# MRI Protocol Harmonization for Neurodegeneration, Vascular Diseases and Brain Injury: regional, provincial and national cohorts.

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The landscape of large-scale neuroimaging projects is constantly evolving and the new frontier of research necessarily involves extensive collaboration by diverse groups in order to maximize efficiency in an era of ever dwindling and increasingly competitive funding sources. As such, there is an immense need for harmonization of imaging protocols across projects, vendor platforms (GE, Philips, Siemens) and recruitment sites. This harmonization aims to optimize the compatibility of the imaging acquired at each scanner-site so that data from many sources can be pooled and shared, allowing for many projects to leverage the resources of others, both financially and in terms of the sometimes limited number of patients with a given condition that are available for recruitment.

One such initiative has been termed the Canadian Dementia Imaging Protocol (CDIP), championed by a group of physicists, physicians and research coordinators from across Canada, representing a multitude of projects including the Canadian Alliance for Healthy Hearts and Minds (CAHHM); the Consortium d'Identification de la Maladie d'Alzheimer – Québec (CIMAQ); the O2 study from the Consortium Québécois de Découverte du Médicament; the Medical Imaging Trials Network of Canada (MITNEC) – C6; and the Ontario Brain Institute's Ontario Neurodegenerative Disease Research Initiative. Additionally, several other organizations and projects such as the Toronto Dementia Research Alliance (TDRA) have already committed to adoption of this protocol, as well as many other studies in various centres throughout Canada and it is foreseen that CDIP will also be used throughout the upcoming Canadian Consortium for Neurodegeneration and Aging (CCNA).

The protocol proposed by this collaborative effort includes a series of advanced imaging sequences with high utility across many disease states including but not limited to stroke, dementia, neurodegeneration, traumatic brain injury (TBI), amyotrophic lateral sclerosis (ALS) and Parkinson 's disease. The protocol includes a high-resolution 3D isotropic T1-weighted scan for assessing fine anatomical detail, an interleaved proton-density/T2 weighted image for reliable skull-stripping and lesion assessment of deep grey structures, a fluid-attenuated inversion recovery (FLAIR) image for quantification and assessment of small vessel disease (SVD, a.k.a. white matter hyperintensities), a T2-star gradient echo for identification of microbleeds, a diffusion tensor image (DTI) for assessment of microstructural and white matter integrity, and resting state blood oxygen level dependent (BOLD) functional MRI for assessment of networks and functional pathways. While arterial spin labeling (ASL) for measurement of regional cerebral blood flow is not yet a part of the CDIP, it is being considered as an add-on for other cohorts.

Other large-scale studies of dementia like the Alzheimer's Disease Neuroimaging initiative (ADNI) have sought to collect large amounts of imaging data and have also made attempts to harmonize across platforms. However, the variety of sequences that are acquired for ADNI is somewhat limited and because the sequences were designed several years ago, current hardware and software technology has allowed for many improvements. Additionally, recent work by the group at Sunnybrook has demonstrated that the ADNI population primarily represents those with purer forms of Alzheimer's Disease, with low representation of those with SVD, as compared to subjects from the Sunnybrook Dementia Study (figure 1), which may somewhat diminish the generalizability of findings from this cohort to the broader population.

Although this ambitious harmonization effort is still in its early stages, through these combined projects it aims to image well over 15,000 Canadian participants from a wide variety of populations and will allow for an unprecedented understanding of the brain through the stages of normal aging and disease.