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Computational pathology in 2030: A Delphi study forecasting the role of AI in pathology within the next decade

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[Sociedad Española de Anatomía Patológica]
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1. Topol EJ. *Nat Med.* 2019;**25(1)**:44–56.
2. Meskó B et al. *NPJ Digit Med* 2020;3:126.
3. Abels E et al. J Pathol. 2019;249(3):286–94

Introduction

- Artificial intelligence (AI) is set to transform healthcare by contributing to more accurate diagnoses, more agile, cost-effective, and standardized clinical workflows, and more effective and personalized treatments.[1,2]

- Pathology has attracted attention as an image-rich specialty likely to be strongly impacted by advances in AI.

- The development of machine learning-based tools for image analysis has led to a surge in AI applications promising to revolutionize pathology workflows, and the advent of a new field, computational pathology (CPath).[3]

4. Steiner DF et al. Biochim Biophys Acta Rev Cancer. 2021;1875(1):188452.
5. Kearney SJ et al. Front Med (Lausanne). 2021;8:765385.
6. Chauhan C et al. Am J Pathol. 2021;191(10):1673–83.

Introduction

- However, few algorithms are currently in routine clinical use,[4] and there is a dearth of studies evaluating their impact in clinical settings.[5]

- Simultaneously, ethical concerns have been raised regarding potential data privacy breaches, systemic algorithmic bias, harm related to erroneous AI-generated outputs, and exacerbation of healthcare disparities.[6]

- Along with hurdles related to regulatory approval and reimbursement for AI products, these have contributed to a significant AI "translation gap" in pathology.[4]

7. Nasa P et al. *World J Methodol.* 2021;**11(4)**:116–29.
8. Rowe G et al. *Int J Forecast.* 1999;**15(4)**:353–75.

Purpose

- To date, there has been no systematic survey regarding this topic from the short-to-medium term perspective of digital and CPath experts.

- To address this gap, we conducted a consensus survey to gain insight into the current challenges and perspectives surrounding the role of AI in pathology, from the standpoint of an international panel of "early adopters", most of them pathologists in active clinical practice with firsthand experience developing and evaluating the clinical utility of AI algorithms.

- For this survey, we applied the Delphi method, a robust, widely accepted tool for building consensus among experts[7] which has outperformed standard statistical methods.[8]

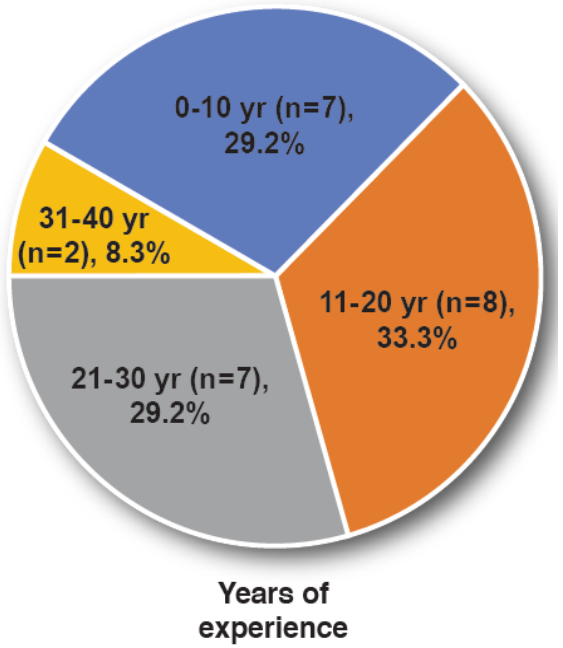
Goals

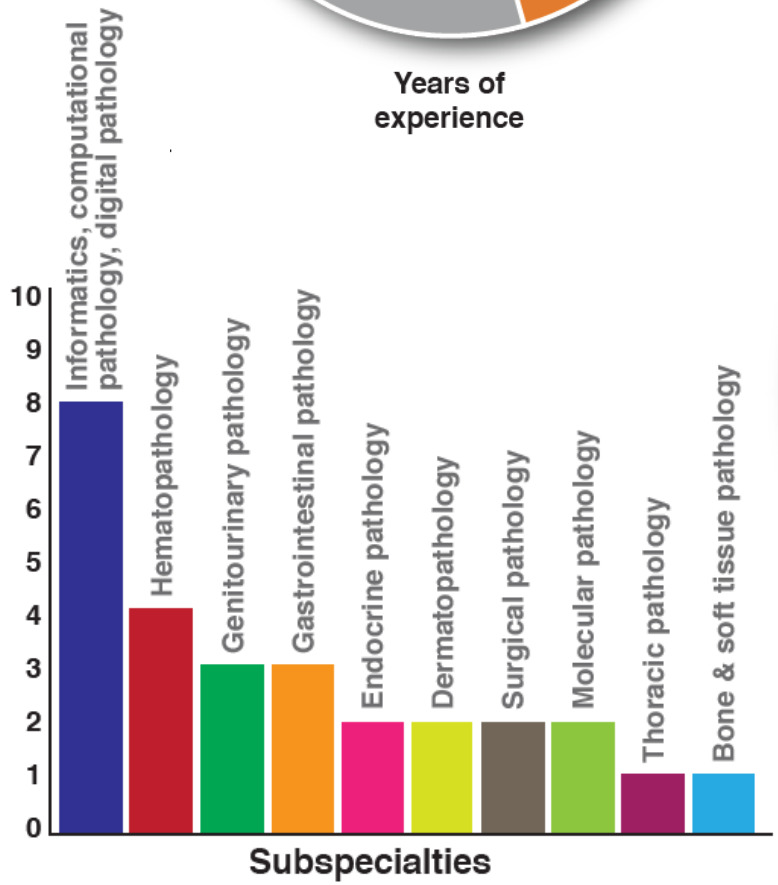
1. Investigate the expected impact of AI on pathology
2. Forecast the extent of clinical AI implementation by 2030
3. Provide specific insights into which technical, legal, regulatory, and ethical aspects of AI integration will require the most attention in the coming years.

Expert Panel Recruitment

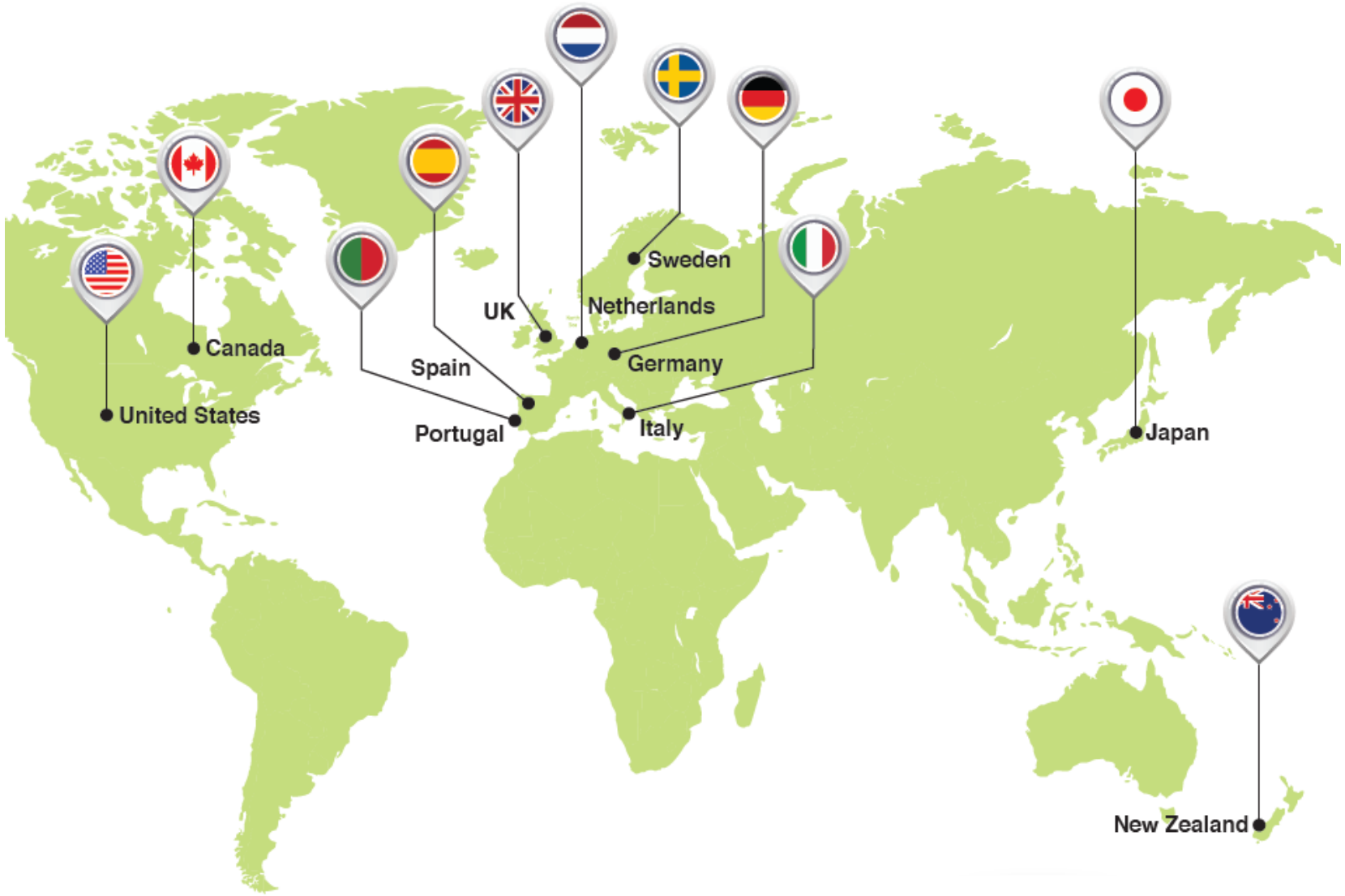
Recruitment criteria:

1. Pathology professionals with an MD (or equivalent medical degree) and/or PhD
2. Authorship of at least one PubMed-indexed CPath/AI publication between 2016–2020

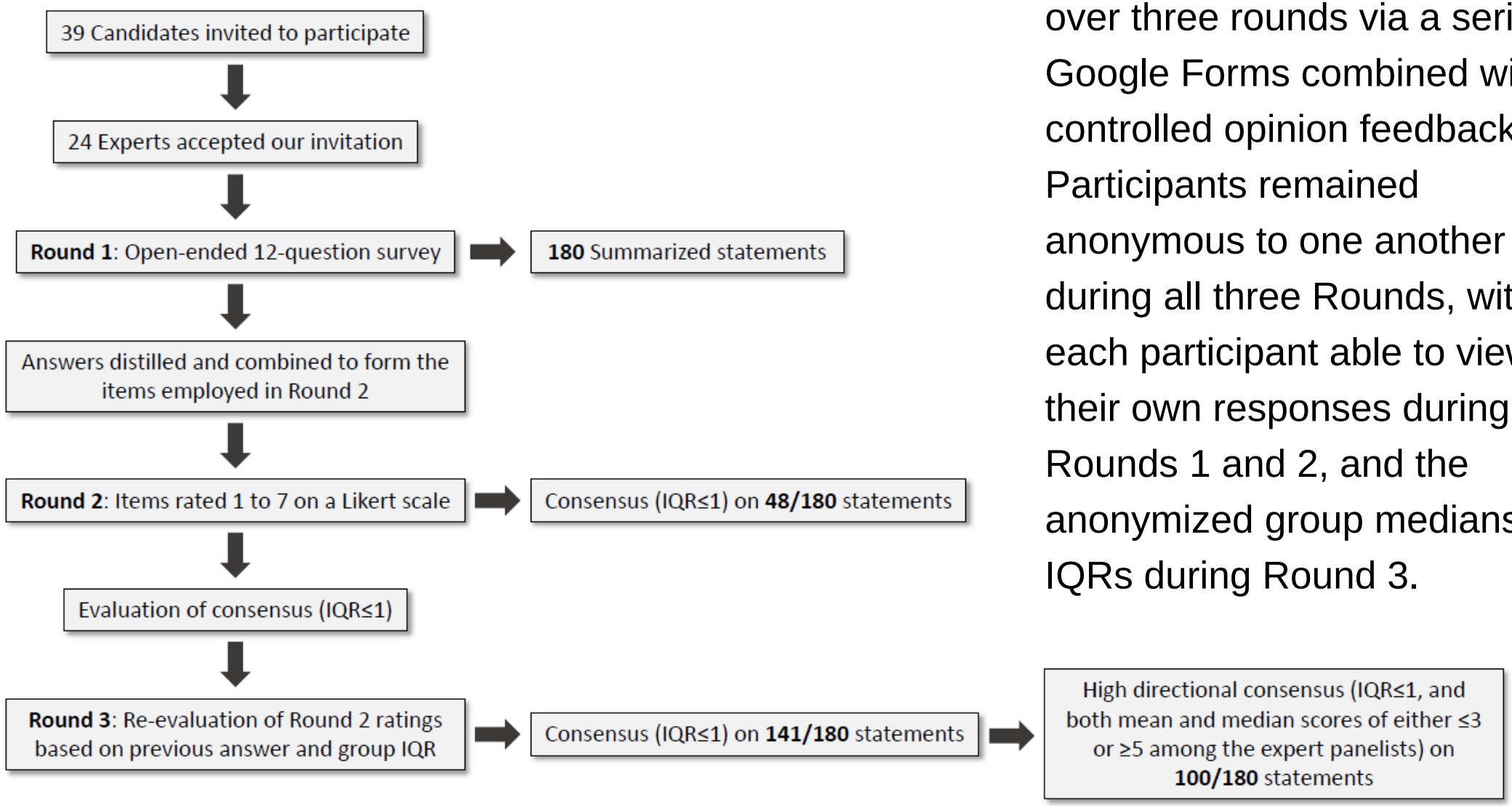




Expert Panel Recruitment



Delphi Study Procedure



This Delphi study was conducted over three rounds via a series of Google Forms combined with controlled opinion feedback.[9] Participants remained anonymous to one another during all three Rounds, with each participant able to view only their own responses during Rounds 1 and 2, and the anonymized group medians and IQRs during Round 3.

Round 1

Open-ended questionnaire containing 12 questions regarding: 1) forecasting the future of AI in pathology, 2) specific pathology AI applications, and 3) ethical and regulatory aspects. Panelist responses were either directly reproduced as, or combined and distilled into, the statements comprising the questionnaire items used in subsequent rounds.

Section 1: Forecasts about the future (please answer according to what you believe will happen by 2030, instead of what you would like to see happen)	
1	On what key performance indicators related to pathology do you believe AI will have a positive impact?
2	How do you think AI will impact the pathology workforce (jobs which will be created and jobs which will be destroyed) by 2030?
3	What new tasks will pathologists be involved in?
4	What new tasks will pathology technicians be involved in, or what existing tasks will they take on more responsibility for?
5	Which tasks currently performed by pathologists will be fully automated by AI by 2030?
Section 2: Applications of AI in pathology (please cite any existing or potential AI-based tools which, in your opinion, would bring value to pathologists. Be as specific as possible)	
6	In what ways can AI be used to improve diagnostic precision?
7	In what ways can AI be used to speed up or facilitate the work of pathologists?
8	What examples of AI tools or applications would bring value to the analysis and interpretation of histological images?
9	What examples of AI tools or applications would bring value to other aspects of the laboratory workflow?
10	In what ways can AI be used to bring value to integrated diagnostics? (integrated diagnostics refers to the convergence of two or more diagnostic techniques, such as pathology, radiology, genomics)
Section 3: Ethical and regulatory aspects	
11	What regulatory challenges will have to be overcome for the generalized adoption of AI in the pathology setting?
12	What ethical issues could arise from the use (and potential misuse) of AI in the pathology setting?

AI, artificial intelligence.

Round 2

The panelists rated each item on a 7-point Likert scale, with different scores designed to fit different question categories, with higher scores generally representing more favorable opinions toward the future role or impact of AI on Pathology.

Point Score	Agreement scale	Probability scale	Job number variation scale	Involvement scale
1	Very strongly disagree	Impossible	Disappear	Not involved at all
2	Strongly disagree	Very unlikely	Greatly decrease	Rarely
3	Disagree	Unlikely	Somewhat decrease	Somewhat
4	Neither agree nor disagree	Even chance / neutral	Remain the same	Sometimes
5	Agree	Likely	Somewhat increase	Often
6	Strongly agree	Very likely	Greatly increase	Routine
7	Very strongly agree	Certain	Dramatically increase	Daily

Round 3

- The panelists were asked to re-rate all items not reaching consensus (defined as an interquartile range (IQR)≤1 for ratings along the Likert scale21) during Round 2. They were shown their Round 2 ratings on each item with the group median and IQR, and given the option to change their previous ratings, if desired.

- Wilcoxon rank-sum exact tests (two-tailed, alpha=0·05) were performed using STATA v16 to examine for significant differences in panelist scores by practice location, pathology subspecialty, and years in practice.

Survey Round Results

- Round 1 resulted in 180 summative statements spanning nine domains: (1) key performance indicators (KPIs), (2) the pathology workforce, (3) pathologist tasks, (4) technician tasks, (5) specific AI applications, (6) role of AI in integrated diagnostics, (7) tasks likely to be fully automated by AI, and (8) regulatory/legal and (9) ethical aspects of AI integration.
- After Round 2, responses to 48 (26·7%) statements reached consensus
- Consensus further increased to 141 (78·3%) after Round 3
- 100 statements achieved high directional consensus (defined as IQR≤1, *and* both mean and median scores of either ≤3 or ≥5).
- For these, two-tailed Wilcoxon rank sum tests demonstrated no significant differences in Likert scores between the comparison groups on 85 statements.

Impact of AI on Pathology KPIs

- There was agreement that, by 2030, there will be growth in CPath as a subspecialty, with AI applications assisting pathologists in making more accurate, standardized, objective, quantitative, and complete diagnoses.

- Statements on the likelihood of cost-per-case and number of second-opinion consultations decreasing with AI use failed to reach consensus.

By 2030, due to the integration of AI in the pathology setting…				
Key performance indicator	*Item #*	*Mean (SD)*	*Median (IQR)*	*Result*
Standardization of pre-analytical processes (staining and slicing techniques) will increase	3	5·38 (0·92)	5·0 (5·0-6·0)	Agree
Diagnostic accuracy will increase	6	5·67 (1·05)	6·0 (5·0-6·0)	Strongly agree
Diagnosis and grading of tumors will be more standardized, bringing more objectivity to the diagnosis of certain entities that are currently subject to high interobserver variability	7	6·04 (0·62)	6·0 (6·0-6·0)	Strongly agree
Detection of rare events (small metastases, small tumor foci) will increase	8	5·88 (1·03)	6·0 (6·0-6·0)	Strongly agree
Analyses will be more quantitative	9	6·21 (0·72)	6·0 (6·0-7·0)	Strongly agree
Completeness of reports will increase	10	5·13 (1·03)	5·0 (5·0-6·0)	Agree
Complexity of reports will increase	11	5·13 (1·12)	5·0 (5·0-6·0)	Agree
Quality of reports will increase	12	5·38 (1·24)	5·0 (5·0-6·0)	Agree

AI's Impact on the Pathology Workforce and Tasks

By 2030, due to the integration of AI in the pathology setting…				
Task	*Item #*	*Mean (SD)*	*Median (IQR)*	*Involvement/Agreement Level*
The number of jobs for IT staff will…	18	5·54 (0·93)	5·0 (5·0-6·0)	Somewhat increase
The number of specialized “computational” pathologists will…	22	5·75 (0·79)	6·0 (5·0-6·0)	Greatly increase
Pathologists will be more involved in diagnostic tumor boards	44	5·58 (1·06)	6·0 (5·0-6·0)	Strongly agree
Pathologists will be more involved in multidisciplinary conferences	45	5·63 (1·06)	6·0 (5·0-6·0)	Strongly agree
Pathologists will be more involved in research activities	46	5·42 (1·06)	5·0 (5·0-6·0)	Agree
Pathologists will be spending more time in the study of rare lesions	47	5·13 (1·03)	5·0 (5·0-6·0)	Agree
By 2030, the degree of involvement of pathologists in these tasks will be…				
Digital pathologic diagnosis without the use of physical glass slides	29	5·58 (1·64)	6·0 (5·5-6·5)	Routine
Interpretation of computationally derived measurements and evaluations	30	6·08 (1·10)	6·0 (6·0-7·0)	Routine
Collaboration with EHR teams regarding the use of laboratory data for a wide range of clinical decision support tools	31	5·25 (1·03)	5.5 (5·0-6·0)	Routine
Evaluating different kinds of AI software and deciding whether these are appropriate for their workflow	35	5·54 (1·14)	6·0 (5·0-6·0)	Routine
Validation and QA/QC of AI solutions	36	5·63 (1·13)	6·0 (5·0-6·0)	Routine
Validation and QA/QC of AI-rendered diagnoses	37	5·88 (1·23)	6·0 (6·0-7·0)	Routine
Defining new categories of patients, based on new data made available through AI	38	5·04 (1·43)	5·0 (5·0-6·0)	Often
By 2030, the degree of involvement of pathology laboratory technicians in these tasks will be…				
Operation of digital slide scanners, digitization, and image management	48	6·25 (1·22)	7·0 (6·0-7·0)	Daily
QA/QC of digitized images	49	6·08 (1·41)	6.5 (6·0-7·0)	Daily
Digital pathology support for pathologists and other users, such as device calibration	50	5·88 (1·12)	6·0 (6·0-6·5)	Routine
Assessing histology consistency, i.e., re-addressing SOPs to make slides and corresponding images more suitable for AI (more consistent tissue and staining quality)	51	5·83 (0·70)	6·0 (5·5-6·0)	Routine
Validation and QA/QC of AI-rendered diagnoses	56	5·17 (0·96)	5·0 (5·0-6·0)	Often

Specific applications of AI being routinely used

By 2030, the probability of these AI tools being routinely used in pathology labs is…				
AI application	*Item #*	*Mean (SD)*	*Median (IQR)*	*Likelihood*
Identification of micrometastases	78	6·17 (1·09)	6·5 (6·0-7·0)	Certain
Detection of lymph node metastases	79	6·33 (0·87	7·0 (6·0-7·0)	Certain
Quantification of IHC or IF stains, such as Ki-67, ER, PgR, PD-L1	85	6·67 (0·56)	7·0 (6·0-7·0)	Certain
Quantification of number of mitoses in H&E-stained images	86	6·33 (0·76)	6·5 (6·0-7·0)	Certain
Counting lymphocytes	87	6·42 (0·65)	6·5 (6·0-7·0)	Certain
Automated ordering of IHC for specific applications / assisting with selection of immunohistochemical stains needed	61	5·46 (0·93)	6·0 (5·0-6·0)	Very likely
Automated QA/QC of IHC positive and negative controls	62	5·75 (0·90)	6·0 (5·0-6·0)	Very likely
Proposing specific IHC or other molecular methods to solve a specific diagnostic problem	68	5·17 (1·34)	5·5 (5·0-6·0)	Very likely
Prioritization of cases (such as cases with neoplasia and infectious organisms in immunosuppressed patients)	69	5·50 (1·10)	6·0 (5·0-6·0)	Very likely
Quality control of whole-slide images (scanning process), and detection of poor-quality slides (tissue folds, poor staining)	73	6·13 (0·68)	6·0 (6·0-6·5)	Very likely
Quality improvement of whole-slide images	74	6·00 (0·92)	6·0 (6·0-6·5)	Very likely
Pre-selecting regions of interest suspicious for cancer for pathologists to view	76	6·29 (0·75)	6·0 (6·0-7·0)	Very likely
Identification of hotspot areas	77	6·25 (0·85)	6·0 (6·0-7·0)	Very likely
Detection of microorganisms (AFB, *H. pylori*)	81	6·17 (0·87)	6·0 (6·0-7·0)	Very likely
Assisting with tumor grading	82	6·21 (0·59)	6·0 (6·0-7·0)	Very likely
Quantification of eosinophils in eosinophilic esophagitis	88	6·13 (0·68)	6·0 (6·0-7·0)	Very likely
Quantitation of features (e.g., fibrosis in various organs, liver steatosis, etc.)	89	6·29 (0·55)	6·0 (6·0-7·0)	Very likely
Marking of perineural invasion, lymphovascular invasion	90	5·79 (0·98)	6·0 (5·0-6·0)	Very likely
Automated measurements (e.g., of tumor areas)	94	6·21 (0·66)	6·0 (6·0-7·0)	Very likely
Ensuring all diagnostically relevant areas on the slide are viewed prior to report finalization	95	5·42 (0·83)	6·0 (5·0-6·0)	Very likely
Mandatory second reads when the pathologist diagnosis does not match the potential AI diagnosis (within a predefined range/percentage; e.g., if the AI tool detects potential tumor on a biopsy but the pathologist reads the biopsy as no evidence of tumor)	97	5·79 (0·83)	6·0 (5·0-6·0)	Very likely
Standardization of pathology reports	98	5·88 (0·68)	6·0 (6·0-6·0)	Very likely
AI-assisted laboratory workflow management, including workload assignments to pathologists, residents, and technicians	59	5·33 (1·31)	5·0 (5·0-6·0)	Likely

Applications of AI to Pathology and Integrated Diagnostics

AI was expected to foster the integration of pathology with other diagnostic modalities, with multimodal-AI enabling the combination of diverse data types (gross/macroscopic, microscopic, radiologic, and genomic) in a single interface and facilitating integrated diagnostic reporting

By 2030, the probability of these integrated diagnostic applications being used routinely is…				
AI application	*Item #*	*Mean (SD)*	*Median (IQR)*	*Likelihood*
Identification of histologic regions to be sampled for genomic testing	104	5·38 (1·13)	5·0 (5·0-6·0)	Likely
Prediction of biomarker status and clinical outcomes for personalized medicine, based on integrated diagnostics	109	5·08 (1·14)	5·0 (5·0-5·5)	Likely
Selection of patients with prostate cancer for active surveillance versus radiotherapy/surgery, based on integration of pathology and radiology data	118	5·00 (1·22)	5·0 (5·0-6·0)	Likely
Creation of new categories of patients by integrating all “big data” from pathology, clinical lab, radiology, and genomics	119	5·04 (1·16)	5·0 (5·0-5·0)	Likely
Building risk stratification (prognostic) roadmaps for individual patients based on input from histology, radiology, and genomics	120	5·13 (0·99)	5·0 (5·0-6·0)	Likely
Use of integrated reports for select conditions, e.g., prostate cancer	121	5·33 (1·31)	5·0 (5·0-6·0)	Likely

Tasks of pathologists fully delegated to AI

It was thought likely that AI would fully replace pathologists on the tasks included on the table, and that work assignment and case triage were likely to be fully AI-automated.

By 2030, the probability of these tasks being fully delegated to AI in pathology labs is…				
Task	*Item #*	*Mean*	*Median*	*Likelihood*
Verification of positive and negative controls for IHC	124	5·71 (0·91)	6·0 (5·0-6·0)	Very likely
Prioritization of cases	125	5·54 (1·47)	6·0 (5·0-6·0)	Very likely
Triage of cases to appropriate pathologists	126	5·46 (1·25)	6·0 (5·0-6·0)	Very likely
Contextual data lookup on patients from the EHR relevant to the pathology case being reviewed	127	5·25 (1·15)	6·0 (5·0-6·0)	Very likely
Slide QC (e.g., detection of tissue folds and tears, stain quality evaluation, etc.)	128	5·88 (1·03)	6·0 (6·0-6·0)	Very likely
Screening for microorganisms, such as AFB and *H. pylori*	129	5·96 (0·75)	6·0 (6·0-6·0)	Very likely
Screening of colorectal polyps	130	5·58 (1·02)	6·0 (5·0-6·0)	Very likely
Cervical cytology screening	131	6·21 (0·78)	6·0 (6·0-7·0)	Very likely
Screening lymph nodes for metastases	132	5·83 (0·76)	6·0 (5·0-6·0)	Very likely
Measurement tasks	135	6·17 (0·92)	6·0 (6·0-7·0)	Very likely
Quantification of IHC or IF stains, such as Ki-67, ER, PgR, PD-L1	137	6·29 (0·69)	6·0 (6·0-7·0)	Very likely
Quantification of mitotic count on H&E-stained images	138	6·08 (0·72)	6·0 (6·0-7·0)	Very likely
Bone marrow differential counts	139	5·54 (1·02)	6·0 (5·0-6·0)	Very likely
MIB-1 scoring	141	6·04 (0·91)	6·0 (6·0-7·0)	Very likely
Assessing extent of liver steatosis and fibrosis	143	5·54 (1·14)	6·0 (5·0-6·0)	Very likely
Screening of tissues with a cancer diagnosis to select regions for tissue coring or macroscopic dissection	122	5·08 (1·02)	5·0 (5·0-5·5)	Likely
Slide screening for regions of interest	134	5·13 (0·99)	5·0 (5·0-6·0)	Likely
Grading of breast cancer	145	5·42 (1·14)	5·0 (5·0-6·0)	Likely
Grading of colorectal cancer	146	5·33 (1·09)	5·0 (5·0-6·0)	Likely

Regulatory and Ethical Aspects of AI Integration in Pathology

By 2030, regarding the integration of AI in pathology…				
Aspect	*Item #*	*Mean*	*Median*	*Likelihood*
A set of new guidelines will be developed, specifically addressing the integration of AI in pathology	150	6·63 (0·82)	7·0 (7·0-7·0)	Very strongly agree
Specific validation procedures for different types of AI tools will be defined by regulatory bodies	151	6·46 (0·72)	7·0 (6·0-7·0)	Very strongly agree
The introduction of AI-based diagnostic modalities will require regulatory supervision, both related to the quality of the rendered diagnosis and the ultimate destination of the diagnostic information	161	6·83 (0·48)	7·0 (7·0-7·0)	Very strongly agree
As long as AI is used as a supportive method, ethical issues will be minor. However, when AI takes over tasks from the pathologist, i.e., making a diagnosis without human oversight, it will face major ethical challenges.	166	6·58 (0·93)	7·0 (6·5-7·0)	Very strongly agree
Pathologists will still be legally responsible for diagnoses made with the help of AI	173	6·25 (1·39)	7·0 (6·0-7·0)	Very strongly agree
Meeting regulatory requirements for most AI applications will be a lengthy and costly process, as it will involve large-scale prospective studies	157	5·46 (1·25)	5·5 (5·0-6·0)	Strongly agree
Definition of endpoints for clinical validation studies will be a common problem	158	5·50 (1·14)	6·0 (5·0-6·0)	Strongly agree
Post-marketing surveillance will pose important challenges, due to algorithm drift	159	5·50 (1·06)	6·0 (5·0-6·0)	Strongly agree
Regulatory approval of AI tools used for definitive (primary) diagnosis will be very strict, but AI used for advisory purposes (secondary) will also have to meet strict regulatory conditions	162	6·04 (0·55)	6·0 (6·0-6·0)	Strongly agree
CLIA regulations and clarification surrounding the use of laboratory data within pathology and laboratory processes versus outside of the laboratory will be reviewed and updated	163	5·63 (0·97)	6·0 (5·0-6·0)	Strongly agree
Governments will actively promote innovation in the areas of AI and medicine, fostering the advancement of AI in pathology	164	5·88 (0·74)	6·0 (5·0-6·0)	Strongly agree
Legal disputes will often arise regarding who should assume liability (pathologist, institution, developer, commercial vendor…) for diagnostic errors induced by AI	165	5·67 (1·05)	6·0 (5·0-6·0)	Strongly agree
AI and technology will be included in the educational curricula for medical students, pathologists, and analysts to help them deal with this rapidly evolving method of support and its ethical implications	180	5·88 (0·80)	6·0 (6·0-6·0)	Strongly agree
Hurried pathologists will often take “shortcuts” by accepting AI interpretations without verification	171	5·08 (1·02)	5·0 (5·0-6·0)	Agree
Potentially-biased algorithms due to lack of demographic diversity in training datasets will lead to diagnostic errors	174	5·13 (0·95)	5·0 (5·0-5·5)	Agree
Data inferences that may impact on patient anonymity will lead to ethical issues	178	5·17 (0·87)	5·0 (5·0-6·0)	Agree

Conclusions

- The panelists were able to reach consensus agreement on 140 (78·3%) of the 180 items surveyed.
- It was felt to be *almost certain* that specific pathology AI applications would be routinely used by 2030
- There was particularly strong consensus that AI would improve the KPI of diagnostic accuracy, and that the number of specialized CPathologists would greatly increase

Conclusions

- It was also thought *very likely* that algorithms would be routinely used for specific pre-analytical, analytical, and post-analytical tasks, and that many of these tasks, along with colorectal polyp and cervical cytology screening, case triage/assignment, and contextual electronic health record data lookup, would be *fully delegated* to AI.

- Many applications projected to be routinely used by 2030 address basic tasks currently performed by pathologists, rather than "aspirational" tasks such as prediction of molecular biomarker status or clinical outcomes directly from morphologic features.

- Our panelists were optimistic regarding the impact of AI on the pathologist workforce, although there was reservation regarding whether AI would truly lead to increased efficiency.

Conclusions

- Our panelists could not reach consensus on whether:
  - AI would reduce the cost-per-case or number of cases requiring pathologist review or increase patient satisfaction
  - AI outputs for clinical decision-making would always need to be reviewed by a pathologist
  - AI´s “black box” nature would cause pathologists to make diagnoses without enough clinical explainability
  - Pathologists would make diagnoses contrary to their own judgment because of AI software recommendations

Conclusions

- Our panelists could not reach consensus on whether:
  - Other healthcare professionals could use AI tools to diagnose cases without pathologists
  - AI would lead to de-skilling of pathologists
  - It would be possible to ensure that pathologists took full responsibility for double-checking and confirming AI-rendered diagnoses

The lack of consensus regarding these is expected to be resolved as more AI tools are evaluated and more consideration is directed toward ensuring that tools are integrated into workflows in ways that maximize safety, efficiency, and positive patient outcomes.

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