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Master thesis

Building a platform for integration of AI-based algorithms into oncology diagnostic workflow

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МІНІСТЕРСТВО ОСВІТИ І НАУКИ УКРАЇНИ ЗВО
«УКРАЇНСЬКИЙ КАТОЛИЦЬКИЙ УНІВЕРСИТЕТ»

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Магістерська робота

на тему: Розробка бізнес-рішення для інтеграції алгоритмів ШІ в процес діагностики онкологічних захворювань

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Introduction

Humanity generates more data today than any period before. Nearly 90% of all online data volumes were generated during the last two years [1]. 2 500 000 terabytes are generated daily [2]. The majority of the experts agree that these numbers will continue growing in the future at nearly exponential pace [3]. Accordingly to Moore's Law, we can inspect the non-linear growth of the computational power [4]. Different new computing units, introduced by large IT companies like TPU from Google [5], allowed processing large amounts of data even more effectively.

These two aspects described above played a critical role in the explosion of Artificial Intelligence development during the last decade. Today, AI empowers companies, governments, and communities to develop an effective ecosystem to serve the entire world. Its indispensable impact on human lives allows solving the challenges across various range of fields.

AI in the medical field is one of the most vivid examples of such a positive impact on Humanity. Medicine is irrevocably transformed by AI. It helps clinicians analyze medical data, speeds up drug development and gene editing, and many more. We have gathered a team of artificial intelligence engineers and a doctor to challenge the traditional cancer detection workflow.

Cancer is the second cause of death worldwide, killing millions of people per year, nevertheless, near 50% of cancers preventable by avoiding risk factors and applying evidence-based prevention methods. The cancer burden can be reduced drastically by early detection and appropriate treatment.

Evaluating cancer dynamics from computed tomography is crucial for assessing malignancy status and selecting prospective treatment. It is a time-consuming task for radiologists requiring manual mapping and measuring of

malignant lesions across multiple studies. More complex abdominal cases can take 20-60min to report, causing long waiting queues and late cancer diagnosis. Different studies on the same patient can be evaluated by different radiologists practicing different measuring and reporting styles and varying eye sensitivity to shades of grey. These differences can introduce uncertainty that might prevent correct assessment of the lesion's dynamics and lead to mistreatment.

Despite the fact that we have tons of research papers about AI applications in cancer detection, we can witness extremely isolated cases of it in clinical use. This research aims to develop a solution that will fit into the radiologists' workflow that will speed up evaluating cancer dynamics by saving time radiologists spend on manually measuring and comparing malignant lesions in CT scans. We will free up to 50% of their time performing this task.

For achieving our goal, the following tasks were formulated:

1. Analyze existing solutions and trends on the market.
2. Identify the specific global problem in the cancer treatment domain, which presents in both EU and US markets.
3. Investigate the regulation field of AI in medicine and corresponding “go to market” strategy of such products.
4. Develop an effective business model, budget, and roadmap of the project for the next three years.

Chapter 1. Problem

Problem description

Cancer is the second leading cause of mortality in the EU, accounting for 26% of all deaths in 2013 [6]. The EU spends €57.3 bln on cancer, productivity losses due to morbidity and premature death were €10.6 bln, and €47.9 bln. With informal care costs of €26.1 bln, the total burden rose to €141.8 bln, 1.07% of GDP [7]. EU states have been implementing strategies to improve radiology services and outcomes of cancer patients. One of the significant factors that influence patient outcomes is timely diagnosis. According to the NHS, delaying cancer treatment by just four weeks increases the risk of death by 10% [8]. The number of CT scans is growing by 6-16% annually in Europe, while the number of trained radiologists stagnates due to aging. This poses a threat to the accessibility of radiology services. By speeding up radiology workflow and making it more accurate, we aim to reduce both the growing demand for the radiology workforce and waiting times for patients while improving care quality.

Regular CT scans are performed on cancer patients every 3-6 months to monitor the disease's dynamics. This provides input for treatment decisions and understanding how the cancer is responding to treatment. Therefore, evaluating cancer dynamics is crucial for assessing the status of malignancy and selection of prospective treatment. It is a time-consuming task for radiologists requiring manual mapping and measuring malignant lesions across multiple CT studies. More complex abdominal cases can take 20-60 min to report. Different studies on the same patient can be evaluated by different radiologists practicing different measuring and reporting styles and varying eye sensitivity to shades of grey. These differences can introduce an unwanted variability that might prevent the correct assessment of the lesion’s dynamics and lead to mistreatment. Different reporting

styles make studies harder to compare and interpret during interdisciplinary clinical decision making.

There were 146,084 CT studies performed in Estonia and more than 60 million in the European Union in 2019 (according to Eurostat and Estonian National PACS) [9]. Radiologists from Tartu University Hospital reported that 50-60% of all CT scans are done for cancer patients. In customer discovery interviews radiologists indicated (see to **Chapter 2. Customers Discovery** for more details) that CT as a modality takes up most of their work time. Radiologists further reported that when performing an oncological CT examination - near 50% of time is spent on assessing the cancer dynamics i.e., manual mapping and measuring of the malignant lesions across multiple CTs of the same patient. Such cases take 20-60 min to measure and report. Roughly estimated 19 000 hours of radiologists' work can be freed annually using our product in Estonia alone. This is equivalent of about 11 full-time radiologists. Translated into DE and NL markets with 12M and 1.6M annual CT studies respectively the number of hours saved would increase by a factor of 100.

Solution

Our first product called OncoSense. We use AI combined with the best possible user experience for radiologists to automatically assess the tumor dynamics, i.e., measuring the volume change (growth/shrinkage) of the same tumor across multiple CT scans. We plan to target a broad range of cancer types in the full-body CT of a patient. We build a product for all organs of the ventral cavity, starting with the kidney and expanding later in further findings in others. We are going to work with organs, which are most vulnerable to cancer disease (refer to Error! Reference source not found.) and use CT as the main screening p rocedure — lung, colorectum, stomach, liver, bladder, spleen, pancreas,

gallbladder and biliary tract. We speed up evaluating cancer dynamics by saving time radiologists spend on manually measuring and comparing malignant lesions in CT scans. Our tools provide a more unified measuring technique and ease reporting with auto-generated standardized reports validated by the radiologist. This provides a more standardized input for clinical decision making, resulting in decreased reporting times, waiting times.

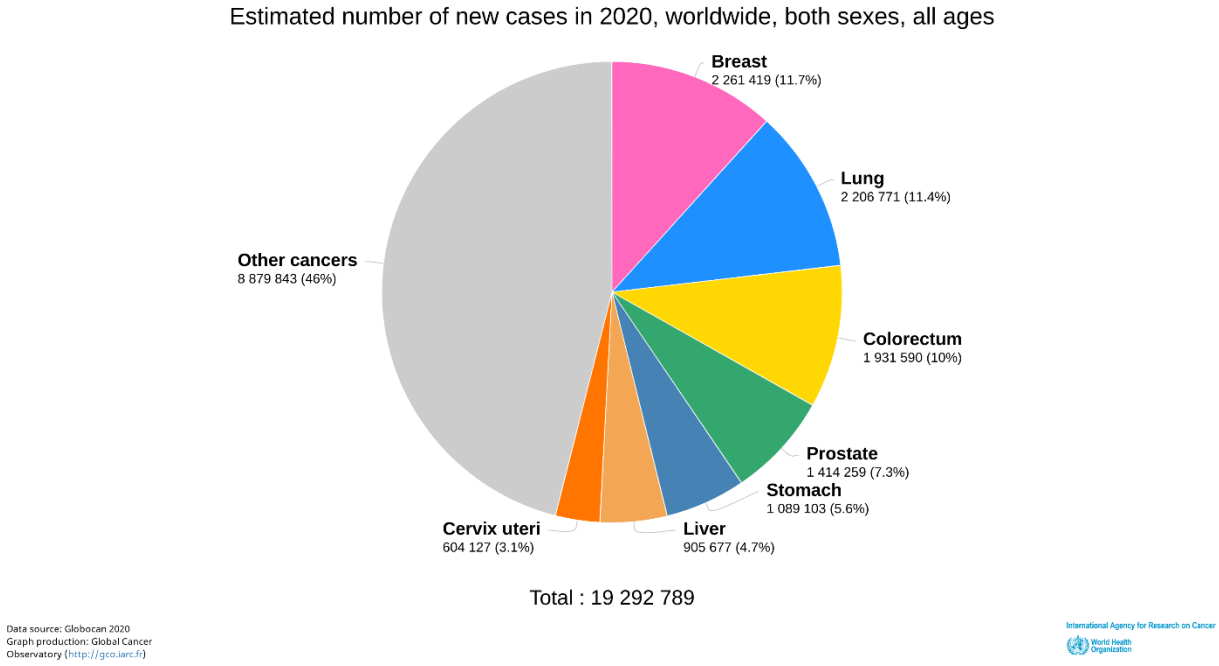

Figure 1. Number of new cases in 2020 worldwide by organ.

We bring an assessment of the cancer dynamics to the next level by employing modern Deep Learning (AI) techniques and other modern computer vision algorithms that enable a fully automated decision support for radiologists for cancer dynamics assessment. We save up to 50% of the time compared to the current practice, improve assessment accuracy, and offer a more unified measuring workflow. Concurrently, we also introduce a more structured reporting system (developing into a new standard for radiologists and the radiology industry), which increases the reporting quality and saves time on “return trips” for double-checking the same report.

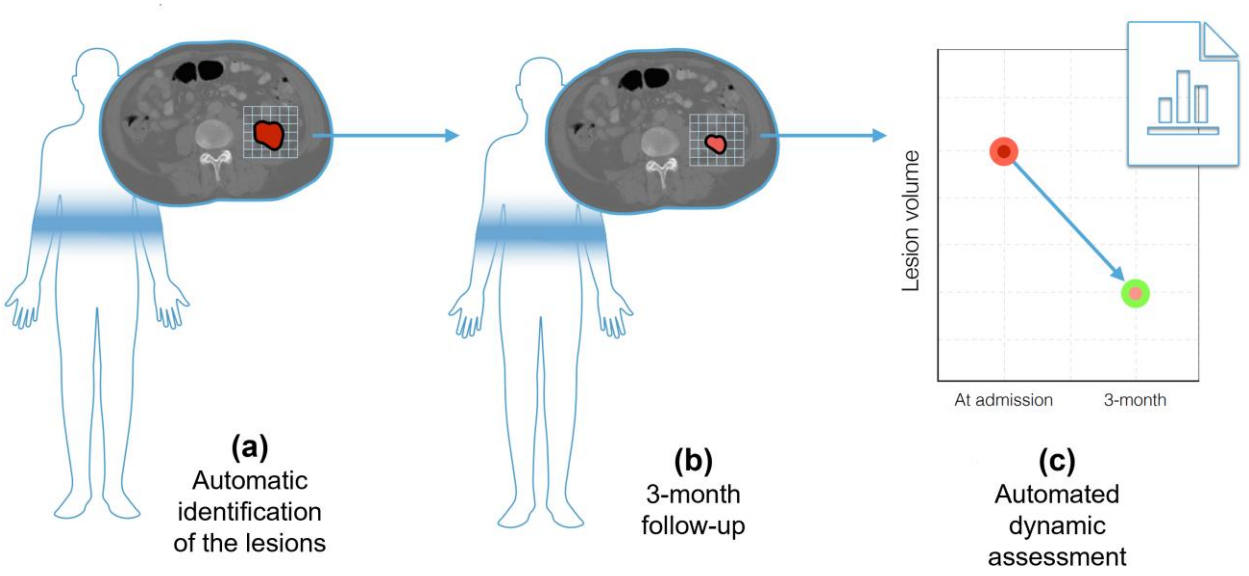

Figure 2. Value, which our product generates for the radiologists. (a) automatic lesion detection & classify to benign, suspicious, and malignant, (b) apply AI algorithms for every follow-up CT studies, (c) estimate dynamic of the lesion over several CT studies.

We will put our solution directly into the clinic workflow. The artificial neural networks will be utilized at the admission of every CT study (refer to Error! R eference source not found.):

1. Our solution will analyze the whole CT scan for cancerous anomalies, find all lesions, delineate them, and measure all clinically significant biomarkers (area, volume, etc.).
2. All masses will be classified into three main categories: malignant, benign, and suspicious. These two steps will be done for every CT study of every case.
3. Considering all CT and clinical history of the patient, we will analyze the tumor dynamics over several CT studies.
4. Finally, taking into account algorithms' predictions and doctors' input concluding standardized report will be generated.

We will present the algorithms' predictions in our web-based image viewer, integrated with the hospitals' PACS systems. Another way we deliver our

algorithms' value by integrating our solution into PACS image viewers of the existing biggest PACS provides like GE, Philips, Sectra, etc. (refer to **Figure 3**).

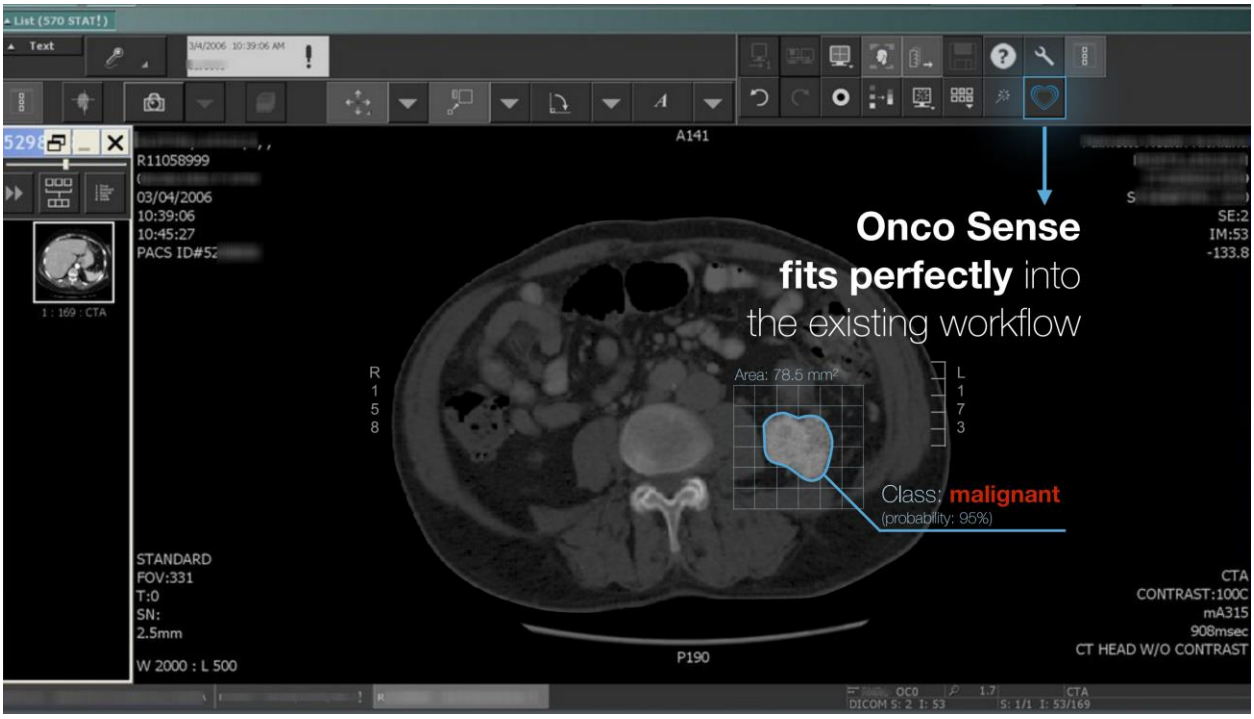

Figure 3. An example of the interface of our product, which is integrated into the PACS Image Viewer.

We have already implemented the PoC version of AI algorithms of a few organs in the open datasets. We have tried our approach on kidney, pancreas, lung, and colorectal cancers. Our approach secured first place on the online international challenge KiTS19 *[10]*. Refer to the quantitative (*Figure 4*) and qualitative (*Figure 5*) results of our AI algorithms on kidney lesions.

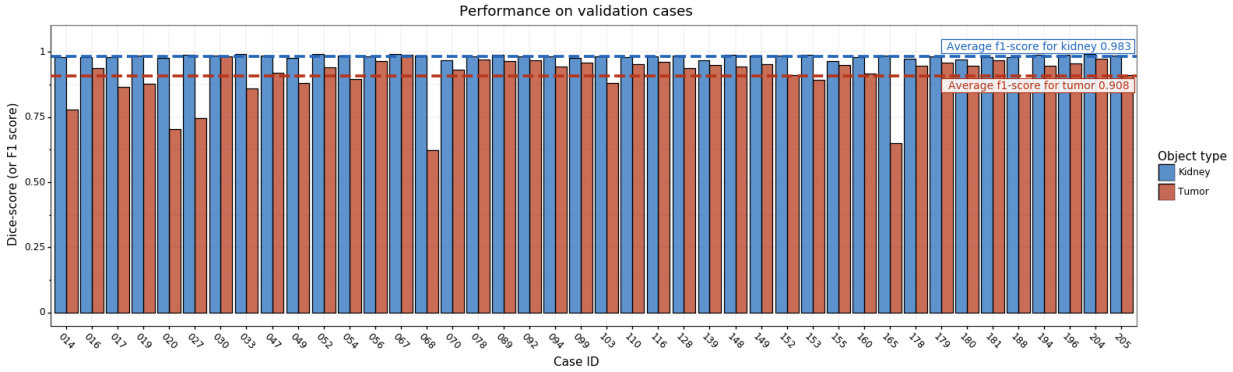

Figure 4.Dice score for our algorithm on the test set of patients. DICE score is a measure, which reflects how good our model guessed the objects on the images; 1 - perfect, 0 - complete failure.

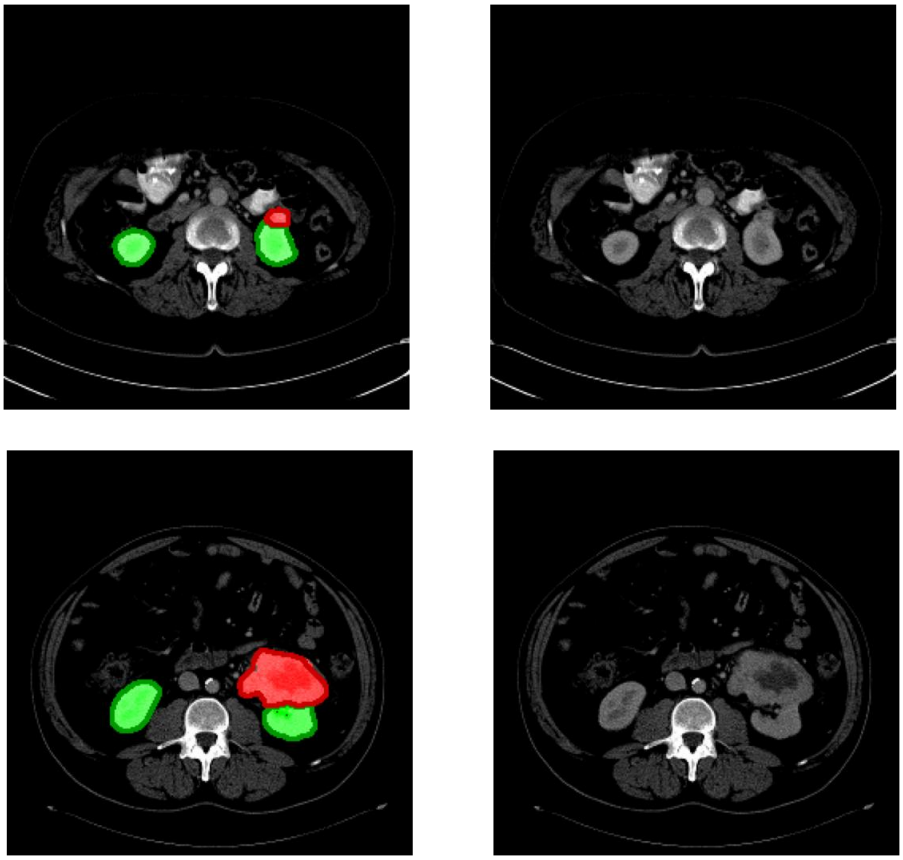

Figure 5. Examples of AI prediction. Dark green and red boundaries are doctors' delineation of kidney and lesion, and light green and red are the AI prediction of kidney and lesion correspondingly.

Chapter summary

Cancer is among the most dangerous diseases nowadays, causing near 10 million deaths yearly. The cancer burden increases, bringing enormous financial, emotional, and physical losses, leading to an unbearable load to people, communities, and healthcare systems.

Fast and accurate cancer diagnosis, especially in the early stages, significantly increases survival and successful treatment. Computed tomography is considered the dominant imaging screening test for oncological problems. The number of radiologists remains the same, while the number of images in radiology

skyrocketing. This gap causes a tremendous workload on radiologists. Thus, more than 80% of their working time they spend on manual mundane, repetitive, exhausting work, which can be automated.

The first product of our startup is OncoSense. We entirely concentrated on diagnosis workflow optimization problems. The main aim of our solution is to automate exhausting and time-costly parts of CT studies interpretation routine, allowing up to 60-70% of time saves. Firstly, from every CT study, we identify the lesions from the CT study, then we classify them into malignant, benign, and suspicious. Finally, we estimate the dynamics of cancer, and in conjunction with the radiologists' judgments, generate a concluding standardized report.

We are a hard MedTech startup that builds a product based on Artificial Intelligence and Machine Learning technologies firmly based on an evidence-based scientific approach. The innovation lies directly in our core solution. We have analyzed a wide range of companies/startups which build products on an AI basis. We found out that nobody does the AI-based fully automatic dynamic lesion assessment from the CT scans. Additionally, to the novel algorithm, we also propose an extensive value proposition, which in contrast to most of our competitors, integrally covers the whole radiologists' workflow of a cancer diagnosis from CT scans of the ventral cavity.

Chapter 2. Customers Discovery

According to a postmortem research of global startups conducted by the venture capital database CB Insights [11], the most common reason why new ventures fail is because they build and launch something customers do not want. Thereby, we extensively approached to the problem of customer and actual needs investigation.

Target customers

We have segmented our target customers into several groups based on their functions and value, which we provide to them. Our user customers are radiologists performing the dynamics assessment task, spending time on the mundane tasks of manual measurements. Our paying customer is the radiology department in the hospital - having overall workload issues and a growing number of studies to report, which leads to longer waiting times, and the hospital management team, which faces a diagnostic throughput and waiting times. Also, alternative paying customers are health care financiers/insurance looking for cost savings through more accurate diagnoses and less cancer financial burden. We also create an impact for patients, who have to wait a long time to get their CTs done and have higher chances of developing life-threatening complications.

Customer interviewing

As a main methodology for interviewing our customers we took a fundamentals, covered in The Mom Test book [12]. The interviews were taken in We investigated the following directions:

Part	Question
Intro	How you average workday look like?
	Do you see any kind of problems, which should be solved in your work? (Time consuming, manual work, accuracy, annoyance)

	What is common and what is different in different countries? Different countries - common problems?
Candidate Challenges (Hypo)	Can you describe the process in assessing the Dynamic for lesions?
	Have you practiced double reading in diagnostic radiology? your experience with double reading
	Have you seen situations where there is problem visible in an earlier study which was not detected at the time of the study?
	Do you see any problems when patients move between hospitals?
Final questions	What is the most important thing in your work for you?
	What questions should I be asking when I would like to understand problems & challenges in radiology?
	Is there anybody you would recommend I should talk to?
	Would you be willing to have another call once we have come up with some kind of solution?

Table 1. Interview questions to our user customers (radiologists).

To identify our problem and gain international background in the field, we have interviewed radiologists (targeted users of our core product) and oncologists from 9 different countries: Estonia, Finland, Lithuania, Croatia, Slovenia, UK, US, Germany, and the Netherlands. All experienced radiologists we talked to admitted that assessing malignant lesions is an existing critical problem in a modern diagnostic workflow. Some of them even showed strong feelings about it, like "I hate this bit, many cancer patients, a lot of follow-up scans.", "and you scroll, scroll and scroll, no tools for comparison.". Also, important insight for us was that the functionality of dynamic lesion assessment which is in high demand completely missed in the market (it is also additionally proven by our research in **Chapter 4. Competitive Landscape**).

Product-solution fit

To clearly state existing problems for each group of our customers and propose the solution which matches their needs, we have outlined a product-solution fit for every one of them.

Radiologist		
Problem	*Our Solution*	*Outcome*
Increasing nr of CTs => increasing workload automatization of repeating tasks	Automatization of repeating tasks	Less time spent per CT
Mundane and manual tasks	Automatization of repeating tasks	More time for meaningful tasks: focus on expert opinion not measuring; time for reflection and innovation; time for interaction with the patient/colleagues; time for research; time for self-auditing
Errors (missed lesions + wrong classification)	"Second pair of eyes"	Less errors (missed & misinterpreted lesions) + higher confidence
Expectation for high q. work increasing workload == pressure	Automatization + higher accuracy	Higher confidence of outcomes (lesions found + if none, that there are none)
Fatigue	"Second pair of eyes"	Higher confidence & accuracy less errors
		Higher confidence more time for meaningful tasks => higher job satisfaction
		Higher confidence more time for meaningful tasks => higher job satisfaction
Non-standardized reporting	Automatic detection +	Faser, more convenient

and struggle of interobserver differences	marking + summary of findings and dynamics Easy to use findings that are semi-implemented in structured reporting system / pre-filling; visualized changes in cancer dynamics	workflow
	Higher accuracy in detection, and classification	Less misinterpretations => mitigated legal risks

Table 2. Undeserved needs, our value proposition and outcome for the radiologist, main user of our product

Our main paying customer is the radiology department or top management of the hospitals, depending on the hospital's infrastructure. We position ourselves to hospitals as a workflow optimizer company, which will make the diagnosis process of cancer from CT scans more effective for the whole radiology department.

We have agreed on joint clinical studies of our product with 4 medical centers across Europe and the US - University Medical Center Groningen, Tartu University Hospital, German Cancer Research Center, and Duke University School of Medicine (read more about clinical study in **Chapter 3. Product certification**). They invested time, intensive labor, and huge interest. It serves as a positive indicator that our product idea is viable on the market also for payable customers.

Healthcare Provider (Radiology Department, Hospital)		
Problem	*Our Solution*	*Outcome*
Raising nr of CTs => increased workforce needs	Faster diagnosis	Higher throughput
		Less stress on hiring
Errors / misdiagnosis	Higher accuracy higher standardization	Mitigate malpractice exposure
		Seamless work between departments
Low service availability => low patient satisfaction	Faster diagnosis higher accuracy	Improved patient care

	higher standardization	
Burnout of radiologists	Atomization of annoying tasks, better workflow, and adequate workloads	Happy radiologists -> better care

Table 3. Undeserved needs, our value proposition and outcome for the healthcare providers

An alternative or additional paying client also will be health insurance companies. We consider an option of selling our product separately to insurance funds and propose to them a faster cancer diagnosis and less economic burden for their customers. It will help us sell faster and more globally. However, this strategy is strongly dependent on the medical care systems from country to country (read more about the business model in **Chapter 5. Business Model**). We have already started negotiations with Haigekassa Estonian Health Insurance Fund concerning our collaboration and finding possible future deals.

Health Insurance Company		
Problem	*Our Solution*	*Outcome*
Cancer costs	Early detection Higher service availability More accurate diagnosis	Lower costs
Complications costs	Higher service availability More accurate diagnosis	Lower costs on dealing with complications
Delayed diagnosis leads to higher costs	Faster process to diagnosis => higher service availability	Lower costs in the future

Table 4. Undeserved needs, our value proposition and outcome for the health insurances

We plan to sell directly to hospitals or insurance companies. Patients will not utilize our product, but it will intensively improve the services which they use. Thus, they will have access to better healthcare services and, as a result, higher life expectancy and added productive years of life. Moreover, our company's broader vision of the cancer problem goes beyond just diagnosis. We may sell create separate additional products, especially for oncology patients, in the future.

Patient		
Problem	*Our Solution*	*Outcome*
Might get cancer	Screening	Early detection => Higher survival
Might have cancer	More accurate diagnosis	More suitable treatment => Higher survival
	Faster diagnosis	Shorter time to diagnosis => Higher survival
Have cancer (in treatment / follow-up) + Afraid of outcomes	More accurate results	More suitable treatment => Higher survival
	Faster diagnosis	Shorter time to diagnosis => Higher survival
Have cancer (in treatment / follow-up) Treatment is harsh	More accurate results	More suitable treatment => More suitable treatment choices
Had cancer (in follow-up) Afraid it comes back	More accurate results	Early detection of relapse => Higher survival
		Shorter time to diagnosis => Higher survival
Complication from harsh treatment	More accurate & faster diagnosis	Maybe easier treatment

Table 5. Undeserved needs, our value proposition and outcome for the patients of the hospitals

Financial aspect of generated value

We counted radiologists' time, which we save for hospitals in Estonia:

Estonia	**Pessimistic (min)**	**Optimistic (max)**	**Reasonable**
Population 2019	1325000		
Nr of CTs in 2019	146084		
% of onco CTs	50%	60%	50%
Onco CTs	73042	87650.4	73042
Avg time-spend on onco CT in min	30	45	30
Time-save per CT	25%	50%	50%
Timesave in hours, per year	9130	32869	18261

Timesave / y man months	57.06	205.43	114.13
Full time radiologists / y	5.19	18.68	10.38
Radiologists' salary fund / mo	7500	7500	7500
Yearly value generated	**€466,888**	**€1,680,796**	**€933,776**
10% yearly earnings from value	**€46,689**	**€168,080**	**€93,378**
Earnings per 1 mil population	€35,237	€126,853	€70,474

Table 6. Financial value generated for Estonia (calculated only time savings)

Chapter summary

We have identified four main segments of our customers: radiologists, healthcare providers, insurance companies, and patients. By conducting interviews with radiologists from different countries across the EU and US, we discovered that the tools for lesions dynamics tracking are in huge demand among clinicians but are not present on the market. We also validated this idea on different healthcare providers across the EU, which agreed to conduct clinical studies with our company. We have elaborated on the values chain we create for every group of our customers to identify actual problems and align proposed values and outcomes.

Chapter 3. Product certification

Even though AI in medicine is proliferating, there is a considerable bottleneck before being intensively used in clinical practice. Every AI-based product must be certified before being deployed into the clinic and monetized. Nothing in medicine is 100% accurate and perfect. So, that is why all manufacturers of medical devices (software that utilizes AI also is considered a medical device) must provide evidence that they have done all their best to ensure that the benefits of using the device surpass any risks and that these risks are acceptable. Depending on the primary market, the CE and FDA certification is required for EU and US markets correspondingly. We plan to sell for both markets; thereby, we will face CE and FDA.

CE certification

This mark shows that the current product meets the essential requirements of the corresponding directives, and it can be freely distributed throughout the market in European member states. In the case of medical devices, the product must meet the EU Medical Device Regulation 2017/745 (MDR) [13] requirements set by the European Commission.

To pass the CE sertivication the following steps should be done:

1. ***Intended Use***

   It is a clear and carefull description of what AI algorithm does. It is usually broken up into several components like name, model, device description and class, principle of work, intended use environment, risks of use, intended users, conditions of normal use, outcome limitations. It is a first step towards regulatory approval. It is crucially important to outline it right. The future product will be judged based on the description provided here. Any change in

the Intended Use will start the certification process again.

We have already nailed down the intended use document for our product.

2. ***Class of the device***

   There are 3 main classes of the medical devices based on their potential risks to patients. Our product supports doctors in their decision making. It is known as as Clinical Decision Support software (CDS) and regarded as Class II. We formulated our Intended Use in such a way to be as a IIa device.

3. ***Notified Body nomination***

   It is an independent external organization that audits how companies make and test their products. From gained experience, there will be a massive lack of NB in Europe soon, making this step a bottleneck in the future.

4. ***Prepare QMS (Quality Management System)***

   It is a series of documents and Standart Operating Procedures, which describe the company's development processes, risk management, and testing. There is a standard, which describes the structure of QMS known as ISO13485:2016 [14]. It is essentially the only standard you need for medical device CE marking. It is obligatory to pass two-stage audit with Notified Body to get the ISO13485 accreditation

5. ***Clinical evaluation report***

   We need to conduct a clinical study and publish a scientific manuscript about the results. It is a bunch of all clinical testing, that has been performed on our device during pre-market and post-market development. We are in the process of elaborating the clinical study to develop AI kidney cancer detection algorithm with the Tartu University Hospital.

After getting the functioning QMS, ISO 13485 certification, and a finished Clinical Evaluation Report, we will be ready for the final CE audition. It is not a

final step towards the CE mark. Once we get it, we will also need to maintain our ISO certification and regularly re-audit and re-test our device's performance.

FDA approval

Entry to the American market involves stringent Food and Drugs Administration (FDA). It is similar but a much more stringent and detailed process to go through than CE. However, lots of startups prefer to start from FDA as it is much more predictable. Some startups like Ezra did it in only 9 months. Another critical reason for going through FDA is the post-COVID-19 consequence in AI regulation processes. Traditionally, the FDA reviews medical devices through a premarket pathway, such as premarket clearance (510(k)) [15], De Novo classification [16], or premarket approval [17]. With the new changes, medical AI products will be single out as a Software as a Medical Device (SaMD) and will allow companies to certify and maintain FDA much easier.

Alternative paths to market without certification

The industry-regulated medical field hinders the main principles of lean startup, limiting players on the market to rapid product delivery at a compromised quality. AI engineering requires continuous retraining and improvement. However, products can not be drastically changed once they have been certified. It is one of the central bottlenecks to fast growth and product development for most startups nowadays.

One possible way to get a considerable advantage over our competitors may be to formulate our product value so that we can generate revenue without being certified. With our regulatory expert, we have generated a set of ideas, which are in a phase of testing out.

Double reading CTs – retrospectively

The idea is to prospectively double-read CT scans for the presence of cancerous lesions, which have been done during the night. According to the [18], radiologists make more errors interpreting off-hours body CT studies during overnight assignments than daytime assignments. In Estonia, it is done only in severe cases. UK's Kings College Hospital does that with the additional human labor. We will not be built into the radiologists' workflow avoiding the certification requirement. Thus, being able to get first payable customers 10 times faster.

Clinical studies for pharma companies

Pharma companies, which develop drugs for cancer, intensively test the treatment effect and usually make their conclusions based on the biomedical data, most often CT. They use such biomarkers as the area/volume of the found lesions to estimate how the lesion responds to their drugs. The idea is to sell them the detection results of our AI and automatically generated biomarkers. Thus, speeding up their drug testing and making the process of CT analysis much cheaper. Such products usually also do not require CE/FDA certification.

Tool for the patients for CT self-interpretation

Patients should wait for a few weeks for the interpretation results after the CT study was performed. The idea is to propose an oncological CT interpretation service, aka AI-online-clinic, for the patients. If malignancy is found, the patient will get an appointment from ER to the oncologists. We are in the process of interviewing cancer patients, whether it may bring some value to them and the oncology departments.

Chapter 4. Competitive Landscape

Market overview

The field of AI in medicine is becoming hotter and hotter every year. According to Statistics MRC [19], the Global Healthcare AI Market is accounted for $0.95 billion in 2017 and is expected to grow to $19.25 billion by 2026, growing at a CAGR of 39.7% during the forecast period. There are clear reasons for such an optimistic market segment growth.

First of all, data generation volumes increased, opening the doors for AI developers. CT, MRI, Ultrasound imagery become more accessible to the hospitals, DNA sequences analyze in the labs, sleep activities, and blood pressure tracked and recorded over various smart devices. On the other hand, data access is highly regulated by privacy and security rules. This obstacle put many newly born startups into a loop of jumping through the compliance processes and getting the needed licenses to deliver their products to the market. Starting from 2014, more than 50 companies [20] got FDA clearance for their AI algorithms.

Secondly, the COVID-19 pandemic underlined the power of information technologies. The startups have been speeding up their delivery processes from telemedicine to high-speed testing and respiration monitoring because of the urgent demand for certain services and products. To enforce the battle against the pandemic, the US government even set up the entire program [21] to speed up corona-related R&D.

Thirdly, growing demand for more personalized and connected healthcare. The main focus is shifting into preventive care models and new ways of reducing overall costs of care. These tasks especially include AI-enabled solutions.

Finally, the leading countries' governments set AI in healthcare among the main priorities, especially amid the pandemic. According to AI Index Report [22], AI

development has gained the special attention of the U.S. Congress. The Chinese government set the goal to be an AI leader by 2023. In 2019, a year-on-year investment growth rate of 54%, with a total sum of $7.4B.

We are in an active phase of looking for the right market for our product. The field of medicine is fragmented, stagnant, and hugely regulated. The regulations laws highly depend not only on the region but even on the country level. We faced different healthcare systems in countries within the EU. All these limitations may hinder our sales and product adaptation in the future.

We have started our MVP development in Estonia because of a bunch of reasons. Firstly, half of our founders' team are Estonians. Thus, we have strong network connections in both business and medicine fields. Secondly, Estonia lies in the topmost digital countries in the world. Medicine is not an exclusion. They have a gold mine for AI-based medical startups - a national database of image data from all hospitals across the country. Finally, from our experience, Estonian top management in the hospitals is very open to innovations, making innovation happen with much less resistance. However, Estonia would rather be a playground where we can fastly test our product and go to market strategies. Our next primary market would be the US because of one but strong reason. Contrary to the EU, AI-based medical product regulation (read more in **Chapter 3. Product certification**) is much heavier and clearly regulated in the US. Thus, we can easily predict and plan the outcomes of the go-to-market strategy or our future product.

The two main groups of our competitors were identified. The first one is the big companies, which create software in the healthcare sector and develop or integrate other AI solutions into their products. The second one is the small and growing companies/startups, which produce AI products in medicine (for more details, refer to **Big players** and **Startups** sections).

Comparison criteria

We have developed our comparison criteria, which deeply reflect all crucial technical properties for the solutions available on the market. While comparing our product with others, we mostly pay attention to the following aspects:

1. What are the types of lesions they are working with (e.g., lung nodules, liver metastases, lymph nodes, etc.)
2. What image modality the solution/study uses (CT, MRI, CT/PET, etc.)
3. Is it fully automatic? (lots of the AI-based solutions require additional manual doctor's input to make the algorithm work)
    a. Automatic lesion identification/classification (classification of the anomaly into malignant/benign, cystic/solid masse, etc.)
    b. Automatic segmentation (delineation of all image pixels, which belong to the lesion body)
    c. Automatic measurements of the lesion (generation of the clinically important features like area, volume, max/min HU value, etc.)
    d. Automatic lesion tracking? (linking founded lesions between studies)
    e. Automatic lesion detection in follow-up studies (comparison of the founded lesions and corresponding clinically significant features across multiple CT studies of one patient)
    f. Fully automatic report generation
4. Data requirements (whether contrast-enhanced, CT phase, so on)
5. Is it based on AI/DL? Is it use ANNs?
6. The reference base for later navigation to lesions?
7. Summary of results for dynamics assessment?
8. Research background:
    a. Which company/university is behind this solution/study?

b. Performance of the method (accuracy, sensitivity, specificity, F1 score)?
c. When was it published?
d. How many cases did they use to training/validating their solution?

We provide a detailed analysis of the competitor companies and startups regarding these criteria in the **Big players** and **Startups** sections.

Competitors interviewing

There is no sense in reinventing the wheel. Lots of problems have already been solved by other teams in this domain. We continuously keep educated ourselves about the field by having experience sharing with our competitors. We usually investigate the following interview structure:

(Main value proposition):

- Tell about your product - what does it do?
- What is the main value you generate for a radiologist and the hospital?

(Workflow + integrations):

- How does your product exactly fit into the hospital workflow?
- Do you have to work with our IT department to get you up and to run?
- How hard is it to get you integrated with informational systems - PACS, viewers, etc.?

(Certification & compliance):

- Do you have all the certifications and necessary paperwork done to use you?
- To get this, this must have been hard? How long did it take to get this far?

(Business size, markets):

- How many hospitals/clients?
- (if many hospitals - follow with) how have you achieved this?

(Revenue streams):

- What is the main business model for software tools in the Medical industry?
- How do you guys earn money?

(Pricing):

- How expensive are you? /What is the Pricing model? (If no details)

  However, roughly, what is the rough ballpark figure? What are the main components of the price?

(Deployment / Integration):

- What is needed, what are the first steps if a hospital wants to start using you?

(Plans):

- What can we expect from your product and your company in the future?

We have interviewed three startups, which develop AI-based products in medicine: Combinostics, Oxipit, and Zebra medical vision. We gained a range of important insights. Firstly, startups we interviewed had/took from the very beginning a Chief Compliance Officer responsible for the ISO/IEC 27001, ISO 13485, CE, and FDA certification, not to speak about GDPR, HIPPA, etc. Secondly, to be able to sell our product we firstly need to certify it. The certification process requires a solid scientific research basis (see in **Chapter 3. Product certification**). Thus, we need to have a team of deep learning scientists for conducting clinical studies (in Combinostics, 5 founders out of 4 have Ph.D.'s in medical image processing). Thirdly, we understood that the collaboration with the startups, to which our idea may be complementary would be a beneficial . For example, Perspectum does AI-based analysis of liver from MRI scans. It would be a perfect match to our solution, which analyzes liver from CT. Finally, they helped us much more realistically formulate our financial needs and budget for investments (see in **Chapter 6. Finances**).

Big players

Big players are the companies that offer enterprise imaging solutions which include PACS for imaging-intense departments in the hospitals (cardiology, pathology, radiology), VNA, and image viewers, which enable an effective and fast image diagnosis process. These companies usually mature and are for a long time on the market. According to Klaus statistic [23], there are leading big players who own the major market share, like Sectra, Intelerad, GE Healthcare, FUJIFILM, Philips, Agfa. Usually, these companies develop their own AI algorithms to strengthen their products' value. Another common strategy for them is to serve as a marketplace for other AI-based startups and integrate their solutions into medical image viewers. Refer to the **Startups** section to read more about integrated AI solutions into the image viewers. Here, we describe the native products developed by PACS providers closely related to our product.

We have summarized all products of Big Players and corresponding features, which we considered for comparison. We have analyzed the closest competitors below the table.

Feature	**GE**	**Philips**	**Agfa**	**Siemens**	**SECTRA**	**Carestream**
Opening up several studies in parallel	YES	YES	NA	NA	YES	YES
Automatic registration (sync of studies)	YES	YES	NA	NA	YES / SEMI	YES
Automatic lesion detection	NO	NO	NA	NA	NO	NO
Automatic segmentation	YES / SEMI	SEMI	NA	NA	NO	NO / SEMI
Automatic lesion detection in followup scans	NO / AIDED	NO / AIDED	NA	NA	NO	NO / MAYBE
Automatic lesion measurements	YES	YES	NA	NA	NO	YES
Summary tables and graphs	YES	YES	NA	NA	NO	YES

Modality	CT, MR, PET/CT, 3D X-ray	CT, MR, PET/CT, SPECT/CT	NA	NA	CT	CT

Table 7. Summary of the image viewers, which has similar functionality to our product

Sectra Lesion Tracking Tool

Short info:

It is a tool that is integrated into the diagnostic application of the Sectra Imaging Solution for reading and reporting findings relevant to follow-up over time. It provides help to radiologists in organizing, comparing, and measuring significant lesions in a standardized manner.

Danger for us:

- They put stress not on standardized UI/UX standardized reporting but on automation of lesion finding and tracking.

Why we are different:

- We automate lesion finding.
- We use AI algorithms.
- Our main focus lies on double reading and fully automated finding of tumors.

Syngo.via for oncology

Short info:

It is an application, which help doctors to deal with the oncological findings in the multi-modality imaging. It has convenient delineation tools and quantitative evaluation of tumor response, standardized reporting, and follow-up.

Danger for us:

- They change their product and will develop AI for their image viewer.

Why we are different:

- We utilize AI

- We automate lesion finding
- Our main focus lies on double reading and fully automated finding of tumors

Philips Multimodality Tumor Tracking

Short info:

Specified module for image viewer, which allows manually segment lesions, volumetric measurements optimized for different modalities and quantify anatomic and metabolic state over time.

Danger for us:

- Same as upper examples

Why we are different:

- Our solution thrives to be fully automated support for onco-dynamics and we look at the whole ventral cavity - all regions, all internal organs.

Startups

We have done a thorough investigation of startups and small companies that utilize AI in medical imaging. We have paid attention to most companies in the field, which raised investments, FDA cleared, CE marked, have patents, and have already conducted clinical studies and published scientific results (any of these criteria).

COMPANY NAME	HQ / YEAR FOUNDED	MODALITIES	AMOUNT RAISED, $	INVESTORS	DOMAIN
Arterys	US / 2011	MRI, CT	43.7M B	Temasek Holdings, Emergent Medical Partners, Asset Management Ventures (AMV)	Oncology
Koios	-	-	-	-	Oncology
CureMetrix	US / 2014	Mammography	Series A	EvoNexus, Analytics Ventures	Oncology
MaxQ AI	Israel / 2013	-	40M	Xplorer Capital, Exigent Capital, W&S Partners	-
Paige	US / 2018	Histology	70M B	Healthcare Venture Partners, Breyer Capital	-

Profound AI	-	Mammography	-	-	Oncology
Screen-point medical	-	Mammography	-	-	Oncology
Voxel-cloud	China / 2016	CT	78.5M B	Shenzhen Hongtai Capital Management Group, Tencent Holdings, Sequoia Capital	Oncology
Braid	US / 2018	CT	12M A	Lux Capital	-
See-mode	Singapore / 2017	CT, MRI	10M A	MMV SEA, Cocoon Capital, Entrepreneur First	-
Gleamer	France / 2017	X-Ray	10.6 M A	Xange, Elaia, BPI France, MACSF, Majycc esante invest, Crista Galli Ventures	Patient triage
Viz.ai	US / 2016		81M A	Kleiner Perkins, DHVC	Stroke
VIDA	US / 2004	-	20.4M	Unity Point Strategic Investment	-
Lunit	South Korea / 2014	CXR, MMG, Digital pathology images	60M C	Kakao Ventures, Softbank Ventures Asia, Formation 8, Legend Capital, LG CNS, Intervest, Fujifilm, others	Oncology
Quantib	Netherlands / 2012	-	5.5M A	Holland Venture	-
Butterfly	US / 2011	-	350M D	Fidelity	Ultrasound
Ezra	US / 2018	MR	22M Seed	FirstMark Capital, Accomplice, Founders Future	-
AIDOC	Israel / 2016	CT, X-Ray	41.5M B	Square Peg Capital, TLV Partners, Shahar Tzafrir, Magma Venture Partners	General medical AI
Zebra Medica Vision	Israel / 2014	CT, X-Ray	50M C	aMoon Fund, Intermountain Healthcare, Khosla Ventures	General medical AI
Qure	India / 2016	X-Ray, CT	16M A	Sequoia India, MassMutual Ventures Southeast Asia	X-ray findings
Proscia	US / 2014	Histology	12.3M A	Flybridge Capital Partners, Emerald Development Managers	Oncology
InferVision	China / 2015	CT	68M C	Sequoia Capital China, CDH Investments, Qiming Venture Partners, others	Oncology
PathAI	US / 2016	Histology	75.2M	LabCorp, General Atlantic, General Catalyst	Hitology
TeraRecon	-	CT	-	-	
Therapixel	-	CT	-	-	-
DeepPathology	Israel / 2017	Histology	-	-	Histology

NucleAI	Israel / 2017	Histology	5M Seed	Grove Ventures, Vertex Ventures, Vertex Ventures Israel	Histology
CoreLine	-	CT	-	-	-

Table 8. List of startups that create AI-powered products for interpretation of medical image data.

The following startups turned out to be closest to our company, product, and vision in general:

Arterys

Short Info:

Arterys is the medical imaging AI platform allowing to weave leading AI clinical applications directly into existing PACS or EHR-driven workflow to make it a natural extension of what doctors already do. The company has a LungAI product. The LungAI finds lung nodules on CT images and provides detection, volumetric segmentation, longitudinal tracking, and standardized reporting (Lung-RADS) product features.

The company was the first to receive FDA clearance for a cloud-based product with Artificial Intelligence, and currently has 5 FDA clearances, and is active in 28 countries.

Danger for us:

- Their product LungAI, which identifies cancer from Lung CT

Why we are different:

- We do kidneys, then other organs on CT, not only Lung.
- We will classify malignant VS benign lesions, not only localize them
- Do volumetric tracking across different CT studies of a patient.

Lunit

Short Info:

With AI, they aim to make data-driven medicine the new standard of care. They are especially focused on conquering cancer (like our product does), one of the

leading causes of death worldwide." They are working with X-Ray imaging, Mammography, and digital pathology - microscope images (Biomarker for Immuno-Oncology). CE marked with two products: Lunit INSIGHT MMG & Lunit INSIGHT CXR

Danger for us:

- Jumping from XRay (CXR) and Mammography (MMG) (2D) to 3D CT and MRI is most likely very doable for them.
- They are being integrated with Philips Diagnostic X-ray Suite.
- Collaboration with GE Healthcare

Why we are different:

- We specialize in other image modalities — CT scans of the ventral cavity.
- Do volumetric tracking across different CT studies of a patient.

Quantib

Short Info:

The main focus is neuroimaging. It is a spin-out from Erasmus MC, University Medical Center Rotterdam. Quantib now has AI partnerships with the three largest academic hospitals in the Netherlands and private providers internationally. The company has three products, only one work with cancer — Quantib Prostate. It analyzes MRI prostate. AI-driven prostate volume measurements, AI-supported ROI segmentation of suspicious.

Danger for us:

- Quantib PROSTATE product as it finds cancer in the Prostate from MRI.
- In collaboration with GE Healthcare, they developed a machine learning application as an Advantage Workstation (Server) plug-in.

Why we are different:

- Our area is the ventral cavity
- We work with CT, not MRI (they work with CT but for the brain)

- We analyze kidneys -> other organs, not only Prostate

Ezra

Short Info:

Ezra's mission is to enable early cancer detection for everyone by using AI and advanced medical imaging technology. Ezra's full-body MRI protocol detects up to 13 cancers in women, 11 in men. They are building the Ezra AI, designed to assist radiologists in their analysis and increase their accuracy and productivity.

They have only 1 FDA for Prostate:

- Accurate prostate volume measurements.
- Semi-automatic lesion segmentation.
- Slice-by-slice segmentation and 3D volume creation.

Danger for us:

- Their primary focus is extremely close to ours, but another modality.

Why we are different:

- We are working with CT modality.
- We have another business model. They offer the entire service, including MRI machines, radiologists' stuff, AI-powered analysis, not only SaaS.
- Lesion tracking. Our competitors do not promise this feature anywhere.

InferVision

Short Info:

Infervision is an AI high-tech company that uses deep learning technology and computer vision to help diagnose cancers. They have a wide range of AI-powered products, including InferRead CT Pneumonia, CT Lung (finding nodules), CT Stroke, CT Bone.

By 2020, Infervision's AI products have gained several regulatory clearances, including PMDA in Japan, CE, the FDA 510(k), and China's NMPA.

Danger for us:

- They are well-financed and have lots of hospitals as partners, meantime being quite close in our field (CT and Cancer) + have experience in developing AI for CT.

Why we are different:

- We work with Kidney CT → cover full-body CT workflow with automated dynamics assessment

Chapter summary

The interviews and research of companies and startups from Finland, Lithuania, Estonia, Croatia, Slovenia, and the UK did not bring up even semi-automated lesion tracking solutions. It strengthens the observation that the market is both slow and very fragmented. The solutions from GE, Philips, and other big players are not that wide-spread (or at least not used by the radiologists and companies/startups we have interviewed).

We can observe that most startups have a laser focus on specific problems (organ and related diseases). However, they do not consider radiologists' entire workflow. We also found out that there are no products on the market, which are FDA cleared on kidney and colon organs, opening the doors for innovation creation.

In contrast to competitors, our solution thrives on being fully automated support for dynamic lesion tracking. We start from the exact organ, which nobody does — the kidney. Lately, we will cover the entire ventral cavity - all regions, all internal organs. CE is an acronym for the French phrase "Conformité Européene". This mark shows that the current product meets the essential requirements of the corresponding directives, and it can be freely distributed throughout the market in European member states. In the case of medical devices, the product has to meet

the EU Medical Device Regulation 2017/745 (MDR) requirements set by the European Commission.

Chapter 5. Business Model

Business model

Characteristic	Our Offer
Clients	*Clients, we want to sell:* We have two main groups of clients in this cohort. The first group is radiologists who open to innovations and care about their productivity and focus on meaningful tasks. They will be end-users of our solution. The second one is the hospitals, which have big oncological departments and willing to optimize diagnosis processes. *Clients, we do not want to sell:* Hospitals, with small or absent oncological departments. *Profitable clients:* Clinics that are happy with our solution and ready to contribute to our product development (clinical study, doctors for data labeling, etc.). They also would be glad to promote us on the medical oncological meetings/webinars/conferences.
Unique Value Proposition	We propose an AI-based, workflow-optimization integral tool, which will speed up the interpretation of the oncological full-body CT scans five times. The radiologists will become much effective and concentrated in more essential tasks. The hospitals will increase the throughput of the oncological department up to five times.
Profit Model	Income Sources: 1. Fee-per-CT scan 2. Annual/monthly subscription 3. Annual maintenance contract 4. Selling AI in other marketplaces Our main delivery model is SaaS (software as a service). The subscription plans which we offer vary considerably depending on the hospital, multi-subscription plans are also available.
Strategic Control	1. *AI algorithms for unique organs* (kidney and

	colorectal): nobody in the market has done the CE/FDA certification of AI algorithms on these organs. 2. *Patents and product certification* 3. *Huge biobank for training AI*: we are the first startup, which gained access to the National PACS database of Estonia. 4. *Our value proposition and product concept*: we propose a unique workflow-optimization tool for radiologists. 5. *Customer relationship*: unique approach for every hospital and abundant consultation for product use and troubleshooting. 6. *Alternative certification-free product dev.*: not to be locket into regulation field we develop an alternative product, which may be modified and improved more productively and faster than already certified products.
Focus of Activity	R&D, UI/UX design.
Key Partners	1. Biggest biobanks 2. Cancer Research centers 3. Health organizations 4. Tartu University's computational cluster 5. Cloud computing providers 6. Medical oriented AI research labs 7. Healthcare part of the government in Estonia 8. Perspectum (AI-based startup in medicine)
Organizational Structure	• Strong R&D lab • Regulatory office • Team of medical experts

Table 9. Business-model for the BetterMedicine company according to the Slywotzky methodology.

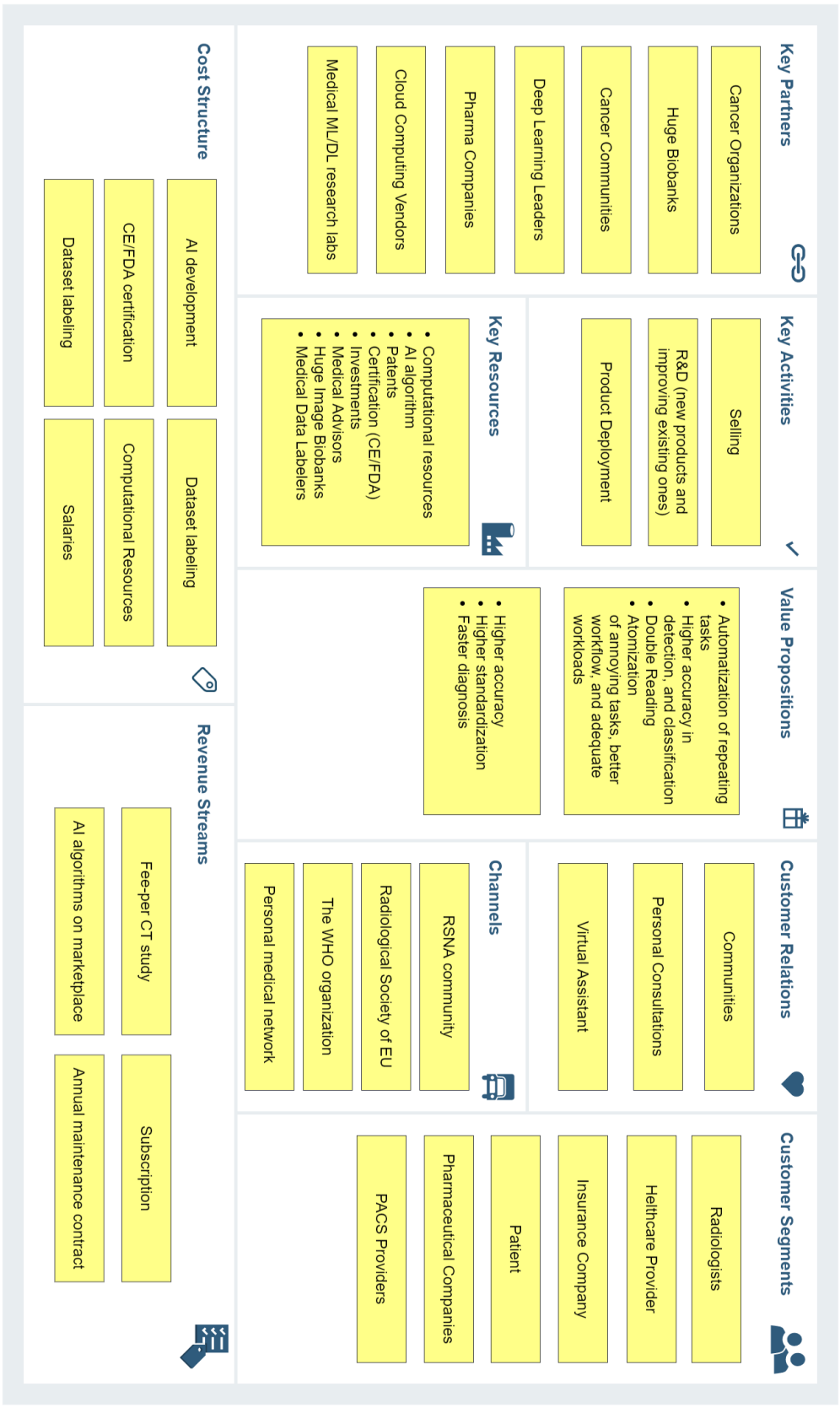

Figure 4. Business model canvas by Osterwalder

We have described our primary business model following two main methodologies by Adrian Slywotzky [24] and Alexander Osterwalder [25]. However, as we mentioned in **Chapter 3. Product certification**, the classical path to market in medical AI startups is too long and risky. That is why we actively find an additional complementary appendix to the given business model, allowing us to gain revenue streams much faster with fewer investments.

Product distribution and marketing

As a B2B business, we will sell directly to the top people in the hospitals at the first stages of the product. One of our founders is Martin Reim, head of the Society of Radiology of Estonia. Thus, we have a broad network of contacts all over Europe. After running our pilot product, we also, in parallel, boost promoting our product by involving the Estonian government and international cancer organizations like the American Cancer Society, RSNA, the WHO, Imperial Cancer Research Fund, etc.

We have successfully applied some steps of the following selling strategy to 3 clinics:

1. Understand the context of the product in the current hospital/country, how will it help, what value does it bring.
2. Find The Key Opinion Leader in the department which we are going to sell. It is usually done by talking to people - it is an unwritten list of people in the sub-specialties per Hospital. For example, the leading oncologist in a hospital might not be the Head of Oncology. In surgery, for liver-related products - it is possible to find people who primarily deal with liver problems. Etc.
    1. Talk to and convert The Key Opinion Leader to be an internal Champion. They need to believe in the product and its value.

    2. Find out who is in the associations - the key people in the related professional association have to agree with the product idea.
    3. Then with the internal champion approach the Head of the Department and sell the product.
3. Then it is time for a product demo.
4. Figure out the financing - how is the Hospital motivated to carry the cost.
5. Create good relations with the head of a department, head of the clinic - they are the decision-makers. Get the decision made.
6. After the buy decision is made, it will move to the formalizing of the buy decision. We should keep our eye on the Procurement and talk through the things to make sure they buy the right thing. It might mean parameters, but also proper training - all of it.

Chapter 6. Finances

Budget

Runway in mo	24	Apr '21 - Apr '23	Full On!!!	Less on	Q2 2021	Q3 2021	Q4 2021	Q1 2022	Q2 2022	Q3 2022	Q4 2022	Q1 2023
Team	**/mo**	**one time**										
CEO	€6,000		€144,000	€123,840	€18,000	€18,000	€18,000	€18,000	€18,000	€18,000	€18,000	€18,000
CMO	€1,500		€36,000	€30,960	€4,500	€4,500	€4,500	€4,500	€4,500	€4,500	€4,500	€4,500
CSO	€1,500		€36,000	€30,960	€4,500	€4,500	€4,500	€4,500	€4,500	€4,500	€4,500	€4,500
Chief of AI Engineering	€6,000		€144,000	€123,840	€18,000	€18,000	€18,000	€18,000	€18,000	€18,000	€18,000	€18,000
CPO (-6mo)	€6,000		€108,000	92880			€18,000	€18,000	€18,000	€18,000	€18,000	€18,000
Chief Compliance Officer	€6,000		€144,000	€123,840	€18,000	€18,000	€18,000	€18,000	€18,000	€18,000	€18,000	€18,000
CTO	€6,000		€144,000	€123,840	€18,000	€18,000	€18,000	€18,000	€18,000	€18,000	€18,000	€18,000
Frontend Engineer (-6mo)	€6,000		€108,000	92880			€18,000	€18,000	€18,000	€18,000	€18,000	€18,000
Frontend Engineer (-12mo)	€6,000		€72,000	52560					€18,000	€18,000	€18,000	€18,000
Backend Engineer (-6mo)	€6,000		€108,000	92880			€18,000	€18,000	€18,000	€18,000	€18,000	€18,000
Backend Engineer (-12mo)	€6,000		€72,000	52560					€18,000	€18,000	€18,000	€18,000
QA (-12mo)	€4,500		€54,000	37800					€13,500	€13,500	€13,500	€13,500
Team total - full on!!!		€1,170,000										
Team total - less on		€978,840										
Product outsourcing												
Branding CVI & Landing		€8,000	€8,000	€8,000	€8,000							
UX/UI design		€30,000	€30,000	€30,000			€15,000	€15,000				
Data & Computational resources												
Annotation (10 organs by 2023 apr)		€187,500	€190,000	€75,000	25000	25000	25000	25000	25000	25000	25000	15000
Computations training		€5,000	€60,000	€15,000	€10,000	€5,000	€10,000	€5,000	€10,000	€5,000	€10,000	€5,000
Computations detection		€1.00	€54,000	€16,200		€10,000	€2,000	€2,000	€10,000	€10,000	€10,000	€10,000
Computational overhead / y		€15,000	€15,000	€6,000	1000	2000	2000	2000	2000	2000	2000	2000
Legal												
General	€2,500		€60,000	€60,000	€7,500	€7,500	€7,500	€7,500	€7,500	€7,500	€7,500	€7,500
IPR - freedom to operate		€5,000	€5,000	€5,000	5000							
IPR - patent application (1)		€10,000	€10,000	€8,000			10000					
Regulatory Compliance (CE Marking)												
Compliance Partners		€300,000	€300,000	250000	60000	60000	60000	60000	60000			
Implementation internally	opt	€62,400	€62,400	€31,200	15600	15600	15600	15600				
Notified Body (first round and yearly audit)		€100,000	€70,000	€70,000			50000				20000	
Clinical Studies												
1st Clinical study in Tartu		€100,000	€100,000	€100,000	25000	50000	25000					
Clinical study in Germany + Netherlands + Austria		€400,000	€1,200,000	€400,000				240000	240000	240000	240000	240000
Distribution												
Reimbursement study in Estonia		€50,000	€50,000	€50,000			50000					
Reimbursement study in Germany + Netherlands		€100,000	€200,000	€100,000				40000	40000	40000	40000	40000
Pilot Hospital - Integration + Feasibility study / alternatively F		€400,000	€400,000	€400,000				80000	80000	80000	80000	80000
Sales & Markeging in Germany		€60,000	€60,000	€60,000						20000	20000	20000
Office / Backoffice												
Workspaces	12	€30,000	€30,000	€30,000	15000		7500		7500			
Rent	€2,160		€12,960	€12,960			€2,160	€2,160	€2,160	€2,160	€2,160	€2,160
Finances	€1,000		€24,000	€24,000	3000	3000	3000	3000	3000	3000	3000	3000
Total			**€4,111,360**	**€2,730,200**								
Full on Quaterly					**€256,100**	**€259,100**	**€419,760**	**€632,260**	**€671,660**	**€619,160**	**€644,160**	**€609,160**

Figure 6. Optimistic and pessimistic versions of our budget for 2021-2023.

We have created optimistic and pessimistic versions of the budget based on the fundraising results (refer to **Figure 6**) for the next 3 years. The outcome of the optimistic (4.1$ mil.) one is the following. We plan to conduct 4 clinical studies with the 4 hospitals across the EU. Ideally, 1 out of 4 hospitals should be from the US. Consequently, we will spend this budget to obtain CE mark and FDA approval for 4 separate organs (kidney, colon, lung, and liver) of the ventral cavity while getting 4 customers, including all deployment infrastructure, security, and product branding. The pessimistic version (2.7$ mil.) of the budget will allow us to finish

the clinical study with Tartu University Hospital on kidney tumors and start the new one with the University Medical Center Groningen regarding colon cancer.

Sources of investments

Vast sums of money are required to create freedom of movement (dedicate ourselves to the company, hire people, annotate datasets, hire consultants for FDA and CE marking, IP protection etc). Firstly, we planned to bootstrap by pre-selling our product. It turned out that in the medical field, the pre-sale strategy did not work in our case. Then we moved into finding grants for the AI projects in medicine. There are plenty of opportunities in public money. Despite this type of financing equity-free, it requires tons of time - applications, reporting, research activity obligations, etc. Another bottleneck is significant research and innovation funding programs that offer up to $5 mil. of funding like Horizon Europe, European Institute of Innovation & Technology Call, etc. They have strong requirements for the applicants. We tried to apply for EIT Innovation call 2021. However, they usually take only mature startups, which have already fundraised up to $2 mil. of private investments previously.

So, our current fundraising strategy is a combination of both private and public money. We plan to fundraise $2.5 mil. in angel investors and specified medical VCs. The rest of the required sum should be covered by public investment, aka EIT Innovation call 2022, or Horizon 2022.

Chapter 8. Project Roadmap

Stakeholder analysis

We have divided our stakeholders into internal (see Table 9) and external (see Table 10) ones.

Internal stakeholders	Their interests
Founders	• Better cancer treatment • Brand development • Income • Experience of hard MedTech startup development
Regulatory experts & doctors in a team	• Additional income • Experience in AI project in medicine • Experience in oncology field
Advisory board	• Income • Curiosity to cancer projects (As one of the board members stated) • Sport excitement
Other team members	• Project, which creates important impact • Strong team • Salary in time
R&D lab	• Interesting research projects • Big budget • High publication pace • Access to the huge clinical datasets • Access to world class leaders in the field(Fei-Fei

	Li, Andrew Ng, DKFZ, etc)

Table 10. Internal stakeholders of our project

External stakeholders	Their interests
Tartu University Hospital	• Publications • Free product • Brand development • Financing
Estonian Government	• Healthy nation • Effective technical support of the medicine field • Brand of the country
Pidlipank (national medical database of Estonia)	• Self-branding • Utilization of their datasets • Financing
Other clinics, ready to run clinical studies	• Competitive advantage • Grant access • Cheaper product • Research publications
Duke University	• Access to the huge medical database • Publications • Joint research • Financing • Access to people resources
Perspectum Company	• Our complementary AI algorithms • Our expertise in CT

Ezra Company	• Our tumor segmentation expertise on CT • Our AI algorithms • Pidlipank data access
DKFZ lab	• Access to huge database • Joint research • Experience sharing • Financing

Table 11. External stakeholder of our project

For every group of stakeholders, we have provided the levels of influence (strong, medium, low) and the level of interest and corresponding risks in Table 12. Influence and risks of the stakeholders.

Stakeholder	Influence level	Interest level	Risks
Founders	Strongest	Strongest	Will burn out
Advisory board	Strong	Strong	Will leave the company
Tartu University Hospital	Strong	Strong	We do our first clinical study. If we fail, we will lose a year of time, what is critical in our case.
Estonian Government	Medium	Strong	We lose support and will be blocked to our other stakeholders.
Pidlipank (national medical database of Estonia)	Strong	Strong	It is one of the main resources and competitive power we have (core of our AI)
Other clinics,	Medium	Medium	Our hot possible

ready to run clinical studies			customers. If we lose them, we will lose time in the future.
Duke University Hospital	Medium	Medium	One of our main potential first customer in US.
Perspectum Company	Low	Strong	Will buy us in the future. Will try to copy our solution
Ezra Company	Low	Medium	Lock us in collaboration with them.
DKFZ lab	Low	Low	Reimplement our idea.

Table 12. Influence and risks of the stakeholders

Stakeholder	Inform	Convince	Encourage action	Ignore
Founders	+		+	
Advisory board	+		+	
Tartu University Hospital	+	+	+	
Estonian Government	+			
Pidlipank (national medical database of Estonia)	+		+	
Other clinics, ready to run clinical studies	+	+	+	
Duke University	+	+	+	

Hospital				
Perspectum Company	+	+		
Ezra Company	+	+		
DKFZ lab		+	+	

Table 13. Forms of interaction with the stakeholders.

Implementation stages

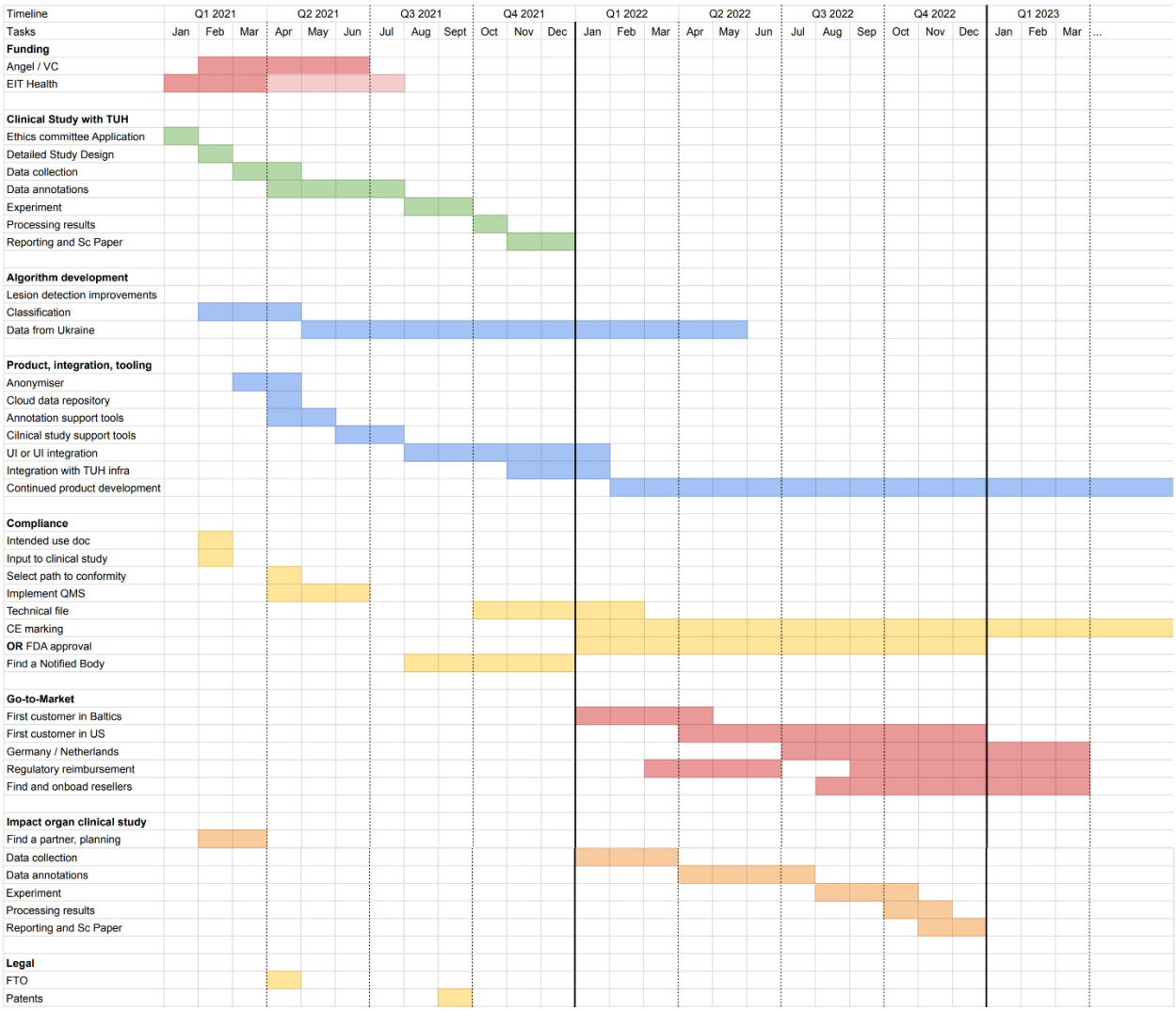

Figure 7. Roadmap of the project for the next 3 years (2021-2023)

We see several critical steps before getting the first revenue.

1. *Get funding.*

We have a concrete plan and gathered lots of institutions and teams around it. In order to move this machinery on, we need lots of investment. During the next 3 months, we will intensively fundraise money for the project.

2. *A clinical study with Tartu University Clinic*

The clinic is our first customer who willing to support us with the data volumes for AI training, doctors, medical expertise, and a playground for running our first clinical study, which is a critical bit towards the next step.

3. *CE/FDA marking*

To sell a product, we need a CE marking, which will allow us to operate on the EU market and FDA. We plan to get our first CE mark for kidney lesion detection algorithm based on the clinical study we do with the Tartu University Clinic.

4. *Clinical deployment & integration*

After auditing the CE/FDA mark, we will need to deploy AI into the clinic infrastructure and develop UI/UX of the AI algorithms. Additionally, security modules that anonymize, encrypt and deanonymize data from the clinic should be implemented.

5. *Product distribution*

Find a reseller / distribution partner to implement our Sales & Marketing strategy for the given market. Contact and negotiate deals with big player 3rd party solution networks or marketplaces - Philips, GE, Siemens, Agfa, etc. Scale up the sales & marketing activities. Get deals signed, generating income.

6. *Quality monitoring*

Set up a Post-Market Surveillance (PMS) system to help update CE marking, keep using the QMS properly.

7. *More clinical studies and AI development for other organs*

Our general approach is the following. Bring into the market kidney lesion AI algorithm as soon as possible. After that, in parallel, certify and develop algorithms for other organs of the ventral cavity with the existing clinics' network over the EU and US.

Chapter summary

Our primary stakeholders are big clinics with oncological departments, AI research laboratories, biobanks, insurance companies, and other AI medical startups. Our main forms of interaction with our target audience are personal contacts via founders, advisory boards and supporters of our company, medical conferences, and other types of events. By utilizing our main ways of communication, we will interact with our audience and stakeholders and will be able to attract them to active cooperation and deliver personified informing.

We also developed a detailed roadmap for the next three years, including our main directions of activities like AI development, research activities, product development/compliance/certification/standardization, clinical study.

Chapter 7. Risk Estimation

We bring scientific technology into the market. We see dozens of obstacles and threats on the way to achieving our goals. We have provided the list of most dangerous from our perspective:

Fail to fundraise

We have pitched the idea to a wide range of investors. It seems that the idea of the project seems challenging for realization. There is a danger that we will not be able to fundraise the sum, which we stated in the pessimistic version of the budget.

Solution: Change the roadmap of the project and fundraising strategy. We will cut the budget and fundraise a much smaller amount of money with the smaller valuation of the company.

AI will not work in the clinic.

It is often the case that AI, which showed high results in the control group of patients, performs poorly in the clinic conditions.

Solution: Analyze most common mistakes, add more challenging cases into the training set, change neural networks architecture, retrain AI models.

Big companies implement our idea faster.

Even with the granted financing to speed up AI development in medicine is a challenging task. There are a set of bottlenecks, which do not allow to do that. Firstly, the product certification process, which takes a minimum of ten months per organ. Secondly, in order to train AI, we need to annotate the dataset. Medical annotated datasets are created exclusively by medical experts, which are in a colossal shortage even for medical services.

Solution: Continue building our biobank with access to national medical databases like Pidlipank. In parallel, develop a community of radiologists willing to help our

idea and contribute to the data labeling process. Money is often not the primary driver in this scenario.

AI with the given accuracy and speed will not bring enough business value to the hospitals.

It may be that the hospitals themselves will not get enough economic value from our developed product.

Solution: Sell our product to other stakeholders like insurance companies, pharmaceutical companies, other AI-based startups, maybe even patients.

Fail to achieve market/sell hospitals

The medical market is desperately fragmented. It may be challenging to sell products to many hospitals as product deployment processes, AI adaptation, personnel training, etc., take tons of time.

Solution: sell AI algorithms via additional distribution channels, like marketplaces created by other startups or big companies.

Chapter 9. Team

PoC phase

At the very beginning, it is crucial to have a few founders to start AI medical startup effectively. We have thoroughly built our team.

Our **Chief Executive Officer (CEO)** is Priit. A software engineer, product manager, and serial entrepreneur with experience from multiple startups and a corporate - Nokia. He has founded two successful companies. The latest, Mooncascade, has built digital products for four out of five Estonian unicorns: TransferWise, Bolt, Playtech & Skype. As a community enthusiast, he has been a co-founder/initiator in a series of nonprofits: Garage48, Latitude59, The Global Hack & Solaride. Board Member in Geneto - genetic testing startup to impact lifestyle choices.

Our **Chief Medical Officer (CMO)** is Martin Reim. He is a practicing radiologist and interventional radiologist; president of the national radiology society; chairman of European Society of Radiology RTF workgroup and a member of several other bodies within ESR, national representative for clinical radiology in IAEA and UEMS, member of Tartu University Hospital development committee, expert consultant for the Ministry of Social Affairs in Estonia, vast medical-network across Europe from the international cooperation projects with different organizations.

Chief Science Officer (CSO) is Dmytro Fishman. He is a computer scientist with an extensive background in biology and medicine. Holds a Ph.D. in Bioinformatics/Biostatistics; Lecturer of Artificial Intelligence and a Medical Imaging group leader at UT; working on a non-invasive blood test for endometrial carcinoma, one of the research leaders of the Autonomous Driving Lab project, an author of the reporting standards of ML methods in biology (article published in

Nature Methods); reviewer of top ML conferences and journals, e.g., ICML/ICLR/Nature Machine Intelligence; Received a prize for the contribution to the development of the Information Society in Estonia.

Our **Chief of AI Engineering** is Bohdan Petryshak, responsible for the core product development, hand in hand with scientific aspects. Take part in the company presentation and fundraising processes. Provides expertise in selling processes to Ukrainian hospitals.

Product development phase

During the active phase of product development, we will necessarily need the following players.

Technology stack:

- Chief Technology Officer (CTO / Chief Engineer / VP of Engineering) - building the whole product for our users around the AI. Accompanying software infrastructure. (missing - covered by Priit)
- Chief Product Officer (CPO) - product expert on the customer, UX & deployment. (until then covered by Priit)

Quality/Compliance/Regulatory:

- Chief Quality Officer (CQO) and Chief Regulatory Officer (CReO) XOR Chief Compliance Officer (CCO) if combined - responsibility: compliance
- CQO - responsible for QMS (quality management system) & RMS (risk management system) implementation and operations. Their job is to get the FDA and CE marking. (QA in software dev terms is part of it later). Close coop with Technical.
- CCO - regulatory compliance works hand in hand with quality. Re: consensus standards, HIPAA requirements, and bio-compatibility. Clinical

studies. If capable can be the same person as CQO. Close cooperation with Medical.

Business development:

- Chief Revenue Officer (CRO / Head of Business Development) - responsible for marketing and sales. (until covered by Priit)
- Chief Financial Officer (CFO) - keeping financials in order, modeling revenue streams, cost predictions, etc.

Later Also: IT & Security; HR & recruitment; legal; etc.

Chapter 9. Conclusions

We have interviewed radiologists out of 9 countries and successfully identified a nerve-racking part of the radiological workflow - lesions dynamic assessment from the computed tomography scans. Dozens of medical AI startups and mature companies were thoroughly analyzed. We found out that there is a lack of solutions, which solve the above-described problem.

We already developed the first version of the AI algorithms, which identify cancer from computed tomography on the kidney, liver, lung, and pancreas. In parallel, we have attracted three hospitals to conduct clinical trials in different countries across the EU: Estonia, Netherlands, and Germany. We are the first medical startup in history that achieved access to the most prominent medical database in the EU - Pidlipank, National Database of Medical Imaging, giving us a strategic advantage over our competitors who work with AI technologies.

We develop a medical hard tech product. It is a very strongly regulated, fragmented, and hard-to-crack industry. The main principles of the lean startup “fail fast and break things” will not work in a healthcare. A slower, more deliberate route to market and reimbursement is required. After pitching to a range of angel investors (co-founder of Skype Jaan Tallinn, co-founder of PipeDrive Martin Henk, etc.) and VCs (NordicNinja, Tera Venture, etc.), we found out that traditional fundraising strategies and approaches also do not work here. We need firstly to attract people with solid experience in the field (for example, Sir. Mike Brady) to the advisory board, get lead medical investors, raise the rest starting budget, and follow developed roadmap.

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Appendix

TPU —tensor processing unit

AI — Artificial Intelligence

ANN — artificial neural network

DL — deep learning

ML — machine learning = AI = DL (in the context of this master thesis)

R&D — research and development

HER — electronic health record

CT — computed tomography

MRI — magnetic resonance imaging

PET/CT or **PET-CT** — positron emission tomography-computed tomography

PACS — picture archiving and communication system (a medical database with all patient information including EHR, all types of image modalities, diagnosis conclusion)

VNA — vendor neutral archive. It is a standardized format of storing medical images and documents (any clinically relevant files), distinct from traditional PACS.

HU value — Hounsfield scale value. It is a quantitive scale for describing radiodensity. It is often used in CT imaging to understand which pixels belong to which type of inner tissues (for instance, 0 is water, 300-400 is bone tissue, etc.)

FDA — Food and Drug Administration

CE — The Conformitè Europëenne, marking represents a manufacturer's declaration that products comply with the EU's New Approach Directives

RADS — Reporting and Data Systems provide standardized imaging findings terminology, report organization, assessment structure, and classification for reporting and data collection in the image diagnosis process.

ROI — a region of interest, a part of the image, where important information is presented. For example, the boundaries of the cancer tumor.

Semi-automated algorithm — algorithms, which require manual input from the user. It cannot perform well without user interaction.

ISO — International Organization for Standardization

Ph.D. (Latin philosophiae doctor or doctor philosophiae) — a Doctor of Philosophy

QMS — Quality Management System

PoC — Proof of concept

VC — Venture capital