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Canadian Medical Imaging Inventory Service Report

The Role of Neuroimaging in Drugs Targeting Amyloid-Beta in Alzheimer Disease: Part 1

Context

Alzheimer disease (AD) is a progressive neurodegenerative disorder and the most common cause of dementia. Current understanding of AD suggests that the main pathological hallmarks of the disease include the widespread accumulation of amyloid plaques and neurofibrillary tangles in the brain.[1] A buildup of amyloid plaque may activate the propagation of neurofibrillary tangles in the brain.[2] Together, these proteins reduce the capacity of neural circuits to work properly, leading to memory dysfunction and cognitive impairment.[3]

There are 190,000 people in Canada living with mild Alzheimer-type dementia and a further 532,000 to 799,000 people with amnestic mild cognitive impairment.[4] With an increasing aging population, where 25% of Canadians will be seniors by 2030,[5] the number of cases of AD is expected to increase.

Amyloid-targeted therapies belong to a new class of AD drugs that aim to treat a possible cause of the neurodegenerative disease, unlike current drugs that address symptoms by delaying memory loss by a few months.[6] The new drugs are intended to remove amyloid plaques from the brain,[4,7] which some researchers believe is the root cause of AD,[6] and subsequently delay or prevent disease progression.[4]

The recent clinical trials for aduncanumab, ENGAGE and EMERGE, used PET-CT and MRI to assess patients.[8] PET-CT imaging involves the use of a PET-CT scanner and a radiopharmaceutical that is injected into the patient's bloodstream. The production of radiopharmaceuticals requires a particle accelerator known as a cyclotron. Radiopharmaceuticals are produced with the assistance of radiopharmacists, radiochemists, and radiotechnicians, as well as cyclotron operators and maintenance staff.[9]

PET-CT may be regarded as a critical and decisive tool in the early diagnosis of AD[10] because, unlike MRI, it can detect the presence of amyloid plaque, as well as small cellular changes before structural changes are visible with MRI.[11] Within the context of amyloid-targeted drugs, a single PET-CT exam (or a lumbar puncture)[7] is needed to confirm both the presence of brain amyloid and to diagnose AD.[8]

It is recommended that a minimum of 4 MRI exams must be undertaken per patient.[8] The number of MRI exams per patient will vary, depending on both the patient's eligibility for the therapy and response to it.[8] Initially, individuals are required to undergo a baseline MRI within 1 year before treatment to rule out other conditions that could present with cognitive decline (e.g., normal pressure hydrocephalus, vascular dementia, slow-growing neoplasm, subdural hematoma) and to assess possible exclusions for the use of aducanumab.[8] After treatment initiation, at least 3 additional scans between drug infusions are recommended to check for amyloid-related imaging abnormalities (ARIA), particularly microbleeds and edema or effusion, which are the main side effects of aducanumab.[8]

In addition, MRI exams are recommended at any time patients have symptoms suggestive of ARIA such as headache, vomiting and/or nausea, confusion, dizziness, visual disturbance, gait difficulties, loss of coordination, tremor, transient ischemic attack, new onset seizures, or significant and unexpected acute cognitive decline.[8] As well, in individuals with confirmed ARIA, monthly MRIs are suggested until treatment can be reinitiated or terminated.[8]

With the potential arrival of these drugs to Canada, an assessment of the infrastructural readiness of the health care system is needed to ensure the optimal delivery of patient care. From a neuroimaging perspective,[8] the comprehensive use of MRI and PET-CT may be limited by the health care system's capacity and availability to conduct this testing. In particular, the high capital and operational costs of equipment,[12] accessibility, wait times, and competing clinical priortities[13] will likely present a barrier to the delivery of optimal patient care.

Objective

The report summarizes information on the infrastructural readiness from a neuroimaging perspective of Canada's health care system for the optimal delivery of new drugs targeting amyloid-beta in AD.

About This Document

This document summarizes information identified through the Canadian Medical Imaging Inventory (CMII)[14] and a limited literature search. The methods for this analysis have been previously described in the CMII report published in 2021[13] and are based on a web-based survey that was distributed to 455 sites with MRI, PET-CT, CT, single-photon emission computed tomography (SPECT), and SPECT-CT.

Data on MRI are presented first, followed by data on PET-CT.

Results

MRI

Number of Units

There are 378 MRI units in Canada (including 65 privately operated units), representing 10.0 units per million population. All provinces and 1 territory have at least one unit. Ontario (33%) and Quebec (27%) have the most units, followed by British Columbia (14%) and Alberta (12%). Figure 1 shows the geographical distribution of MRI units across Canada, mapped to the level of settlement (city or town) with the circle diameter proportional to the number of units. Counts for all sites within a city were aggregated. (Table 1 in Appendix 1 provides details on the number of units per province and territory.)

Compared to 35 other OECD countries, Canada ranks 26th in MRI units per million population.

Volume of Exams

The volume of publicly funded MRI exams across Canada in the fiscal year 2019–2020 was 2.33 million, representing 61.6 exams per thousand population (Table 2 in Appendix 1 provides details on the number of exams, and the number of exams per thousand population, per province and territory). This represents a 62% increase in exam volume from a decade before.

Figure 1: Geographic Distribution of MRI Units in Canada

Type of Use

The highest overall use of MRI by broad clinical indication is split evenly between neuroimaging and musculoskeletal imaging, each accounting for 28% of all MRI exam volume in Canada. Oncology exams account for 18% of all MRI exams, followed by hepatobiliary exams, accounting for 12% of overall usage.

Hours of Use

On average, MRI units operate for 14.1 hours per day. Almost half of MRI units operate between 12 to18 hours a day, 22% of units operate between 8 to 12 hours a day, 15% operate for less than 8 hours a day, and about 13% of sites operate at least 1 unit for 24 hours a day. More than half of MRI units operate on weekends.

Wait Times

The average wait time for an MRI exam (prior to COVID-19) was 89 days, which is 59 days longer than the recommended 30-day wait time target.[15] The anticipated wait time for an MRI in 2022 is 133 days.[15]

PET-CT

Number of Units

There are 57 PET-CT units in Canada (including 7 PET-CT that operate in the private sector), representing 1.5 units per million population. Prince Edward Island and the territories do not have PET-CT capacity. Figure 2 shows the geographical distribution of PET-CT units across Canada, mapped to the level of settlement (city or town), with the circle diameter proportional to the number of units. Counts for all sites within a city were aggregated. (Table 1 in Appendix 1 provides details on the number of units per province and territory.)

Compared to 32 other OECD countries, Canada ranks 21st in PET-CT units per million population.

Volume of Exams

The volume of publicly funded PET-CT exams across Canada in the fiscal year 2019–2020 was 125,775, representing 3.3 exams per thousand population (Table 2 in Appendix 1 provides details on the number of exams, and the number of exams per thousand population, per province and territory). The average number of exams per unit was 2,206.

Type of Use

The primary focus of PET-CT is oncology exams, with 79% of its overall use dedicated to this purpose and with some variation from province to province. The second most common use of PET-CT is for cardiac exams, at 11%. Neuroimaging accounts for 6% of all PET-CT exams.

There is some variability across Canadian provinces in accessing PET-CT specifically for dementia imaging. One province (New Brunswick) does not currently fund this indication and 2 others (British Columbia and Ontario) provide funding for dementia imaging on a case-by-case basis.[16]

Hours of Use

On average, PET-CTs operate for 9 hours per day. Almost half of PET-CT units operate between 8 to 12 hours a day, 38% of units operate for less than 8 hours a day, 12% for between 12 to 18 hours, and no units are used for more than 18 hours a day. Most PET-CT units do not operate on weekends. As well, the operating times of PET-CT units are closely tied to the operating times of the cyclotrons that supply the radiopharmaceuticals used in PET-CT exams.

Wait Times

While the average wait time for a PET-CT exam is unclear, for oncology exams they are beyond provincial targets in some provinces and, subsequently, requests for non-oncologic exams may not always be fulfilled.[9]

Figure 2: Geographic Distribution of PET-CT Units in Canada

Human Health Resources Considerations

Staffing

The availability of trained personnel to conduct, read, and interpret imaging exams is an ongoing concern in Canada.[15] Currently, there are 2,582 radiologists, 271 nuclear medicine specialists, 25,033 technologists, and 47 imaging medical physicists. (Table 3 in Appendix 1 provides details on the number of imaging staff, and the number of imaging staff per million population, per province and territory.) Increasing imaging capacity will require an investment in imaging staff. From an MRI perspective, there is already a shortage of radiologists, particularly in rural and remote communities.[17] For PET-CT, the predicament is similar for nuclear medicine physicians, with recent shortages made more acute due to a wave of upcoming retirements.[9] Shortages in nuclear medicine technologists, particularly those with experience in PET-CT is common across provinces with PET-CT capacity.[9] In some jurisdictions, staff shortages with medical physicists, radiochemists, and medical physicists have been reported.[9]

Education and Training

Overall, many physicians will require additional training for this new indication and for new radiopharmaceuticals, as well as training for managing spills and contamination events.[9] More specifically, radiologists experienced with recognizing ARIA are needed, as there are concerns that inexperienced radiologists may miss signs of ARIA.[8] As well, the PET-CT amyloid scan should be conducted by an imaging expert with experience in determining the presence or absence of amyloid plaque deposition. The imaging expert is usually a nuclear medicine specialist or radiologist with specific training in the interpretation of amyloid PET.[18]

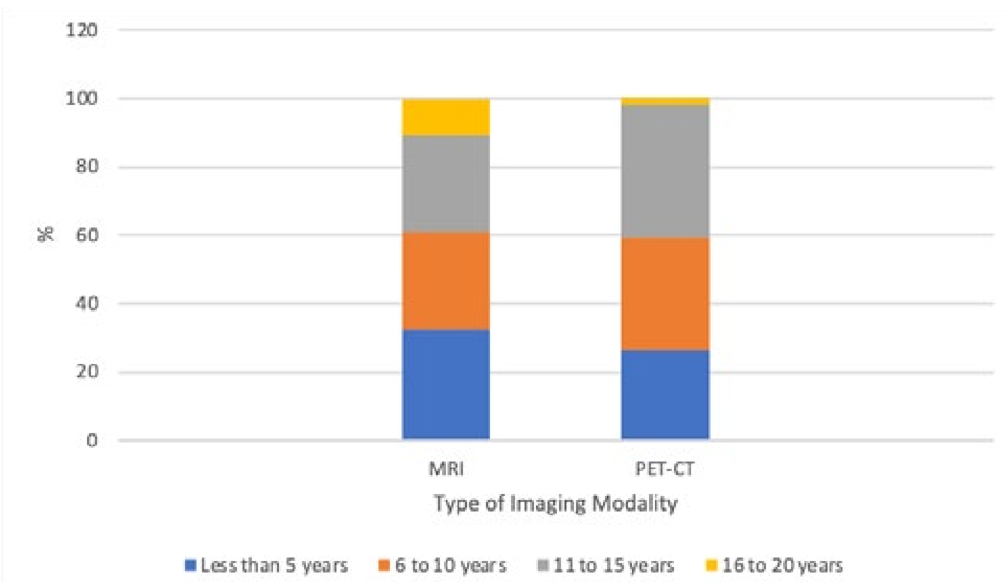
Most technologists are trained in nuclear medicine but require additional training for PET-CT. Currently, there are limited programs in Canada that provide PET-CT training for technologists.[9]

Equipment Considerations

Age of Imaging Equipment

According to life cycle guidance, equipment older than 10 years should be considered for replacement [19,20] because, compared to newer equipment, it may be less operationally reliable, use higher doses of radiation, have reduced diagnostic capabilities, and permit a lower throughput of patients.[21] Older imaging equipment may also be more likely to break down and may be more challenging to maintain and repair.[22] When considering Canada's future imaging capacity needs, the age of the existing armamentarium of imaging equipment should be taken into account. Currently, approximately 40% of both MRI and PET-CT units are older than 10 years[23] and subsequently may be affecting the health care system's ability to provide a timely diagnosis and treatment of patients.[19,20] Figure 3 indicates the average age of MRI and PET-CT in Canada.

Figure 3. Age Ranges of Imaging Equipment



CMII = Canadian Medical Imaging Inventory.

Access to Imaging Equipment

Currently, not all provinces and territories have access to MRI or PET-CT, and for those that do, access is mostly limited to densely populated urban centres. Travel burden is a barrier to optimal patient care, particularly for patients who may be too sick to travel, have mobility limitations, or are unwilling or unable to travel long distances.[24] Populations in rural and remote communities incur out-of-pocket travel expenses when travelling to urban centres for imaging.[25] Costs are also incurred through work absenteeism and other incidentals[25] by patients and their caregivers,[24] and may present a disincentive to seeking a diagnosis.[26]

Health care systems are increasingly using mobile imaging equipment as a means of expanding imaging capacity to underserved locations. The extension of diagnostic imaging to unconventional settings — such as rural and remote communities, and long-term care facilities — helps reduce disparities in the delivery of health care.[27]

PET-MRI

Neuroimaging using a hybrid modality that combines PET and MRI into a single unit may be of interest to clinicians. In dementia, compared to PET-CT, PET-MRI may provide additional insight into underlying anatomical, metabolic, and functional changes associated with disease progression.[28] This information may improve diagnostic classification and may have important implications for the clinical management of individuals with dementia compared to PET-CT alone.[28] Currently, there are 3 PET-MRI units in Canada: 2 in Ontario and 1 in Alberta. Because PET-MRI is only used for research purposes in Canada at this time, it is unlikely that this new hybrid modality will play a meaningful role in assessing patients for new AD drugs in the near future.

Conclusion

The fact that Canada's existing wait lists for MRI and PET-CT are past clinically recommended targets indicates that the potential approval of amyloid plaque-removing drugs will require an investment in new imaging equipment. For PET-CT, in particular, if each of the 190,000 people in Canada living with mild Alzheimer-type dementia (and not including the additional 532,000 to 799,000 people with amnestic mild cognitive impairment who would potentially be eligible) were to receive a single PET-CT exam as recommended for amyloid-targeted treatments, it would exceed the total annual volume of PET-CT exams conducted in Canada in 2019–2020 for all clinical indications by approximately 64,225 exams.

While there are approximately 6 times more MRI than PET-CT units in Canada, because MRI is used to monitor the side effects of amyloid-targeted drugs, the demands on MRI will be at least 4 times greater than those on PET-CT. To ensure the delivery of optimal patient care, procurement strategies that consider investment in both imaging modalities and that take into account that 40% of existing equipment is older than 10 years and should be considered for replacement may be better positioned to accommodate the anticipated accelerated demand in services.

In addition to investing in new equipment, decision-makers may look for opportunities to maximize the use of existing imaging capacity. This may involve extending hours of operation of equipment, particularly for evening and weekend use. It may also involve providing training opportunities for staff, as well as the wider adoption of tools, such as clinical decision-support software, artificial intelligence, and centralized order entry systems, all intended to promote appropriate equipment use and support efficiencies in imaging equipment management and workflow.

Whether expanding imaging capacity by maximizing the use of existing equipment and/or acquiring new equipment, decisions should be made in the context of health system constraints such as human resources shortages, education and training requirements, and the availability of supporting technologies such as cyclotrons and radiopharmaceuticals for PET-CT.

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Appendix 1: Supplementary Summary Tables for the 2019–2020 Canadian Medical Imaging Inventory

Table 1: Total MRI and PET-CT Units and Units Per Million Provincial or Territorial Population in 2019–2020

	MRI	PET-CT
Units (units per million population)		
Alberta	44 (10)	4 (0.9)
British Columbia	52 (10.2)	4 (0.8)
Manitoba	14 (10.2)	1 (0.7)
New Brunswick	14 (17.9)	2 (2.6)
Newfoundland and Labrador	5 (9.6)	1 (1.9)
Northwest Territories	0 (0)	0 (0)
Nova Scotia	11 (11.3)	1 (1)
Nunavut	0 (0)	0 (0)
Ontario	124 (8.5)	20 (1.4)
Prince Edward Island	1 (6.3)	0 (0)
Quebec	102 (12)	23 (2.7)
Saskatchewan	10 (8.5)	1 (0.8)
Yukon	1 (24.4)	0 (0)
Canada	378 (10)	57 (1.5)

Table 2: Total MRI and PET-CT Exams and Exams Per Thousand Provincial or Territorial Population in 2019–2020

	MRI	PET-CT
Exams (exams per thousand population)		
Alberta[a]	215,593 (49)	12,175 (2.8)
British Columbia	255,038 (50)	11,286 (2.2)
Manitoba	95,250 (69.3)	2,180 (1.6)
New Brunswick	46,309 (59.4)	2,149 (2.8)
Newfoundland and Labrador	21,929 (42)	1,704 (3.3)
Northwest Territories	0 (0)	0 (0)
Nova Scotia	50,664 (51.9)	2,818 (2.9)
Nunavut	0 (0)	0 (0)
Ontario	1,107,814 (75.6)	23,564 (1.6)
Prince Edward Island	5,348 (33.9)	0 (0)
Quebec	448,130 (52.6)	67,849 (8)
Saskatchewan	81,652 (69.3)	2,050 (1.7)
Yukon	2,496 (60.8)	0 (0)
Canada	2,330,223 (61.6)	125,775 (3.3)

[a] Fiscal year 2018–2019.

Table 3: Number of Radiologists, Nuclear Medicine Specialists, Medical Radiation Technologists, and Imaging Medical Physicists in Canada in 2018

Province/ territory	Radiologists[29]		Nuclear medicine specialists[30]		Medical radiation technologists[31]		Imaging medical physicists[a]	
	Count	Per million population	Count	Per million population	Count	Per million population	Count	Per million population
Alberta	294	65.7	28	6.3	2,416	540.2	7	1.6
British Columbia	314	61.5	29	5.7	2,128	417.0	9	1.8
Manitoba	88	63.6	6	4.3	841	608.6	5	3.6
New Brunswick	57	73.5	3	3.9	595	767.1	0	0.0
Newfoundland and Labrador	52	99.6	5	9.6	396	758.2	1	1.9
Nova Scotia	85	87.9	8	8.3	609	629.7	2	2.1
Ontario	939	64	79	5.4	10,720	730.3	18	1.2
Prince Edward Island	9	57.2	0 [b]	0.0	113	718.0	0 [c]	0.0
Quebec	661	77.8	107	12.6	6,587	775.4	5	0.6
Saskatchewan	83	69.5	6	5.0	628	525.0	0	0.0
Territories	0	0	0	0.0	NR	0.0	0	0.0
Canada	2,582	68.2	271	7.2	25,033	661.0	47	1.2

NR = Not reported.

[a] (Gisele Kite, Administrator, COMP–Canadian Organization of Medical Physicists, ON: personal communication, Sept 17, 2020).

[b] Although not reported by the Canadian Medical Association, there is one radiologist practising in Prince Edward Island who is fellowship trained in nuclear medicine (Grant McKenna, Health PEI, Queen Elizabeth Hospital, PE: personal communication, Oct 20, 2020).

[c] There is 1 imaging medical physicist practising in Prince Edward Island who is certified in mammography(Grant McKenna: personal communication, Oct 20, 2020).

ABOUT CADTH

CADTH is an independent, not-for-profit organization responsible for providing Canada's health care decision-makers with objective evidence to help make informed decisions about the optimal use of drugs and medical devices in our health care system.

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