Professional MBA
Entrepreneurship & Innovation

TU WIEN CONTINUING EDUCATION CENTER

WU EXECUTIVE ACADEMY

Cloud-based characterization of tumour lesions in cancer patients.
A business plan for a University spin-off.

A Master's Thesis submitted for the degree of "Master of Business Administration"

Supervised by

Prof. Dr. Marc Gruber, EPFL, Lausanne, CH

Submitted by

Thomas Beyer, PhD

h1527628

Vienna, May-27, 2017

AFFIDAVIT

I, Thomas Beyer, hereby declare

1. that I am the sole author of the present Master's Thesis "Cloud-based characterization of lesions in cancer patients. A business plan for a University spin-off.", 100 pages, bound, and that I have not used any source or tool other than those referenced or any other illicit aid or tool, and
2. that I have not prior to this date submitted this Master's Thesis as an examination paper in any form in Austria or abroad.

Vienna, May-27, 2017

ACKNOWLEDGEMENTS

I like to thank the PMBA 2015-7 course instructors for being inspiring enough for me to see this last part of the PMBA course through with pleasure and devotion.
Marc Gruber has provided insightful and helpful advice throughout the composition of this thesis – thank you.
I am indebted to many colleagues who supported me with hands-on information and hindsight: Laszlo Papp, Anthony Stevens, Jim Williams, Richard Zimmermann and many more. I appreciate my team and friends who tolerated my past disappearance from the social scene: Florian, Frank, Ivo, Lutz, Markus, and Sieggie, to name a few.
My sincerest gratitude goes to my dear wife, Bärbel, who put up with me for the time of this course, and specifically during the past months dedicated to this work, and, last but least, for the past 11 years; no words can make up for this.

Several icons for building elements of the figures have been sourced from Google Images: https://images.google.com.

PREFACE

Here, I present a business plan for an academic spin-off (ASO). The product is a cloud-based computing platform for on-demand tumour characterization as part of oncology patient management. In this work, I will highlight the origin of the idea and its innovation potential for the healthcare industry. A literature review of past experiences of academic spin-offs shall present key insights in light of plans for turning the above business idea into a viable start-up business. This desk research is complemented by field research that included open interviews with stakeholders in the healthcare industry. To conclude, a few learning points from this study shall be juxtaposed with reflections on current state of affairs with regards to USO in Austria, before presenting the actual plan.

Today, healthcare costs make up for a significant fraction of the GDP in industrialized countries, and costs are rising. The growth of these costs is caused by multiple factors. First, the population grows and life expectancy increases, and, thus, more people require medical attention. Second, examinations and, more so, therapies become more complex and more expensive. Additional costs arise from choosing therapy options for patients who do not benefit from them because of an incorrect a priori diagnosis. Overall, there is striking evidence of sunk healthcare costs from failure of delivering proper treatment at the right time, as well as overtreatment.

The observation of choosing ineffective therapies for selected patients and patient groups arises from the fact that frequently the diagnostic pathway to determining and grading disease in these patients employs insufficient diagnostic means. For example, it is known that certain tumours cannot be diagnosed properly by standard medical imaging examinations that rely solely on depicting anatomical details, but instead require insight into the biological, molecular and signaling pathways. Therefore, other, biology-driven imaging modalities and diagnostic tests are needed for efficient patient management.

Driven by technical innovation, more and more data are generated in our societies today. So far many of these data are not utilized. The concept of *big data* or *data lakes* describes the availability of large amount of data of all types of formats that can and should be utilized to advance our knowledge. One mean to go about this is to employ *artificial intelligence* (AI) or *machine learning* (ML), i.e. higher-level computer-based algorithms that can advance through the use of validated training data sets. Healthcare benefits a great deal from the combination of big data and AI. Pilot proofs have been produced by various groups and companies that demonstrate the diagnostic power of `AI as well as its potential to save costs.

Our business concepts rests on the idea of combining diagnostic imaging and non-imaging information for building *supervised ML* (SML) algorithms that are ultimately capable of predicting the existence and type of a tumour in oncology patients. Here, a cloud-based computing platform on a pay-per-use basis is perceived as a viable business model. In the latter part of this thesis, a business plan details all major assumptions and parameters for this business opportunity.

The idea for this concept arose from a multidisciplinary engagement of various clinical and non-clinical experts. Therefore, a number of formal aspects regarding the set-up of such a company shall be reviewed. This includes, access to data that are used to train the ML[1] algorithms, associated intellectual property rights (IPR) and discussions of realistic licensing agreements. These points shall be discussed in the context of building a healthcare business on the grounds of an innovative technical and methodological value proposition.

Since the idea for a holistic-type type tumour characterization originated from an academic partnership at a major national university, the specifics of translating an innovative idea from an academic project into a product as part of an ASO strategy shall be studied. More specifically, a strategy, and later on a business plan for an ASO will be derived from a review of the theoretical constituents of developmental phases and critical junctures in the development of a company. Of note, a recent Opportunity Assessment Plan on this very idea did already indicate a market potential for this "cloud-based and computer-supported characterization of tumour lesions", and it is hoped that this thesis will help with the preparation of a lasting business strategy.

[1] For the sake of simplicity, the more general term "machine learning – ML" shall be used for the remained of the thesis.

ABSTRACT AND STRUCTURE OF THE THESIS

This project aims at deriving a business plan for an academic spin-off (ASO). The business idea is a cloud-based computing platform for characterizing tumour load in oncology patients based on the provision of non-invasive biomarker information. Subsequent tumour characterization through predictive analytics shall be used for the stratification of individual treatment options, specific to the patient, thus, helping to bring down overall healthcare costs.

First, the *concept of state-of-the-art cancer patient management* will be introduced. Today, cancer patients are diagnosed through non-invasive anatomical and/or molecular imaging as well as a series of clinical tests that frequently include invasive biopsies. Medical experts face a diagnostic dilemma that is two-fold. On the one hand, not all tests may be performed for a particular patient to support the most accurate diagnosis. On the other hand, many more data from other but similar patient cohorts are available, yet remain inaccessible and understood by the very medical expert, and, therefore, cannot be used easily as part of the knowledge build-up of that expert. As a consequence, diagnostic interpretations may be challenged in complex cases, and suboptimal or inefficient therapies may be ordered that do not help the patient.

With the onset of high-power IT structures, the *concept of big data* has made its way to *healthcare*. Numerous data (imaging, immuno-histochemical markers, clinical records, etc.) are available and await conjoint analysis for the generation of new knowledge that can be absorbed by the medical expert. Today, several companies offer on-demand services through cloud-based data sharing and analysis tools. A recent survey conducted by the author provides insight into the readiness of healthcare stakeholders to adopt a cloud-based decision support algorithm specifically for tumour characterization. The results indicate a generally positive perception of such a service if it was approved by the authorities. The second part of this thesis highlights the business idea and value proposition, which is that of a dedicated *computer-supported clinical decision system*.

As the idea for a cloud-based tumour characterization span out of ongoing academic research, the third part of this thesis will probe the *theoretical framework for turning such an innovative idea into a business* considering the specific boundary conditions of an ASO. These conditions entail the need to complement academic know-how with business expertise, the need to address various interests over intellectual property rights, and the start-up and early growth strategy, to name a few.

The fourth section of this work is dedicated to the *actual business plan*. Here, important learning points from the earlier theoretical work shall be highlighted to support the choice of arguments and quantitative estimates for the planned business. Finally, this work will conclude with a summary of the main teaching points from the development of a strategy and a business plan for a ASO and a very specific cloud-based service offering in the context of oncology healthcare.

TABLE OF CONTENT

LIST OF FIGURES

LIST OF TABLES

ABBREVIATIONS

AI	Artificial intelligence
ASO	Academic spin-off
CAD	Computer Aided Diagnosis
CAGR	Compounded Annual Growth Rate
CE	Conformité Européene
CT	Computed Tomography
CDSS	Clinical Decision Support System
CRO	Clinical Research Organization
DDP	Discovery-driven planning
DICOM	Digital Imaging and Communications in Medicine
EORTC	European Organisation for Research and Treatment of Cancer
FDA	Food and Drug Administration
FDG	[18F]-labeled fluorodeoxyglucose
GDP	Gross Domestic Product
IoT	Internet of Things
IPR	Intellectual Property Rights
IT	Information Technologies
ML	Machine Learning
OAP	Opportunity Assessment plan
PET	Positron Emission Tomography
PET/CT	Positron Emission Tomography/Computed Tomography
PET/MRI	Positron Emission Tomography/Magnet Resonance Imaging
PMI	Precision Medicine Initiative
PPP	Public Private Partnership
MRI	Magnetic Resonance Imaging
SaaS	Software-as-a-Service
SML	Supervised Machine Learning
SPECT	Single Photon Computed Emission Tomography
SW	Software
TTO	Technology Transfer office
US(A)	United States (of America)
WHO	World Health Organization

GLOSSARY FOR NON-BUSINESS TERMINOLOGIES

Agnostic Clinical Enterprise	New approach of big healthcare providers, whereby they broaden their footprint through the inclusion (buy-in) of individual, advanced processing and analysis functionalities so as to position themselves as central healthcare platform providers.
Artificial intelligence	A higher order of machine learning (ML) to indicate the ultimate potential of computer-based systems to render analytic and/or predictive recommendations.
Big data	Very large data sets that may be analyzed by computers (and through ML) to reveal patterns and information not easily accessible to the human observer.
Biomarker	A measured or evaluated descriptor that serves as an indicator for normal biological or pathogenic processes, or responses to therapeutic interventions.
Biopsy	A procedure whereby a small tissue sample is extracted from a living subject for subsequent diagnostic work-up in an attempt to discover the presence or extent of a disease.
Clinical Decision Support	A mechanism or tool that provides healthcare stakeholders with essential information that is extracted from a wide range of variables and that is used as an additional information during patient management.
Computer aided diagnosis	A part of a clinical decision support system that employs IT to, e.g., render a lesion automatically based on a large cohort of reference data.
Computational Pathology	A diagnostic approach that encompasses multiple sources of information of which non-invasive imaging and digitized histopathological samples are of the essence.
Discover-driven Planning	A planning technique for a strategy or business that accounts for changes in input parameters as the plan proceeds. Interim funding of the project is made contingent on the achievements at milestones, unlike in conventional planning where the final outcome is judged against initial projections.
Expert system	A computer-based system that emulates or supports the decision making process of a human professional.

Feature vector	A list of (numerical) values extracted from an object of interest. A feature vector is the digital manifestation of what was measured and what is to be to evaluated by machine learning.
Histology	The examination and study of the cellular microstructures of samples from living organisms.
Human-machine approach	Combination of expert reading and computer-support system analysis for the best possible accuracy of a diagnosis.
Imaging	Non-invasive means of assessing the anatomy (e.g., X-ray, CT, MRI) and metabolism (e.g., SPECT, PET) of patients in search of aberrations of normal anatomy and metabolic pathways as indicators for the presence and aggressiveness of disease. Hybrid imaging refers to the physical combination of two complementary medical imaging modalities within a single gantry.
Machine learning	A method of computer-based data analysis that builds on iterative "learning" experience from complex data sets. The capabilities of these algorithms get better with higher orders of data complexity and size. *Supervised* ML employs known reference values to guide the learning process. In *unsupervised* ML no such reference information is available. Subgroups are identified from measured data only (*clustering*). *Reinforcement* ML automatically determines its ideal behaviour based on feedback from its environment as a result of its long-term actions. Reinforcement ML is a type of self-establishing AI.
Omics	Informal name for technological fields in medicine and biology that end on "omics", such as *genomics*, *proteomics* and *metabolomics*.
Precision medicine	*aka* Personalized Medicine; buzzword to describe the field of medicine that tailors therapies according to personal needs and pre-dispositions of patients, based on large amounts of data (incl. imaging and non-imaging examinations) from a single individual
Predictive analytics	The process of learning from retrospective data in order to build an analytical model that helps make predictions.
Radiomics	Approach to extracting new levels of information and knowledge from medical images, preferentially radiology-type images.
Telemedicine	The use of IT and telecommunication to provide healthcare services from a distance.

Theranostics	*Thera*py and Diag*nostics*; term to describe ongoing efforts to combine diagnostic and therapeutic capabilities within one single agent (e.g., a molecule labeled with different radioisotopes).
Tracer	*aka* Radiotracer, is a biomolecule that is labelled with a radioactive isotope so as to follow its biodistribution through external measurements of the emitted radiation. A tracer is frequently called also a "molecular contrast agent".
Tumour	A lesion in the body that is made of cancerous cells, i.e., cells with abnormal signaling and growth.
Tumour heterogeneity	Intra-tumour-lesion heterogeneity of tissues and cell structures, indicative of tumour aggressiveness.

1. AN INTRODUCTION TO ONCOLOGY HEALTHCARE

This chapter will present cancer care as part of modern healthcare systems and describe the standard workflow for the diagnostic and therapeutic workup of cancer patients. Shortcomings of today's current diagnostic pathways and subsequent choices for – frequently – ineffective therapies will be deduced ("diagnostic dilemma") and presented as a business opportunity.

1.1 HEALTHCARE AND COSTS

Providing affordable access to healthcare for every citizen should be a prime objective of society. However, healthcare politics and financing vary widely across countries. Spending on healthcare is higher in economically advanced countries [1]. By 2040, capita health spending will double; total spending globally will be around 24 trillion$. This increase is driven, in principal, by rising expenditures in upper/middle-income countries. In most OECD countries, healthcare costs measured as a share of GDP are significant at 10%, and more [2]. Causes for increasing health expenditures include the technical progress of healthcare instruments, the increasing life expectancy of people and the ability to contain formerly terminal diseases as chronic diseases over more life years. A 2008 study has pointed to the *Baumol effect* as a major cause for rising health expenditures, primarily in developed countries. The Baumol effect describes an economic state where labour productivity in healthcare grows slower than that in the overall economy. In that case, the study found that 1% growth in total labour productivity is associated with a 0.5% growth in healthcare spending [3].

Increasing life expectancy and the costs to manage serious diseases are a concern for most healthcare systems today. By 2050, the number of over-65s worldwide will have tripled [4], thus leading to more citizens requiring medical attention without them co-financing healthcare by large. As life expectancy increases, so will the number of age-related diseases, such as cancer. The latest report by the American Society for Clinical Oncology mentions that according to the WHO the number of new cancer diagnoses will be 22 mio per year until 2030, up from 14 mio in 2012 [5]. About 60% of the new cancer cases will be in emerging market economies [4], many of which have limited access to cancer screening and appropriate treatment. Nonetheless, thanks to clinical advances, today, two of three people with cancer live 5 years, or more after the first diagnosis, up from about one out of two in the 1970s. In line with increasing incidence of cancer, healthcare costs are expected to rise as a proportion of GDP.

1.2 CANCER PATIENT MANAGEMENT

Rising healthcare costs are caused also by "waste" in healthcare systems that affects public and private payers alike. An US-based study from 2012 points to cost saving potential of 158b$ – 226b$ from avoiding "overtreatment" alone [6]. Overtreatment, i.e. subjecting patients to care that cannot help them according to best practice, science and patient's own judgement, is a major cost driver in cancer patient management. The diagnosis of cancer frequently happens too late with patients

presenting in advanced stages of disease concurrent with symptoms, such as pain or palpable lesions. Obviously, the earlier cancer is detected the more likely it can be treated effectively, since the disease is at an early stage and several therapeutic options still exist. To date, cancer diagnosis is based mainly on *medical imaging*. Imaging describes a number of non-invasive anatomical and molecular imaging methods, which subjects with the suspicion of cancerous disease are referred to (**Error! eference source not found.**).

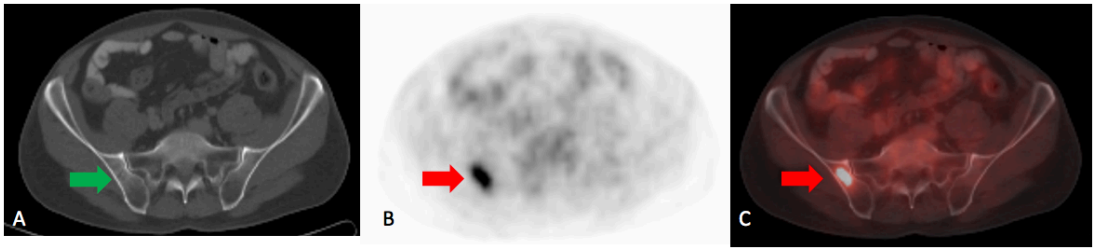


Figure 1. Axial views of a patient undergoing (A) anatomical, CT, and (B) molecular, PET, imaging as part of a combined, dual-modality PET/CT examination (C). The panels clearly demonstrate the tumour lesion (arrow) through its subsequent anatomical alteration and increased biological activity, measured as an increase in PET image contrast.

In general, anatomical imaging uses a source of ionizing radiation placed outside the patient to measure the amount of radiation passing through the body, thus, depicting morphological information with high spatial precision (**Error! Reference source not found.**A). In contrast, molecular imaging ses internalized sources of radiation that distribute along a pre-selected biological or molecular pathway, thus, representing biological information (e.g., concentration) at a given time in the body of the patient, with high functional sensitivity but generally low spatial accuracy (**Error! Reference ource not found.**B). The use of molecular imaging methods, such as Positron Emission Tomography (PET) or Single Photon Emission Computed Tomography (SPECT) has been shown to provide relevant diagnostic information for the management of cancer patients. The use of anatomical imaging, mainly through X-ray imaging and Computed Tomography (CT) imaging, on the other hand, has been shown to yield valuable diagnostic information at advanced stages of disease when anatomical alterations from normal morphology become apparent (if at all). The combination of both, anatomical and molecular information, through the use of combined or hybrid imaging (**Error! eference source not found.**C**)** to yields a higher diagnostic accuracy than either modality alone [7].

In addition to non-invasive imaging, frequently invasive biopsy procedures are applied to patients with the suspicion of cancer lesions so as to extract histological samples for subsequent tissue analysis and tumour grading (Figure 2). In some cases, the lesion is removed surgically and worked up histopathologically afterwards to support subsequent therapeutic choices. A main disadvantage of biopsy procedures is that tumours (of any size) are heterogeneous and that standard, core-needle biopsies frequently do not suffice addressing this heterogeneity. Standard biopsy procedures may miss the (most) aggressive parts of the tumour and, thus, render the extracted biological materials useless for a coherent differential diagnosis. Other challenges for biopsies include cost, logistics and harm to patients [8].

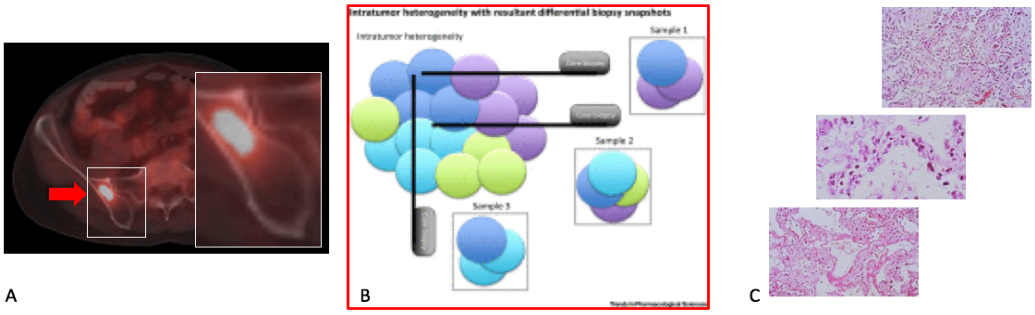


Figure 2. Image-guided fine-needle biopsy to extract tissue samples from region suspicious of tumour growth. (A) Suspicious bone metastasis in patient with lung cancer. (B) Fine needle tissue sampling from various regions of the tumour lesion, subject to tissue heterogeneity [8]. (C) Example cellular structures of biopsy samples (non-clinical). In case of significant tumour heterogeneity, fine needle biopsy cannot sample the lesion with sufficient accuracy and may miss the most aggressive regions.

Nevertheless, both – non-invasive imaging and invasive bioptic sampling – are used to render a diagnosis of the patient (Figure 3). Depending on the tumour type, the location of the lesion and tumour aggressiveness, distinct therapeutic regimes or combinations thereof are selected to treat the patient. Such therapy options include, in general, surgery (if the tumour is singular and well described), radiotherapy (if the lesion is close to sensitive organs, or if the disease is spread) and chemotherapy (if the disease is spread). Once the patient has completed a treatment/cycle he/she is subject to periodic follow-up examinations to pick up any recurrent disease early. While, individual and national healthcare costs may vary along the diagnostic and treatment pathway (Figure 3), it is interesting to note that global spending on cancer drugs amounted to 91bEUR in 2013, which is twice as much as in 2010 [4].

1.3 DIAGNOSTIC DILEMMA AND COMPUTER-SUPPORT ALGORITHMS

Healthcare costs can be contained if treatment options are selected based on personalized, accurate biomarker information so as to ensure that patients respond to a particular treatment most effectively. While several concomitant sources of biomarker information are available today and – when used together - promise to yield an increased level of diagnostic accuracy and/or confident reading, an individual reader is challenged by the sheer volume of information [9]. Today, such information typically includes various imaging data sets, biopsy-based tissue samples, genetic profiles, blood serum levels, physical examination results and alike. The diagnosis made by the *medical expert* reader (Figure 3) rests on the accuracy of the individual pieces of information, the level of expertise of the reader and a set of rules for making a decision. The "diagnostic dilemma" describes the need to bridge the gap between the wealth of useful information available today and the inability of an individual expert reader to comprehend the whole lot of it easily. Costs are incurred, for example, through the continuous engagement of a highly-trained medical experts and the provision of access points to various data formats stored in different ways at multiple locations in the healthcare system.

With the onset of personal computers and wider accessibility of IT infrastructure, healthcare professionals have tried to automate parts of the decision making process, including the collection of

the piece-wise information and subsequent basic analysis. With the introduction of *expert systems* in the late 1990's and early 2000's diagnoses were made with the help of semi-automated computer algorithms (Figure 4). The algorithms were provided by programmers who liaised with medical professionals to learn rules and criteria for making a decision and for translating these decision paths into software code [10], so as to building a healthcare expert system that emulates the principles and actions used by the medical doctors. Example for such algorithms, were *computer aided diagnosis* (CAD) packages for the detection of lung lesions (aka cancer) on X-ray or CT images and for the image-based detection of breast and colon cancer [11].

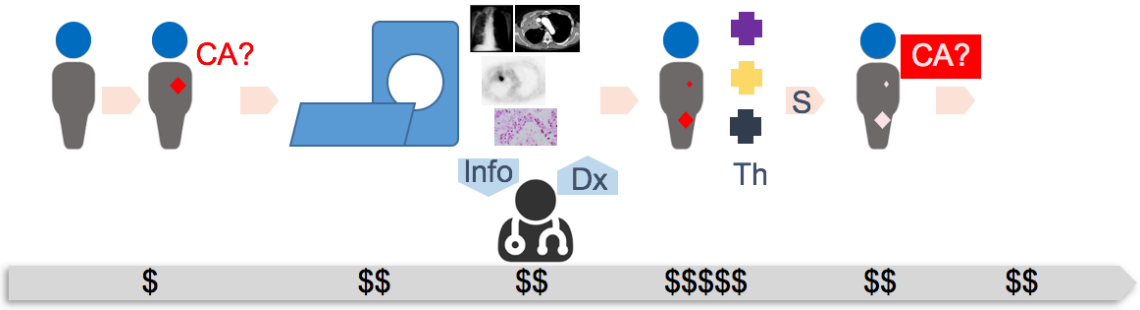


Figure 3. Flow chart of typical cancer patient management: A patient with a suspected cancerous disease (CA?) is referred to a number of imaging examinations and medical tests, including biopsy. All relevant information (Info) is collected (if possible) and used by a medical expert to render a formal diagnosis (Dx). Pending the detection and characterization of a cancer, a subsequent treatment plan is made by the medical doctor. Then, patients are sent for therapy (Th), which may include either of the following or combinations thereof: chemotherapy, surgery and radiation therapy. Following therapy, cancer patients are subject to treatment effect surveillance (S) and additional therapies, if needed. Relative healthcare costs are marked as $.

CAD approaches rely on the ability of software tools to recognize abnormalities amidst a normal background information (say, a CT image with a lung lesion), or to pick a patient with a disease from a cohort of normal subjects. This requires the algorithm to be accurate and reproducible. With the introduction of CAD, more and more experts have asked to support the decision making process by an individual doctor with know-how derived from large cohorts of healthcare data, so as to minimize the risk of making an incorrect diagnosis in view of the many variants of a disease. The paper by Lusted has been one of the first to instigate the idea of a more holistic approach to gathering diagnostic information and rendering a recommendation for an optimum therapy: "… even when the roentgenologist does make use of clinical data and functional studies, he still may not make a correct interpretation because he does not include all possibilities in his differential diagnosis. …Symbolic logic and probability contribute to our understanding of the reasoning process in diagnosis, while value theory can aid our choice of an optimum treatment." [12].

As a first step, this encompassing approach entails searching larger cohorts of patients with similar type symptoms and disease for frequent and reproducible patterns of information and to correlate them with a given parameter (e.g., presence or absence of a tumour, tumour grade, and even overall patient survival). In a very simple manner this is done in *expert systems* already that search a thorax

X-ray or CT image volume for common features (e.g., the outline of the lungs) and that denote any unusual finding (e.g., a dense lesion within the lungs). Taking this approach further, conclusions can be drawn from reappearing shapes, density distributions and locations of tissue densities on anatomical images with regards to the presence and aggressiveness of disease. Such *pattern recognition* mandates training of computer algorithms using large cohorts of patients with confirmed diagnosis. This approach is referred to as *radiomics*, thus, describing the intent to bring radiology (aka anatomical) imaging to the same level as genomics, proteomics etc., and making it part of a multi-modal reasoning [13] of the medical expert (Figure 4). To date, the field of radiomics is in active pursuit of academic researchers, and multiple commercial software tools are offered to healthcare professionals for automated diagnosis.

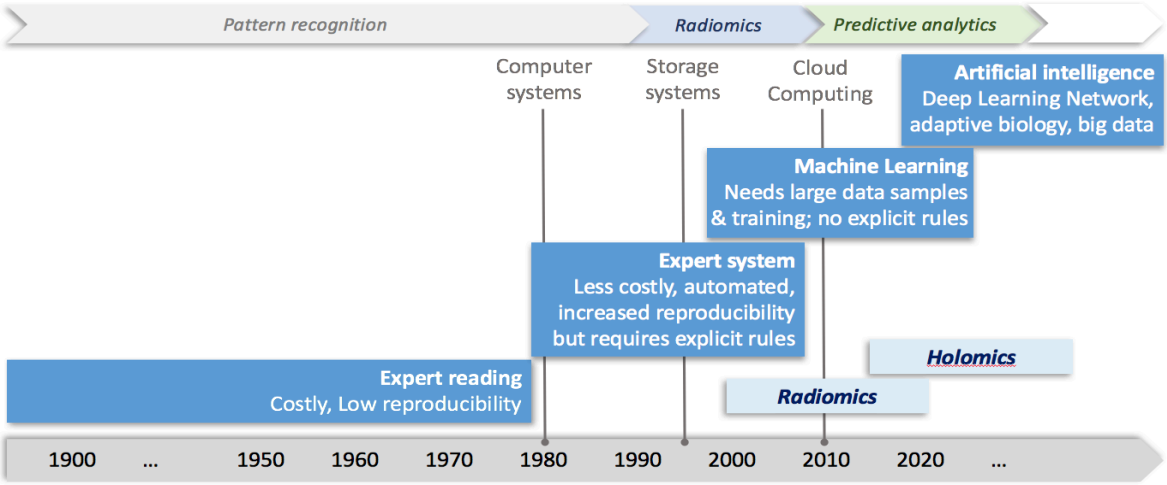


Figure 4. The approaches towards medical diagnosis have changed over time. *Expert reading* was replaced to a large extent by *expert systems*, offering computer-supported automation of the diagnostic decision making. With the onset of high-performance computer power and access to larger (big) data cohorts, *machine learning* (ML) has been proposed to provide more substantiated decision making. The complexity of ML-algorithms can be increased by *artificial intelligence* (AI). Also shown are technology turn points and trends that supported the progress of computer-support algorithms.

While radiomics entails, for the largest part, some sort of pattern recognition, leading to selecting structures and patterns that are outside a normal distribution, there is more to utilizing large data cohorts. *Machine learning* (ML) is a computer-implemented, statistical process that – based on a body of (coherent) data - derives a rule or procedure that can explain these data and that predict future data [10]. There are three types of ML: *supervised*, *unsupervised* and *reinforcement*. Of note, in this work we focus on *supervised ML* (*SML*). In contrast to the aforementioned expert system, ML-algorithms can be used also in cases when it is difficult to pinpoint and code explicit rules to solve a given problem. In the context of medical diagnosis and through the application of mathematical models, ML aims at deriving new diagnostically-useful information from the incorporation of multiple sources of information (e.g., images, lab tests, medical records, genetic profiling etc.). This concept is also referred to as *computational pathology*, which helps "generate diagnostic inferences and predictions" about disease [9]. Following the *radiomics* approach, the *predictive analytics* approach describes the

next layer of computer-supported diagnostic means [14], a more holistic perspective on how to source knowledge from the overabundance of (healthcare) data.

Figure 5 summarizes the core principle of *supervised machine learning* (*SML*) as one component of the *predictive analytics* approach (see section 1.4). An expert defines the task for which a machine learning algorithm is to be developed (e.g., Based on the input CT images, does this patient have a tumour?). A sufficiently large historical data set is used and split into a *training* and a *test* data set. A model with a number of parameters is defined and an objective function is selected. By iteratively applying the model and adjusting the parameters the objective function is maximized (and its difference to the original function is minimized). In that case, the model has been trained successfully. Following further validation with test data, the model can be applied then to similar type prospective data, with the final reading being expected to be as good as the expert reading, or better.

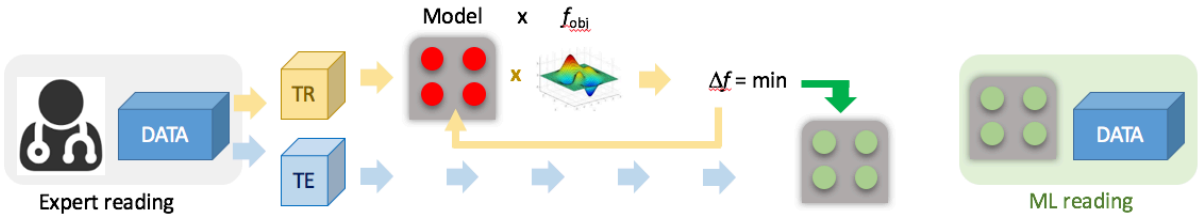


Figure 5. Supervised Machine learning (SML) approach: A historical data set is split into *training* (TR) and *test* (TE) data. A *model* is chosen to represent decision making. Further, an objective function, f_{obj} (e.g., tumour y/n?) is chosen. The model has parameters that can be adjusted so as to maximize f_{obj}. The model is applied and parameters are adjusted iteratively until f_{obj}=max. The resulting model is applied to TE for verification. It is expected that the resulting ML reading is as good as the expert reading, or better.

The above approaches towards (clinical) decision making by employing computer systems are brought together by the term *artificial intelligence* (AI). There is no single widely accepted definition of AI, but in colloquial terms, AI may be described as a process of mimicking cognitive functions by means of non-human computer-based set-ups. It has been hypothesized already in the 1940s that machines may do a better job at rendering a solution to a problem than humans [15]. The field of AI was founded in the mid 1950s but progress and interest slowing in the 1970s. The concept of AI was revived in the 1980s with first commercial success of expert systems (Figure 4), and again in the late 1990s and 2000s with first successful applications of ML in data mining and medical diagnosis.

The current wave of enthusiasm for AI, beginning in 2010, was driven by the availability of *big data* from various sources (incl. large databanks, social networks, information systems etc.), evidence for the usefulness of *ML approaches* to sourcing new knowledge from the data, and the ever increasing power and accessibility of *computers and storage systems*. While, most people (52%) today think that AI is still at its infancy, it is anticipated that AI will have a positive impact (51%) rather than a negative (7%). In the same study from KRC Research [16] over 50% respondents considered AI trustworthy for providing healthcare advice. And, of interest to this project, 11 of the 100 most promising global AI companies, were situated in the healthcare sector [17].

1.4 CDSS – CLINICAL DECISION SUPPORT SYSTEMS

Many terminologies exist today that describe the introduction of machine (aka computer) based support mechanisms into healthcare. The most generic terminology is perhaps *Health Information Technology*, referring to different technologies (IT, data storage, e-communication, etc.) to assist in the handling of health information as well as in the extraction of patient-specific information as part of patient management. Recent studies have shown that *human-machine teams* can be more effective than either alone with significant (>80%) reductions in errors [18]. However, for now neither of the computer-based support algorithms is likely to replace the human observer [19].

Clinical Decision Support Systems (CDSS) encompass computer-aided support functionalities for health information management. In the context of this work, we will focus on ML-algorithms (Figure 5). CDSS benefit from the following major technology trends [20]: (1) *machine learning*: fast progress in training automated IT-based algorithms for decision making; (2) *humanized big data*: perception that knowledge can be created from gathering more information from large (aka *big*) data cohorts, and (3) *on-demand*: readiness to access data anytime from anywhere in the world. CDSS help extract valuable information from *big data* and translate that information into knowledge. In the words of Obermeyer and Emanuel "… data by themselves are useless. To be useful, data must be analyzed, interpreted and acted on. Thus, it is the algorithms – not the data sets – that will prove transformative." [21]. The authors encourage the readers to turn attention from data to ML approaches in order to uncover rules or predictive models that can help make reproducible decisions on new data. As such, ML and AI will open vast new possibilities in medicine.

Already today, a number of commercial service providers engage increasingly in the area of CDSS. IBM, for example, offers several computer-support tools with multiple layers of complexity, all focusing on providing *multi-modal reasoning* as support for healthcare professionals when making conscious decision on patient management [13]. Increasingly, this landscape of ML service providers is also becoming more competitive [22], thus, giving an indication of the market potential for CDSS (see section 2.3).

1.5 PERSONALIZED MEDICINE: DIAGNOSIS AND TREATMENT

In the past, patient management (individual or cohort) would have been subject to an *expert reading* (section 1.3), and, therefore, successful treatment outcome would very much depend on the level of expertise of the decision making expert. This approach would be synonymous with a "one-size fits all" approach whereby little patient-specific and relevant adjustments to the choice of diagnostic means and therapeutic choice would have been made. Today, the inclusion of novel imaging techniques and biomarker information as well as the adoption of computer-support algorithms can be used to help improve patient management through *personalized medicine*. This approach aims at tailoring diagnostic choices and therapeutic options to patient groups or individual patients (Figure 6).

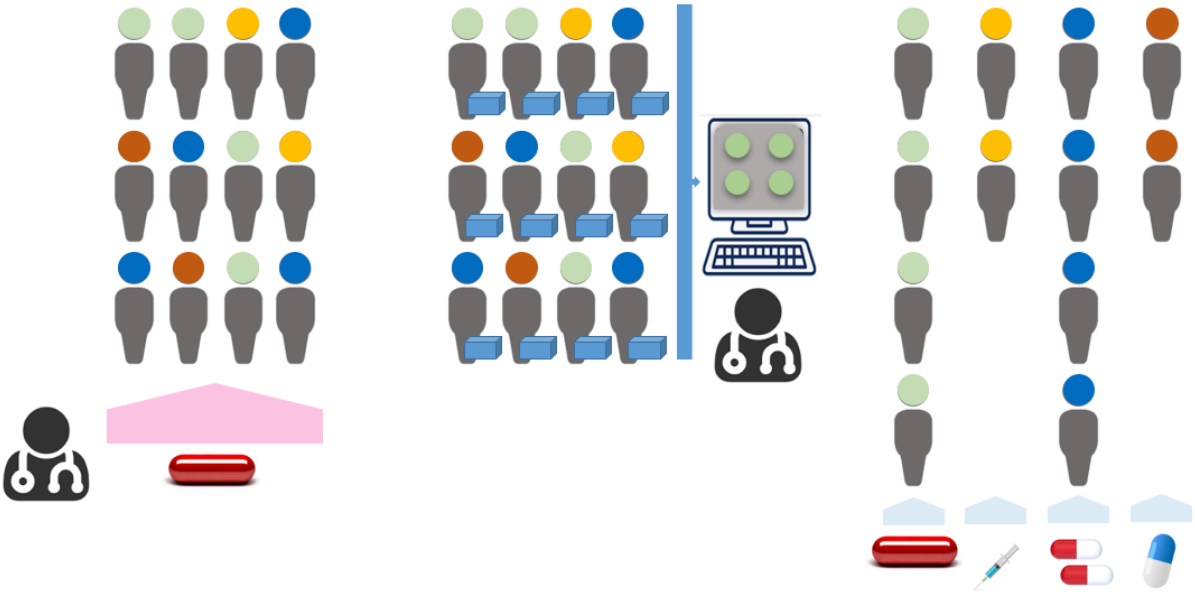


Figure 6. Concept of Personalized Medicine and the use of CDSS. With an *expert reading* the same drug may be applied to a cohort of patients although these patients will not respond equally well to that drug (left). When adopting a h*uman-machine approach* (expert system and ML), data from each patient are analyzed by the model (*predictive analytics*) and patients can be tailored to sub-cohorts that will receive disease-specific medication, so as to increase the efficiency of an individualized treatment and, thus, reduce overall costs.

The selection of these groups and individuals is based on either very sensitive diagnostic tests (imaging and -*omics*) or the use of CDSS. In case of the latter, models can be applied to patients that guide the expert to the location of a tumour and further help characterize that lesion, so as to provide the medical professional with expert knowledge for the subsequent choice of an optimum therapy. For example, highly-specific chemotherapeutic drugs require the existence of a given receptor on the tumour cell; in the absence of that receptor the drug will be of no use while in the presence of that receptor the drug will work most efficiently. A CDSS can help characterize tumours based on the engrained "knowledge" of a wide range of tumour appearances and, thus, stratify patients to specific diagnostic and treatment workflows, so as to match tumour receptors and targeted drugs. Of course, a CDSS gets better and more accurate, the more training data (aka *reference data*) are available for building the inherent ML engine.

As such, an CDSS can become an efficient tool in *personalized medicine*, which describes the means to individualize diagnostic and treatment options to what is most beneficial, helpful and – ideally – cost-effective for a given patient (in a given healthcare system). Table 1 lists the key components of the concept of personalized medicine that can help lower costs of healthcare for individual patients and healthcare systems [23]. The translation of this concept into clinical routine is challenged frequently by the complexity of the (training) data and by the need to communicate across specialties, both of which frequently go missing in light of the egos of many healthcare stakeholders.

In response to the promises of personalized medicine, a dedicated Precision Medicine Initiative (PMI) was launched by the US government in 2016 together with a 215 M$ investment [24] of which 70 M$ are dedicated to scaling up "efforts to identify genomic drivers in cancer and apply that knowledge in

the development of more effective approaches to cancer treatment". The main objectives of this initiative resonate with the ultimate promises of precision medicine and include: (1) more and better treatments of cancer, (2) modernization of regulation to facilitate innovative research and translation of research results, (3) creation of large data cohorts with associated effective data protection, and (4) support strategies for public-private partnerships (PPP).

Table 1. Key aspects of the concept of Personalized Medicine, incl. benefits, challenges and opportunities; see also [25].

Benefits	**Consequences**
Improve targeting of (tumour) receptors and signaling pathways	Increasing precision and effectiveness of treatment - potential cost savings for healthcare providers. Expedited and efficient drug development - cost saving potential for pharma industry.
Avoid futile therapies and toxic treatment side effects by tailoring right treatment to right patients	Cost savings for payers, providers and insurances
Existing pilot evidence of increased diagnostic accuracy and therapeutic efficacy	Positive connotation and promotion of concept of personalized medicine in healthcare industry
Challenges	**Consequences**
Include multiple, complex data for decision making	Software investment. Clarify liability issues
Cross-specialty communication (stepping out of comfort zones)	Need for professional engagement and training
Convince all stakeholders of the potential of Personalized Medicine	Communication strategy for benefits
Opportunities	**Consequences**
Tackling *big data*	Draw new knowledge
Cross-specialty training	Similar to an open innovation process with medical stakeholders

1.6 PHARAMCEUTICAL DRUG DEVELOPMENT

Chemotherapeutic drugs make up for a significant portion of costs for managing cancer patients (Figure 3). Typically, chemotherapeutic options are the most expensive therapy options, ranging from 10kEUR to 100KEUR per treatment cycle; a recently introduced immunotherapy costs 12.5kEUR per month [4]). Medicine expenditure forecasts predict that spending on cancer drugs in developed markets exceeds spending on treating other diseases by a factor of 2, or more [4]. The cost per treatment has risen exponentially over the past years serving as an indication of the increasing costs of development of effective cancer drugs. On average, new drug development and market entry cost about 1 bEUR for a process that may take a decade (Figure 7). Most of these costs and the time needed are attributed to early phase development. Frequently, phase II and III trials bring the development to an irreversible halt with millions of Euros wasted without bringing the anticipated drug to the market.

Drug discovery and development is essentially a 4-step process [26]: first, a target for the drug needs to be selected; second, an appropriate molecule that will become the drug linking to the target must be determined; third, convincing evidence must be created that the drug-target interaction is effective and measurable in the context of human biology; and, fourth, demonstrate that the new drug is beneficial to patients. It has been shown that molecular imaging can help expedite drug development [27] and, thus, bring development costs down. This is based on the ability to image and quantify metabolic and signaling pathways non-invasively.

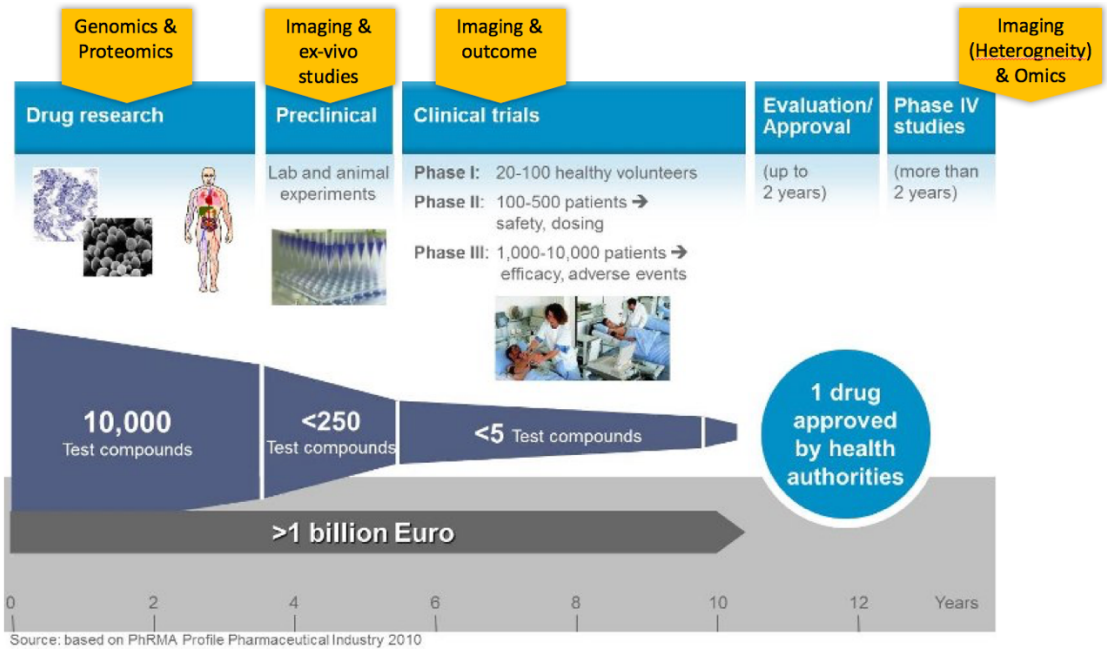


Figure 7. Main road to pharmaceutical drug development. Thousands of compounds need to be screened to select a few hundred for pre-clinical development and testing in animals. Once complete, very few test compounds can be brought into human subjects (phase I-IV). Following successful completion of phase III drugs can be evaluated for market approval. Molecular imaging and machine learning have the potential to expedite drug development and bring development costs down (yellow arrows). From [28].

Therefore, molecular imaging (SPECT and PET) can help depict non-invasively whether a drug reaches the target and it can help quantitate target occupancy, and, hence, drug efficiency. Assuming that pre-clinical tests for that drug have passed, molecular imaging can serve as a gate keeper to expensive phase I-IV studies. Integrating molecular imaging and non-imaging *omics* data as part of a predictive analytics concept (Figure 4) has the potential to move this gatekeeper function further to the left of the drug development process (Figure 7) by generating trained models to confirm or predict congruence of animal imaging studies and ex-vivo histology.

Taking this perspective further, in theory, ML could be used to more effectively select from thousands of compounds those that make sense to label and pass on to pre-clinical testing, by exploring correlations of genomic and proteomic information [8]. ML can be used also post-phase III track and predict tumour biology and response through the treatment, and possibly indicate a suitable alternative drug once a given treatment ceases to be effective since the tumour biology has adapted. A recent meta-analysis has demonstrated that cancer patients who received a personalized treatment – based on a biomarker-based drug selection – had a significantly higher median response rate and a longer median progression-free survival than patients in the non-personalized treatment group [29].

1.7 SUMMARY

The burden of cancer is growing worldwide with an aging population and with more diagnostic options at hand. Research efforts are geared towards turning cancer into a type of chronic disease so as to contain the disease for extended periods of time while providing patients with a high quality of

life. Accordingly, healthcare costs – already accounting for 10% GDP, or more - need to be contained through various measures. Most importantly, means must be provided that help diagnose cancer early and accurately. Non-invasive imaging has proven to provide valuable diagnostic information during the diagnosis, therapy planning and response prediction. Lately, clinical decision support systems (CDSS) have been proposed that entail computer-based ML approaches to include meaningful hindsight from large data cohorts (*big data*) so as to support the expert decision making during patient management. It is expected that these algorithms help increase diagnostic accuracy, provide additional patient-specific information that allows selecting specific therapeutic options faster and more effectively, and, thus, help bring down costs of cancer care by avoiding futile therapies and reducing harmful side effects from (ineffective) treatments. In particular, ML-/AI-based algorithms as part of predictive analytics concepts are expected to advance the concept of personalized medicine, and, thus, promote a paradigm shift in cancer medicine while reducing overall healthcare costs.

2. THE BUSINESS IDEA: A CLOUD-BASED CDSS

This chapter introduces the business idea of the perceived start-up company: a computer-supported, automated tumour characterization tool based on user-provided reference biomarker data. First, the market for similar type solutions will be described. Second, a survey among healthcare stakeholders is presented to further solidify the business idea. Third, the (revised) business model is presented. Intermittent summary perspectives will highlight the most important facts to support the proposed business idea and model.

2.1 THE INTERNET OF THINGS AND CLOUDS

The ability to digitize large amounts of data and the increased connectivity of people via the internet has changed the way we source and share knowledge. The digitization of our business relationships has created "huge business opportunities" and "consumers seem readier to accept digital products than just a few years ago." [30]. Data storage and sharing is linked with the *cloud* - virtual access points that can be reached from any computer and internet point. Starting out as a simple storage solution, the cloud has matured into a business proposition that entails the analysis of large amount of coherent data, also referred to as big data. Major IT players engage in big data and cloud computing. A recent article in the Wall Street Journal points to an estimated revenue of 17 b$ for Amazon, Microsoft and Google together in 2016, which is expected to grow to 30 b$ in 2018 [31]. There is a marked trend for firms to consider cloud-based applications as beneficial for their business; this includes improved agility (68% companies rate this as important), lower total costs (68%), improved sharing of information (66%) and delivery of unique functionality (59%) [32].

The availability of (stored) data through the cloud together with rapid advances in the IT processing speed has expedited the use of ML and AI. A 2016 survey among IT professionals (incl. healthcare IT) demonstrated that 8% users employ ML already and 45% plan to do so within the next 5 y, only 18% have no plans yet [33]. In a way, big data has entered the mainstream; 70% of firms view big data as very important or critical to the success of their business (*vs* 54% in 2014). It provides them with greater insights into their customers (37%), faster time-to-decision (17%) and greater analytics capabilities (9%) [34]. Of note, the core element of this thesis is to present a business idea for healthcare services based on the use of the cloud, big data and machine learning – in the context of oncology patient management.

2.2 BUSINESS IDEA FOR A CLOUD-BASED CDSS

As discussed in section 1.2, timely and accurate patient diagnosis, treatment planning and therapy response assessment are critical for efficient cancer patient management and for containing healthcare costs. This process entails the use of non-invasive and invasive biomarker information, adequately trained medical professionals and access to IT infrastructure, including promising ML-type algorithms. Our business idea is to build a supervised ML (SML) engine that provides predictive analytics as part of oncology patient management (Figure 8).

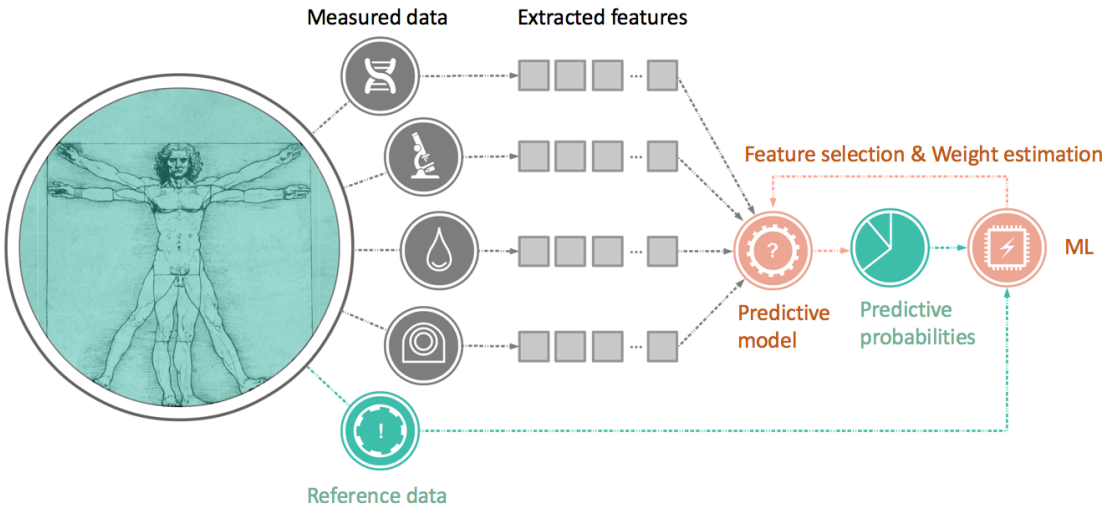


Figure 8. Workflow for the ML algorithm within the CDSS. Based on validated reference data a ML-algorithm is built, whereby various information sources can be used. When providing new information (measured data) the predictive model estimates probabilities for individual input features without the need of a semi-/automated feature pre-selection. Instead, the workflow selects and weights features based on their importance for the decision making. Weights are relative over the entire feature space. (Courtesy of Laszlo Papp, Vienna/AT)

More specifically, this CDSS, shall help medical doctors in the field of oncology in making a diagnosis and tailoring treatment on a per-need basis (Figure 9). Specifically, this CDSS will:

- be able to handle binary (e.g., tumour: y/n?) and multi-class predictive models (e.g., different grades of a tumour),
- build on a multi-layer architecture to automatically perform feature selection and feature weight estimation for the prediction model (Figure 8),
- not require prior information about the features,
- utilize cross-validation to accurately estimate the accuracy and robustness of the predictive model across unknown samples, and
- be applicable to a range of cancer types.

In order to avoid heavy data traffic and bottlenecks from local legal requirements (e.g., need to anonymize data or restrictions to share data at all), the concept is to make users transfer only the segmented tumours to the cloud-based CDSS (following automated anonymization on-site). At this stage we are developing a potential customer base (Table 2) with the following target groups:

- medical doctors, who base their routine diagnosis on biomarker information,
- medical doctors, who seek a second opinion reading,
- pharma industry during drug development and testing (see Figure 7),
- Clinical Research Organizations (CRO) for reporting standardized results of imaging trials,
- (Educated) patients interested in providing their doctors with additional information, and
- Insurances, which may consider paying for a (chemotherapeutic) treatment only if additional proof of receptor/target expression is provided, and
- Radiopharmaceutical companies, which are interested in providing their customers with a molecular contrast agent and a matching automated data analysis functionality.

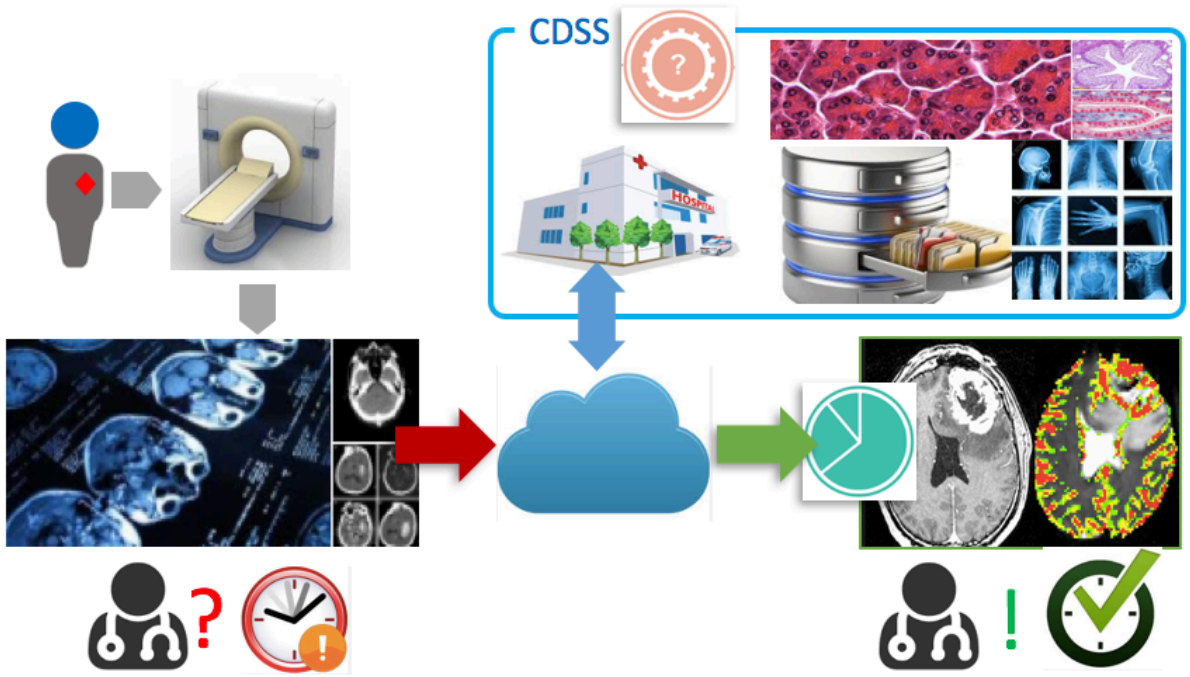


Figure 9. Business model for CDSS: A CDSS is developed based on a validated database of a large cohort of reference data (upper right). This CDSS is made available through the cloud on a need-basis. A medical doctor (lower left) receives diagnostic information from a cancer patient with suspected disease (upper left). This can be from anywhere on this planet. The data are anonymized and fed to the cloud, where the CDSS generates the predictive analytics that are fed back automatically to the doctor. The output of the predictive analytics toolbox can be, e.g., a tumour probability map (right). This service is a pay-per-use model. The CDSS is provided for a specific cancer at the time.

Table 2 provides further details on the added values for each of these customer groups. Added value could be additional information to a client, which could be integrated (and charged for) in different ways in their service offerings, it could be a cost saving potential or an incentive. Target customers are anticipated to benefit (time, accuracy, costs) from the use of a CDSS in light of the information provided by the predictive analytics module. This information includes tumour characteristics (e.g., heterogeneity and expression of specific receptors for targeted therapies) and ultimately also a decision on the presence or absence of disease.

Table 2. Business opportunities and added value for target customer groups for the CDSS. Cost saving potential is relative (+ little, +++ high)

Target customer	CDSS application	Results and added value	Cost saving potential
MD: private practice	Use as 2nd opinion	Confirmatory	+
	Use on need-basis	Lower investment in hard/software needed	++
	Added value	Strengthen profile towards referrals	(+ revenue)
MD: public hospital	Personalized treatment	A priori choice of treatment option	+++
Pharma industry	Drug development	Downsize study groups	+++
CRO	Standardized reading	Additional value offered to sponsors	(+ revenue)
Patients	Added value	Convince their caring physician	(no direct impact)
	Sensitize to sharing	Sharing data = strengthening the ML engine	(no direct impact)
Insurances	Personalized medicine	Use tool for standardized workflows	++
Radiotracer provider	Personalized diagnosis	Use tool for automated, tracer-specific reading	++

The business model is a *B2C model*. It depends on the availability of a validated ML engine. Validation is currently work-in-progress for three types of cancers: breast cancer, prostate cancer and

glioblastomas. Other cancer types will be addressed through new CDSS, which, however, require the set-up and access of validated databases. Options to access these data and to incentivise stakeholders to share their data will be discussed in section 2.6. In the short term, the business (Figure 9) shall be started with service provisions for these three types of cancers, while more reference data for other important clinical indications (see section 2.5) are being collected.

The *value proposition* of our business for an oncology CDSS includes:

1. On-demand, non-invasive risk stratification and tumour characterization,
2. The identification of specific treatment-relevant target structures of whole-body tumour lesions for therapy response estimation,
3. The adoption of ML/AI algorithms based on the integration of anatomical, genomic and molecular information,
4. Operational agility through automatic selection and weighting of features of the input data,
5. Cloud-based service and functionalities for easy accessibility and use, and
6. Scalable service with regards to cancer type, access and image modality.

While existing competitive products and non-commercial solutions mirror individual values from the list above, none of these tools covers the whole range of it. We believe, however, that only through the combination of ML, cloud computing and advanced molecular imaging, such CDSS algorithm becomes unique and helps contain costs in oncology healthcare, and thus, is of interest to a wider range of customers (Table 2).

2.3 MARKET ANALYSIS FOR ML, AI AND CDSS

2.3.1 MARKET TRENDS - IT

The seven most prominent *Technology Trends* can be summarized as (1) Internet-of-Things, IoT, and smart Home-tech, (2) Augmented and virtual reality, (3) Machine learning, (4) Automation, (5) Big Data, (6) Physical-Digital interaction, and (7) On-demand services [20]. System support of handling large volumes of both structured and unstructured data (as part of big data) will continue to rise and the need to secure governance of big data (transfer, access and handling) will increase significantly [35]. In addition, the same report highlights the following aspects that pertain to the business proposed here: (i) customers will demand analytics on all available data, (ii) organizations will demand agile and repeatable use of big data reservoirs (called *data lakes*), (iii) IT architectures will move away from a one-size-fits-all approach to become reconfigurable to evolving needs, (iv) analytics tools need to adjust to the variety of big data formats, (v) big data analytics need to prepare for computation-intensity, (vi) big data is deployed more and more via cloud services, and (vii) business users want analytics at no cost of manual preparation of data.

A recent report highlights the growing demand for computer-support algorithms in healthcare: "… machine learning will displace much of the work of radiologists and anatomical pathologists. These

physicians focus largely on interpreting digitized images, which can easily be fed directly to algorithms instead. Furthermore, patient safety movements will increasingly advocate the use of computer-based algorithms over humans for their inherent auditable validation and working hours-independent capacities." [21].

In summary, the market goes fully digital with the empowerment of big data and cloud services for adoption, also, in healthcare.

2.3.2 MARKET TRENDS – HEALTHCARE IT

Healthcare costs are under scrutiny. Subsequent efforts – in the industrialized world - are geared towards containing costs while permitting technological progress (Figure 10). A recent report by PWC points to six top health industry issues: diet-related health, electronic health records and emerging technologies, volume to value and risk sharing approaches, insurance plans, training of medical professionals and drug prices [36]. Another report by HIT consultants points to the same trends that relate to healthcare cost containment (incl. achieving more value at lower costs) and the adoption of technological advances (incl. AI) [37]. The use of machine learning as part of CDSS is resonated on multiple occasions, also in scientific reports: "… machine learning will improve diagnostic accuracy. A recent Institute of Medicine report highlighted the alarming frequency of diagnostic errors and the lack of interventions to reduce them. Algorithms will soon generate differential diagnoses, suggest high-value tests, and reduce overuse of testing." [21]. Cloud computing in the context of healthcare is on the rise. In 2011, 4% healthcare industry used cloud computing; this number is expected to rise by 20% per year [38].

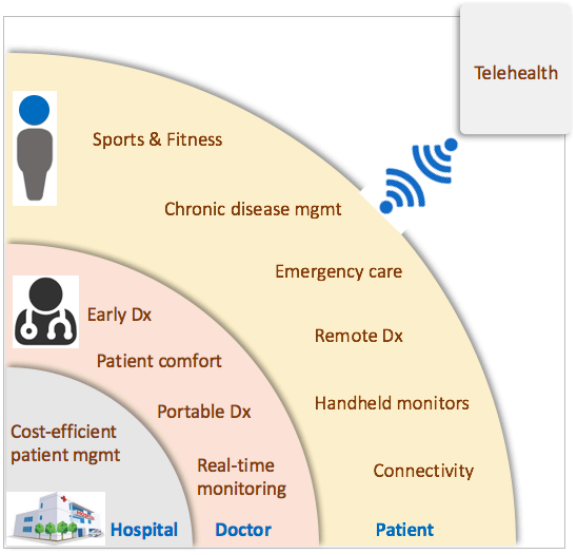


Figure 10. Three levels (hospital, doctor, patient) of Healthcare and related trends in 2017. The onset of technological innovation (real-time and handheld monitoring) generating loads of data that can be assessed for predictive information will help bring down costs in the mid-/long-term.

mgmt = management, Dx = diagnosis

In addition to the diagnostic market, many pharmacology companies start to engage in the cloud. For them, the explosion of available data (e.g., next generation sequencing) renders cloud data storage/access and cloud-based computing an increasingly important aspect of their research and drug development. Commercial cloud vendors have developed pharma-specific clinical research cloud offerings with the goal of lowering the cost and development of new drugs.

In summary, efforts are being made in healthcare to contain the rapidly growing costs. This is facilitated through the adoption of new (monitoring) technologies and the utilization of all diagnostic and biomarker data at hand to render patient-specific diagnoses more reliable and efficient.

2.3.3 MARKET TRENDS - BIOMARKER

Non-invasive imaging has become an integral part of oncology patient management. Molecular imaging, by means of PET, is commercially available since the 1980s. Following the reimbursement policies in the USA in the late 1990s and the success of [18F]FDG-PET imaging in oncology [2], the market for whole-body PET examinations grew rapidly. With the introduction of combined PET/CT systems the sales of PET-only went down while the number of integrated PET/CT systems grew exponentially. In the first 3 years (2001-3) more than 500 systems were sold worldwide. Sales increased further and then plateaued around 2006-8 following reductions in reimbursement rates before picking up again. Today, over 5'000 PET/CT systems are operational throughout the world, with 30-40% and 40% installations being in Europe and in the USA, respectively. Combined PET/MR systems were introduced commercially in 2010. Since then the total number of installations worldwide is 120, which is a factor of 50 less than that of PET/CT. Also, the adoption rate of PET/MR is significantly lower. Together (PET, PET/CT and PET/MR) make for about a 10th of the CT market.

Figure 11 illustrates the number of all PET systems per 1 mio capita in various European countries. The workload per PET system varies with the country and installation. For example, the annual throughput ranges from 600 (Switzerland) to 1'500 (UK), 2'000 (BeNeLux) and 2'500 (Italy, France). This compares to about 1.6 mio PET examinations performed per year in the USA (*vs* 23 mio CT examinations). Assuming an average annual workload of about 1'000 patients/year, a total of 6 Mio PET exams is performed each year [39]. This subjective estimate is very close to the total number of PET examinations performed in 2016 (6.2M) as derived from Figure 12. The same data project a growth rate of 7%-12% onwards towards 2021.

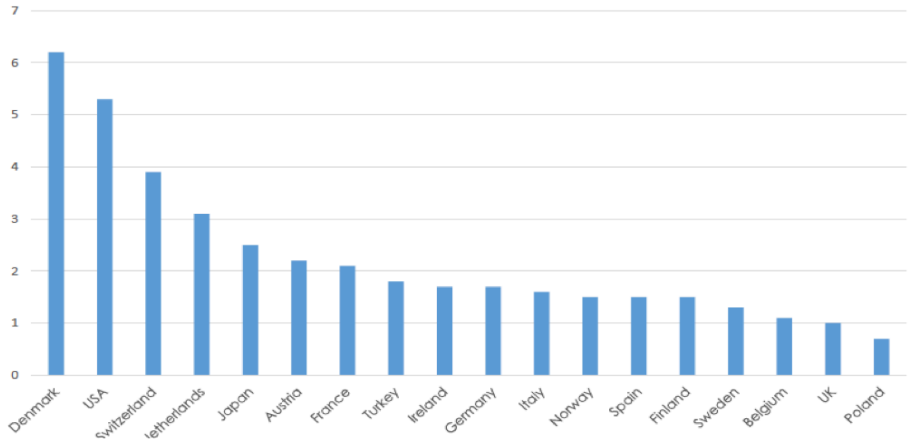


Figure 11. Number of PET systems installed per 1M people in European countries (2014).

Data courtesy of Anthony Stevens, UK.

[2] FDG describes glucose labelled with radioactive 18F-fluorine; glucose is a source of energy consumption for the body; tumours require a lot of energy and, therefore, they can be picked up by an increased FDG signal on PET images.

Of note, 90% of PET examinations are performed with [18F]FDG as the tracer-of-choice. It is assumed that around 10% of the PET based examinations are concordant with the availability of a biopsy specimen. However, less than 10% of patients undergoing a biopsy procedure also undergo a PET-based imaging examination as part of their diagnostic work-up [40]. Still, non-invasive real time tumour characterization adds to the diagnostic accuracy and, thus, will improve therapy guidance and monitoring. The CDSS engine proposed in chapter 4 is able to provide these means for an improved personalized medicine approach to cancer patient management while helping to reduce costs through, for example, avoiding biopsy procedures where applicable.

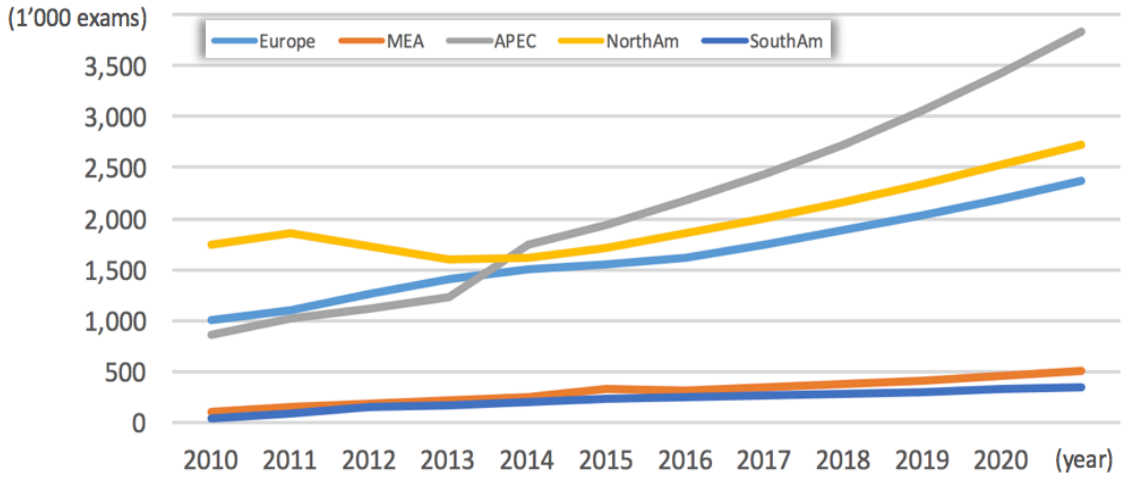


Figure 12. PET and PET/CT examinations in main regions worldwide from 2010 to 2021; numbers are estimates from 2016 onwards. Data courtesy of Anthony Stevens (http://www.medicaloptions.co.uk).

In summary, throughout the past 20 years, PET has established itself as a routine clinical diagnostic modality in the management of patients with oncological as well as neurological and cardiovascular diseases. The majority of PET examinations is performed for oncology indications with radioactively labelled glucose (FDG) as the tracer of choice.

2.3.4 MARKET CHALLANGES

Major challenges and barriers for an ML-based CDSS in the cloud include:

- *the need to ensure privacy and security of the image data and health records.*

  This entails automated measures to anonymize all data used for training the ML algorithms and for user-specific input data. Mandates the ability to handle DICOM tags of data.

- *Variations in national legislation in view of confidential and private information and sharing thereof.*

  Data exchange and access to cloud-based services may not be permitted by local legislation, hospital politics etc. Here, a solution that avoids transferring entire image data sets to the cloud are preferred.

- *Reliability and accuracy of the CDSS service.*

  ML-/AI-algorithms must be trained sufficiently and validated. This entails the availability of and access to a sufficiently large training data set for a given CDSS application [41].

- *Integration of CDSS into local workflow.*

  Local sites must be prepared to adopt CDSS, to ensure optimum incorporation of CDSS into patient management on site, and to accept the consequences (e.g., dismiss biopsy or deal with conflicting tumour indicators). Warrants staff training and optimized workflows.

- *Ensure data portability.*

  In agreement with the major healthcare trends, biomarker will present with various data formats that need to be handled automatically. This entails investments on the developer's side.

The biggest market challenge may yet to come. While in social networks, people are prepared and motivated to share all sorts of (very) personal information, a similar readiness is not yet seen with patient data. Sharing important biomarker information and associated information on diseases, clinical management etc. will be of essence to leverage data lakes for predictive analytics. Thus, business models on CDSS hinge on the accessibility of *data lakes*. A recent report in HBR highlights restrains on the willingness to share patient data as a current obstacle to advancing cancer care [42]. Other barriers, not to be discussed here, include the "black box" character of ML algorithms, the general resistance of imaging experts who see ML and AI as a threat, the unresolved legal implications of rendering an incorrect diagnosis from CDSS analytics, to name a few [43].

2.3.5 MARKET GROWTH

Market revenue from medical image analysis software, which comprises CAD, quantitative analysis (e.g., size measure) and decision support tools is predicted to grow by 20%, or more from 2018 to an estimated 650M$ in 2018 [44]. Analysts predict that by then 30% of IT providers will employ cognitive (ML and AI) analytics on patient data [45]. The onset of predictive analytics may be significant in the years to come, but the prospective validation will require several more years of data collection [21]. The market for cloud-based computing is expected to grow by 28% per year [46]. Between 2015 and 2018 the three big internet rivals (Google, Microsoft and Amazon) alone predict revenues of 10b$ and 31.5b$, respectively [31]. In comparison, worldwide spending on public cloud services will grow at 19% from 70b$ (2015) to 141b$ (2019) and 173b$ (2026) [47]. Spending on cloud IT (CAGR 15%) will gradually replace spending on traditional IT. By 2020 penetration of Software-as-a-service (SaaS) *vs* traditional SW deployment will be over 25% and packaged SW will shrink to 10% of new enterprises, thus, reflecting the aforementioned trends [20,35]. Main cloud providers include Agfa HC [48,49], CareCloud, Dell, GEHC and Merge HC (bought by IBM in 2015 [50]).

Of interest, growth in revenues is mirrored by a growth in venture funding. Digital Health funding grew at an annual rate of 31% from 2008, to a total of 2.8b$ in 2013 [51]. Growth of funding is expected to continue to 6.5b$ (2017) with the majority of funds being allocated to "creating a seamless physical and digital experience" and to the "aging and chronically ill population". Funds are directed towards: infrastructure, treatment (incl. personalized medicine), engagement and diagnosis. A

recent analysis of venture capital investment into companies offering diagnostic analytics reported 52 deals between 2014 and early 2016 with a total investment of 265M$ (average deal size: 5.1M$, max investment: 31M$) [52]. Funding of dedicated medical imaging AI companies between 2014 and 2017 grew also, to a total of 114M$ with an average deal size for AI start-ups of 2.6M$ (and max order of 12M$) [53].

The global healthcare cloud computing market is expected to reach 9.5b$ in 2020, up from 3.7b$ in 2015, growing at a CAGR of 20.5%. The market is expected to be dominated by North America, followed by Europe, Asia, and the Rest of the World, with Asian markets expected to have the highest growth rates [50,54]. Zooming into the specifics of the *radiomics* (Figure 4) service market, revenues are expected to exceed 500M$ in 2021, up from 180M$ in 2015 [55]. Growth is expected to be significant despite the lagging clearance by health care authorities and the yet limited areas of application (e.g., single imaging modality, single disease).

The global diagnostic imaging market is estimated to grow with a CAGR of 6% between 2015-20 [56] and the global market is to reach 33b$ by 2020. The global PET system market will grow at 4.7% CAGR until 2026 [57]. North America is likely to dominate the market, while the fastest growth is expected in Asia. The report indicates that the hospital market will be in balance with the diagnostic centre market (33%-36% each). Of interest, the global isotope (i.e., tracer or "molecular contrast agents") market, the fuel for the nuclear medicine examinations, will grow at 9% CAGR until 2020 [58], thus, attesting to an anticipated stronger utilization of the installed base of nuclear medicine imaging systems.

In summary, there is a healthy market growth of IT, cloud-based SaaS and healthcare IT as measured by revenue and venture investments. This is mirrored by the market potential for molecular PET imaging, with an expected annual growth of PET-based imaging procedures of 10% (7-12%).

2.3.6 MARKET OFFERING AND COMPETITION

Considering the rapid technological progress in IT and the growing interest in CDSS, commercial enterprises offering CAD and CDSS services are plentiful. A desk research study was conducted between 10/16 and 03/17 in order to gather an informative perspective on the market and competitive products. *Methods*. This study was based on composing a list of companies that offered solutions in the context of "healthcare", "IT", "cloud" and "predictive analytics". Entries to this list were determined as follows. First, an extensive web search was launched using the following key words: "healthcare", "imaging", "cloud computing" and "oncology". Second, a number of reports on trends in healthcare was identified that listed individual companies matching the above key words [14,53, 55,59,60]. The list of companies was amended by companies that the author knew personally from past and ongoing collaborations. In total, the web portals of about 70 companies were studied. Of these, 43 were included in the final list of healthcare companies that employ ML or AI (Appendix 1).

Each company was assessed on eight accounts along the lines of the value proposition of the CDSS (section 2.2). Here, "CAD", for example, was considered an entry-level engagement to computer-supported diagnosis that indicates some know-how in the field but that is not sufficient to support a predictive analytics model. Likewise, "image viewing" related to any advanced offerings of image display functionalities that could be easily added to any CDSS. "Lead users" are indicative of an existing customer base that is not necessarily related directly to innovative product development. Table 3 summarizes all key specifications for this assessment. A scoring system (1-lowest to 10-highest) was used based on review of the information provided on the firms' web pages.

Table 3. Scoring model for market analysis of healthcare companies engaged in predictive analytics. Scores ranged from 1 (not existent) to 10 (complete fit).

Specification	Reasoning
Hybrid Imaging	Is the company engaged in multi-modality imaging (**Error! Reference source not found.**) for providing biomarker information?
Digital Pathology	Is the company recognizant of the potential of pathology-based biomarker information (as reference standard and input) for disease characterization?
CAD	Does the company offer solutions to automated disease characterization (e.g., tumour size)?
Machine learning	Does the company engage in adopting AI and cognitive data mining for predictive analytics?
Cloud	Does the company provide cloud-based services (e.g., storage and processing)?
Image viewing	Does the company possess know-how in dealing with various medical image data formats?
Tumour characterization	Is the company in pursuit of product offerings that enable medical professionals to more accurately and easily characterize individual tumours for improved therapy pre-selection?
Lead user	Is the company known for lead users who help advance healthcare into the direction of image data mining and oncology?

Results. Figure 13 summarizes the subjective scores of the assessed healthcare providers. The figure includes only the scores for "hybrid imaging", "digital pathology", "ML", "tumour characterization" and "cloud". It is clear that none of the assessed companies spans all areas of engagement equally well. Few companies engage in tumour characterization, which is considered the ultimate application of predictive analytics in the context of oncology patient management.

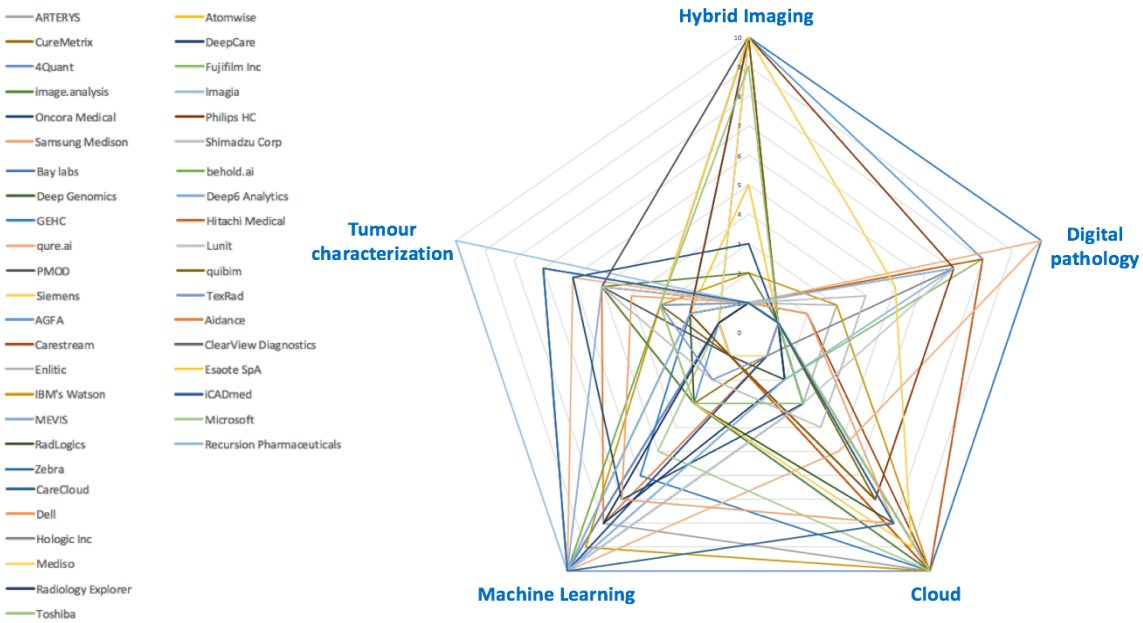


Figure 13. Spider graph indicating the scoring (1-min fit, 10 – max fit) of the assessed healthcare companies with regards to their capabilities in predictive analytics (Table 3). Of note, only five parameters are included; see Appendix 1 for the full listing. Many firms engage in ML and the cloud, but very few also offer tumour characterization.

Most of the companies do engage in ML, but only few of those utilize hybrid image information (**Error! Reference source not found.**) or biomarker information from pathology (Figure 2) to train their ML engine. A reasonable number of companies engage in cloud-based IT services, but this engagement is yet short of the trends described above.

Based on the information provided in their web presence, the following companies claim a convincing engagement in predictive analytics, imaging and oncology and, therefore, are considered *direct competitors* to our venture for the very close similarity of their product offering:

- *Imagia* offers a combination of AI and liquid biopsies for the detection and quantification of cancer changes – although little detail is provided as to the core process [61],
- *qure* provides healthcare professionals with deep-learning solutions that help physicians during diagnosis – although this appears limited to anatomical imaging and biopsy sections [62],
- *Lunit* provides AI algorithms for tumour description on anatomical imaging (only) and including tumour probability maps [63], and
- *Shimadzu* launched first R&D support initiatives for genotyping as part of a deep learning initiative for cancer lesion characterization in breast cancer [64],

Indirect competitors include companies that engage in AI and ML, but without an immediate focus on oncology. Here, a number of companies engage in AI for lesion detection in mammography [65-67]. Lately, there is a lot of press about healthcare dinosaurs (Siemens, GE etc.) investing into a HealthTech. Siemens recently purchased Germany-based company called NeoOncology for their offering in analysing therapy-relevant genome alterations for individual cancer treatments [68]. GE announced a 500M$ investment into data and image analytics (compared to 18b$ revenue stream in 2016) [69]. IBM purchased MergeHealthcare for 4b$ and announced MEDIAL SIEVE [70] as one of "longer range initiatives" [71] with a 50-100M$ investment that includes ML and patient-centric tumour characterization. Thus, major vendors are in the process of positioning themselves as *central platform providers*, so as to "leverage their clinical expertise and modality hardware footprint to expand the breadth of their IT offerings, including analytics …" [69]. These new solutions are termed *Agnostic Clinical Enterprises*. These global healthcare providers are considered *future competitors* for now, given the lack of visibility in oncology CDSS as described in Figure 9.

In conclusion, desk research demonstrated the availability of numerous, commercially-available IT solutions for the automated and computer-supported diagnostic decision making as part of the oncology patient value chain. However, the majority of these algorithms falls short of the big data potential in light of advanced diagnostic imaging. There is an obvious trend towards employing the cloud as a media for storage and data sharing. Still, today, the number of direct competitors for a cloud-based CDSS for oncology patients is limited, thus, offering a window of opportunity for our business model.

2.4 BUSINESS OPPORTUNITY

Several trends in the IT and healthcare industry provide new business opportunities. In general, *digital healthcare*, for example, is considered a "huge business opportunity", with an increasing customer readiness to accept digital products [72]. Through the growing adoption of telemedicine, predictive analytics and early diagnosis of diseases are expected to deliver lower health care costs (Table 4), for example, through tailored patient admission schemes. However, regulated healthcare systems will likely require lengthy dealings with the challenges of accuracy, security and privacy of the data.

Table 4. Selected market trends [20,35,36] and resulting opportunities for Cloud-based CDSS.

Market Trend	Business opportunity	Cost savings potential
IT		
Rising demand for analytics of existing data	Offer tools for predictive analytics to support medical decision making	Faster diagnosis. More accurate diagnosis (avoid repeat scans and ineffective therapies).
IT architecture must adapt quickly to changing customer needs	Cloud-based analytics models for need-based access	No license fee. No hardware maintenance. Pay-per-use models.
Raising interest in Cloud services	Provide Cloud solution	Join marketing trend. Lower fixed costs.
Users do not want to engage in manual preparation of data	Automatic feature selection and weighting in AI	Customers spend less time upfront on their data
Healthcare		
Cost containment	(Accurate) Analytics on pay-per-use	Pay-per-use model.
Contain drug prices	Include predictive analytics in drug development	Avoid expensive therapies when ineffective.
Biomarker		
Growing number of PET(/CT, /MR) systems	Offer predictive analytics together with systems	Liaise with imaging vendors and package flat-fee services.
Growing interest in incorporating multiple biomarker information in decision model	Offer scalable predictive analytics system	Offer customers to share data in return for reduced fees.
Healthcare and insurance providers request prospective tests for targeted therapies	Use predictive analytics to assess tumour receptor status prior to therapy [73]	Avoid futile therapies. Engage pharma so as to reduce minimum group sizes during drug tests [28].

In addition, the CDSS business model suggested here (Figure 9), has the potential to be transformative [74] in the sense that it combines *innovation* and *market trends* for a potentially sustainable and scalable value proposition. As such, this CDSS may lead to a long-term change of the healthcare industry in the way that key stakeholders make use of this service instead of stand-alone imaging. Figure 14 illustrates this further through a correlative network approach to the CDSS. The more innovative features are integrated in a business model, the higher the chances of that model to be successful and transformative. Specifically, the CDSS business model addresses five of the six key factors of a successful innovation and, therefore, has a higher chance of succeeding [74].

Personalization is provided through the provision of a patient-specific tumour characterization that can be picked up by doctors for treatment planning and by patients to solicit a second professional opinion, or to provide their treating physicians with more helpful information. *Asset sharing*, as a means for cost reduction, can be facilitated in two ways. First, we foresee providing our ML output to

interested users in return for their data (they test the algorithm on their data, we get their data and scale our value proposition). Second, we can provide *sparring partners* an interface to our ML engine and data base in an effort to continuously cross-check performance and innovation on the current state of service. *Usage-based pricing* is engrained in the SaaS model of our cloud solution. *Collaborative ecosystems*, as a means to make a business more sustainable, come with engagements in cooperation with patient advocacy groups and pharma/CRO. And finally, *agility*, is seen in the ability of the medical doctors to include the CDSS-based tumour information in their patient-specific treatment planning, thus, getting ready to move outside and beyond existing tracks.

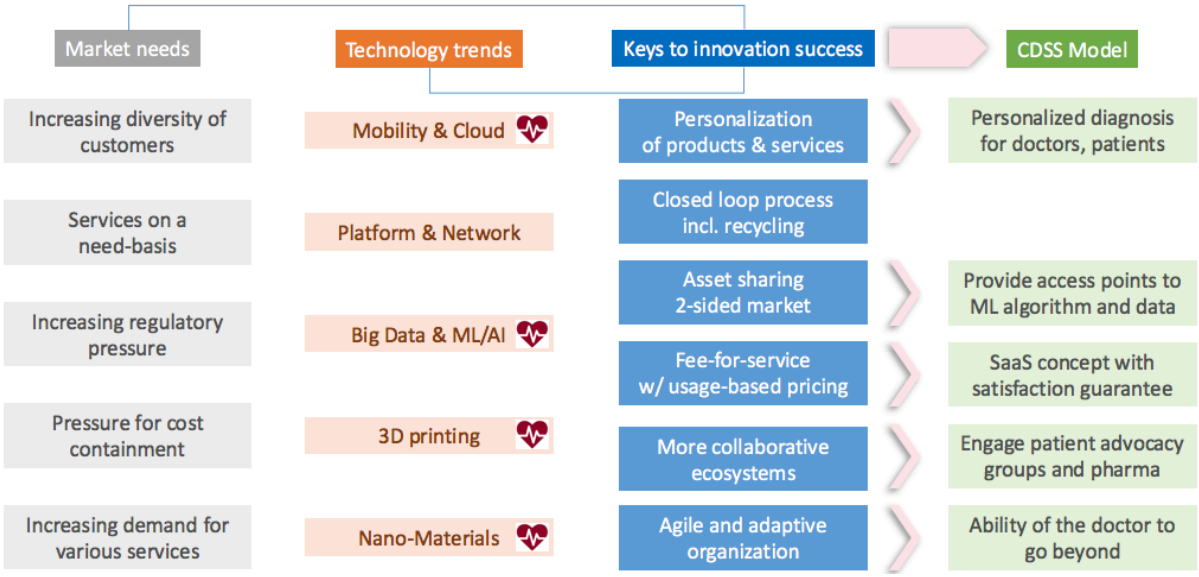


Figure 14. Our CDSS business model matches 5 of 6 key features to successful innovation when interlinked with market needs and technology trends [adapted from [74]. Features characterizing innovation success (blue) link recognized market needs (gray) and technology trends (orange), of which the marks a relevance for healthcare. Of note, the market needs are reflected in Table 4 above, while technology trends were discussed in sections 2.3.1-2.3.3.

In summary, cancer patient management is known to benefit from complementary biomarker information. When combined with other diagnostic information as part of a *big data* concept, a number of business opportunities arise from offering computer-based tools for highly accurate and predictive information on the investigated tumours. Such services can be rendered as a pay-per-use, cloud-based computing. Beneficiaries are primarily patients. Cost-savings are located with medical imaging centres and hospitals, pharma, CRO, insurances and patients. Through the integration of a number of key factors to successful innovation, the CDSS business model is likely to become successful.

2.5 STAKEHOLDER ANALYSIS AND BUSINESS VIABILITY

Following the derivation of a business opportunity (section 2.4) a survey was conducted among potential stakeholders of cancer patient management. *Methodology*. The survey (Appendix 2) consisted of 2 demographic questions and 10 questions related to a cloud-based CDSS along the lines of the value proposition laid out in section 2.2. The survey was conceived to be web-based and the

questionnaire were prepared in GoogleDocs [75]. Table 5 recaps the questions asked and provides some hindsight to the reasoning. The link to this survey was promoted through various media relations (European Society of Hybrid Imaging, AuntMinnie Radiology Services) and personal invitations using the author's email lists and LinkedIn network. This directional field research for input was aimed at healthcare professionals who either reported clinical images or were engaged in producing, adopting and distributing imaging equipment. This survey was sent primarily to imaging experts and *not* to pathologists, which can be seen as a limitation for the validity of the responses.

Table 5. Web-based survey on cloud-based CDSS (see chapter 4).

Question	Reasoning	Implications
Demographics		
What is your professional background	Separate doctor, IT specialist and other	NA
What is your place of work	Gather info on public vs private practice	NA
Strategy and use-case		
Would you employ a cloud-based CDSS?	Gather general interest and readiness for such a product	If *no*, then change value proposition.
Would you be willing to pay for such a service?	Gather willingness to invest (pay-per-use?)	If *no*, then adapt pay-per-use model.
Would you consider this service if the use of a selected treatment compound (e.g., chemotherapy) was linked to the proof of therapy target expression?	Gather willingness (change thereof) if pre-therapy personalization of treatment was required	If *yes*, then reach out to pharma/insurances (marketing) If *no*, then reinforce current direct marketing strategy.
Would you consider this service without a CE certificate?	Check on adherence to legal requirements	If *no*, then start-up investment must include certification fees.
Please provide the 3 most important tumour entities for which you would use this service?	Prioritizing indications	Focus on training the CDSS for high-priority tumours first. Focus marketing plan.
What imaging methods would profit most from this service?	Prioritizing methods	Focus on training the CDSS for first-line methods. Focus marketing plan.
Does your place of work permit the transfer of image data?	Check on IT structure (large amount of data) and on-site firewall restrictions	If *no*, then provide customers with interface to transfer feature vectors only.
Would you be willing to sharing data for the sake of training a new model (kind of community service)?	Check on growth potential for such a product	If *yes*, then leverage data sharing with customers for building reference data base. If *no*, then build alternative incentivized data sharing schemes.
Are you using similar type software already at your site?	Check on competing products	If *yes*, then focus on value proposition and pricing. If *no*, then leverage first-mover advantages.

Results. Between January and May 2017, 58 anonymous responses were collected (multiple responses were permitted). Most of the responders were imaging experts (60%). Other backgrounds included imaging physicists (21%) and IT specialists (7%) and other (26%). The majority was employed in public hospitals (62%) followed by other (industry: 33%, private clinics: 5%). Most importantly, 86% responders were willing to consider cloud-based services as part of a clinical decision support. In general, the responses were encouraging for our value proposition. In more detail,

- 2/3 responders would pay for such a service (either fee-for-service (38%) or flat-fee (33));
- 90% responders would use this system if their choice of targeted cancer treatment was dependent on the result;

- 38% responders would mandate a CE certificate for this service; 40% would wish for it, the rest (22%) would not require such a certificate; and
- 90% responders have no such or similar CDSS at hand for their routine work; only 3 sites reported on in-house developments within a research-type setting.

Figure 15 provides a summary of responses in favour of a given imaging modality that would benefit most from the use of a CDSS (Figure 9). Here, the majority voted for PET/CT and PET/MR followed by CT, attesting to the engrained perception of *radiomics* as a current trend in healthcare. When asked about the most important tumour entities for which the stakeholders would employ such a CDSS the responses varied fairly. The most frequently cited indications were: lung cancer (29), breast cancer (22), prostate cancer (16), colorectal cancer (9) and other less significant mention of brain tumours, melanoma, lymphoma, neuroendocrine tumours and liver. Of interest, these priority applications resonate well with the relative expenditures for cancer care [76]: breast cancer (13%), colorectal (11%), lung (10%), lymphoma (10%), prostate (9%) and brain (4%). Furthermore, breast imaging accounted for 25% of the market for image analysis software, incl. computer support systems in 2016, with cardiology and neurology being the runners up [77].

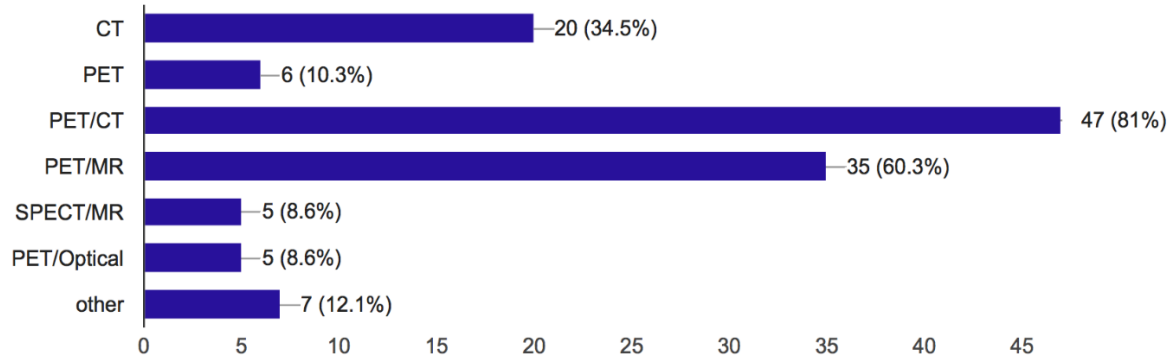


Figure 15. CDSS survey: %responses to which imaging modality would benefit most from a cloud-based CDSS. The majority of responses was in favour of PET-based hybrid imaging (PET/CT and PET/MR).

The survey probed the willingness of the stakeholders to partake in scaling the initial value proposition to other tumour entities. This would mandate access to additional data cohorts that can be used to build a new ML algorithm. Of all responders, 28% would support such product developments through prospective sharing of their non-/imaging data, while 31% would consider it and another 33% would make it conditional. Anonymized image data could be shared easily (59%) and possibly (37%).

Despite the general willingness of the interview partners to share their data, the general willingness of users to do so is limited. A recent HBR article laid out opportunities for cancer researchers to learn from direct-to-consumer companies [78]. The authors state that while many patients share personal data through all kind of social platforms they remain hesitant to share their health data. Two strategies to entice patients (and stakeholders) to share their data entail *storytelling* and *value creation through membership programmes*. The first option gears towards a content-driven marketing campaign (chapter 4) while the second could entail a credit system for CDSS use in return for a data pool

shared. The need to enhance data sharing for the benefit of enlarging the *data lake* has been pointed out elsewhere [5], with the same report eluding to the need to incentivize patients to share their data. This may be supported by ongoing efforts to provide cancer patients with web-based tools for patient navigation and self-monitoring that can be used to source that information for the purpose of building even stronger predictive analytics models. These challenges will be addressed in the marketing plan (chapter 4). In general, an appropriate incentive system must be conceived to help expand on the available training data and to motivate early adopters to use the CDSS system even without a CE label while sharing their data even for the benefit of developing even more reliable ML engines.

In conclusion, this web survey supported the hypothesis that a cloud-based CDSS would be of interest to stakeholders involved in oncology patient management. Moreover, no similar (commercial) solution was available and used on-site at any of the responding centres. There is a general willingness of the stakeholders to engage in such services and to support further developments, and users from the PET/CT and PET/MR camps may be good first target customers. Nonetheless, the importance of a CE-label for a CDSS was highlighted, and will be addressed through early investment into a quality management system for the company.

2.6 UPDATED BUSINESS MODEL AND VALUE PROPOSITION

We identified *cost containment* as the key market need in healthcare. Our business model of a pay-per-use CDSS for advanced tumour characterization addresses this need (Table 2). Desk and field research of the market further supported this type of B2C model. Therefore, no major adjustments of the actual model are required just now (Table 6).

Table 6. Original business idea and updates following desk and field research.

Original	Update	Reasoning and comments
Business idea		
Pay-per-use	Pay-per-use	Acceptable, no change needed
Market segments		
Medical doctor Pharma and CRO	+ Patients + PET tracer providers/distributors	Incentivized sharing for building ML New sales channels
Marketing strategy		
Direct B2C	Focus on MD with access to PET/MR Lead academic users Partner with global player	High-growth potential Visibility and input Seed investment and sales channels
Operations plan		
1st stage: no CE label, 2nd stage: CE	CE label by year-2	Need for higher seed investment
Risk management		
Known risks	+ CE label requirement higher costs	Seek early investor and grant support (PPP?)
Variability of ML engine	Test multi-centre data	Image data from different centres/ systems may yield different patterns or information, thus, causing a variability of the prediction tool
Financial plan		
Fast profits	Fairly fast profits	Balance with first mover advantage (must grow fast)

However, field research indicated a preference (and need) for a CE label of the CDSS. Only 22% responders would use the cloud-based CDSS without a CE label. The CE certification is a generally costly and time consuming procedure. This was now made a priority and is reflected in the business plan (chapter 4) through the added costs for a quality manager software engineer (50%) for year 1-2.

A major risk identified is the lack of large cohorts of reference data. Data sharing is problematic. However, the more reference and training data are available, the better the SML engine and the more applications the SML engine can be trained on. There is "some evidence that participation in research benefits participants. Increases in participation in clinical trials in the context of specialist care have translated into better outcomes at the population level." [79]. Therefore, we plan to roll out the CDSS product to academic research centres in an attempt to generate large cohort evidence of the benefit of the CDSS, and we plan to start early in liaising with patient advocacy groups in an attempt to entice them to share important data that help build the SML engine (chapter 4: Marketing). Even when data are shared, differences in the acquisition and image reconstruction may introduce a variability in the prediction analytics, thus, leading to a limited robustness. In order to evaluate this effect, we will analyse retrospectively cohorts of image data from the same tumour type but different patients (sourced locally), and measure relative differences in the output of the ML engine. This analysis may delay the deployment of a commercial product offering by 6 months.

Pharma industry, CROs and insurances have been identified as potential target customers. We will consider directed efforts in communicating with these three stakeholders on potential use case scenarios for our CDSS in the context of their services. This requires an increase in the marketing budget but may help venturing new markets or adapting our product offerings (chapter 4: Marketing). Lastly, portability of (training) data requires further research and investment prior to rolling out the CDSS platform. We will aim at addressing this point more rigorously prior to starting the ASO. Table 6 summarizes the main takeaway points from the original strategy and its revision, which will be reflected in the business plan in chapter 4.

3. DEVELOPING A START-UP STRATEGY

This chapter starts with a theoretical introduction to new ventures / start-up's and their strategy. This includes a reflection on various factors influencing new venture creation and its success factors. In particular, the main developmental phases for an Academic Spin off (ASO) will be discussed. The theoretical background will be complimented by the results from open interviews on strategic planning prior to/during start-up that were conducted with selected CEOs of start-up healthcare firms. Outcome and teaching points will be used to fine-tune of the business plan for the perceived ASO (chapter 4).

3.1 START-UP AND ENTREPRENEURSHIP

3.1.1. START-UP AND GESTATION

Many people like to leave a footprint. They do so through writing books, composing an opera, teaching students, researching phenomena and alike. Others like to turn an idea into a product that can be offered and - ideally - sold to other people, for the inventor to make a living. The reasons for an individual to turn either way, or to do nothing are manifold and the framework for analyzing the creation of a commercial entity is very complex. Numerous studies have been published on this topic and yet there is a residual myth about people who have the will to become entrepreneurs. Their mindset shall be discussed in more detail in section 3.1.2.

Entrepreneurs create ventures or engage in them. Ventures are created for one ultimate reason: to generate value. Whether this value is monetary, tangible or intangible depends on the causes of the creation of that firm and the entrepreneur. These causes can be complex, as discussed by Gartner in 1985 [80], who points to an interplay of the individual entrepreneur, the environment, an organization and the entrepreneurial process, also calling this "the four dimensions of venture creation" (Table 7).

Table 7. Selected key variables in new venture creation regarding the individual entrepreneur, the business environment, the organization and the process of creation.

Individual	Environment	Organization	Process
Locus of control	Access to incubation funds	Cost structure	Act on business opportunity
Perseverance	Culture/bureaucracy	New service/market/product	Gather resources
Curiosity/creativity	Security	Political landscape	Create product/service
Demographic background	Access to labour force		Legalization of firm
Risk taking propensity	Entry barriers		Societal embedding of firm

Here, the *entrepreneur* is the key figure and, many times, the lead in the firm creation. The lowest common denominator for entrepreneurs is the drive to achieve, the intent to exert control over personal actions and a certain affinity to taking risks (see also section 3.1.2). The *environment* is described as a set of external conditions for the entrepreneur to relate to; they can be supportive or not. The *organization* is related to the value proposition and product of the new firm, and as such, is indicative and determinant of the entrepreneur's background. Finally, the *entrepreneurial process*

attests to the observation that setting up a firm is a temporal process that is affected by multiple actions.

These four dimensions span a continuum in which a new firm can be created. This creation process is often more complex than just putting an idea to work [81]. The creation of a new firm can be described simply as a 2-phase process [82]. First, the founding process extends from *conception to birth*, also referred to as "screening process ahead of a go/no-go decision" (p. 140 in [83]). The following, second, phase is called *post-birth period*. The length of these phases varies with the firm and the key events of the incubation process (phase 1) can take place in any sequence; not all key events are required for gestation. Nonetheless, the most common initial event is the *personal commitment* (Figure 16, *PersCom*).

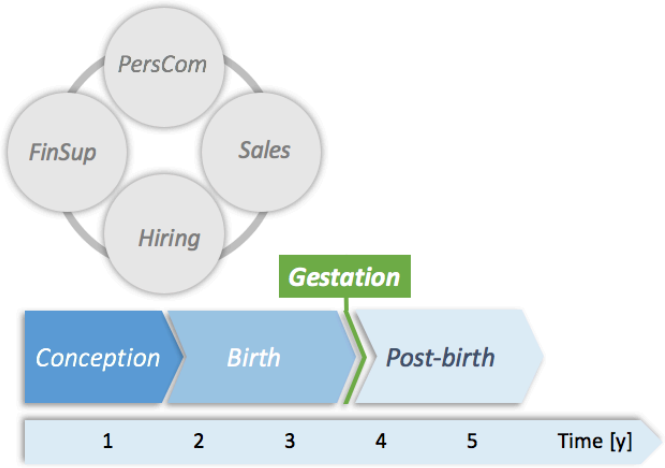


Figure 16. Timelines and processes during start-up. Phase 1 (incubation) mandates at least one of the key events (PersCom, FinSup, Sales, Hiring) to take place. Nine out of 10 firms report a gestation period of 3-y, or less, with a range from 1-mo to 10-y [80].

PersCom = Personal commitment of time and resources; *FinSup* = External financial support; *Sales* = First revenue; *Hiring* = first staff.

Many studies point to the importance of the commitment of the (nascent) entrepreneur [78,80,82]. Carter et al could show that activity profile during the gestation period is an indicator for the success of the start-up [84]. The more activities a nascent entrepreneur would engage in the more likely the start-up firm would be a successful [85]. These activities include efforts directed at the start-up organization as well as toward making the start-up real to the outside world. The less active an entrepreneur is, the more likely the start-up will not get off the ground and remain in a "still trying" phase or be moved to a "giving up" state [84]. However, more research was suggested by the authors as to understand how much planning (*thinking*) was done by successful nascent founders prior to acting (*doing*).

3.1.2. FOUNDING ENTREPRENEUR

Entrepreneurs in general are strongly-minded individuals with a set of "connectivity skills" and "discovery skills" [81] that may lead the individual to a strong business commitment. Entrepreneurs at the stage of a *founder* must exhibit an even broader set of skills and personal traits that can be leveraged during the gestation period (Figure 16). While in larger firms, these skills and traits can be shared among several managers, in a start-up setting, a single entrepreneur most frequently must exhibit all of them as one individual.

The set of skills and traits correlates positively with the success of the start-up [85]. In the case of intellectually challenging product offerings in start-ups, the following entrepreneurial traits were identified as key: education and experience, internal locus of control, clear business concept and sweat equity. Entrepreneurs should also have the ability of swift *opportunity recognition*, which is said to describe a mental ability of "recognizing meaningful patterns in complex arrays of events or trends" [86]. Gatewood and colleagues take this concept further towards identifying specific cognitive factors that set successful entrepreneurs apart from those "trying". They were able to show that successful entrepreneurs have a *cognitive orientation* that supports their "persistence in entrepreneurial activities in the face of difficulties" [87]. In other words, it is not only time but perseverance that entrepreneurs must bring to the start-up process. This trait should be combined with the ability of the entrepreneur "to offer … explanations for their plans for getting into business". In short, "attributions matter". Table 8 lists the most important skills and traits of a successful start-up entrepreneur.

Table 8. Entrepreneurial traits and skills that promote success of a start-up; in alphabetical order

Traits and skills	Effects and benefits
Attribution	The ability to express oneself clearly
Education	Positive influence on profitability
Experience	Product related experience is generally more valuable than management-related experience
Locus of control	A healthy belief of being able to control the outcome of an action
Opportunity recognition	The ability to identify meaningful information in a complex environment
Perseverance	The ability to adapt along the planned process in view of un-/solicited challenges
Risk taking	Readiness and ability to deal with un/foreseen risks along the developmental path of the firm

Nascent entrepreneurs have a vested interest in making their business a success. However, there is no simple means to measure the performance, and hence the success of a start-up. Jo and Lee chose to employ *profitability* and *growth*, and assess their correlation with the background of the entrepreneur [88]. Based on their study of 48 Korean start-ups they were able to show that education was correlated with profitability but not growth. Interestingly, a background in social sciences added to profitability while a background in natural sciences added to growth, thereby attesting to the close link of science and innovation. The authors were also able to show that prior managerial experiences were less promotional to the performance of the start-up than experiences related to the actual product, which resonates with prior studies [85].

Start-ups typically engage in very innovative products or services. In that case, the *tacit knowledge* of an entrepreneur has a direct implication for the success of the start-up [89]. Tacit knowledge describes the knowledge that cannot be created from a pure consumption of information and that cannot be transferred from one person to another. Instead it is very much related to the experience of a particular person and it is employed sub-/consciously by that individual. Koskinen and Vanharanta argue that tacit knowledge plays an essential role in innovation start-ups, primarily in the early phases of the innovation process (Figure 17) [90]. Here, the new venture is likely exposed to numerous internal and

external risks. The entrepreneur's tacit knowledge, when leveraged for active engagement in multi-disciplinary communication and for setting up and operating a non-bureaucratic organizational structure, for example, is highly beneficial for the success of the start-up.

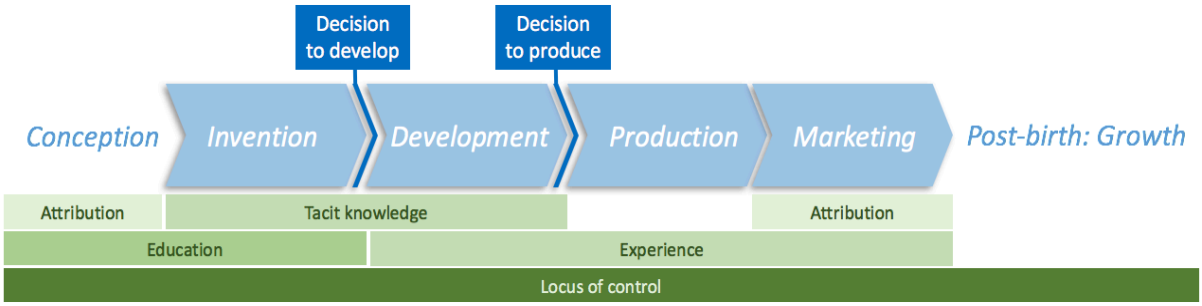


Figure 17. Early progression of (technology) start-ups with supportive entrepreneurial traits. Steps in light blue correspond to birth phase in Figure 16. Following a general willingness of an individual to become entrepreneurial, the process entails a 4-step process (from the invention to marketing the product). The supportive entrepreneurial traits and skills are outlined in green. Tacit knowledge should, of course, be complemented by explicit knowledge.

This success scales with the *human capital* of the firm, which tacit knowledge is a part of [91]. As stated by the authors: "Human capital increases the owner's capabilities of discovering and exploiting business opportunities.", and, therefore, is essential throughout the start-up (innovation) process. However, the direct benefit of human capital on the success of the firm is higher for the outcome of human capital investments (i.e., skills and knowledge) than for the actual investment itself, primarily in technology-driven industries. As a consequence, investing into human capital only is not enough, but it must be translated into the accumulation of explicit and tacit knowledge within the company (Figure 17).

3.1.3. ASO: ACADEMIC SPIN-OFF

University spin-offs, or Academic spin-offs (ASOs), are amorphous organizations that are somewhat difficult to define. Typically, they describe commercial enterprises that are founded by scientists in an attempt to translate an idea and/or results from research activities into a commercial product or service [92]. Many times, the idea originates from publically funded research projects and in all cases at least one founder originates from that academic institution that the start-up emerges from. Pirnay and colleagues offer a more refined typology of academic spin-offs along two dimensions: the status of the individuals involved and the nature of the knowledge to be transferred [93]. Depending on the type of the ASO, related activities, financial needs and other requirements as well as growth perspectives may vary. Figure 18 illustrates some of the facets of an ASO.

ASOs gained traction following the 1980 Bayh-Dole Act in the US, and sometime later in Europe as well, following similar changes in national legislative systems. Through this Act, universities were permitted to license patentable inventions that arose from federally funded research [94]. The right to license supported the commercialization of inventions, and, thus, helped exploit inventions more rigorously.

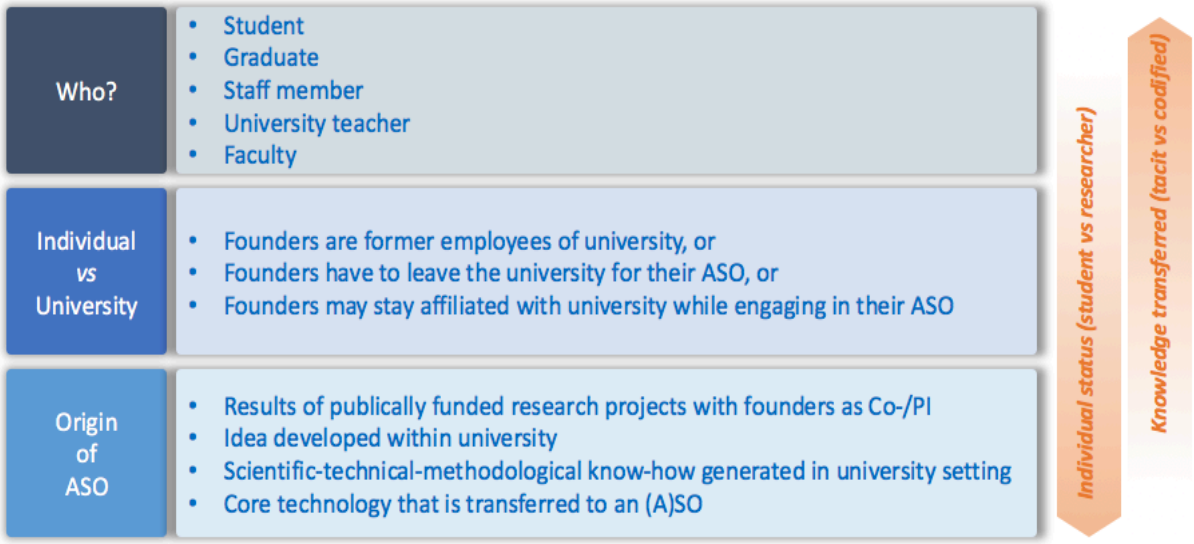


Figure 18. Range of key definition parameters for an ASO with 2-dimensional typology to describe the involved individuals and the transferred know-how. Modified from [93].

In contrast to purely commercial start-ups, ASO face a number of specific challenges when advancing a research result or invention into a successful business (Table 9). While all steps and actions are important in either scenario, the order of events as well as the magnitude of each event may differ. A study by DeCleyn and colleagues produced the surprising result that none of the key traits of an early entrepreneur (Table 8) appeared to affect the success of an ASO, which is in contrast to prior studies, that, however, involved a more diverse range of start-ups. Nonetheless, the authors call for a focus on founder's team characteristics that are complementary, and argue "Given the complexity of the tasks in early stage ASOs … the required expertise is hardly to be found in a single person." [95].

Table 9. Critical steps in the creation of a new venture (start-up) and comparison of general start-up and academic spin-off.

Technology/Innovation start-up	Critical steps	Academic spin-off (ASO)
Typically preceded by opportunity recognition	**Proof of concept**	Typically objective-driven with public funding of research projects
Comes first and typically yields a proof of concept that is used for pitching investors	**Opportunity recognition**	Recognize an opportunity upon successfully answering a part. research question or completing a project
May be linked to the prior proof-of-concept in many cases, depending on the funding situation.	**Functional prototype**	Possibly in sync with the next step. May require extra-mural funding (independent grant application). Must be clear about IPR.
Prior experience likely. Not very challenging to core team. Consider IPR.	**Developing a business model**	Challenging to most academics given different mental concepts.
Means available to attract support, given an existing business-type network.	**Attracting financial support**	Challenging to many academics because of lack of overlap of their science-network with business angel network. Support from CTOs.
Facilitated through existing network.	**Acquiring first customers**	Supported by broad academic network.
Costly and appreciated from the start.	**Testing and certification**	Costly and new to many academics.
Benefits from immersion of start-up in business world.	**Production and Marketing**	Here, additional support from (experienced) entrepreneurs is welcome.
More likely to gain experience and advise through existing network.	**Growth strategy**	Again, in/external support and expertise welcome. Decide on duality-of-interests.

The biggest challenge for an ASO, however, is the typical non-commercial background of the inventor and entrepreneur [95,96]. This is in addition to a technological and market risks. Above all, the inventor must decide very early during a potential gestation phase (Figure 16) between moving

entirely into entrepreneurship, engaging in both academia and the start-up at the same time ("*entrepreneurship faculty*" [97]), or staying out of business altogether. Conflicts of interest and conflicts of (lifestyle) values may arise easily for a faculty with entrepreneurial inclinations [98]. Here, clear procedural guidelines as to obeying to a *duality-of-interests,* or even a conflict of interest [99] must be followed. While there are common ethical standards, each academic institution may set forth their own guidelines and procedures that vary widely in their success [94,100-102,104]. Such guidelines also help avoid dispute over intellectual property rights (IPR) that are considered most important when planning the transfer of "embryonic inventions" into a commercial context [94], and, moreover, help "stimulate technological spillover from universities to firms" [104]. This spillover is most effective if a TTO was set up as a *for profit extension*, which, however, is the case only in less than 10% of university TTOs [105].

A survey of inventions from USA-based universities concluded that 63% inventions originated from federally funded research, while only 17% were sponsored by industry [106]. Inventions were highly variable with regards to their commercial potential, and only 12% were ready for commercialization at the time. To promote an efficient transfer of a patentable invention from academic research onto a commercial development path, either the invention is picked up by the university and licensed to an independent entrepreneur or the university supports the creation of an ASO. In either case, the development of the invention is guaranteed only if the inventor partakes in the revenue stream from the licensing fees, or if the inventor is permitted to explore his/her within an ASO with the university receiving royalties [106]. Typically, the University-based TTO can help in the proper arrangements [101,107]. Such licensing and royalty agreements are central to the support that a University can offer to an ASO and the degree of which has been shown to be an important factor for the success of the ASO [92].

When implemented effectively, an ASO policy by the university can create a mutually beneficial situation. An ASO can provide revenue (as little as it may be) to the former parent organization (e.g., royalties, licensing, etc). At the same time, the first successful ASO start-up can entice other entrepreneurial faculty to follow suit, so as to again create value to the university and society.

3.1.4. START-UP LANDSCAPE

ASO activities occur in a complex environment. In order to understand the founding of an ASO (or the reasons for not founding it) as well as to predict its chances for success, one has to consider multiple factors (section 3.1.1.-3.1.3.). As such, *academic entrepreneurship* is a multi-dimensional phenomenon. Here, many inter-related factors are to be considered that include the cultural environment, the institutional culture, its support of entrepreneurial activities, the inventor's organization, the immediate eco-system and the social dynamics between the inventor and/or academic and the actors of the ASO. Frequently, universities are challenged to provide competent support during the transfer of an invention to the market [108]. This is highlighted also in a report by

Friedrich Schneider (Johannes-Kepler University, Linz, Austria) who points to the shortage of university-based support structures for the creation of ASO [109]. Of note, this shortage of support was recognized by the Austrian Government, and a new Programme – "Young Innovators Austria" - was instated with a funding volume of 15MEUR.

While such initiatives are to be appraised, the AIT study further exacerbates that, in general, start-ups in Europe rely more on incubator funding from public sources compared to US-based start-ups [108]. More than half (55%) the founders of all start-up firms in Austria, for example, did receive public funding at least once during their gestation, with a total funding in 2016 of 270MEUR [110]. The AIT study found an even higher fraction of public funding for university start-ups (ASO) of 80% in Austria versus 70% for Europe [108]. In contrast, only one in four (28%) ASO in the USA did receive public funding.

Whatever the public support for ASO, which was seen critically by the authors, more start-up support organizations are considered beneficial to facilitate early entrepreneurship. Academic entrepreneurship, in particular, can generate societal value: following some initial support (know-how, financing, etc.), a successful ASO creates social and financial capital that can be re-inserted into the founding processes of new start-ups through shared expertise, co-financing other support; all to up the chances for more successful ASOs. In addition, more formal structures are called for that can act as mediators, or intermediaries between universities and the market [108].

In addition to the detailed insights on the environmental factors for a start-up, and an ASO in particular, the European Startup Monitor provides a broader perspective on the European start-up scene. For the sake of completeness, the following paragraph summarizes a few key observations [111]:

- 77% start-ups were founded by teams (Austria 77%) and with one (49%), two (34%) or three (12%) managing directors
- 76% start-ups prefer a flat organizational hierarchy of 1-2 levels
- 9.7% EU start-ups were founded as ASO (Austria: 9%) with Switzerland taking a lead (18%)
- 46% founders had founded a venture previously (Austria 41%)
- 12% start-ups build their venture on SaaS
- 52% start-ups consider their product an international market innovation
- 80% start-ups intend to gain access to customers/market through partnerships with established firms (Austria 84%)

The responding start-ups considered the following issues as critical to their success:

- going international and facing differences in legislation/regulations (30%) as well as adapting the product to local customer preferences (19%)

- politician's understanding of and support for start-ups (45%, down from 55% in 2015, vs Austria 57%)
- readiness of the educational system to relay entrepreneurial thinking (45%, Austria: 37%)
- the general business situation (40% good, 51% satisfying, 9% bad) vs Austria (40%, 62% and 8%)

In conclusion, the planned ASO is very much in line with the average range of European start-ups; for example, it will have a team of three founders (all of who come with prior business and founder's experience). The ASO will be built around a scalable SaaS product. For the sake of seed investment and growth potential the founders plan to engage their start-up in a PPP scheme together with an Austria-based venture engaged in customized solutions for biomarker research and a global healthcare provider.

3.2 STRATEGY

3.2.1. WHAT IS STRATEGY AND STRATEGIC PLANNING?

So far the origins of a start-up venture have been discussed with a focus on ASO. To some extent, the gestation period (Figure 16) comprises a number of actions and associations that are neither directional nor do they follow a specific strategy that is a pre-conceived line of actions in support of a long-term goal. Only when the (anticipated) entrepreneur makes a *go-decision* to bring his/her idea to market, the gestation period moves from the concept phase to the birth phase, which is normally the time when a strategy is needed. Strategizing always involves *planning* and *acting*. *Strategy* by the words of Michael Porter is "…the creation of a unique and valuable position, involving a different set of activities …" [112]. As such it seeks to employ a distinctive feature, service, or product of a company to obtain and defend a competitive advantage for this firm. In his position paper, Porter reflects in more detail on the do's and don'ts of strategic planning and positioning. He argues that plain *operational effectiveness* is not a strategy. Instead, strategy is about acknowledging and bolstering a *difference*. A firm should create customer value through establishing, preserving and adapting a "different set of activities". With regards to "emerging industries and technologies", such as those that engage cloud-based computing and ML/AI (section 2.3.1), Porter argues that "companies that are enduringly successful will be those that begin as early as possible to define and embody in their activities a unique competitive position" [112]. This is done as part of the development and execution of a strategy (Figure 19).

Devising a strategy can be very challenging for a start-up for its intrinsic difference from a strategy for an established firm. The latter, like start-ups eventually, wants to create value and seeks to maximize the return on shareholders' investments. A start-up is faced with a much more fundamental issue, which is to get the firm off the grounds and make it go through the post-birth phase into a growth phase, which is, where most of the established firms are already. Therefore, strategy planning should consider the following points, thereby re-iterating what has been discussed by Porter in [112]:

(1) Picking talented staff that is willing to share the goals and objectives of the start-up, (2) Choosing a market passionately, (3) Raising capital in light of other financing sources without losing control of the company, (4) Gathering market share fast by turning to high-need customers to act as role models, and (5) Being prepared to adapt to a changing environment [113].

Figure 19. Strategy in the context of a start-up creation: from gestation to post-birth and growth (and exit). During gestation (concept and birth) at least one actor needs to make a decision to become an entrepreneur. At that time, at the latest, a strategy must be conceived and started to be acted on. The strategy should provide guidance to the venture and help make conscious decisions in a highly uncertain environment. Likewise, the company should measure its adherence to the strategy as well as its value output (performance), which can start as early as during gestation.

Once the start-up is moving well along the post-birth phase (Figure 19), more attention must be centred on reaching the growth phase, and the strategy may need to be adjusted to provide the means to overcome the shortcomings and risks of a start-up in light of larger firm competition. These strategic objectives include: the need to remain relevant by all possible means (leverage free advertisement through word-of-mouth, social media, publications, etc.), the need to provide an ultimately good experience to customers, to embrace the right technology, to maintain risk-taking, to keep engaged in what is selling well and move out from products/services that do not sell [114]. And finally, a strategy must be executed. This is where an experienced entrepreneur may be invited to the board, or at least to an Advisory Committee [115].

3.2.2. IMPLICATIONS FOR A CDSS STRATEGY

The CDSS product should be positioned clearly along the customer *needs* (e.g., add-on diagnostic information during oncology patient management), *access* (e.g., cloud) and *variety* (e.g., focus on selected tumour entities). Based on resources (staff, financing, computing power, reference data etc) trade-offs will need to be made, which – according to Porter [112] – will mandate a strategy. Based on the market analysis in section 2.3, a significant growth potential is expected for this service. However, the entrepreneurial skills of the founders must be reviewed critically in light of the suggested traits (Table 7 and Table 8). In case selected traits are missing, then the founders should seek to engage advisors or investors who may help fill in these trait gaps.

3.2.4. STRATEGY AND BUSINESS PLANNING OF START-UPs / INTERVIEWS

Figure 16 illustrates the start-up process as being a lengthy process. Van de Ven and co-authors argue that the more the entrepreneur follows this process by means of a structured plan, the higher the chances for the success of the new firm. This process includes an understanding of a problem (aka market opportunity), the development of a business plan and the actual start-up process [83].

Naturally, a *business plan* (Chapter 4) is considered a documentation of a strategic plan for a (start-up) firm.

Business plans are composed of a general analysis of the market, the business opportunity and growth potential. Any quantitative estimate is based on an interpretation of the past (market, firm, etc.) and subsequent predictions on the future. Typically, such predictions are positive, but frequently they are subject to an overconfidence bias, too. Furthermore, entrepreneurs may have the right data at the time of the start-up, but they assume a static environment without change. If, however, key assumptions change, then their predictions falter and the business plan is challenged. Therefore, more effective and successful planning would entail a "systematic way to uncover the dangerous implicit assumptions that would […] slip unnoticed and thus unchallenged into the plan" [116]. This type of alternative business planning is also called *Discovery-Driven Planning* (DDP), thereby giving reference to the fact that the real value of a firm becomes apparent (aka *discovered*) only as it develops. In the author's interpretation, the DDP concept could be described as an iterative approach towards standard business planning: both make solid assumptions based on a sincere, one-time market analysis, both need to define objectives and success and both do not obviate the need for the entrepreneur to repeatedly benchmark the new firm against the targets. The difference is, however, that DDP puts an emphasis on "milestones and repeated benchmarking of key revenue and cost against the market", which is further supported by encouraging DDP-centric entrepreneurs to start with a reverse income statement [117]. For the purpose of this thesis, however, a standard business plan will be developed. Time permitting in real-life, the founders are prepared to adopt a DDP approach.

Over the past years, the author came across a number of entrepreneurs who reported – rather unexpectedly – that they did not have a fully-fledged business plan at the time of the gestation of their firm, but instead worked along a core concept with a few key assumptions that were updated more or less continuously as the company evolved. In order to gather more insight and to probe business and strategic planning for start-up companies in the healthcare sector, a series of interviews with CEOs of small healthcare companies was conducted.

Methodology. For this study a questionnaire was employed that consisted of a mix of 22 multiple-choice and open questions regarding the following main topics: (1) demographic hindsight, (2) start-up phase and affiliation with universities, (3) value proposition and product description, (4) founders and management team, (5) strategy, (6) growth phase, (7) potential for optimization of the business, and (8) trends and comments. The questionnaire was made available as a Text file and in GoogleForms – together with an introduction letter describing the project idea and the reasoning for this interview (Appendix 1). The contact persons to receive an invitation to participate in this survey were sourced from the author's personal network and network recommendations. In total 19 interviews were completed between February and April 2017. Of these, 8 interviews were conducted over the phone (60 min, or less) while 11 interviews were completed by the managers and returned via email without a follow-up verbal interview.

Results. Of the 19 responders, 17 and 2 were male and female, respectively. Most entrepreneurs had a PhD degree or higher. Most start-ups (11/19) were founded after 2010. Table 10 lists the main reasons for the founders to become entrepreneurs. Interestingly, the argument (by academics) to turn their idea into a product for a more sustainable impact was brought forward repeatedly. Other trigger points were *ownership* and *thrill/fun* factor. Of the 19 start-ups, 8 are actual academic spin-offs (ASO), and 7/8 did receive support from the university, which included access to infrastructure, advice and access to external networks as well as the permission to engage in both academic and business work (see duality-of-interest, section 3.1.3) and in 1 case co-investments by the university. It is, therefore, no surprise that all start-ups that did receive university support consider a TTO valuable. The other, non-"beneficiaries" had more balanced views with only 1 considering the TTO to be of no use. When asked for more comments, responders gave credit to TTOs for their support during early IPR negotiations but then pointed out that support was sometimes slow or actions were not taken to the advantage of the start-up but more to the benefit of the TTO. These examples resonated more with the lower end of the performance spectrum (section 3.1.3). Finally, 11/19 start-ups had no licensing agreement with a university while 6/19 gave clear indication that they did enter such an agreement.

Table 10. Entrepreneurial triggers for 19 founders of interviewed healthcare start-ups. There was a balance of start-ups responding to a "market-pull" vs a "technology-push". Note, the repeated mention of turning a research result into a product (gray).

	Service	Effects and benefits
1	Consulting	To do what I did as part of a big company on my won and with more enthusiasm/return
2	Radiology reporting	To facilitate the application of academic research in clinical practice
3	Cardiac analysis	To cater to external interest in a product version of the presented research functionalities
4	Education	Always wanted to, but had to wait for the right moment
5	Web & cloud solutions	Ownership of preferred and enjoyable professional activities
6	Imaging systems	To commercialize academic research for more sustainable impact
7	Imaging systems	Fun factor
8	CRO	Conviction and ownership
9	Image reconstruction	In response to a request for a product-type solution
10	Consulting	Opportunity recognition of a change in the legal system
11	Image analysis	Ownership and fun factor
12	Image & data analysis	In response to a request for a product-type solution
13	Image analysis	Opportunity recognition
14	Surgery planning	Turning a convincing idea into a product, paired with entrepreneurial ambition
15	Communication	Passion to work and personal freedom
16	NA	Thrill and fun factor
17	Video consultations	To facilitate the application of academic research in clinical practice
18	Pharma	Fun factor
19	Data acquisition	Readiness for a professional change based on a convincing product idea

Of the 19 start-ups, only 7 (37%) had a full business plan ready at the time of the founding, 9 (47%) firms did not have such a plan and 4 reported that they used a simplified plan. Interestingly, only 50% of the responders with a full business plan reported the firm's growth to be as expected, and a third of those who did not have a plan still reported a positive (expected) growth. Founder teams were diverse

in terms of gender, nationality and experience. Of note, in most start-ups at least one person with a non-academic background (i.e. business, legal) was part of the founders' team.

Table 11 summarizes the feedback provided by the founders as to their perspectives on key factors for success for a start-up. Access to a fitting team and partners/networks was seen as a key success factor, as well as well-identified market needs and the usual personality traits that help stay innovative while enduring the stress of starting a new venture.

Table 11. Most popular key factors to the success of a start-up as per interviews of 19 healthcare start-ups.

Key factors	Advise and choices
Partners/Team	Choose wisely, respect and trust them
	Prior mutual engagement of team members is beneficial
	Never set-up a company on your own, always do it with a partner
	Foster complementarities and multi-disciplinarily
	Don't shy away from sourcing external support/advise during start-up
Market	Need for good market understanding
	It's the market (know-how), not the product that is important
Traits	Perseverance, Determination, Agility
Ideas/Products	Have a unique idea/technology that – ideally – addresses an identified market need
	Clarify IP
Finances	Be realistic and have access to back-up funding

Discussion. The main reasons for people to become entrepreneurial in start-ups (interviews above) resonate with the discussions from the literature (section 3.1.1., Table 8). In this cohort fewer entrepreneurs had a full business plan ready compared to the cohort in the report by Reid and Smith [118] who had interviewed CEOs of 150 start-ups and found that 89% of the owners had a business plan. Of these plans 79% were formal and complete. While the fraction of firms that had a formal business plan was high, the authors could demonstrate also that the mere existence of such a plan did not correlate with the success of the firm when categorized into "low, medium and high performance" firms, which is in line with the responses to our questions about growth. They conclude that entrepreneurs should make parsimonious assumptions as to the financial performance of their company, while at the same time being cognizant of non-tangible indicators, such as personal drive, imagination, creativity and flair.

In conclusion, these interviews support the main take home messages from larger, prior studies that point to the benefits of team diversity, an appreciation of the benefits and risks of becoming an entrepreneur as well as to the inclusion of several entrepreneurial traits (Table 8) in the founder teams. In line with prior studies, the gestation of an ASO was observed as being highly variable. The bottom line of start-up success was seen by the interview partners in the ability "to identify the right problem" and to act on "good know-how, good ideas and good contacts".

3.3 SUMMARY AND IMPLICATIONS FOR CDSS BUSINESS MODEL

The healthcare industry is growing fast (Chapter 1) and business opportunities are abound (Chapter 2). The growth is rooted in the growing interest of patients, the general public and society at large in

better and cheaper healthcare products. Fortunately, healthcare suffers from comparatively little public scrutiny despite the complexity and variable efficacy of new technologies. Instead, the business models of traditional service providers are challenged by the onset of platforms, be it for social networking, for rating services or for comparing prices. This is the time for incumbents with new business ideas and value propositions. Such ideas have a good chance of turning into successful products/services if they meet a trend (section 2.3.2). The interview partners from section 3.2.4 were also asked about their understanding of current trends in the healthcare sector, and most of them resonated the 3 megatrends: ML/AI, digitization and big data, followed by the need for cost containment (Figure 20).

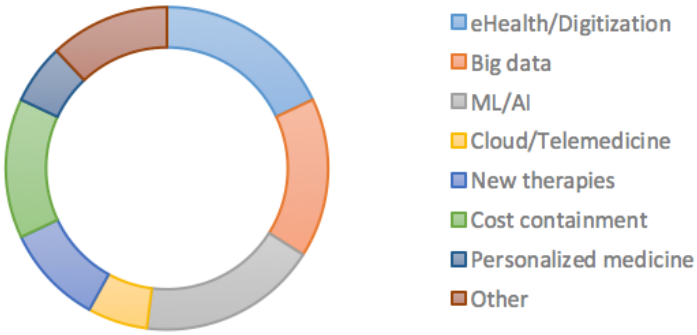


Figure 20. Absolute responses during interviews with healthcare start-ups with regards to the three biggest healthcare trends. Over half the votes were on *digitization*, *big data* and *ML/AI*.

In conclusion, there is an opportunity for a CDSS for tumour characterization, which can be considered both, a *technology-push* and a *market-pull* technology. This opportunity shall be realized as an ASO (Figure 21) following the process of an opportunity recognition by a group of technology innovators with a background in entrepreneurship (founders). As discussed earlier in this chapter, an ASO must "provide a business idea that is attractive to the market" [119]. The market attractiveness is "positively influenced by the market orientation of the academic start-up founders", while prior experience "positively affects the articulation". Therefore, the founders plan to spend particular efforts on the business proposal and communication to the financing bodies and customers.

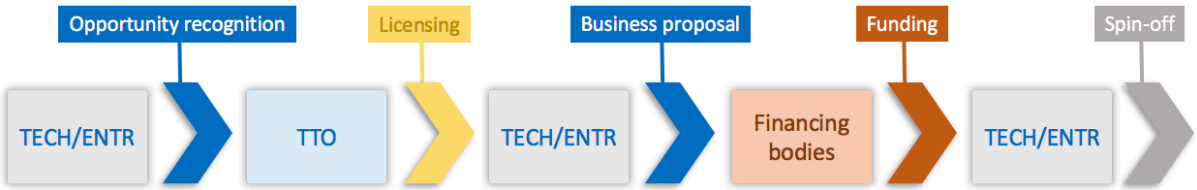


Figure 21. Stage-based model of technology push and market pull with an entrepreneurial technology originator [98]. The technology originator (TECH) is within the same group as the entrepreneur (ENTR). Following an opportunity recognition, the Technology Transfer Office (TTO) and the originators agree on a licensing scheme. This process should precede the business planning. The originators then seek investments from funding agencies or financing bodies before spinning-off.

A spin-off is also referred to as a "mechanism for technology transfer" [92]. The founders will engage in a licensing agreement with the university. To date, the university TTO offered a term sheet along the lines of a minimal down payment and a royalty payment on the order of 3% after first positive cash flow (Personal communication). Looking ahead into the short-term future, none of the three

founders expects to leave their academic position anytime soon. Instead, the founders seek to act as "entrepreneurial staff and faculty" with the first investment going into full-time staff of the new venture. While they consider themselves as excellent academics, they do recognize that the same level of excellence is lacking from an entrepreneurial human capital perspective [120]. Hence, the founders have contacted an Austrian incubator and applied for participation in their start-up camp, which would provide them with access to entrepreneurial and business coaching as well as to a network of business coaches who may be invited to the founder's team or to the Board of Advisors.

4. BUSINESS PLAN "ADx 2017"

This chapter presents the business plan for the perceived company "ADx" (Advanced Diagnostics). Within each chapter of the business plan individual learning points from the theoretical framework and surveyed aspects are highlighted and further reasoning for the use of particular parameters or choice of assumptions is given.

"*Der Plan ersetzt den Zufall durch den Irrtum*."

(Anonym)

In general terms, a business plan is a written document prepared by the entrepreneur responsible for that business. The document describes important aspects (internal and external) that are relevant for the business. On top, the business plan provides direction for the firm and its operation, thus, helping the entrepreneur to move from *A* (start) to *B* (growth, exit, etc.). As such it contains details on, for example, financial, marketing, sales and operation plans [121]. A business plan may also be composed to help the entrepreneur to determine the amount and range of required resources, or to obtain financing from investors. A business plan may also help during periodic evaluation of the performance of the firm by "management of deviation" [121]. The pure composition of a business plan, however, does not guarantee the success of the company. Of note, this may be one reason, why the majority (63%) of the start-up entrepreneurs in section 3.2.4 reported during the interview that they had no complete business plan ready at the time of the starting-up.

In this chapter, the layout of a business plan as suggested by Hisrich and colleagues in Chapter 7 of [121] will be followed. This includes in the order of appearance the following parts: Introduction page, Executive summary, Industry analysis, Description of the venture, Production plan, Operation plan, Marketing plan, Organizational plan, Risk assessment, Financial Plan and Appendices. Of note, blue info-boxes will be inserted that further motivate the assumptions and choices made during the planning process.

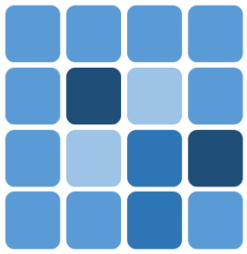
INTRODUCTORY PAGE

Business Plan for ADx – Advanced Diagnostics Ltd

ADx GmbH

[Name] Street, A – [ZIP] [City], Austria

Vienna, May, 2017



Co-Founders: Founder 1, PhD founder1@adx.com
Fon / Fax
Founder 2, MSc founder2@adx.com
Fon / Fax
Founder 3, MD founder3@adx.com
Fon / Fax

Web: www.[tbd].com

Description.

This business offers cloud-based solutions for the characterization of tumours of cancer patients. The service is conceived as a pay-per-use model. To date, proof-of-concept is available for three types of cancer. Our target customers include medical experts and pharmaceutical industry. Based on the provision of non-invasive, medical imaging data an artificial intelligence programme will provide characteristic tumour descriptors for a particular patient. This information can be used for supportive diagnostic means and for pre-selecting a personalized therapy for that very cancer patient. This tumour characterization model is scalable to more cancer types.

Financing: Initial financing requested is 500'000 EUR to be paid off over five years. The debt will cover utilities and salaries of 3 computational scientists for two years, as well as the preparatory work for CE-labeling and advertising campaign.

Confidentiality. This report is confidential and is the property of the co-founders listed above. The information provided should not be shared with external parties except those involved in the review of the business plan for the purpose of becoming an investor.

EXECUTIVE SUMMARY

Healthcare burden measured as a fraction of the GDP is generally high, and on the order of 5-17% depending on the country and the health system. Over the past decades, following medical advances and societal changes, healthcare costs have risen steadily. At the same time the population has grown older and a number of diseases that formerly were considered terminal have been transformed and contained to chronic disease. At the same time, **technological progress**, paired with the general wish to obtain any treatment anywhere at any time have caused the **costs** of the public healthcare system to grow fast. With the advent of medical technology, numerous information can be generated for a given patient, or an entire study population, that cannot be coped with by an individual medical expert any more easily. Therefore, a large portion of information and know-how goes missing in untapped data. The concept of **big data** describes means of employing computer algorithms to gather and filter the vast amount of data to titrate essential information and know-how that can be used to diagnose a patient more efficiently and to help choose a most effective treatment options. Choosing the right therapy at the right time helps the patient and also helps bringing healthcare costs down since futile therapies can be avoided. This applies to patients with cancer, in particular.

Cancer patients require an accurate diagnosis and personalized treatment. Today, multiple biomarker information is available to render such a diagnosis. These include imaging, blood samples, genetic profiles, etc. The more information is available the more complex the decision process by the care physician. Today, cancer treatments, that involve chemotherapeutic drugs or targeted therapies, are quite effective but also expensive, costing up to several ten thousand Euros per treatment cycle. It is, therefore, important - to the patient and to the healthcare system alike - to choose a therapy that is most efficient to the individual patient and to avoid futile therapies.

Our solution can help in assessing an individual patient suffering from cancerous disease more accurately and efficiently and in choosing the most appropriate therapy option. In essence, we propose a **clinical decision support system** that predicts **tumour characteristic information** on the basis of the provision of patient-specific, non-invasive imaging information, such as from hybrid imaging (e.g., PET/CT and PET/MR). Prediction is based on a **machine-learning algorithm**, which is trained on a growing cohort of reference data of cancer patients. Machine leaning and clinical decision support are integral parts of the mega trend of digitization in healthcare. Both make use of big data and are capable of extracting specific information and know-how that otherwise may go unnoticed by a single human observer. As such, both can support a conscious human decision making and **predict** tumour- and patient specific parameters, such as receptor expression or long-term survival, respectively.

We intend to offer such a service to the cancer patient management cycle, in an effort to expedite decision making, to help **personalize diagnosis and treatment** and – eventually – to help **containing healthcare costs**.

Our **business model** is a **cloud-based, pay-per-use clinical decision support system**. To date, pilot evidence exists for the ability to predict tumour grading and receptor expression with high accuracy for three types of cancer: **breast, glioma and prostate**, that together account for 26% expenditure for cancer care. The prediction algorithm is based on a supervised machine learning algorithm that has been trained with a wide range of medical imaging and non-imaging data, which include histopathological information as the reference standard. The algorithm can be scaled to other tumour entities and prediction functionalities pending the availability of large training data cohorts. Currently, that availability is limited since medical data and records are not shared widely among healthcare stakeholders; this is a known phenomenon.

We intend to place this business model in the framework of an academic spin-out of a medical university in Austria. Our **founders team** is made of three medical imaging experts: a software engineer and developer with 15+ years of industry background in medicine, an imaging physicist with 20+ years of academic and industrial experience in healthcare, and a molecular imaging specialist and medical doctor with 20+ years of clinical and research experience. All three have worked together for at least 1.5 years under auspice of a number of academic projects in the context of non-invasive imaging, biomarker research and machine learning. While the start-up has not matured into a legal venture yet, we have passed the first stage of application for a national incubator support in 05/2017.

Our **vision** for the start-up is as follows: "We want to improve the quality of life of people by providing those in need with innovative services that are built on scientifically proven results. At the centre of our business is the human being". In order to achieve this vision, we propose the following: "With our machine-learning based predictive analytics model for tumour characterization in cancer patients, medical doctors - who face the time-consuming and complex task of diagnosing cancer - will be able to employ an on-demand service to provide them with additional valuable insight into the disease that will be helpful in subsequent personalized treatment planning. This will help increase patient benefit and reduce costs."

Our decision support system is based on non-invasive hybrid (i.e., anatomical-molecular) tomographic images (e.g., PET/CT and PET/MR) and non-imaging biomarker information (e.g., immune-histochemistry, genotype etc.). Customers who seek to use this service can do so based on the availability of similar image data from a given patient. Following the manual definition of the tumour lesion in a thin-client application, that lesion information is provided to the ML engine, where it is processed as a feature vector as part of the trained prediction functionality. A tumour characteristic's report is generated automatically and returned to the customer. The report includes information on the grade (and likelihood) of the cancer and a receptor status of the delineated tumour lesion(s). This information can be used by the caretakers on site as part of a personalized diagnosis and treatment plan for that particular patient (e.g., a targeted therapy best fitting to the target expression of the tumour).

Based on this model, we expect a **total revenue stream** of about 2MEUR in years 1-3, when assuming a single use fee of 100EUR per case (incl. VAT). **Break-even** is possible to achieve in year 1, and **net profits** should be 150kEUR and 490kEUR in year 2 and 3, respectively. Our financial plan assumes the use of PET-based hybrid imaging data and we make concessions to several gatekeepers along the revenues downstream. Gatekeepers include the willingness to utilize CDSS-type service and the readiness to do so, the ability of imaging centres to communicate clearly, preferably (for now) in English and German proficiently, and, finally, the actual frequency of breast, glioma and prostate cancer patients on-site.

We have identified two main **risk factors** to the success of our business. First, this start-up may suffer from a falling-out of the founders or a shortage of funds. This risk can be mitigated through continuous communication and engagement of the founders in the gestation phase of this company. We are prepared to accept a fourth founder (co-investor) who has not yet engaged in a professional relationship with either of three founders. Shortage of funds can be addressed within reasons through the application for incubator co-financing (ongoing). Likewise, we are in early-phase negotiations with a potential large scale customer who seeks to utilize part of our machine learning engine for predictive analytics of non-imaging biomarkers.

Second, a **shortage of training d**ata may render our existing decision support system less robust than what is required by the market. In order to increase the robustness and, further, to scale the value proposition to other tumour types, more and larger training cohorts must be ceased. Here, we are planning to partner with a global player in healthcare industry as part of a PPP that is co-funded by an Austrian Research Organization. Funds can be used to pay for assessing and analyzing reference data.

In summary, we propose a tool that provides clinicians with complementary information and know-how on cancer – sourced from reference cohorts – that can be used to personalize diagnosis and treatment, thus, contributing to cost containment in healthcare. Desk and field research demonstrates a fit with the megatrends of **healthcare digitization** and **cost savings**. There is no direct competition to our perceived product. Following the identification of some key risk factors and challenges to the model and the robustness of the prediction functionality, in particular, we propose a series of marketing and operational steps to mitigate these risks. Our business is likely to generate a net profit of 150kEUR and 490kEUR in year 2 and 3, respectively.

ENVIRONMENTAL AND INDUSTRY ANALYSIS

Our data confirm the mega trend towards utilizing *big data* and *computer-based knowledge creation*. A main obstacle to growing and scaling this type of business within imaging healthcare is the limited willingness to share patient relevant information despite a general willingness of the public to give away all sorts of personal information. Further, our market analysis has evaluated value propositions from 70+ companies (see Thesis chapter 2) to single out four direct competitors (*Imagia*, *qure*, *Lunit* and *Shiadzu*). Indirect competitors with similar value propositions but services limited to anatomical imaging exist as well; existing global healthcare service providers may turn into future competitors, although currently their CDSS offerings are limited. The value of cloud-based computing of image-based biomarker information has been demonstrated successfully by the value of the company Heartflow (www.heartflow.com).

Environment. The world population in 2017 is estimated to hit 7.5 billion people at an average yearly growth rate of 1.1% (80M). In addition, the world population is aging. Between 2015 and 2030 the number of people aged 60 years or over will grow by 56%, from 901 million to 1.4 billion. By 2050, the global population of older persons is projected to double compared to that in 2015, reaching nearly 2.1 billion. Life expectancy of people would be higher if major diseases, such as cancer and cardiovascular disease were contained. In 2014, 14.1 million people worldwide were diagnosed with cancer and 8.2 mio people died of the disease. Despite major technical and medical progress life expectancy of people with cancer has not improved much over the past 60 years. This is despite the increasing healthcare spending across the globe. In 2014, average healthcare expenditure was 9.9% GDP across all countries, while the USA healthcare spending was above average at about 17.1% GDP[a]. Between 2010 and 2020 absolute cancer costs in the USA alone were expected to rise from 124 b$ to 156b$. The total economic burden of "premature death and disability" from cancer was 895b$ in 2008[a]. While these costs did not include direct costs of treating cancer, they were 20% higher than the healthcare burden from cardiovascular diseases. The three types of cancer with the most significant economic conundrum were lung, colorectal and breast cancer. In light of this business proposal it is to be noted that while cancer diagnosis mandates non-invasive imaging, the associated costs of imaging make up for only 1.5% of the total cancer costs[a].

With the onset of affordable, high-power computing and IT, digitization of our world has become a mega trend. Information of any kind is available at anytime from anywhere in the world. This has brought up the concept of *data lakes* making reference to the vast volumes of information that are to be utilized and absorbed. Digital health has the potential to become a disruptive concept in healthcare. While established global firms gather speed on the digital path only slowly, small and medium size incumbents make their way into the market quickly with very attractive digital health services. Digital

[a] http://data.worldbank.org/indicator/SH.XPD.TOTL.ZS

health funding grew at an annual rate of 31% (2008-13) culminating in 2.8 b$[b]. Funding drivers are the need to reduce "system waste" and contain healthcare costs as well as the perceived benefits from physician and digital blending of technologies and know-how.

The environment is challenged by two general legal concerns. First, imaging examinations that are required for effective cancer staging prior to therapeutic decisions and during follow-up are not reimbursed fully across different countries, and, therefore, may not be available to all cancer patients in need. And, second, data pooling and sharing for the sake of exploring big data is currently in a premature state and not yet widely accepted, although an increasing fraction of people conceives the potential of big data and AI as positive for their own well-being and for society as a whole. Very soon, AI-based CDSS are expected to play a big role in diagnostic imaging by complementing medical experts with advanced image information[c].

Industry analysis. It is understood by all players in the market that the available (patient) data hosts a wealth of information that can be translated into information and turned into knowledge. This concept of *big data* is synonymous with the use of *machine learning* and *artificial intelligence* routines that are used to master that wealth of data. In the next years, CDSS that employ quantitative molecular image information and non-imaging biomarkers arte expected to facilitate personalized diagnostic and therapeutic treatment plans. In this context, healthcare related data are expected to grow from 500 Petabytes (2012) to 25'000 Petabytes (2020), a factor 50 increase[d]. Both concepts, ML and AI, have been demonstrated to yield knowledge that a single medical expert has no ability to source alone. A growing number of incumbent firms engage in the use of ML and AI to provide accurate healthcare information faster and on a need basis. Of the 100 top AI companies, 11 are healthcare companies[e]. Between 2014 and 2016, a total of 114 M$ was invested into AI start-ups with an average deal size of 2.6M$. The focus was on USA-based companies engaging in general imaging[f]. In 2010 4 healthcare start-ups engaged in ML were founded, with this number rising to 16 in 2016. Between 2015 and 2017, 25 start-ups engaged in ML for healthcare entered the market of which a third was based in the USA.

Typical product offerings of these start-ups include semi-/automated lesion detection and demarcation on tomographic images (mainly radiological: Computed Tomography) and basic functional analysis of dynamic contrast-enhanced images. Likewise, some companies engage in genetic profiling and prediction of alterations and occurrence of disease based on ML-algorithms. However, very few

[b] https://www.accenture.com/t20160602T011605__w__/us-en/_acnmedia/Accenture/Conversion-Assets/DotCom/Documents/Global/PDF/Industries_13/Accenture-Fueled-Healthcare-IT-Start-Up-Funding-Digital-Disruption-Knocking.pdf

[c] Frost&Sullivan Global Healthcare Industry Outlook 2017, K152-54, Feb-2017: p. 40

[d] M Gandhi and T Wang. The Future of Personalized Healthcare: predictive Analytics. Rock+Health Report 2017. https://rockhealth.com/reports/predictive-analytics/

[e] CBinsights. The AI 100 Ranking, 2017. https://www.cbinsights.com/research-reports/CB-Insights_AI-100-2017.pdf

[f] S Harris. Funding Analysis of Companies developing ML solutions for Medical Imaging. Mar-10, 2017. http://signifyresearch.net/knowledge-centre/funding-analysis-of-companies-developing-machine-learning-solutions-for-medical-imaging/

companies offer a combination of non-/imaging biomarker information for ML- or AI-based disease characterization. Most companies engage in cloud storage and remote data exchange. One company, Heartflow, for example successfully launched an on-demand service for assessing cardiac function based on the remote provision of CT image data. None of the companies assessed, however, proposes a strong commitment to molecular biomarker information and complementary big data information as a basis for disease characterization. Direct competition is currently limited to four companies that appear to engage in a combination of AI and anatomical imaging and liquid biopsies: *Imagia*, *qure*, *Lunit* and *Shimadzu*.

DESCRIPTION OF VENTURE

A recent OAP indicated a business opportunity for a cloud-based service for tumour characterization following the remote provision of non-/image based biomarker information and a validated machine learning algorithm. It is understood that the start-up would benefit from additional entrepreneurial expertise. Their expertise must be complemented by a core business expertise and that the firm needs seed financing.

Our venture is an academic spin-off from a medical university in Austria. Following the megatrend of digitization of healthcare and our own research, we have agreed to create a product offering for service-based tumour characterization as part of state-of-the-art cancer patient management. The mission of our firm is to provide a validated ML-based engine that assesses and describes tumour heterogeneity, that provides individual risk stratification for cancer patients and that predicts receptor expression for use in pre-therapeutic, personalized treatment planning. The ultimate goal is to provide the medical expert with additional information (aka clinical decision support) for making a diagnosis in light of a range of complex data, in shorter time and with a higher accuracy, so as to help bring healthcare costs down through increased efficiency and the avoidance of ineffective therapies.

An effective cancer therapy hinges on the ability to accurately determine the type and grade of tumour. This is done with non-invasive imaging examinations and frequently concurrent and invasive tumour tissue biopsies. However, such histological data is available neither for the whole tumour lesion nor for multiple lesions, in case they are suspected to bear cancerous cells. Therefore, real-time molecular imaging has the potential to identify the spread of cancer inside the body and, together with the CDSS concept described above, to provide tumour diagnostics along the lines of an *in-vivo histology* without the need to actually perform an invasive and frequently very challenging bioptic procedure.

The actual product is a remote, computer-based service. For a given patient, users are asked to mask a tumour[g] and submit the tumour mask via a web portal. Our ML-engine will access the data and a norm database and return probability maps for histological tumour grading as well as expression status of treatment relevant, tumour-specific receptors or target structures. The data are returned to the user automatically in DICOM format together with a report. Return time can be measured in hours (or shorter for a premium). At the start, this service shall be available for [18F]FDG-PET/CT imaging and breast cancer. In phase 2 and pending access to a large training database for other type of cancers (e.g., lung and colorectal), this service shall be expanded.

An opportunity assessment plan (OAP) from October 2016 has indicated a business opportunity for this cloud-based CDSS. Also, we have applied with the Austrian incubator INITS (www.inits.at) for start-up funding and experts advice (final verdict pending at the time of this write-up). Further, the

[g] In the future, an additional service can be conceived, which automatically delineates the tumours/lesions.

founders have completed some proof-of-concept testing using scientific data from the university database. The founders have also started negotiations with the university's TTO regarding access to a norm database for training the ML engine and for subsequent licensing schemes. The TTO has indicated a willingness to delay royalty payments until first positive cash flow (discussions ongoing).

The ASO will be founded as a Limited (GmbH) company in Austria. All founders have a background in healthcare imaging business and academia. We anticipate 2.5 full-time employees (software engineers) in year 1 and 2. Following seed funding and pending the decision with INITS, the company may be located during year 1 in the premises of the incubator. If no start-up seeding is available at this time, the company will rent an office space in a building elsewhere. The firm will require access to a large grid computer for fast computation time and data storage. The computer and storage will be bought and operated by a third-party. The actual ML engine is a software that is hosted on the Founder's main computer. A safety copy and regular updates thereof will be stored in a safe.

PRODUCTION PLAN

No production of hardware or goods, other than virtual analysis tools, is planned for now. Our business is based on a machine learning engine (Fig A). Data and materials used for the initial training and validation beyond existing pilot proof will be sourced from the university (licensing discussions are ongoing).

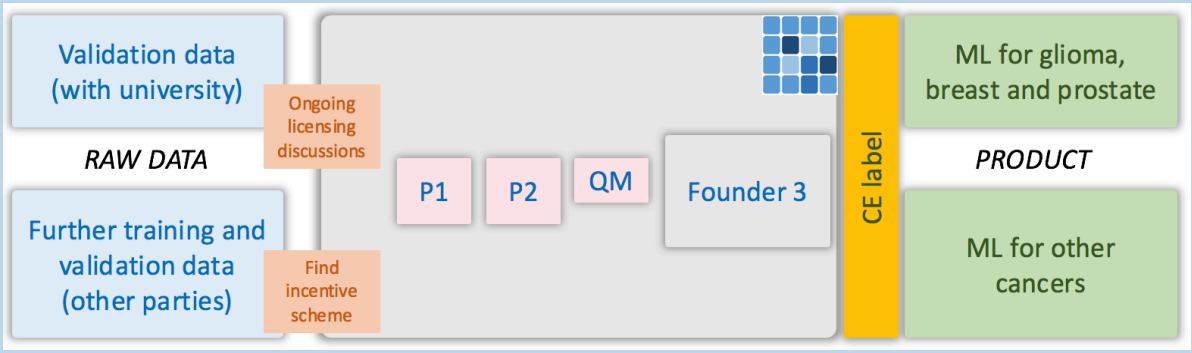


Figure A. Virtual production plan. Validation data from the university will be licensed to our start-up, ADx, for validation of the ML engine. At the same time, other data shall be sourced through direct engagement (academic) and marketing as well as PPP funding schemes. The two SW engineers (P1 and P2) together with the IT savvy founder_3 shall produce a validated ML engine, which – following CE certification (with the help of the Quality Software Engineer, QM) – is offered as a product.

Figure A. Virtual production plan. Validation data from the university will be licensed to our start-up, ADx, for validation of the ML engine. At the same time, other data shall be sourced through direct engagement (academic) and marketing as well as PPP funding schemes. The two SW engineers (P1 and P2) together with the IT savvy founder_3 shall produce a validated ML engine, which – following CE certification (with the help of the Quality Software Engineer, QM) – is offered as a product.

Production of goods will relate to the development of a machine learning (ML) algorithm as part of the CDSS and to the provision access points for customers and users. We consider “Raw data” as the data used for the training and validation of the ML engine. These data will be sourced from current research activities by the founders. Data belong to the university (employer), and first negotiations to license these data for a one-time validation are ongoing.

Future data (as provided from other sources) will be stored and hosted on IT infrastructure that is part of maintained server that belongs to ADx. All manufacturing (aka programming) will be governed by a strict internal quality management, which goes hand in hand with our intent to obtain a CE-label (stage 1) in year-2 of operations.

No physical plant is required but office space and IT architecture will be needed. In-house IT infrastructure from year 1 will include 3 high-performance computers and a server structure.

To date, no plans exist for any type of outsourcing; all SW developments are planned solely as in-house developments.

OPERATIONS PLAN

Operations shall start with the provision of CDSS services for the three types of cancer for which pilot proof exists today (glioma, breast and prostate cancer). ML-based predictive analytics benefit from fast computing power. As the numbers of users increases and the amount of accessible data goes up, more advanced (and expensive) IT infrastructure will be employed.

The operations plan for ADx entails a directional approach towards providing predictive analytics services. The core ML engine - within ADx – is fed with clinical data. Following the pilot proof of applicability to three types of cancer, more validation data sets will be sourced to make the ML engine robust for general applicability. Here, ADx will access a large data pool residing with the university. This access does not entail the transfer of physical goods. Accessing will be governed by a licensing agreement. Once the ML engine is validated, no immediate access to this data cohort is required; see Figure B for a flowchart of goods and services.

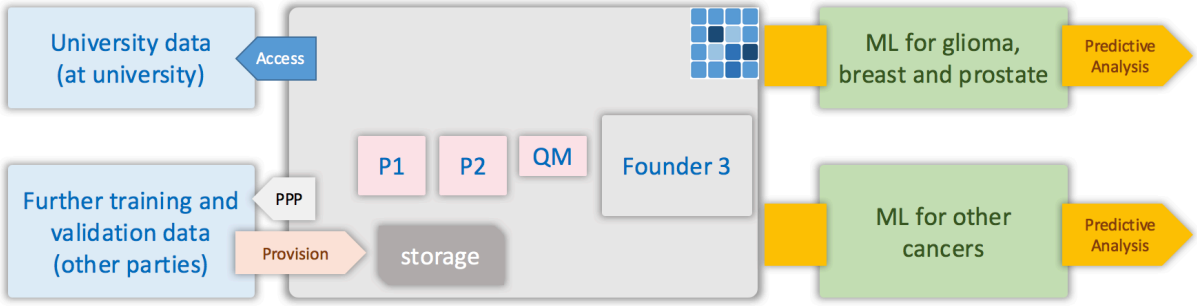


Figure B. Operations plan for ADx. Transfer of goods is perceived only for the sourcing of data other than the validation data set from the local university (lower left). Flow of services is to the right, following the validation of the ML engine and the CE labelling to outside customers on a per-need-basis.

At the same time, ADx will provide incentivized means to owners of other topical data to share and provide their data with the company. Here, the intent is to support a transfer of goods (data) that will become part of a training data repository. For now, this repository shall be in the ownership of ADx; alternative open data set-up's can be considered. Another, option for ADx is to engage with an external partner, through a co-funded PPP (Figure B), for example.

All production (aka programming and quality control) will be maintained in-house. Predictive analytics (aka CDSS services) will be offered on a pay-per-use model, thus, customers will be required to register with the ADx platform and pay (per case). Naturally, there is no inventory involved.

The founders will stay with the current employer for now; thus, all services will be built by the staff employees of ADx. CE labelling will be essential for the roll-out of the services and special attention will be given (funding, 50%quality software engineer).

MARKETING PLAN

Our field research indicated a willingness and general readiness to adopt CDSS services for oncology patient management with users of combined PET/CT and PET/MR imaging. Our market studies highlight six key customer target groups: medical doctors in private and public hospitals, insurance companies, pharma industry, Clinical Research Organizations, providers of molecular biomarkers (radiotracers), and patients. Marketing in year 1 will be geared towards establishing the venture in the market, sensitizing users of hybrid imaging to the use of CDSS and providing proof points. A particular focus shall be given to pharmaceutical industries, for who the lack of a CE label for the CDSS during the 1st year of operations may be less critical.

The goal of our company is to improve the quality of life of cancer patients by providing them and their medical doctors with predictive and analytical information for the sake of faster, accurate and personalized diagnosis and therapy planning. Healthcare costs can be contained by avoiding invasive biopsy procedures and futile therapies of cancer. Our *marketing strategy* in year 1 aims at preparing the grounds for a wide adoption of a CDSS for oncology patient management, and at addressing the needs of the target customers with existing services. Our strategy shall also incentivize users in sharing data for further training and validation of the ML engine. We target customers in the realms of non-invasive medical and molecular imaging in the context of oncology.

Market and Market size. The *potential market* (PotM) is that of all people who utilize PET (aka molecular imaging, Thesis **Error! Reference source not found.**) as part of their patient management. This extends beyond general oncology, since all PET users may be interested in buying this product. The *total available market* (TAM) is that portion of the PotM that is interested in buying our particular CDSS. This would be people who employ PET imaging as part of oncology patient management in case of one of the three types of cancer covered today (breast, glioma and prostate). The *served available market* (SAM) is the size of the *TAM* that we wish to serve. The penetrated market (PenM) is the size of the SAM that we capture (Figure C). Assuming a PotM of roughly 6M PET examinations per year, then TAM would be 5.1M while SAM would be 1.5M. Our field research indicated that 22% target customers would be ready to use the CDSS service without a CE label today. Therefore, we assume a PenM of 330'000 PET examinations per year.

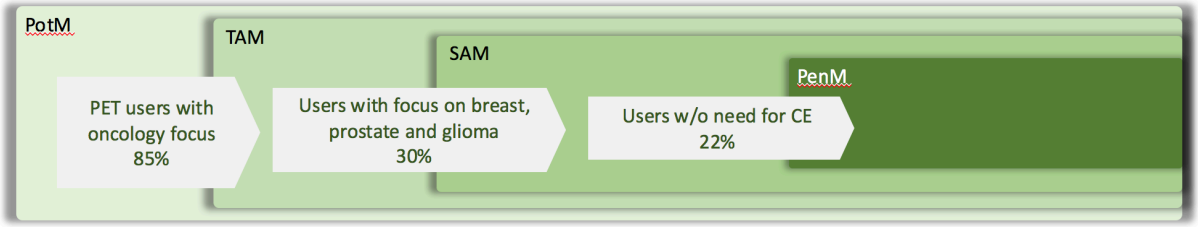


Figure C. Markets and downstream key estimates for our CDSS product. Starting from a global market size of 6M PET examinations per year we estimate our penetrated market to be on the order of 0.3M PET exams per year.

Strategy Part 1 – Patenting. The founders will apply for a patent of the ML engine during the first half of year 1. This shall help increase the value of the assets of the company and build entry barriers for competitors. Following the patent application, a communication will be prepared to highlight the innovativeness of our start-up.

Strategy Part 2 – Preparing the grounds. In continuation of early pilot research and pending the legal implications following the patent application, we seek to communicate our ML engine capabilities at scientific meetings. This will be done by the founders as part of their academic activities with clear notification of the duality-of-interests with regards to this start-up. Such communications will entail opinion papers, commentaries and network communication to "spread the word" on the company. Lastly, pilot evidence for a clear demonstration of the cost saving potential of the CDSS in clinical routine (e.g., through the reduction of biopsy procedures[h]) must be created during this phase. This is planned as part of in-house collaborations and academic partnerships with other imaging centres.

Strategy Part 3 – Market push. Table I provides a short overview of the marketing mix used in part 3 of our strategy to address the 6 key customer groups.

Pricing. A one-time access is priced at 100 EUR (incl. VAT), independent of the tumour type. This corresponds to about 5-10% of the fees for a hybrid imaging examination. In general terms, as confidence-based service fee could be conceived, meaning if the ML engine returns an image interpretation with a high or low probability, customers would be charged the full and a reduced fee, respectively.

Distribution and Promotion. Promotion can be started – at no cost – through the founder's network and academic presentations. At the same time, promotion should be supported through a web-based initiative and messaging on LinkedIn and alike. Also, personal contacts at senior levels of healthcare companies should be targeted and informed by means of a short video clip and electronic/handout materials. Distribution is foreseen direct in year 1 and via distributors from year 2. In that case, we plan to engage with an Austrian biomarker bank, which may order an ML engine for analyzing non-imaging data. We intend to distribute our solution through their network as an OEM (solely for non-imaging data). The same network could be used for our image-based ML prediction at the cost of a shared revenue scheme. Lastly, we are considering the option of partnering with a global healthcare provider in a PPP (sourcing matching funds from the State) in return for well-defined distribution rights to part of our (joint) services[i].

[h] Costs for biopsy procedures vary with the location of the lesion and the use of image guidance (ultrasound or MRI). On average bioptic procedures in Austria cost 1000 EUR (200-1700 EUR) with additional cots for the pathological work-up (40-600EUR).

[i] Harris S. how to sell machine learning algorithms to healthcare providers. Signify Research Mar-30, 2017: http://signifyresearch.net/analyst-insights/how-to-sell-machine-learning-algorithms-to-healthcare-providers/

Product forecast. To date, ML-based predictive analysis is offered for breast cancer, glioma and prostate cancer patients undergoing a specific imaging examination as part of their work-up. There will be no CE label as of year 1, and, therefore, marketing will focus on sensitizing customers, incentivizing them to share their data and become part of an early testing of the functionalities. In year 2 we plan to provide the CDSS with a CE label, and as of year 3 we plan to extend this service to other tumours.

Table I. Marketing strategy for a CDSS in oncology patient management and pharmaceutical research. MD = medical doctor, B2C = Business-to-Customer. Marketing investments measured on scale of low ($) to very high ($$$).

	Value proposition	Marketing mix	Investment	Critical success factors	Comments
MD – public	A comfortable support system for high-quality reporting of complex diseases; helps strengthen the report.	Approach employer/hospital. Promote increased quality of services and potential for reading time reduction.	$$ Mainly B2C	Find contacts into hospital administration. Legislation critical.	Start with PET/MR users.
MD – private	Added benefit for attending physician. Added information that can be sold to patients.	Approach practice owner and MDs. Provide cost estimates for fee-per-service *vs* investment on SW platform.	$$$ Mainly B2C but scattered.	Hinges on personal contacts.	Start w/ direct network.
Insurance	Critical information prior to targeted therapies.	Propose joint study to assess efficacy and cost saving potential from personalizing treatment.	$$$ B2C only with referred contacts.	No pilot proof yet on therapy effect. May consider prospective proof of concept study at reduced service rates.	No contacts. Need to build network.
Pharma	Promising information in early drug testing in patients that potentially leads to smaller study groups	Pitch CDSS idea to pharma as part of early phase trials. Cost saving potential from smaller subject cohorts. Likely no need for CE label.	$$$ B2C.	Fraction of trials with molecular imaging is small, since considered expensive. Must find proof points fast.	Limited contacts
CRO	New, standardized parameters in response to therapy evaluation; raises value of study management to pharma.	Pitch CDSS as complementary analysis tool to existing modes of reporting. Entice CRO to provide CDSS information to sponsors.	$$$ B2C.	Find CRO that engage in molecular imaging.	Limited contacts.
Radiotracer companies	Added value for users of (new) radiotracers. Supportive diagnostics for inexperienced readers (sites with low throughput)	Pitch CDSS as added value to radiotracer. Approach companies for access to retrospective data (market authorization) for training CDSS, and prospective data.	$$ B2C.	Multiple licensees for the same tracer/CDSS not possible. Prospective training data are limited. Costs for CDSS incurred on end user of companies?	Good contacts.
Patient	Provision of add-on information that can be used for better therapy planning and for engaging referring physician.	Work with patient advocacy groups to incentivize them to share their data.	$$ B2C.	May require financial reward for advocacy group.	No contacts to advocacy groups.

Data sharing and incentive schemes. Through our academic networks we will approach high-throughput imaging centres for accessing their data (one time) and training our ML engine in return

for free access to the functionalities and joint research papers (following a patent application). First, we will focus on PET/MR users and breast cancer patients. At the same time we will engage in shaping regulatory processes through the founder's engagement in scientific associations. Access to existing databases, such as that from the European Organisation for Research and Treatment of Cancer, EORTC shall be explored [j]. It appears that access can be granted for subsequent developmental work in return of (only) giving credit to the host of the dataset; further insights will be sought to verify this. Finally, patient advocacy groups will be approached at meetings or directly, to probe their willingness to share their data for the benefit of building a robust ML engine. Here, storytelling and value creation for patients will be of the essence. Communication strategies and incentive schemes will be drawn from past positive experiences with chronically ill patients who are willing to share their data with drug companies. Lastly, a complete new approach to data sharing could be built up with providers of radiopharmaceuticals; their customers could be invited to share their data (also with new tracers) in return for free feedback from the CDSS. Once validated, the CDSS service could be offered by the tracer producers as part of a distribution agreement.

CSR. The founders will strive to obtain the PlanetMark (www.theplanetmark.com) Business certificate in recognition of efforts towards a sustainable business operation.

[j] www.eortc.org/data-sharing/

ORGANIZATIONAL PLAN

In order to gather an independent perspective on our personality traits with regards to becoming entrepreneurs of a start-up for CDSS, the three founders have completed the *Get2Test* on Enterprising tendencies (www.get2test.net). The overall scores were 89% (Founder 1, TB), 67% (Founder 2, MH) and 83% (Founder 3, LP). Figure D shows the scores for the individual ratings on personality traits and skills. We identified a need to supplement our locus of control through external support.

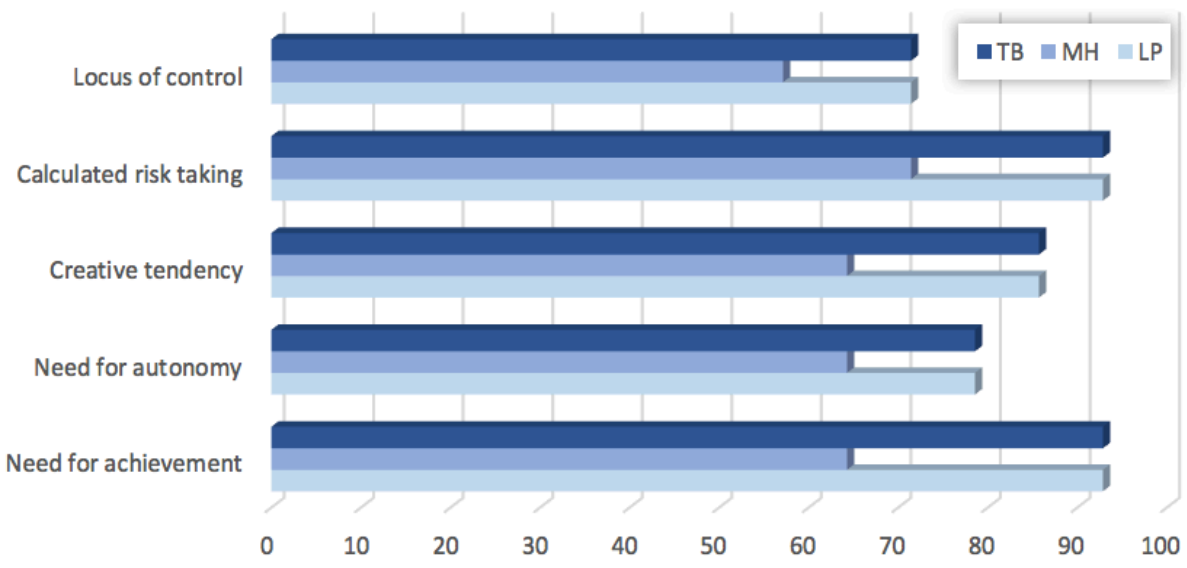


Figure D. Individual scores of entrepreneurial skills of the three founders of the CDSS company (as assessed by Get2Test). The distribution of scores indicates shortcomings on the need for achievement and locus of control.

Structure and ownership. The company will be founded as a limited liability corporation (LLC) under Austrian legislation. The three founders (Founder 1-3, see below) will hold 30% equity each with 10% equity allocated to a fourth seed investor at the time of the foundation (Figure E). The founders will take on one main responsibility each: Chief Executive (CEO) for representing the company to the outside and for ensuring internal communication/organization, Chief Medical Officer (CMO) for commanding all operational and strategic aspects related to medical applications and Chief Technical Officer (CT) for acting on all technical and technological aspects of the company.

The CEO will have check-signing authority, with the CTO and CMO having the mandate and authority to view and cross-check financial transactions (during the start-up phase). All decisions on the company and its strategy (incl. investments and revenue stream) must be made unanimously by the CEO, CTO and CMO. Regular meetings will facilitate an efficient communication and information flow. A legal document detailing the individual responsibilities and mandates will be prepared.

The management team. All 3 founders[k] work at the same university in Vienna where they engage in advancing quantitative, molecular imaging. Founder 1 is full professor of physics of medical imaging with 20+ years of experience in hybrid imaging. He has been working in industry and academia with

[k] The real BP will detail their full name and contact.

close engagements and responsibilities in global collaboration management. Founder 2 is a full professor of nuclear medicine with a background in cardiac and oncology imaging. He has over 20+ years of clinical and clinical research experience spanning from small animal and translational imaging to clinical molecular imaging and image-guided therapies. Founder 3 is a computer scientist with 10+ year experience in imaging industry where he led a development team of 20+ people. His experience extends from computer hard- and software to applying machine learning (ML) algorithms to delineating lesions on hybrid imaging. Since January 2016 he is staff scientist at the university Medical University where he engages in ML-based approaches to tumour characterization.

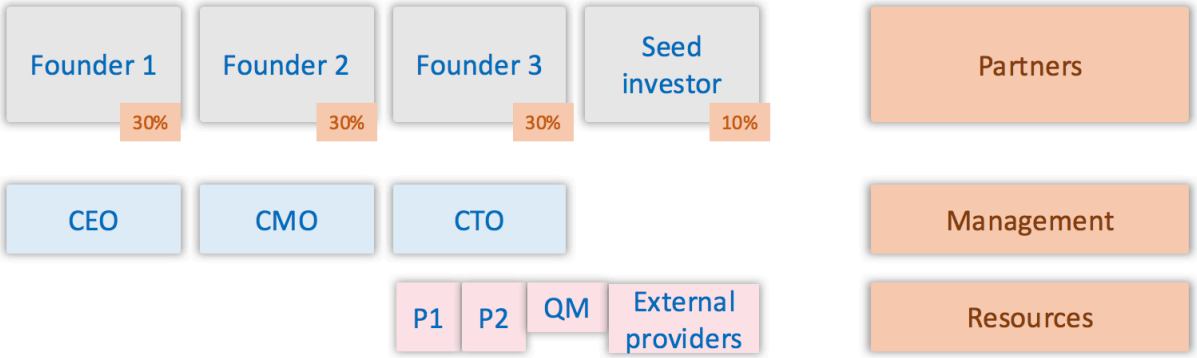


Figure E. Organizational chart for ADx GmbH. The 3 founders each and the seed investor hold 30% and 10% equity, respectively. Founder 1 will be CEO, founder 2 will be CMO and founder 3 will be CTO. In the beginning, the 2 anticipated staff hires (Programmers P1+2) will be with the CTO in order to excel the developments of the ML engine. External providers will be sourced as needed.

Together, our educational and professional experiences cover important aspects of product development and deployment. We are actively engaged in applying medical technology in healthcare, we conceive new trends in medical imaging and we successfully pursue innovative research projects. All 3 founders will stay with their university during the first 1-2 y of operation.

We consider our general business skills as complementary to our academic skills and to those of each other. All founders have the ability to articulate themselves clearly and to relay complex issues comprehensively to varieties of audiences (*attribution*). *Founder 1* is experienced in open innovation with a background in academic and academic-industrial cooperation, founder 3 is experienced in cooperative engagements between industry and academia, and founder 2 is a versatile SW development manager with a clear understanding of product development cycles (see blue box for self-assessment of the founders). It is evident that together we require more *locus of control* and *need for achievement*, in short, we lack plain business expertise for starting a company of that type of growth potential. More specifically, we need short-term *marketing expertise*, mid-term *financial expertise* and input to the product development, incl. CE certification and FDA approval. Looking long-term and with the business growing, we require *growth expertise*, incl. choosing (financial) partners and legal advice. We intent to source that knowledge from engaging a seed investor (with his/her business hindsight) and from engaging an Advisory Board.

Advisory Board. We anticipate an advisory board that provides us with most of the skills we lack at this stage. Currently, we plan for 4 members: (A1) oncologist for expertise in applying our product to various clinical workflows (and optimizing it), (A2) molecular imaging specialist based in the US for intellectual support and messaging to a target market, (A3) a pharma consultant with in-depth business experience for his/her contacts and helping to build the CRO business, and (A4) start-up entrepreneur with expertise in healthcare. All Advisory Board members would be offered 2kEUR during year 1 (bi-annual video conferences and 1 face-to-face meeting with all travel costs covered). From year 2, a vested equity share (1.5%, no voting rights) could be conceived.

RISK ASSESSMENT

Desk and field research as well as our own experience point to three main risk factors: (1) insufficient traits and funds to pull this business off the ground, (2) a shortage of data to validate and expand the ML engine for a range of cancer types, and (3) the current lack of cost savings in pilot set-up's of the CDSS model in oncology.

Major potential risks to the new venture are (in order of perceived descending importance):

1. *Lack of sufficient funds to establish the idea as a business*
2. *Lack of sufficient data sets to train and validate the ML engine across imaging centres*
3. *Lack of current proof of cost saving potential from clinical adoption of CDSS*
4. *Short- to mid-term competition from global companies,*
5. *Legal implications and liability issues*
6. *Plagiarism of the ML approach*
7. *Falling-out of the founders*

If these risks became reality, the implications and consequences would be diverse and range from closing the ASO during gestation to long-term legal implications. Here, we discuss practical consequences and contingency plans.

1. *Lack of sufficient funds*. To date, we estimate that 500kEUR are needed for 2y of operations. At the end of this period we will have a completed technical development for an ML engine that can be employed for predictive analytics for min. three cancer types. In case, no funds were available, the business could not be started or the start-up would be delayed. In that case, and assuming that cloud-based CDSS continues to gather momentum, direct and indirect competition may grow and the window of opportunity may close. Therefore, our plan is to engage in an incubator programme (we have passed the first stage in 04/17; pending positive reviews of our business idea and execution we may be in line for some incubator support and separate seed funding at max 200kEUR over the next 2y). In parallel, we will explore the option of setting up the company and engaging in a PPP-type research project with a 1-to-1 matching of funds. We seek to engage either a global healthcare provider in becoming a partner in such a PPP, or, alternatively, in conducting pilot data evaluation for an existing Austrian company engaging in biomarker research and, pending the successful completion of this pilot, in sourcing their first order, which will help us expand on the existing ML engine.
2. *Lack of data*. In order, to provide customers with a CDSS for routine use we require on the order of 1'000 data sets each (today: 300 total). General access to such data cohorts is limited. Even within academia the willingness to share these type of data is limited. Moreover, the prediction for the same type of tumour may vary with the type and quality of non-invasive images supplied (i.e., patients with similar tumour but imaged with different hybrid imaging systems of variable resolution and contrast). The fewer data are available, the less robust the

algorithm is and the slower we can provide a product and generate revenue. Therefore, our plan is to (1) assess the variability of the prediction with the quality of the data (as part of current academic research), (2) partner within a PPP to gather funds for broader data access (incl. cohort at our university), (3) crowdsource data through personal and academic networks (in return for joint publications), and (4) to check options for tapping into existing external databases (e.g., EORTC). If variability was low (1), then productizing was faster. Top (3) and (4) mandate stakeholder engagement and incentives, which, however, are not linked to larger investments but are rather supported via our personal networks and academic resources.

3. *Lack of current proof points and cost saving potential.* The CDSS model builds on the assumption that an image-based predictive analytics model is eventually ready to replace bioptic tumour characterization. Here, technical and methodological progress may precede the willingness of medical partners to change their patient management. Our plan, is to a) conduct smaller scale and dedicated research studies on site that proof the cost saving potential, and b) to engage with academic partners elsewhere to generate similar, off-site case studies.
4. *Competition*. Currently, no commercially-available CDSS solution appears to be used by customers with access to hybrid imaging. This immediate, direct competition on the current value proposition appears limited. If a direct or indirect competitor came out with a similar service offering anytime soon, our revenue stream, or chances thereof would be reduced. Therefore, our contingency plan rests on three pillars. First, we seek to partner with an indirect competitor in a PPP (under the auspices of a common research proposal objective and agreement on IPR). Second, we shall monitor potential competitors closely through our network and our attendance at scientific meetings. And, third, we would refocus our marketing strategy on our holistic approach to CDSS (thereby leveraging the founder's experience and current occupation), in case we would be threatened on our product.
5. *Legal implications*. Field research indicated a preference for a CE label, or alike. However, other legal implications, such as using the CDSS output during the course of rendering an incorrect diagnosis, exist as well and cannot be addressed at this stage. Incorrect diagnosis in light of ML and AI (even though we provide probabilities only) are topics of ongoing discussions. Our plan is to monitor the field closely and to engage proactively in expert discussions whenever suitable.
6. *Plagiarism of the ML approach*. ML algorithms can be plagiarized; there uniqueness lies with their target application. In our case, the uniqueness is with the training data sets (and the expertise of the founders). Our plan is to develop the ML engine in-house and store copies of the algorithm in a safe. Users will be given only an entry port to the "import functionality" of the engine. When engaging with the crowd, sparring contesters are permitted to test their algorithm on the same (shared) data but not on the algorithm itself. We will follow-up on the idea of patenting (part of) our ML engine.

7. *Falling out of the founders.* Currently, all three founders work at the same university and with two being linked hierarchically. It is possible, although not very likely, that the founders may be falling out for reasons of stress at work, disagreement over the start-up or any other topic. In that case, the business would die. Our plan is to continue our regular meetings to strategize and align. These meetings shall include regular formal retreats, possibly supported or moderated by an independent expert. Also, we hope to benefit from our application with INITS (start-up incubator). Lastly, we are prepared to accept a fourth investor who may moderate in case of a conflict. Our last resort would be our Advisory Board (see Organization).

FINANCIAL PLAN

Our financial plan rests on three assumptions. First, the founders have applied to become part of an Austrian start-up camp (INITS), which – if completed successfully – will provide us with in-kind support and interest-free investment. Second, we will apply for seed financing from the Austrian Bureau of Economy (AWS) to cover costs for pilot evidence. And, third, we will explore two options for stage 2 financing, involving the use of funds from a first order (ongoing discussions) and cross-financing from a PPP to subsidize our developments of an ML engine (Figure F).

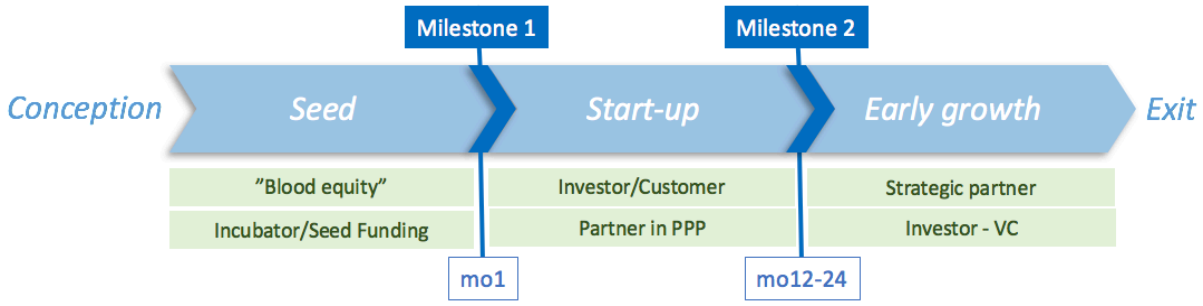


Figure F. Financing strategy for start-up: During the seeding we seek to work with the founder's investments and financial/in-kind support from a national start-up camp (application process ongoing) followed by financial support from the AWS (application in progress). When reaching "Milestone 1" (foundation of company) we will explore the next stage of financing. Here, we will work with a potential high-level customer who seeks to employ the ML engine for biomarker research; part of his order volume will be directed towards optimizing the ML engine for image data. At the same time, we will apply for PPP funding with a global HC provider. When reaching "Milestone 2" (CE label, CDSS roll-out for 3 tumour types) we will go after VC financing.

Financial support is expected during the seed phase from a seed funding agency (AWS, application in progress). The funds shall be used to generate further pilot evidence for the accuracy and robustness of the ML engine of the predictive analytics functionality. Upon starting the business (in month 12-24) we assume the availability of further pilot data and a user interface that permits users to upload tumour lesions for predictive analysis; this is required prior to generating revenue. Figure G lists the operations budget for the ASO "ADx" with a total of 67kEUR for the first 3 months. Here, we assume the engagement of 2 full-time software engineers for building the ML engine, and 50% engagement of a quality manager/software engineer who shall prepare the CE certification for the product. Also, we plan to purchase 2 high-power and 1 standard PC for programming and QM. This is in addition to renting/maintaining server space.

Expense	M1	M2	M3	*Comments*
Salaries (all incl)	17,083	17,083	17,083	2 FTE SW engineers + 50% FTE QM-SW engineer
Bookkeeping	500	500	500	Tax lawyer and book keeping
Services/Maintenance	2,500	2,500	2,500	Renting server space and processing power
Utilities	6,500	0	0	2 high-performance + 1 standard PC
Advertising	3,000	0	0	web page set-up
Selling expenses	0	0	0	on-the-fly through university engagement; no conference visit
Insurance	0	0	0	SW coding, no insurance needed
Depreciation	200	200	200	Fraction of HW / PC costs
Office expenses	100	100	100	Office covered by start-up camp (pending decision) + Comm.
Total expenses (EUR)	**29,883**	**20,383**	**20,383**	**70,650**

Figure G. Operating budget for the first 3 months with key assumption and explanations.

Figure H shows the pro forma IS for the 1st year of operation. Our calculations and estimates are based on the penetrated PET imaging market, which is on the order of 300'000 PET examinations per year. We assume a revenue stream of 300 kEUR in year 1, which is based on the total revenue estimated from the penetrated market, of which we account for 22% (response rate of interviewed parties who would be willing to use our service w/o a CE label). Further, we assume a revenue stream that varies by month (mo 1-12) to indicate a turbulent market. Note, we also allow for support of an Advisory Board.

(EUR)	mo1	mo2	mo3	mo4	mo5	mo6	mo7	mo8	mo9	mo10	mo11	mo12	*Total*
Sales	20,000	20,000	10,000	0	50,000	40,000	10,000	60,000	5,000	50,000	20,000	10,000	*295,000*
COGS	600	600	300	0	1,500	1,200	300	1,800	150	1,500	600	300	*8,850*
Gross profit	19,400	19,400	9,700	0	48,500	38,800	9,700	58,200	4,850	48,500	19,400	9,700	*286,150*
Operating expenses													
Salaries	17,083	17,083	17,083	17,083	17,083	17,083	17,083	17,083	17,083	17,083	17,083	17,083	*205,000*
Advsory Board (4 pax)	0	0	0	0	0	0	0	0	8,000	0	0	8,000	*16,000*
Bookkeeping	500	500	500	500	500	500	750	750	750	750	750	750	*7,500*
Services/Maintenance	2,500	1,200	1,200	1,200	1,200	1,200	5,000	5,000	5,000	5,000	5,000	5,000	*38,500*
Utilities	6,500	0	0	0	0	0	0	0	0	0	0	0	*6,500*
Advertising	3,000	0	0	0	0	0	0	2,000	0	0	0	0	*5,000*
Selling expenses	0	0	0	0	0	0	0	0	0	0	0	0	*0*
Insurance	0	0	0	0	0	0	0	0	0	0	0	0	*0*
Depreciation	200	200	200	200	200	200	250	250	250	250	250	250	*2,700*
Office expenses	100	100	100	100	100	100	600	600	600	600	600	600	*4,200*
Total operating expenses	29,883	19,083	19,083	19,083	19,083	19,083	23,683	25,683	31,683	23,683	23,683	31,683	285,400
EBIT	-10,483	317	-9,383	-19,083	29,417	19,717	-13,983	32,517	-26,833	24,817	-4,283	-21,983	*750*

Figure H. Pro Forma Income statement (pfIS), first year per month (EUR).

Of note, the *pfIS* does not include yet the following aspects: (i) service fees to leverage the data from existing non-/imaging cohorts at the local university, (ii) a potential lease (instead of purchase) of the IT infrastructure (see service/maintenance), (iii) an engagement with a seed funding organization in year 1, (iv) engagement with a potential customer as part of a PPP, (v) no probability (result) based fee structure (revenues), and (iv) no concession to a different pricing scheme for "fast" versus "standard" turnaround times for the report (revenues). Of note, these times may be affected by high processing loads in case of high case submission rates.

Further, individual calculations and assumptions for the *pfIS* are detailed in the Appendix of this Business Plan for all three tumour entities: breast cancer, glioma and prostate cancer. In short, we arrange the PET imaging institutions according to regions. We target English and German speaking sites only and focus on centres/examinations for oncology patient management. We account for a "reach&response factor" (3%-10%) that represents the limited response rate from users to our product (given their interest, funding, etc). Finally, we anticipate the provision of a "customer satisfaction programme", which requires users to pay only if they consider this information helpful (in 60%-90% of cases).

Costs per CDSS use are set to 100 EUR (incl VAT) w/o regional variations. This corresponds roughly to the equivalent of a 10 min time saving on reading an examination by a medical professional, which is what we would expect from the use of our CDSS. Thus, our projected revenue for year 1 is: 270 kEUR (breast cancer), 6 kEUR (glioma) and 17 kEUR (prostate cancer), or about 300 kEUR in total.

Figure I shows the *pfIS* for year 1-3 with the following assumptions: (1) sales double in y-2 (following CE certification) and again in y-3 (engine scaled to new tumour entities, e.g., lung cancer);

(2) service fees for computing capacity in safe service rack grow exponentially; (3) utilities (IT infrastructure) scale with sales; (4) advertising increase in y-2 and again in y-3; (5) selling expenses enter in y2 and y3 to cover sales activities (e.g., participations at shows); (6) an advisory board will be engaged as of year 1 (with 2 kEUR/advisor and 10kEUR per year and advisor's meeting); (7) depreciation increases by 20% per year; (8) office expenses include rent (free for M1-6) and communication; and (9) taxes are assumed to be 25% in Austria without taking out dividends from the company.

(EUR)	%	Year 1	%	Year 2	%	Year 3
Sales	100	295,000	100	590,000	100	1,180,000
COGS	3	8,850	3	17,700	3	35,400
Gross profit	97	286,150	97	572,300	97	1,144,600
Operating expenses						
Salaries	69	205,000	52	205,000	26	205,000
Book keeping	3	7,500	1	7,500	1	7,500
Advisory Board	5	16,000	3	16,000	1	16,000
Services/Maintenance	13	38,500	10	57,750	10	115,500
Utilities	2	6,500	2	13,000	2	26,000
Advertising	2	5,000	3	20,000	3	30,000
Selling expenses	0	0	7	40,000	7	80,000
Insurance	0	0	0	0	0	0
Depreciation	1	2,700	1	3,240	0	3,888
Office expenses	1	4,200	1	7,200	1	7,200
Total operating expenses		285,400		369,690		491,088
Gross profit (loss)		750		202,610		653,512
Taxes (25%)	25	188	25	50,653	25	163,378
Net profit		**563**		**151,958**		**490,134**

Figure I. Pro Forma Income statement (pfIS), for year 1-3 (EUR). The company becomes profitable in .-1 with gross profits growing to 25% and 42% revenue in y-2 and y-3, respectively.

Figure K shows the pro forma cash flow for year 1 based on the following assumptions: (1) 50% of each month's sales will be received in cash while the remainder will be paid in the next month and (2) COGS disbursement is 90%. Equipment purchase refers to 2 high-performance computers. The CF statement shows positive CF from M4. Figure L provides the pro forma balance sheet at end of year 1.

(EUR)	mo1	mo2	mo3	mo4	mo5	mo6	mo7	mo8	mo9	mo10	mo11	mo12
Receipts												
Sales	20,000	20,000	10,000	0	50,000	40,000	10,000	60,000	0	50,000	20,000	10,000
Disbursements												
COGS	540	600	330	30	1,350	1,230	390	1,650	315	1,365	690	330
Salaries	17,083	17,083	17,083	17,083	17,083	17,083	17,083	17,083	17,083	17,083	17,083	17,083
Advisors	0	0	0	0	0	0	0	0	8,000	0	0	8,000
Services	1,200	1,200	1,200	1,200	1,200	1,200	5,000	5,000	5,000	5,000	5,000	5,000
Utilities	6,500	0	0	0	0	0	0	0	0	0	0	0
Advertising	3,000	0	0	0	0	0	0	2,000	0	0	0	0
Selling expenses	0	0	0	0	0	0	0	0	0	0	0	0
Insurance	0	0	0	0	0	0	0	0	0	0	0	0
Depreciation	200	200	200	200	200	200	250	250	250	250	250	250
Office expenses	100	100	100	100	100	100	600	600	600	600	600	600
Inventory	0	0	0	0	0	0	0	0	0	0	0	0
Total disbursements	28,623	19,183	18,913	18,613	19,933	19,813	23,323	26,583	31,248	24,298	23,623	31,263
Cash flow	-8,623	817	-8,913	-18,613	30,067	20,187	-13,323	33,417	-31,248	25,702	-3,623	-21,263
Beginning balance	100,000	91,377	92,193	83,280	64,667	94,733	114,920	101,597	135,013	103,765	129,467	125,843
Ending balance	91,377	92,193	83,280	64,667	94,733	114,920	101,597	135,013	103,765	129,467	125,843	104,580

Figure K. Pro Forma Cash Flow for y-1. Note, variable monthly income in view of likely turbulent/new market.

Assets		
Current assets		
Cash	104,580	
Accounts receivable	5,000	
Inventory	0	
Total current assets		109,580
Fixed assets		
Equipment	6,500	
Less depreciation	2,700	
Total fixed assets		3,800
Total assets		113,380
Liabilities and Owner's equity		
Current liabilities		
Accounts payable	30	
Total liabilities		30
Owner's equity		
Founder 1	33,333	
Founder 2	33,333	
Founder 3	33,333	
Retained earnings	12,480	
Total owner's equity		112,480
Total liabilities and owner's equity		113,380

Figure L. Pro forma balance sheet at end of year 1.

Based on the assumptions and calculations above, we can assume the following break-even point: fixed costs in year 1 (285kEUR) divided by (the sales price per unit = 100EUR minus variable costs per unit (300 EUR / 285 kEUR)), which results in 2900 units. That is, the company needs to sell just over 2900 use cases for the CSS to make a profit in year 1.

Finally, figure M illustrates the disposition of the earnings from operations and from other sources of financing at the end of year 1. Here, the net increase in working capital is on the order of 100KEUR.

	(EUR)	(EUR)
Source of funds		
Founders	100,000	
Net income (loss) from Ops	750	
Add depreciation	2,700	
Total funds provided		103,450
Application of funds		
Purchase of equipment	6,500	
Inventory	0	
Total funds expended		**6,500**
Net increase in working capital		**96,950**
		103,450

Figure M. Pro forma sources and applications of funds, end of year 1.

APPENDIX TO BUSINESS PLAN

Market Research Data

Note, data are available in Thesis Chapter 2; given the limited space, these data are not replicated here again.

Market Revenue.

Overview of revenue stream calculation and key assumptions (Figure N-P).

All calculations are based on the regional distribution of PET systems (Thesis Chapter 2). We assume that some imaging centres in selected geographic regions operate more than 1 PET system per centre (1.00-1.25).

The fraction of English (and German) speaking[l] sites varies between 0.3 and 1.

We account for a general readiness to use CDSS type services (85%, as per survey (section 2.5)).

Then, we single out centres/exams for oncology imaging (70-90%).

Depending on the application of the CDSS we make concessions to the fraction of oncology examinations performed with the following radiotracers: [18F]-FDG (breast): 75-100%, [18F]-MET (glioma): 0%-5%, and [18F]FCH (prostate): 0%-24%[m].

Subsequent estimations assume a fraction of examinations performed for breast cancer (5-20%), glioma (5-20%) and prostate cancer (1-20%).

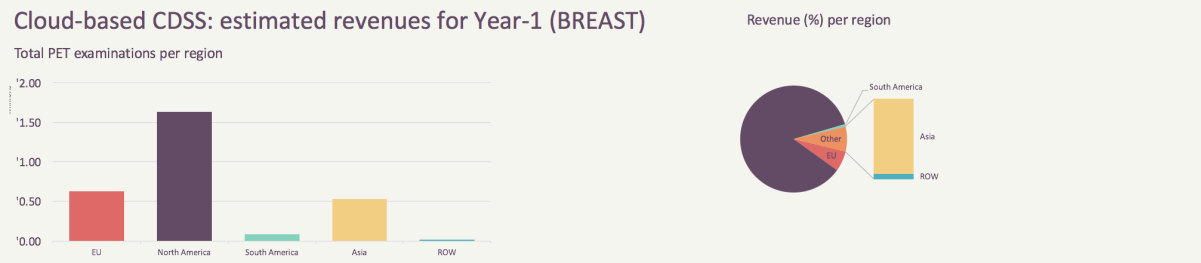
Then, we account for a reach factor, i.e. only a fraction of people will respond to the product offering (0.5-15%).

And finally, we make a very conservative concession of a "money-back-guarantee" during the launch of the product, which represents a mix of a probability-based result and a general result-driven acceptance rate of the users. We assume that 10-50% will make use of it in return for accessing their data.

Predictive analytics are assumed to cost 100 EUR per case, incl. VAT.

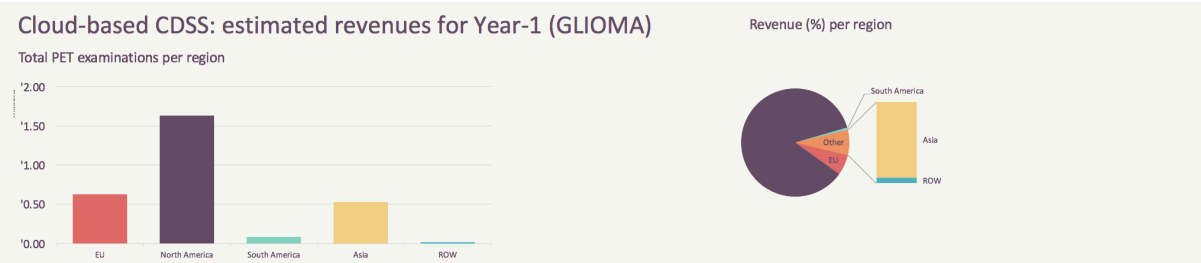
[l] We target English and German speaking sites during start-up in order to avoid costs for translations. However, during early growth materials should be made available in Mandarin, for example.

[m] Beyer T, Czernin J and Freudenberg L. Variations in clinical PET/CT operations. J Nucl Med 52: 303-10, 2011.



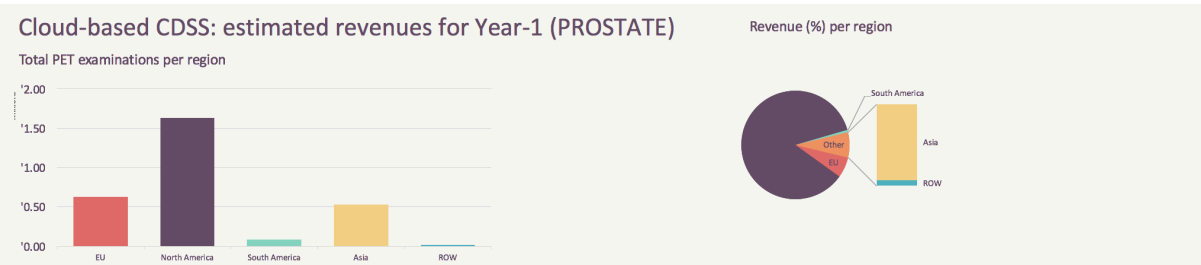
Regions	PET systems	Systems per ctr	PET Centres	English/ German speaking	English/ German speaking	CDSS Survey positive response	Potential customer centres	PET exams per system	Total PET exams	Oncology	Eligible oncology PET exams	FDG Oncology	Eligible FDG Oncology	BreastCA indication	Eligible breastCA PET exams	Reach& Response	Accessible PET exams tot	Money-back	Revenue PET exams	Costs/Case [EUR]	Total Income
EU	976	1.10	887	0.65	577	0.85	490	1,160	625,518	0.80	500,415	0.75	375,311	0.05	18,766	0.050	938	0.80	751	100	EUR 75,062
North America	2,340	1.25	1,872	1.00	1,872	0.85	1,591	820	1,630,980	0.90	1,467,882	0.95	1,394,488	0.10	139,449	0.100	13,945	0.75	10,459	100	EUR 1,045,866
South America	187	1.00	187	0.50	94	0.85	79	1,075	85,425	0.80	68,340	0.95	64,923	0.05	3,246	0.030	97	0.90	88	100	EUR 8,765
Asia	2,110	1.20	1,758	0.30	528	0.85	448	983	529,125	0.75	396,844	0.90	357,159	0.05	17,858	0.080	1,429	0.60	857	100	EUR 85,718
ROW	58	1.00	58	0.40	23	0.85	20	948	18,700	0.70	13,090	1.00	13,090	0.20	2,618	0.030	79	0.80	63	100	EUR 6,283
Total	5,671		4,763		3,093		2,629		2,889,748		2,446,570		2,204,971		181,936		16,488		12,217		EUR 1,221,694

Figure N. Revenue stream for predictive analytics for breast cancer patients following an [18F]-FDG PET/CT examination.



Regions	PET systems	Systems per ctr	PET Centres	English/ German speaking	English/ German speaking	CDSS Survey positive response	Potential customer centres	PET exams per system	Total PET exams	Oncology	Eligible oncology PET exams	MET Oncology	Eligible MET Oncology	Glioma indication	Eligible glioma PET exams	Reach& Response	Accessible PET exams tot	Money-back	Revenue PET exams	Costs/Case [EUR]	Total Income
EU	976	1.10	887	0.65	577	0.85	490	1,160	625,518	0.80	500,415	0.050	25,021	0.05	1,251	0.050	63	0.80	50	100	EUR 5,004
North America	2,340	1.25	1,872	1.00	1,872	0.85	1,591	820	1,630,980	0.90	1,467,882	0.020	29,358	0.10	2,936	0.100	294	0.75	220	100	EUR 22,018
South America	187	1.00	187	0.50	94	0.85	79	1,075	85,425	0.80	68,340	0.005	342	0.05	17	0.030	1	0.90	0	100	EUR 46
Asia	2,110	1.20	1,758	0.30	528	0.85	448	983	529,125	0.75	396,844	0.007	2,778	0.05	139	0.080	11	0.60	7	100	EUR 667
ROW	58	1.00	58	0.40	23	0.85	20	948	18,700	0.70	13,090	0.000	0	0.20	0	0.030	0	0.80	0	100	EUR 0
Total	5,671		4,763		3,093		2,629		2,889,748		2,446,570		57,498		4,343		368		277		EUR 27,735

Figure O. Revenue stream for predictive analytics for glioma cancer patients following an [18F]-MET PET examination.



Regions	PET systems	Systems per ctr	PET Centres	English/ German speaking	English/ German speaking	CDSS Survey positive response	Potential customer centres	PET exams per system	Total PET exams	Oncology	Eligible oncology PET exams	FCH Oncology	Eligible FCH Oncology	Prostate indication	Eligible prostate PET exams	Reach& Response	Accessible PET exams tot	Money-back	Revenue PET exams	Costs/Case [EUR]	Total Income
EU	976	1.10	887	0.65	577	0.85	490	1,160	625,518	0.80	500,415	0.200	100,083	0.10	10,008	0.050	500	0.80	400	100	EUR 40,033
North America	2,340	1.25	1,872	1.00	1,872	0.85	1,591	820	1,630,980	0.90	1,467,882	0.030	44,036	0.05	2,202	0.100	220	0.75	165	100	EUR 16,514
South America	187	1.00	187	0.50	94	0.85	79	1,075	85,425	0.80	68,340	0.030	2,050	0.01	10	0.030	0	0.90	0	100	EUR 28
Asia	2,110	1.20	1,758	0.30	528	0.85	448	983	529,125	0.75	396,844	0.100	39,684	0.10	3,968	0.080	317	0.60	190	100	EUR 19,049
ROW	58	1.00	58	0.40	23	0.85	20	948	18,700	0.70	13,090	0.005	65	0.20	13	0.030	0	0.80	0	100	EUR 31
Total	5,671		4,763		3,093		2,629		2,889,748		2,446,570		185,919		16,202		1,039		757		EUR 75,654

Figure P. Revenue stream for predictive analytics for prostate cancer patients following an [18F]-FCH-PET/MR examination.

Letters

Here, a statement of interest would be provided by an investor.

Leases and Contracts

If any leases of office space were signed, a copy would be placed here.

Price list of suppliers

Here, a price list for IT infrastructure could be provided.

Management team

Resumes of the management team (founders and advisors) would be included.

5. CONCLUSION AND OUTLOOK

This chapter summarizes take home messages from the theory review and main conclusions from this study. This section contains an up-to-date summary of the status of the firm for future reference.

A **professional engagement in healthcare** can be rewarding for many reasons. First, it may hold new insight into the causes of disease and corresponding choices of treatment options for a given patient (*personalized medicine*). Second, there is **financial reward** for **innovative solutions** that provide accurate diagnoses, reliably and fast. Ultimately, any progress in healthcare should benefit patients and their families. Preferably, healthcare innovations should help **contain costs** of the healthcare services, also in light of the growth of the (elderly) population.

In this work, the idea of an **advanced clinical decision support system (CDSS)** for **cancer** patient management is proposed. Cancer related costs to the healthcare system are on the order of several hundred billion Euros. Non-invasive imaging can help diagnose cancer disease early, thus, paving the way for an efficient therapy (**chapter 1**). However, frequently, additional invasive biopsy sampling of the lesion(s) suspected of cancer is indicated. Biopsy procedures are challenged by the heterogeneity and multiplicity of lesions, and, therefore, bioptic tumour characterization is limited. However, it was shown that both, imaging and non-imaging biomarker information taken together, and referred to advanced data processing can help improve the diagnosis of cancer patients. The use of a ***big data*** approach to **characterizing tumours** is of great potential. Analyzing big data in healthcare as part of a CDSS should be considered as a complementary armamentarium to the medical doctors rather than their short-term replacement. A CDSS provides supportive data for their readings and diagnoses, which will help them **choose the right therapy** for the benefit of the patients and healthcare systems.

Chapter 2 describes the business opportunity for utilizing a big data approach to non-invasive tumour characterization. This opportunity resonates with **current megatrends in modern healthcare**, incl. *digitization, cloud storage and computing, big data, molecular imaging* and *cost containment*. These trends have become obvious through extensive desk research as part of this thesis work. The business idea of a CDSS for **predictive analytics for non-invasive tumour characterization** as part of oncology patient management is intended to be turned into a viable business. Prior to developing a business plan additional field research has been conducted to determine key product definition parameters and to help better **define the target customer groups**. Interviews with healthcare actors indicated a general interest in a CDSS type service and a willingness to adopt such services in case they are certified (e.g., CE mark). Non-invasive tumour characterization is conceived particularly valuable in breast and prostate cancer as well as lung and colorectal cancer. While pilot data exist for the first (as well as glioma), the CDSS functionalities for the other types of tumours do not exist yet. Here, the biggest obstacle to an immediate and wide-spread distribution of a CDSS service offering is the **shortage of large data cohorts** that are accessible to train and validate our ML engine. However,

this is a general challenge for any big data type analysis tool in healthcare, and given that **direct competition** on this business idea to date is limited, a very promising business opportunity is perceived for cloud based tumour characterization. **Target customers** were identified as well, that span from the patients, medical doctors to stakeholders in pharmaceutical developments and insurance providers (chapter 2). Without a doubt, the entire healthcare industry will benefit from the adoption of predictive analytics, pending a coherent and **joint approach with the regulatory bodies**.

The above business idea originated from past and current research engagements of three founders who intend to productize this idea as part of an ***academic spin off*** **(ASO)**. Starting a business, and an ASO, in particular, requires the appreciation of a number of key variables and processes, which are reviewed and discussed in **chapter 3**. For example, in order for inventors and innovators to become **successful entrepreneurs**, they must exhibit a number of **personal traits and skills** that extend beyond curiosity and determination. Furthermore, **starting a business from academia** can be more complex, given the frequent lack of entrepreneurial and business background and networks, while it may hold a number of advantages, such as the ability to quickly engage in well-defined research activities to further generate specific proof points or support a given value proposition. At the same time, **agreements** (**licensing, royalty** and alike) must be made with the host university to ensure data access, if required, and to further agree on the terms for a joint engagement of the faculty in academia and their spin-off (*cf* **duality-of-interest**). In the case of the CDSS model proposed here, special agreements must be made with the university to access training data that are needed for building the ML engine (aka licensing agreements). The **theoretical background** in this chapter highlights the entrepreneurial traits and their value during conception and birth (*aka* **gestation**) of the start-up, before pointing to a series of actions and measures to take when moving from an idea to an actual company start-up (**post-birth**). The implications for the CDSS based start-up have been reviewed and used to update the business model where applicable, following additional field research with a series of healthcare start-up managers. Following this theoretical background review, the founders felt more content in developing a **business plan**.

This plan is laid out in **chapter 4**. This plan is for real and the information provided therein should not be disclosed to third parties for the wilful purpose of mimicking this business idea. Specifically, our **financial plan** indicates a total revenue of 2MEUR and a gross net profit of 0.7MEUR after the 3rd year of operations. The business plan addresses the shortcomings in entrepreneurial traits, risks and financial strategy based on the findings from chapter 1-3. **Specific summary boxes** are given at the beginning of each section of the plan. As of May 2017, the company has not been founded yet, but the future founders have applied with an Austrian incubator (stage2/3) and an application for seed funding with the Austrian Bureau of Economy is work in progress. Readers are now invited to judge whether the persons involved in this start-up are capable of dealing with the uncertainty, which is considered a core ability of an entrepreneur, and whether they consider this a promising business model.

BIBLIOGRAPHY

[1] Global Burden of Disease Health Financing Collaborator network. Future and potential spending on health 2015-40: development assistance for health, and government, prepaid private, and out-of-pocket health spending in 184 countries. The Lancet Apr-19, 2017; http://www.thelancet.com/journals/lancet/article/PIIS0140-6736(17)30873-5/fulltext

[2] http://data.worldbank.org/indicator/SH.XPD.TOTL.ZS

[3] M Pomp and S Vujic. CPB Discussion Paper. Rising health spending, new medical technology and the Baumol effect. No 115. 2008; ISBN 978-90-5833-386-5.

[4] A Ward. Healthcare: Counting the cost of cancer. FT Jan-15, 2015.; https://www.ft.com/content/5e0b1f54-9ca0-11e4-a730-00144feabdc0

[5] HJ Burstein et al. Clinical Cancer Advances 2017. J Clin Oncology 35: 1-27, 2017

[6] DM Berwick and AD Hackbarth. Eliminating waste in US health care. JAMA 307(14): 1513-6, 2012

[7] I Rausch and T Beyer, PET/CT-Atlas. Interdisziplinäre PET/CT- und PET/MR-Diagnostik und Therapie (editors: W Mohnike, G Hör, A Hertel and H Schelbert), p 5-35, Springer, ISBN 978-3-662-48842-3, 2016

[8] DC Collins et al, Towards Precision Medicine in the Clinic: From Biomarker Discovery to Novel Therapeutics. Trends Pharma Science 38: 25-40, 2017; https://www.ncbi.nlm.nih.gov/pubmed/?term=Collins%2C+SUndar%2C+Lim%2C+2017

[9] DN Louis et al., Computational Pathology – An emerging definition. Arch Pathol Lab med 138: 1133-1138, 2014

[10] Preparing for the future of artificial intelligence. A report by the National Science and Technology Council Committee on Technology. October 2016. https://www.whitehouse.gov/sites/default/files/whitehouse_files/microsites/ostp/NSTC/preparing_for_the_future_of_ai.pdf

[11] J Shiraishi et al, Computer-Aided Diagnosis and Artificial Intelligence in Clinical Imaging. Seminars in Nucl Med 41(6): 449-62, 2011; http://www.seminarsinnuclearmedicine.com/article/S0001-2998(11)00074-2/pdf

[12] lB Lusted. Logical Analysis in Roentgen Diagnosis. Radiology 74(2): 178-193, 1960; http://pubs.rsna.org/doi/10.1148/74.2.178?url_ver=Z39.88-2003&rfr_id=ori:rid:crossref.org&rfr_dat=cr_pub%3dpubmed

[13] Tanveer Syeda-Mahmood plenary talk: The Role of Machine Learning in Clinical Decision Support): https://www.youtube.com/watch?v=A4Uk88-DOBA

[14] M Gandhi and T Wang. The Future of Personalized Healthcare: predictive Analytics. Rock+Health Report 2017. https://rockhealth.com/reports/predictive-analytics/

[15] AM Turing. Computing Machinery and Intelligence. Mind 49: 433-60, 1950; https://www.csee.umbc.edu/courses/471/papers/turing.pdf

[16] L Gaines-Ross. What do people – Not Techies, Not Companies – Think About Artificial Intelligence?. Harvard Business review – Technology. Oct-24, 2016; https://hbr.org/2016/10/what-do-people-not-techies-not-companies-think-about-artificial-intelligence

[17] CBinsights. The AI 100 Ranking, 2017. https://www.cbinsights.com/research-reports/CB-Insights_AI-100-2017.pdf

[18] D Wang et al, Deep Learning for Identifying Metastatic Breast Cancer. Jun-18, 2016; https://arxiv.org/pdf/1606.05718v1.pdf

[19] Defining the opportunity for machine learning in radiology Signify research Nov-16, 2016, http://signifyresearch.net/analyst-insights/defining-the-opportunity-for-machine-learning-in-radiology/

[20] https://www.forbes.com/sites/jaysondemers/2016/11/16/7-technology-trends-that-will-dominate-2017/#d78bc724a51d

[21] Z Obermeyer and EJ Emanuel, Predicting the Future – Big Data, machine learning, and Clinical Medicine. NEJM 375(13): 1216-9, 2016; https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5070532/

[22] S Zilis and J Cham. The Competitive Landscape for Machine Intelligence. HBR Technology, Nov-02, 2016; https://hbr.org/2016/11/the-competitive-landscape-for-machine-intelligence

[23] AIPES Symposium "Saving costs in cancer patient management through Nuclear medicine. Sep-28, 2016: http://www.aipessymposium.eu

[24] https://www.whitehouse.gov/precision-medicine

[25] J Schaffhausen. What precisely is precision Medicine? Trends Pharmacol Sci 38(1): 1-2, 2017; https://linkinghub.elsevier.com/retrieve/pii/S0165-6147(16)30162-6

[26] P Vallance. Industry-Academic Relationship in a New Era of Drug Discovery. J Clin Oncol 34(29): 3570-5, 2016; http://ascopubs.org/doi/pdf/10.1200/JCO.2016.68.4217

[27] PM Matthews et al. PET molecular imaging for drug development. Br J Clin Pharmacol 73(2): 175-86, 2012. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3269576/

[28] http://management-of-innovation.over-blog.com/pages/Fun_For_Medicine_A_Unique_NPO_For_The_Medical_Progress-8921500.html

[29] M Schwaederle et al, Association of Biomarker-Based Treatment Strategies With Response Rates and Progression-Free Survival in Refractory Malignant Neoplasms: A Meta-analysis, JAMA Oncol 2(11): 1452-9, 2016; http://jamanetwork.com/journals/jamaoncology/fullarticle/2527365

[30] Health care. The wonder drug. The Economist Mar-4, 2017; p49-50; http://www.economist.com/news/business/21717990-telemedicine-predictive-diagnostics-wearable-sensors-and-host-new-apps-will-transform-how

[31] J Nicas and J Greene. Google chases Rivals in Push Into Cloud Computing. The Wall Street Journal. B4, Mar-9, 2017.

[32] Forrester's Global Business Technographics Software Survey, 2016; in: The Wall Street Journal Mar-7, 2017: R8. https://www.forrester.com/data/business/dashboards

[33] How AI will Change Everything. The Wall Street Journal R2, Mar-7, 2017

[34] Big Data Executive Survey 2016. New Vantage Partners 2016. http://newvantage.com/wp-content/uploads/2016/01/Big-Data-Executive-Survey-2016-Findings-FINAL.pdf

[35] https://www.tableau.com/resource/top-10-big-data-trends-2017

[36] http://pwchealth.com/cgi-local/hregister.cgi/reg/pwc-hri-top-healthcare-issues-2017.pdf

[37] http://hitconsultant.net/2017/01/09/7-healthcare-trends-to-watch-in-2017/

[38] https://www.google.at/url?sa=t&rct=j&q=&esrc=s&source=web&cd=1&ved=0ahUKEwij-O_V8IbUAhVQKywKHaTBC6kQFggoMAA&url=http%3A%2F%2Fwww.eweek.com%2Fc%2Fa%2FHealth-Care-IT%2FCloud-Computing-in-Health-Care-to-Reach-54-Billion-by-2017-Report-512295&usg=AFQjCNGS4oEUk9kPnZgIBelNWrYAMCzmBA&sig2=IdXNhAcLHyZEQrjCXW9RYw

[39] 8.6 mio PET examinations per year worlwdie. Personal communication, Carl von Gall, Siemens Healthcare, Sep-28, 2016

[40] Personal communication Marcus MD, Medical University Vienna, Austria

[41] RL Winslow, N Trayanova, D Geman and MI Miller. Computational medicine: Translating models to clinical care. Sci Transl Med 4(158): 1-21,2012.

[42] RG Hamermesh and K Guisti. One obstacle to curing cancer: patient data isn't shared. HBR Nov-28, 2016. https://hbr.org/2016/11/one-obstacle-to-curing-cancer-patient-data-isnt-shared

[43] 5 Reasons why radiology needs artificial intelligence. Signify Research, Oct-25, 2016, http://signifyresearch.net/knowledge-centre/5-reasons-why-radiology-needs-ai/

[44] S Harris. Machine learning in radiology targets efficiency. AuntMinnieEurope Feb-6, 2017. http://www.auntminnieeurope.com/index.aspx?sec=sup&sub=adv&pag=dis&ItemID=613990

[45] http://m.healthcareitnews.com/news/artificial-intelligence-cognitive-computing-and-machine-learning-are-coming-healthcare-it-time

[46] http://www.datamation.com/cloud-computing/110-billion-cloud-market-growing-28-annually-synergy-research.html

[47] http://www.forbes.com/sites/louiscolumbus/2016/03/13/roundup-of-cloud-computing-forecasts-and-market-estimates-2016/#3b733a5e74b0

[48] http://global.agfahealthcare.com/main/enterprise-imaging/

[49] http://global.agfahealthcare.com/us/enterprise-imaging/managed-services/

[50] https://techcrunch.com/2015/08/06/ibm-buying-merge-healthcare-for-1b-to-bring-medical-image-analysis-to-watson-health/

[51] https://www.accenture.com/t20160602T011605__w__/us-en/_acnmedia/Accenture/Conversion-Assets/DotCom/Documents/Global/PDF/Industries_13/Accenture-Fueled-Healthcare-IT-Start-Up-Funding-Digital-Disruption-Knocking.pdf

[52] Signify Research. Analysis of venture Capital investment in Diagnostic Analytics Companies. http://signifyresearch.net/knowledge-centre/venture-capital-investment-diagnostic-analytics/

[53] S Harris. Funding Analysis of Companies developing ML solutions for Medical Imaging. Mar-10, 2017. http://signifyresearch.net/knowledge-centre/funding-analysis-of-companies-developing-machine-learning-solutions-for-medical-imaging/

[54] http://www.marketsandmarkets.com/Market-Reports/cloud-computing-healthcare-market-347.html

[55] S Harris. Quantitative Imaging Software Market to Exceed 500 m$ in 2021. Signify research. Jan-27, 2017. http://signifyresearch.net/analyst-insights/quantitative-imaging-software-market-exceed-500m-2021/

[56] http://www.marketsandmarkets.com/Market-Reports/diagnostic-imaging-market-411.html?gclid=CILS5qKdyM8CFYky0wod0mwBLg

[57] PET market is poised for healthy growth. Aunt Minnie Oct-11, 2016: http://www.auntminnie.com/index.aspx?sec=sup&sub=mol&pag=dis&ItemID=115325

[58] Global isotope market could reach 7b$ by 2020. Aunt Minnie Jul-8, 2015: http://www.auntminnie.com/index.aspx?sec=sup&sub=mol&pag=dis&ItemID=111381

[59] S Zilis and J Cham. The competitive landscape for machine intelligence. HBR Nov-2, 2016. https://hbr.org/2016/11/the-competitive-landscape-for-machine-intelligence

[60] B Meskó. Top Artificial Intelligence Companies in Healthcare to Keep an Eye On. Healthcare Technology Feb-2, 2017. https://www.linkedin.com/pulse/top-artificial-intelligence-companies-healthcare-keep-meskó-md-phd

[61] https://www.imagia.com

[62] http://qure.ai

[63] http://lunit.io/publications/

[64] http://www.shimadzu.com/an/industry/pharmaceuticallifescience/drugdiscovery0101020.html

[65] https://www.clearviewdiagnosticsinc.com

[66] http://curemetrix.com/how-it-works/

[67] http://www.icadmed.com

[68] http://www.fiercebiotech.com/medical-devices/siemens-buys-german-liquid-biopsy-startup-to-enter-molecular-oncology-dx

[69] Is $500M enough? The Signify View on GE Healthcare's investment in digital health. http://signifyresearch.net/analyst-insights/is-500m-enough-the-signify-view-on-ge-healthcare-investment-in-digital-health/

[70] https://www.youtube.com/watch?v=0i11VCNacAE

[71] https://www.youtube.com/watch?v=A4Uk88-DOBA

[72] Health care. The wonder drug. The Economist, Mar-4, 2017, p49-50

[73] For example, in Germany 42 drugs are approved only in conjunction with a genetic test prior to therapy. This was discussed in an article on the company Qiagen (FAZ Jan-11, 2017).

[74] S Kavadias, K Ladas and C Loch. The transformative business model. HBR Oct 2016, https://hbr.org/2016/10/the-transformative-business-model

[75] https://docs.google.com/forms/d/1P0BogSRwIJtTMzz-2PVc-o_eV16eYvR6G_hQEVOCZ8g/edit

[76] National Cancer Institute. Cancer prevalence and cost of care projections 2010-20: https://costprojections.cancer.gov/expenditures.html

[77] S Harris. Target applications for machine learning in medical imaging. Signify research Apr-13, 2017: http://signifyresearch.net/analyst-insights/target-markets-for-machine-learning-in-medical-imaging/

[78] K Giusti and RG Hamermesh. What cancer researchers can learn from DTC companies. HBR Marketing. Jan-12, 2017: https://hbr.org/2017/01/what-cancer-researchers-can-learn-from-direct-to-consumer-companies

[79] R A-S Alman et al. Increasing value and reducing waste in biomedical research regulation and management. The Lancet 383: 176-185, 2014

[80] WB Gartner. A conceptual framework for describing the phenomenon of new venture creation. Academy of Management Review 10(4): 696-706, 1985

[81] A Vohora, M Wright and A Lockett. Critical junctures in the development of university high-tech spinout companies. Research Policy 33: 147-75, 2004

[82] P Reynolds and B Miller. New firm gestation: conception, birth, and implications for research. J Business Venturing 7: 405-17, 1992

[83] P Burns. Entrepreneurship and small business. Start-up, growth and maturity. 4th edition. Palgrave. ISBN 978-1-137-43035-9, 2016

[84] NM Carter, WB Gartner and PD Reynolds. Exploring start-up event sequences. J Business Venturing 11: 151-66, 1996.

[85] AH Van de Ven et al. Designing new business startups: Entrepreneurial, organizational and ecological considerations. J of Management 10(1): 87-107, 1984

[86] RA Baron and MD Ensley. Opportunity recognition as the detection of meaningful patterns: Evidence from comparisons of novice and experienced entrepreneurs. Management Science 52(9): 1331-44, 2006

[87] EJ Gatewood, KG Shaver and WB Gartner. A longitudinal study of cognitive factors influencing start-up behaviors and success at venture creation. J Business Venturing 10: 371-91, 1995

[88] H Jo and J Lee. The relationship between entrepreneur's background and performance in a new venture. Technovation 16(4): 161-71, 1996

[89] A Rauch and M Frese. Let's put the person back into entrepreneurship research: A meta-analysis on the relationship between business owner's personality traits, business creation and success. Eur J Work and Org Psychology 16(4): 353-85, 2007

[90] KU Koskinen and H Vanharanta. The role of tacit knowledge in innovation processes of small technology companies. Int J Production Economics 80: 57-64, 2002

[91] JM Unger, A Rauch, M Freese and N Rosenbusch. Human capital and entrepreneurial success: A meta-analytical review. J Busines Venturing 26: 341-58, 2011

[92] M Steffensen, EM Rogers and K Sopeakman. Spin-offs from research centres at research universities. J Business Venturing 15: 93-111, 1999

[93] F Pirnay, B Surlemont and F Nlemvo. Toward a typology of university spin-offs. Small Business Economics 21: 355-69, 2003

[94] J Coyvas, M Crow, A Gelijns, R Mazzoleni, RR nelson, N Rosenberg and BN Sampat. How do university inventions get into practice? Mgmt Science 48(1): 61-72, 2002

[95] SH DeCleyn, J Braet and M Klofsten. How do human and social capital contribute to the early development of academic spin-off ventures? Frontiers Entrepreneurship Research 31917): 567-81, 2011

[96] DJ Bower. Business model fashion and the academic spinout firm. R&D Mgmt 32(2): 97-106, 2003

[97] BJ Bird, DJ Hayard and DN Allen. Conflicts in the commercialization of knowledge: Perspective from science and entrepreneurship. Entrepreneurship Theory and Practice. Jun-22: 57-77, 1993

[98] J Lerner. The university and start-up: Lessons from the past two decades. J Technology Transfer 30: 49-56, 2005

[99] T Beyer and J Czernin. Is conflict of interest in our best interest. Eur J Nucl Med Mol Imag 37(6): 1063-8, 2010

[100] EB Roberts and DE Malone. Policies and structures for spinning off new companies from research and development organizations. 1-31, 1995: https://dspace.mit.edu/bitstream/handle/1721.1/2569/SWP-3804-32616509.pdf

[101] D DiGregorio and S Shane. Why do some universities generate more start-ups than others? Research Policy 32: 209-27, 2003

[102] A Lockett, M Wright and S Franklin. Technology transfer and university's spin-out strategies. Small Business Economics 20: 185-200, 2003

[103] JB Powers and PP McDougall. University start-up formation and technology licensing with firms that go public: a resource-based view of academic entrepreneurship. J Business Venturing 20: 291-311, 2005

[104] AN Link, JT Scott and DS Siegel. The economics of intellectual property at universities: an overview of the special issue. Int J Industrial Organizations 21: 1217-25, 2003

[105] GD Markman, PH Phan, DB Balkin and PT Gianiodis. Entrepreneurship and university-based technology transfer. J Business Venturing 20: 241-63, 2005

[106] R Jensen and M Thursby. Proofs and protoypes for sale: The tale of University licensing. National Bureau of Economic Research. Working paper 6698. August 1998: www.nber.org/papers/w6698

[107] MJ Lynskey. The entrepreneurial university and spin-out firms in the UK. Industry & Higher Education 22(2): 81-98, 2008

[108] G Fürlinger and K-H Leitner. The role of social capital for university start-up incubation: A multi-level comparison of USA and Europe. Final report on the ÖNB project 15500, AIT Vol 123, 2016: http://austrianstartupmonitor.at/wp-content/uploads/2016/05/Endbericht-OeNB-Projekt-nr-15500-März-2016_final.pdf

[109] J Ruzicka. Kleinfirmenförderung bei Hochschulen verankern. DER STANDARD. Dec-5, 2016

[110] R Singer. Startschwierigkeiten. Kein Land fördert seine start-ups so sehr wie Österreich. Wiener Zeitung, Feb 18-19, 2017

[111] European Startup Monitor 2016: http://europeanstartupmonitor.com/esm/esm-2016/

[112] ME Porter. What is strategy? HBR Nov-Dec 1996, https://hbr.org/1996/11/what-is-strategy

[113] PS Cohan. Does your startup have a strategy? Entrepreneur. Jun-4, 2014, https://www.entrepreneur.com/article/234473

[114] M Newlands. 9 strategies all startups must have to sustain growth. StartUpGrind 2015, https://www.startupgrind.com/blog/9-strategies-all-startups-must-have-to-sustain-business-growth/

[115] G Deeb. For a successful startup, you need strategy and execution. Entrepreneur. Feb-3, 2015, https://www.entrepreneur.com/article/242457

[116] R McGrath and I MacMillan. Discovery-Driven Planning. HBR Jul-Aug 1995, https://hbr.org/1995/07/discovery-driven-planning

[117] A Gallo. A refresher on discovery-driven planning. HBR Feb13, 2017, https://hbr.org/2017/02/a-refresher-on-discovery-driven-planning

[118] GC Reid and JA Smith. What makes a new business start-up successful? Small Business Economics 14:165-182, 2000

[119] A Grandi and R Grimaldi. Academics' organizational characteristics and the generation of successful business ideas. J Business Venturing 20: 821-45, 2005

[120] A Vohora, M Wright and A Lockett. Critical junctures in the development of university high-tech spinout companies. Research Policy 33: 147-75, 2004

[121] RD Hisrich, MP Peters and DA Shepherd. Entrepreneurship. McGraw Hill Education. 9th edition. ISBN 978-007-132631-5, 2013

[122] Harris S. how to sell machine learning algorithms to healthcare providers. Signify Research Mar-30, 2017: http://signifyresearch.net/analyst-insights/how-to-sell-machine-learning-algorithms-to-healthcare-providers/

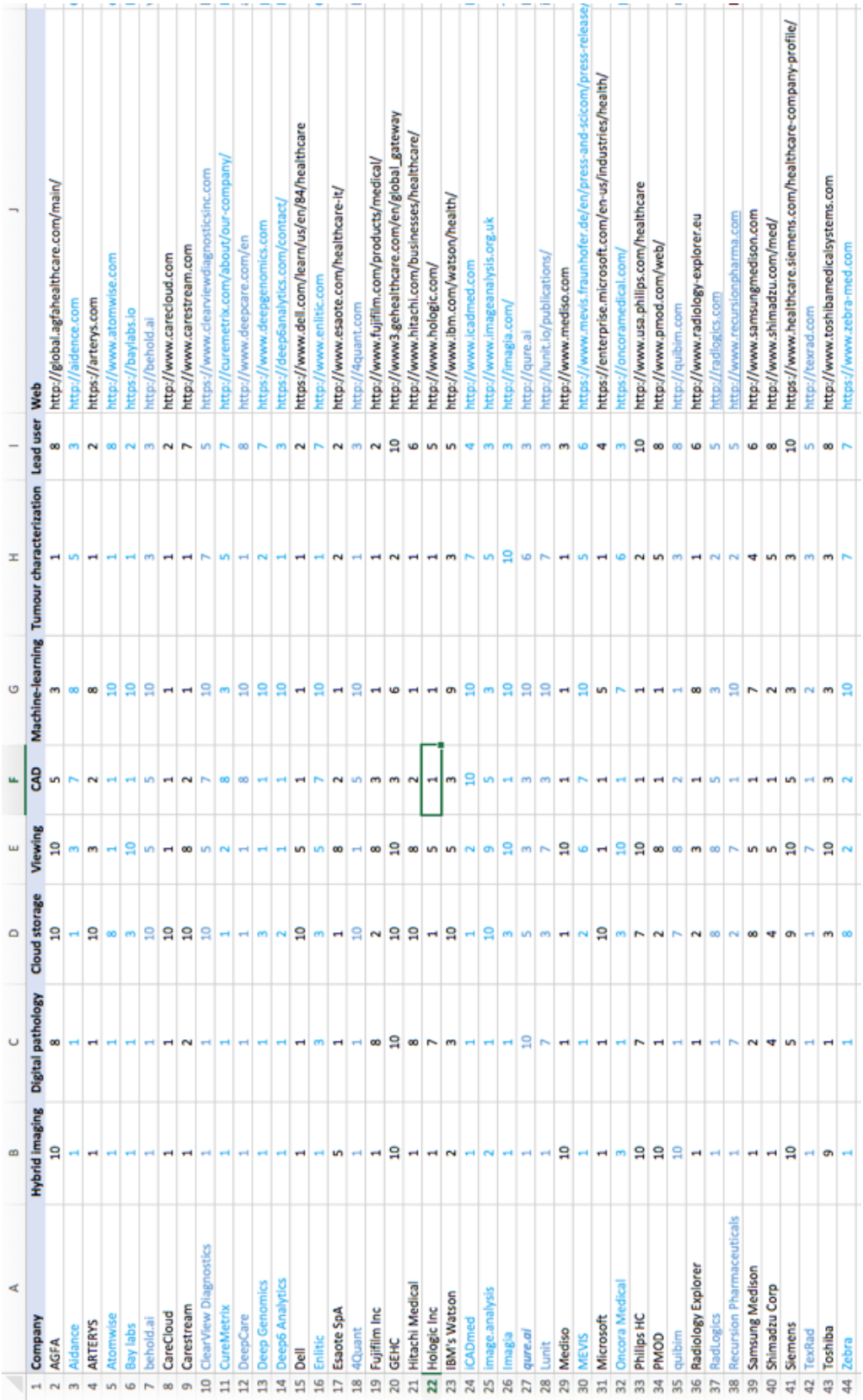
[123] www.eortc.org/data-sharing/

[124] T Beyer, J Czernin and L Freudenberg. Variations in clinical PET/CT operations. J Nucl Med 52: 303-10, 2011

[125] 7 Healthcare Trends to Watch in 2017. http://hitconsultant.net/2017/01/09/7-healthcare-trends-to-watch-in-2017/

APPENDIX

Appendix 1. Complete list of healthcare companies analyzed in section 2.3.6.



Company	Hybrid imaging	Digital pathology	Cloud storage	Viewing	CAD	Machine-learning	Tumour characterization	Lead user	Web
AGFA	10	8	10	10	5	3	1	8	http://global.agfahealthcare.com/main/
Aidance	1	1	1	3	7	8	5	3	http://aidence.com
ARTERYS	1	1	10	3	2	8	1	2	https://arterys.com
Atomwise	1	1	8	1	1	10	1	8	https://www.atomwise.com
Bay labs	1	1	3	10	1	10	1	2	https://baylabs.io
behold.ai	1	1	10	5	5	10	3	3	http://behold.ai
CareCloud	1	1	10	1	1	1	1	2	http://www.carecloud.com
Carestream	1	2	10	8	2	1	1	7	http://www.carestream.com
ClearView Diagnostics	1	1	10	5	7	10	7	5	https://www.clearviewdiagnosticsinc.com
CureMetrix	1	1	1	2	8	3	5	7	http://curemetrix.com/about/our-company/
DeepCare	1	1	1	1	8	10	1	8	http://www.deepcare.com/en
Deep Genomics	1	1	3	1	1	10	2	7	https://www.deepgenomics.com
Deep6 Analytics	1	1	2	1	1	10	1	3	https://deep6analytics.com/contact/
Dell	1	1	10	5	1	1	1	2	https://www.dell.com/learn/us/en/84/healthcare
Enlitic	1	3	3	5	7	10	1	7	http://www.enlitic.com
Esaote SpA	5	1	1	8	2	1	2	2	http://www.esaote.com/healthcare-it/
4Quant	1	1	10	1	5	10	1	3	http://4quant.com
Fujifilm Inc	1	8	2	8	3	1	1	2	http://www.fujifilm.com/products/medical/
GEHC	10	10	10	10	3	6	2	10	http://www3.gehealthcare.com/en/global_gateway
Hitachi Medical	1	8	10	8	2	1	1	6	http://www.hitachi.com/businesses/healthcare/
Hologic Inc	1	7	1	5	1	1	1	5	http://www.hologic.com/
IBM's Watson	2	3	10	5	3	9	3	5	http://www.ibm.com/watson/health/
iCADmed	1	1	1	2	10	10	7	4	http://www.icadmed.com
image.analysis	2	1	10	9	5	3	5	3	https://www.imageanalysis.org.uk
Imagia	1	1	3	10	1	10	10	3	http://imagia.com/
qure.ai	1	10	5	3	3	10	6	3	http://qure.ai
Lunit	1	7	3	7	3	10	7	3	http://lunit.io/publications/
Mediso	10	1	1	10	1	1	1	3	http://www.mediso.com
MEVIS	1	1	2	6	7	10	5	6	https://www.mevis.fraunhofer.de/en/press-and-scicom/press-release/
Microsoft	1	1	10	1	1	5	1	4	https://enterprise.microsoft.com/en-us/industries/health/
Oncora Medical	3	1	3	10	1	7	6	3	https://oncoramedical.com/
Philips HC	10	7	7	10	1	1	2	10	http://www.usa.philips.com/healthcare
PMOD	10	1	2	8	1	1	5	8	http://www.pmod.com/web/
quibim	10	1	7	8	2	1	3	8	https://quibim.com
Radiology Explorer	1	1	2	3	1	8	1	6	http://www.radiology-explorer.eu
RadLogics	1	1	8	8	5	3	2	5	http://radlogics.com
Recursion Pharmaceuticals	1	7	2	7	1	10	2	5	http://www.recursionpharma.com
Samsung Medison	1	2	8	5	1	7	4	6	http://www.samsungmedison.com
Shimadzu Corp	1	4	4	5	1	2	5	8	https://www.shimadzu.com/med/
Siemens	10	5	9	10	5	3	3	10	https://www.healthcare.siemens.com/healthcare-company-profile/
TexRad	1	1	1	7	1	2	3	5	http://texrad.com
Toshiba	9	1	3	10	3	3	3	8	http://www.toshibamedicalsystems.com
Zebra	1	1	8	2	2	10	7	7	https://www.zebra-med.com

Appendix 2. Survey and interview template with CEOs of small firms (Section 3.3)

Cloud-based characterization of lesions in cancer patients.
A business plan for a University spin-off (USO).

INTERVIEW
with managers of USO and SME
on Innovation and Strategy for start-up businesses

Mar-03, 2017
thomas.beyer@s.wu.ac.at

BACKGROUND

I would like to ask you as few questions regarding innovation and strategy for start-up businesses. The results from this survey are planned to be used as part of an MBA dissertation with the Business University Vienna (WU). With this, I intend to develop a business plan for a cloud-based computing platform for tumour characterization as a fee-per-use scenario. I reach out to managers of start-up's and SMEs in healthcare and other industries.

All interviews can be anonymized, if so wished. Please take a moment to review the following questions and provide your responses. This survey should take about 10-15 min of your time, and you input and insights would help me a great deal with the sourcing of valuable materials for this thesis.

Thank you in advance for your time and consideration.

Kind regards,

Thomas Beyer, PhD

Professor of Physics in Medical Imaging
Medical University Vienna
General Hospital Vienna, 4L
Waehringer Guertel 18-20
A-1090 Vienna, Austria

Email: thomas.beyer@s.wu.ac.at
Mobile: +43 664 800 163 3520

Thomas Beyer LinkedIn

INTERVIEW: INNOVATION & STRATEGY OF START-UP'S

- **YOUR BACKGROUND**
  - *age / gender / highest degree*
  - *your business, possibly w/ web link*
  - *founding year of your main business*
  - *What triggered you to become an entrepreneur ?*
- **START-UP**
  - *Does your firm originate from a University spin-off (USO)* [y/n]
  - *If "y",*
    - *did you get support from your university and if so, what support :*
    - *do you have a licensing/ equity / royalty agreement with your university ?*
  - *If "n"*
    - *does your firm license from a University ?*
  - *Do you consider a Technology Transfer Office valuable for starting up a business ?*
- **VALUE PROPOSITION and PRODUCT**
  - *How would you describe the value proposition of your firm / product ?*
  - *Does your value proposition address a "technology push" or a "market pull" ?*
- **FOUNDERS, MANAGEMENT AND TEAM**

- *Please describe briefly the founders and their level of experience at the time of the start-up (please pick one)*
  - *Academic only and #years of experience* [ ]
  - *Academic with prior industry exposure and #years of experience* [ ]
  - *Industry background and #years of experience in the same / different industry.*
  - *Other: …*
- *Please describe in short the diversity of your team with regards to nationality, locations, gender, experiences, know-how, talents, etc*

- **STRATEGY**
  - *At the start of your company, did you have a business plan ready: y / n; comments*
  - *Did you know of the concept of "Discovery-driven planning" as an alternative to conventional (linear) business planning for very new / innovative firms: y / n; comments*
  - *What type of external financing (business angels, crowd, VC ...) did you source during the first five years of your start-up and at what stage(s) ??*
- **GROWTH**
  - *Did your company grow as expected (business plan): y / n / comments*
  - *Did you make adjustments to the strategy of your company in y1-5, pls comment .*
  - *Did these adjustments have any effect on the structure of the team / management, and if so, how ?*
- **OPTIMIZATION**
  - *What, would you say, are the 3 key factors to launching a successful start-up / USO ?*
  - *In retrospect, what were the biggest mistakes you made when setting up your firm, and what were the things you did right from the start?*
- **TRENDS**
  - *What are the three biggest trends in healthcare today ? Where do you see opportunities for growth and what excites you at the moment in the healthcare space?*
- **COMMENTS**
  - *Feel free, to add any comments ...*

Appendix 3. Questionnaire "Cloud-based Tumour characterization" as generated with GoogleDocs and shared with stakeholders in healthcare.

PREFACE.

A new University spin-off offers a cloud-based computing service for image-based tumour characterization. The backbone of this characterization is an artificial intelligence algorithm trained on a database of 3D PET data and tissue samples. To date, tumour characterization is offered for 3 cancer types with dedicated input requirements for image data. The algorithm delivers an individual risk profile, as well as probability maps for the expression of key therapy targets for the tumour lesions. In the future, tumour characterization can be expanded to other cancers and using alternative image information pending the availability of alterative databases.

We kindly invite you to complete this short survey on the usefulness of such a cloud service. All responses will be treated anonymously.

QUESTIONS.

Q1. Would you use cloud-based services to support your clinical decision making?

Y / N

Comment:

Q2. Would you be willing to pay for these services?

Y – monthly / annual rate or Y – use-case per patient

N

Q3. Would you consider this cloud service, if the use of selected treatment compounds is linked to a required proof of therapy target expression?

Y / N

Comment: …

Q4. Would you consider this cloud service also without a CE certificate?

Only with – With/Without (doesn't matter) – Only without

Comments: ….

Q5. Please provide the three most important tumour entities for which you would employ the above cloud service:

1. …….. 2. …….. 3. …..……..

Q6. What image modalities would profit most from computer-based support algorithms for tumour characterization:

CT – PET – PET/CT – PET/MR – SPECT/CT – SPECT/MR

Q7. Does your place of work permit the transfer of anonymized image data (e.g., PET, PET/CT, PET/MR)?

Y / N

Specify requirements: ….

Q8. Would you be willing / able to share data (image data, biopsy, whole-mount histology, genetic profiles etc) to build a new data base on which the algorithm can be trained for new cancer types:

Y / N

Maybe - under the following circumstances: ….

Q9. Are you using similar type support software already in your clinical routine?

Y – Pls comment: since when, which (home-made, commercial)? …

N

Q10. What is your background?

Imaging expert (rad/nuc) - oncologist – pathologist – other: ……

Q11. What is your place of work?

Public hospital – Private clinic – Other: ……

Thank you very much for your input. Please drop the completed form at the front desk or mail it to thomas.beyer@meduniwien.ac.at.