



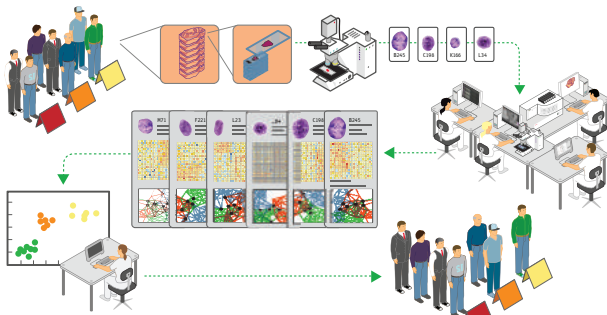
Do More!

The DoMore! project addresses the significant problem in pathology that is heterogeneity in cancer. Our purpose is to improve cancer diagnosis by utilizing big data and software-driven automation of pathology. In brief, our three main objectives are: to automate lab procedures to attain a higher throughput and thereby generate a more representative sample size; to create an efficient pipeline for digitalization of microscopy and analysis; and to utilize the Big Data produced to identify and establish robust generic biomarkers for cancer prognosis and prediction.

We will DoMore! – Increasing quality and productivity

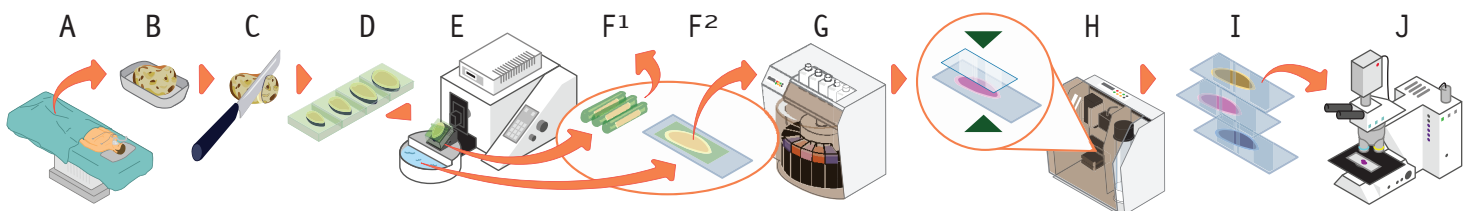
Our goal is to completely transfer today's very complex thinking and decision-making within cancer care, currently based on visual observation, to a computer basis with objective, reproducible algorithms. The concepts involved are based on image analysis and more specifically: deep learning, texture analysis, and quantification of DNA.

The implementation of this project would be groundbreaking and would allow us, substantially, to DoMore! for patients.



Automatic analysis and more accurate patient diagnostics The figure above depicts how (here prostate-) cancer patients qualify for different treatment plans. By analysing their specific cancer types, each cell's specifics, hereditary disease, patients history etc we may find more accurate treatment options for more patients.

Automation The figure below depicts the progression from tumor resection to final analysis. Following a cancer diagnosis, (A) the tumor is surgically removed from the patient and (B) is set in formalin for preservation. (C) It is then divided into smaller pieces, with (D) each piece embedded in separate blocks of paraffin wax. (E) Using a microtome, the paraffin block is sectioned into slices used for different analyses. (F¹) Thick tissue sections are used to extract single nuclei and (F²) thin sections are taken for in situ tissue analysis. (G) Various stains are applied to identify nucleic acids, proteins or cellular structures. (H) A cover glass is affixed onto the slide and finally, (I) the finished slides (J) are analyzed. As opposed to what is now a largely manual process, steps (E) through (J) will be fully automated by one of the DoMore! project partners by 2019.



We will DoMore! – Challenges we address

Cancers are heterogeneous and can follow multiple paths. Some will progress to metastases and death, while others will prove to be indolent, causing little or no harm during a patient's lifetime. This heterogeneity, as it's called, poses a great challenge to those assessing the prognosis of cancer.

The biomarkers we use to identify the aggressiveness of tumor progression are not distributed evenly throughout the tumor. This introduces a first issue: under sampling. Sampling for markers (other than for histological grading) is normally only performed on a small tissue sample or a small fraction of a single block of tissue. Using prostate cancer as an example, the sample that is usually examined represents a mere 1:1000 of the tumor. By sampling such a minuscule amount of the tumor, there is a great risk of missing the cells that actually go on to kill the patient.

Tumors are assigned a histological grade based on their growth pattern, which serves as a biomarker used to determine adjuvant therapy. Unfortunately, the prognostic value of histological grading also varies between pathologists, as it is a subjective process. Grading depends heavily on the pathologist's expertise, and inter-observer and intra-observer agreements are moderate only. Furthermore, the inter-observer agreement among specialist pathologists is better than that of general pathologists.

The ability to assess the likely outcome of cancer is crucial, and the importance of prognostic methods and markers cannot be overrated. A successful treatment often relies on a correct diagnosis, preferably at an early stage of the disease.

These are precisely the challenges we address in the DoMore! Project. Selected as one of three Lighthouse projects, the Norwegian Research Council is funding DoMore! for five years as of July 2016.

We will DoMore! – Goals

The goal of DoMore! is to explore a unique combination of academic and industrial competence to radically improve prognostication and hence treatment of cancer by using digital tools in pathology.

We are beginning with the three most common cancer types - lung, colorectal and prostate cancer. These three cancers account for 50% of all cancer diagnoses as well as 50% of all cancer deaths. We are working toward increased efficiency in pathology, and finding methods and markers that can aid the clinician to give better and more personalized treatment to cancer patients.

We will DoMore!

– Automation and in silico pathology

Biomarkers that could be used to identify the aggressiveness of tumor progression are unevenly distributed throughout the tumor. In order to get a complete and accurate picture of the disease, it will first require greater sampling. By the completion of the project, we expect to increase laboratory production by a factor of 5 to 10 through automation of the majority of the manual lab techniques we use today.

The real economic and societal difference will be made when we use in silico pathology to its full extent to improve diagnosis by utilizing Big Data and software-driven automation of pathology. This will enable us to address each challenge in an objective and reproducible way, reducing human error and removing subjective and time-consuming analyses.