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Artificial Intelligence and Tools for Clinical Decision Making in Precision Oncology

Manish Patel, MD

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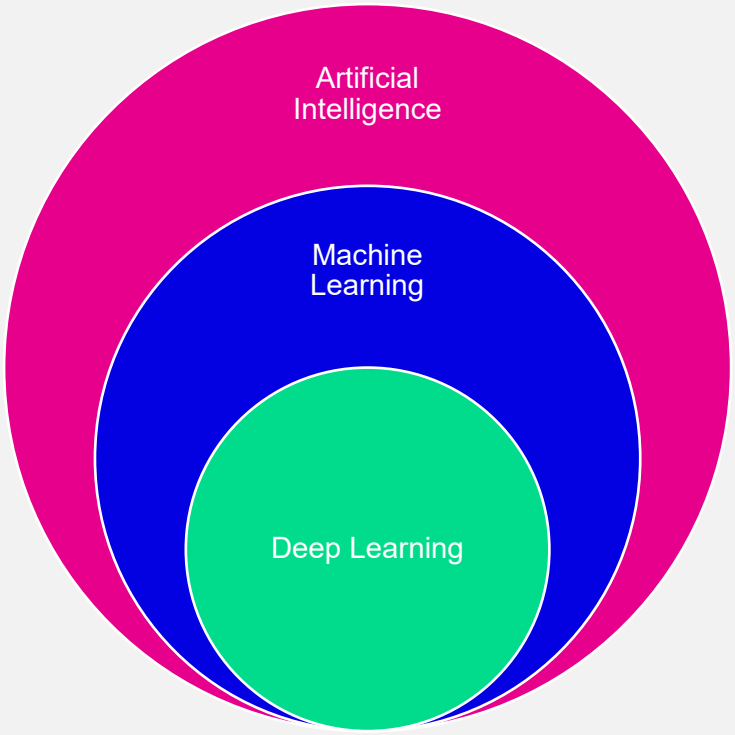

What Do We Mean by *Artificial Intelligence* (AI)?

Tools that can improve efficiency and precision by synthesizing and analyzing complex data from multiple sources to acquire insights.

- A model or algorithm is used to train the machine to recognize patterns, identify characteristics and interactions, and extract relationships.

Machine learning (ML)

- A method that applies statistics and mathematics to develop and iterate—in essence, learn
- Computers are trained by exposure to data input, rather than extensive programing before implementation.

Deep learning (DL)

- A type of machine learning that incorporates complex neural networks, based on how the human brain processes information
- "A well-designed and well-trained DL model is able to perform classification tasks and make predictions with high accuracy."[1]

More high-quality data = Better predictions and decisions

[1]National Cancer Institute. Artificial intelligence: opportunities in cancer research. www.cancer.gov/research/areas/diagnosis/artificial-intelligence

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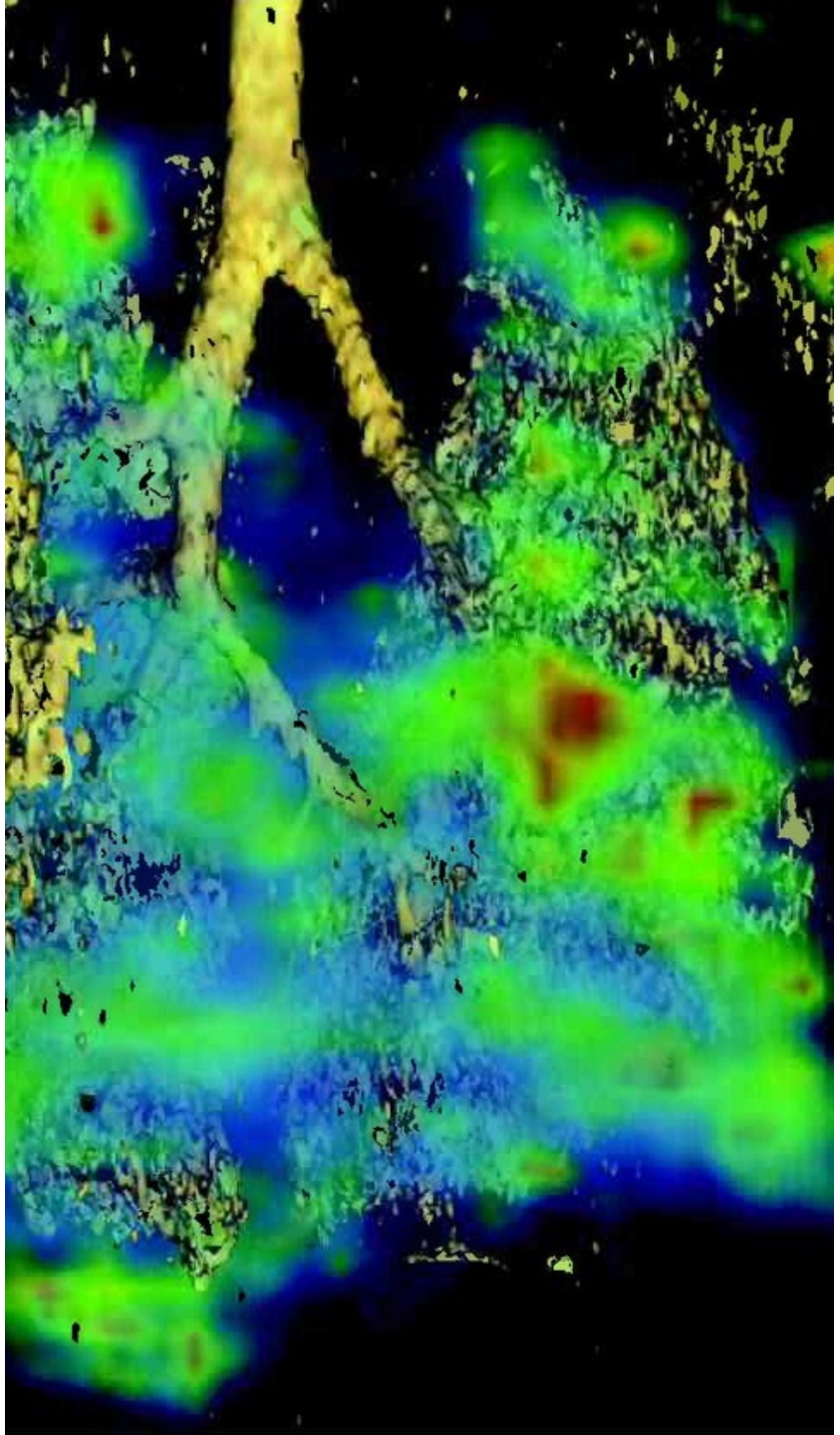
Utilization in Oncology



Utilization in Oncology

The vast amount of data generated almost daily, combined with rapidly evolving testing and treatment paradigms, makes it impossible to stay current without assistance.

- Most extensive use is in imaging, including digital pathology, radiographic imaging, and clinical photographs.[1]
- Currently more than 70% of devices that are authorized by the FDA as artificial intelligence and machine learning are used in radiology or pathology, primarily in the area of diagnostics.[2,3]
- AI, ML, and DL integrate data obtained from imaging results with other information, such as biomarkers, to provide more information, improve accuracy, and guide treatment.

[1] Chua IS et al. Artificial intelligence in oncology: path to implementation. Cancer Med. 2021.
[2] Luchini C et al. Artificial intelligence in oncology: current applications and future perspectives. Br J Cancer. 2022.
[3] FDA. Artificial intelligence and machine learning (AI/ML)-enabled medical devices. www.fda.gov/medical-devices

Utilization in Oncology

Evaluate disease risk

Pancreatic cancer is often not detected until a late stage.

Early detection may lead to more treatment options for individuals and improved survival rates overall.

ML was used to analyze time sequences of events over 41 years in more than 8.6 million patients from EMRs within the Danish National Patient Registry.

Models could learn diagnosis patterns most predictive of pancreatic cancer risk.

Defined patterns of symptoms within the records that could identify patients at high risk of pancreatic cancer within 36 months.

Raises the state-of-the-art performance level for cancer risk prediction on real-world data and supports design of future screening trials for high-risk patients.

Placido D et al. AI predicts risk of pancreatic cancer from disease trajectories using real-world electronic health records (EHRs) from Denmark and the USA. Cancer Res. 2022.

Clinical Research

Research is also becoming increasingly complex with more varied data, and AI can be useful for synthesizing and analyzing that data.

- Development of new treatments, especially targeted therapies
- Additional and improved use of existing therapies
- Clinical trial matching
  - AI, sometimes with natural language processing (NLP), can sift through patient records to extract and match patients to open clinical trials.
    - May also be useful for reducing population heterogeneity and improving prognostic and predictive enrichment.[1]

[1]Taylor K et al. Intelligent clinical trials: transforming through AI-enabled engagement. 2020. Deloitte insights. www2.deloitte.com/content/dam/insights/us

Use in Clinical Research

Process

Using structured and unstructured data, one AI program collected and sorted data from EMRs, medical literature, and public clinical trial information to improve the matching process. The machine read and identified inclusion/exclusion criteria for the trials, determined populations, and matched to data from EMRs.

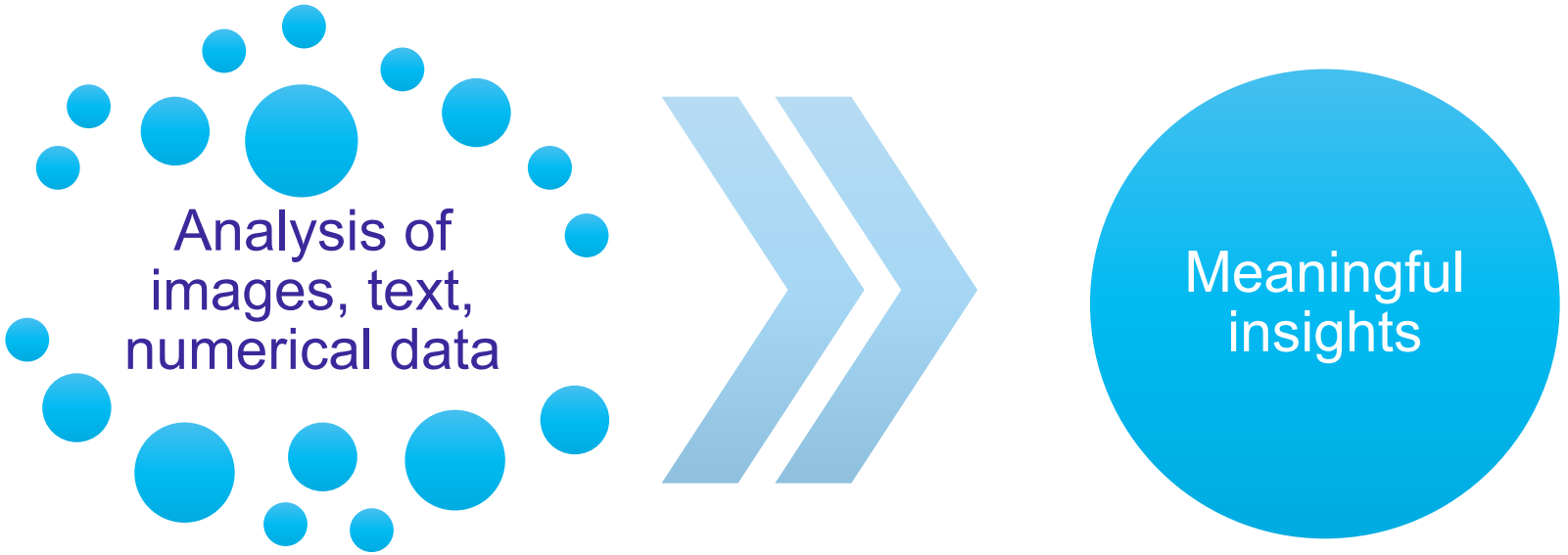
Results

- When used by the Mayo Clinic, within 11 months enrollment for breast cancer systemic therapy clinical trials increased by 80%.
- In a pilot study, this AI program processed data for 90 patients 78% faster than the clinical trial coordinator.

Taylor K et al. Intelligent clinical trials: transforming through AI-enabled engagement. 2020. Deloitte insights. www2.deloitte.com/content/dam/insights/us

Use in Precision Medicine

AI can amplify and supplement our clinical knowledge and skills, not replace it.



Recognize patterns, details

Examine, compare, quantify interactions

Precision Medicine Focus

Screening and detection

Whole-genome evaluation

Prebiopsy diagnosis

Reduced time to diagnosis

Diagnosis

Improve accuracy

Extract additional valuable data

- Grade
- Gene methylation
- PD-1 status

Decision making

Provide more input for consideration by clinicians

Risk stratification

Outcome prediction

Prognosis

Response to treatment

- Including likelihood of toxicity

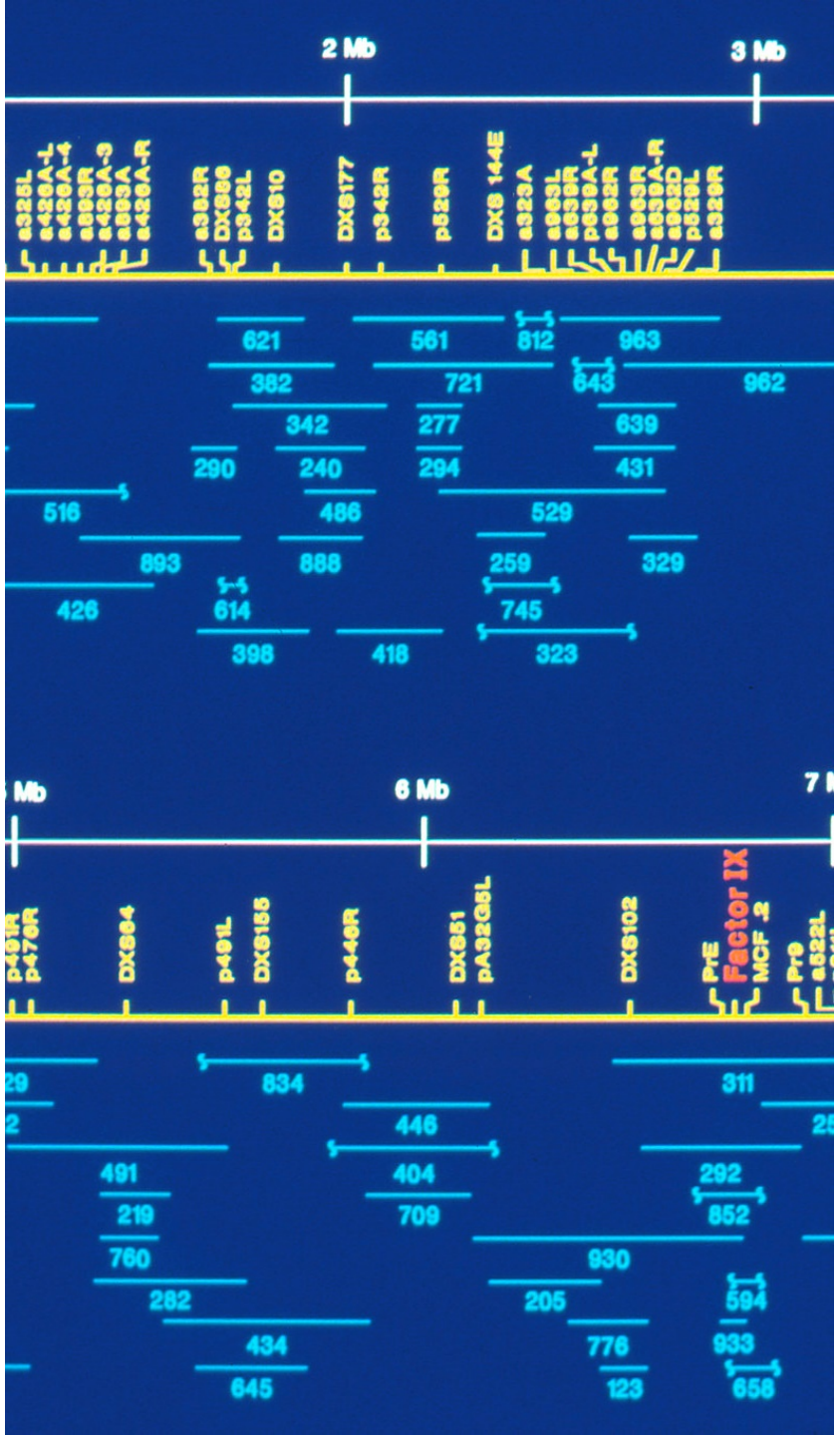
Metastasis prediction

Precision Medicine Focus

Screening

Lung tissues are often analyzed visually by pathologists, which can be challenging and time-consuming. A DL convolutional neural network model classified histopathology images of 1176 tumor and 459 normal tissues as cancer or normal.	DL method accurately distinguished tissues with slightly better sensitivity and specificity than the pathologists.
	DL accurately predicted the presence of 6 commonly mutated genes from the image: *STK11, EGFR, FAT1, SETBP1, KRAS,* and *TP53*.
	About 1/3 of the slides misclassified by the DL model were also misclassified by the specialists.
	22 of the 26 slides misclassified by the specialists were correctly classified by the DL model.

Coudray N et al. Classification and mutation prediction from non-small cell lung cancer histopathology images using deep learning. Nat Med. 2018.



Precision Medicine Focus

NGS results are highly complex and may be difficult to apply clinically. AI may be used to more effectively evaluate these results and guide treatment decisions.

A few current challenges of interpreting results are

- Many of the reported results are not relevant (or their importance is unknown).
- The significance of combinations of alterations is not known.
- Tumors may exhibit a large degree of intratumor heterogeneity.
- New research is published almost daily, with new data to consider.

We need to know which information is most important and actionable in order to determine diagnosis, guide therapy, and provide prognostic information.

Precision Medicine Focus

Predictive biomarkers

Immune checkpoint inhibitor (ICI) monotherapy may be an option in non-small cell lung cancer (NSCLC), depending on PD-L1.	Tissues from 518 patients with advanced NSCLC treated with ICIs were classified by immune phenotype as inflamed, immune-excluded, or immune-desert, which correlated with PD-L1 status ≥ 50%, 1% to 49%, or < 1%.
AI may be efficient, objective, and accurate for spatial analysis of tumor-infiltrating lymphocytes, aiding in predicting response.	AI effectively segmented and quantified H&E-stained whole slide images. PD-L1 tumor proportion scores identified by AI and by pathologists showed significant positive correlation.
	Patients in the inflamed immune phenotype group had higher overall response rates and longer progression-free survival.
	AI can objectively classify immune phenotype as a complementary biomarker to PD-L1 to supplement pathology review and optimize treatment selection by predicting response to therapy.

Park S et al. Artificial intelligence–powered spatial analysis of tumor-infiltrating lymphocytes as complementary biomarker for immune checkpoint inhibition in non–small-cell lung cancer. J Clin Oncol. 2022.

Precision Medicine Focus

Predictive signatures

Treatment response monitoring using cell-free DNA (cfDNA)

Minimal residual disease (MRD) testing

Adjuvant chemotherapy benefit for early-stage ER+ breast cancer

Immunotherapy responsiveness

Precision Medicine Focus

Analysis of EMRs using natural language processing

Targeted DNA sequencing results from 1018 patients with any type of cancer were evaluated by a molecular tumor board (MTB) and by AI.	AI and MTB identified the same patients, plus AI indicated 323 additional patients eligible for newly approved therapies or open clinical trials.
	The algorithm determined 8 additional genes that could be actionable.
	AI execution was also faster than humans could have processed this information, averaging less than 3 minutes per case.

Patel NM et al. Enhancing next-generation sequencing-guided cancer care through cognitive computing. Oncologist. 2018.

Precision Medicine Focus

Predicting site of tumor origin

Determining the site of tumor origin is critical, even when using molecularly targeted therapy. AI can be a complementary method used with conventional histologic review.	ML analyzed DNA tissue sequencing results of 7791 advanced cancer patients and predicted cancer type accurately in 73.8% of cases.
	In genomic analysis of cfDNA, predictions were accurate in 75% of cases.
	A likely site of origin for cancers of unknown primary was predicted in 67.4% of patients.
	A woman with breast cancer history presented with a lymph node lesion that was classified as ER+ breast cancer; hormonal therapy was planned. Diagnosis was revised to metastatic lung adenocarcinoma, based on high mutational burden (including *KRAS* G12Cf).
	Algorithm predicted with 96% confidence that a cancer of unknown primary in one man was colorectal, based on mutations. Combined *BRAF, MEK*, and *EGFR* therapy resulted in clinical response.

Penson A et al. Development of genome-derived tumor type prediction to inform clinical cancer care. JAMA Oncol. 2020.

Precision Medicine Focus

Classification of images

About 25% of the time there is disagreement between experts about whether lesions are benign nevi or malignant melanoma, based on H&E staining of biopsies.	595 slides were analyzed by 11 expert histopathologists and ResNet50 convolutional neural network (CNN) trained with deep learning techniques.
	The accuracy of the pathologists was 59.2%, and the accuracy of the CNN was 76% (p=.016).

Hekler A et al. Deep learning outperformed 11 pathologists in the classification of histopathological melanoma images. Eur J Cancer. 2019.

Point-of-Care Decision Making

AI can be used effectively in real-time pathology or image analysis because of speed and accuracy.

Uses include identifying patients with higher risks, such as predicting the risk of adverse effects to allow preventive or preemptive measures to be taken.

Algorithms can analyze symptom reports to enhance prioritization and early intervention.

Point-of-Care Decision Making

The SELECT framework uses the tumor transcriptome to determine optimal treatment, by analyzing for a synthetic lethal partner of the drug target.[1]	The algorithm was tested on 35 published trials in 10 types of cancer and successfully predicted patient response in 80%.
	It was further tested on 3 multi-arm trials in 21 cancer types and predicted alternative drugs for 65% of patients.
Colonoscopy may miss up to 25% of malignancies.	A computer-aided polyp detection system improved adenoma detection rates during exams by as much as 14.4%.[2]

[1]Lee JS et al. Synthetic lethality-mediated precision oncology via the tumor transcriptome. Cell. 2021.
[2]American Association for Cancer Research. AACR Cancer Progress Report 2021. www.cancerprogressreport.org/

Point-of-Care Decision Making

Classification of images

Cancer screening can be difficult in remote locations, leading to delayed diagnosis or even lack of diagnosis and treatment.

AI system developed to provide access to digital microscopy diagnostics in a rural location.

740 cervical screening samples were digitized, uploaded to a cloud server, and analyzed with a DL system to detect cervical cellular atypia.

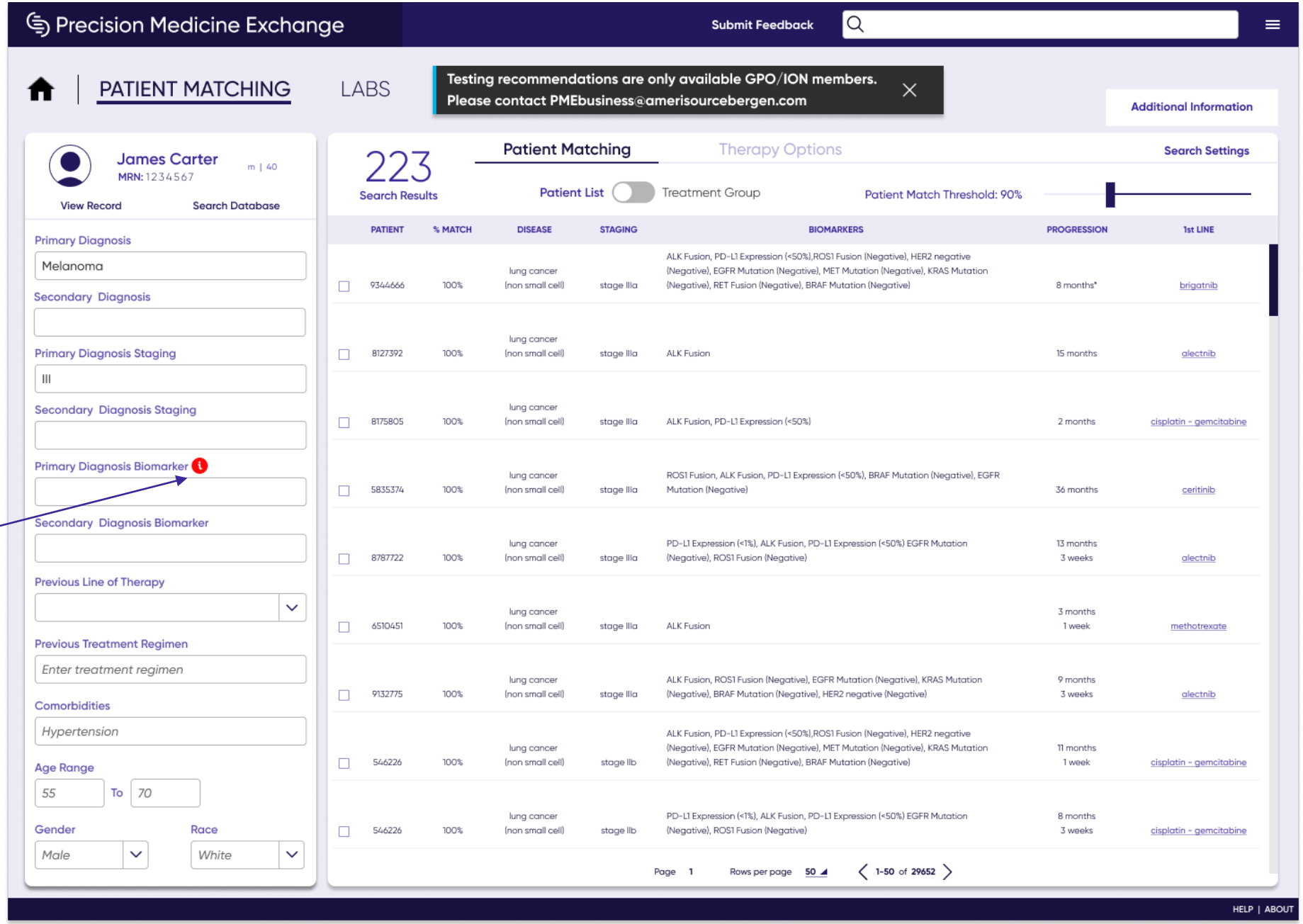
Compared with a pathologist's analysis of digital slides, sensitivity was 96% and specificity was 85%.

Negative predictive values and accuracy were high, especially for high-grade lesions.

Holmström O et al. Point-of-care digital cytology with artificial intelligence for cervical cancer screening in a resource-limited setting. JAMA Netw Open. 2021.

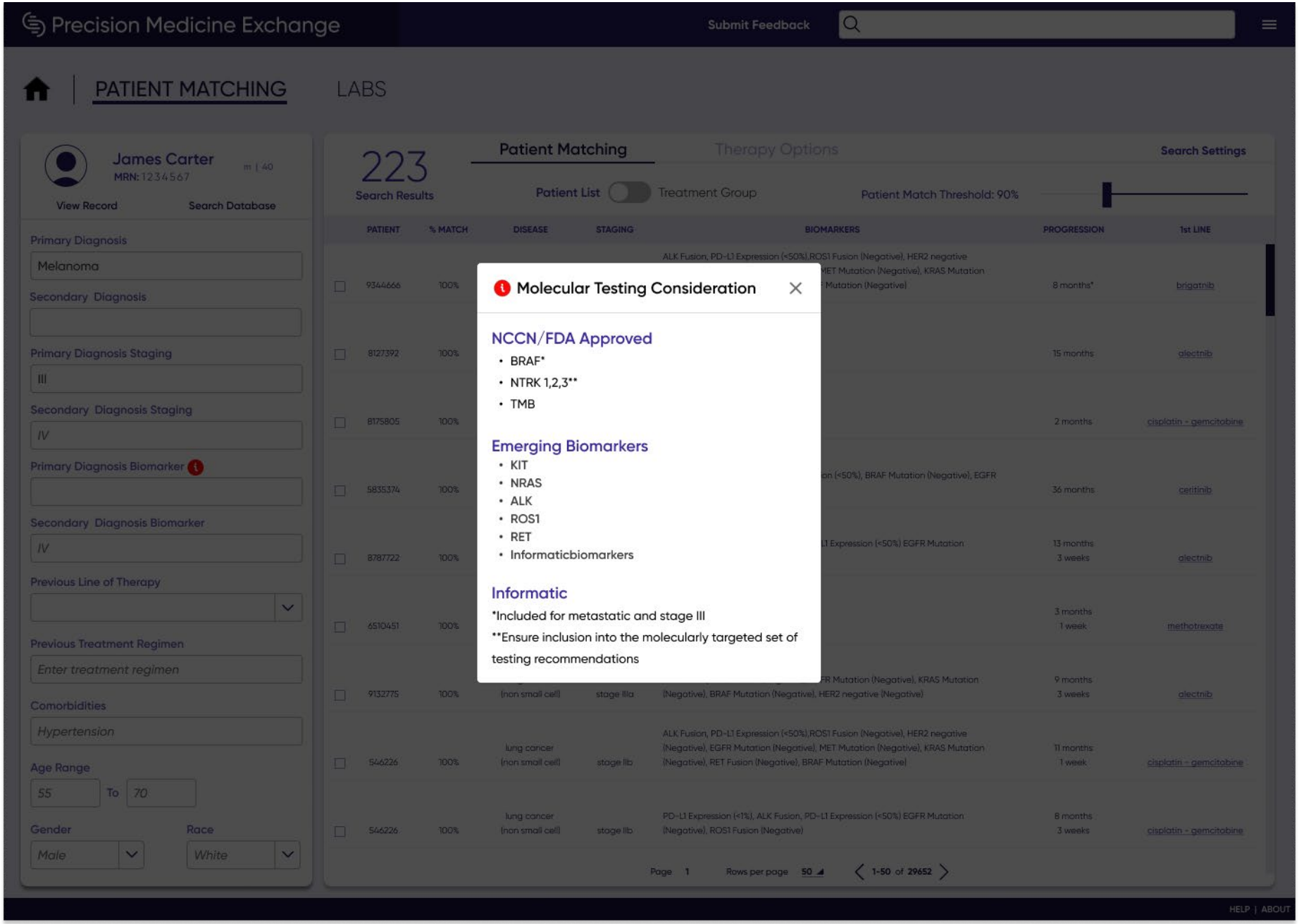
Precision Medicine Exchange supports real-time application of the latest precision medicine treatments within the workflow.

- This patient has a melanoma diagnosis, but no biomarker results.
- Information on the left was mapped from patient's chart.
- Red icon above biomarker field indicates additional information available.



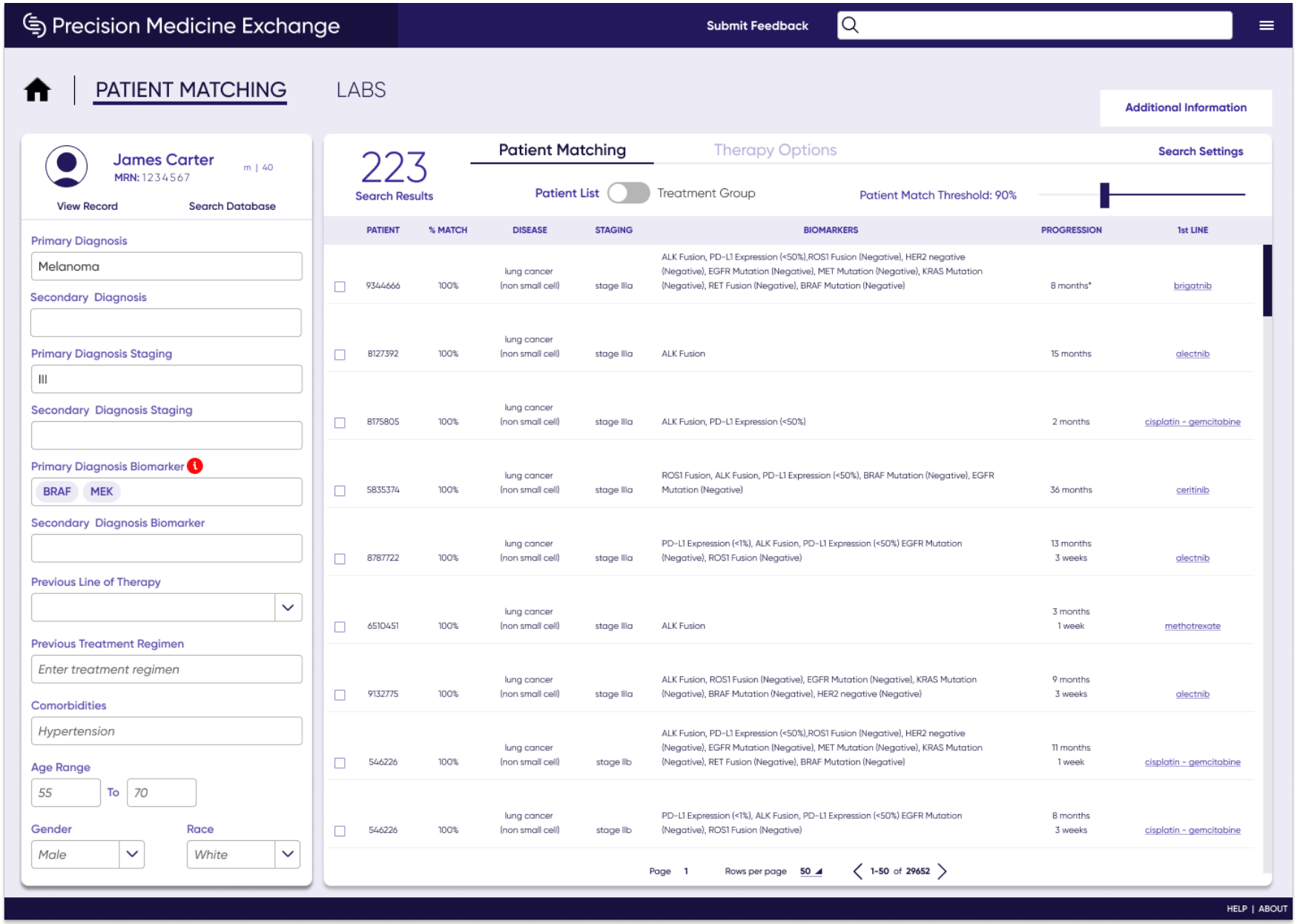
Precision Medicine Exchange

- Testing recommendations displayed based on diagnosis.
- In this case, the patient did not have any existing biomarker results.
- If biomarker information exists, more content could be displayed, including physician education.



Precision Medicine Exchange

- “Patients Like Mine” can be viewed on the right panel.
- Deidentified patient data are shown, matched by biomarker and/or diagnosis.
- Historical treatment data available for physician consideration.



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Data Quality

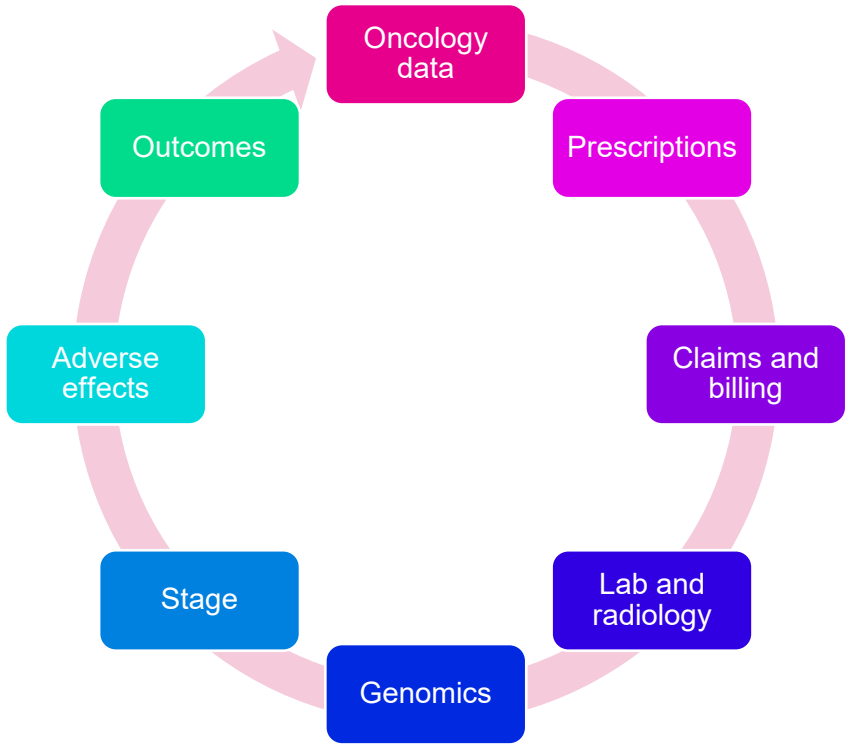
Data Quality

Quality output depends on quality input.

Good data representing all populations must be used to train the machine, or the results will not be applicable across all patients.

AI works best when models are based on robust, consistent data from large data sets.

Data Quality



Many EMR systems collect different types of data, use different terms to describe the same data, or collect data in different formats. Lack of interoperability limits the usefulness of data.

- Accurate, useful output depends on a consistent information pipeline. EMRs and other sources must be uniformly structured for analysis across multiple data sets.
- Much of the data that could be utilized—such as cancer staging, NGS results, adverse effects, outcomes—are collected only in unstructured text, making vital information difficult to access and analyze.
- Manual abstraction with natural language processing (NLP) can be used to extract data, but this requires more time and effort and may yield inconsistent or incomplete results.

Wang L et al. Assessment of electronic health record for cancer research and patient care through a scoping review of cancer natural language processing. JCO Clin Cancer Inform. 2022.
Osterman TJ et al. Improving cancer data interoperability: the promise of the Minimal Common Oncology Data Elements (mCODE) initiative. JCO Clin Cancer Inform. 2020.

mCODE

mCODE: Minimal Common Oncology Data Elements

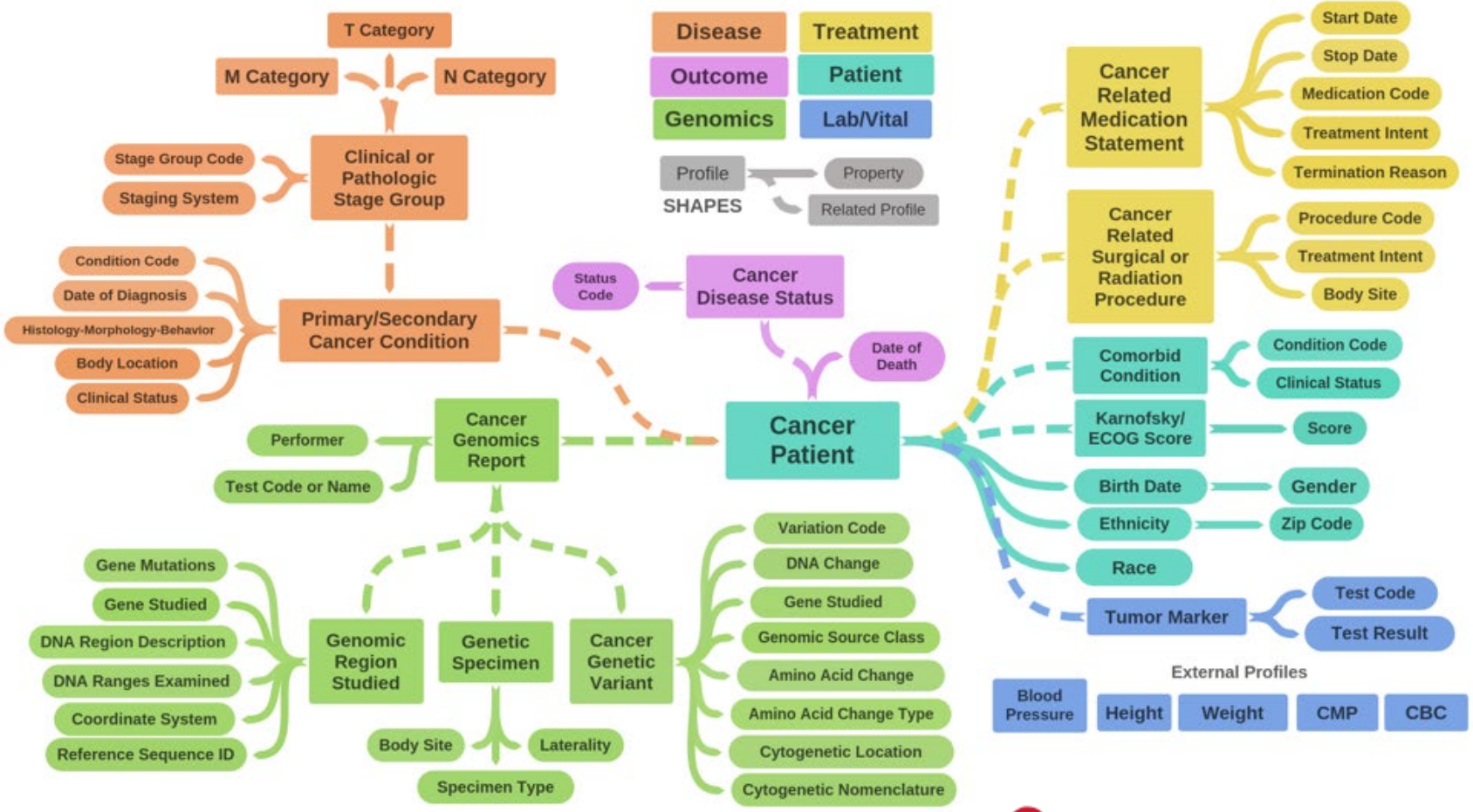
- mCODE standard seeks to ensure EMRs and other clinical systems share standard oncology data in a consistent format.
- 6 primary *domains*: patient, disease, laboratory/vital, genomics, treatment, and outcome
- Domains contain 23 *profiles* associated with 90 *data elements*

Domain	Profile
Disease	Primary cancer condition
Disease	Secondary cancer condition
Disease	TNM clinical distant metastases category
Disease	TNM clinical primary tumor category
Disease	TNM clinical regional nodes category
Disease	TNM clinical stage group
Disease	TNM pathologic distant metastases category
Disease	TNM pathologic primary tumor category
Disease	TNM pathologic regional nodes category
Disease	TNM pathologic stage group
Genomics	Genetic specimen
Genomics	Genomic region studied
Genomics	Cancer genetic variant
Genomics	Cancer genomics report
Laboratory/vital	Tumor marker
Outcome	Cancer disease status
Patient	Comorbid condition
Patient	ECOG performance status
Patient	Karnofsky performance status
Patient	Cancer patient
Treatment	Cancer-related radiation procedure
Treatment	Cancer-related surgical procedure
Treatment	Cancer-related medication statement

Osterman TJ et al. Improving cancer data interoperability: the promise of the Minimal Common Oncology Data Elements (mCODE) initiative. JCO Clin Cancer Inform. 2020.

mCODE: Minimal Common Oncology Data Elements

- AI works better with robust, consistent data to base models on.
- This has been a major limitation in application of AI in oncology.



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The real promise lies in the synergy between AI and clinical expertise and dedication

Potential

Saving time and resources and improving quality of care

Mitigation of disparities by providing additional resources, freeing up clinical time, and improving access to clinical trials

Drug discovery and development

Challenges

Must have large, accurate data sets to properly train machines

Potential negative effects on the physician-patient relationship and patient engagement, accuracy/risk of medical errors, liability questions, and issues with privacy


thank you

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Q&A