-Net	Link
D52	COVID19-Lung-CT-Challenge	Link	CT	D143	Visio-SEG	Link
D53	LITSC	Link	CT	D144	BKAI-RH NeoPolyb	Link
D54	NSCLC	Link	CT	D145	ColoreSegNet	Link
D55	UREST- COVID-19	Link	CT	D146	4Scan	Link
D56	MSD COVID 19	Link	CT	D147	PolyGen	Link
D57	DeepMed CT	Link	CT	D148	RadTool	Link
D58	Pneumax	Link	CT	D149	abuse	Link
D59	AbdomenCT-1k	Link	CT	D150	MICCAI Instrument Seg (EndoVis)	Link
D60	CHDcast	Link	CT	D151	EndoCast 2020	Link
D61	COVID19-CT-Seg	Link	CT	D152	ETIS-Larsh	Link
D62	GLIS-RT	Link	CT	D153	AudiLapras	Link
D63	HCC-TACE-Seg	Link	CT	D154	Kvasir-Instrument	Link
D64	INSTANCIE	Link	CT	D155	CVC-ColonDB	Link
D65	KIPA	Link	CT	D156	CVC-300	Link
D66	LymphNodes	Link	CT	D157	IBRID	Link
D67	NSCLC-Pe-Theta	Link	CT	D158	PAPILA	Link
D68	NSCLC-Radiogenomics	Link	CT	D159	PaPACSp	Link
D69	TotSegGenerator	Link	CT	D160	Debris-GS	Link
D70	WORD	Link	CT	D161	RM-GANv2	Link
D71	ChestCT	Link	CT	D162	REFUGE	Link
D72	MALBCV	Link	CT	D163	PRVES	Link
D73	Verse 2019	Link	CT	D164	CHASDB	Link
D74	Verse 2020	Link	CT	D165	DRIVE	Link
D75	4C201 CSM TL501	Link	CT	D166	iChallengeAMD	Link
D76	SLIVER07	Link	CT	D167	iChallengePALM	Link
D77	AbdomenAtlas-3K	Link	CT	D168	STARD	Link
D78	LUNA16	Link	CT	D169	Interacranial Cystoid Fluid	Link
D79	COVID-19 CT	Link	CT	D170	OCT DMEI	Link
D80	CTFUS	Link	US	D171	ABOS	Link
D81	CAMUS	Link	US	D172	BOSE	Link
D82	Nerve	Link	US	D173	OCTA-500	Link
D83	HC18	Link	US	D174	CHAOS	Link
D84	Breast US	Link	US	D175	AMOS	Link
D85	CTFUS	Link	US	D176	MSD	Link
D86	US-Muscle	Link	US	D177	Lung-PETCT	Link
D87	Abdomen US	Link	US	D178	AutoPET	Link
D88	Breast Cancer US	Link	US	D179	HECKTOR	Link
D89	MMOTU	Link	US	D180	Tenets et al	Link
D90	FHPS US	Link	US	D181	QASIS-3	Link
D91	ThyroidUS	Link	US	D182	RadiImageNet	Link

TABLE IV
LIST OF ALL REVIEWED INTERACTIVE METHODS WITH PUBLICLY AVAILABLE CODE

Paper	Code
DeepGeoS [5]	https://github.com/HITLAB-DeepGeoS/
Zhou et al. [111]	https://github.com/DLwhm123/OCMIST
iWNet [14]	https://github.com/gmaresat/iW-Net
UGIR [22]	https://github.com/HiLab-git/UGIR
NuClick [26]	https://github.com/navidstuv/NuClick
MidDeepSeg [38]	https://github.com/HiLab-git/MidDeepSeg
Sambaturu et al. [41]	https://tinyurl.com/ym4hypr2
Zhou et al. 2 [42]	https://github.com/lingorX/Mem3D
Zhang et al. [47]	https://github.com/sunahbert/Sequential-patch-based-segmentation
Zheng et al. 2 [48]	https://github.com/ritminglab/CLIS
DINs [49]	https://github.com/Jarvis73/DINs
Sun et al. 2 [60]	https://github.com/Tian-lab/IGMedSeg
iSegFormer [64]	https://github.com/uncbiag/iSegFormer
ECONet [65]	https://github.com/masadv/ECONet-MONAILabel
i3Deep [66]	https://github.com/Karol-G/i3Deep
DeepEdit [67]	https://tinyurl.com/cyck2uf
Liu et al. [68]	https://wtliu7.github.io/tis/
Shi et al. [69]	https://github.com/lyuueshi/Hybrid-Propagation
AnatomySketch [70]	https://tinyurl.com/45tmh96n
Gallsot et al. [71]	https://tinyurl.com/4et77jpf
Zhou et al. 3 [81]	https://github.com/lingorX/Mem3D
Hallitschke et al. [82]	https://github.com/verena-hallitschke/pet-ct-annotate
Liu et al. 2 [83]	https://github.com/uncbiag/iSegFormer
Asad et al. [85]	https://github.com/masadv/MONet-MONAILabel
Wei et al. [89]	https://tinyurl.com/3r7b4yw7
Zhuang et al. [90]	https://github.com/DlutMedimgGroup/Scribble-Guided-Segmentation
Zhuang et al. 2 [87]	https://tinyurl.com/yemvnyh9
GiG [91]	https://github.com/Zrr1997/Guiding-The-Guidance/tree/main
Qu et al. [92]	https://github.com/MrGiovanni/AbdomenAtlas
SAM-Media [93]	https://github.com/mazurowski-lab/segment-anything-medical-evaluation
MedSAM [120]	https://github.com/bowang-lab/MedSAM
MedSAM-Adapter [99]	https://github.com/WuJunde/Medical-SAM-Adapter
SAM-Adapter [98]	https://tianrun-chen.github.io/SAM-Adaptor/
OphthalmologySAM [100]	https://github.com/Qsingle/LearnablePromptSAM
GazeSAM [103]	https://github.com/ukaukaaa/GazeSAM
Mattjie et al. [107]	https://github.com/Malta-Lab/SAM-zero-shot-in-Medical-Imaging
PolypSAM [108]	https://github.com/ricklisz/Polyp-SAM
PromptUNet [109]	https://github.com/WuJunde/PromptUNet
IAMSAM [111]	https://github.com/portrai-io/IAMSAM
DeSAM [112]	https://github.com/yifangao12/DeSAM
3DSAM [118]	https://github.com/med-it/3DSAM-adapter
MedL-SAM [116]	https://github.com/openmedlab/MedL-SAM

comprehensive conclusions and identify overarching patterns and trends. Our review’s synthesis methods (rows 13a-13f in Table VIII) encompass the following elements:

TABLE V
LIST OF ALL LITERATURE DATABASES USED IN STEP 1 OF OUR SYSTEMATIC SEARCH

Literature Database	Link
Google Scholar	https://scholar.google.com/
PubMed	https://pubmed.ncbi.nlm.nih.gov/
IEEE Xplore	https://ieeexplore.ieee.org/Xplore/home.jsp
SpringerLink	https://link.springer.com/
arXiv	https://arxiv.org/

TABLE VI
LIST OF ALL CONFERENCES, JOURNALS, AND CONFERENCE WORKSHOPS USED IN STEP 4 OF OUR SYSTEMATIC SEARCH. ALL PROCEEDINGS OF THE VENUES IN THE TABLE ARE INSPECTED FOR ELIGIBLE STUDIES PUBLISHED BETWEEN 2016 AND 2023 FOR THE REVIEW

Venue	Abbreviation	Type	Link
Applied Sciences	Appl. Sci.	Journal	Link
Artificial Intelligence in Medicine	Artif Intell Med	Journal	Link
BioScience Trends	TIP	Journal	Link
Biomedical Signal Processing and Control	Biomed Signal Process Control	Journal	Link
Cytometry Part A	Cytometry A	Journal	Link
Diagnostics	-	Journal	Link
Frontiers of Information Technology & Electronic Engineering	FITEE	Journal	Link
IEEE Journal of Biomedical and Health Informatics	J-BHI	Journal	Link
IEEE Transactions on Image Processing	TIP	Journal	Link
IEEE Transactions on Medical Imaging	TMI	Journal	Link
IEEE Transactions on Pattern Analysis and Machine Intelligence	TPAMI	Journal	Link
International Journal of Computer Assisted Radiology and Surgery	IJCARS	Journal	Link
Journal of Biomedical Semantics	J. Biomed. Semant.	Journal	Link
Journal of Digital Imaging	JDI	Journal	Link
Journal of Pathology Informatics	JPI	Journal	Link
Machine Learning and Knowledge Extraction	MAKE	Journal	Link
Machine Learning with Applications	MLWA	Journal	Link
Medical Image Analysis	MedIA	Journal	Link
Medical Physics	Med Phys	Journal	Link
Neurocomputing	-	Journal	Link
Physics and Imaging in Radiation Oncology	-	Journal	Link
Physics in Medicine & Biology	Phys. Med. Biol.	Journal	Link
Radiology: Artificial Intelligence	Radiol. Artif. Intell.	Journal	Link
Scientific Reports	Sci. Rep.	Journal	Link
AAAI Conference on Artificial Intelligence	AAAI	Conference	Link
ACM International Conference on Multimedia	ACM-MM	Conference	Link
Annual International Conference of the IEEE Engineering in Medicine and Biology Society	EMBC	Conference	Link
Asian Conference on Pattern Recognition	ACPR	Conference	Link
IEEE Global Conference on Consumer Electronics	GCCE	Conference	Link
IEEE International Conference on Multimedia Big Data	BigMM	Conference	Link
IEEE International Conference on Research, Innovation and Vision for the Future	RIVF	Conference	Link
IEEE International Symposium on Biomedical Imaging	ISBI	Conference	Link
IEEE/CVF Conference on Computer Vision and Pattern Recognition	CVPR	Conference	Link
IEEE/CVF International Conference on Computer Vision	ICCV	Conference	Link
IEEE/RSJ International Conference on Intelligent Robots and Systems	IROS	Conference	Link
International Conference on Medical Image Computing and Computer-Assisted Intervention	MICCAI	Conference	Link
International Symposium on Image Computing and Digital Medicine	ISICDM	Conference	Link
Medical Imaging with Deep Learning	MIDL	Conference	Link
SPIE Medical Imaging	-	Conference	Link
Applications of Medical Artificial Intelligence	AMAI	Conference Workshop	Link
Eurographics Workshop on Visual Computing for Biology and Medicine	VCBM	Conference Workshop	Link
International MICCAI Brainlesion Workshop	BrainLes	Conference Workshop	Link
International Workshop on Deep Learning in Medical Image Analysis	DLIA	Conference Workshop	Link
International Workshop on Graph Learning in Medical Imaging	GLMI	Conference Workshop	Link
International Workshop on Hardware Aware Learning for Medical Imaging and Computer Assisted Intervention	HAL-MICCAI	Conference Workshop	Link
International Workshop on Large-scale Annotation of Biomedical data and Expert Label Synthesis	LABELS	Conference Workshop	Link
International Workshop on Machine Learning in Medical Imaging	MLMI	Conference Workshop	Link
MICCAI Workshop on Data Augmentation, Labeling, and Imperfections	DALI	Conference Workshop	Link

TABLE VII
RETRIEVED STUDIES FOR EACH KEYWORD COMBINATION

Keywords	Interactive Segmentation Medical Deep	Interactive Delineation Medical Deep	Human-in-the-Loop Segmentation Medical Deep	Human-in-the-Loop Delineation Medical Deep
Google Scholar	296	19	29	13
PubMed	262	36	10	1
IEEE Xplore	110	2	11	0
SpringerLink	318	2	2	0
arXiv	78	4	10	10
Total	1064	63	62	14

- Tabular representation of all studies: A structured arrangement of studies and their corresponding data items in a clear and accessible format. This information is presented in Table I and Table II, located on pages 4 and 5, respectively.

- Introduction of a taxonomy: A taxonomy tree, introduced in Section III, paragraphs 1-3, to offer a structured categorization of the reviewed studies.
- Visual rationale for study categorization: We utilize Fig. 4 to visually illustrate the rationale guiding the categorization within the taxonomy tree, ensuring transparency throughout the categorization process.
- Visualization and analysis of the data items of the reviewed studies: We analyze the distribution of data items to unveil patterns, visually presented in Fig. 5, and provide a comprehensive discussion of potential reasons for these patterns in Section V-A.
- Analysis of the cross-comparisons: We analyze the comparisons between reviewed studies in Fig. 7, and explore the underlying reasons for the absence of systematic comparisons within the field in Section V-D.

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TABLE VIII
PRISMA 2020 CHECKLIST

Section and Topic	Item	Checklist Item	Location where item is reported
TITLE			
Title	1	Identify the report as a systematic review.	Title
ABSTRACT			
Abstract	2	See the PRISMA 2020 for Abstracts Checklist.	Appendix F, Table X
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of existing knowledge.	Page 1, Section I, paragraph 4
Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.	Page 1, Section I, paragraph 5 (bulleted list)
METHODS			
Eligibility Criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses	Page 3, Section III, paragraph 1
Information sources	6	Specify all databases, registers, websites, organizations, reference lists, and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted.	Page 2, Section III, paragraph 1
Search strategy	7	Present the full search strategies for all databases, registers, and websites, including any filters and limits used.	Page 2, Section III, paragraph 1; and page 3, Section III, paragraphs 1 and 3
Selection process	8	Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, and whether they worked independently.	Page 3, Section III, paragraph 2
Data collection process	9	Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, and any processes for obtaining or confirming data from study investigators.	Page 3, Section III, paragraph 4
Data items	10a	List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results to collect.	Page 3, Section III, paragraph 4
	10b	List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information.	Page 3, Section III, paragraph 4
Study risk of bias assessment	11	Specify the methods used to assess the risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study, and whether they worked independently.	-
Effect measures	12	Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results	-
Synthesis methods	13a	Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item #5)).	Page 3, Section IV, paragraphs 1-3; page 6, Fig. 3; and page 7, Fig. 4
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions.	Page 3, Section IV, paragraphs 1-3
	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	Page 3, paragraphs 1-3; page 4, Table I; and page 5, Table II
	13d	Describe any methods used to synthesize results and provide a rationale for the choice(s).	Page 3, Section IV, paragraphs 1-3; and page 7, Fig. 7
	13e	Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression).	Page 15, Section V-D; and page 6, Fig. 6
	13f	Describe any sensitivity analyses conducted to assess the robustness of the synthesized results.	-
Reporting bias assessment	14	Describe any methods used to assess the risk of bias due to missing results in a synthesis (arising from reporting biases).	-
Certainty assessment	15	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.	-

TABLE IX
PRISMA 2020 CHECKLIST, CONTINUED

Section and Topic	Item	Checklist Item	Location where item is reported
RESULTS			
Study selection	16a	Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram.	Page 2, Fig. 2; page 3, paragraph 3; and Appendix F, Table VII
	16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.	Page 3, Section III, paragraph 5
Study Characteristics	17	Cite each included study and present its characteristics.	Pages 3-12, Sections IV-A, IV-B, and IV-C (all paragraphs each) cite and describe all studies in detail; page 4, Table I; page 5, Table II; and page 14, Fig. 6 contains citations to all studies
Risk of bias in studies	18	Present assessments of risk of bias for each included study.	-
Results of individual studies	19	For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision (e.g. confidence/credible interval), ideally using structured tables or plots.	-
Results of syntheses	20a	For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies	-
	20b	Present results of all statistical syntheses conducted.	Pages 12-13, Section V-A (all paragraphs); and page 13 Fig. 5
	20c	Present results of all investigations of possible causes of heterogeneity among study results.	-
	20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results.	-
Reporting biases	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.	-
Certainty of evidence	22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.	-
DISCUSSION			
Discussion	23a	Provide a general interpretation of the results in the context of other evidence.	Page 15, Section VI, paragraph 1
	23b	Discuss any limitations of the evidence included in the review.	-
	23c	Discuss any limitations of the review processes used.	-
	23d	Discuss implications of the results for practice, policy, and future research.	Page 15, Section IV-B (all paragraphs)
OTHER INFORMATION			
Registration and protocol	24a	Provide registration information for the review, including register name and registration number, or state that the review was not registered.	The review was not registered
	24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared.	A protocol was not provided
	24c	Describe and explain any amendments to the information provided at registration or in the protocol.	A protocol was not provided
Support	25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review.	-
Competing interests	26	Declare any competing interests of review authors.	-
Availability of data, code and other materials	27	Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review.	-

TABLE X
PRISMA 2020 ABSTRACT CHECKLIST

Section and Topic	Item	Checklist Item	Reported (Yes/No)
TITLE			
Title	1	Identify the report as a systematic review.	Yes
BACKGROUND			
Objectives	2	Provide an explicit statement of the main objective(s) or question(s) the review addresses.	Yes
METHODS			
Eligibility criteria	3	Specify the inclusion and exclusion criteria for the review.	No
Information sources	4	Specify the information sources (e.g. databases, registers) used to identify studies and the date when each was last searched.	No
Risk of bias	5	Specify the methods used to assess risk of bias in the included studies.	No
Synthesis of results	6	Specify the methods used to present and synthesize results.	Yes
RESULTS			
Included studies	7	Give the total number of included studies and participants and summarize relevant characteristics of studies.	Yes
Synthesis of results	8	Present results for main outcomes, preferably indicating the number of included studies and participants for each. If meta-analysis was done, report the summary estimate and confidence/credible interval.	No
DISCUSSION			
Limitations of evidence	9	Provide a brief summary of the limitations of the evidence included in the review (e.g. study risk of bias, inconsistency, and imprecision).	No
Interpretation	10	Provide a general interpretation of the results and important implications.	Yes
OTHER			
Funding	11	Specify the primary source of funding for the review.	No
Registration	12	Provide the register name and registration number.	No

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