Artificial Intelligence in Cancer Care:
An Environmental Scan

CANADIAN PARTNERSHIP AGAINST CANCER
PARTENARIAT CANADIEN CONTRE LE CANCER

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ACRONYMS

Acronym	Term
AI	Artificial intelligence
AML	Acute myeloid leukemia
ANN	Artificial neural network
CADe	Computer-aided detection
CADx	Computer-aided diagnosis
CNN	Convolutional neural network
DCNN	Deep convolutional neural network
DL	Deep learning
EHR	Electronic health record
KNN	K-nearest neighbour
LLM	Logic learning machine
ML	Machine learning
NHS	National health service
NLP	Natural language processing
NN	Neural network
NSCLC	Non-small cell lung cancer
PNN	Probabilistic neural network
RF	Random forest
SBRT	Stereotactic body radiation therapy
SREs	Skeletal-related events
SRS	Stereotactic radiosurgery
SVM	Support vector machine
VTE	Venous thromboembolism

Executive Summary

INTRODUCTION

Health care in Canada faces geographic barriers to access such as large distances between health care delivery centres, population concentrated in the southern part of the country, and a federated health care system. As the number of Canadians diagnosed with cancer increases, new models of care delivery that improve access and efficiency and reduce costs are needed. The Canadian Partnership Against Cancer (the Partnership) is the steward of the recently refreshed 2019-2029 Canadian Strategy for Cancer Control (the Strategy), which articulates that technology needs to play a more prominent role in accelerating the improvement of cancer outcomes for Canadians. New technological approaches such as artificial intelligence (AI) have the potential to offer solutions to these geographic challenges, as well as other challenges in the system.

While there is no standard definition of AI, it can be understood as computer programs and technologies that use processes that resemble human intelligence (e.g., reasoning, learning and adaptation, sensory understanding, interaction).[1] AI includes machine learning (ML) and deep learning (DL), where machines provide the analytic power to analyze large amounts of data and can make predictions or decisions based on the patterns the machine identifies in the data. In order to learn more about how AI is being used in cancer care in support of potential future work in this area, the Partnership has undertaken this environmental scan. This report presents findings from a review of the grey and academic literature and interviews with five Canadian key informants.

FINDINGS: AI IN CANCER CARE

Technology is increasingly being used across the health care system to improve the quality and efficiency of care. AI is one of these important technologies and has the potential to change the way cancer care is delivered. In recent years, there has been an explosion of research exploring the use of AI in health care, and the AI market in health care is expected to grow exponentially going forward. Overall in the health sector, some of the largest areas of expansion for
AI technologies are expected to be:

- Process optimization (particularly for back-end processes like procurement and scheduling, as well as clinical flow processes)
- Preclinical research (e.g., drug discovery)
- Clinical decision support, especially in the areas of diagnosis and prognostication
- Using AI to interact directly with patients through patient-facing applications
- Using AI to analyze population-level data to identify health trends and changes (e.g., monitoring disease spread)

While system-wide adoption of AI technologies appears to be somewhat limited, there are many examples of AI being used by individual health care organizations. The areas of radiology, pathology, and dermatology seem to be the furthest advanced in implementing AI technologies. For example, in a small survey of people working in radiology in the US, over half reported they were already using AI technology or planning to use it within the next two years. Data collection and data processing tasks are the most susceptible to being transformed with technology, including AI, to improve automation and efficiency.

Within cancer care specifically, the key areas in which AI is being used or explored include:[i]

- Analyzing data in support of **detecting cancer earlier** and/or **identifying those at higher risk** of cancer. Some of these approaches use methods that are less invasive than traditional imaging and biopsies (e.g., extracting and analyzing data from blood such as genetic markers or basic blood work results like complete blood count).
- Using AI to **support the cancer diagnosis process**, potentially making it more efficient and enhancing access, through:
  - Reviewing diagnostic and clinical images (e.g., MRI, CT, x-ray, endoscopy images, images of skin lesions, etc.), segmenting images, highlighting suspicious regions in images for pathologist/radiologist review, and/or classifying findings as benign or malignant. In some cases, research has reported performance of AI algorithms that is comparable to or better than experienced clinicians in making a diagnosis.
  - Classifying pathology findings and identifying biomarkers that can be associated with imaging features (radiomics) for the purposes of diagnosis.
- Supporting **cancer treatment planning and decision-making** by:
  - Assembling and reviewing patient clinical data, published literature, and/or other medical evidence (e.g., past treatment plans) to inform individualized treatment.
  - Supporting the delivery of precision medicine (i.e., a personalized approach to cancer treatment and follow up care) through the ability to predict disease progression, survival, and treatment response, and adapt patient care based on these factors. In the area of precision medicine AI is also being used to support drug development.
- **Better identifying and proactively managing symptoms and complications** cancer patients may experience (e.g., depression/anxiety, hospital readmission after surgery, clinical deterioration).
- Making the **care process more efficient by automating tasks** that were previously done by humans (e.g., radiotherapy planning, scheduling for health care providers and patients, capturing hands-free documentation from providers in real time using AI-powered natural language processing).
- **Supporting quality improvement** by extracting data and real-world evidence from electronic health records (EHRs) to inform quality indicators and monitoring (e.g., assessing actual care delivery against standards established in guidelines) and drive treatment decisions and system change.
- **Improving patient experience** by more easily providing patients with information and tailoring support to their specific needs.

Each of these areas are explored in more detail in the report with explanations of how AI technologies and algorithms are being used in each area. The report also includes examples of specific AI innovations in the above categories that are being used or tested in clinical practice. These examples help to illustrate the possibilities for using AI in real-world contexts.

i There is also extensive work taking place in drug development using AI but this area is outside the scope of this environmental scan.

FINDINGS: CONSIDERATIONS FOR IMPLEMENTATION

Extensive research and development is happening in AI and cancer care, and AI technologies have the potential to enhance cancer care. While the specific conditions for successful implementation of AI technologies are not yet known, criteria are likely to vary based on the technologies being implemented and the context in which they are being used. However, this environmental scan identified many important elements that need to be considered and addressed to support widespread implementation of AI technologies as AI moves from research into practice.

Ethical Issues

- **Context and Challenges:** There are many potential ethical issues associated with AI such as legal and medical accountability for AI decision-making, potential for bias and inequity, access to and privacy of data, impact on patients and health care providers, etc.
- **Solutions:** The Canadian government recently issued a *Directive on Automated Decision-Making* that requires all automated decision systems used by the federal government to undergo a detailed impact assessment before they are implemented and lays out the required evidence and monitoring for a given technology based on its expected impact. This directive could provide a framework for assessing ethical issues and concerns within cancer care. Internationally, the Institute of Electrical and Electronic Engineers (IEEE) is developing standards for ethical use of AI, and other countries (e.g., UK) are also starting to implement guidance and standards. Engaging patients in the process of addressing ethical questions associated with using AI is also critical.

Access to Data, Patient Privacy and Data Security

- **Context and Challenges:** AI needs access to very large amounts of high-quality data to be developed (trained) and tested. Small datasets, datasets that are not connected, data that is not accessible, and data that is incomplete or includes errors/inconsistencies can affect the quality of AI development. Access to data also influences which AI technologies are developed as data availability is a prerequisite for testing new AI algorithms. There are also concerns about how patient privacy and security will be addressed.
- **Solutions:** Collaborative efforts are needed to create integrated and secure data sources that can be used for AI development, and improve the accuracy and consistency of these datasets. Building trust in AI among patients, providers and the public; engaging patients in the data governance and management process and educating them about how data will be used, collected and stored; and developing appropriate regulations and security requirements could help to improve acceptance of AI access to health data. Government regulators will play a critical role in this process.

Equity

- **Context and Challenges:** AI algorithms could create inequity through biases in the training datasets used to develop the algorithm (e.g., if certain populations are excluded or not well-represented), and biases in those who develop the algorithms. Barriers to accessing technology (e.g., inability to afford technologies, discomfort or resistance to using technologies, poor technological literacy) could also create inequity.
- **Solutions:** Considerations of diversity and equity should be at the forefront of AI development and implementation, and it may be helpful to establish criteria for training datasets in terms of the equity/inclusiveness of the patient cohort.

Transparency, Replication, Validation, and Testing

- **Context and Challenges:** Many AI approaches are too complex for humans to understand, and it can be unclear exactly how an algorithm arrived at a decision. This leads to difficulty replicating decisions and may hide problems with the decisions that are made, such as errors or bias.
- **Solutions:** In addition to educating and building trust in AI, it will also be important to establish validation and testing standards, define a threshold or requirements for when technology is ready to be tested in real-world settings, and provide a controlled environment for initial testing and validation. Standards that ensure consistent reporting of bias in research, and increasing emphasis on interpretable AI may also be beneficial, as well as having a continued human presence to review the outcomes from AI algorithms.

Impact on the Health Workforce

- **Context and Challenges:** Widespread implementation of AI technologies could have an impact on the overall composition of the health care workforce, as well as the specific skills and expertise needed by health care providers.
- **Solutions:** Health care providers have essential abilities that AI tools are not able to reproduce (e.g., compassion, understanding of patient context), and clinicians will still be needed to interact with patients and complete higher value work. The most likely scenario is for providers to work in cooperation with AI tools, not be replaced by them. However, some changes to training/education may be needed, and engaging and building buy-in among health care providers will be critical.

Costs and Cost-effectiveness

- **Context and Challenges:** There is currently very little publicly available evidence on the costs and cost-effectiveness of AI. Direct costs of implementation include hardware and software costs, training, and adapting workflows to accommodate new technology. Larger health system impacts may also occur based on how AI changes the care process. For example, a technology that identifies those at high risk of developing cancer earlier may increase upstream costs (e.g., costs for primary care providers and screening), but decrease the costs of treatment and follow up.
- **Solutions:** Understanding the costs and cost-effectiveness of different technologies will be critical in determining which AI tools should be widely implemented. Appropriate costing studies should assess costs and short- and long-term benefits and include a range of perspectives (e.g., patients, clinicians, administrators, experts, etc.) in the economic evaluation process.

CONCLUSION

AI technologies for cancer care is an expanding area of research and development, with exciting possibilities for improving cancer care. AI for cancer care is already being tested or implemented in real-world contexts on a smaller scale in areas such as diagnostics, treatment planning, and process efficiencies. However, more work is needed to support the shift of AI from research into practice. As AI technologies continue to move towards more widespread use in Canada, AI developers, governments, and health system partners and stakeholders must work collaboratively to address the factors that could pose roadblocks to implementation. To continue to support moving research into practice, more collaboration between organizations to develop, test, and implement AI is needed, starting first with smaller manageable AI projects that have the potential to be scaled up. Conversations among health system stakeholders about the challenges and benefits of using AI more widely in cancer care are also critical, and this is an area in which the Partnership will provide support as an enabler of the refreshed Strategy.

Introduction

The Canadian Partnership Against Cancer (the Partnership) has been the steward of the Canadian Strategy for Cancer Control (the Strategy) since 2007, and together with its many partners, has changed the pace of cancer reform in Canada. The recently refreshed 2019-2029 Strategy articulates that technology needs to play a more prominent role in accelerating the improvement of cancer outcomes for Canadians. Almost 1 in 2 Canadians will be diagnosed with cancer in their lifetime.[2] The costs of cancer care in Canada also continue to rise, more than doubling from $2.9 billion in 2005 to $7.5 billion in 2012.[3] As the number of people with cancer in Canada grows along with the costs of caring for them, it is critical to explore evidence-based strategies for delivering care more cost-effectively. Increased use of technology and new innovations that improve decision-making and care processes is an important area that could potentially contribute to improving both the quality and efficiency of cancer care and help us use scarce health care resources more wisely.

The Partnership is exploring how to best work with its partners to support the adoption of new innovations and increase the use of digital technology to improve Canadian cancer care. One important area of technological innovation in cancer care is artificial intelligence (AI). The term "artificial intelligence" was first used by scientist John McCarthy in 1956, and he defined AI as, "the science and engineering of making intelligent machines." One of the strengths of AI technologies is that they are able to process and analyze large amounts of data and they can also 'learn' from this data. While AI has been in existence in various forms for many years, the pace of development has accelerated in recent years thanks to the increased availability of both more powerful computing technology and large amounts of electronic data. In health care for example, clinical and pathological imaging and patient health records are increasingly being stored digitally.

AI technologies are now being researched and applied in many areas of cancer care, including drug discovery and development, early detection and/or prevention of cancer, diagnosis, treatment decision support, personalized medicine, patient experience, research, and more. AI tools have the potential to make cancer care more efficient and less labour-intensive, reducing costs to the system. The Canadian Agency for Drugs and Technologies in Health (CADTH) notes that AI technologies may be able to reduce the costs of health care by providing more accurate diagnoses and detecting and diagnosing disease earlier to reduce the costs of treatment and complications.[4] To learn more about the work taking place related to using AI in cancer care, the Partnership engaged Research Power Inc. to conduct an environmental scan on this topic. The findings from this environmental scan will be used to inform the Partnership's future work to support implementation of the priorities and actions in the refreshed Canadian Strategy for Cancer Control.

Methodology

RESEARCH QUESTION

The following research question was used to guide this work:

1. What AI innovations exist across the cancer control continuum (with a focus on early detection, diagnosis and treatment), that are being used or piloted in practice (primary importance), or are being developed/studied in a research context (secondary importance)?

Out of Scope

The following topics were out of scope of this search:

- AI innovations used generally across health care (i.e., not cancer-specific) were not reviewed in detail in order to keep the scope of this research manageable. However, many of these innovations will be relevant in cancer care as well and are discussed briefly in the report.
- Robotics (e.g., robotic-assisted surgery), unless specifically referencing use of AI in robotics.
- Use of AI to inform drug development or identify potential treatment targets or pathways for cancer.

LITERATURE REVIEW

A review of the academic/peer-reviewed and grey literature was conducted to address the identified research question. An analytic framework was first developed to guide the literature review process and ensure that information was captured in a consistent and comprehensive manner.

Academic Literature

To identify academic literature, the PubMed, Cumulative Index to Nursing and Allied Health Literature (CINAHL), and Health Business Elite databases were searched for related English language articles published since 2013. The search strategy that was used is summarized below. Terms were used in various iterations and combinations, and the strategy was modified as required to use appropriate terminology, alternative spellings and synonyms, Boolean operators, and relevant syntax for the requirements of each database. Because of the large number of results, MeSH terms and keywords were restricted to “Major” Mesh subject headings and free text keywords were limited to be found in the title of references to narrow the results.

- detect*[Title] OR screen*[Title] OR diagnos*[Title] OR treat*[Title] OR therap*[Title] OR “Early Detection of Cancer”[Majr] OR “Mass Screening”[Majr] OR “Therapeutics”[Majr] OR “therapy”[Subheading]
- AND cancer*[Title] OR neoplasm*[Title] OR oncolog*[Title] OR malignan*[Title] OR “Neoplasms”[Majr] OR “Medical Oncology”[Majr]
- AND “artificial-intelligence”[Title] OR “machine-learning”[Title] OR “machine-intelligence”[Title] OR “thinking-systems”[Title] OR “thinking-system”[Title] OR “microsoft-hanover”[Title]) OR “lymph-node-assistant”[Title] OR “lymph-node-assistants”[Title] OR “IBM-watson”[Title] OR “artificial-technologies”[Title] OR “artificial-technology”[Title] OR deepmind*[Title] OR “deep-learning”[Title] OR “machine-perception”[Title] OR “machine-perceptions”[Title] OR “google-ai”[Title] OR “Artificial Intelligence”[Majr]

The searches yielded over 2,000 results, which were narrowed down by a skilled reference librarian to approximately 660 results. The titles and abstracts of these results were reviewed by the consultants for relevance. From these results, relevant articles were obtained in PDF and reviewed in further detail.

Grey Literature

Relevant grey literature was identified through systematic searches of relevant provincial/territorial, Canadian, and international websites (see list below), as well as through general Google searching and review of reference lists from other relevant articles/documents.

Canadian

- Alberta Machine Intelligence Institute (AMII)
- BC Cancer Agency
- Canadian Agency for Drugs and Technologies in Health (CADTH)
- Canadian Association for Health Services and Policy Research (CAHSPR)
- Canadian Association of Radiologists (CAR)
- Canadian Institute for Advanced Research (CIFAR)
- Canadian Institutes of Health Research (CIHR)
- Canadian Personalized Healthcare Innovation Network
- Cancer Care Ontario
- CancerCare Manitoba
- CancerControl Alberta
- Direction de la lutte contre le cancer (Québec)
- MILA (Institut Québecois d'intelligence artificielle/Québec Artificial Intelligence Institute)
- Quebec Network for Personalized Health Care
- Saskatchewan Cancer Agency
- Techna Institute
- Vector Institute

International

- Alliance for Artificial Intelligence in Healthcare (AAIH)
- American Society of Clinical Oncology
- AIMed
- Agency for Healthcare Research and Quality (AHRQ) (USA)
- Cancer Research UK
- Clinical Oncology Society of Australia
- Computational Intelligence Society, IEEE
- Emerj (USA)
- European Organization for Research and Treatment of Cancer
- European Society for Medical Oncology
- Engineering in Medicine and Biology Society (EMBS), IEEE
- Healthcare Information and Management Systems Society (HIMSS)
- IEEE (Institute of Electrical and Electronics Engineers)
- Innovation Centre Denmark (USA)
- National Cancer Institute (NCI) (US)
- National Comprehensive Cancer Network (NCCN) (US)
- National Institutes of Health (NIH) (US)
- National Institute for Health and Care Excellence (NICE) (UK)
- National Health System (NHS) (UK)
- The Institute of Cancer Research (UK)
- The Partnership on AI to Benefit People and Society

In addition, a targeted search of major cancer centres in Canada and internationally was completed to try and identify any centres that may be using AI technology in daily clinical practice (only sites available in English were searched). The centres included in this search were:

- British Columbia
  - Centres included in the cancer agency website search (noted above)
- Alberta
  - Cross Cancer Institute
  - Tom Baker Cancer Centre
- Saskatchewan
  - Allan Blair Cancer Centre
- Manitoba
  - Centres included in the cancer agency website search (noted above)
- Ontario
  - Juravinski Regional Cancer Centre
  - Odette Cancer Centre - Sunnybrook Hospital
  - Ottawa Regional Cancer Centre
  - Princess Margaret Cancer Centre and University Health Network
- Québec
  - CHUS - Centre Hospitalier Universitaire de Sherbrooke
  - CSSSL - Hôpital de Laval; Jewish General Hospital
- Nova Scotia
  - Provincial Cancer Centre at QEII Health Sciences Centre
- Newfoundland and Labrador
  - Dr. H. Bliss Murphy Cancer Clinic

- Australia
  - Calvary Mater Newcastle Hospital
  - Epworth Radiation Oncology
  - Genesis Cancer Care
  - Lyell McEwin Hospital
  - Monash Health
  - Olivia Newton John Cancer and Wellness Centre
  - Peter Maccallum Health Centre
  - The Crown Princess Mary Cancer Centre
  - Townsville Cancer Centre
- United States
  - Dana-Faber Cancer Institute
  - Georgetown Lombardi Comprehensive Cancer Center
  - Hospital of the University of PA – Abramson Cancer Center
  - James Cancer Hospital & Solove Research Institute
  - Johns Hopkins Hospital Sidney Kimmel Comprehensive Cancer Center
  - Massey Cancer Centre of Virginia Commonwealth University
  - Mayo Clinic
  - Memorial Sloan-Kettering Cancer Center
  - Roswell Park Cancer Institute
  - The Ohio State University Comprehensive Cancer
  - UMass Memorial Medical Center
  - UNC Lineberger Comprehensive Cancer Center
  - University Hospitals Seidman Cancer Center
  - University of Chicago Medicine Comprehensive Cancer Center
  - University of Colorado Cancer Center
  - University of Texas M.D. Anderson Cancer Center
  - University of Washington Medical Center/ Seattle Cancer Care Alliance
  - USC Norris Comprehensive Cancer Center
  - Wake Forest University Baptist Comprehensive Cancer Center
- United Kingdom
  - Alaw Unit, Ysbyty Gwynedd
  - Chelsea and Westminster NHS Foundation Trust
  - Christie Hospital NHS Foundation Trust
  - HCA Healthcare
  - Royal Surrey County Hospital
  - St. George's Hospital NHS Trust
  - St. Luke's Cancer Centre
  - The Christie NHS Foundation Trust
  - The Royal Marsden NHS Foundation Trust
  - Velindre Cancer Centre
- Other International
  - Apollo Hospitals (India)
  - Hong Kong Adventist Hospital (China)
  - Institut Gustave Roussy (France)
  - Karolinska Institutet (Sweden)
  - Netherlands Cancer Institute (Netherlands)
  - Oslo Comprehensive Cancer Centre (Norway)
  - Spanish National Cancer Research Center (Spain)
  - Vall D'Hebron Institute of Oncology (Spain)

KEY INFORMANT INTERVIEWS

Five interviews were conducted with Canadian key informants with expertise in the area of AI and cancer care. Potential key informants were identified by the Partnership through their networks and knowledge of work in this area. Key informants who participated in the interviews are listed in Appendix A.

An interview guide was developed with the Partnership's input to help ensure all areas of interest were addressed (provided in Appendix B). All interviews were conducted by telephone and lasted approximately 45-60 minutes. Detailed notes were taken during the interviews, and the notes were sent to key informants for their review and validation following each interview.

ANALYSIS

Information collected through the literature review and key informant interviews was thematically analyzed, which involves identifying common threads across sources (i.e., literature and transcripts). Sources were first coded to reveal broader themes, as well as sub-themes/categories that illuminate the data in ways not provided by the main themes/concepts. The themes and sub-categories were then compared across data sources to further formulate the themes and categories. Systematic comparisons and verifications ensure that important categories are not overlooked, and that emerging categories and concepts are properly identified. The strength of response from key informants is reflected in the use of the descriptors "many", "some" and "a few". Information provided by key informants is integrated with the findings from the literature review throughout the report.

AI INNOVATION EXAMPLES

Throughout this report, specific innovations are highlighted in text boxes as examples of AI innovations that are being used or tested in real-world cancer care settings. Each of these innovations is also described in greater detail in Appendix C, where there is a table for each innovation with the following data captured to the extent information is available:

- Innovation Name
- Description
- Where Developed/ Implemented
- Developer (Individual or Org)
- Cancer Continuum
- Disease Site
- Use/Testing in Clinical Settings
- Results
- Clinical/Health System Impacts
- Training/Research/Development
- Other

CONSIDERATIONS

- While AI innovations used more generally across all health care settings were not the focus of this environmental scan, some information on these more general innovations is included where relevant. However, an exhaustive search and review was not conducted on these topics.
- In some cases interesting innovations were identified but it was unclear the specific technology that was used to support these innovations. Unless an innovation specifically referenced AI or other related terms (e.g., machine learning, intelligent system, neural networks, natural language processing, etc.), it was excluded from this review.
- There is an extensive amount of research and development being conducted on AI and cancer care and the field is changing rapidly. While this report provides a very good picture of the key trends and current status of this work, it is by no means an exhaustive list of all the innovations and research underway. In particular, there are many, many private companies around the world working on developing AI technologies that could be useful in cancer care, but it can be challenging both to identify these companies and to gather information about any relevant work.
- Throughout the report, when there were many publications addressing a specific topic area (for example, in many of the sections on diagnosis), we have compiled the relevant findings in literature tables that are included in Appendix D. The text in the report summarizes the more detailed findings described in these tables. In other sections of the report where there are not many relevant sources, sources are referenced directly rather than being included in a separate table.
- This environmental scan forms a scoping review of current work taking place related to the use of AI in cancer care. The studies described and included in this report are provided more for illustrative purposes of examples of work that is currently underway. Formal assessment of the quality of the studies that are included was out of scope for this report.

Findings

ORGANIZATION OF THE FINDINGS

The report findings are presented in three main sections:

Overview: This section provides some helpful context for understanding the environmental scan findings, including key AI concepts and definitions, how AI development is being supported in Canada, and the broader context of how AI is being/could be applied across the health care sector.

Artificial Intelligence in Cancer Care: This section describes how AI is being researched and applied in cancer care in the areas of prediction and early detection of disease; diagnostics; treatment planning and decision-making; managing symptoms and complications; evaluating quality of care; process efficiencies and support for health care providers; and improving patient experience.

Considerations for Implementation: This section discusses considerations in moving forward with implementing AI in cancer care, including ethical issues and questions; issues affecting access to data and data privacy and security; the transparency of AI algorithms and the ability to validate and replicate findings; equity issues; potential effects on the health workforce; costs and cost-effectiveness; and moving AI from research into practice.

OVERVIEW

What is Artificial Intelligence?

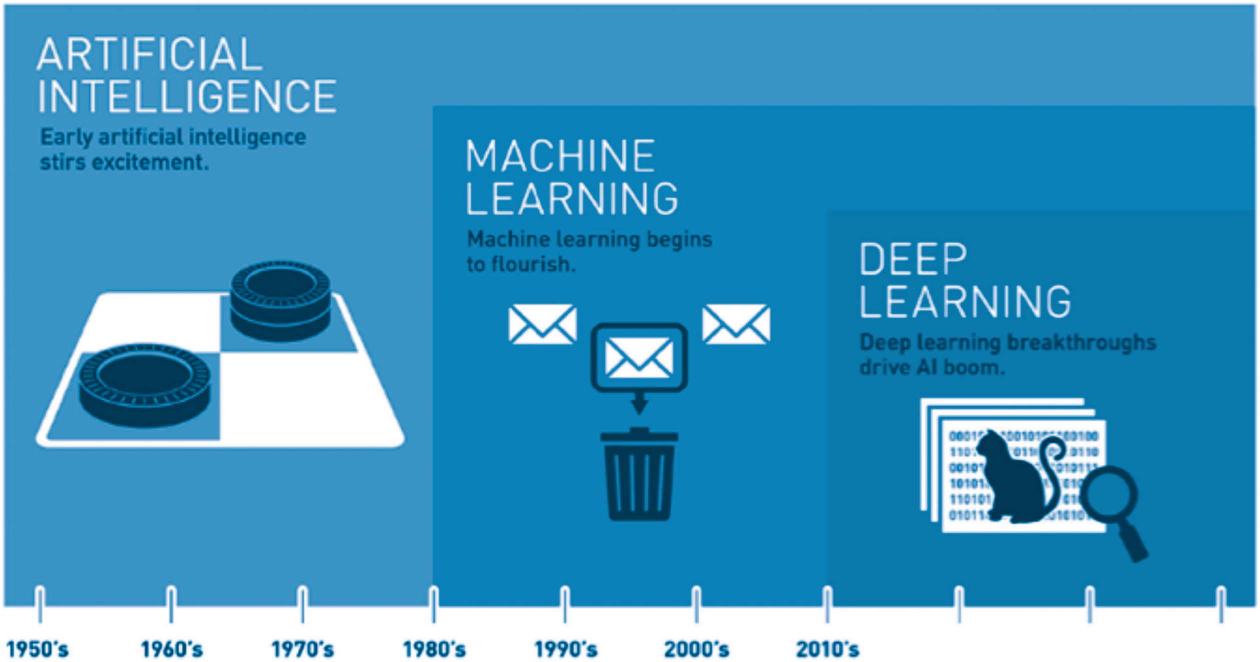
While there is no standard agreement on a definition of AI, scientist John McCarthy first defined AI in the 1960s as, “the science and engineering of making intelligent machines.” AI can further be defined as “computing technologies that resemble processes associated with human intelligence, such as reasoning, learning and adaptation, sensory understanding, and interaction.”[1] Within AI, there are different types of approaches/technologies that can be used. Below are some helpful definitions:

Machine learning (ML): a system that is able to learn to recognize patterns on its own and make predictions, contrary to hard-coding a software program with specific instructions to complete a task.[5]

Deep learning (DL): a subset of machine learning modelled after how the human brain makes decisions. Deep learning uses a layered structure of algorithms where each layer feeds into/out of the layers above/below. There are many hidden layers between inputs and outputs in deep learning (i.e., decisions are made in a black box).

Figure 1 gives an overview of how AI, ML, and DL have developed over time.

Figure 1: AI Development over Time[5]



ML/DL programs thrive on and require access to large datasets for both "training" and validation. AI algorithms are initially trained using an existing dataset, and then validated with another dataset (i.e., where a human can verify results).[4] This training process can be **supervised** (the inputs and outcomes are already known and the technology is finding the patterns that predict the outcomes) or **unsupervised** (the outcomes are unknown, and the technology is trying to summarize or explain patterns in the data).[4,5] In addition, even once training is complete, ML/DL algorithms continue to learn and improve their decision-making as they review and analyze new data.

Within ML/DL, there are many different specific techniques that can be used. The most commonly used techniques reported in research include neural networks and support vector machines. Other techniques that are also used, though less frequently, include decision tree, logistic or linear regression, nearest neighbour, discriminant analysis, random forest, hidden Markov, and naïve Bayes.[6] This report is not intended to provide technical discussion of how AI technologies work and the specific techniques that are used, but definitions for the most commonly used approaches include:

- **Artificial neural network (ANN):** a computer model that mimics the neuron connections found in the human brain. An ANN can learn from complex data and automatically generate decisions or conclusions. The networks are typically layered and the decision-making process between inputs and outputs is hidden.[4] There are different kinds of neural networks (NNs) including feedforward NNs, recurrent NNs, self-organizing NNs, convolutional neural networks (CNN), etc.[7] NNs excel at interpreting non-linear data, and provide excellent image recognition abilities.[8] They are therefore often used in AI technologies that analyze medical images.[9] Many DL models use layers of ANNs, but other types of algorithms can also be used (e.g., **support vector machine**).
- **Support vector machine (SVM):** a type of machine learning that is used to classify subjects into two groups and can be used to support diagnosis/prediction of disease.[4]
- **Natural language processing (NLP):** an approach that helps computers understand, process and manipulate natural human language expressed through text or voice (e.g., chatbots that respond to patient questions, automatic reading of information entered into patient charts, etc.).[4]

- **Fuzzy systems:** use a "fuzzy logic" method of reasoning modelled after human decision-making that takes into account imprecision (i.e., all possible responses that lie between yes and no or between 0 and 1) and is able to solve uncertain problems based on a generalization of traditional logic.[7]
- **Logic learning machine (LLM):** a supervised ML approach that is able to generate intelligible threshold-based rules to enable classification of inputs.[10]

Support for AI Development in Canada

Developing and expanding the use of AI has become an important priority for many governments, including the Canadian government. A strong Canadian network/infrastructure to support AI development has been created, with major centres dedicated to supporting the advancement of AI technologies across sectors in Toronto (Vector Institute), Montreal (MILA), and Edmonton (Alberta Machine Intelligence Institute, AMII). The Government of Canada has provided $125 million in funding to implement the Pan-Canadian Artificial Intelligence Strategy, managed and led by the Canadian Institute for Advanced Research (CIFAR). Funding is also available for research on "Artificial Intelligence, Health and Society" through the Collaborative Health Research Project competition.[4,11] Other countries/regions have also launched strategies to support AI development across sectors (e.g., the European Union has funded a European AI strategy with €20 billion, and the Chinese government has made significant investments in AI). In addition to supporting research and development of new AI technologies, the AI community in Canada is also working to address some of the existing barriers/challenges that could affect the implementation of AI in health care, such as regulation of new technologies and access to data (this work is discussed in more detail later in this report, in the section *Considerations for Implementation* beginning on p. 24).

Applying AI in Health Care

Technology is increasingly being used in many different ways across the health care sector. A variety of different technologies have and are supporting changes in the way the health care system operates, including enhanced access to care through telemedicine, digitization of health data to enable better access to data and more effective practice, and increasing efficiency in the system through process automation (i.e., using technology to perform repetitive tasks). The technologies being used range from standard computer programs and applications to more advanced applications such as robotics, 3D printing, virtual and augmented reality, nanotechnology, wearable/mobile health apps, trackers and sensors, and of course, artificial intelligence.[12]

AI is a critical and growing piece of the technology puzzle across health care and much work is being done in this area. For example, in recent years, there has been an explosion of research exploring the use of AI in cancer care specifically. In the search of the academic literature conducted for this environmental scan, we identified over 600 articles published in the last five years that explore various aspects of how AI is being used in cancer care. However, it appears that thus far the vast majority of work is still at the development and testing phase, and few AI tools are actually being used in daily clinical practice. All of the key informants interviewed for this environmental scan agreed that implementation of AI technologies in regular clinical practice is limited, and researchers reviewing AI applications in cancer concluded that most applications are "still far from being incorporated into clinical practice".[13]

One key informant noted that it is estimated that fewer than 0.1% of all technologies developed in a research context are put into practical application. In the research world, this is known as the "valley of death", and there is often a lack of resources and expertise focused on translating research into practice that presents a barrier for widespread implementation.[14] In Canada, only six AI products have been approved to date by Health Canada, but two of these are related to diagnosis and imaging and have relevance for cancer care: the Powerlook Density Assessment software assesses breast density in mammogram images, and MICA, a medical imaging cloud-based AI software developed by Arterys that includes support for diagnosing cancer in imaging for breast, lung and liver.[15]

Although current use of AI technologies in health may be limited, it is expected to grow exponentially. One estimate of the use of AI in health care in the US predicts that the health AI market will grow more than ten times larger in the next five years.[16] There are many Canadian and international companies working in the area of AI and health care or cancer care. Much of the private sector innovation in AI and cancer care internationally seems to be occurring in China, the US, and the United Kingdom (UK). China in particular may have an advantage in developing AI due to its large population and high volume of health data available for analysis.[17]

It is unclear exactly how and when the predicted growth in the AI sector may be translated into widespread clinical use, due in part to implementation challenges such as regulatory requirements and data access (implementation challenges and solutions are discussed in more detail later in this report, in the section *Considerations for Implementation* beginning on p. 24). Looking at other countries with publicly-funded health care systems similar to Canada's, at a system level it appears that the UK is one of the leaders in planning for and exploring the implementation of AI in health care. For example, NHS (National Health Service) England has developed and funded a Test Beds program that brings together health system organizations and industry partners to test implementation of digital technology including AI in real-world clinical settings.[18] Public Health England is also in the process of developing guidance for using AI in screening that will provide guidelines for AI developers.[19]

Overall in the health sector, it is estimated that some of the largest areas of expansion for AI technologies will be virtual nursing assistants, and supports for administrative work flows.[16] A recent report on AI In health care in the UK identifies five key areas where AI technologies could be used[20]:

- Process optimization (particularly for back-end processes like procurement, scheduling, logistics, etc., as well as clinical flow processes)
- Preclinical research (e.g., drug discovery)
- Integrating AI into clinical workflows to support diagnosis and prognosis
- Using AI to interact directly with patients through patient-facing applications
- Using AI to analyze population-level data to identify health trends and changes (e.g., monitoring disease spread)

Across these different areas or types of tasks, a report by the Canadian Agency for Drugs and Technologies in Health (CADTH) identifies the areas of radiology, pathology, and dermatology as those that may first experience large-scale change due to AI technologies.[4] The Canadian Association of Radiologists has highlighted radiology in particular as a candidate for early adoption.[14] In a survey of 133 people working in radiology in the United States (US), 23% reported that they are already using AI technology and another 38% said that they plan to adopt some type of AI within the next two years. Breast and lung imaging were by far the most common applications of AI identified by survey respondents.[21]

In cancer care, tasks related to data collection and data processing are likely the most susceptible to being transformed with technology (broadly, not just AI) to improve automation and efficiency.[22] Technology that supports the back-end of health care delivery (e.g., scheduling of patients or staff, data collection, etc.) may be more likely to be adopted than technology related to patient care because of the lower risks if an error is made.

The key informants interviewed for this environmental scan were asked to identify the trends in AI and cancer care, many of which are applicable across health care more broadly. Key informants noted that AI may be used to:

- Identify potential disease pathways and therapeutic targets and **develop new drugs**.
- Analyze population-level health data to better **identify risk factors and support early detection** of disease.
- Improve the efficiency and quality of the **cancer diagnosis** process.
- Support **treatment planning and decision-making**.
- Improve **patient experience** and provide better patient information.
- Make many **processes more efficient** and less resource-intensive.
- Enhance **safety, quality, and data security**.
- Inform **cancer system design**.

Most of these trends are discussed in greater detail in the next section of this report (*Artificial Intelligence in Cancer Care*).

ARTIFICIAL INTELLIGENCE IN CANCER CARE

This section describes the advancements related to AI and cancer care that are occurring in research and provides examples of technologies that are being used or tested in clinical practice where this information is available. These examples are highlighted in text boxes, and more information about each example is available in Appendix C. Identifying specific applications that use AI can sometimes be challenging as there can be cross over between different types of technologies. For example other technologies such as virtual care platforms, patient portals, robotic surgical devices, and mobile health trackers or sensors may or may not also make use of AI. AI can be used to add value to existing technologies such as these or other medical technologies (e.g., in radiology or pathology) through its data analysis and interpretation capabilities. Process automation is another example of an area where AI can be applied but is not always included in technologies that support automation. Sometimes information about a specific application/software or device is limited and it is unclear exactly why and how AI is being used. For the purposes of this environmental scan, unless an innovation specifically referenced AI or other related terms (e.g., machine learning, intelligent system, neural networks, natural language processing, etc.), it was not included in this review.

Although this report presents research that is currently taking place on AI in cancer care, it does not assess the quality of the studies that are discussed.

One recent author noted that "most studies evaluating AI applications in oncology to date have not been vigorously validated for reproducibility and generalizability,"[23] and another notes that the variation in AI techniques and parameters used in research makes it difficult to get a clear understanding of how accurate or reproducible the technology might be in clinical practice.[24]

This report focuses specifically on how AI is being applied within cancer care. However, many AI innovations being applied more broadly across the health care sector or even in other sectors also have relevance for use in cancer care. For example, voice recognition software using AI natural language processing has become ubiquitous across many consumer applications (e.g., Apple's Siri, Amazon's Alexa) and is being used in different health care contexts as well.[25] While these broader health care innovations were not reviewed in detail for this environmental scan, key trends are discussed briefly in the report.

The following sub-sections describe the key research and development in AI and cancer care identified through this environmental scan related to prediction and early detection of cancer; diagnostics; treatment planning and decision-making (e.g., decision support, radiotherapy planning, clinical trial matching, and precision medicine); managing complications; supporting and assessing quality of care; process efficiencies and support for health care providers; and improving patient experience.

Prediction and Early Detection of Disease

AI technologies can be used to identify potential cancer risk factors and predict who may be at greater risk of being diagnosed with cancer. This could ultimately facilitate earlier and more accurate detection of cancer and reduce the need for more invasive diagnostic procedures that could potentially cause harm, such as biopsy, imaging, or colonoscopy. Work in this area currently being explored includes:

- Using neural networks (NNs) and other ML techniques to **predict colorectal**[27,28]**, prostate**[29,30]**, and breast**[31] **cancer based on patient clinical data** such as age, bloodwork, family history, and physical examination.
- Using **NLP to extract information from an electronic health record (EHR) or clinical report** to help identify patients that may be at higher risk of colorectal and pancreatic cancer.[32,33]
- Using AI to **detect cancer using a blood-based test** (i.e., liquid biopsy) to detect epigenetic changes. Research has explored this in pediatric patients with Li-Fraumeni syndrome (a syndrome that predisposes them to cancer)[34], as well as in other populations such as women with ovarian cancer.[35-37] Liquid biopsies are already being implemented in some clinical settings, such as at University Health Network in Ontario.[38]

ColonFlag

ColonFlag uses routinely available data (age, sex, and complete blood count) to identify people who are at high risk of developing colorectal cancer. It was developed using a ML algorithm and datasets from nearly 3.5 million patients. It has not yet been implemented in clinical practice but was explored for use by the National Institute for Health and Care Excellence (NICE) in the UK.[26,27]

A few of the key informants interviewed for this environmental scan also highlighted the area of prediction and early detection of disease as an important field where AI has the potential to make a significant impact. Key informants noted that AI could be applied at the population health level to better understand risk factors, barriers to participation in screening, and epidemiological information to enhance understanding of cancer.

AI is also being used to support diagnosis in health care more generally, which could also have relevance for earlier detection of cancer. For example, Babylon Health provides an application that allows patients to input their health data and symptoms and consult with a chatbot (using NLP) about their health. The chatbot gives patients health information and advice. The platform also provides physicians with tools that use AI to help assess patient symptoms and determine next steps. A platform like this has the potential to support both patients and health care providers in detecting possible cancer symptoms and sending patients for additional diagnostic screening at an earlier stage.[39]

Diagnostics

Improving the cancer diagnosis process is one of the biggest areas of investigation for AI and cancer care. Machine learning algorithms have been developed to review digitized radiology and pathology results and both detect (i.e., determine the presence of cancer) and diagnose (i.e., determine malignancy and staging) cancer accurately. Many cancers are diagnosed at later stages and therefore have poorer prognosis and outcomes. For example, half of lung cancers in Canada in 2017 were diagnosed at Stage IV when they had already metastasized, resulting in a five-year survival rate of just 17%.[2] Half of colorectal cancers were diagnosed at Stage III or IV.[2] Technology that can improve the detection of cancer and shift diagnosis to an earlier stage could have a significant impact on reducing morbidity and mortality. These technologies also have the potential to make the diagnosis process more efficient.

AI technologies are increasingly being applied to traditional diagnostic imaging, including MRI, CT, x-ray, ultrasound, and histological images. AI can support detection and diagnosis of disease in the following ways:[23]

- Detecting disease by highlighting suspicious regions in images, identifying indeterminate findings, and reducing the rate of false positives and false negatives.
- Characterizing tumours through image segmentation, diagnosing tumours as benign or malignant, staging tumours, and associating genomic factors with imaging features.
- Monitoring tumours for changes over time.

AI is also being used to support efforts to reduce invasive diagnostic procedures such as imaging and biopsies, and replace them with less invasive approaches such as: liquid biopsy where genetic features of cancer are assessed through a blood test[38,40], analyzing data from breath tests that detect cancer through analysis of volatile organic compounds[41,42], and combining features identified in images with genomic factors that increase understanding of disease and guide treatment approaches (i.e., radiomics).[43,44]

Radiomics is a relatively new field that extracts a large number of quantitative features from medical images that could potentially be linked to specific genetic mutations or other clinical information in cancer care to better understand tumour phenotypes and develop decision support tools.[14] Radiomics has the advantage of being less invasive than traditional biopsies and can potentially be combined with other methods and data to improve the ability to detect and diagnose cancer.[45]

The sections that follow discuss how AI has been applied to diagnosing lung, colorectal, breast, prostate, skin, and brain cancer. These cancer types are discussed in more detail as they seem to be the areas where the greatest volume of work in using AI technology to support diagnosis is taking place (based on the findings of the literature search). However, similar AI approaches are also being researched and tested to inform detection and diagnosis of other cancers, including:

- Detecting malignant liver lesions in ultrasound[46-48], CT[49,50], and MR images[51].
- Detecting gastric cancer with endoscopy.[52-54]
- Detecting leukemia using microscopic blood images.[55,56]
- Detecting thyroid cancer using ultrasound.[57-64]
- Detecting ovarian cancer in ultrasound[65] and photoacoustic imaging[66].
- Detecting cervical cancer in pap-smear images.[67]
- Detecting esophageal cancer.[68,69]

Lung Cancer

Lung cancer is one of the most commonly diagnosed cancers in Canada. CT scans have been shown to be more effective at diagnosing lung cancer earlier compared to the traditional chest radiograph (x-ray), but review of CT scans takes valuable radiologist time,[70] and malignant nodules can be difficult to identify, resulting in both missed diagnoses and a high rate of false positives.[71] AI can help to address these issues. A systematic review of computer-aided diagnosis (CADx) that included eight studies found that using CADx helped to improve accuracy of diagnosis.[72] Another review of convolutional neural networks (CNNs) in lung cancer detection found that this is an effective strategy to improve the sensitivity of pulmonary nodule detection but notes that the research is limited by small, non-validated datasets, computational constraints, and incomparable studies.[73] The research work on AI approaches to support lung cancer diagnosis includes the following key areas (for more information see Table 1 in Appendix D):

- Improving the accuracy and efficiency of malignant **lung nodule detection in CT images** using approaches such as fuzzy clustering, CNN, SVM, genetic algorithms, and other deep learning approaches.
- Improving the accuracy of malignant **lung nodule detection in radiography** (chest x-rays) using computer-aided detection (CADe) and probabilistic NNs.
- Using **biomarkers** to detect lung cancer and support differential diagnosis (e.g., adenocarcinoma vs. squamous cell carcinoma) using particle-swarm optimization-enhanced algorithms, CNN, and logic learning machine.
- Using a combination of **both imaging and biomarkers** to diagnose and detect lung cancer with SVM.
- Using SVM to analyze data from a sensor that captures data from a **breath test** that can be used to diagnose lung cancer.

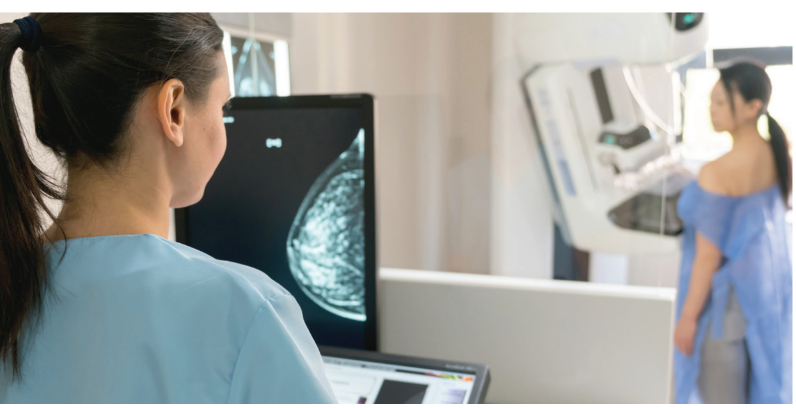
Doctor AIzimov System for Lung Cancer Diagnosis
Russian researchers have developed an AI image classification system that analyzes CT images within 20 seconds and clearly marks areas for radiologist attention. The software uses the chord method to measure and classify images. Open tests of the system are being conducted at the St. Petersburg Clinical Research Center for Specialized Types of Medical Care (Oncological) starting in 2019.[74]

In Canada, MICA, a medical imaging cloud-based AI software developed by Arterys that includes support for diagnosing cancer in lung imaging (as well as breast and liver imaging for diagnosis) was approved for use by Health Canada in late 2018.[15,75] However, it is unknown to what extent this device has been implemented in clinical practice.

Colorectal Cancer

Detecting and removing precancerous polyps via colonoscopy is the gold standard for preventing colon cancer, but the detection rate of adenomatous polyps can vary significantly between endoscopists.[77] AI techniques are beginning to emerge in gastrointestinal endoscopy as one way to improve the ability to detect and remove polyps. The most promising of these efforts have been in CADe and CADx for colorectal polyps, with recent systems demonstrating high sensitivity and accuracy even when compared to expert human endoscopists.[78] Table 2 provides an overview of the growing body of literature illustrating **improvements in the detection and classification of polyps via colonoscopy** in real time during either live colonoscopy or video recording, primarily using deep learning built on NNs. Other emerging areas in AI related to colorectal cancer diagnosis are **improving diagnosis of pathology images** using SVM; and using biomarkers to enhance detection and diagnosis (for more information see Table 2 in Appendix D).

ai4gi and Olympus
Canadian company ai4gi has recently entered into a co-development partnership with Olympus, a major manufacturer of endoscopic devices, to implement ai4gi's AI solution for early colon cancer detection and diagnosis, which uses DL for real-time assessment of endoscopic video images of colorectal polyps. This partnership is the first of its kind in the US and will help to bring this product to market.[76]



Breast Cancer

Breast cancer is the third most commonly diagnosed cancer in Canada, and almost all Canadian provinces and territories now have organized breast cancer screening programs that screen women using mammography.[2] The largest body of academic literature that explores how AI technologies could improve diagnosis is in breast cancer. There are several relevant systematic reviews that provide insight into the current work underway:

- A systematic review of CAD systems for breast cancer diagnosis using digital mammogram, ultrasound, MRI, histological images, or infrared thermography included 154 studies. The majority of included studies focused on **mammogram images**. The review found that the most commonly used techniques were **SVM and NNs**. The accuracy levels of the various algorithms ranged from 61.8% to 100%, with many that were above 90% accurate in predicting cancer diagnosis.[79] A separate systematic review of CAD systems that included 13 studies found that CAD was **effective in increasing sensitivity and/or cancer detection rate** when adding CAD to a single reviewer of mammography images.[80]
- A mapping review of AI application to breast MRI found that the majority of included studies were focused on diagnosis (i.e., breast lesion identification), and that **ANN, SVM and clustering were the most frequently used algorithms.** The review identified supervised learning algorithms as most commonly used in diagnosis, with accuracy ranging from 74% to 98%.[13]
- Another review and meta-analysis that included 11 studies found that **SVM algorithms** had the highest levels of accuracy in predicting breast cancer diagnosis, with an accuracy of 85.6%.[81]

In terms of clinical application of this work, many of the methods identified in these systematic reviews are still in the testing stages.[13] However, a few examples of AI software being used in practice for breast cancer diagnosis were identified in this environmental scan. One of these is Mia (see text box). Google is also doing work in this area. They have developed LYNA (LYmph Node Assistant), a deep learning–based approach to improve diagnostic accuracy in digital pathology by detecting cancer in pathology slides of lymph nodes from breast cancer patients. LYNA was able to correctly distinguish a slide with cancer from a slide without cancer 99% of the time and helped to shorten review

Mia
Mia is a DL-based breast cancer screening software that can read screening mammograms like an independent reader alongside expert radiologists. Mia uses artificial NNs to analyze the mammogram images and provide results to clinicians within seconds, within existing workflows. Mia is currently being tested as part of the Wave 2 Test Beds in the UK's NHS, to test the technology with pathway redesign in real-world settings. The software has the potential to reduce the number of radiologists required to review mammogram images from two to one.[18,82]

time for each slide.[83,84] Another Google project in this area is a partnership between Google's DeepMind, the Cancer Research UK Imperial Centre at Imperial College London, and the Jikei University Hospital in Japan to train the DeepMind breast cancer diagnosis algorithms on de-identified mammograms from both countries.[85]

Prostate Cancer

Prostate cancer is the most commonly diagnosed cancer in Canadian men.[2] The diagnosis process typically includes a prostate-specific antigen (PSA) test, biopsy, and/or imaging (usually ultrasound or MRI). A comprehensive review of CAD technology to diagnose prostate cancer in MR images over the last 10 years found that most of the included studies did report performance improvements, but noted that it is difficult to draw conclusions across studies because of the variability in the datasets used and the results reported.[86] Another more recent review of CAD in prostate cancer notes that although the performance of some CADx systems is good, these systems are not widely used in clinical practice and more work is needed to adapt them to clinical needs.[87] Other research work on AI approaches to support prostate cancer diagnosis includes the following key areas (for more information see Table 3 in Appendix D):

- Improving the accuracy of **diagnosis of prostate cancer from MR images** using NNs and CADx systems.
- Using **temporal enhanced ultrasound** (TeUS) to detect prostate cancer, a new approach to tissue characterization based on ultrasound radio frequency data.
- SVM and other approaches (random forest) are used to **classify pathology findings** and identify prostate cancer.

Skin Cancer

Skin cancer, the most common human malignancy[90], is primarily diagnosed visually, beginning with initial clinical screening followed potentially by dermoscopic analysis, a biopsy and histopathological examination. Automated classification of skin lesions using images can be a challenging task because of the fine-grained variability in the appearance of lesions.[90]
The main focus of AI research in the early detection and diagnosis of skin cancer has been on DL methods, primarily CNN[90-93] but also using other methods such as SVM[94,95] and fuzzy logic[96], to **diagnose cancer from lesion images** (for more information see Table 4 in Appendix D). Findings from research have shown that AI is capable of classifying skin cancer with a level of competence comparable to dermatologists.[90,93,97]
In a frequently-cited study of more than 120,000 images of malignant melanoma and benign moles, CNN was compared to the performance of 21 international dermatologists in classification of skin cancer and found to have missed fewer melanomas and made fewer false positive diagnoses (i.e., diagnosing benign moles as malignant) than the dermatologists.[90] This use of AI technology could assist dermatologists in more accurate diagnoses and provide improved management options for patients, though validation and large-scale trials are needed before AI algorithms can be put into clinical practice.[98] The next phase of research is to transition the algorithm, which currently exists on a computer, to mobile devices.
The authors of the sentinel study noted that outfitted with DNN, mobile devices have the potential to extend the reach of dermatologists outside of the clinic with the potential to provide low-cost universal access to diagnostic care, including in remote and underserved populations.[90]

MoleMapper
MoleMapper is a mobile app designed to help individuals map, measure, and monitor moles over time. While the app does not currently use AI technology, researchers hope to eventually use AI to allow MoleMapper to detect suspicious lesions in images (i.e., give individuals the ability to self-diagnose).[88,89]

Brain Cancer

Brain cancer is not as common as the other types of cancer discussed in this section, but has a poor survival prognosis.[2] It is diagnosed through imaging (MRI and CT) as well as neurologic exam and biopsy. Much of the work related to diagnosing brain cancer using AI focuses on gliomas. A review on information-based medicine in glioma patients highlights the benefits of deep learning in providing clinicians with insights from imaging data that can be used to aid in diagnosis.[99] AI is being used to support brain cancer diagnosis through NNs and/or CAD systems:

- CADx systems were found to be effective in detecting and diagnosing gliomas from MRI.[100,101]
- NNs[102,103], fuzzy image processing [104], and other deep learning models[105] have also been used to enhance brain tumour detection and grading in MRI, including both gliomas and astrocytomas.

Treatment Planning and Decision-making

AI technologies can be applied to many aspects of cancer treatment planning and decision-making. This section discusses advances in treatment decision support, AI for clinical trial matching, AI tools that improve radiotherapy support and planning, and how AI can support personalized medicine.

Although robotic-assisted surgery is a separate area of technology that is already being used extensively in cancer care, this environmental scan did not find evidence of surgical robots used in cancer care that also incorporate AI technologies (existing robots respond to the commands of a human clinician), so robotic-assisted surgery is not discussed in detail in this report. However, work is underway to integrate AI algorithms into surgical robots, particularly in the area of orthopedics.[16] If these AI algorithms are ultimately applied in cancer surgeries as well, AI-powered surgical robots could potentially improve the precision and quality of cancer surgeries.[106]

Treatment Decision Support

Watson for Oncology
IBM's Watson for Oncology is intended to use AI to analyze and interpret the clinical information of a patient and identify individualized, evidence-based treatment options appropriate for that patient drawing from its analysis (using AI) of medical evidence. Watson for Oncology worked with Memorial Sloan Kettering Hospital in the US to train the system.[107]

AI can be used to support clinicians in determining the best course of treatment for a patient. These decision support tools automatically consider the relevant oncology knowledge base (i.e., extracting information from the research literature and clinical practice guidelines) as well as information abstracted from patient charts. They can then use this information to recommend a course of treatment appropriate to the patient. The most well-known example of this kind of application is probably IBM's Watson for Oncology (see text box). Some of the research work and product development taking place in this area includes:

- A rapid learning utility for melanoma was effective in identifying known trends in melanoma using data from existing patient charts, and clinicians expressed interest in being able to use this information to support treatment decision-making in the future.[108]
- Oncology Expert Advisor (OEA) uses ML algorithms to summarize patient history, recommend treatment options, and advise on patient management based on patient characteristics and published literature (23 million abstracts from the Medline database).[109]
- A clinical decision-support tool is being developed to provide personalized treatment recommendations for managing sepsis in cancer.[110]
- Work to effectively and automatically extract information from a patient's electronic record to inform treatment decision-making.[111]

Clinical Trial Matching

Another potential area of application for AI in supporting cancer treatment is in helping to efficiently match patients who may benefit with appropriate clinical trials in order to both enhance patient treatment and improve clinical trial research. Ni et al. (2015) developed an automated process to review and match patients with clinical trials using NLP and other technologies to extract information. The AI algorithm accurately identified patients who were appropriate for clinical trials and reduced the workload required by the clinician by 85%.[114]

Watson for Clinical Trial Matching
IBM offers a tool called Watson for Clinical Trial Matching that uses AI to match patients with clinical trials. This software has recently been used by the Mayo Clinic in the US to increase enrollment in clinical trials for breast cancer by 80% and reduce the time required to screen patients.[112,113]

Radiotherapy Support and Planning

Radiation therapy, where radiation beams are used to destroy cancer cells, is an important treatment tool for people who have cancer. However, proper planning of radiotherapy is critical to ensure that the treatment impacts nearby organs that are not affected by cancer as little as possible. Radiotherapy planning is a time-consuming task as the plan needs to take into account the unique anatomy and tumour shape for each patient. Much research is underway to develop and test a more efficient and quicker approach to radiotherapy planning using AI. The research work taking place in this area includes investigating AI for the following (for more information see Table 5 in Appendix D):

AutoPlanning at University Health Network (UHN)
AutoPlanning uses AI to analyze a database of gold standard treatment plans and develop new patient-specific radiation therapy plans. AutoPlanning is now being used in clinical practice at UHN, and the technology has also been licensed to be integrated into the RayStation treatment planning system, currently used in over 2,600 clinics in more than 65 countries.[115,116]

- **Image segmentation** (auto-contouring), i.e., delineating tumour volume (clinical target volume (CTV)) and identifying and defining organs at risk (OAR).

- **Dose optimization and the development of knowledge-based treatment plans** that are comparable to those developed manually.
- **Quality assurance processes** such as comparing planned and delivered radiotherapy to ensure accuracy and identifying patients that may require adjustments to their radiotherapy plans due to anatomical variations.
- **Decision support systems** that help clinicians better understand potential outcomes and complications of radiotherapy treatment.[117]
- **Tracking tumour position in real time** so that models can be used to reduce tumor tracking errors and improve accuracy.

AI and Precision Medicine

There is an increasing shift in health care generally and cancer care specifically to deliver precision medicine. Precision medicine can be understood as adapting the approach to care (i.e., diagnosis, treatment, ongoing management) to each individual patient, taking into account variation in a patient's genetics, environment, and lifestyle factors. The increasing availability of genetic data about a patient is helping to support this shift.

Research is exploring the use of AI technologies to advance precision medicine by using AI to review genetic and other data to inform treatment decision-making. In fact, one author notes that, "there is no precision medicine without AI".[118] AI allows researchers and clinicians to analyze large amounts of genetic data to identify patterns and make predictions that will affect patient care. AI could be used to support precision medicine in a number of ways (for more information see Table 6 in Appendix D):

- **Predict treatment response:** AI can be used to better understand the effect of different treatments (e.g., chemotherapy, stereotactic radiosurgery) on cancer cells and therefore predict treatment outcomes for each patient. This approach could eventually support oncologists in designing treatment regimens that maximize therapeutic effectiveness while minimizing adverse effects.[121] This review identified work in predicting treatment response in brain, breast, esophageal, head and neck, leukemia, liver, lung, ovarian, and other types of cancers.
- **Understand and predict progression and survival outcomes:** AI models have been used to predict progression and survival outcomes for cancer patients based on factors such as genomics, radiomics, imaging, and other clinical data. Survival and progression predictions could ultimately be used to help guide which treatments are offered to which patients as well as when they are provided.[122] For example, patients with poor survival expectations may be screened out of riskier or more aggressive treatments, with the goal of improving quality of life for patients.[123,124] This review identified work to predict outcomes in many different types of cancer, including bladder, brain, breast, cervical, colorectal, gastric, head and neck, leukemia, liver, lung, ovarian, pancreatic, prostate, sarcoma, and testicular.
- **Identify biomarkers that determine outcomes:** AI can be used to identify biomarkers that can have an effect on treatment response and survival outcomes. This is also an important part of drug development, i.e., identifying potential therapeutic targets for cancer treatment. AI can be used in this way to support drug discovery and development. However, this area of research was out of scope for this environmental scan and is therefore not discussed in detail here.

Precise MD

Precise MD is a pathology platform that uses AI to translate data into clinical knowledge. Precise MD is currently in use in the Department of Pathology at Mount Sinai Hospital in New York. Precise MD developed a new approach for assessing risk in prostate cancer patients that predicted significant disease progression with a greater degree of accuracy compared with models that incorporated only clinical features such as the traditional Gleason score, or a Prostate-Specific Antigen (PSA) test. Men identified as high risk by the Precise MD test may be appropriate candidates for additional monitoring and treatments, including chemotherapy and radiation.[119,120]

Managing Symptoms and Complications

AI tools can be used to better understand potential patient symptoms and complications and predict which patients will be affected. If health care providers can identify which patients may experience certain symptoms or complications, they can intervene to potentially improve outcomes.[125] Some of the areas where AI has been used to understand and predict symptoms and complications include (for more information see Table 7 in Appendix D):

- Using network analysis to understand the complex **relationships among 38 common symptoms** experienced by oncology patients undergoing chemotherapy.[126] For example, this research could identify which patients are at higher risk to experience **psychological symptoms such as depression and anxiety**.[127]
- Predicting which patients with bone metastases are more likely to experience **skeletal-related events** (SREs).[130]
- Predicting **complications from chemotherapy and radiation therapy** such as acute mucositis in head and neck cancer patients[131], late rectal bleeding and erectile dysfunction in prostate cancer patients[132], and rectum toxicity in cervical cancer patients.[133]
- Predicting the **risk of venous thromboembolism** (VTE) for cancer outpatients.[134]
- Predicting **delayed discharge and readmission** in enhanced recovery following laparoscopic colorectal cancer surgery.[135]

PATHFx

PATHFx is an AI adaptive treatment support tool for patients with metastatic bone disease. It uses AI to analyze data and provide the patient with a survival prognosis to aid the orthopaedic surgeon's decision-making regarding whether to offer surgery to a patient with a pathologic fracture and which implants are suitable. It also helps avoid under-treatment and over-treatment. PATHFx is linked to the International Bone Metastasis Registry in order to continually improve and update its prognoses as new cancer treatments are introduced. It is in clinical use at the orthopaedic clinic at Karolinska University Hospital in Sweden.[128,129]

- Predicting **clinical deterioration** (ICU transfer and cardiac arrest) in patients with hematologic malignancies.[125]
- Predicting **acquired resistance** to epidermal growth factor receptor tyrosine kinase inhibitors.[136]
- Predicting **risk for patients with acute leukemia** before undergoing allogeneic hematopoietic stem-cell transplantation.[137]

Evaluating Quality of Care

AI tools are being developed that support evaluating the quality of cancer care. Performance indicators are an important tool in cancer care to support monitoring and quality improvement initiatives. The largest contribution of AI to this area is using NLP to extract data from EHRs, particularly from free text/clinical notes fields to inform quality indicators. For example:

- NLP was used to extract data on **adenoma detection rates** as a metric for colonoscopy quality[138-140], and also used to determine **whether surveillance intervals for colorectal cancer are guideline adherent**[139].
- NLP was used to extract data from the EHR on **end-of-life process measures** (e.g., documented goals of care discussion) for cancer patients receiving gastrostomy with sensitivity and specificity comparable to manual chart abstraction[141] and has been used more broadly across palliative care to ensure that providers are having appropriate end-of-life care discussions with patients.[142]
- NLP has been used to analyze **patient-reported outcomes** (including functional and emotional outcomes) reported in online cancer support groups for men with prostate cancer.[143]

Process Efficiencies and Support for Health Care Providers

AI has the potential to support health care providers in doing their work and improve efficiency in the care delivery process. This environmental scan identified several areas where AI can be used to help support efficiencies in cancer care. Several of these were already discussed, for example, more efficient clinical trial matching and faster radiotherapy planning. In health care more broadly, AI is also being explored to improve efficiency and support health care providers in the following ways:

- Better organize and coordinate **scheduling of care**, including scheduling health care providers and allowing patients to self-schedule appointments.[146,147]
- Using NLP to automatically read the results of diagnostic reports and create **real-time alerts and follow up reminders** for both patients and health care providers.[148]
- Using NLP to automatically **extract data from patient charts** and deliver it to health care providers to **inform clinical decision-making**.[32,108,111,149,150]
- NLP techniques that use voice recognition could be used to support **hands-free documentation** by health care providers. For example, physicians could document findings in real-time during a clinical procedure by talking through their findings or have more opportunity to interact freely with patients during appointments if notes from the visit are automatically entered into the patient's EHR.[151-153]

Docbot
Docbot is an integrated AI tool that applies AI to polyp detection in endoscopy/colonoscopy images and also integrates with EHR systems to auto-document procedures and associated quality measures. This will help to reduce specialist time in inputting patient data manually, resulting in a quicker turn around on reporting and any required follow up.[144,145]

Improving Patient Experience

AI also has a role to play in supporting patients and improving patient experience during cancer care. The system and health care provider-focused AI technologies previously discussed in this report could also be important contributors to improving patient experience (e.g., better patient management using AI-driven outcome prediction; quality improvement initiatives powered by data collected with AI; AI process efficiencies that support patient convenience such as allowing patients to schedule their own appointments, etc.). Patient-facing AI technology and applications are also important strategies to enhance patient experience. This environmental scan did not identify many innovations in this area that were specific to cancer care. However, within health care more broadly there are many efforts underway to improve the patient experience that could be relevant for cancer care. Some of the key trends include:

- Use of **chatbots** and/or **virtual assistants** to support patient care, for example answering patient questions or reminding patients about appointments.[154]
- **Apps** that provide patients with **personalized information and resources** based on the patient's specific circumstances (e.g., type of cancer, symptoms, treatment course, etc.).[155]

While not cancer-specific, the Alder Hey Children's Cognitive Hospital currently being developed in the UK is an interesting example of how AI technology can be implemented across a health care organization to support improved patient experience. Alder Hey is working with IBM Watson to integrate technology throughout the hospital experience. This will include providing a child-friendly app that can provide a virtual hospital tour, answer questions patients and their families may have, provide reminders of appointments and care instructions, and track symptoms and other concerns (e.g., patient anxiety). The app will even ask about patient preferences and likes (e.g., a child's favourite animal) so that these can be integrated into the patient's experience. All feedback collected by the app is also shared with clinicians and other hospital staff so that they can use this information to personalize the care process.[156-159]

CONSIDERATIONS FOR IMPLEMENTATION

There are many considerations in moving forward with implementation of AI in regular clinical practice, including ethical issues and questions; issues affecting access to data and data privacy and security; equity issues; the transparency of AI algorithms and the ability to validate and replicate findings; potential effects on the health workforce; and the costs and cost-effectiveness of technologies. These are all important elements that need to be addressed to support moving AI technologies from research into practice. The specific conditions for successful implementation of AI technologies will be different depending on the technology being implemented and the context in which it is being used. While many of these considerations are relevant in implementing AI in any context, health care poses a particular challenge because of the sensitivity of health data and the potential for negative outcomes that affect the life and death of individuals.

The issues in this section are discussed in the context of AI in health care generally and are also relevant specifically within cancer care. Key informants interviewed for this environmental scan discussed many of these implementation considerations as well. While a comprehensive search and review of each topic was outside the scope of this report, the report sections that follow provide a general overview and key findings related to each topic.

The Ethics of AI

Context and Challenges

Interest in the possible advantages that AI could bring to the health care system is high. However, the use of AI in health care also raises many potential ethical concerns and challenges.[1,118] Balancing the potential benefits and risks of using AI is an important consideration before use of AI in health and cancer care can become widespread. The Nuffield Council on Bioethics in the UK highlights the following potential ethical questions related to AI:[1]

- Who is **accountable** for decisions made by an AI algorithm? This is particularly important as there is always the potential for AI to make incorrect decisions.
- How are the outputs from AI technologies developed, understood and **validated**?
- What **biases** exist in the data used to develop and train AI systems and how will these impact outcomes? What about **inequity in access** to technology?
- Who has **access to data** and how will sensitive data be protected? Studies have found that patients may be uncomfortable with allowing AI systems to access their health data for example, particularly if private sector companies are involved.[160,161]

- How might using AI affect **an individual's experience of care** and/or sense of dignity? A few key informants noted that patients may prefer not to receive care from an automated source compared to a live person.
- What is the **impact** of AI technologies on **health care providers**?
- How can we prevent AI from being used for **malicious purposes**?
- What about the **unintended consequences** of AI? For example, could the technology or data be used in a manner for which it was not originally intended?[162]

Some of these issues are further discussed in later sections of this report (e.g., data use, access and security; equity; impact on health care providers).

Solutions

Ethical standards are needed to guide AI in health/cancer care.[118] Developing these standards and ensuring they are followed should involve a collaborative effort that engages governments and regulatory agencies, researchers, private sector developers, health care system administrators, frontline providers, patients, and the public. Many organizations and individuals in Canada and internationally are working towards addressing the ethical issues involved in using AI in health care:

- Many Canadian organizations are focused on ethical development and implementation of AI in health, including the Canadian Institutes for Health Research (CIHR), CIFAR, the National Research Council, and others.[163,164] In February 2019, the Government of Canada issued a *Directive on Automated Decision-Making* to **ensure that any government process that uses an automated decision system (i.e., using AI) is "compatible with core administrative law principles such as transparency, accountability, legality, and procedural fairness"**. The directive requires that all automated decision systems undergo a detailed impact assessment before they are implemented, and lays out the requirements for a technology based on its expected impact.[164,165] While this directive applies specifically to public-facing decisions within the federal government's jurisdiction, it could provide a framework for these types of technologies within health care at the provincial level as well.
- The Canadian Standing Senate Committee on Social Affairs, Science and Technology recommended in 2017 that **working groups be established to address many of these ethical issues**, and that Health Canada **assess the current regulatory environment** for medical devices in Canada to explore whether any changes to regulatory processes are needed.[166] The Canadian Agency for Drugs and Technology in Health (CADTH) notes that regulation of AI applications in health may require additional considerations, such as meeting the same rigorous clinical criteria that would be applied to any other type of health innovation.[4] Vector Institute and other partners have emphasized the need for an adaptive approach to regulation in this area.[167]
- In Canada, the *Montreal Declaration for a Responsible Development of Artificial Intelligence* was developed and recently launched with the aim of providing an **ethical framework for developing and implementing AI** and helping to guide the transition to new technologies. This could serve as an important ethical framework for AI implementation in Canada.[168]
- Internationally, the Institute of Electrical and Electronic Engineers (IEEE) launched the IEEE Global Initiative for Ethical Considerations in Artificial Intelligence and Autonomous Systems in 2015 and just released *Ethically Aligned Design* in late March 2019. This document will provide insights and **recommendations to inform development and implementation of technology so that it aligns with ethical principles.** The group is also working towards developing **standards** in this area.[7]
- Other countries such as the UK are also developing **guidance documents** and recommendations for how AI should be used or applied in practice (e.g., in screening).[19]
- A few key informants highlighted that **educating patients and health care providers** about AI is also critical to building trust and understanding of AI technologies.

Access to Data, Patient Privacy and Data Security

Context and Challenges

Around the world an increasingly large volume of health information is being created and captured from a variety of sources, such as EHRs, mobile health apps, wearable health devices (e.g., FitBit), digital imaging and pathology results, and the administrative records of health care organizations. One of the critical needs for AI technologies to continue to develop and become more accurate is access to large amounts of data. In order to learn, AI algorithms need access to high-quality datasets that can be used for training. In an ideal world, datasets would also be linked so that findings from one data source could be combined with other data sources to better inform a final conclusion (e.g., linking information from a patient's chart to pathology and/or radiology results).[169] In addition to training purposes, one key informant noted that real-world, high quality linked datasets can be used with AI systems to inform hypothesis generation and generate insights or potential solutions to problems that humans are not yet considering.

Unfortunately, there are still many limitations on the amount of high-quality data that is potentially available to inform the development of AI, as well as concerns about the privacy and security of datasets used by AI technologies. All key informants identified challenges related to access to data of adequate size and quality as a key factor limiting the development and implementation of AI. The challenges include:

- **Limited Access to Data:** In some cases, large datasets are simply not yet available. For example, there may be a limited number of genetic profiles for a specific type of cancer[170], or the information collected in a patient's chart may not yet be available in a digital format.[166] Even if data does exist, researchers/developers may not be able to access this data.[171] One key informant indicated that geographic and political barriers that exist around data sources may also complicate access issues. Key informants noted the following potential negative impacts of limited access to data:
  - Research and development of AI tends to focus where data is most readily available, so access barriers may also ultimately influence what technologies get developed.
  - Small datasets can affect the accuracy of algorithms and results as AI thrives on access to large amounts of data.
- **Errors and Inconsistencies in Data:** Unfortunately, many available datasets contain errors and/or inconsistencies[1], or are incomplete (e.g., lacking a confirmed diagnosis for diagnostic imaging).[23] The performance of an AI algorithm can only be as good as the quality of the training dataset that is used, so data errors can affect performance. For example, if outcome labels are unclear or missing in a dataset (i.e., confirmation of a cancer diagnosis for each image included in training), this will impact the accuracy of the algorithm.[172] Data also may not be collected in a consistent way across different sources, leading to difficulties linking or comparing datasets.[1]
- **Privacy Concerns:** Patients and health care providers may have concerns about sharing health data to support development and testing of AI technologies, particularly if this data is being shared with private companies.[1] For example, a recent agreement between Google's DeepMind and a London, UK hospital to share patient data for training and development purposes was ruled to be a violation of privacy by the UK's data protection regulator.[173]
- **Data Security:** In this age of online access to data, there may also be concerns about the security of data and the need for protection against malicious access to and use of health data (e.g., through hacking).[174]

Solutions

Potential solutions that could help to address some of these challenges include:

- Efforts are underway to **develop integrated and secure data sources**. This will require appropriate investment in the staffing and infrastructure needed to develop and maintain these data sources. One example of this is Health AI Data Analysis Platform (HAIDAP) being developed collaboratively by ICES, HPC4Health (at the Hospital for Sick Children in Toronto), and the Vector Institute. The HAIDAP will move "population-wide longitudinal health data holdings into a secure environment with the compute power required for modern machine learning research."[163] One key informant noted that Canada should consider a hub and spoke type of model for its data infrastructure so that data integrity can be maintained and access can be appropriately managed. The National Institutes of Health (NIH) in the United States recommends that existing federal, academic, and commercial computer systems for data storage and analysis be leveraged.[175]

- Work towards **improving the accuracy and consistency of datasets**. For example, additional work may be needed to ensure that training datasets for cancer diagnosis include accurate labelling from a later stage of the diagnosis process (e.g., biopsy results).[172]
- **Build trust in the use of AI technologies** in health care through a range of approaches, including public consultation with plain language materials and patient and health care provider involvement in data regulatory decisions.[161,167] Education is also needed for patients around how their data will be collected, stored and used.[20]
- Experts in ethics and patient privacy in the context of big data have highlighted the importance of **equity, consent, and patient governance** in data collection and management.[176]
- Implement **FAIR Data Principles** to help support the development of data that is findable, accessible, interoperable and reusable.[175] Following these principles would ensure that AI developers can find the data they need and access the data once it is identified (with proper authorization as appropriate). It also supports integration (interoperability) of different datasets for analysis/processing and storage. All of this contributes to making the data reusable so that work can be replicated.[177]
- Transition data collection tools such as EHRs to **a more secure technology** such as blockchain to help increase security and guard against hacking. Blockchain is a secure, decentralized online ledger (database) that has been used extensively in cryptocurrencies such as Bitcoin.[178]
- **Regulations** will also need to address data access, privacy and security concerns. For example, in the European Union, the recently enacted European General Data Protection Regulation (GDPR) establishes specific requirements for informed consent for all uses of data and outlines the rights of individuals that are providing their data.[166]

Equity

Context and Challenges

AI algorithms are only as equitable as the data they are built on and those who are involved in building them. AI may therefore pose several challenges in relation to equity:

- **Bias in the Data:** AI algorithms are subject to selection bias, i.e., if patients of certain ethnic backgrounds are under- or over-represented in the training dataset, this may impact the ability of the algorithm to properly assess some patients.[169] While not specific to the use of AI in health care, one author notes that AI in general often reproduces racist and sexist biases in society because these are inherent in the data used by the technology.[179]
- **Bias in the Developer:** In addition to biases in the datasets used to develop AI technology, biases that reflect the beliefs and prejudices of the developers may be embedded from the beginning, before data is even analyzed.[1]
- **Barriers to Accessing Technology:** In areas where technology is less accessible, this may affect the ability to develop and use AI. This could apply to individual patients as well as to given geographical areas (e.g., individuals or communities with lower socioeconomic status may face additional challenges accessing technology).[1] Individuals may not have access to the technology needed to use tools such as mobile apps or wearable health monitoring devices. Some individuals and/or communities or cultural groups may also be more hesitant about or resistant to the use of technology in their health care, or they may lack the digital literacy to use these tools.[20]

Solutions

- It could be helpful to **establish criteria for the patient cohorts** that will be used for training purposes.[4] For example, training datasets should include a diverse range of cases considering factors such as demographics, patient clinical factors, and disease outcomes (e.g., variation of cancer stages in imaging technology).[180]

- Ensure that **equity is a consideration when assessing the potential impacts** or outcomes of AI, including both equity of access and equity of outcomes.[20]
- Support and encourage **diversity** among those working to develop and implement AI.[1]

Transparency, Replication, Validation, and Testing

Context and Challenges

One of the challenges with many AI techniques, especially deep learning, is that they occur inside a "black box", i.e., the decision-making process is too complex for humans to understand. In addition, private companies developing AI technologies may deliberately keep their technology secret as proprietary information.[1,4] This presents several challenges:

- **Difficulty of Replication and Validation:** It can be difficult for other scientists to test a technology and replicate results if the mechanisms and processes are not clear.
- **Difficulty Detecting Errors or Bias:** If the decision-making process is not well-understood, it can be difficult to identify cases where the AI technology may be making errors or using biases to inform its decisions.[24]
- **Lack of Trust in AI:** Lack of knowledge about how AI technologies actually operate may be a factor in limiting trust in their results for both patients and health care providers. Europe's GDPR includes a regulation that provides individuals with the "right not to be subject to a decision based solely on automated means."[4] Understanding the decision-making mechanism may be an important factor in acceptability for patients.

Solutions

- Key informants noted that **validation and verification methods** for AI tools must be rigorous and must be conducted regularly even after official approvals and implementation, especially as the technology will continue to learn from existing data. The Canadian Association of Radiologists (CAR) recommends that **standards for validating and testing** AI tools and reporting findings be developed.[4] Fröhlich et al. (2018) recommend that validation processes include internal validation with the initial training dataset (e.g., using cross-validation), external validation with an independent dataset, and validation through a prospective clinical trial to demonstrate any benefit compared to standard of care.[169] Consistency in reporting across different technologies or studies is also important.[24]
- One key informant said that there needs to be mechanisms for identifying situations when an AI model is not functioning correctly, and **disagreement and contesting decisions** should be welcomed as part of the development process.
- Key informants also indicated the need for a **human presence** for some time to review and validate AI decisions. This will also help to build trust in the technology.[160]
- One key informant suggested that there is a need for a **controlled environment for testing and refinement of technologies** once they are ready. The test beds being used in the UK are one example of this approach.[18] The CAR recommends a standardized approach for benchmarking and implementation of AI applications in radiology.[14]
- There is a need to define a **threshold or requirements for when a technology is ready to be tested in a real-world setting and/or implemented in daily clinical use**. NHS England in the UK has developed an evidence standards framework for digital health technologies to provide guidance on what level of evidence is needed to approve these technologies and takes a proportionate approach to risk where the highest level of evidence is required for tools that involve determining a patient's diagnosis or treatment. While these standards are only applicable to AI that uses fixed algorithms and not to DL techniques where the algorithms are continuously changing in response to new data, it could serve as a model for determining evidence standards for implementation.[181]
- Emphasize the importance of **interpretable AI** in health care, i.e., ensure that there is plain language information on the technology and explain how human monitoring and verification is used in the decision-making process.[167] This is currently an active field of research.[23]

Impact on the Health Workforce

Context and Challenges

Health care has been built on relationships between patients and their health care providers. Adding AI technologies to health care has the potential to shift these relationships, and in fact to alter how health care is structured and provided. This could have a significant impact on the health care workforce, including:

- **Skills and Expertise:** The skills and expertise required by health care providers may need to change. For example, AI could change the focus to spending more time building relationships with patients. AI may have a particular impact on radiologists and pathologists as much of the current work is taking place in imaging and pathology.[14] Although AI technologies may be able to make decisions more effectively than humans in some cases, humans will still need to maintain their expertise and skill so that they are able to recognize and correct errors, and/or step in when the AI system fails.[1,20]
- **Workforce Composition:** AI may change the overall composition of the workforce in cancer care by automating some tasks that previously were done by people.[1,4] Concerns about job losses or impact on roles may lead to resistance to implementing new AI technologies among some health care providers, although most key informants felt that the majority of health care providers would generally be supportive.
- **Potential for Process Inefficiencies:** One key informant noted that any technology that is poorly implemented can actually have the unintended consequence of making work less efficient rather than more efficient. For example, if a program takes time to load or requires the user to enter the same data multiple times, or switch back and forth between screens, or other processes that take time, this can lead to inefficiencies.
- **Threats to Independence:** Health care providers may feel their independence or autonomy is threatened by AI.[1]

Solutions

- Most key informants noted that **health care providers will still have a critical role** in interacting with and verifying findings from AI technologies, and other researchers share this view as well.[4,99,182] Studies have found that AI **technology is most accurate when used as a support** to a physician (compared to the algorithm or the physicians alone).[83] In addition, key informants also suggested that the **empathy and compassion** that health care providers have for patients, as well as their **understanding of patient context**, will not be easily replaced by AI.[1,20]
- **Restructured training and education** may be needed for health care providers. For example, providers may need more soft skills around interacting with patients rather than focusing as much on knowledge acquisition, recall, and building specific skills (e.g., reading radiology or pathology images).[183] One key informant highlighted the need for expertise in data science among health care providers and researchers, and the CAR recommends that radiology residency programs integrate health informatics, computer science, and statistics courses in AI in their curriculum.[14]
- Ensure that AI algorithms that are implemented are **effectively integrated into existing clinical work flows** so that they improve both efficiency and quality.[83] Aside from issues related to the accuracy and effectiveness of the AI algorithms themselves, any implementation barriers or functionality problems for day-to-day users must be proactively addressed. One key informant suggested that it may be more effective to focus first on AI technologies that make care processes more efficient (e.g., using NLP to automate data entry through speech to speed up data capture processes), and then move into more clinical applications.
- **Building buy-in and support among health care providers** will be critical.[4] Health care providers need to have a clear understanding of how and why a technology will be implemented and how it will benefit them.

Costs and Cost-effectiveness

Context and Challenges

In implementing any AI technology in cancer care, it will be critical to have a good understanding of both the costs and cost-effectiveness of the technology. Unfortunately, most of the sources reviewed for this environmental scan did not provide detailed information on the costs or cost-effectiveness of proposed AI technologies. In terms of costs, both hardware and software expenses could be direct costs of implementation. Computers first need to have the required capacity to support the software or processing of the AI algorithm. CADTH suggests that it may be relatively inexpensive to add the required capacity to existing computers (e.g., $1,000 USD for a graphics processing unit to rapidly perform required calculations).[4] Software that runs the AI technology may also need to be purchased, and the costs of this could vary widely. For example, the cost of ColonFlag, a machine learning software to identify people who are at high risk of developing colorectal cancer, is approximately $90,000 CDN for installation and another $70,000 CDN annually for ongoing support,[26] while the costs for a technology like IBM Watson may be in the millions.[184] There may also be costs associated with training staff and changing existing workflows to accommodate the technology.

It will also be important to properly evaluate new AI technologies from a cost-effectiveness perspective. AI technologies may result in both increased and decreased costs. For example, in its analysis of ColonFlag the UK's National Institute for Health and Care Excellence (NICE) notes that the software may increase costs by requiring an increased number of family physicians and gastroenterologists to support more colonoscopies to screen patients identified as being at risk; and may also reduce costs to the system if it improves outcomes and reduces the need for more advanced cancer treatment and support.[26]

Solutions

Understanding the balance between increased costs and cost savings will be critical in determining which AI tools should be widely implemented, and this is an area where more research is required. Appropriate costing studies should include both costs and short- and long-term benefits. Ideally AI developers will collect the necessary information during the development process so that costing studies can be conducted. Proper economic evaluation of these new technologies should include multidisciplinary teams with representation from patients, clinicians, health economists, health system experts, experts in informatics, etc.

Moving AI from Research to Practice

Many key informants made suggestions for what is needed to move all of the AI work that is happening in research into practice in cancer care. Addressing the considerations for implementation discussed above will be critical, along with the following:

- Building collaboration between organizations to develop, test, and implement AI.
- Engaging health care providers, patients and the public in conversations about the challenges and benefits of AI in cancer care.
- Starting with smaller manageable projects that have the potential to be scaled up, and projects/technologies that are low threat, i.e., addressing a small and controlled aspect of care such as radiation planning, or starting to use AI to improve back-end health care processes rather than starting with complex health care decisions.

A few key informants noted that the Partnership could play an important role in bringing stakeholders together to support moving AI more effectively into practice in cancer care. For example, the Partnership could help develop relationships between researchers and clinical care systems or explore how datasets can be established and expanded to support AI.

Conclusion and Next Steps

This report has described the extensive research and product development that is now taking place to integrate AI technologies into cancer care and health care more broadly. AI has the potential to improve cancer care across the continuum and is suited to tasks such as:

- Identifying and predicting cancer without using invasive diagnostic procedures;
- Making cancer diagnosis more accurate and efficient;
- Supporting treatment planning and decision-making to ensure that each patient gets the optimal treatment (i.e., precision medicine);
- Predicting patient symptoms and complications, making management more effective and proactive;
- Increasing efficiency in the cancer care system by supporting providers in treatment planning and administrative tasks (e.g., radiotherapy planning, hands-free and real-time patient chart dictation);
- Gathering data to inform quality improvement; and
- Enhancing and improving patient experience.

While many AI technologies are still some time away from widespread application in real-world practice, it is encouraging that there is so much interesting work happening around the use of AI in cancer care and some innovative approaches being tested that have the potential to transform the way cancer care is delivered. This could help to support new priorities in cancer care that have been identified in the recently updated Canadian Strategy for Cancer Control.

As AI technologies move further towards widespread use, AI developers, governments, and other stakeholders in Canada and around the world are working to address many of the factors that could impact or limit implementation. Some of these considerations include finding solutions to the ethical questions associated with AI decision-making; improving access to and quality of data to inform AI technologies while still ensuring patient privacy and data security; identifying and addressing equity issues that could be inherent in the use of AI; working to ensure and enhance the transparency, validation, and testing of AI technologies; and considering and mitigating potential impacts on the health workforce. Critical next steps in broader implementation of AI in cancer care may include clarifying the regulatory environment and requirements in Canada and providing opportunities for testing AI technologies in real-world clinical workflows with appropriate evaluation and oversight. The evaluation and testing process in particular is critical, as this will help to build buy-in and support for implementation among health care stakeholders such as patients, clinicians, health system leaders and administrators, etc.

AI technologies have exciting potential for improving cancer care. It will take continued collaboration among the stakeholders involved in both AI development and cancer care to realize this potential. In its role as the steward of the Canadian Strategy for Cancer Control, the Partnership will contribute to supporting partners in the process of thoughtful implementation of more widespread use of AI where it can help advance the priorities and actions of the refreshed Strategy.

Appendix A: Key Informants

The following five key informants participated in interviews as part of this environmental scan.

Name	Title	Organization
Dr. Angel Arnaout	Breast Surgical Oncologist	Ottawa Hospital
Dr. David Jaffray	Senior Scientist Executive VP Technology and Innovation Director Research Institute and Core Lead	Princess Margaret Cancer Centre University Health Network Techna Institute for the Advancement of Technology for Health (Techna)
Dr. Alison Paprica	VP, Health Strategy and Partnerships	Vector Institute
Dr. David Armstrong	Associate Professor of Medicine Gastroenterologist	McMaster University Hamilton Health Science
Dr. Stephen Lam	Professor of Medicine Distinguished Scientist, Leon Judah Blackmore Chair in lung cancer research, MDS-Rix endowed Director of Translation Lung Cancer Research	University of British Columbia BC Cancer Research Centre

Appendix B: Interview Guide

KEY INFORMANT INTERVIEW GUIDE

February 14, 2019 – Final

Purpose of the Guide

This document will be used by the interviewer to guide the interview discussion and ensure all areas of interest are covered.

Introduction and Purpose

As the number of people with cancer in Canada grows, along with the costs of cancer care, it is critical to explore evidence-based strategies for delivering care more cost-effectively. Increased use of technology and new innovations that improve decision-making and care processes is an important area that could potentially contribute to improving care. The Partnership is exploring how to best work with its partners to help support the adoption of new innovations and increase the use of digital technology to improve Canadian cancer care. As a first step in this process, to learn more about work in this area, the Partnership's Digital Strategy team has engaged Research Power Inc. to conduct an environmental scan to identify new and existing innovations leveraging AI in cancer care. This environmental scan will help to inform the Partnership's future work to support implementation of new technology.

An important component of this environmental scan is interviews with experts in this area, such as yourself. Information collected through this interview will be compiled into a report, and this report will be reviewed by the Partnership. To help with the analysis of the information, I would like to take notes during the interview. If you wish to do so, you will have an opportunity to review these notes in order to ensure accuracy and validate the information provided. The notes from your interview will be shared with the Partnership, and you may be cited in the report for any factual information. Opinion-based information (e.g., description of challenges or trends in the field) will be reported in aggregate across all key informants and not be linked to a specific individual. All key informants who participate in the interviews will be listed by name in the Appendix of the report, which will be used internally by the Partnership and may be shared publicly.

Do you have any questions?

Do you agree to participate in the interview?

Questions

1. Please briefly describe your role and how it is related to the use of AI in cancer care.
2. What are the major trends in AI and cancer care right now?

   Sub-questions:
   - How might these trends change in the future?
3. From your perspective, what is the most important innovation related to AI and cancer care?

   Sub-questions:
   - Who developed this innovation?
   - How is it being used (research, practice, etc.) and where?
   - Has it been evaluated? If so, what is the evidence of effectiveness?
4. Are you aware of any AI innovations that are being used in day-to-day clinical practice in cancer care? If so, please describe.

   Sub-questions:
   - Who developed these innovations?
   - Where are they being used?
   - Have they been evaluated? If so, what is the evidence of effectiveness?
5. What innovations related to AI and cancer care are you aware of that may not be as well-known by others?

   Sub-questions:
   - Who developed these innovations?
   - How are they being used (research, practice, etc.) and where?
   - Have they been evaluated? If so, what is the evidence of effectiveness?
6. What are the barriers to implementing AI technologies in cancer care in Canada?

   Sub-questions:
   - How could these barriers be addressed?
   - What supports or changes are needed to successfully implement AI technologies?
7. If you were advising a Canadian provincial government or cancer agency on how to implement an AI innovation in cancer care, what top three pieces of advice would you give?

   Sub-questions:
   - How can we encourage buy-in and support for adoption of AI among health care providers (e.g., physicians, nurses)?
8. Are there any key documents/reports or websites related to AI in cancer care that we should review?
9. Are you interested in continuing to work with the Partnership as this work moves forward?
10. Is there anything else you would like to share related to this topic?

Thank you for your thoughtful input and time.

Appendix C: AI Innovations

Throughout this report, specific innovations are highlighted in text boxes as examples of AI innovations that are being used or tested in real-world cancer care settings. Each of these innovations is described in greater detail in this Appendix. Innovations are listed here in the same order they are presented in the report. The innovations include:

ColonFlag

Innovation	ColonFlag[26,27,185]
Description	ColonFlag is a web-based machine learning algorithm that is designed to help identify people aged 40 years or over who are at high risk of having colorectal cancer. The algorithm uses existing datasets containing age, sex and complete blood count (CBC) test results to generate a risk score for a person. People with a high-risk score can be referred for further assessment, potentially before they show any symptoms. ColonFlag will automatically processes new data once it is saved in the healthcare network database.
Location	Unknown
Developer	Medial Early Sign
Cancer Continuum	Early Detection
Disease Site	Colorectal
Use/Testing in Clinical Settings	ColonFlag is a commercially-available product and has been explored for use in the UK's National Health System (NHS)
Results	Four studies have been conducted including 3,485,065 patient records from populations in Israel, the UK and the US. The overall performance of the algorithm was reasonably consistent across the different populations. The reported ORs showed that ColonFlag is potentially useful for identifying people at 10 to 30 times increased risk of colorectal cancer (CRC).
Clinical/ Health System Impacts	ColonFlag could have the effect of moving care upstream (i.e., more patients may be identified as being at risk of CRC and require intervention from their primary care provider). It could also put pressure on the system if more colonoscopies are needed for CRC diagnosis.
Training/ Research/ Development	The model was developed and validated using primary care data collected from a cohort of 606,403 Israelis (of whom 3,135 were diagnosed with CRC) and a case control UK dataset of 5,061 CRC cases and 25 ,613 controls. The model was developed on 80% of the Israeli dataset and validated using the remaining Israeli and UK datasets. Performance was evaluated according to the area under the curve, specificity, and odds ratio at several working points.
Other Information	Costs include an initial installation fee (estimated to be approximately £50,000 ($90,000 CDN) in the UK's analysis) plus an additional £40,000 ($71,000 CDN) annually for clinical and technical support. No studies have evaluated cost-effectiveness. ColonFlag may increase costs by requiring an increased number of family physicians and gastroenterologists to support more colonoscopies to screen patients identified as being at risk; and may also reduce costs to the system if it improves outcomes and reduces the need for more advanced cancer treatment and support.

Doctor AIzimov

Innovation	Doctor AIzimov System for Lung Cancer Diagnosis[74]
Description	Russian researchers have developed an intelligent image classification system, Doctor AIzimov (AI for Artificial Intelligence), that analyzes CT images within 20 seconds and clearly marks areas for radiologist attention. The software uses the chord method to measure and classify images. Open tests of the system are being conducted at the St. Petersburg Clinical Research Center for Specialized Types of Medical Care (Oncological) starting in 2019.
Location	Russia
Developer	St. Petersburg Clinical Research Center for Specialized Types of Medical Care (Oncological)
Cancer Continuum	Diagnosis
Disease Site	Lung
Use/Testing in Clinical Settings	System is able to analyze CT images within 20 seconds and marks areas for radiologist attention. The system will be at first used at the St. Petersburg Clinical Research Center for Specialized Types of Medical Care (Oncological). In the future, the project will be extended and more medical institutions will be involved. There are also plans to adapt the system to analyze other types of imaging (e.g., ultrasound, x-ray) and for other organs in the body.
Results	At the end of 2018, the first tests of this intelligent system were carried out. The system analyzed anonymized CT images of 60 patients at the Oncological Center. According to the radiologists, the tests were successful, as the system has found focal nodules in lungs of small sizes (2 mm). Open tests of the system are being conducted at the St. Petersburg Clinical Research Center for Specialized Types of Medical Care (Oncological) starting in 2019.
Clinical/ Health System Impacts	This innovation is expected to significantly reduce the time needed for analysis and diagnostics by radiologists.
Training/ Research/ Development	The system was trained by analyzing 1000 CT images from LUNA 16 and LIDC datasets. Russian researchers have also collected their own dataset named LIRA - Lung Intelligence Resource Annotated. Currently, the dataset holds CT images of about 250 patients. The scientists are planning to increase the number of images by four times by mid-2019.

ai4gi

Innovation	ai4gi[76,186,187]
Description	Canadian company ai4gi has recently entered into a co-development partnership with Olympus, a major manufacturer of endoscopic devices, to implement ai4gi's AI solution for early colon cancer detection and diagnosis, which uses DL for real-time assessment of endoscopic video images of colorectal polyps. This partnership is the first of its kind in the US and will help to bring this product to market.
Location	Canada
Developer	ai4gi
Cancer Continuum	Diagnosis
Disease Site	Colorectal
Use/Testing in Clinical Settings	Not yet used in clinical settings but Olympus is a major manufacturer of endoscopic devices so the deal will help to bring the product to market.
Results	The AI model works with a confidence mechanism and did not generate sufficient confidence to predict the histology of 19 polyps in the test set, representing 15% of the polyps. For the remaining 106 diminutive polyps, the accuracy of the model was 94% (95% CI 86% to 97%), the sensitivity for identification of adenomas was 98% (95% CI 92% to 100%), specificity was 83% (95% CI 67% to 93%), negative predictive value 97% and positive predictive value 90%.
Training/ Research/ Development	The model was tested on a separate series of 125 videos of consecutively encountered diminutive polyps that were proven to be adenomas or hyperplastic polyps.

Mia

Innovation	Mia[18,82,188,189]
Description	Mia is a deep learning-based breast cancer screening software that can read screening mammograms like an independent reader alongside expert radiologists. Mia's deep learning uses powerful artificial neural networks and high-performance computing to analyze complex medical images with tremendous precision. Clinicians are able to receive results within seconds, directly into their existing workflows, incorporating case-wise recall decision support and lesion localization. It allows for intelligent triaging of imaging studies prior to review, enabling radiologists to prioritize studies based on the algorithm's findings.
Location	London, UK
Developer	Kherion Medical
Cancer Continuum	Diagnosis
Disease Site	Breast
Use/Testing in Clinical Settings	Currently being tested as part of the Wave 2 Test Beds in the UK's National Health Service (NHS) in partnership with East Midlands Radiology Consortium (EMRAD). The Test Beds program brings NHS organizations and industry partners together to test combinations of digital technologies with pathway redesign in real-world settings.
Results	The company commissioned an independent multi-centre clinical study to evaluate their software's performance. This retrospective study demonstrated that the software surpassed recognized standards for single radiologist reporting accuracy. The firm found Mia beat the average performance of a human radiologist when tested against 3,500 scans. Kheiron is already launching further multi-phase clinical evaluations across the UK, Europe and US to further assess and improve performance, and the potential impact on breast screening outcomes.
Clinical/ Health System Impacts	Potential to reduce from two to one the number of radiologists required to review breast imaging.
Training/ Research/ Development	Kheiron's technology has already been trained on about 500,000 scans from hospitals in Hungary.
Other Information	- The software has received CE marking, which means that it meets EU safety, health or environmental requirements, complies with EU legislation, and is able to be used in the UK and across Europe. - Application for FDA approval of Kheiron's software is underway (October 2018).

MoleMapper

Innovation	MoleMapper[88,89,190,191]
Description	MoleMapper is a cellphone app designed to help individuals map, measure, and monitor moles over time. It does not currently use AI technology. However, the app's optional data collection function utilizes Apple's ResearchKit platform and gives users the option to contribute to melanoma research by sharing anonymous photos of how their potential trouble spots evolve over time. The research partners involved in MoleMapper hope to eventually use AI techniques to detect suspicious lesions in MoleMapper images (i.e., give individuals the ability to self-diagnose).
Location	United States
Developer	Sage Bionetworks and Oregon Health & Science University
Cancer Continuum	Diagnosis
Disease Site	Melanoma
Use/Testing in Clinical Settings	MoleMapper is now available to people in the US but does not currently include any AI or diagnosis capabilities.
Results	Though the app itself does not yet include AI, research has shown that AI can perform as well or better than dermatologists to diagnose melanoma from images, and this may be able to be applied in a mobile app in future.
Clinical/ Health System Impacts	No current impacts, but if the technology eventually enables self-diagnosis this could have a significant impact on access to care and required resources in the system for patients with possible melanoma.
Training/ Research/ Development	MoleMapper was developed by a Ph.D. cancer biologist, Dan Webster, to help his wife (who is at high risk of melanoma) monitor her moles between visits with her dermatologist.

Watson for Oncology

Innovation	Watson for Oncology[107,192,193]
Description	Watson for Oncology combines leading oncologists' deep expertise in cancer care with the speed of IBM Watson to help clinicians as they consider individualized cancer treatments for their patients. Watson for Oncology is a solution that is fueled by information from relevant guidelines, best practices, and medical journals and textbooks. The solution assesses information from a patient's medical record, evaluates medical evidence, and displays potential treatment options ranked by level of confidence, always providing supporting evidence. The oncologist can then apply their own expertise to identify the most appropriate treatment options. Staff at Memorial Sloan Kettering worked with IBM to train the software.
Location	United States
Developer	IBM
Cancer Continuum	Treatment
Disease Site	Not specific to one disease site
Use/Testing in Clinical Settings	Watson for Oncology was trained by staff at Memorial Sloan Kettering. IBM reported in an article that more than 230 hospitals are using Watson oncology tools and the number of patients reached is over 100,000 as of the end of 2018.
Results	A study assessed concordance between Watson for Oncology (WFO) breast cancer treatment recommendations and recommendations from a multidisciplinary tumor board (MMDT) at Manipal, a quaternary health care centre in India. This study found that about 73% of the MMDT treatment recommendations were also recommended by WFO, but noted that with respect to metastatic disease and hormone positive HER2 negative disease, improvement in recommendations from WFO was needed.

Watson for Clinical Trial Matching

Innovation	Watson for Clinical Trial Matching[112,113,194]
Description	Watson for Clinical Trial Matching enables clinicians to more easily and quickly find a list of clinical trials for an eligible patient. Similarly, it enhances the ability of clinical trial coordinators to find patients that are potentially eligible for any of the site's trials. The improvement in screening efficiency and more effective patient recruitment can help increase clinical trial enrollment and opportunities to offer patients the option of a clinical trial for treatment.
Location	United States
Developer	IBM
Cancer Continuum	Treatment
Disease Site	Not specific to one disease site
Use/Testing in Clinical Settings	Watson for Clinical Trials Matching worked with the Mayo Clinic to determine optimal workflows and screening processes for clinical trial matching, and then began implementing the system in 2016 with a team of screening clinical research coordinators in its ambulatory practice for patients with breast cancer.
Results	In the 11 months after implementation, there was on average an 80 percent increase in enrollment to Mayo's systemic therapy clinical trials for breast cancer. The time to screen an individual patient for clinical trial matches also fell when compared with traditional manual methods.
Clinical/ Health System Impacts	Potential to improve efficiency in clinical trial matching significantly to save clinician time. May also contribute to improved patient outcomes if more patients are able to access clinical trials.

AutoPlanning

Innovation	AutoPlanning[115,116,195,196]
Description	Researchers at University Health Network in Toronto have developed an automated planning tool for radiotherapy using AI. AutoPlanning technology makes the complex radiation therapy planning process much quicker and more efficient and generates highly-personalized plans for each patient, correctly balancing the need for directing sufficient radiation at tumours while avoiding healthy organs and tissues. The AutoPlanning technology is now being used in clinical practice at UHN, and the technology has also been licensed to RaySearch Laboratories to be used in RaySearch's RayStation treatment planning system, currently used in over 2,600 clinics in more than 65 countries.
Location	Canada
Developer	University Health Network
Cancer Continuum	Treatment
Disease Site	Not specific to one disease site
Use/Testing in Clinical Settings	In 2018, AutoPlanning was used to treat the first patient, someone with prostate cancer, after meeting all the appropriate protocol and quality assurance metrics. This may be the first time anywhere that a patient was actually treated with a radiation plan based only on AI technology. The clinical team continued with large-scale clinical roll out of the AI technology for planning radiation treatments in 2018 and 2019. The technology has also been licensed to RaySearch Laboratories to be used in RaySearch's RayStation treatment planning system, currently used in over 2,600 clinics in more than 65 countries.
Results	Published preliminary testing of the technology showed that automated plans achieved an average of 0.6% higher dose for target coverage evaluation criteria, and 2.4% lower dose at the organs at risk criteria levels evaluated compared with clinical plans. The technology can generate complete treatment plans in 12-13 min without user interaction.
Clinical/ Health System Impacts	This innovation will significantly reduce the time required by clinicians to develop radiotherapy plans, from days to minutes.
Training/ Research/ Development	The preliminary research compared four versions of the dose prediction pipeline using a database of 54 training and 12 independent testing patients by evaluating 14 clinical dose evaluation criteria.

Precise MD

Innovation	Precise MD[119,120]
Description	Precise MD is a pathology platform that uses AI to translate data into clinical knowledge. Precise MD developed a new approach for assessing risk in prostate cancer patients that predicted significant disease progression with a greater degree of accuracy compared with models that incorporated only clinical features such as the traditional Gleason score, or a Prostate-Specific Antigen (PSA) test. Men identified as high risk by the Precise MD test may be appropriate candidates for additional monitoring and treatments, including chemotherapy and radiation.
Location	United States
Developer	Department of Pathology and Icahn School of Medicine at Mount Sinai Hospital
Cancer Continuum	Treatment
Disease Site	Prostate
Use/Testing in Clinical Settings	Precise MD is currently in use in the Department of Pathology at Mount Sinai Hospital in New York.
Results	Initial testing of the software was conducted in 2016 and 2017. The Precise MD test reclassified 58 percent of intermediate risk patients as low risk and 42% as high risk for significant disease progression.

PATHFx

Innovation	PATHFx[128,129,197]
Description	PATHFx is an AI adaptive treatment support tool for patients with metastatic bone disease. It uses a survival prognosis to aid the orthopaedic surgeon's decision-making regarding whether to offer surgery to a patient with a pathologic fracture, and which implants are suitable. It also helps avoid under-treatment and over-treatment. PATHFx is linked to the International Bone Metastasis Registry in order to continually improve and update its prognoses as new cancer treatments are introduced.
Location	Sweden
Developer	Karolinska University Hospital
Cancer Continuum	Complications
Disease Site	Bone metastases
Use/Testing in Clinical Settings	PATHFx is in clinical use at the orthopaedic clinic at Karolinska University Hospital in Sweden.
Results	PATHFx is thoroughly externally validated in the Nordic countries, Italy and Japan, and has proven to provide reliable survival prognoses.
Training/ Research/ Development	The model has been extensively validated in several published articles (see list at https://ki.se/en/mmk/new-digital-decision-support-gives-gravely-ill-cancer-patients-the-right-fracture-treatment).

Docbot

Innovation	Docbot[144,145]
Description	Docbot is an integrated AI tool that applies AI to polyp detection in endoscopy/colonoscopy but also integrates with EHR systems to auto-document procedures and associated quality measures.
Location	United States
Developer	Doc Bot
Cancer Continuum	Process Efficiency
Disease Site	Not specific to one disease site
Use/Testing in Clinical Settings	No data is available on use, but Docbot was aiming to commercialize a fully functional system by September 2018.
Clinical/ Health System Impacts	The Docbot system will help to reduce specialist time in inputting patient data manually, resulting in a quicker turn around on reporting and any required follow up.
Training/ Research/ Development	Prior to commercialization, public beta was conducted with physician groups from several other academic medical centers, ambulatory surgery centers and acute care hospitals.

Powerlook Density Assessment

Innovation	Powerlook Density Assessment[198]
Description	Powerlook Density Assessment is an automated breast density solution that is designed to standardize the assessment of breast density in 2D and 3D mammography. PowerLook Density Assessment assists radiologists in evaluating and scoring breast density to identify patients who may need supplemental screening or be at higher risk of developing breast cancer. This solution uses an appearance-based approach to assess dense tissue, to deliver automated, rapid and reproducible assessments of breast structure, texture, and fibroglandular dispersion. This innovative technique calibrates the patient's breast density to the appropriate density category corresponding to BI-RADS® reporting system.
Location	United States
Developer	iCAD
Cancer Continuum	Early Detection
Disease Site	Breast
Use/Testing in Clinical Settings	No data on use in clinical practice, but this software has been approved for use by both the US Food and Drug Administration (FDA) and Health Canada.
Results	In a clinical study, PowerLook Density Assessment was shown to have statistical agreement with a panel of 10 expert radiologists specializing in breast imaging when assessing the percentage of breast density of over 500 mammography cases. The radiologists' results were used to align PowerLook Density Assessment's percentage of breast density to the BI-RADS® breast density assessment categories
Clinical/ Health System Impacts	Mammography is considered to be the gold standard in breast cancer screening. However, mammography has been proven to be less effective in women with dense breast tissue. Patients may experience reduced sensitivity of digital mammography based on their dense breast tissue. PowerLook Density Assessment adds a critical dimension to the analysis of dense breast tissue. It aligns with the BI-RADS® standard of identifying dense tissue in the breast that could be masking cancer, potentially making the identification/early detection and diagnosis of breast cancer easier in women with dense breast tissue.

Appendix D: Literature Review Tables

The tables included in this section provide more detailed information on the literature summarized in the report. The included tables are listed below:

Table 1: AI Technologies to Improve Lung Cancer Diagnosis

Area	Approach	Findings
Nodule Detection in CT	Fuzzy Clustering	• Able to detect regions that may be nodules in CT studies.[199] • Effectively distinguish between adenocarcinoma, large cell carcinoma, small cell carcinoma, and squamous cell carcinoma.[200] • Detects lung lesions in CT images using the fuzzy local information cluster means automatic segmentation algorithm and back propagation network classification.[201] • An effective fuzzy auto-seed cluster means morphological algorithm produced a good sensitivity, specificity and accuracy of 100%, 93% and 94%, respectively.[202]
	CNN	• A CNN was used to reduce the rate of false positives in lung nodule detection by 93%.[203] • A multigroup patch-based learning system is efficient to improve the performance of lung nodule detection and greatly reduce the false positives (sensitivity of 80.06% with 4.7 false positives per scan).[204] • A system using a deep 3D residual CNN with an additional spatial pooling and cropping (SPC) layer improves the accuracy of identifying malignant lung nodules.[205] • A CADx system using a deep CNN had an accuracy of up to 68%.[206] • A CNN had improved accuracy (89.9%) in detecting lung cancer nodules compared to a CAD system (84.8%).[207] • A single 3D CNN with dense connections, trained in an end-to-end manner outperforms the current literature (89.7%).[208]
	SVM	• A pulmonary nodules detection algorithm based on SVM and CT image feature-level fusion with rough sets shows improvement in effectiveness.[209]
	Genetic Algorithms	• Accuracy of determining malignant vs. benign tumours as high as 92.52%.[210]
	General Deep Learning	• A deep learning system accurately (91.2%) detected lung cancer nodules.[211] • A deep learning algorithm used data produced through Coherent anti-Stokes Raman scattering (CARS) images achieved 89.2% accuracy in classifying normal, small-cell carcinoma, adenocarcinoma, and squamous cell carcinoma lung images.[212]

Area	Approach	Findings
Nodule Detection in Radiography	CADe	• A currently available CAD system marked 71% of radiologist-identified lung nodules in a large consecutive series of CXRs, and 41% of "false" marks were caused by pathologic findings.[213]
	PNN	• A PNN provides good results and can detect low-contrast nodules in CXR. The simpler approach of a PNN also lowers the computational burden of the trained network.[214]
Using Biomarkers for Detection and Diagnosis	Particle-swarm Optimization-Enhanced Algorithms	• Used to select biomarker panels for tumour-educated blood platelets from RNA-sequencing libraries to accurately detect early- and late-stage non-small-cell lung cancer.[215]
	CNN	• Levels of three-gene promoter methylation were effective in diagnosing patients with lung cancer.[216] • A CNN system was able to automatically classify adenocarcinoma (LUAD), squamous cell carcinoma (LUSC), and normal lung tissue with an accuracy rate of 97%. The system was trained to detect the presence of six of the most common genetic mutations in lung cancer adenocarcinoma (STK11, EGFR, FAT1, SETBP1, KRAS and TP53).[217]
	Logic Learning Machine (LLM)	• A logic learning machine technique used three tumour markers (CEA, CYFRA 21-1 and SMRP) to accurately (77.5%) assess the differential diagnosis of pleural mesothelioma.[10]
Combining Imaging and Biomarkers	SVM	• Computer-aided diagnosis combines CT imaging features and serum biomarkers to improve diagnosis performance in classifying between malignant and benign pulmonary nodules.[218]
Diagnosis Using Breath Test	SVM	• A breath test for detecting lung cancer using a chemical sensor array and support vector machine techniques was found to have high accuracy.[219] • SVM and a breath sensor device was able to correctly differentiate individuals with cancer (87.3%).[220]

Table 2: AI Technologies to Improve Colorectal Cancer Diagnosis

Area	Approach	Findings
Polyp Detection and Classification in Endoscopies/ Colonoscopies	CNN, DCNN	• A deep convolution neural network (DCNN) was tested on 125 videos of consecutively encountered diminutive polyps and achieved a 94% accuracy of classification for 106 of the 125 videos. For these 106 polyp videos, the system was able to detect adenomas with a sensitivity of 98% and a specificity of 83%.[78] • With CNN learning, cT1b colon cancer diagnosis is possible (sensitivity, specificity and accuracy were 67.5, 89.0 and 81.2% respectively and AUC was 0.871) without relying on the skill and experience of endoscopists.[221] • Joint detection and classification of a proposed Spatially Constrained Convolutional NN (nucleus detection) and a novel Neighboring Ensemble Predictor (NEP) (classification) produced the highest average F1 score as compared to other recently published approaches.[222] • A computer-assisted image analysis using CNNs improved polyp detection with cross-validation accuracy of 96.4% and an area under the receiver operating characteristic curve of 0.991 (8,641 colonoscopy images containing 4,088 unique polyps).[223]
	CADx	• A novel CADx system for endocytoscopic imaging of colorectal lesions had a sensitivity of 92.0% and an accuracy of 89.2%; these were comparable to those achieved by expert endoscopists and significantly higher than those achieved by trainee endoscopists. This tool provides fully automated instant classification of colorectal polyps with excellent sensitivity, accuracy, and objectivity and can be a powerful tool for facilitating decision making during routine colonoscopy.[224] • A CADx system based on linked colour imaging (to predict the histological results of polyps by analyzing the colours of the lesions) identified adenomatous or non-adenomatous polyps in the test set with an accuracy of 78.4%. The accuracy of the CADx system was comparable to that of the expert endoscopists.[225] • A CADx system that uses ultra-high magnification endocytoscopy diagnosed invasive colorectal cancer with an accuracy of 94.1%.[226]
Diagnosis with Pathology	SVM	• A novel colon cancer diagnostic system initially classified colon biopsy images into normal and malignant classes, and then automatically determined the grades of colon cancer for malignant images. Radial basis function kernel of SVM were used as classifiers. Compared with previous techniques, the proposed system has demonstrated better cancer detection (classification accuracy=95.40%) and grading (classification accuracy=93.47%) capability. Therefore, the proposed CCD system can provide a reliable second opinion to the histopathologists.[227] • A hybrid feature spacebased colon classification technique used hybrid features for differentiating normal and malignant colon samples. Various kernels of SVM were employed as classifiers, and their performance analyzed on 174 colon biopsy images. The proposed geometric features achieved an accuracy of 92.62%, and the proposed technique achieved 98.07% testing and 99.18% training accuracy.[228]
Using Biomarkers for Detection and Diagnosis	SVM and NN	• By inspecting serum tumour marker levels in colorectal cancer patients and healthy subjects, early diagnosis models for colorectal cancer were built using three ML algorithms (logistic regression, SVM and Back-propagation NN). The models showed high diagnostic value and can help obtain evidence for the early diagnosis of colorectal cancer.[229]

Table 3: AI Technologies to Improve Prostate Cancer Diagnosis

Area	Approach	Findings
Diagnosis with MRI	NNs	• An automated method based on multimodal CNNs alleviates requirements for interpretation of radiologists while improving diagnostic accuracy. It achieved 89.85% sensitivity and 95.83% specificity for distinguishing cancer from noncancerous tissues and 100% sensitivity and 76.92% specificity for distinguishing indolent prostate cancer from clinically significant prostate cancer, which is superior to previous state-of-the-art method.[230] • A study assessing the accuracy of an ANN model in detection found that automatic analysis of prostate magnetic resonance spectroscopic imaging (MRSI) using this model is feasible, and application of anatomical segmentation of MRI as an additional input to ANN improves detection.[231] • High level feature representation with deep NNs for detection achieved better performance than conventional handcrafted features and is effective in refining cancer detection.[232]
	CADx	• A texton-based CAD system that focuses on the peripheral zone (where 75% of prostate cancers start) bypasses typical feature extraction which can be time consuming and inefficient. Accuracy rates were between 86.9% and 92%, comparable to state of the art technologies in the literature.[233] • A CAD technology using a two-stage approach performed well and was not significantly different from the radiologist, suggesting that it could be used as an independent second reader and has potential in a first-reader setting.[234] • A CAD diagnostic technology using diffusion-weighted MRI and a trained deep learning network achieved 92.3% accuracy, 83.3% sensitivity, and 100% specificity and could be used as a reliable non-invasive diagnostic tool.[235]
	Multiple ML techniques	• ML techniques such as SVM and others were used to detect prostate cancer and found that the highest accuracy rate of 99.71% was found by using a combination of features.[236]
Diagnosis with Ultrasound	NNs and tissue mimicking simulations	• Temporal Enhanced Ultrasound (TeUS) is proposed as a new paradigm for tissue characterization based on a sequence of ultrasound data combining deep NNs and tissue mimicking simulations. This can be used for detection of prostate cancer.[237]
Diagnosis with Pathology	SVM	• SVM and random forest (RF) classifiers were used to analyze digital pathology images and classify the tissue as stroma, benign, or prostate cancer. This approach may be helpful in clinical studies where the quantification of the tumour content is necessary to understand the course of the disease.[238]

Table 4: AI Technologies to Improve Skin Cancer Diagnosis

Area	Approach	Findings
Lesion Classification with Visual Exam/ Dermoscopy	CNN	• In a study of more than 120,000 images of malignant melanoma and benign moles, CNN was compared to the performance of 21 board-certified dermatologists in classification of skin cancer and found to have missed fewer melanomas and misdiagnosed benign moles less often as malignant than the group of dermatologists.[90] • A comparative cross-sectional reader study using a 100-image test-set compared a CNN's ability to review dermoscopic images and make an appropriate diagnosis to an international group of 58 dermatologists, including 30 experts. Most dermatologists were outperformed by the CNN.[97] • Two deep learning methods (fully convolutional residual networks [FCRN] and CNN) were used to address three main tasks in the area of skin lesion image processing (lesion segmentation, lesion dermoscopic feature extraction and lesion classification). Results show the promising accuracies.[91] • Findings from a study to assess melanoma detection by analysis of clinical images using CNN revealed that the proposed method is superior in terms of diagnostic accuracy in comparison with the state-of-the-art methods.[92] • A CNN for diagnosis was applied to dermoscopy images of acral melanoma and benign nevi on the hands and feet. The sensitivity and specificity of the CNN was 83.51% and 80.23%, a better performance than the evaluation of non-experts and similar to the performance of the dermatologists (81.08%, 81.64%).[93]
	SVM	• SVMs were used to classify melanoma in the early stage of development. The algorithm was tested on 200 images and achieved sensitivity of 90% and specificity of 96%. The results indicate that the proposed approach captured most of the malignant cases and could provide reliable information for effective skin mole examination.[94]
	CNN and SVM	• NN and SVM algorithms were tested and validated with nearly 992 images (malignant and benign lesions) and showed a high classification accuracy of 93%, which can assist dermatologists to confirm the diagnosis and to avoid excisional biopsies.[95]
	Fuzzy Logic Image Analysis	• Fuzzy logic image analysis techniques were used to analyze three shades of blue in dermoscopic images for melanoma detection. A logistic regression model provided up to 82.7% accuracy for melanoma discrimination. This fuzzy logic technique applied to multiple shades of blue could therefore assist in melanoma detection.[96]

Table 5: AI Technologies to Support Radiotherapy Planning

Area	Cancer Type	Findings
Image Segmentation	Breast Cancer	• A deep dilated residual network (DD-ResNet) was used for fast and consistent auto-segmentation of the CTV for breast cancer (BC) radiotherapy. Mean segmentation time was 4s to 15s per patient and the proposed method segmented the CTV accurately with acceptable time consumption.[239]
	Cervical Cancer	• A machine learning approach using voxel classification provided an automatic method for delineating locally advanced cervical cancers, and combining all relevant MR image series resulted in high sensitivity and specificity.[240]
	Colorectal Cancer	• A deep dilated convolutional neural network (DDCNN)-based method was developed for fast and consistent auto-segmentation of the CTV and organs at risk in the planning CT for rectal cancer. Findings show that the method can be used to segment the CTV and organs at risk (OARs) accurately and efficiently, and potentially improve the consistency of contouring and streamline radiotherapy workflows.[241] • A deep learning algorithm was used to effectively segment rectal tumours based on MRI T2 images with no difference between automated and manual segmentation.[242]
	Head and Neck Cancer	• A NN segmentation method was used to conduct fully automatic multi-organ segmentation on volumetric CT scans for head and neck cancer radiotherapy. The method showed competitive performance and took shorter time to segment multiple organs compared to state of the art method.[243] • A kernel SVM was used to effectively automatically segment parotid MRIs to monitor radiation-induced parotid gland changes in patients after head and neck radiation therapy.[244] • A CNN was used to accurately segment OARs in head and neck cancer CT images, with performance comparable to commercial software.[245]
	Lung Cancer	• ML techniques (ANN, fuzzy clustering, SVM) were used to delineate gross tumour volume regions for stereotactic body radiation therapy with accuracies between 73 and 79%.[246]
	Prostate Cancer	• NNs were used to achieve real-time image processing for image-guided radiotherapy.[247]
Dose Optimization and Knowledge-based Treatment Planning	Head and Neck Cancer	• Knowledge-based automated planning successfully developed high-quality radiotherapy plans without human intervention, with performance comparable to clinical plans.[248] • A vector model reduced planning time by applying optimization parameters from retrieved reference cases to stereotactic radiotherapy planning for brain metastasis.[249] • A dose prediction pipeline using voxel-based dose prediction developed fully automated radiotherapy treatment plans for head and neck cancer. The automated plans were comparable to clinical plans and were completed in only 12-13 minutes.[195] • A KBRT technique (RapidPlan) is used to predict achievable dose-volume histograms (DVHs) for new patients and uses those models for setting optimization objectives that are comparable to clinical practice.[250]
	Pancreatic Cancer	• An artificial neural network dose model showed excellent overall agreement with clinical dose distributions for pancreatic cancer. Accuracy was substantially improved when each physician's treatment approach was taken into account by training their own dedicated models.[251]

Area	Cancer Type	Findings
Dose Optimization and Knowledge-based Treatment Planning (cont'd)	Prostate Cancer	• KBRT plans for prostate cancer were comparable to those developed by experts and achieved a lower bladder dose than those developed by experts.[252] • A vector model reduced planning time by applying optimization parameters from retrieved reference cases to prostate cancer radiotherapy planning without compromising the plan quality.[253] • Models using k-nearest neighbor and logistic regression were able to produce clinical quality treatment plans.[254] • A machine learning algorithm was used to automatically generate high-quality, prostate low-dose-rate (LDR) brachytherapy treatment plans with an average planning time of less than one minute (compared to 18 minutes for the expert planner).[255] • A CNN was used for automated prediction of dosimetric eligibility of patients with prostate cancer undergoing intensity-modulated radiation therapy with prediction accuracies of 56.7% (with a CT image dataset) and 70.0% (with a structure label dataset).[256]
	Multiple	• An ANN was used to generate beam orientations in stereotactic radiosurgery (SRS). ANN models were able to determine beam orientation in SRS. ANN-generated treatment plans were comparable to human-designed plans.[257]
Quality Assurance	Head and Neck Cancer	• Unsupervised machine learning was used to develop a predictive network to identify patients with head and neck cancer that would benefit from a re-planning of their image-guided radiation therapy to correct anatomical variations.[258]
	Prostate Cancer	• A classifier-based expert system was developed to compare delivered and planned radiation therapy in prostate cancer patients and identify which patients would benefit from an individualized adaptive strategy.[259]
Decision Support	Multiple	• An AI-based clinical decision support system connects patients with early-stage lung and postoperative oropharyngeal cancers to past discrete treatment plans in radiation oncology and allows clinicians to use past decisions to help inform current assessments.[260]
Motion Prediction	Lung and Breast Cancer	• NNs were used to predict lung tumour motion during respiration to help improve accuracy of radiation therapy with fast real-time retraining. For a one-second prediction horizon, the proposed techniques achieved accuracy less than one millimeter of 3D mean absolute error in one hundred seconds of total treatment time.[261] • A neuro-fuzzy inference system was used to track moving tumours in external radiotherapy for lung and breast cancers and reduce tumour tracking errors more significantly, as compared with ground truth database.[262]

Table 6: AI Technologies to Support Personalized Medicine

Area	Cancer Type	Findings
Understanding and Predicting Disease Progression and Survival	Bladder Cancer	• A regularized extreme learning machine was able to predict mortality after radical cystectomy for bladder cancer with 80% accuracy.[263] • A ML algorithm was used with gene expression profiling to predict recurrence of nonmuscle invasive urothelial carcinoma of the bladder.[264]
	Brain Cancer	• An AI classifier was able to predict neuroblastoma patients' outcome with a very low error rate.[265] • A SVM algorithm was able to predict survival time outcomes for high grade gliomas with 75% accuracy.[266] • SVM classifiers were used to predict overall survival for glioblastoma multiforme patients with 98.7% accuracy.[267]
	Breast Cancer	• An ANN was used to predict 5-year mortality of breast cancer patients who underwent surgery and found that the 5-year postoperative mortality of breast cancer patients was significantly associated with age, Charlson comorbidity index (CCI), chemotherapy, radiotherapy, hormone therapy, and breast cancer surgery volumes of hospital and surgeon.[268] • A study of ML models in breast cancer survival prediction found that the Trees Random Forest model (TRF), a rule-based classification model, had the highest level of accuracy (96%) in predicting survival.[269] • Unsupervised ML was used to improve understanding and help identify patterns associated with the survivability of breast cancer patients. The results of the analysis can be used to segment the historical patient data into clusters or subsets, which share common variable values and survivability.[270]
	Cervical Cancer	• A probabilistic neural network (PNN) model predicted overall survival in cervical cancer patients treated with radical hysterectomy with an accuracy of 89.2%.[271]
	Colorectal Cancer	• SVM was used to accurately classify colon cancer patients into groups with relapse and no relapse.[272] • A ML model was used to predict clinically relevant outcomes including disease free survival, survival, radio-chemotherapy response and relapse for colorectal cancer patients.[273] • An ANN predicted 10-year survival in stage II A colon cancer patients after radical surgery effectively divided patients into high, moderate and low risk sub-groups.[123]
	Gastric Cancer	• Artificial and Bayesian NNs were used to predict the survival of gastric cancer patients. The age at diagnosis of gastric cancer was most important for predicting survival, followed by tumour grade, morphology, gender, smoking history, opium consumption, receiving chemotherapy, presence of metastasis, tumour stage, receiving radiotherapy, and being resident in a village.[274] • ML methods used radiomics features analysis to predict overall survival for non-small cell lung cancer.[275]
	Head and Neck Cancer	• A radiomics study identified optimal machine-learning methods for the radiomics-based prediction of local failure and distant failure in advanced nasopharyngeal carcinoma.[276]
	Leukemia	• SVM was used to assess genomic alternations in AML and identified 81 biomarkers that could be used as prognostic and predictive markers for disease progression.[277]
	Liver Cancer	• ANNs were used to predict disease-free progression for hepatocellular carcinoma patients after radiofrequency ablation with 67.9% accuracy based on 15 clinical features.[278]

Area	Cancer Type	Findings
Understanding and Predicting Disease Progression and Survival (cont'd)	Lung Cancer	• Gene co-expression network analysis was able to predict lung cancer patients' prognosis independent of other clinicopathological features.[279] • A prediction model for early death in non-small cell lung cancer patients following curative-intent chemoradiotherapy based on performance status, age, gender, T and N stage, total tumour volume, total tumour dose, and chemotherapy timing was more effective than previous prediction models.[280]
	Ovarian Cancer	• An ANN model was capable of predicting overall survival with high accuracy (93%) as well as predict the outcome of surgery for patients with ovarian cancer.[281] • A versatile data fusion (integration) framework was used to identify three ovarian cancer patient subgroups that have significant differences in survival outcomes, as well as potential new driver genes for each group and potential candidate drugs.[282]
	Pancreatic Cancer	• ANNs were used to accurately predict the 7-month survival of pancreatic adenocarcinoma patients, both with and without resection, at a 91% sensitivity and 38% specificity.[124]
	Prostate Cancer	• SVM classification was use to predict recurrence in prostate cancer patients with an accuracy of 95.9%.[283]
	Sarcoma	• Based on scientific literature and clinical expertise, clinicopathological data were analyzed using both a supervised and an unsupervised learning classification method to predict the prognosis for patients with retroperitoneal sarcoma.[284] • A deep-learning-based prediction algorithm was able to predict survival for synovial sarcoma patients.[285] • A machine learning-based prognostic model combined known prognostic factors with treatment- and response-related information and showed high accuracy for individualized risk assessment in patients with soft tissue sarcoma.[122]
	Testicular Cancer	• Deep learning was used to detect tumour-infiltrating lymphocytes in testicular germ cell tumours from histology images. These lymphocytes could be used as a prognostic marker for disease relapse.[286]
	Multiple types	• Machine learning was applied to electronic administrative records from a cancer database to predict survival outcomes for a range of cancers.[287]
Predicting Treatment Outcomes	Brain Cancer	• A CNN-based ensemble radiomics model accurately predicted the response of brain metastases to stereotactic radiosurgery from CT images.[288] • A reinforced learning model was able to generate precision treatment plans for glioblastoma treatments that use a combination of the drugs temozolomide and procarbazine, lomustine, and vincristine, administered over weeks or months. The treatment plans were based on differences in tumour size, medical histories, genetic profiles, and biomarkers.[289]
	Breast Cancer	• An ANN was used to analyze 39 MR image features to predict tumour response to chemotherapy in breast cancer.[290] • CNN was used to predict post neoadjuvant axillary response in breast cancer patients with an accuracy of 83%.[291]
	Esophageal Cancer	• CNNs were used to predicting response to neoadjuvant chemotherapy with PET imaging, with a sensitivity of 80.7% in determining non-responders.[292]
	Head and Neck Cancer	• A fuzzy classification method was used to predict both parotid shrinkage and xerostomia and their influence on outcomes is revealed.[293]
	Leukemia	• The Beat AML (acute myeloid leukemia) project is using AI technology to test the response of patients' leukemia cells to different targeted drugs and combinations of drugs in hopes of determining which medication will be most effective in inhibiting mutations and genetic drivers of the disease.[294]

Area	Cancer Type	Findings
Predicting Treatment Outcomes (cont'd)	Liver Cancer	• A ML algorithm used MRI and clinical patient data to predict treatment response to intra-arterial therapies for hepatocellular carcinoma with an overall accuracy of 78%.[295]
	Lung Cancer	• ANN was used to predict response to adjuvant chemotherapy (ACT) after surgery for patients with non-small cell lung cancer with an accuracy of 65.71%.[296] • SVM was used to predict local tumour control after stereotactic body radiation therapy for early-stage non-small cell lung cancer.[297]
	Ovarian Cancer	• SVM was used to predict drug responses from genetic profiles for ovarian cancer patients.[298] • SVM was used to predict chemotherapy response, progression free survival and overall survival for high-grade serous ovarian carcinoma. This classifier may provide a potential way to predict chemotherapy resistance.[299]
	Multiple types	• Combined genomics data and ML to accurately predict the performance of a wide range of therapies on cancer cell lines.[121] • A ML model was used to identify gene isoforms (different forms of genes) that can be used to predict which cancer treatments will be effective in a given patient.[300,301] • A new ML technique (multimodal deep belief network) was used with genetic data to identify disease sub-types and predict outcomes.[302] • A sub-network based random forest classifier was used to predict the impact of adjuvant chemotherapy on survival for patients with breast and lung cancer.[303]
Identify Biomarkers that Determine Outcomes or Treatment	Brain Cancer	• CNN has been used to classify glioma patients according to chromosome arms 1p/19q status based on imaging features rather than surgical biopsy. This status can be used to predict the chemosensitivity and prognosis of these patients and determine course of treatment.[43,44] • Convolutional recurrent neural network architecture (CRNN) was used to predict the methylation status of the promoter or the enhancer regions of the O6-methylguanine methyltransferase gene, which may impact the efficacy and sensitivity of temozolomide, and hence may affect overall patient survival.[304]
	Leukemia	• ML was used to identify molecular markers for targeted treatment of acute myeloid leukemia (AML).[305]
	Lung Cancer	• Multi-level residual CNNs were used to detect epithelial growth factor receptor (EGFR) mutations on CT images of patients with lung adenocarcinoma. EGFR status impacts how patients are expected to respond to treatment.[306]

Table 7: AI Technologies to Predict Complications of Cancer Care

Area	Approach	Findings
Understanding Symptoms	Network Analysis	• Network analysis was used to analyze the relationships among the occurrence, severity and distress of 38 common symptoms experienced by oncology patients undergoing chemotherapy. For example, this research could identify which patients are at higher risk to experience psychological symptoms such as depression and anxiety.[126,127]
Bone Metastases	SVM	• ML models using SVM or decision tree techniques were found to be the most effective in predicting skeletal-related events (SREs) in cancer patients with bone metastases. Being able to predict patients who may experience SREs could allow for physicians to select the most appropriate analgesic therapies for these patients, with a view to preventing SREs.[130]
Chemo and Radiation Therapy Complications	RF	• Severe acute mucositis commonly results from head and neck (chemo)radiotherapy. A predictive model of mucositis could guide clinical decision-making and inform treatment planning. A random forest model had the best performance in identifying potential causes of mucositis and finds that reducing the volumes of oral cavity receiving intermediate and high doses may reduce mucositis incidence.[131] • A ML algorithm using pre-conditioned RF was able to develop a predictive and clinically useful risk stratification model for predicting radiotherapy complications in patients with prostate cancer. The model also identified important underlying biological processes in the radiation damage and tissue repair process.[132]
	CNN	• A CNN model was used to better understand and predict rectum toxicity in cervical cancer radiotherapy.[133]
Venous Thromboembolism	SVM	• ML models using SVM and random optimization were tested to identify risk predictors for venous thromboembolism (VTE) for cancer outpatients.[134]
Discharge and Readmission	ANN	• An ANN was developed to predict delayed discharge and readmission in enhanced recovery following laparoscopic colorectal cancer surgery and found that factors predicting 30-day readmission included overall compliance with the Enhanced Recover After Surgery program pathway and receiving neoadjuvant treatment for rectal cancer.[135]
Clinical Deterioration	NN	• A NN model using routinely obtained vital signs and laboratory values effectively predicted clinical deterioration (ICU transfer and cardiac arrest) in patients with hematologic malignancies with 82% accuracy compared to 24% accuracy in existing models.[125]
Drug Resistance	ML general	• Acquired resistance to epidermal growth factor receptor tyrosine kinase inhibitors (EGFR-TKIs) is a major issue worldwide, for both patients and health care providers. A ML model that analyzed genomic data cohort data was able to identify generalized predictors for acquired resistance (DDK3, CPS1, MOB3B, KRT6A).[136]
Stem-cell Transplant Risk Assessment	Decision Tree	• Allogeneic hematopoietic stem-cell transplantation (HSCT) is potentially curative for acute leukemia but carries considerable risk. A ML decision tree model was used to develop a robust tool for risk evaluation of patients with acute leukemia before HSCT.[137]

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