

Team Results

Document SenSwiss



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11.08.2023

SensUs 2023

Traumatic Brain Injury

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1. Abstract

Traumatic Brain Injury (TBI) is a major and widespread health concern in contact sports. Due to the lack of standard and comprehensive on-field athlete assessment protocols, the majority of mild TBIs remains undiagnosed. This issue carries substantial health implications, particularly considering that repeated untreated head traumas heighten the risk of neurodegeneration and dementia. Driven by the desire to revolutionize the situation, our team, SenSwiss, has developed a novel biosensor allowing for quantification of Glial Fibrillary Acidic Protein (GFAP) in human plasma.

To achieve precise detection, we have designed an intricate system that amalgamates various technologies. Employing a sandwich bioassay, we incorporated citrate-capped gold nanoparticles functionalized with capture antibodies. By integrating a pump system, we introduce the sample fluid into our microfluidic chip. Furthermore, the microfluidic technology has been ingeniously integrated with the cartridge-based approach. The resultant signal is then converted through an SPRi-based configuration, further enhanced by nanoparticle integration and a grating-based technique.

Thanks to this cutting-edge technology, we anticipate the SenSwiss sensor becoming a valuable tool for implementing new measures to ensure athlete's safety and well-being.

2. Biosensor system and assay

2.1 Molecular recognition and assay reagents

Our sensor utilizes a sandwich assay with two distinct antibodies to capture the GFAP protein. Initially, a self-assembled monolayer (SAM) forms on a gold-coated chip by immersing it in a solution of COOH/OH-functionalized PEGylated alkanethiols. Following this, the EDC/NHS crosslinking solution activates carboxylic groups in the SAM, forming NHS esters that react with amines on the detection antibodies (Anti-GFAP 94cc) (Yan et al., 2015). These antibodies are immobilized on the gold surface through amine bonds. Ethanolamine treatment and Bovine Serum Albumin (BSA) application neutralize remaining reactive COOH groups to prevent non-specific binding. In the subsequent step, GFAP protein mixes with citrate-capped gold nanoparticles (AuNPs) functionalized with capture antibodies (Anti-GFAP 15cc), using the same EDC/NHS crosslinking solution. The resulting solution is added to the chip, allowing GFAP-AuNPs to attach via the antigen to the immobilized detection antibodies, forming the sandwich complex for quantifying GFAP.

2.2 Physical transduction

Utilizing surface plasmon resonance (SPR) for transduction, our device gains from grating integration, which enhances refractive index sensitivity. We achieved this improvement by incorporating metal gratings sourced from DVD-R discs, avoiding costly methods like laser lithography and nanoimprint. These DVD gratings have a periodicity of 740 nm and a modulation depth of 86 nm (Sun et al., 2018). This configuration presents distinct advantages over CDs and Blu-rays, particularly due to its ability to facilitate excitation within the visible spectrum. Our approach involves cleaving the DVD's aluminum surface and performing a treatment regimen (acetone, isopropanol, and DI water) to remove surface dye. A 2 nm Cr layer and 10 nm Au layer are then deposited via sputtering at room temperature using the Alliance Concept DP 650. Post-deposition, the integrity of the gratings was

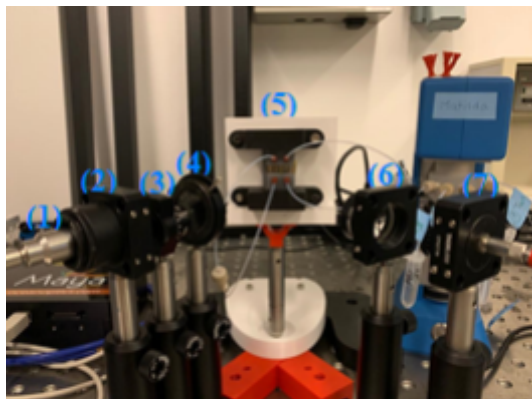


Figure 1: The optical setup. 1) Optical fiber containing white light 2) Collimation lens 3) Polarizer 4) Aperture diaphragm 5) Sample in microfluidics system 6) Focusing lens 7) Optical fiber going to spectrometer

confirmed through microscopic examination at 40x magnification, while gold-coated surface uniformity was assessed using the Bruker Contour X optical profiler.

To enable the detection of GFAP, a broadband LED source (Thorlabs, MBB1L3) is collimated and illuminates the sensing surface at an angle (full optical setup in Figure 1). The metallic grating induces a strong absorption dip in TM polarized light (Guner et al., 2017), shifting when the refractive index (RI) of the solution at the surface of the DVD changes. The change in RI is caused by binding events and is enhanced by the incorporation of nanoparticles, amplifying the signal generated by these interactions (Fathi et al., 2019) and improving the limit of detection (Li et al., 2013).

2.3 Cartridge technology

The microfluidic chip comprises three main components: the glass microfluidic channel, O-rings, and the functionalized gold surface, all held together by a custom-designed aluminum alloy holder. The glass microfluidic channel features two chambers (20 mm² of surface area and 0.32 mm diameter inlet and outlet channels for sample flow). The sample fluid is introduced into the microfluidic chamber using IDEX MicroTight F-126Hx fittings. In collaboration with

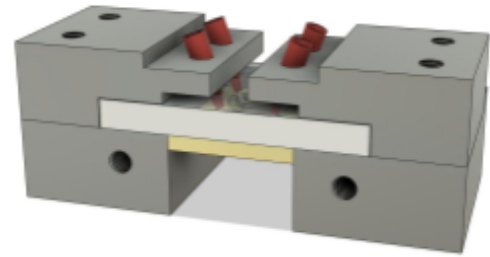


Figure 2: Microfluidic chip

FEMTOprint, the design was optimized and fabricated using Fused Silica, ensuring over 90% optical transmission in the 500-1300 nm spectrum. A dovetail profile integrated within the glass microfluidic channel accommodates HITEC EPDM ID 5.00 x 1.00 mm O-rings (Angst-Pfister), providing a secure seal with a 0.29 mm protrusion. A 10 nm gold-functionalized DVD grating ($P \approx 740$ nm) serves as the sensing surface for optical detection based on surface plasmon resonance. This gold chip is pressed against the O-rings (previously fitted in the glass microfluidic channel) using a rack and pinion-based mechanism. Considering the material properties of EPDM and the fabricated dovetail groove profile, the microfluidic chamber's volume is estimated to be around 2.5 μ L. Material sustainability held a significant influence in the material selection, and further design enhancements were aimed to increase sensor sensitivity. The setup featured a stationary glass chip with O-rings and a movable stage for interchangeable cartridges, streamlining GFAP detection using nanoparticles with a compact micro-volume and easy sensor surface replacement.

2.4 Reader instrument and user interaction

The optical elements consist of a broadband LED source (MBB1L3 by THORLABS) and a spectrometer (Maya 2000 pro by OceanViews) that acts as a reader. The pump used was supplied by AMF (AMF LSPone). These components are controlled via a python-based GUI software, ensuring versatility in both data presentation and storage. The interface is divided into two primary sections: one for microfluidics control and the other for spectrometer control.

The microfluidics control interface offers three command modes for the pump: manual, semi-automatic and automatic. The measured spectrum (wavelength vs intensity) is displayed in real time and the peak of maximum absorbance is saved and displayed as a function of time. We calibrate the spectrometer using both dark field (background noise) and flat field (TE light). Finally, the software performs the post-processing needed to compute GFAP concentration.

3. Technological feasibility

3.1 Molecular Recognition

To ensure optimal molecular recognition within our system, we optimized the antibody pair to achieve the most robust signal in a sandwich assay. We employed the biolayer interferometry technique (BLI), which is renowned for its real-time analysis, label-free detection and high sensitivity. As illustrated in Figure 3, the optimal antibody pair is Anti-GFAP 94cc as capture and Anti-GFAP 15cc as detection. Anti-GFAP 15cc were then functionalized with gold nanoparticles (AuNPs) to increase sensitivity of the biosensor for smaller concentrations of GFAP. In Figure 4, we can observe the difference in the absorbance peak between bare AuNPs and antibody-functionalized AuNPs of 2.5nm for 40 nm AuNPs and 12nm for 100 nm AuNPs with our sensor. The presence of this shift in the absorbance peak towards longer wavelengths is due to the surface chemical changes induced by the presence of antibodies on the AuNPs surface. This method still needs to be tested with GFAP, for which we hope to detect low concentrations.

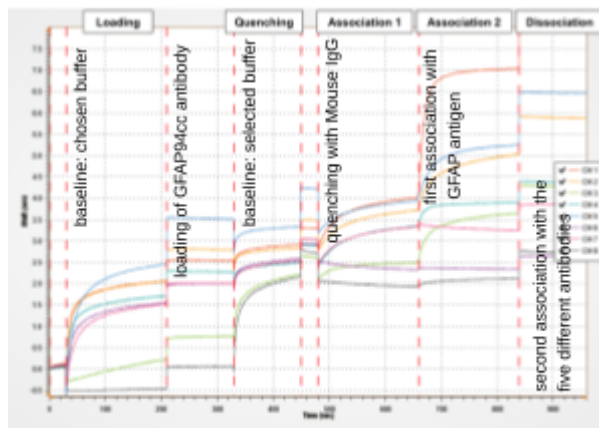


Figure 3: Depiction of the temporal wave shift signal variations for various sandwich pairs utilizing BLI (Can be found larger in Appendix 9.1)

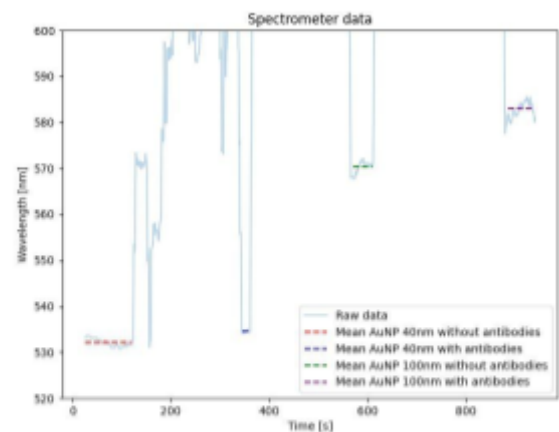


Figure 4: Gold Nanoparticle test with and without antibodies for 40 nm and 100 nm AuNP

3.2 Physical transduction

The DVD grating-based SPR system developed here boasts a sensitivity of 972 nm/RIU when testing with glycerol concentrations ranging from 0 to 75%.

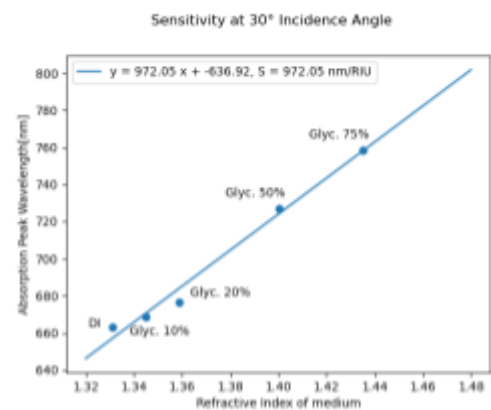


Figure 5: SPR sensitivity results

3.3 Fluidic Cartridge

For our earlier testing phases an alternative cartridge was used for our bio tests. Clear resin was used to print a replica of the glass part and test the leakage of the chambers with O-rings attached to the resin. The resulting chip had good sealing properties however the chamber filling was not ideal due to the non uniformity of the resin prints part.

3.4 Reader Instrument

When developing the Graphical User Interface, we implemented a wide range of commands that allow us to customize the microfluidics and spectrometer settings. In particular, the microfluidics commands allow to choose between the following modes:

1. Manual mode: Sending single commands individually to the pump.
2. Semi-auto mode: Creating a personalized list of commands executed together.
3. Auto mode: Using pre-set sample dispensing, cleaning, command buttons for quicker operation.

This dynamic range of options empowers users with tailored instructions for any requirement. Moreover, the software allows for fine calibration, ensuring more precise results. Additionally, the software is able to recognize whether a spectrometer or a camera is connected to the system. Some smart functionalities such as the automatic detection of a ROI in the image, in the case a camera is connected; as well as spectrometer calibration and noise reduction algorithms and real time signal processing, are all implemented.

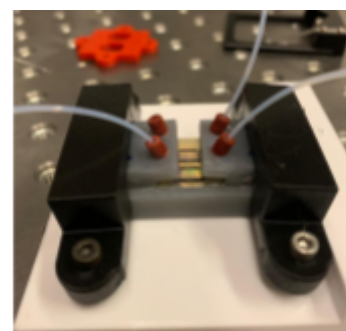


Figure 6: The microfluidic chip held by the aluminum alloy holder

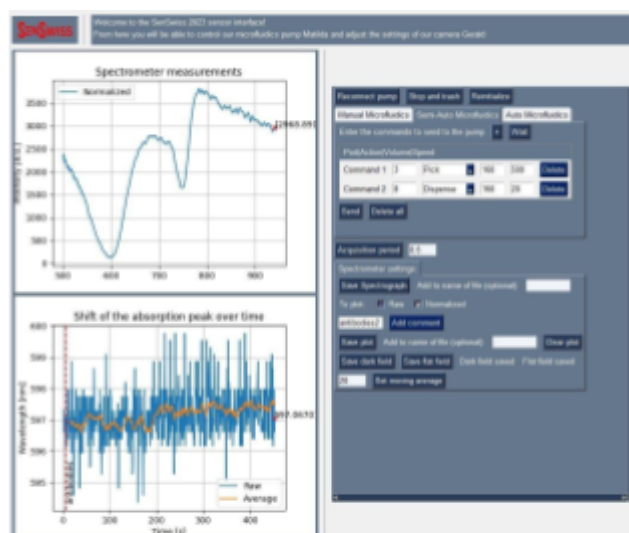


Figure 7: The GUI (Can be found larger in Appendix 9.1)

3.5 Limitations

While our results are promising, there are still uncertainties in reaching the necessary analytical performance in plasma. Presently, we have shown feasibility in the optical and biological systems separately, but are facing difficulties with the plastic microfluidics chip. Due to inhomogeneous filling of the chamber, the signals recorded during flow of samples contain too many artifacts to reliably draw conclusions. Anticipated improvements are expected once the glass microfluidics chip is integrated and nanoparticles are introduced. Further, the biosensor must be validated with plasma, which is a more intricate matrix than PBS.

4. Originality

Team Captains

The SenSwiss biosensor is designed for ease of use as well as ease of fabrication while maintaining high sensitivity. The SenSwiss software builds on the work of team LauSens from the 2022 SensUs competition. We made the graphic user interface both easier to modify and to use as our goal was to make it more accessible to future users. Our software contains safeguards for hazards and real-time signal processing and the graphic user interface allows for flexible data displaying and saving. Insertion of the blood plasma sample is straightforward as all dilution steps are done internally by the Advanced Microfluidics LSPone pump at the press of a button. Together with Abtin Saateh of the EPFL BIOS laboratory, we elaborated a protocol for antibody-oligonucleotide conjugation on the gold surface. This method would allow for continuous biosensing by cleaning and reusing the functionalized sensing surface. This was discontinued due to a lack of time and following recommendations by Prof. Hatice Altug and Dr. Nako Nakatsuka, but may serve as a springboard for future teams.

The sensor technology uses gratings found on commercial DVDs. Chip production is therefore cheap and easy, while the resulting optical system is on par with other high end biosensors. We partnered with FEMTOprint, who provided us with a state-of-the art custom tailored glass microfluidics chip. This novelty boasts over 90% optical permittivity (VIS-NIR) and ensures a leak-free system when coupled with inserts from Postnova and O-rings from Angst+Pfister.

Prof. Hatice Altug

The 2023 SensUs team showed innovative spirit across many aspects of their project. The sensing technology was selected to be different from the previous years as they looked to build their very own sensor with no prior foundation. The team explored a variety of novel methods not used in the final device such as: one-step antibody-oligo conjugation, surface regeneration, magnetic nanoparticles, organic field effect transistor biosensing and real-time identification of nano-particle adsorption. The work done here can be continued in future iterations of SensUs and will help push towards continuous biosensing, key for clinical applications.

The team used the metallic grating found in DVDs inspired by Guner & al. 2016 and Sun & al. 2018. This concept opens up biosensing to the curious without the need for complex surfaces. This year's significant upgrade was the microfluidics chip technology developed with an external partner and will be beneficial to future teams as well as to the BIONanophotonic Systems laboratory.



Abtin Saateh
on behalf of Prof Hatice Altug



Julian Bär
Team Captain



Méline Cretegny
Team Captain

5. Translation potential

Traumatic Brain Injury (TBI) is a major global cause of disability, especially among contact sport athletes. In Switzerland, mild TBI (mTBI) affects 20,000 to 40,000 athletes annually (Rossetto, 2012), with concussions accounting for 17% of ice hockey injuries (Brunner et al., 2020). The multifaceted nature of TBI, ranging from mild to severe, poses diagnostic and treatment complexities. Currently, universally accepted diagnostic and therapeutic standards are lacking (Oris et al., 2023). On-field athlete assessment, if no loss of consciousness is observed, often involves clinical evaluation (e.g. Glasgow Coma Scale) and neuroimaging (Shevelev et al., 2023), but around 80-90% of mTBI cases are missed (Cohen Veterans Bioscience, 2023). Detecting mTBI is vital for athletes' well-being, as undiscovered TBIs increase neurodegeneration and dementia risk (Graham & Sharp, 2019). Research indicates that TBI increases the risk of dementia between 1.5 and 3 fold post-injury (Shively et al., 2012) with up to 5% of all dementia cases attributed to TBI (Graham & Sharp, 2019). Thus, novel tools are imperative for detecting and monitoring mTBI and mitigating long-term effects in athletes.

5.1 Business model canvas

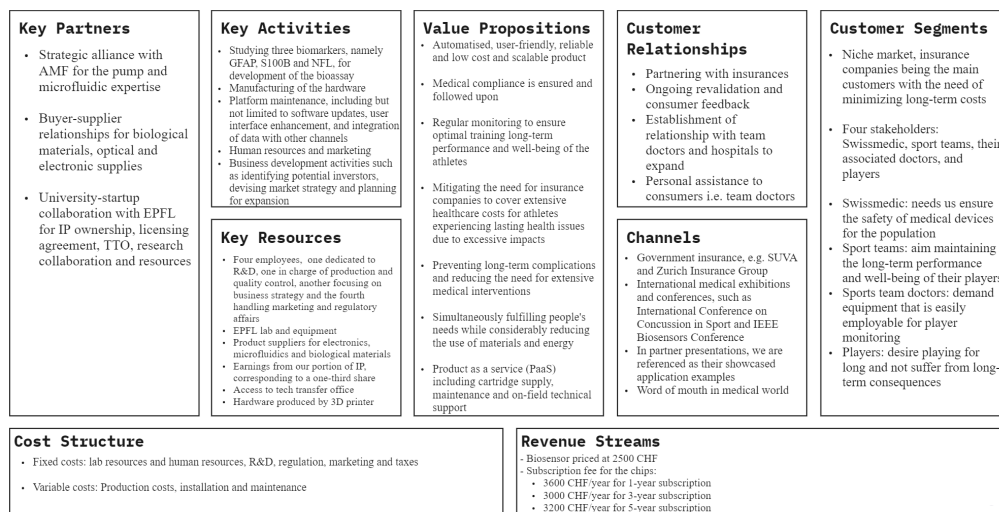


Figure 8: Business Model Canvas (Can be found larger in Appendix 9.2)

5.2 Stakeholder desirability

Frequent TBIs, especially with their link to neurodegeneration (Graham & Sharp, 2019), place a significant financial burden on the healthcare system in Switzerland, where mandatory health insurance is the norm (FOPH, 2023). Considering athletes' emphasis on salary when selecting clubs, these organizations are cautious about reducing their to cover test expenses, preferring insurance coverage, as highlighted by Bearmind—an EPFL start-up specializing in sensor-equipped helmets for brain injury diagnosis. To address this preference, our strategy is to target insurance companies with sizable sports insurance portfolios (e.g., SUVA, Zurich Insurance Group) as customers. By investing in cutting-edge technology that can prevent repeated TBI, these insurers can enhance their services and attract a larger client base. Insurers aim to cut healthcare costs and provide comprehensive coverage. Our sensor aids by providing a reliable diagnosis, ultimately leading to enhanced patient outcomes and reduced insurance claims. It empowers insurers with proactive risk management and strengthens their negotiation stance when implementing safety measures with sports teams.

Other stakeholders include Swissmedic, sports teams, doctors and players. Swissmedic is the governmental authorisation and supervisory authority for drugs and medical products. Complying with their regulations is crucial to ensure the safety, legitimacy, and legality of our product. In the context of sports, our solution enhances the safety measures available to sports teams and, therefore, player safety, while doctors gain access to precise injury assessment tools. This translates to improved patient outcomes and contributes to more effective injury diagnosis and treatment.

Conventional methods like pen and paper exams remain prevalent in sports concussion assessment. However, they can be subjective and influenced by players who are eager to return to gameplay prematurely, as highlighted by Dr. Gaëtan Hirsch, Co-founder of Physio Neo Genève and Member of the Swiss Rugby Union Medical Commission. Our sensor delivers impartial results, preventing players from making decisions against their best interests.

A range of other companies also specialize in mTBI assessment tools and can be classified as either direct or indirect competitors based on whether their assessment techniques employ the detection of biomarkers or not. A comprehensive product comparison is available in the Appendix 9.3.2.

What sets our sensor apart is that it not only promptly informs clinicians about injury severity but also enables long-term monitoring. More details on the multiplex biosensor can be found in Section 5.4. Beyond curbing long-term healthcare costs, our sensor is more cost effective than competitors. Our pricing strategy is based on the monetary valuation estimates of Prof Jean-Charles Sanchez, University of Geneva Group Leader and TBICheck CEO and Co-Founder, ensuring resonance with consumers. Moreover, our athlete-focused product diverges from hospital-oriented competition. Our prototype will allow us to test injured athletes promptly after the game and in the following days, providing quick (under 20 minutes) and objective data for treatment decisions and monitoring.

Consideration of competitor intellectual property (IP) is vital, the most relevant being direct competition using GFAP detection. However, several such patents focus on evading CT scans, which is impractical since suspected moderate or severe TBI cases necessitate CT scans as standard protocol in Switzerland, as explained by Dr. Vincent Darioli, Associate Doctor at Lausanne University Hospital's Emergency Department. Moreover, Abbott Laboratories' patents focus on combined GFAP and UCH-L1 detection (MCQUISTON et al., 2020), which is not applicable to our product. The Banyan patents either stand abandoned (K. K.-W. Wang et al., 2017, 2019) or are limited to the US and expire (K.-W. Wang et al., 2013) after our planned expansion to that market. Furthermore, John's Hopkins' patent encompasses many biomarkers (Everett et al., 2012) that we won't be utilizing.

5.3 Business feasibility

Within the first years we will advance our Proof of Concept (PoC) and prototype, benefiting from the EPFL and BioNanoPhotonic Systems Laboratory partnership for essential resources. Our network of buyer-supplier relationships includes biological supplies (Hytest, Idex), as well as electrical and fluidics materials (Distrelec, Mädler, Angst-Pfister). Our key collaborations with Advanced Microfluidics for flow channel components and Thorlabs for optical materials further enhance our capabilities.

Our R&D team will be tasked with developing an advanced multiplex biosensor capable of detecting the biomarkers GFAP, S100B, and NFL for post-impact TBI assessment across a broad time range.

S100B has the shortest half-life (1.5 hours) while GFAP exhibits a longer half-life (36 hours) (Hier et al., 2021). GFAP has proven effective in predicting CT positivity, whereas heightened S100B levels correlate with impact severity (Potokar et al., 2020). NFL boasts a longer half-life of about three weeks, enabling tracking of damage over an extended period (Hier et al., 2021). Sustained NFL elevations may indicate recurring injury-related biomarker release (McDonald et al., 2021). Consequently, monitoring NFL levels could yield valuable insights into players' conditions, aiding in prevention of neurodegenerative diseases. Dr. Elisa Zanier, Head of the Laboratory of Cranial Trauma and Neuroprotection at the Mario Negri Research Institute in Milan, approved these biomarkers.

In order to maximize the impact of our R&D efforts we will focus on the following domains:

Software Development: Software updates, refining the user interface, and integrating data with other platforms such as phone health apps and medical documentation, fostering seamless data exchange.

Manufacturing Efficiency: Low-cost hardware production via buyer-seller relationships, a key element in making our solution more accessible and scalable.

Scale-Up Manufacturing: Facilitating large-scale production of the bioassay

Our initial team will include a CEO for the business strategy, seeking investors and ensuring a smooth scaling process. Our COO will handle production and quality control, while our CTO will handle R&D and software development. We will also have one employee dedicated to marketing, regulatory compliance and HR tasks.

Strategic partners contribute to licensing, fundraising, rigorous testing, and regulatory strategy. Dr. Craig Cook, Head of Business Development & Licensing at the Wyss Center for Bio and Neuroengineering, will provide invaluable insights into business planning and scaling. Prof. Jean-Charles Sanchez, will provide guidance for clinical studies. Further, Dr. Nako Nakatsuka, Senior Scientist at ETH Zurich, will be pivotal in validating our biosensor technology and ensuring alignment with the latest industry advancements. To enrich our R&D efforts and gather essential consumer insights, we will partner with the Lausanne Hockey Club (LHC) for pilot testing. Our outreach will extend to other contact sport clubs, notably Dr. Davide Bianchi, Member Physician of the World Boxing Council (WBC) Medical Committee and Advisory board has offered to pitch our product within the WBC, aiming to establish it as an integral part of a new standard post-impact assessment protocol. Rigorous tests and clinical trials involving a broader range of athletes are crucial to confirm the biosensor's performance and refine our technology. Our estimations project that this comprehensive validation process will span approximately 7 years (Van Norman, 2016).

To secure capital, we will seek EPFL Startup Launchpad grants like Innogrants, Ignition, and Blaze. Switzerland's innovation-focused programs, including Innosuisse and Venturelabs (Schweizerische Eigenossenschaft, 2023), make it an ideal startup location. Next, we will engage with venture capitalists such as S2S, WCF, Wingman Fund, and Healthcare Angels and pursue grant funding through SNSF and X-Grant to further bolster our financial support and allow us to scale up.

Our biosensor is a Swiss Class C medical device, thus necessitating approval from Swissmedic (Swissmedic, 2019). To begin with, we have produced a risk assessment and mitigation plan (Appendix 9.3.1). For more details on the regulatory aspect see Appendix 9.3.

Prior to launch, securing our IP is crucial. Our MAKE project status at EPFL obliges us to utilize the Technology Transfer Office at EPFL transferring ownership of the patent to the university (EPFL, 2023). This enables us to establish a contract, granting commercialization rights. This approach is beneficial, given the expenses of patent acquisition and defense.

Upon securing regulatory approval for our product's launch, we will embrace a Product as a Service (PaaS) business model. This entails selling the sensor at a set price while offering subscriptions encompassing gold chips, cleaning solution, and maintenance services, notably for the microfluidics pump through a Full Service Contract (FSC) with Advanced Microfluidics. We will distribute through DHL, and customers can handle the installation thanks to the simple process and instructional videos. Our marketing strategy involves collaborating with local sports teams, beginning with the LHC and expanding to other well-known teams first nationally, and then internationally. These partnerships will serve as endorsements, establishing credibility and trust. We will implement a referral program and leverage a website and social media to increase visibility and engage potential customers.

To attract our customers, we will participate in conferences such as the International Conference on Sports Medicine and Biomedical Engineering and host webinars. Additionally, we will gain visibility through publicity from our partners, who are already widely recognized. By combining these approaches, we aim to create brand awareness, forge new strong partnerships, and drive sales growth within the Swiss sports and insurance sectors.

The sales funnel begins with content marketing highlighting our technology's benefits for our customers, followed by webinars and case studies demonstrating the efficacy of our product. We will engage prospects with tailored emails and testimonials, offering in-depth demos and customized packages to meet their individual needs. Once onboard, we will sustain the customer relationship through updates, training, and support, fostering loyalty and referrals.

Our future expansion plans include EU and then later US regulatory approval for global reach. Sustainability will drive our operations, from sourcing to production and waste management. Insurance coverage is key for affordability for patients. Additionally, we will use DVDs instead of manufacturing the grating in-house, reducing healthcare expenses for patients who have not met their insurance deductible (SDG 3.8.2) (United Nations, 2023b). Although recognizing the necessity of our product, we will responsibly minimize material usage (SDG 12.2) (United Nations, 2023c), including reducing packaging, and implementing a chip cleaning protocol for maximum reuse. Further, the PaaS business model, generating recurring revenue through subscriptions, allows to profitably favor a durable sensor. Additionally, we'll make the sensor housing from PETG using a machine that recycles extra 3D printed parts and supports. In terms of additional recycling, Swiss regulations classify serum-contaminated sensor components as medical waste, mandating incineration and, unfortunately, precluding recycling (Schweizerische Eidgenossenschaft, 2005). Our employees' well-being is a top priority, with a focus on mental health (SDG 3.4) (United Nations, 2023b). Gender equality will be actively promoted, encouraging women to take leadership roles (SDG 5.5.2) (United Nations, 2023a).

5.4 Financial viability

Our Costs Of Goods Sold (COGS) table (Appendix 9.4.1) reveals the current sensor production cost of 3972 CHF expected to decrease due to scalability improvements. Individual chip production costs 4.7 CHF and can be used for ten measurements, cleaned using our custom-made cleaning solution in between. The biosensor is made to last a decade. With plans for mass production of over 80 biosensors and 8640 chips by year 9, we will employ an external contract manufacturer with a gross margin of 7%. Distribution, sales and maintenance will be in-house. When expanding to the European market, customs clearance fees and value-added taxes (VAT) are non-negligible added costs.

Our PaaS model involves selling the sensor at 2500 CHF with subscriptions including chips, cleaning solution, and maintenance. Subscription durations of 1 year (3600 CHF), 3 years (9000 CHF), and 5 years (16000 CHF) are available, with additional fees for misuse-related damage or exceeding consumable limits. These costs cover a yearly supply of 90 chips for 900 tests at 4 CHF each. They are estimated for a team of 30 players with 30 tests per year each for monthly monitoring and closer monitoring after impacts (3 tests per impact, average of six seasonal severe hits per player).

Detailed in Appendix 9.4.2, our annual profitability stems from revenue and total expenses analysis. An initial negative net profit extends until year 9, a breakeven point is anticipated in year 3 with a subsequent positive trend by year-end. The negative net profit during the clinical trials and initial two years will be offset by 6.5 million CHF in funding which allows our cash equivalent to be positive.

We will use a business intelligence system that uses data from sales, customer interactions, website analytics, and market research. Cutting-edge software and algorithms will analyze this data, generating customized reports with key performance indicators for informed decision-making. Predictive analytics will forecast demand, detect market trends and allow us to optimize inventory.

Our market entry strategy starts in Switzerland, with an initial focus on hockey. We will then expand to other team contact sports after 3 years. In year 13, we will reach saturation of the Swiss market with 80% of the hockey market and 25% of the other sports'. We will then further expand to the European market after the validation from the European notified body according to the EU 2017/746 regulations. We will start with 5% of the market to an expected 20% after three years.

The total addressable market (TAM) we are targeting are 75'000 adult European hockey, rugby and soccer teams (Appendix 9.4.3). We assume an average of 6 concussive sports injuries/year, some of which will be categorized as mTBI and thus not detected (Cohen Veterans Bioscience, 2023). This results in about 6.8k ER visits of about 500 CHF each (Lausanne University Hospital, 2018), which gives a TAM of 3.4B CHF. At our final estimated 20% penetration rate, we will have a Serviceable Available Market (SAM) of 675M CHF and a Share Of Market (SOM) of 70M CHF, based on 10% of the previous year's sales. This accounts for 2% of the TAM which will generate sufficient revenue for the costs. Neurocognitive tests with possible CT scans remain the golden standard in the market with a price of 300 CHF to 1200 CHF (Schweizerische Eigenossenschaft, 2019). However, according to Dr. Davide Bianchi the neurocognitive tests can be heavily influenced by athletes and are rarely performed after hits to the head in boxing matches due them taking too long as well as the athletes wanting to return to the mat prematurely. Our solution offers a quick, unbiased evaluation of athletes' condition.

6. Team and support

6.1 Contributions of the team members

Meline Creteigny (Team Captain): Coordinated team-organizer communication, explored chip functionalization, and developed the project's business model. **Emilie Jemmi:** Optimized bioassay protocol, tested antibody-gold nanoparticle conjugation, and nanoparticle functionalization with oligos. **Neethu Kizhakkedom:** Determined optimal antibody pairs using bio-layer interferometry and assessed financial viability of the project. **Marin Bricq:** Developed GUI for the pump control, designed prototype components, and conceptualized electrical components. **Arthur Eglin:** Worked on the GUI and on code development of the spectrophotometer and dynamic nanoparticle tracking. **Elena Gado:** Optimized spectrometer code, assisted with deliverables, sponsorship, and explored SPR Microscope via literature review and experiments. **Julian Bär (Team Captain):** Developed a new optical sensing method, microfabricated chips, and oversaw team communication and collaboration. **Ali Elmorsy:** Focused on microfluidics, mechanical design of sensor prototype, electrical element selection, and OFET-based GFAP detection exploration. **Prasanna Surana:** Conceived glass chamber, communicated with sponsors, facilitated collaboration and secured financial support. **Aybüke Çalık:** Worked on electronics conception, microfabricated chips, competitor assessment for the business plan and nanoparticle functionalization. **Bettina Weber:** Strategically planned and executed business plan, developed microfluidics control code, and managed partnership and entrepreneurship sessions. **Chiara Matti:** Contributed to business plan development, deliverables, and SPR Microscope exploration through literature review and experiments.

6.2 People who have given support

We are grateful to **Prof. Hatice Altug** for hosting us in her BIOS lab. A special thanks goes to **Abtin Saateh** for his invaluable guidance and support. Our appreciation also goes to our supervisors **Dr. Nako Nakatsuka**, **Prof. Jean-Charles Sanchez**, and **Dr. Craig Cook**, whose expertise greatly influenced our technical progress and market understanding. We are deeply grateful to medical experts **Dr. Jocelyne Bloch**, **Dr. Elisa Zanier**, **Dr. Ian Fournier**, and **Dr. Vincent Darioli** for their contributions. A special mention goes to the Core Facility Structure team, **Kelvin Lau**, and **Micaela Siria Cristofori**, who granted us access to biolayer interferometry which proved invaluable.

6.3 Sponsors and partners

We greatly value our sponsors' crucial contributions to this project. **Advanced Microfluidics** provided a pump and expertise for the microfluidics system, aiding us in overcoming pump-related challenges. **CMi** funded the use of their cleanroom facility, allowing gold chip production. **FEMTOprint** manufactured the glass microfluidics cartridge and shared their expertise. Financial support was extended by **Wyss Center for Bio and NeuroEngineering**, **Forum EPFL**, **Ligentec**, and **Logitech**. **EPFL** offered vital infrastructure for sensor development, granting access to labs, machinery, and materials.

7. Final Remarks

We have loved working on this cutting edge sensor and hope that one day our technology will have a positive impact on the safety of athletes worldwide. Based on the interviews with medical and sport specialists we conducted, we are optimistic that the sensor will be well received by the world of sports and cannot wait to explore a possible commercialization. We take great pride in our innovative contributions, particularly in microfluidic technology, and we're enthusiastic about pushing the boundaries of innovation even further. In terms of future research, we are eager to extend the number of detected biomarkers and explore various biosensing techniques that we were unable to fully investigate due to project time constraints. Of particular interest are methods enabling continuous sensing through the cleaning and reuse of functionalized sensing surfaces, as these hold significant value for future clinical applications.

8. References

8.1 Interviews

- Interview with Bearmind - EPFL start-up specializing in sensor-equipped helmets for brain injury diagnosis and performance monitoring - 24 May 2023
- Interview with Dr. Gaëtan Hirsch - Co-founder of Physio Neo Genève and Member of the Swiss Rugby Union Medical Commission - 9 August 2023.
- Interview with Jean-Charles Sanchez - University of Geneva Group Leader and TBICheck CEO and Co-Founder - 20 April 2023
- Interview with Dr. Vincent Darioli - Associate Doctor at Lausanne University Hospital's Emergency Department - 19 April 2023
- Interview with Dr. Elisa Zanier, Head of the Laboratory of Cranial Trauma and Neuroprotection at the Mario Negri Research Institute in Milan - 28 July 2023
- Interview with Dr. Craig Cook - Head of Business Development & Licensing at the Wyss Center for Bio and Neuroengineering - 3 May 2023
- Interview with Dr. Nako Nakatsuka - Senior Scientist at ETH Zurich - 27 June 2023
- Interview with Dr. Davide Bianchi - Chief Medical Officer of Swissboxing and Member Physician of the World Boxing Council Medical Committee and Advisory - 11 August 2023

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9. Appendix

9.1 Technological feasibility

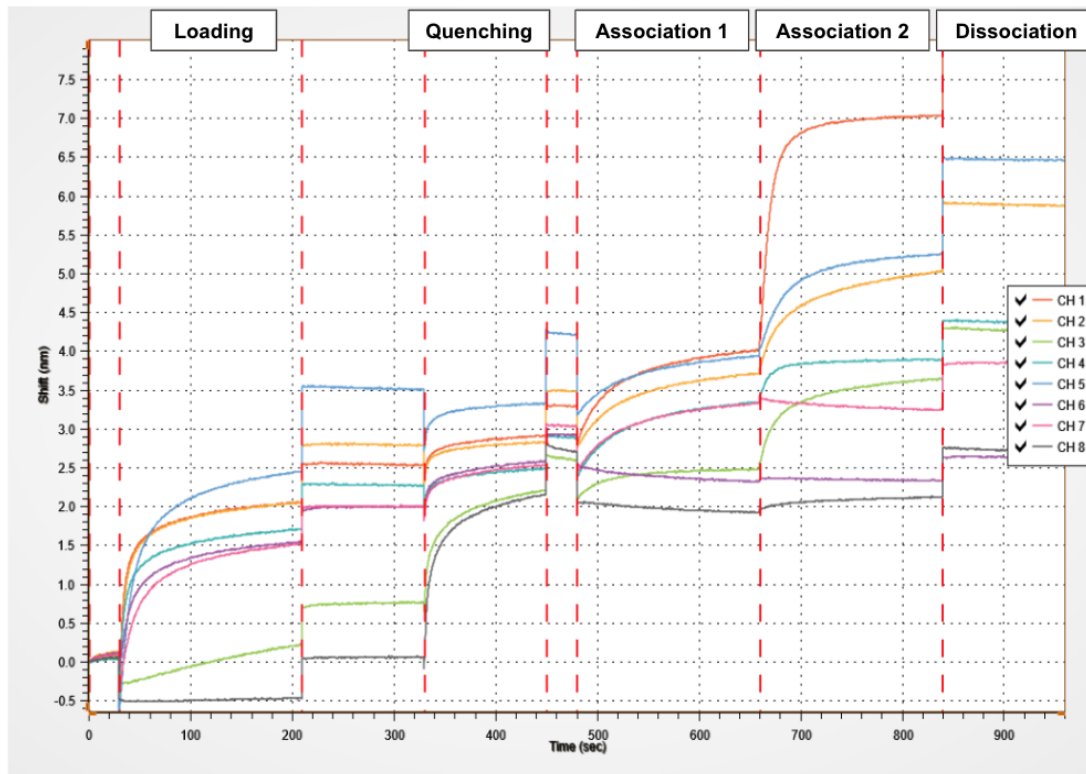


Figure A: Depiction of the temporal wave shift signal variations for various sandwich pairs utilizing BLI. From the right to the left: baseline with the chosen buffer, loading with the GFAP94cc antibody, baseline with the selected buffer, quenching with Mouse IgG, the first association with GFAP antigen, the second association with the five different antibodies and dissociation from the latter.

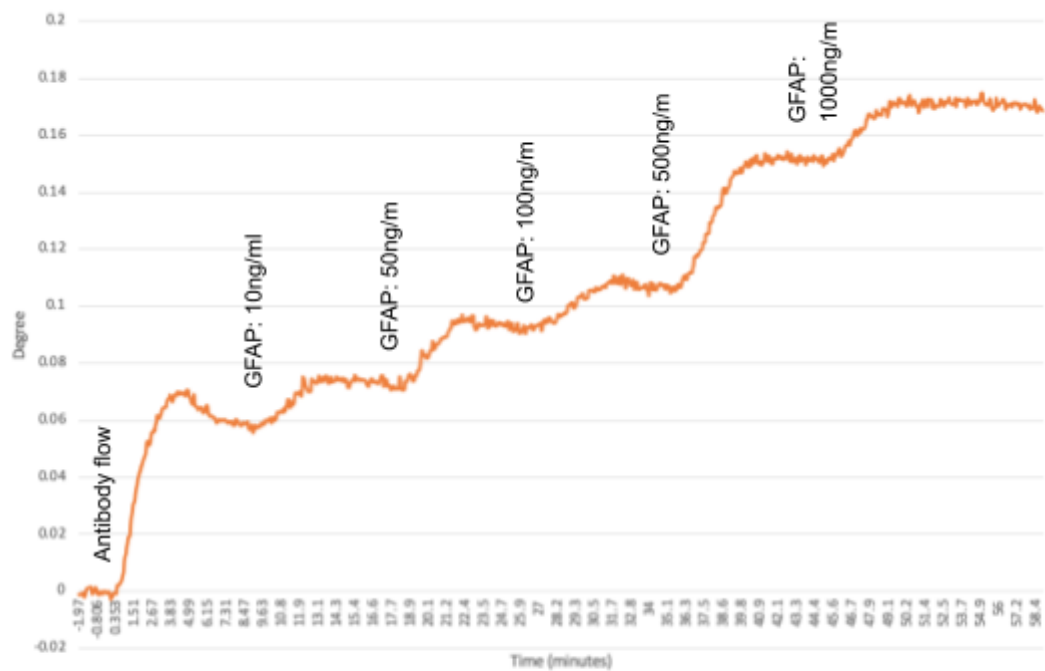


Figure B: Degree shifts as a function of time obtained from SPR experiment on a gold chip with a flow of 50 μ g/ml of GFAP 94cc capture antibodies and different GFAP concentrations

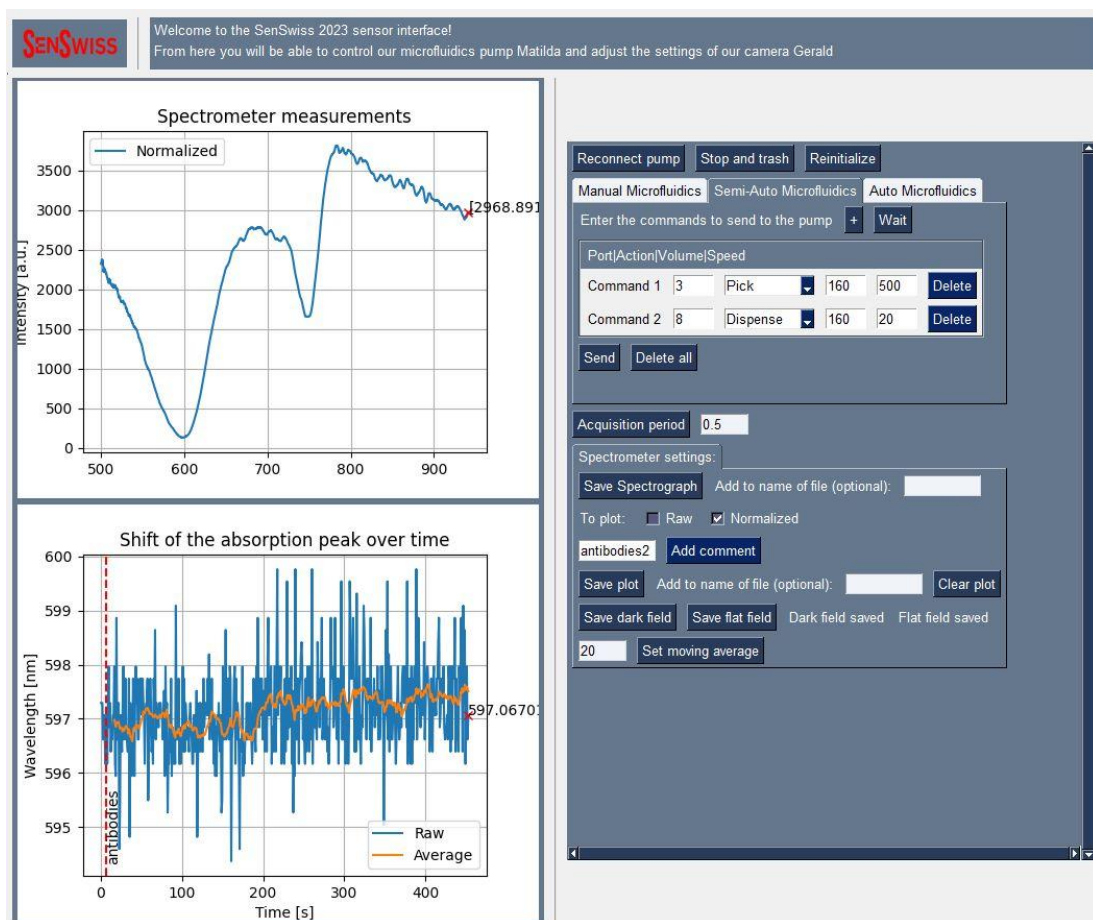


Figure C: Graphical User Interface with spectrometer and pump connected

9.2 Business model

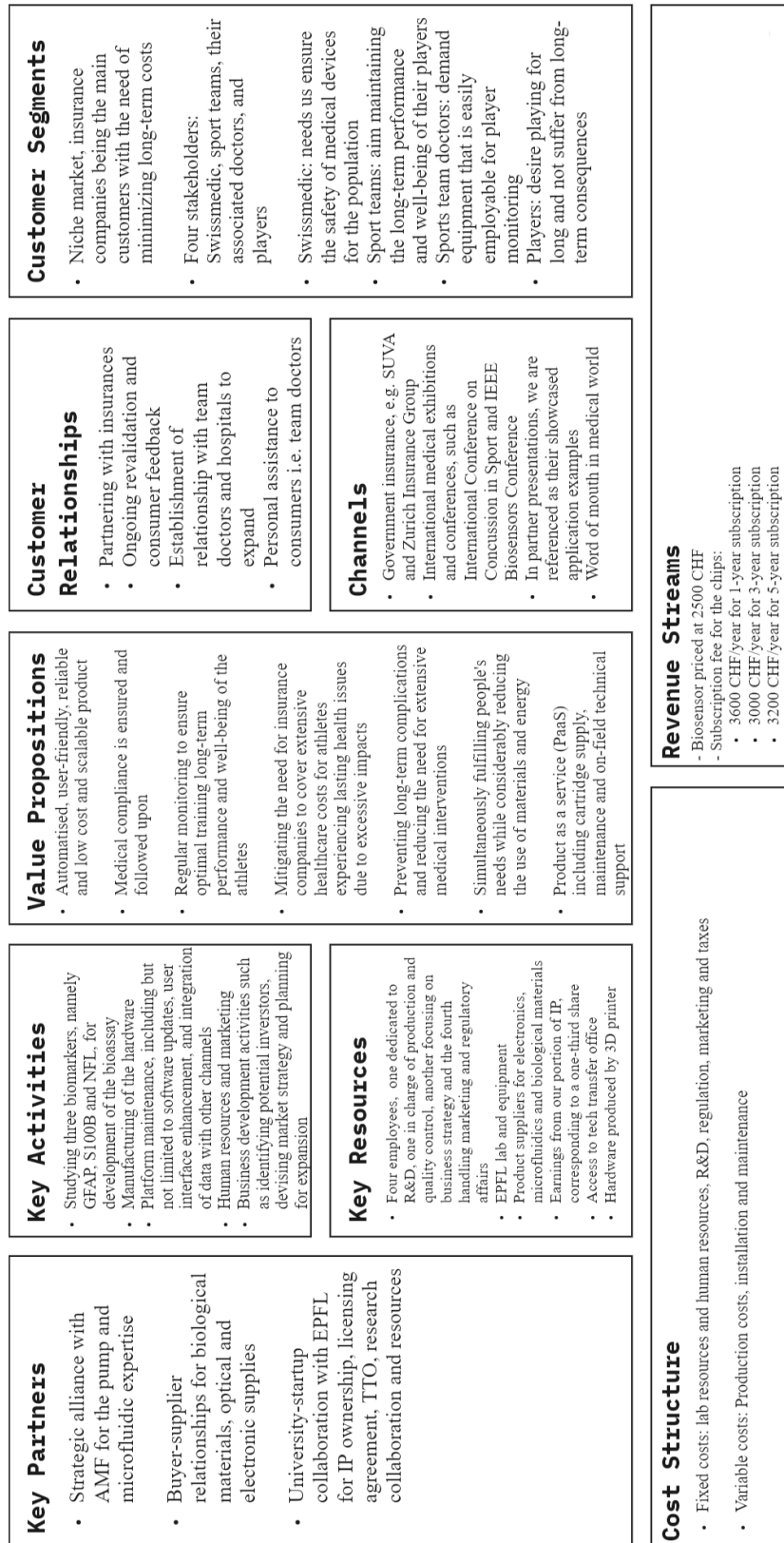


Figure D: Business model

9.3 Business feasibility

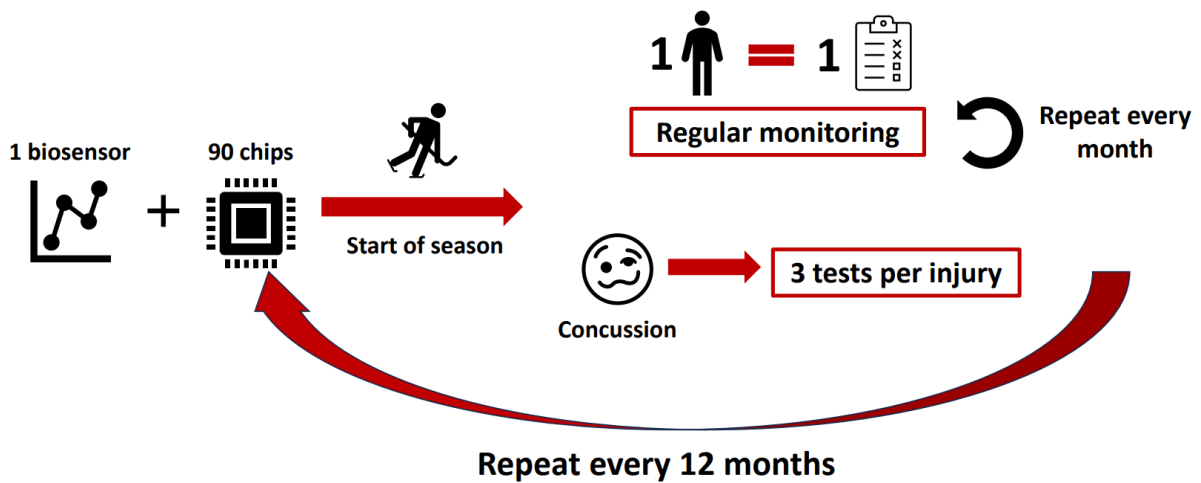


Figure E: Customer and product flow

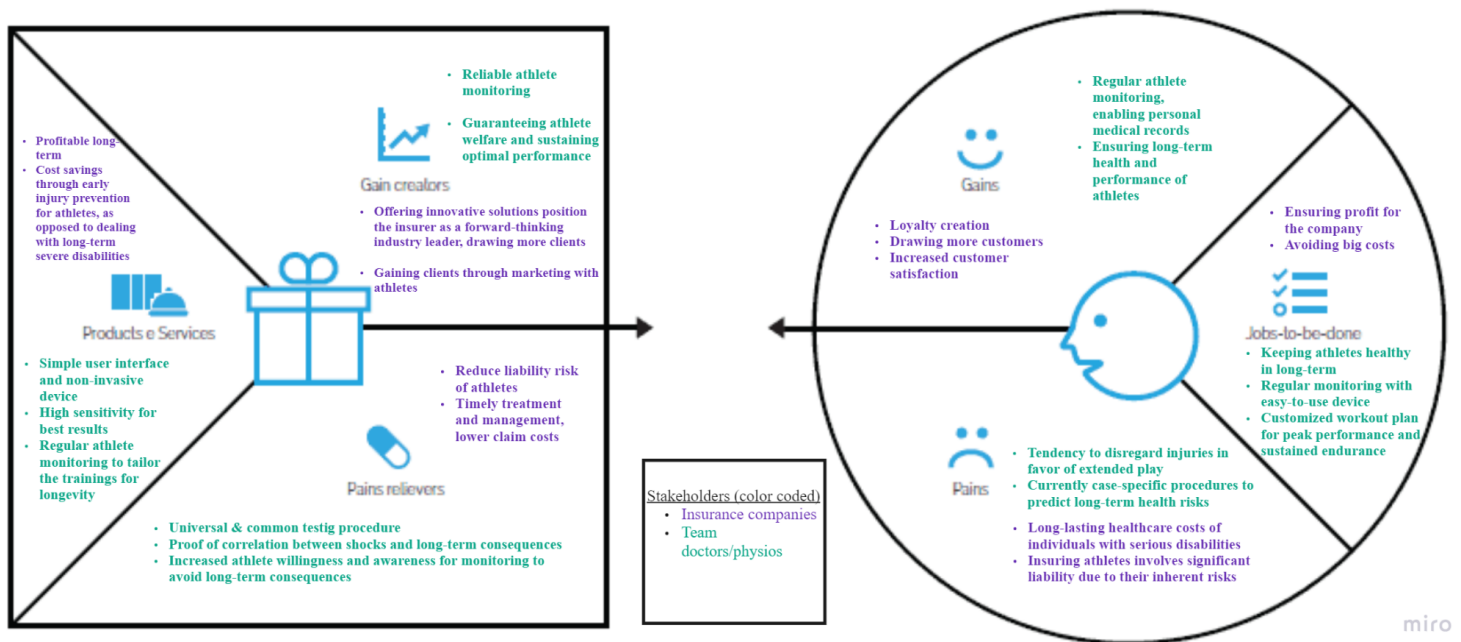


Figure F: Added value canvas

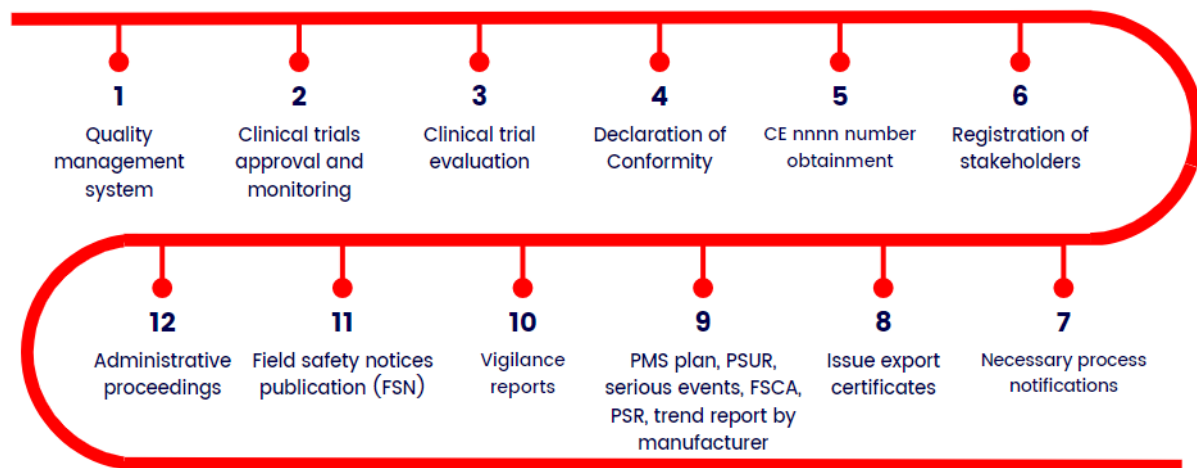


Figure G: Regulatory overview

9.3.1 Risk Assessment

Category	Hazard	Hazardous Situation	Severity	Occurrence	Risk Level	Risk Control Measures
General	Electrical Energy	Electric shock when plugging or unplugging the system	2	1	2	Insulation of the electrical parts
	Functionality	There is a break in the casing of the sensor letting in ambient light and preventing the sensor from functioning	1	1	1	Offer customer support and work with the customer to fix the light leak
Microfluidics	Leakage	The sample leaks out possibly contaminating the sensor and user and influencing the measurement result	3	1	3	Use of gloves when loading the sample and regular testing and replacement of the sealing O-rings to prevent their malfunction
	Mechanical failure	Pump breaks rendering the sensor completely non-functional	1	1	1	Offer customer support and work with AMF to possibly repair the pump or replace it if needed
	Mechanical failure	Clogged tubing	1	2	2	Offer individual replacement parts for the tubing
	Mechanical failure	Liquid is not fully evacuated from the pump and microfluidic channels	1	2	2	Design a cleaning procedure for the pump between samples
Chip	Functionality	Chip to chip variability in manufacturing	3	3	9	Use a multiple channel system to have a reference value for each chip and thus eliminating the variability in data processing
	Sharp edges	The chip has sharp corners and could cause injury	1	1	1	Round the corners of the chip to prevent injury
Software	Functionality	The software malfunctions and gives a false test result	3	1	3	Implement checks for all inputted values as well as feedback messages throughout the processing, if the test fails the result will be marked as invalid
	Cyber security	The software is targeted by hackers, leading into incorrect medical practice due to modified and unreliable test results	3	1	3	Access to software download and installation is restricted to approved and authenticated operators
Sample Preparation	Biological agent	The measured sample contains a hazardous biological agent that could transfer to the user	3	1	3	Include safety warnings and instructions on how to handle biological samples including required personal protective equipment in the manual
	Chemical agent	The chemicals (for example HCl) that must be filled in the sensor are mishandled and cause injury	3	1	3	Include chemical safety sheets in the user manual
	Evaporation	Inaccurate sample volumes due to evaporation could lead to skewed results	2	2	4	The sample will be preserved in a closed chamber. Also, humidity control mechanisms will be incorporated to the measurement chamber and volume accuracy will be validated through quality control mechanisms.
Biological Assay	Functionality	A non-functional assay leads to a false negative result	3	2	6	Multiple channel system allows to measure a known reference, if this reference is measured as zero the test is reported as invalid
Optical System	Light	The user looks directly into the laser	3	1	3	The measurement chamber will have a locking mechanism so the laser can only be turned on when there is no danger
Specificity and Interference	Cross-reactivity of blood proteins	Cross-reactivity with other proteins or interference from blood components could affect the accuracy of the GFAP measurement	3	2	6	Validate the sensor's specificity against potential interfering substances, and assess its performance with a diverse set of blood samples
Data	Data Security	Hackers or unauthorized users intercepting the transmitted data, potentially compromising patient confidentiality	3	1	3	Implement strong encryption protocols, secure authentication mechanisms, and regular security updates. Anonymize or pseudonymize patient data before transmission, and adhere to relevant data protection laws
	Data Tampering	The data alters during wireless transmission due to malicious actions or technical problems, resulting in inaccurate medical information	3	1	3	Use cryptographic hashes and integrity checks to verify data integrity upon transmission and reception
Interference	Electromagnetic interference	Electromagnetic interference with the nearby devices causes noise in the results	2	1	2	Electromagnetic compatibility testing

Table 1: Product risk analysis and management

		Severity		
Occurrence		Low (1)	Medium (2)	High (3)
	Low (1)	1	2	3
	Medium (2)	2	4	6
	High (3)	3	6	9

Table 2: Risk matrix with different levels of severity and occurrence

9.3.2 Competitors

Company	Technology	Upfront cost	Long-term monitoring	Consumer	Time for Test
SanSwiss	Biomarker (GFAP, S100B, NFL)	2500 CHF	Yes	Sport Clubs and Sport-related insurance companies	20 minutes
Direct competitors					
Abbott	Biomarker (GFAP, UCH-L1)	3000 USD	No	Hospitals	18 minutes
Indirect competitors					
BrainScope	EEG based AI	31,500 USD	No	Hospitals and Clinics	<20 minutes
Oculogica	Eye movements	not-specified	Yes	Hospitals and Clinics	< 4 minutes

Table 3: Competitors comparison

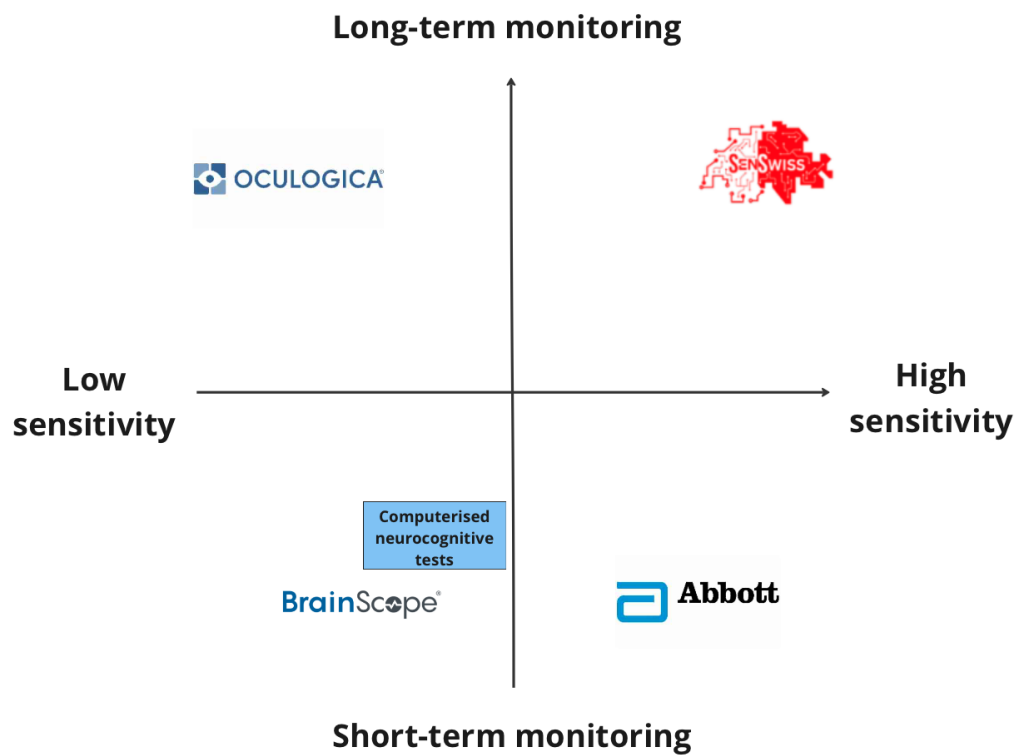


Figure H: Competitors comparison

9.4 Finance viability

9.4.1 Biosensor and consumables cost

System	Component	Number	Price (CHF/unit)	Price (CHF)
Structure	Printed parts	1	150	150
	Mounting kit	1	37,2	37,2
Optics	T-Cube LED Driver	1	303,72	303,72
	ThorLABS M660L4	1	219,42	219,42
	FLIR Blackfly BFS-U3-200S6M-C	1	717,6	717,6
	OceanOptics QP600-2-UV-VIS	1	300	300
	Thorlabs F800SMA-780	1	251,83	251,83
	Thorlabs LPNIR050-MP2	1	415,66	415,66
	Thorlabs AC254-50-AB-ML	1	124,73	124,73
Microfluidics	AMF LSPone	1	1000	1000
	Tubings (20 m) 1/32" OD 0.3 mm ID	1	60	60
	Angst+Pfister HITEC O-rings ID 5 x 1mm	1	12	12
	IDEX F126Hx MicroTight fittings	1	13,5	13,5
Electronics	Micro Motors E192.12.336	1	161,4	161,4
	GEAB2.5-12-25-B-8	1	21,12	21,12
	RGEAR2.5-100-N	1	13,99	13,99
	Arduino Motor Shield Rev3	1	23,04	23,04
	Amewi 922MG	1	16,95	16,95
Packaging		1	100	100
PROTOTYPE PRICE				3942,16

Table 4: Biosensor cost

System	Component	Total units	Price (CHF)	Needed units	Price (CHF/unit)
Chip & functionalisation	Bluray CD	50 units	20	0,8 unit	0,32
	Microfluidics chip pdms	1 kg	3	20 g	0,06
	Capture Abs GFAP 94cc	1 g	50	0,01g	0,50
	EDC	5000 mg	286	19,2 mg	1,10
	NHS	25000 mg	91,75	5,4 mg	0,02
	SH-PEG-COOH (mg)	1000 mg	280	1 mg	0,28
	SH-PEG-OH (mg)	5000 mg	900	1 mg	0,18
	Ethanol	250 mL	31	0,3 mL	0,04
	MES buffer	50 g	244	0,02 g	0,10
	Acetic acid	1L	31	50 µL	0,00
Au-NPs functionalisation	Detection Abs GFAP 15cc	1 g	50	0,01g	0,50
	Nanoparticles	20 mL	70	0,02 mL	0,07
Lab chemicals	Running buffer (PBS 1X)	500 mL	29	1 mL	0,06
	BSA 1% (blocking agent)	50 g	417	50 mg	0,42
	Cleaning solution	1 L	0,167	3 mL	0,50
Packaging	Chips package			1	0,40
	Functionalised nanoparticles			1	0,16
CONSUMABLES PRICE					4,70

Table 5: Consumable cost

9.4.2 Profit and Loss

SenSwiss Profit and Loss statement (CHF)	Sports Penetration rate Phase Year	Clinical Trials							Hockey			Hockey, rugby, soccer				
		Year							Switzerland Expansion			25%				
		Year 1	Year 2	Year 3	Year 4	Year 5	Year 6	Year 7	Year 8	Year 9	Year 10	Year 11	Year 12	Year 13	Year 14	Year 15
Expenses		224962.8	211549.8	210147	210167	210261.4	210346.1	210423.1	47903.8	792544.68	1519294.83	3379851.955	4524915.683	2943329.18	51243163.15	88476757.18
CAPEX (Capital expenses)		236210.94	222127.29	220654.35	220675.35	220774.47	220863.405	220944.255	498648.99	832171.914	1595259.272	3548844.553	4751161.467	3090495.64	5390321.3	92900595.04
IP rights - patent		7000	1531	53	73	158	238	315	408	2195	2288	2430	3258	2753	2928	3115
CE (EU IVDR 2017/46)		0	1531	53	73	158	238	315	408	495	586	730	868	1053	1228	1415
SwissMedic		7000	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Total FSC		0	0	0	0	0	0	0	0	1700	1700	1700	1700	1700	1700	1700
CoGS (Cost of Goods Sold)		7962.8	18.8	94	94	103.4	106.1	108.1	70495.8	359263.92	833787.27	2575890.893	3477505.093	26331486.6	47060668.58	82177897.62
Biosensor components		3972	3972	3972	3972	3972	3972	3972	3972	3972	3972	3972	3972	3972	3972	3972
# of biosensors		2	0	0	0	0	0	0	16	80	180	558	709	5059	8259	14119
Consumable components (1 chip)		4.7	4.7	4.7	4.7	4.7	4.7	4.7	4.7	4.7	4.7	4.7	4.7	4.7	4.7	4.7
# of consumables (average of 90 per BS per year)		4	4	20	20	22	23	23	1440	8640	24840	75060	13870	594180	1337490	2609200
Total components cost		7962.8	18.8	94	94	103.4	106.1	108.1	70320	355368	831708	2569158	3468837	22889994	39090951	68339208
VAT in EU (taxes) and Custom Duties (20%)		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Carriage and Insurance Paid to - CIP (0.25%)		0	0	0	0	0	0	0	175.8	895.92	2079.27	6422.895	8672.0925	57217.485	97727.3775	170848.02
OPEX (Operating Expenses)		210000	210000	210000	210000	210000	210000	210000	404000	431085.76	683219.56	801841.06	1014818.59	3099089.58	4233366.57	6295744.56
Contract manufacturer gross margin (7% of components cost)		0	0	0	0	0	0	0	0	25085.76	58219.56	179841.06	242818.59	1602089.58	2736366.57	4783744.56
R&D budget		0	0	0	0	0	0	0	20000	20000	20000	20000	20000	20000	20000	20000
Payroll		48000	48000	48000	48000	48000	48000	48000	72000	72000	72000	72000	72000	96000	96000	96000
# of employees		4	4	4	4	4	4	4	5	5	8	8	10	15	15	15
Marketing (website, ads, exhibitions...)		2000	2000	2000	2000	2000	2000	2000	5000	10000	10000	10000	10000	15000	15000	30000
Infrastructures (rent, equipment)		16000	16000	16000	16000	16000	16000	16000	16000	16000	16000	16000	16000	16000	16000	16000
Audit		0	0	0	0	0	0	0	3000	3000	3000	3000	6000	6000	6000	6000
Profits		0	0	0	0	0	0	0	119200	791800	1904600	5870000	8599500	51278500	92992500	165943300
Revenues		0	0	0	0	0	0	0	119200	791800	1904600	5870000	8599500	51278500	92992500	165943300
Biosensor		2500	2500	2500	2500	2500	2500	2500	2500	2500	2500	2500	2500	2500	2500	2500
# of biosensors		0	0	0	0	0	0	0	16	80	180	558	709	5059	8259	14119
Yearly fee (90 chips, 40 CHF each)		3600	3600	3600	3600	3600	3600	3600	3600	3600	3600	3600	3600	3600	3600	3600
# of 1y subscription		0	0	0	0	0	0	0	12	58	161	480	885	3775	8495	16563
3 Years fee		9000	9000	9000	9000	9000	9000	9000	9000	9000	9000	9000	9000	9000	9000	9000
# of 3y subscription		0	0	0	0	0	0	0	4	23	51	163	225	1487	3523	4259
5 Years fee		16000	16000	16000	16000	16000	16000	16000	16000	16000	16000	16000	16000	16000	16000	16000
# of 5y subscription		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
NET PROFIT		-238210.84	-222127.29	-220654.35	-220675.35	-220774.47	-220863.405	-220944.255	-379448.99	-40371.914	309340.4285	2321155.47	3848338.533	20373504.36	39187778.7	73042704.96
Cash Flow		1398789.06	277872.71	279345.65	28324.65	279225.53	779136.595	812655.745	-299048.99	10028.086	309340.4285	2321155.47	3848338.533	20373504.36	39187778.7	73042704.96
Investors		1635000	500000	500000	250000	500000	1000000	1033600	80400	50400	0	0	0	0	0	0
SNSF		0	0	0	0	250000	500000	1000000	0	0	0	0	0	0	0	0
EPFL Tech Launchpad Ignition		0	0	0	0	0	0	0	30000	0	0	0	0	0	0	0
EPFL Innogiants		100000	0	0	0	0	0	0	0	0	0	0	0	0	0	0
X-Grant		10000	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Innosuisse		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Venture Capitals		1025000	500000	500000	0	0	0	33600	50400	50400	0	0	0	0	0	0
Healthcare Angels		500000	0	0	0	0	0	0	0	0	0	0	0	0	0	0
CASH EQUIVALENT		1393789.06	1676661.77	1656007.42	1985332.07	2264657.6	3043684.185	3856349.84	3557300.95	3567329.036	3876669.465	6187624.912	10045163.45	30419667.81	68656846.5	142845551.5

Table 6: Profit and Loss statement

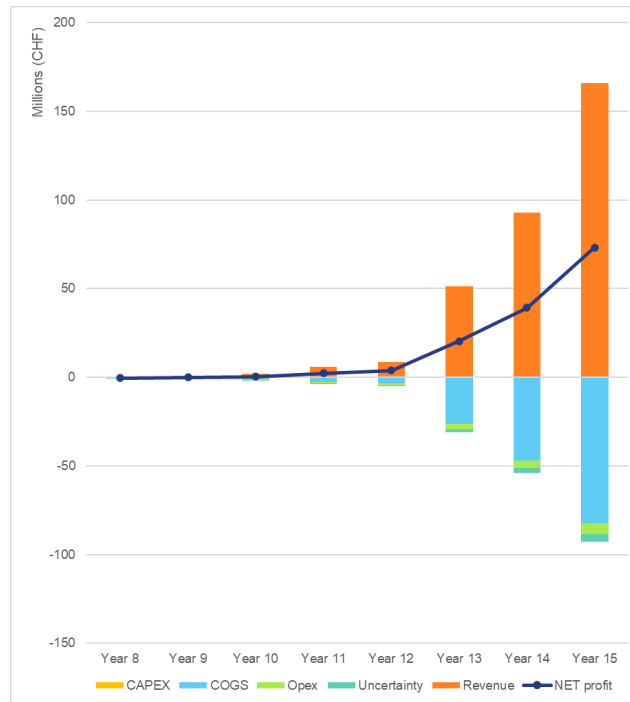


Figure I: Expected Net Profit over the years

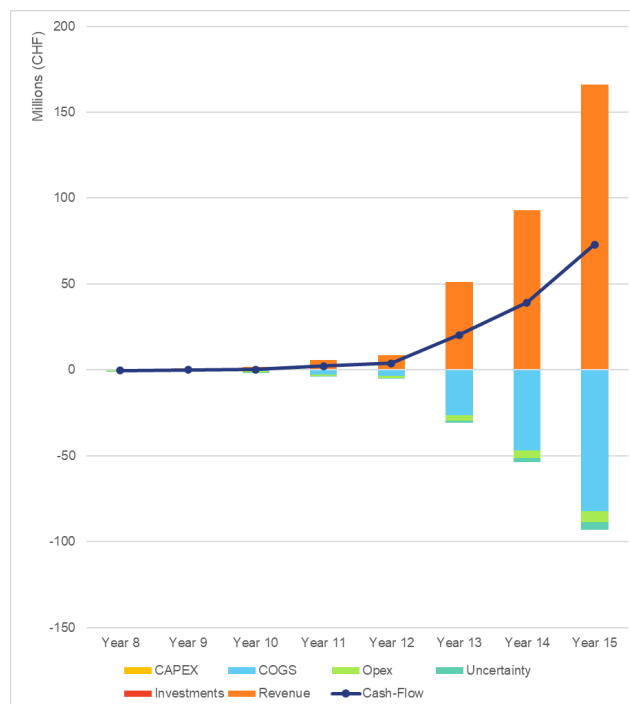


Figure J: Expected Cash Flow over the years

9.4.3 Market evaluation

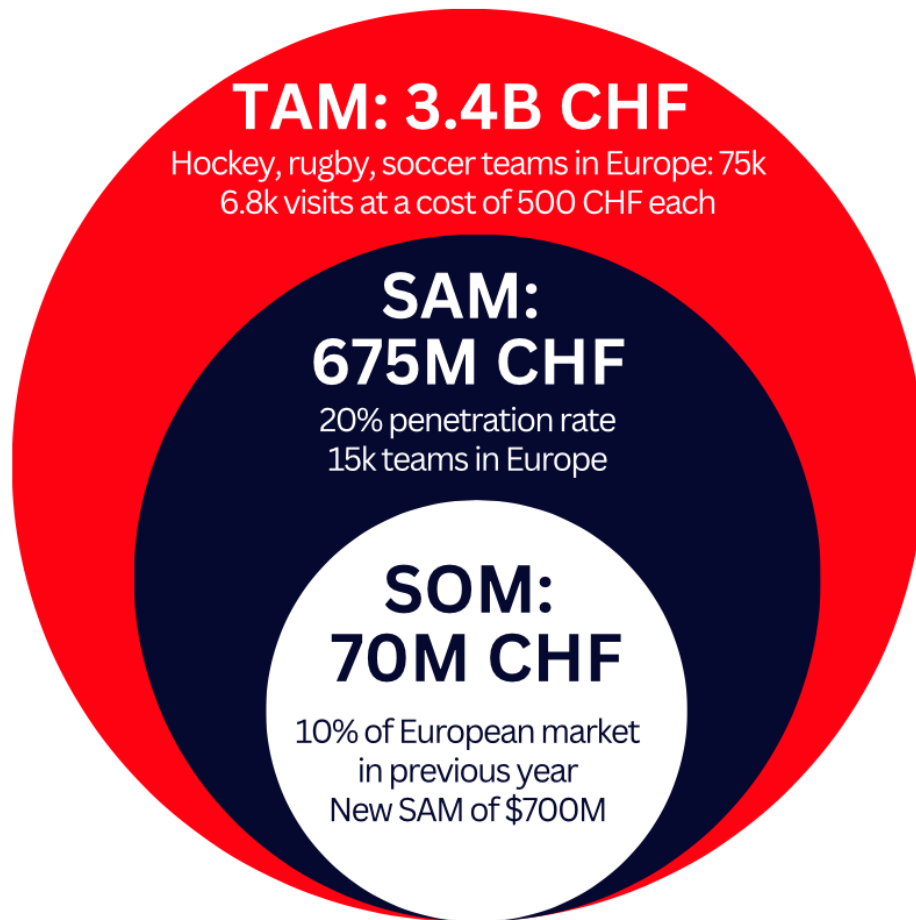


Figure K: Market evaluation

Market size (penetration rate)	Switzerland						Europe		
	Hockey teams	Total hospital visits	Cost (500.- / visit)	Hockey, rugby, soccer	Total hospital visits	Cost (500.- / visit)	Hockey, rugby, soccer	Total hospital visits	Cost (500.- / visit)
2%	17	1530	765000	131	11822	5911200	1500	135036	67518000
5%	43	3825	1912500	328	29556	14778000	3751	337590	168795000
10%	85	7650	3825000	657	59112	29556000	7502	675180	337590000
20%	170	15300	7650000	1314	118260	59130000	15004	1350360	675180000
50%	425	38250	19125000	3284	295560	147780000	37510	3375900	1687950000
80%	680	61200	30600000	5254	472896	236448000	60016	5401440	2700720000
100%	850	76500	38250000	6568	591120	295560000	75020	6751800	3375900000

Table 7: Market evaluation