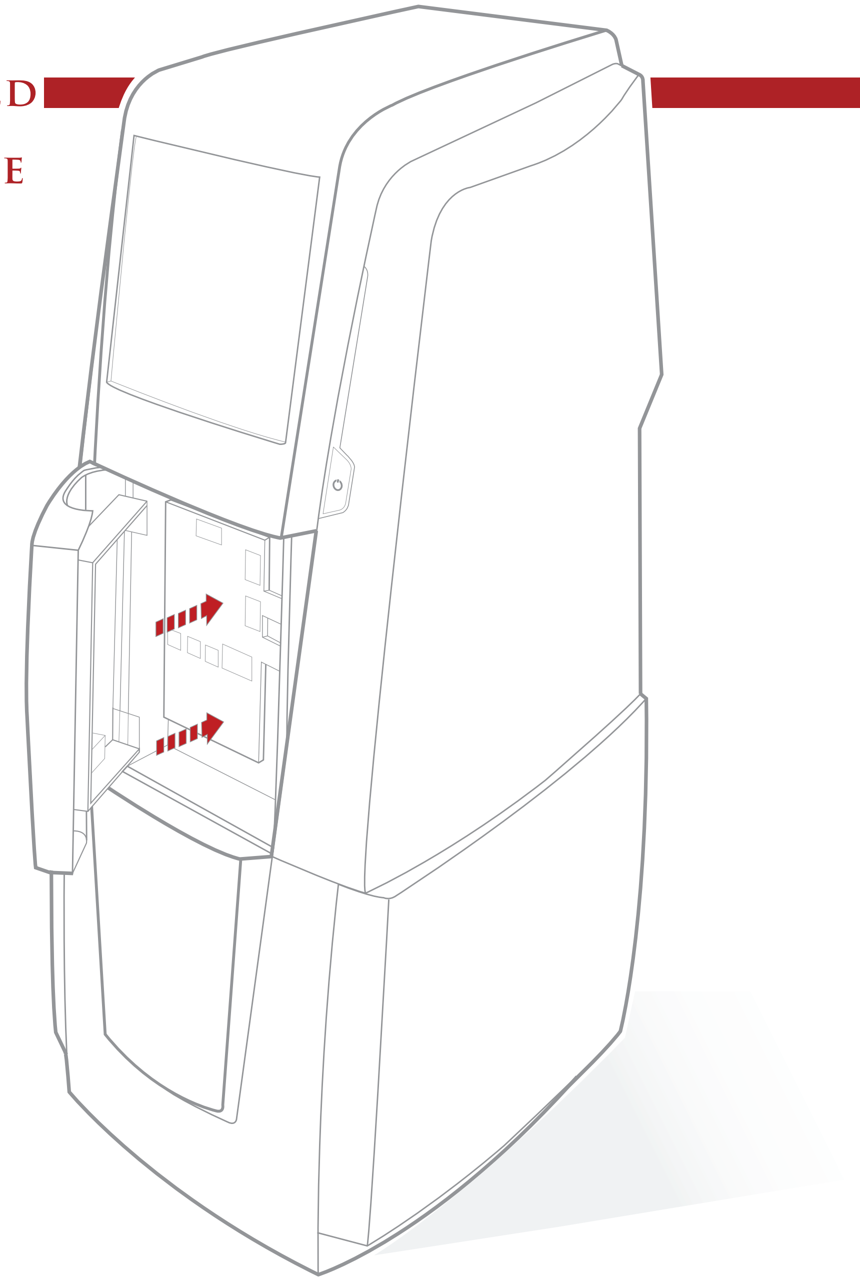
Design & Development of User-Centered Molecular Cancer Diagnostic Device



Applied Research

Amol Surve

College of Design, Arizona State University
Human Factors in Design
Industrial Design
In association with The Center for Applied NanoBioscience,
Arizona State University

surveamol@gmail.com
amolsurve.com

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"It is so hard to wait for test results from your tests. You could spend an entire weekend waiting for results that came in on Friday. Make it a habit to call and ask for results as soon as it's reasonable."

– Steve Singer

Cancer patient

Acknowledgements

I cannot express enough thanks to my parents, to my mentors, Prof. Prasad Boradkar and Dr. Zenhausern, and to my friends and colleagues within and outside ASU who have helped to nurture an environment of creativity and support.

My deepest gratitude goes to Late Prof. Paul Rothstein, for encouraging me to look for meaningful collaboration opportunities outside the College of Design that led to the development of this project.

Prof. Prasad Boradkar for his guidance, endless patience and driving me to achieve a high quality of output. I also wish to express my sincere thanks to my committe members especially Dr. Frederic Zenhausern who listened with endless patience and enthusiasm to my thoughts and helped me to understand the technology and science behind Molecular Cancer Diagnostics.

Abstract

Cancer, which can be defined as the uncontrolled growth of cells due to genetic alterations is the leading cause of death in the United States . Although it occurs in different parts of the body it can exhibit broadly similar characteristics. Cancer patients and the oncologists that treat them face various unknowns as the detailed cause or mechanisms of a particular cancer case can often remain inscrutable. Therefore, the treatment that could be a combination of drugs, coupled with exhausting rounds of chemotherapy may cause undesirable side effects.

However, human genome sequencing coupled with molecular diagnostics may help in early detection and monitoring the state of the disease during progressive cancer. Molecular diagnostics is a new discipline that captures genetic changes and uses the information to distinguish between normal, precancerous, and cancerous tissues at the molecular level in the process helping oncologists to better plan the treatment. However the current devices on the market are cumbersome and are targeted towards the needs of large reference laboratories.

This project applies the convergence of lab-on-a-chip platform, which is being developed at the Center for Applied NanoBioscience (ANBC) at ASU, information technology, and advanced molecular testing in the development of a compact fully integrated device that would rapidly analyze single sample at a time. It would be capable of identifying the nature of cancer, monitoring the state of the disease, guiding therapeutics as well as providing sensitivity data to treatment in a comparatively smaller footprint, ideal for a clinical setup.

This device which is part of a larger ecosystem leverages the fast-growing field of computational biology to speed research and directly impact patients. The device will enable the non-specialized operator to perform sophisticated biological tests in a clinical setting with greater speed and accuracy. Based on ANBC's Lab-on-a-chip technology, this device proposes to test raw biological samples such as blood, urine, solid tissue and perform processes that include sample preparation, DNA quantification, PCR amplification and detection in a single integrated device. The future scenarios showing the use of the proposed device throw light on the possibilities of the strategic decisions that need to be taken today.

Project Overview

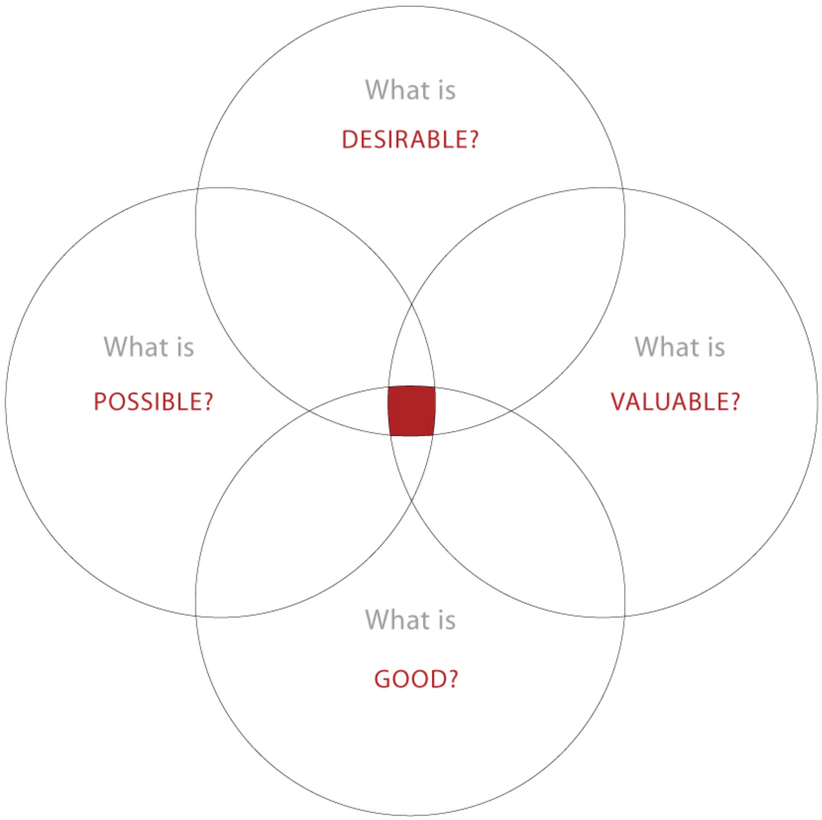
This applied research explores the area of Molecular Cancer Diagnostics with an aim to address a latent need in the Cancer Diagnosis through an advanced 'DNA fingerprinting' platform technology that is being developed at The Center for Applied NanoBioscience (ANBC) at the Biodesign Institute.

This automated "DNA fingerprinting" or Short tandem repeat (STR-typing) lab-on-a-chip platform would ultimately automate the entire process that would read-out an individual's STR (DNA fingerprint) starting with the sample preparation processes, which includes DNA extraction and amplification, to detection of the individual's DNA fingerprint. The platform consists of a plastic cartridge and control instrumentation. Considering that ANBC's core competency lies in developing ways to diagnose disease, monitor health, and create enabling polymer electronics by merging new technology with genomics and molecular biology, it was natural that an interest was shown to further explore the area of Molecular Cancer Diagnostics using their DNA printing platform.

I saw this as a great opportunity to work on a live project and also to collaborate with the core research team of technologists and experts from a variety of areas such as nanotechnology, micro-electromechanical systems (MEMS) technology, polymer technology, molecular biology and genomics. I was inspired by the Innovationspace program that believes in benefiting the society while minimizing the impact on the environment and Late Prof. Paul Rothstein, an ASU associate professor of industrial design who encouraged design students to partner with programs outside the school of design. In his article that was published in Innovation magazine he wrote, "On most university campuses, for example, partnering with programs in science, education, business, medicine or engineering will open doors to an amazing network of connections and resources. But we must give these disciplines compelling reasons for wanting to create partnerships and equitably share funding." In this regard, designers possess a great advantage: applied projects." I chose this opportunity to conceptualize a Molecular Cancer Diagnostic device as my final applied project.

A qualitative research approach consisting of observations, site visits, expert interviews, web searches, blog searches was implemented. "Integrated Innovation" framework was utilized to organize the design research. A strategic concept design was developed and prototyped based on user insights, technological capabilities of the Center and potential funding opportunities in the Valley and outside. Future, scenarios were created showing the device in use. This "system's" approach to the design of device will contribute to the development of future molecular-based genetic testing devices.

Integrated Innovation Model



Innovation Space at Arizona State University

What is desirable to users?
What is possible through engineering?
What is valuable to business?
What is good for society and the environment?

Introduction

Objective in phase 1 was to expand my knowledge regarding cancer, molecular Dx and nanotechnology through literature review, site visits, interviews, web searches, observations and interacting with experts to extract innovative ideas. Product opportunities were then identified by researching relevant social conditions, trends (such as ipod + itunes) and collecting meaningful information related to the users (lab technicians, oncologists, bioengineers, cancer patients-through blogs, cancer care coordinators, stake holders, bioinformation specialists), the market and technology behind Molecular diagnostics. Understand and familiarize myself with the platform technology that was being developed at ANBC, the basic premise of molecular cancer diagnostics and relevant technologies.

Information was collected through discussions with researchers, research technologists at ANBC at the Biodesign Institute, cancer care coordinator and oncologist of a leading healthcare provider, V.P. of Research and Development and Director of software engineering, Manager of a CLIA-certified specialty reference laboratory that helps cancer patients worldwide by applying discoveries of the Human Genome Project to personalized medicine. Other information was gleaned from the official company and academic websites, product brochures and catalogs.

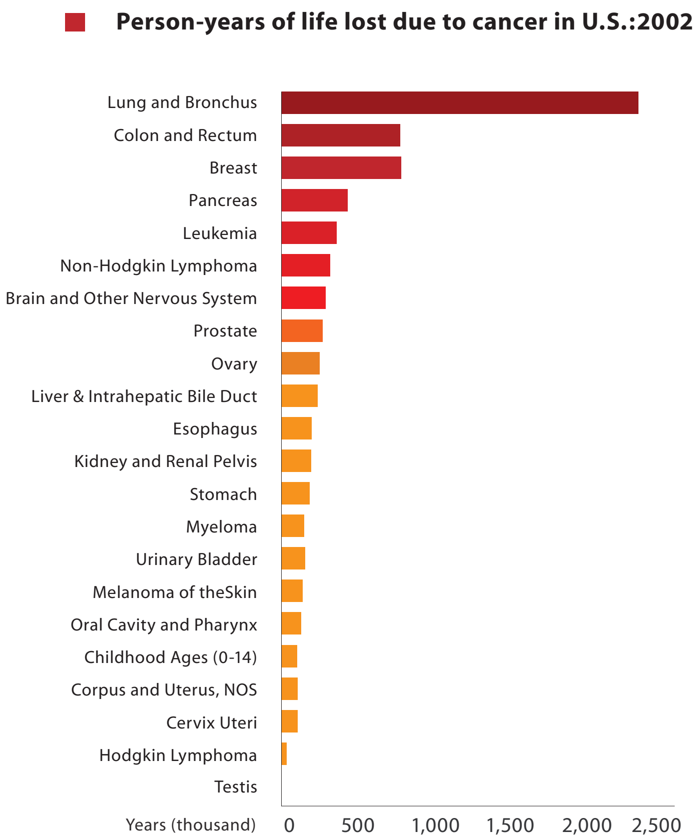
The specific topics in Phase 1 were identified by using the Integrated Innovation factors and related methodologies.

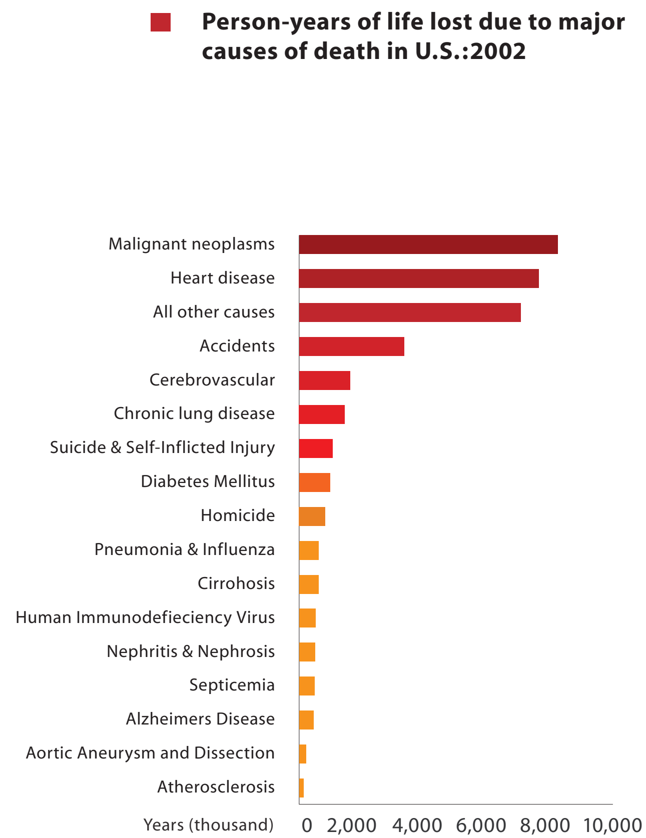
What's desirable?

Obtain an insight into the patient and oncologist behaviors, values and needs in relation to Cancer diagnostics.

Research activities included interviews with oncologists, cancer-care coordinators, lab technicians, MD's and software engineers managing medical data. Reading cancer patient web blogs, literature review, web searches, observing and understanding current practices in cancer diagnostics.

Figure 1. Person-years of life lost due to cancer vs. major causes of death in U.S. in 2002





As seen in the chart above Lung and Bronchus cancer were responsible for most deaths in 2002 in U.S. Also, Fig. 2 above shows Malignant neoplasm (cancer) was responsible for the most Person-years of life lost due to death in U.S. in 2002.

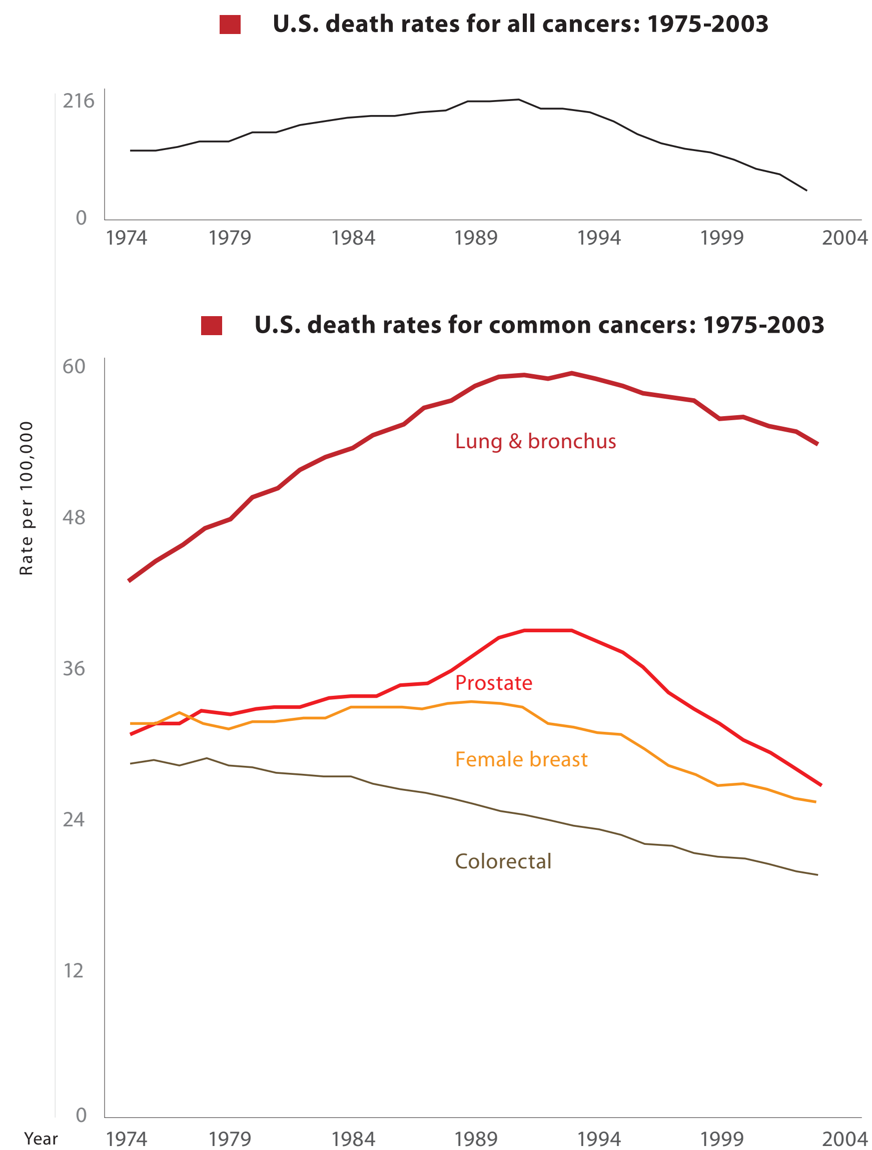


Figure 2. U.S. death rates for all cancers vs. common cancers, 1975-2003.

As seen in the adjoining graphs U.S. death rates for all cancers from 1975-2003 seem to be abating and it may be a result of improved diagnostic procedures and early detection.

Figures 3 and 4 on the right are screen captures of the Molecular Diagnostics webpage on the National Cancer Institute website from 2005 and January 2007 respectively.

A drastic increase in the amount of content shows the growing demand for information on molecular Dx upon the increasing relevance of this type of diagnosis for cancer.

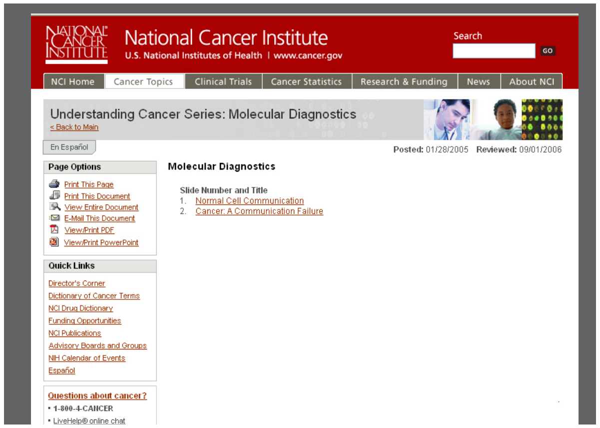


Figure 3: Molecular Dx information on the NCI website in 2005.

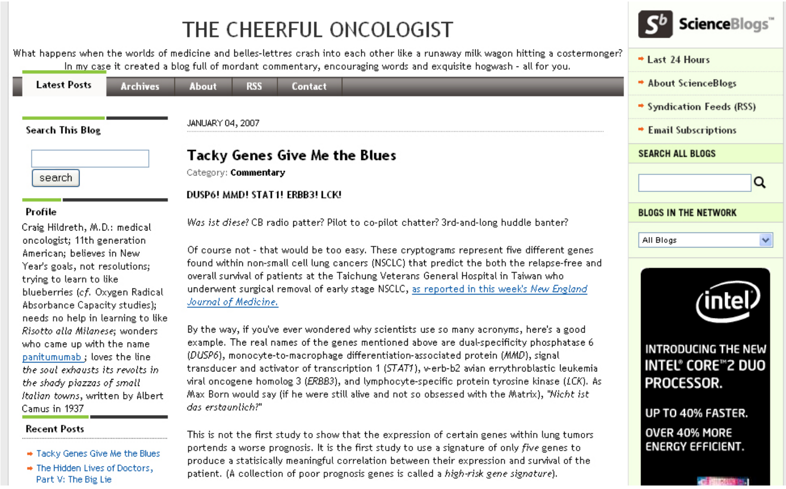


Figure 5: Oncologists are blogging and opening new avenues to share valuable information and develop a rapport with their patients. The above shown screen shot of Dr. Craig Hildreth's blog is called 'The Cheerful Oncologist'.

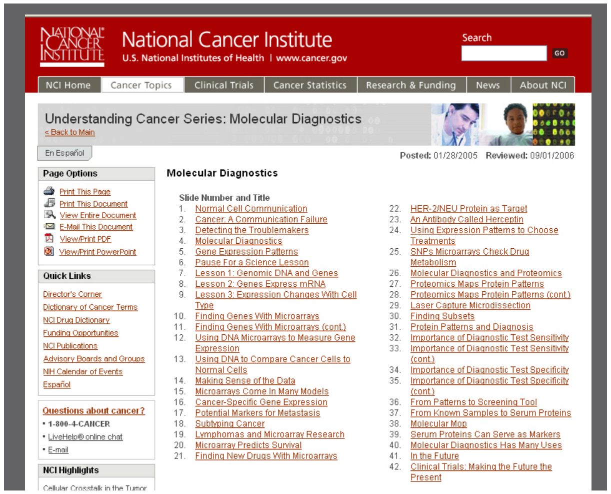
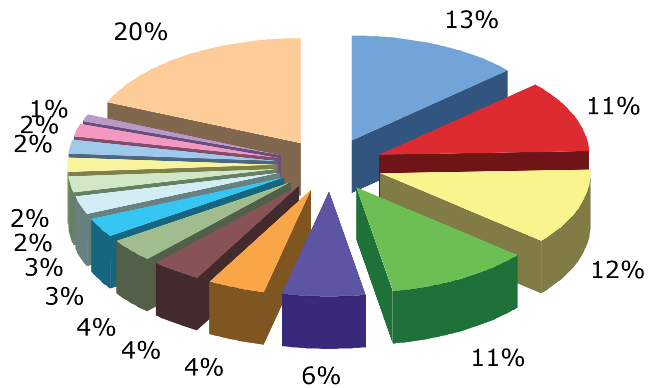


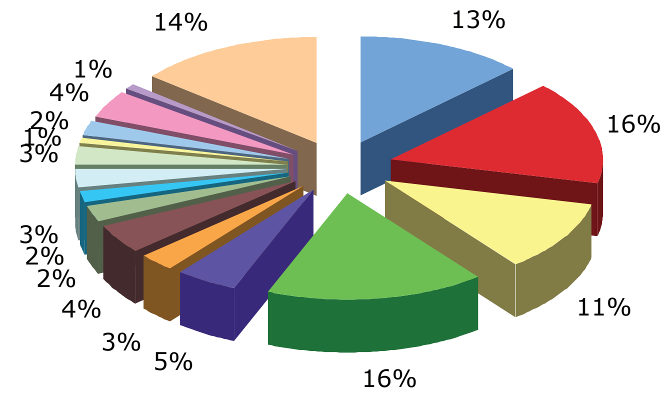
Figure 4: Molecular Dx information on the NCI website in January 2007.

Figure 7. Data of National Expenditures for Medical Treatment 1998 - 2004.

Estimates of National Expenditures for Medical Treatment for the 15 Most Common Cancers 2004



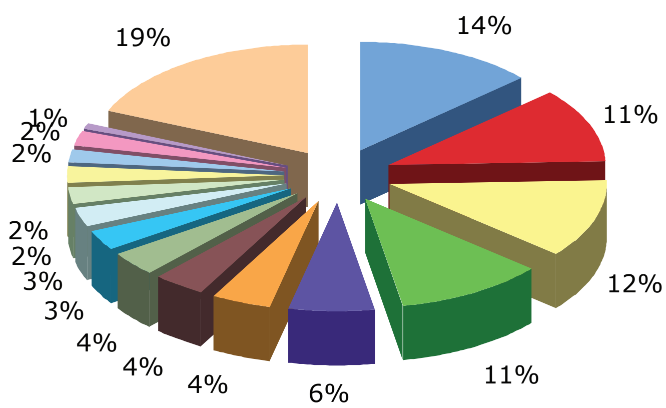
Percent of All New Cancers 1998



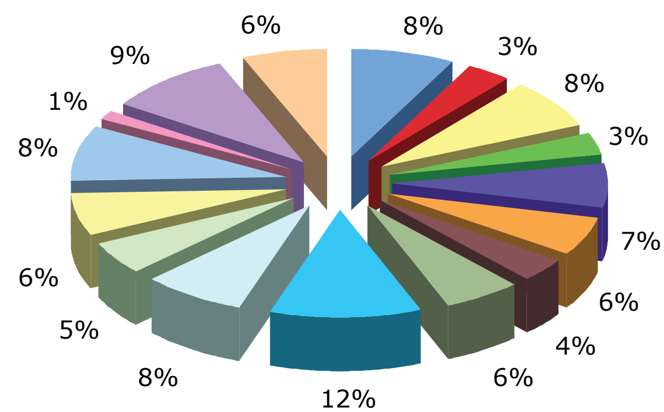
The pie chart above presents the estimate of National Expenditure for Medical treatment of lung cancer was the maximum for 2004 followed by colorectal, breast and prostrate cancer.

In the above pie chart breast cancer had the most new cases of cancer in 1998

Percent of All Cancer Treatment Expenditures



Average Medicare payments per individual in first year following diagnosis 2004

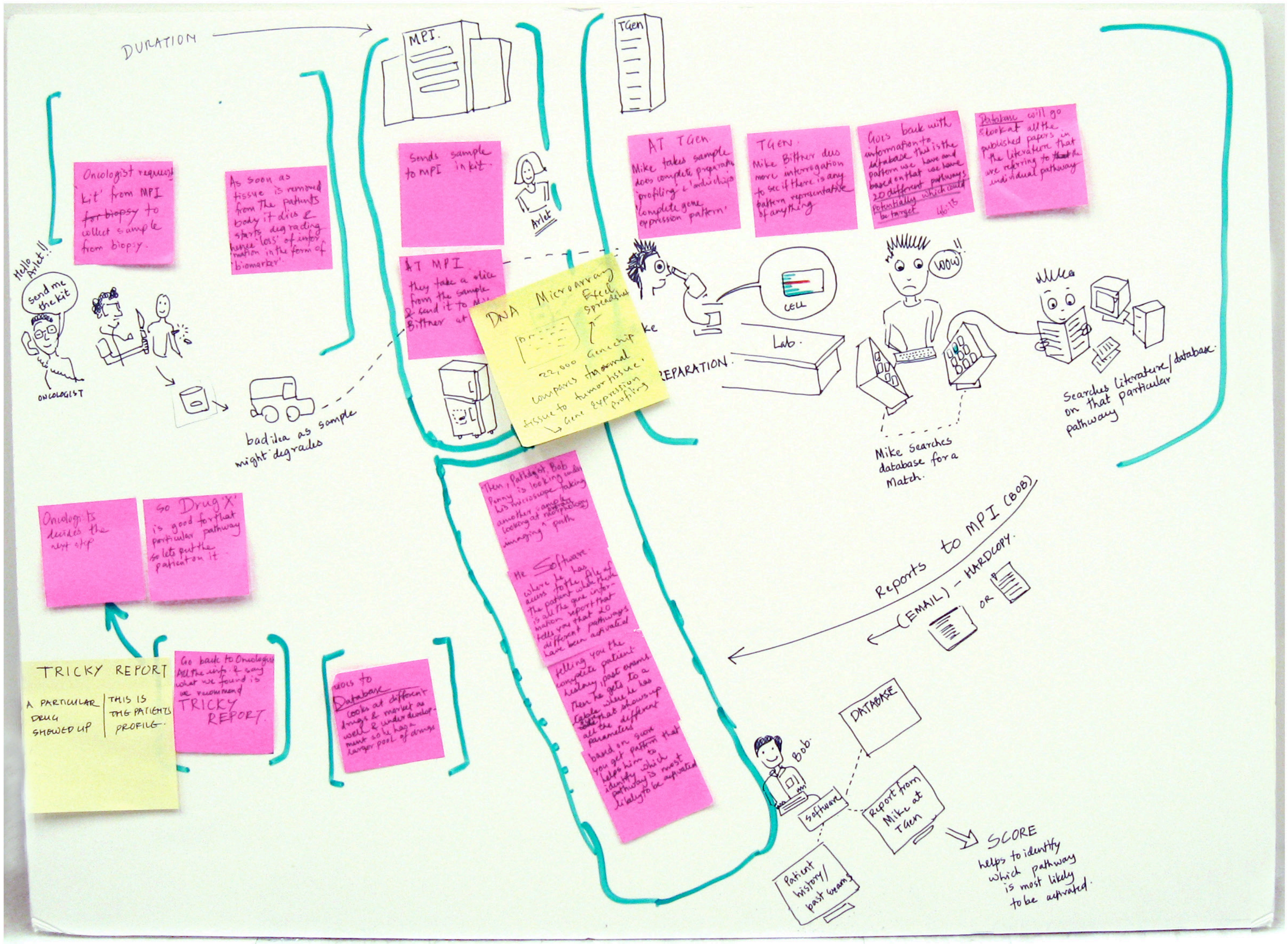


As seen in the above chart the percentage of Lung Cancer Treatment expenditure is the maximum at 14%.in 2004. Also

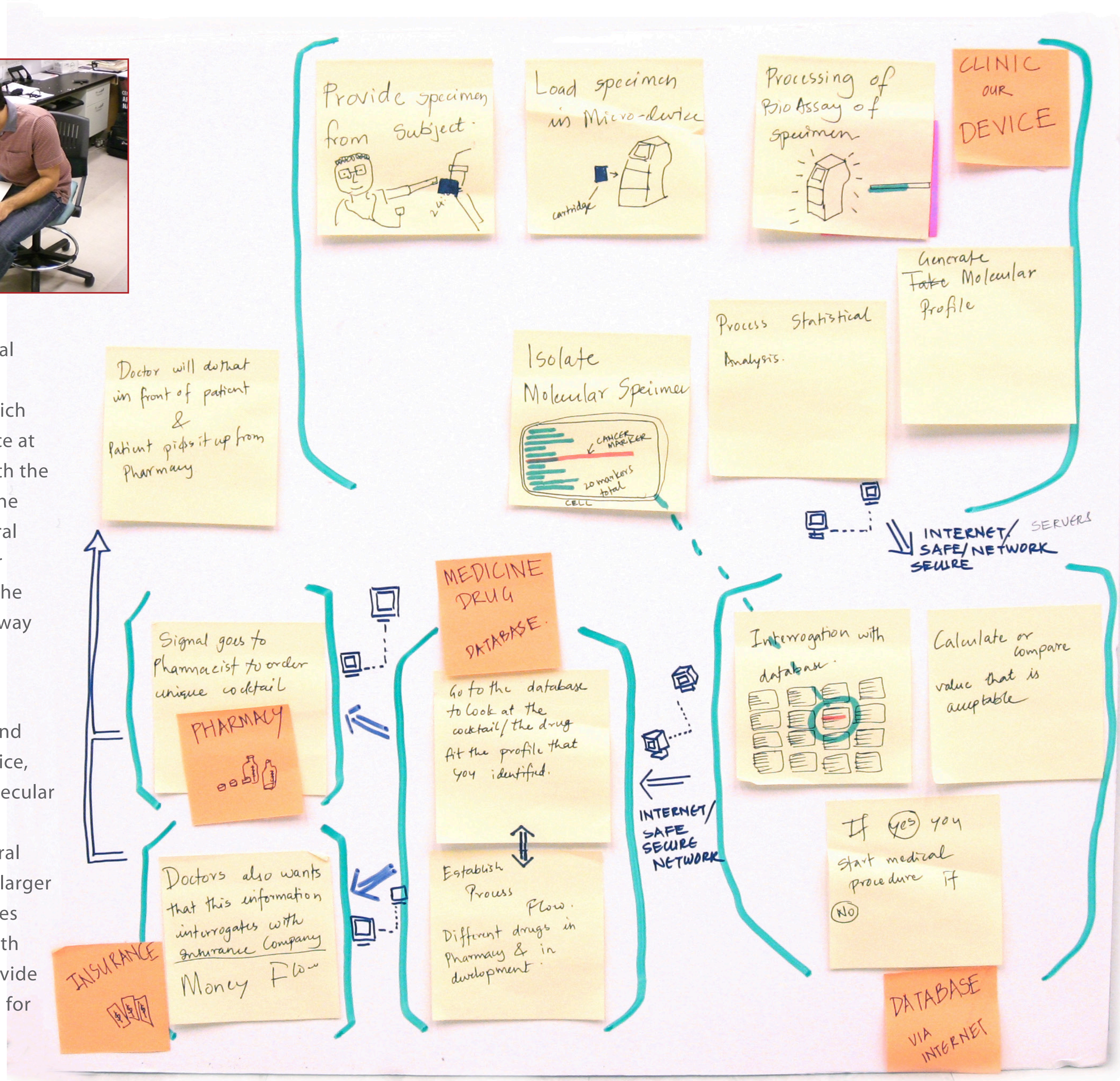
As shown in the above pie chart Ovarian cancer has the most average medicare Payment per individual in the first year following diagnosis as per the data available from 2004.

Interviews

A visual representation of the current Molecular Profiling process at a CLIA certified Reference LAB.



Semi-structured Interviews and discussions were conducted. Seen above is an example of 'visually' transcribing the audio to create meaningful clusters of information. Post-its also help to organize the content and share information with other team members. Original size- 2'x3'



Seen on the right is a visual mapping of the proposed system that consists of a rich Client device (MoDx device at the oncologists' clinic) with the ability to use the Cloud (the internet) to access a Central database running a server application to do part of the task in a complimen-tary way to the local client.

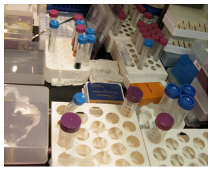
ANBC's would contribute towards the technology and science on the client de-vice, organizations such as Molecular Profiling Institue (would help to populate the central database with data and a larger consortium of IT companies would have to comeup with rich applica-tions and provide technolog-ical innovation for the central servers.

ATMOSPHERE

ARTIFACTS

Cancer Clinics
Hospitals
Smaller Biopharma
IT Services
Academic Medical Centers
Big Biopharma
Foundations
Measurement Platform Cos.

ARTIFACTS



ACTORS

M.D.'s
lab technicians
oncologists
bioengineers
cancer patients
cancer care co-ordinators
stake holders
academic
reference lab
smaller biopharma
IT providers
Academic Medical Centers
Big Pharma
Foundations
Measurement Platform Cos.
bioinformation specialistsz
Research technicians
Bioengineerig Researchers

ACTIVITIES

Reference Lab:
create database
co-ordinate sample collection
provide testing kits
Collect tissue
Process specimen
Isolate Molecular species
Generate Molecular Profile
Process Statistical Analysis
Calculate and/or compare
Provide feedback
Provide decision tools
Smaller Biopharma:
Access database
share bioinformatics capabilities
share tissue access
IT/Service Providers
Maintain supplier relationship
look for development opportunities
Academic Medical Centers
Access database
Retain owenership
Access tissue

Strive for better patient outcomes
Oncologist
Provide specimen from a subject
Prescribe therapy
Monitor progress
Diagnose cancer
Foundations
Advance research
Strive for better patient outcomes
Big Pharma
Access tissue
Share database
Recruit patients for trial
Patients
Looking for better outcomes
Participate in trials and try treat-
ment options
Need privacy
Measurement Platform Cos.
Maintain supplier relations
Create a standard
Exercise complete operational
freedom

What's good?

Research related to new trends and developments in cancer diagnosis and treatment. Social issues such as preventing the loss of a dear one suffering from cancer and ways to improve the quality of life of cancer patients. How could oncologists be assisted to diagnose and treat cancer better? How could we speed up access to reliable molecular and post-treatment data of cancer patients to inturn use it to treat other cancer patients?

Activities included interviews with healthcare professionals (oncologist- expressed the need for upgradable devices) including administrators, literature review and web search. Research socioeconomic issues and environmental responsibilities affecting medical diagnosis through internet. E.g. No testing on third world patients or drastically reduce patient testing for drugs.

What's possible?

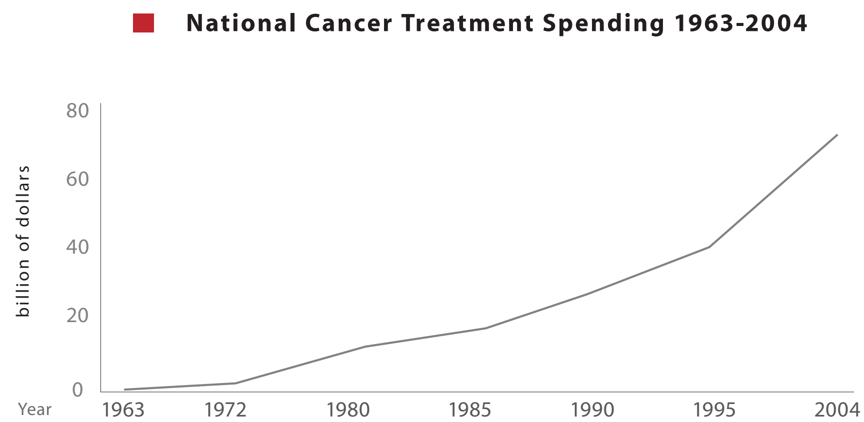
Trends in technology, manufacturing, sustainability and design of healthcare products, as well as equipment.

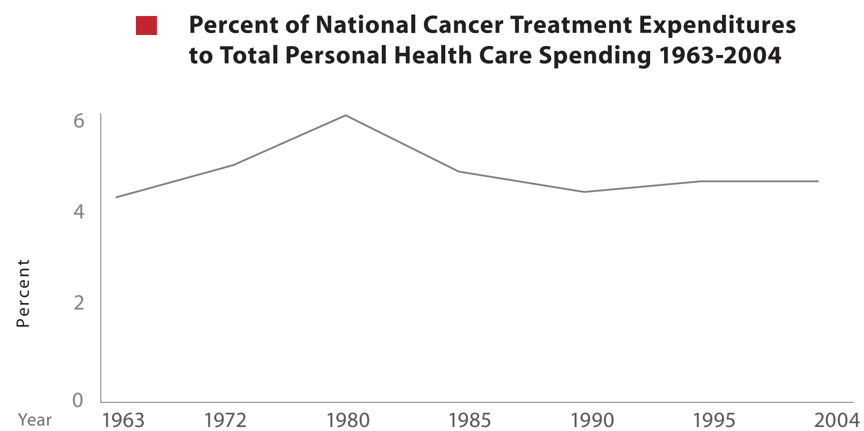
Activities included interviews (discussions+participation in analogous product development) with medical information system designers, program manager and director of ANBC,power source and electrical technologists. Also, internet based research was conducted to gain a better understanding of the topics discussed.

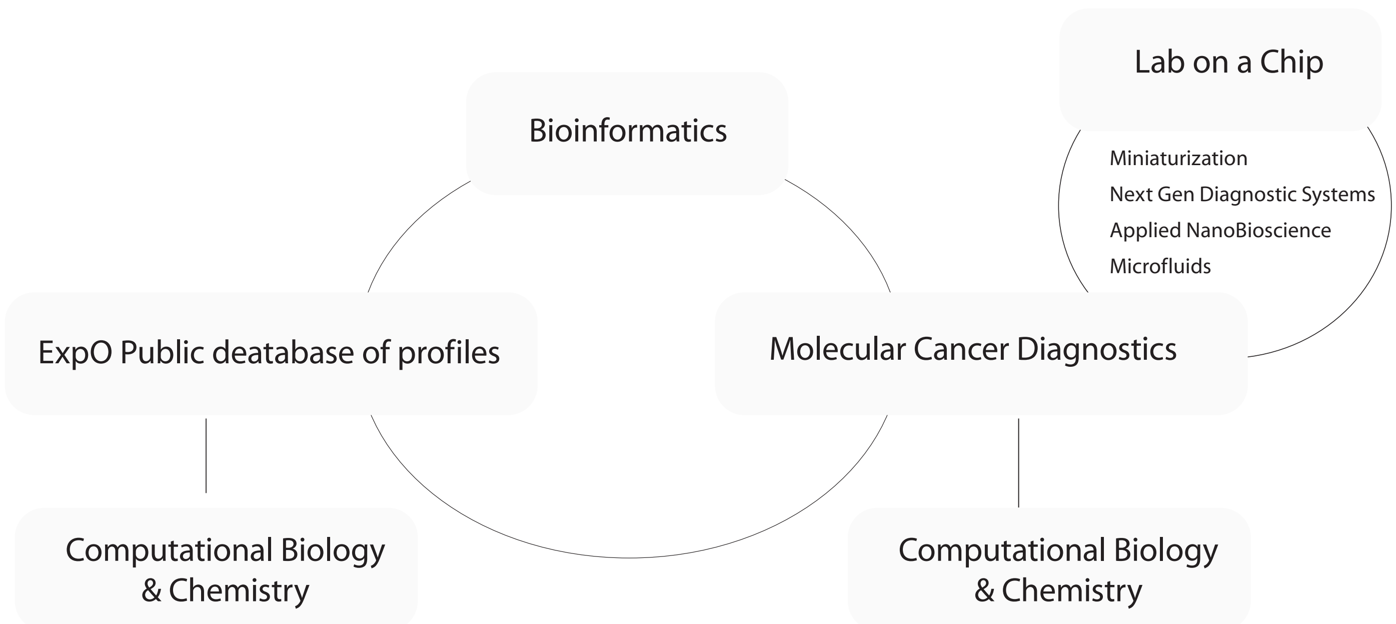
What's valuable?

Current trends in Medical diagnostic systems and administration (insurance), key competitors in market (what is provided by who?) consumer (patient/provider) pattern and trends (eg. indirect use of mol Dx)

Figure 6. National Cancer Treatment Spending and Percent to Total Personal Health Care Spending 1963-2004.






Lab on a Chip
Miniaturization
Next Gen Diagnostic Systems
Applied NanoBioscience
Microfluids
Bioinformatics
ExpO Public deatabase of profiles
Molecular Cancer Diagnostics
Computational Biology & Chemistry
Computational Biology & Chemistry

Phase 2 *Analysis*

Introduction

The objective of Phase 2 is to analyze the meaningful data collected about users, technology and relevant social conditions and trends. Each integrated innovation factor is divided into key findings and actionable insights.

What's desirable?

Introduction

Today oncologists and cancer patients blogging on the same web portal. The new generation desires devices that are empowered by internet connectivity and Interoperability. Any device that works in isolation would not be a good idea.

Key findings

Oncologists need tools to treat their patients better and early detection is one thing that can help fight cancer. Researchers who are profiling cancer tumors and creating a large database need a platform that can be fully automated and has the ability to connect to a central database via the internet. These platforms will need to have the potential to become industry standard as the size of the database increases. Researchers are also facing a challenge in dealing with different device manufacturers and technologies. It would really help their effort if they could ship devices to laboratories all around the world that show interest to participate in their study. The internet would allow all these labs to save and access this data from all over the world.

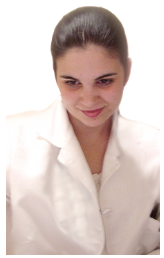
Actionable insights

- Actively participate with the researchers such as Dr. Von Hoff to understand their needs and customize the platform according to their requirements.
- Smaller footprint (12”x12”x24”) for a clinical setting and easy portability.
- Interoperability: Easy USB 2.0 connectivity to printers, monitors, keyboards and interface tools.
- Connectivity: Easy connectivity to remote database through high speed internet.
- Easy learning curve: Windows(R) based operating system with help function.
- Web-based software updates.
- Develop rich client applications that will provide great user experience at the local level.
- Central database running a server application to do part of the task in a complimentary way to the local client Server applications capable to fetch information from other databases belonging to health insurance, pharmacy etc.

Personas

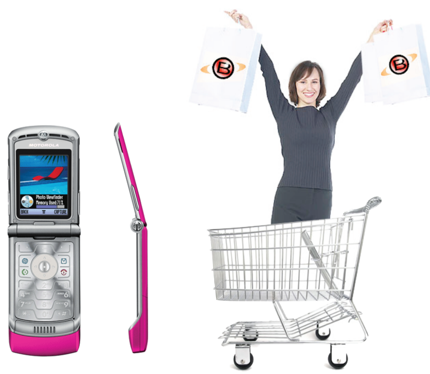
Lab technician

– 23 years
– Works 20 hours per week
– Very enthusiatic, wants more responsibility & has an enterpreneurial spirit
– Very intelligent & lives a simple lifestyle
– He wants to learn operating new equipment in the lab but feels that sometimes training others takes too much of his time. He has a feature right, rotating open Sony MP3 cell phone.



Lab technician

– 31 years old
– Works 8-5 shift
– Does not want much responsibility at work
– Enjoys spending weekends with her husband relaxing
– She is intelligent yet simple. Likes hero Motorola RAZR phone for its thin & stylish. Although a little laid back, she makes it to Thanksgiving sale.



Lab technician

– 36 years old
– Works with a radiologist as a laser support person
– He lovesdriving his new Audi.

Oncologist / Radiologist

– 42 years old
– Likes technology, especially bluetooth. Likes easy interfaces and once upon a type had a subscribtion to I.D. Magazine.

Needs and Desires

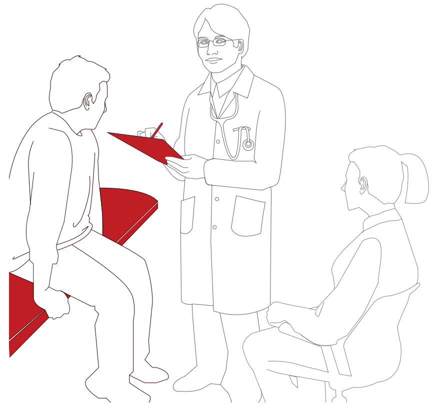
Feature rich
Value for money
Good deal

Value
Style

Performance

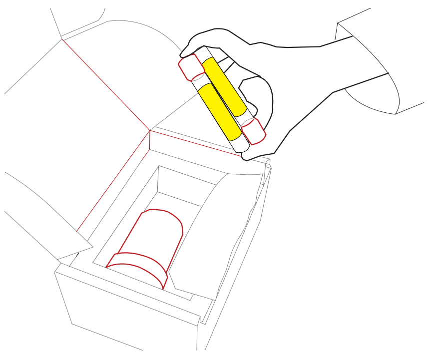
Value for money
Long-term use

Patient requests for an appointment.

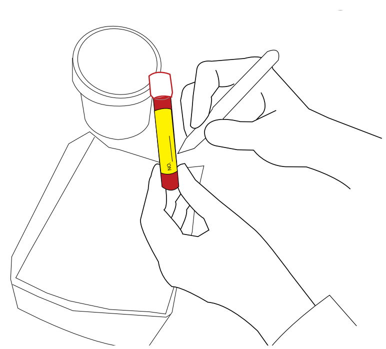


Doctor examines the patient prescribes a biopsy for tumor tissue for profiling.

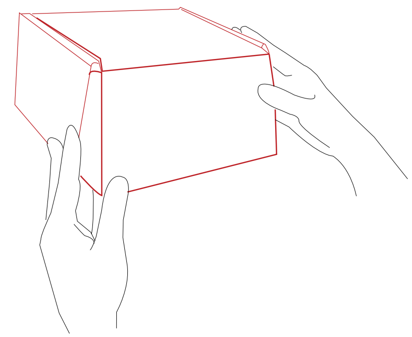
Contacts Reference Laboratory for a testing kit for sample collection.



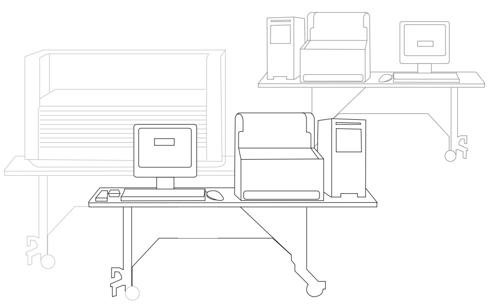
Receives testing kit.



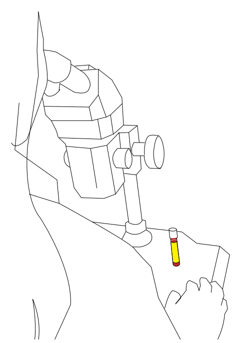
Performs biopsy &carefully stores sample in the kit.



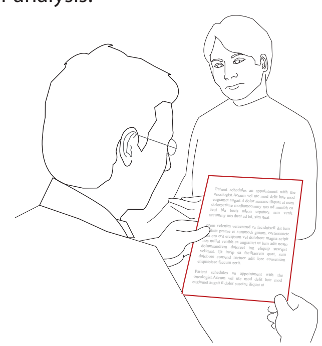
Couriers the kit to Reference Laboratory for analysis.



A big setup consisting of a supercomputer and DNA Microarray device to choose genes that might be of therapeutic value to the patient.



The tumor sample is profiled and recommendation report is sent to the oncologist.



Oncologist reviews the reports and prescribes treatment.

What's good?

Introduction

How could we leverage bioinformatics and computational biology and chemistry to fully exploit the potential of this advance platform to revolutionize Cancer Molecular Diagnostics?

Key findings

Social:
The device would not only be a tool to analyze the blood sample for cancer tests but also to access the central database that would contain billions of data points generated by genetic research.

We need to revolutionized cancer diagnostics at the clinical level so that there are more avenues for profiling and early detection of cancer.

Need for ultra low cost technology in Cancer Diagnostic Application

Need to develop technologies for high-volume production (reliability)

We need to provide the latest and the best testing for cancer patients to a wider patient base.

Environmental:
Need to decrease reagent and sample consumption

Actionable insights

Social:

The protocol can be integrated to reduce the amount of hands-on manipulation using the integrated chip approach.

Employ scalable methods and techniques as alternatives to photolithography

An open source algorithm would be developed to carry out the complex statistical calculations in the main database.

An IT service base would have to be established to handle the high data analysis, management and feedback loop.

Environmental:
Integrate advanced functionality into the same (plastic) substrate (advanced performance)

Using recyclable plastic for the cartridges.

Distribution Network For The Molecular Cancer Diagnostic Device

- Phase 1 Primary Research Centers
- Phase 2 Secondary Research Centers
- Phase 3 Clinical & Reference Labs

Sentinel Events in Diagnostics and health care, 1953-2006

Scientific Advancements

1953
DNA structure defined by Watson & Crick

1964
Cancer marker alpha-1-fetoprotein (AFP) was first described as a tumor-associated marker.

1968
First fully automated discrete chemistry analyzer for whole blood or serum.

1973
First system to measure blood gas, metabolites, electrolytes and CO-oximetry from a single sample.

1976
Discovery of hemoglobin glycosylation

1979
First point-of-care device developed

1985
HER-2/ neu gene is cloned

Mullis develops polymerase chain reaction (PCR) for copying DNA

First diagnostic test to screen blood and blood products for HIV

1986
First automated DNA sequencer is produced

1953 1963 1973 1983

Policy Milestones

1965
Social Security Amendments authorizing Medicare and Medicaid

1966
AMA establishes and publishes first CPT coding system

1967
Clinical Laboratory Improvement Act (CLIA) - Federal government enacts licensing, regulatory authority over clinical laboratories

1973
Federal Register published new FDA regulations on labeling requirements & procedures for standards for diagnostics

1976
Medical Devices Amendments to Food, Drug, & Cosmetic Act

1983
Social Security Amendments enacted, including Medicare prospective payment system based on DRGs.

1984
Deficit Reduction Act requires labs to bill Medicare directly; creates Clinical Laboratory Fee Schedule to cap payments for lab services.

1988
First-generation test kits for Chlamydia trachomatis and Neisseria gonorrhoea infections

1990
Human Genome Project launches

1993
Relationship between severity of Type 1 diabetes and degree of glycemic control demonstrated

1994
BRCA-1, the first breast cancer susceptibility gene, is discovered

1995
First fully automated system for high-volume blood screening laboratories

1998
First targeted treatment (Herceptin) for HER-2/neu positive metastatic breast cancer patients

2001
Launch of a rapid anthrax test

First non-invasive glucose monitor using a low electrical current to take glucose readings without puncturing the skin

Publication of initial Human Genome Program working draft sequence -Collins & Venter

2002
First fully - automated congestive heart failure test for diagnosis and monitoring treatment response

2003
West Nile virus blood screening assay available for use by U.S. manufacturers

First fully automated, high-throughput diagnostic instrument for detecting Chlamydia trachomatis and Neisseria gonorrhoea

2004
First pharmacogenomic array to identify variations in drug metabolism

First oral specimen rapid HIV test

Compilation of the nations first public database of standardized, clinically annotated gene expression data began on March 1 with the launch of the International Genomics Consortium (IGC) expression project for oncology (expo)

2006
Feb 3, 2006 – ASU's Biodesign Institute & the Translational Genomics Research

Sept 7, 2006– Genome Code Cracked for Breast & Colon Cancers: Johns Hopkins Kimmel Cancer Center scientists have completed the first draft of the genetic code for breast and colon cancer

1990 2000 2006

1988
Clinical Laboratory Improvement Amendments consolidate regulation of all clinical laboratories under one statute

1990
Safe Medical Devices Act

Negotiated Rulemaking Act enacted

1992
Safe Medical Device Amendments establish single reporting standard for user facilities, manufacturers, distributors

1993
ICD-10 codes first released by World Health Organization as an option to replace ICD-9 codes.

1996
Health Insurance Portability and Accountability Act (HIPAA) enacted

1997
FDA Modernization Act

1998
EU in Vitro Diagnostics Directive

1999
FDA Draft Guidance on Labeling for Laboratory Tests

Balanced Budget Refinement Act of 1999 pays outpatient clinical laboratory tests as critical Access Hospitals (CAHs) on a reasonable cost basis versus a fee schedule

2000
Medicare, Medicaid, and SCHIP Benefits Improvement and Protection Act of 2000 (BIPA).

2001
Final rule in Federal Register establishes NCDs for 23 diagnostic tests as a result of negotiated rulemaking with industry stakeholders.

2002
Medical Device User Fee & Modernization Act

FDA Office of IVD Device Evaluation and Safety (OIVD) formed to consolidate regulatory oversight of diagnostics

CMS publishes interim final rule regarding inherent reasonableness (IR) authority

2003
Compliance required for IVDD: all IVD products mustbe "CE marked" or be prohibited from sale in EU

FDA draft guidance for pharmacoge-nomic data submissions released

Medicare Prescription Drug, Improvement and Modernization Act(MMA) enacted

2004
Freeze on clinical laboratory fee schdule becomes effective through 2008.

Genetic Information Nondiscrimination Act of 2005

What's possible?

Introduction

ANBC has developed a platform for low cost automated STR typing that utilizes an integrated cartridge for molecular profiling that helps cancer research. Large amount of data is generated during molecular profiling and any ability to search such large volumes of clinical information to compare treatment outcomes, demographics, clinical histories and current disease parameters has potential to add value to the treatment side of cancer as it has on the research side.

Key findings

Connectivity among multiple institutions will be crucial to success. Even today's largest medical centers cannot treat a broad enough patient population to make their own records the sole basis for information-based medicine. Such treatments must cull from millions of records spanning hundreds of disease categories. Patients must come from diverse backgrounds that span a broad range of genotypes, and for each genotype the system must include enough records to generate statistically significant information.

The International Genomic Consortium (IGC) is dedicated to the creation and public-release of clinically annotated molecular databases characterizing human disease. These databases are useful for discovery and validation of new diagnostic markers and therapeutic targets.

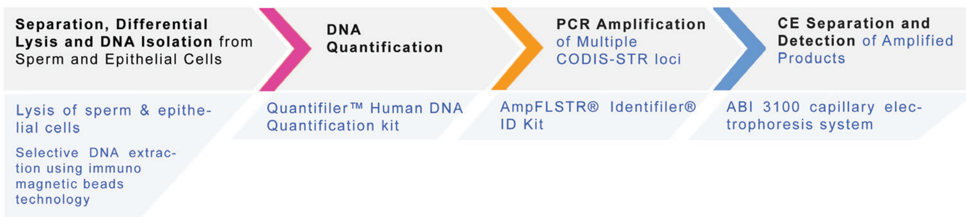
Actionable insights

We propose a system that will use extraordinary power of the supercomputer located at the central data base to quickly analyze the billions of data points generated by genetic research.

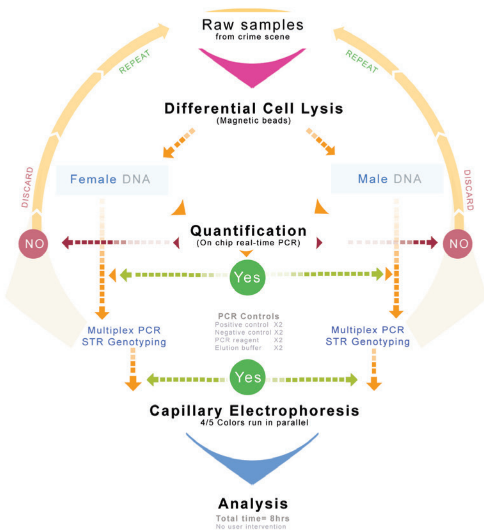
Web-based Central Computing

Web-based central client-server computing would be a powerful and cost effective way to deliver high-performance computing, knowledge-based databases, and application software tools for biomedical data analysis and visualization. Web-based central computing will allow easy upgrades to data bases and an algorithm will be developed to analyze the content of the patients' records to help formulate therapeutic strategies to treat cancer.

Conventional Approach



Integrated Chip Approach

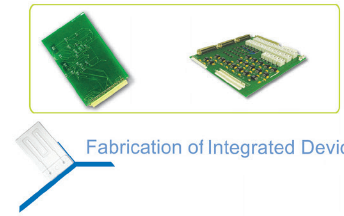


Decreased reagent and sample consumption can be achieved and the protocol can be integrated to reduce the amount of hands-on manipulation using the integrated chip approach.

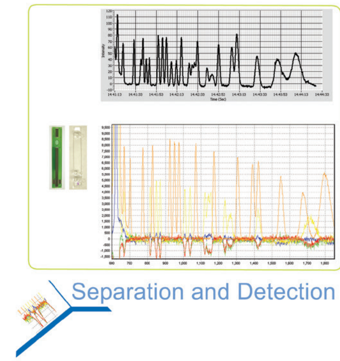
Fabricating such an integrated microfluidic system in plastic provides a disposable and more functional device which minimizes user intervention.

Why a Plastic Platform?
Need for ultra low cost technology in Cancer Diagnostic Application
Need to integrate advanced functionality into the same (plastic) substrate (advanced performance)
Need to develop technologies for high-volume production (reliability)
Accompanying scalable methods and techniques as alternatives to photolithography

Differential DNA Extraction



Fabrication of Integrated Devices



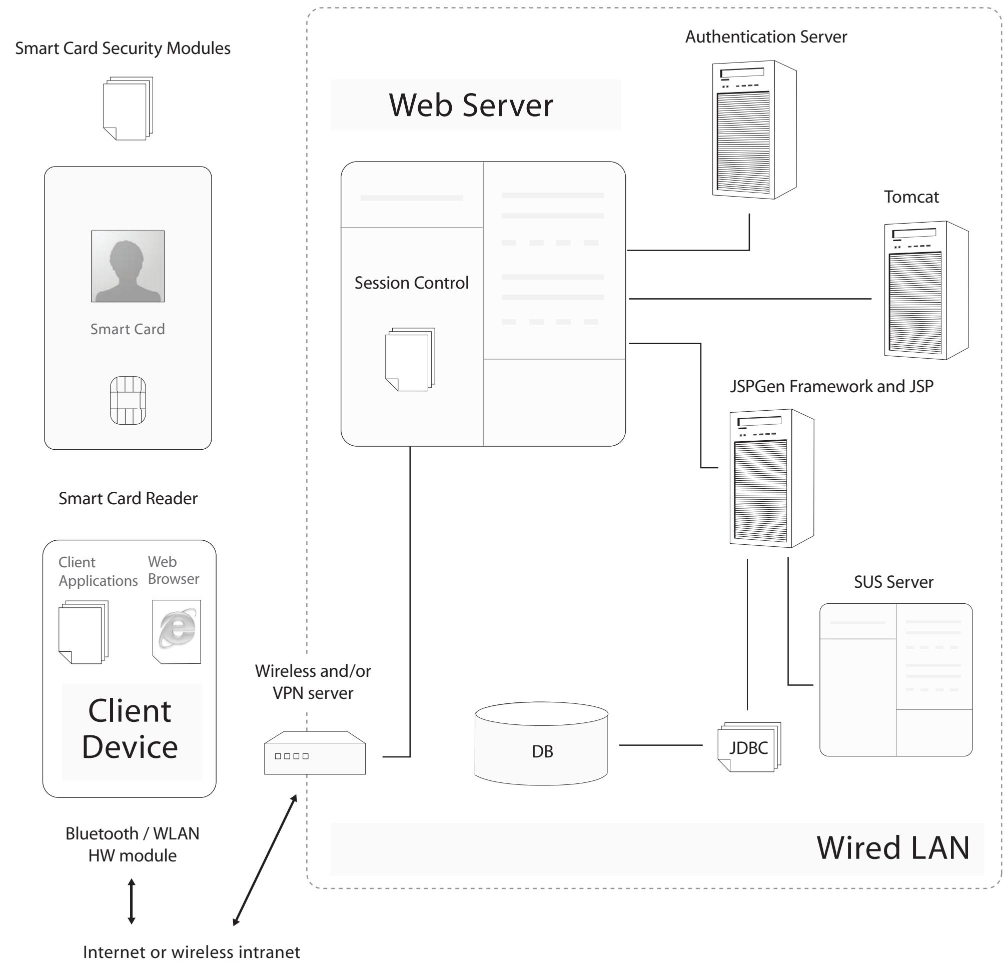
Separation and Detection

Integrated Product Development

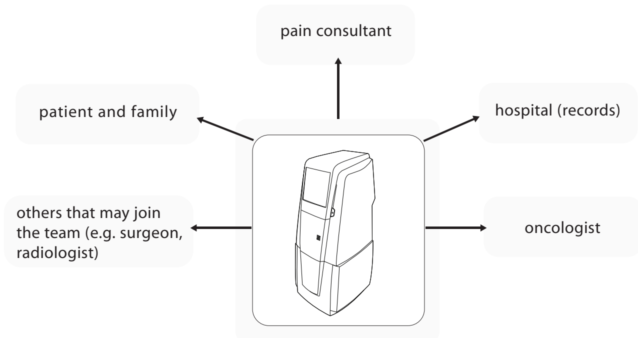
Micro-machined plastic cartridge for differential extraction/PCR

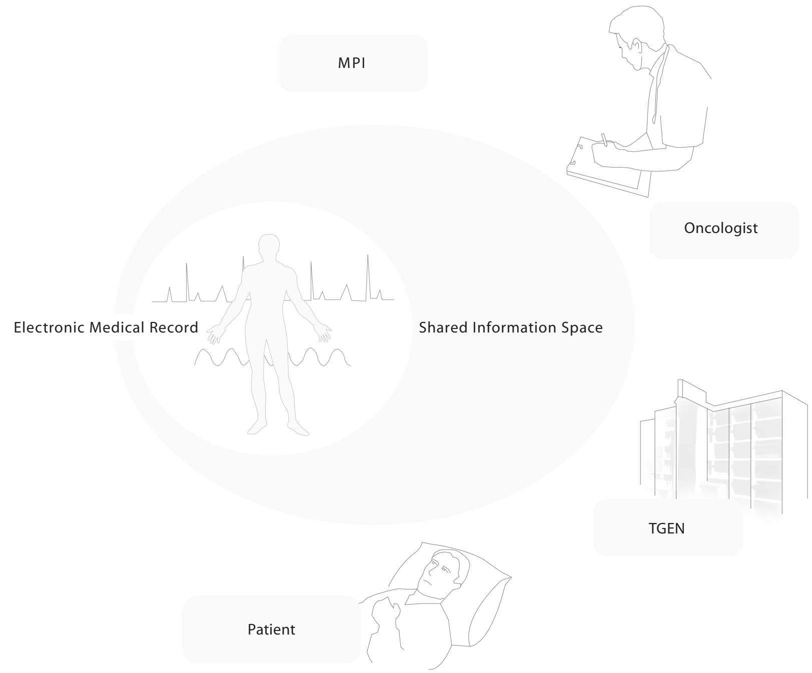
Injection molded PCR-cartridge (top)

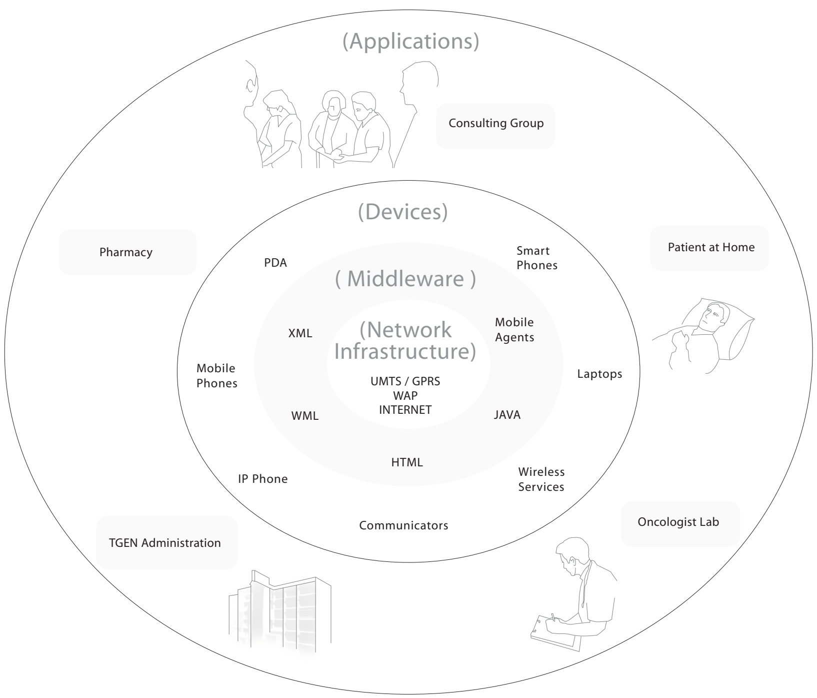
Figure showing the proposed web-based system consisting of the Molecular diagnostic device (client device) and the central database connected through the internet.



Web Mobi-Dev general architecture



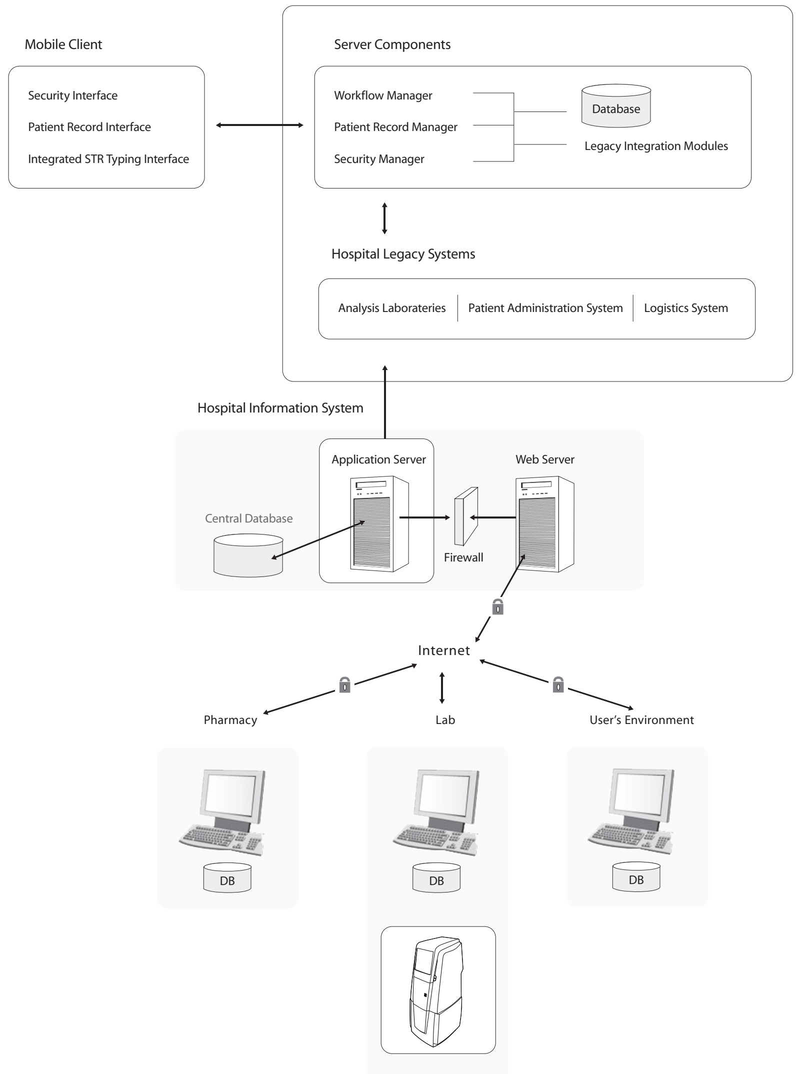




1 | 2

3

1. The client device is at the center of the various entities. The application on the client will gather information from various sources and present it in an actionable format.
2. Figure showing the shared information space which would immensely benefit the cancer patient.
3. The system would be made up of devices, applications running on them, middleware that would enable these applications to interact with the main database and large network infrastructure that would be at the core of this system.



Web-based Central Computing

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Computational Bioscience: High-performance Linux cluster for computation-intensive genomics research.

High-Performance Computing

ASU supercomputers have Linux operating environment due to its high performance and scalability which makes it a great choice for the main database. Linux would provide the open, reliable computing platform at an attractive cost. High-speed LAN and WAN connections are provided for rapid data communications.

Create a knowledge-based Database.

An algorithm capable of carrying three functions would be developed to:

1) Control the analysis of the sample in the device.

2) Trigger the central data base to compare the results to extract and use information from vast amounts of knowledge and data collected from wide-ranging sources such as public and commercial databases.(e.g., gene mapping, gene expression, literature database and pharmacy databases.)

Web Based Central Computing

 SWOT Analysis is designed to help determine the Strengths, Wea kness, Opportunities and Threats of the proposed system.

Weakness

Biological systems are of such complexity, and the ability to assemble the relevant clinical, biochemical knowledge is a serious barrier to the effective use of the diagnostics.

Single sample can be analyzed at a time prohibiting use in large scale reference laboratories where multiple samples need to be analyzed in less time.

R&D expense in perfecting the technology and setting up an entire system of remote clients communicating to the main server via the internet.

The Medicare statute does not provide for reimbursement for screening and prevention services, except as the law has been amended by Congress for particular tests. Only in recent years has Congress granted coverage for such interventions, including three diagnostic tests (Pap smear, fecal occult blood test).

Developing technology might take time to perfect. We do not have the chemistry ready to build the tool and validate the technology.

Strengths

Unique infrastructure:

Platform developer - Center for Applied NanoBioscience.

Clinical Partners - Scottsdale Healthcare, Mayo Clinic Scottsdale and Banner Health
Clinical reference lab - Molecular Profiling Institute.

Scalable IT environment and connectivity:
ASU has a supercomputing infrastructure, consisting of a 1024 Beowulf IBM Linus cluster, the largest cluster of its type focusing on genomic research into diseases such as cancer. Through its affiliation with ASU, our system could be a part of IBM scholar's program, receiving complimentary software and support to create the central server. Web-based software updates and internet connectivity in the device

Lab-on a-chip: Miniaturization and automation of the Molecular Profiling process.

Unique portability features makes it easily deployable to emerging markets allowing new data collection centers possible all around the globe.

Opportunity

Currently there is no device in the market that is capable of performing all the four steps involved in Molecular Analysis from sample preparation to Detection.

No device in the market that could be used in a clinical setting.

Present commercial solutions are expensive, cumbersome and need a complex environment such as a laboratory to operate.

Enable collaboration and interaction between our clinical partners through this technology platform.

Provide rapid and accurate results compared to the current devices that satisfy the demand in a timely manner to treat as many patients as we would like to.

Translation of the discovery in medicine to a clinical application

Technology Platform could also be used for 'Forensic DNA Finger printing' and in 'Drug Discovery'.

Threats

Regulatory threat that the technology of DNA microarray and DNA sequencing may not be accurate and reliable enough to be approved by FDA.

Technology is not mature.

The statistical tools to analyze the complex data may not be available to make the technology robust enough to be used universally.

Legal threat if diagnosis is not accurate enough.

Funding dollars could be spent on projects yielding more immediate benefits in detection and treatment than on efforts to map cancer genes eventually affecting the creation of valuable genetic data.

Clinical M.D.s are risk averse and hence it may take longer to adapt new practices.

What’s valuable?

Introduction

Current trends in diagnostics systems and administration, key potential partners (who, why, and how) were researched. S.W.O.T. analysis was also performed.

Key findings

The majority of US diagnostic testing is conducted within hospitals, accounting for 60% of the industry’s revenue. Labs in physician practices make up 55.4% of all sites of service. Though reference labs comprise only 2.8% of US clinical labs, they account for 32% of the diagnostics industry’s revenue, because of high-volume testing. This could be reversed with the device enabling the oncologist to conduct the diagnostic test within the clinic tapping a large market segment.

The International Genomic Consortium (IGC), National Human Genome Research Institute (NHGRI) and Arizona Cancer Center are pulling together resources to perform gene expression profiles and creating a central database. Their efforts to standardize. Since the technology platform analyses genetic information it could be further adapted to be used for the diagnosis of other genetic diseases.

Forensic agencies all over the world are looking for portable DNA fingerprinting devices to help them with on-site testing of samples recovered from the crime scene.

We need to monetize the system so that a revenue stream is built that could further support this program.

Standardization requires a large population for validation and hence it would be great if we could have these devices in the emerging markets as well.

It would be very valuable for the validation of the device if emerging markets could participate in the Cancer Molecular Diagnostics system.

Actionable insights

The device is to be used for molecular Cancer diagnostic purpose but it is hardware ready to be used for Forensic applications with a simple and flexible Windows®-based system that manages the maintenance and operation of the device. The software would also manage the required accessories connected to it. Connectivity to external printers, keyboards, mouse, fingerprint reader, iris scanner is available through USB ports situated within comfortable reach of the user.

Potential Partnerships:

International Genomics Consortium (IGC)- a non-profit medical research foundation established to serve common, unmet needs.

Translational Genomics Research Institute (TGen)- its mission is to make and translate genomics discoveries into advances in human health.

Molecular Profiling Institute Inc.- provides cutting-edge testing facilities, products, and resources for genomic and proteomic profiling and treatment of cancers and pharmaceutical services to identify populations that may respond to targeted therapies.

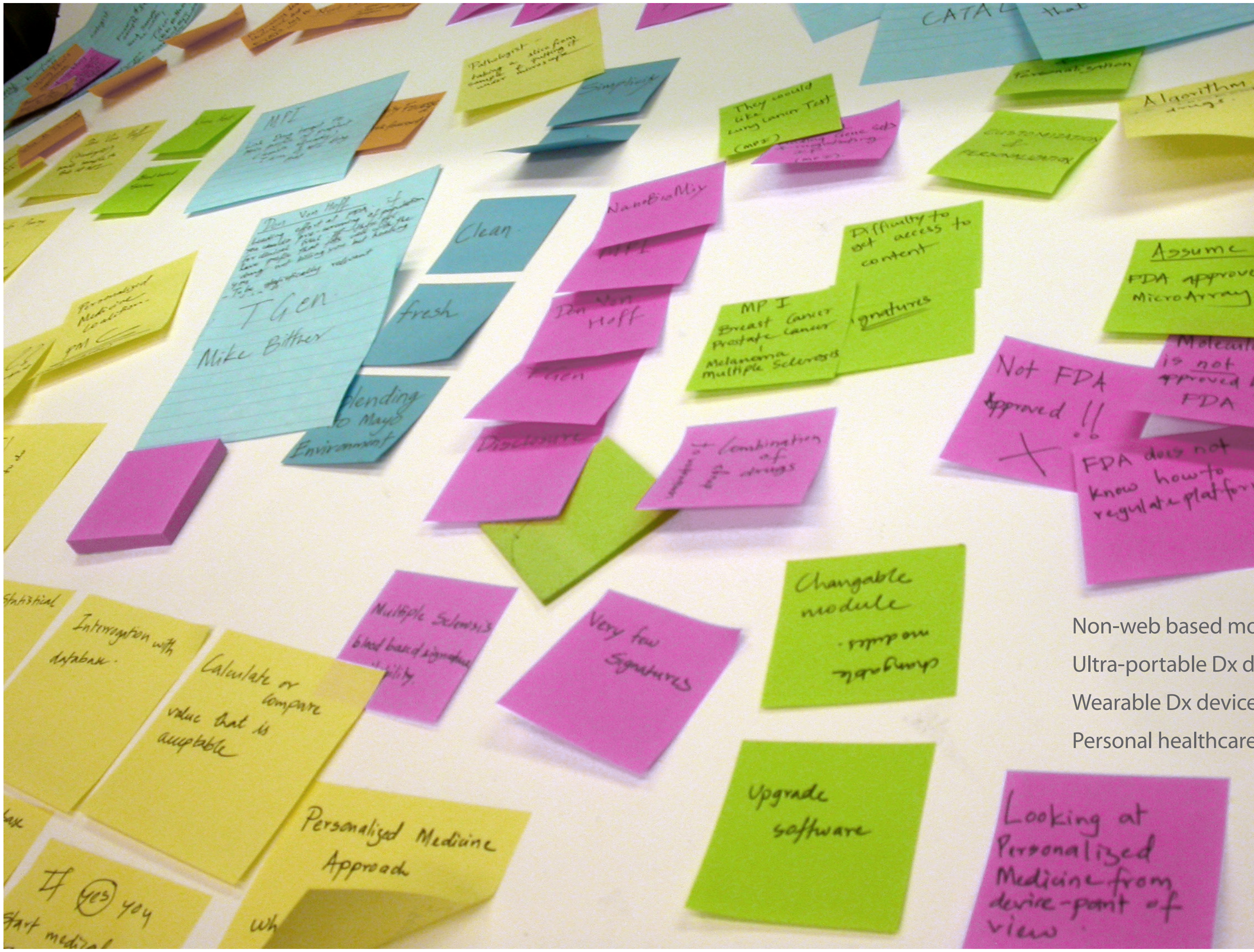
Potential Industry Partners:

Gen-Probe - manufactures a broad portfolio of diagnostic and blood screening products to detect a variety of diseases.

Affymetrix - Affymetrix technology is used by the world's top pharmaceutical, diagnostic and biotechnology companies as well as leading academic, government and not-for-profit research institutes.

Ameripath Inc - offers a broad range of testing and information services used by physicians in the detection, diagnosis, evaluation and treatment of cancer and other diseases and medical conditions.

A few potential ideas:

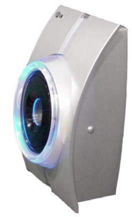
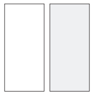
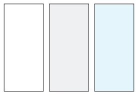
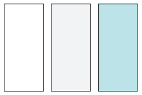
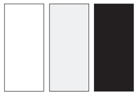
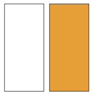


- Non-web based molecular Dx device
- Ultra-portable Dx devices
- Wearable Dx devices
- Personal healthcare management device

Aesthetic

Most current products in the area of genetics
are very medical and technological in appearance
and function.

Design Language

Product					
Personality	Cold, unfriendly, beefy, rudimentary, boring, brawney	Intelligent clever, faithful	Familiar, amiable Easy-going Honest	Complex scientific, unapproachable	Complex Boring Brawney
Form	Geometric, boxy angular, massive sterile	Geometric Massive Sterile	Combination of curves with soft edgy lines. Subtle convex and concave surfaces	Mechanical Cold Advanced Portable	Rounds and radii Sterile
Materials	Textured Plastic, metal, Glass	Metallic Plastic Glass	Plastic	Aluminum Plastic & Glass	Plastic Rubber
Colors					
Metaphor					

Cold, unfriendly,
beefy, rudimentary,
boring, brawney

Straight to
controlled lines,
Flat surfaces

Aluminum

Intelligent
friendly

Geometric
Massive
Sterile

Plastic
Rubber

Friendly, faithful
Accommodating
Helpful

Rounded off
rectangular
shapes and flat
surfaces

Plastic
Rubber

Complex, boring
technological
Demanding

Mechanical
Cold
Advanced
Portable

Plastic
Glass

Complex
Boring, zoomorphic

Geometric
Massive
Sterile

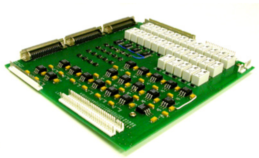
High end Plastic
aluminium body

Functional Development

Off the shelf components

Device	Manufacturer/Model	Size	Power Requirements	Weight	Additional Notes
Microcomputer	VersaLogic, Cobra (VL-EBX-12d)	5.75" x 8.00" x 1.75"	5V ± 5% @ 4.7 A (23.5 W) typ.	0.32 kg (0.72 lbs)	1 GB DRAM, 82541ER based
RS-232 Module					Gigabit Ethernet Controllers
	WinSystems, PCM-COM8	3.8" x 3.6" x 0.6"	+5V ±5% @ 125 mA	0.16 kg (0.36 lbs)	Eight RS-232
I/O Modules (4 ea)	WinSystems, PCM-MIO-1	3.8" x 3.6" x 0.6"	+5V ±5% @ 500mA (Typ.)	0.16 kg (0.36 lbs)	16 Analog Inputs, 8 Analog
					Outputs, 48 Digital I/O
	Douglas, BX-DE-104-163-265	3.8" x 6.3" x 0.6"	N/A		CCD Control
PCI Adapter	Qualtek, 761-18/004	66 x 27 mm	N/A		
AC Power Plug	Cypress Industries, CCUSBA-32003-00X	0.6" x 0.5" x 0.6"	N/A		Male, Metal Housing, DPST,
USB Connector	ICC, IC107C5EBK	0.57" x 1.20" x 0.64"	N/A		Single Fuse 5x20
Ethernet Connector					
		25 x 25 x 17 mm			
R-HP803xx 3W Rectangular Power LED					
	Miller Technologies	7.3" x 5.56" x 0.63"			
8" TFT Open Frame LCD					
Power supply					
High Voltage Power Supply (HVPS)					
Cooling Fan					
Avalanche Diode					
LED light Source					
Spectrometer					

Custom made components



The PCB (printed circuit board)DAQ cards in the PC.

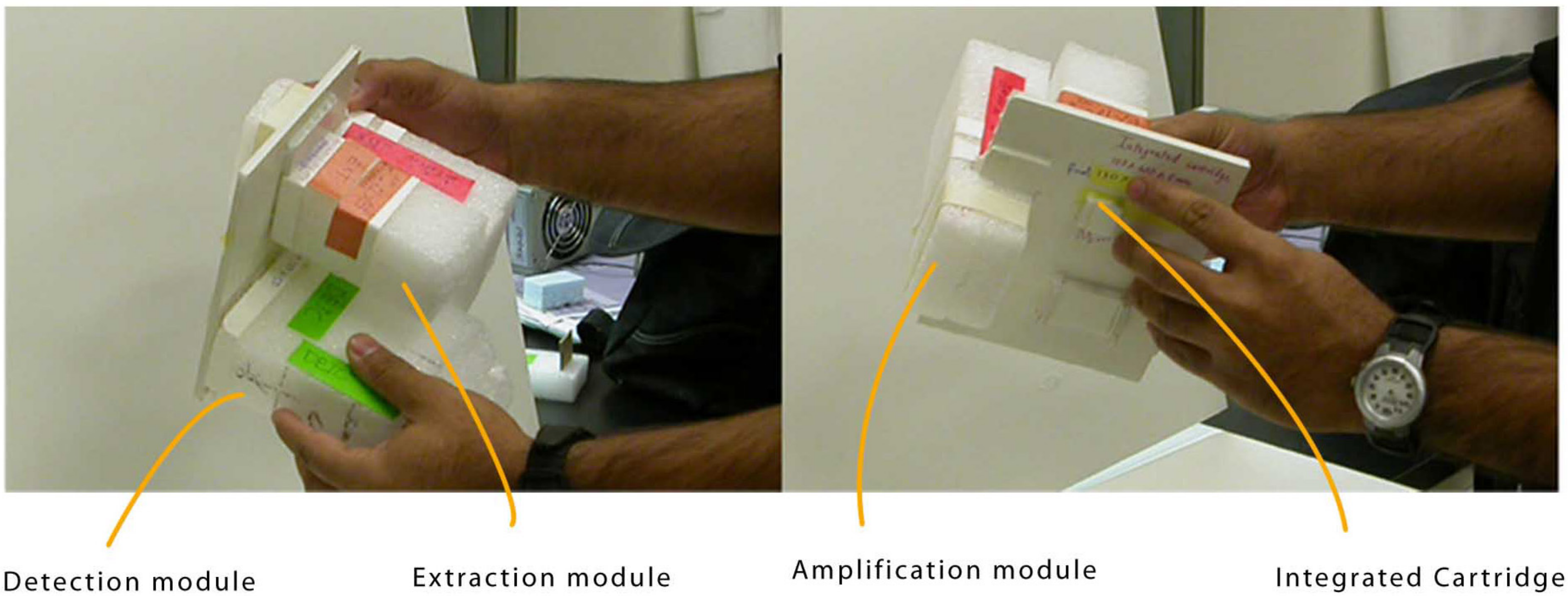
The PCB (printed circuit board) is the control electronics for the Sample Prep Heater Board. It's primarily made up of relays, regulators, and digital trim potentiometers. This will give us precise control and adjustment of each valve heater and pump. The interface to the computer is made up of AMP D Subminiature 050 Series connectors. This also allows simple interfacing with the DAQ cards in the PC.

Printed circuit board for actuation of integrated device

Micro-machined plastic cartridge for differential extration/ PCR

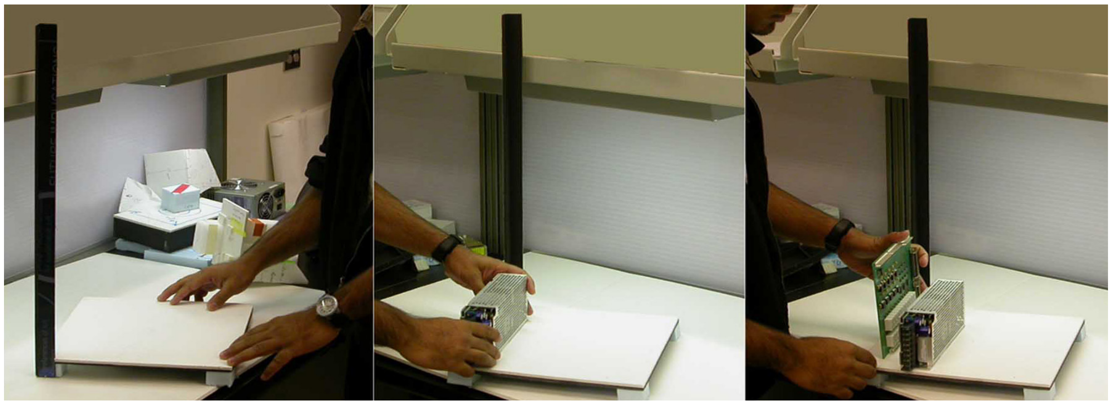
The device would be composed of six vital components:

Detection module
Extraction module
Amplification module
Integrated Cartridge (a plastic cartridge with electronic printed circuit)
Power supply
Computer (integrating the computing ability of individual modules into one)
Display (LCD TFT touchscreen)

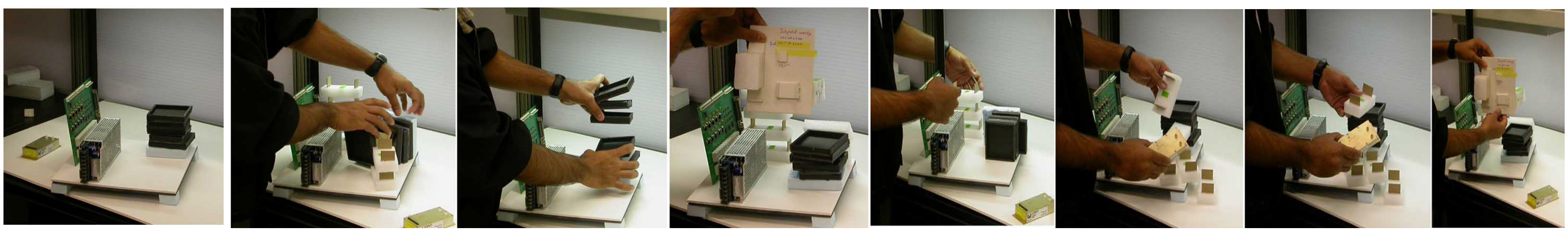


At the heart of this device is an integrated cartridge that would contain the prepared sample of the patient. The rest of the modules, detection, extraction and amplification are built around this cartridge. This cartridge would be inserted into the device just like we load a DVD player or computer with a CD. The other modules were placed in relation to the cartridge.

The device would have a footprint of 30cm (L) x 30cm(W) x 60cm(H)

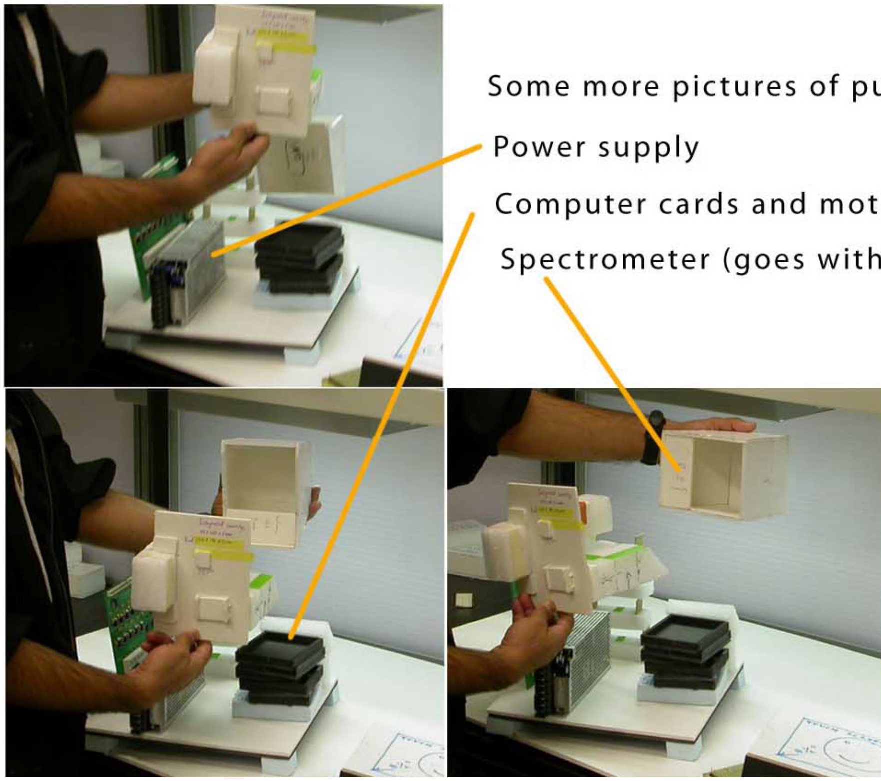


The study model was built with mock-ups of all the components that would be in the device. Most of the modules were individual tests and were separate with their own computing and power supply, but this device would combine all these different modules into one compact and integrated device. It was a challenge to find the smallest and most efficient computing and power supply sources.



A study model was made with a base and a reference for height.

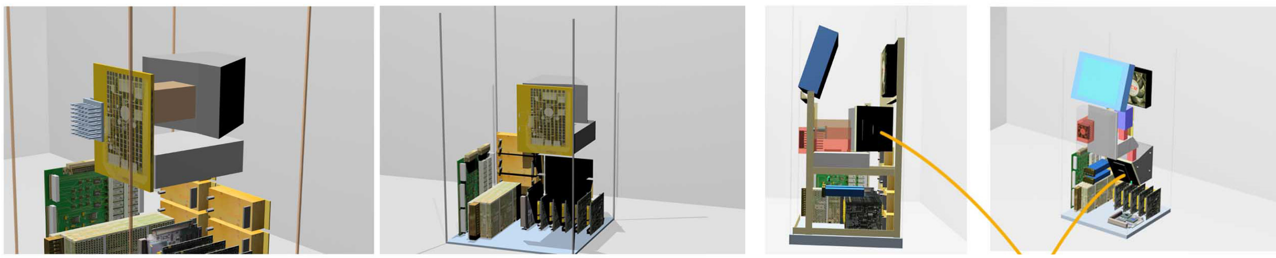
Some more pictures of putting together the rough model.



As seen in the bottom two pictures, the orientation of the spectrometer varies. Mock ups helped the Optical team to realize very early in the development stage that they would have to consider LED source for the laser as opposed to a conventional laser source.

Innovation Trolley

The trolley contained mock-ups of the components, post-it notes, suggestion sheets, exacto knife, styrofoam and double-sided tape.

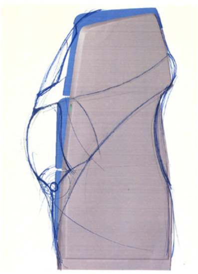


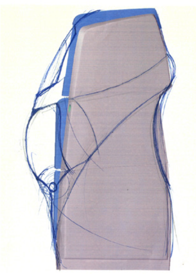
The detection module (which has spectrometer attached to it) was a major are of concern. Finally we reached at a conclusion that in the best case we would go for a LED source of light and in the worst case an external laser unit!!!

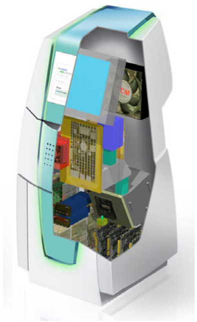
Next Step

Computer modelling in 3D Max after the relative position of the internal components was almost final.

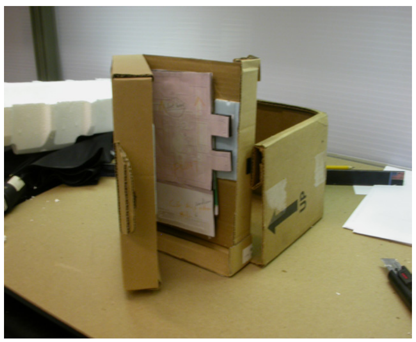
Concepts

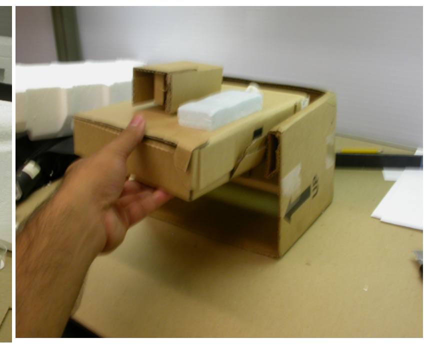


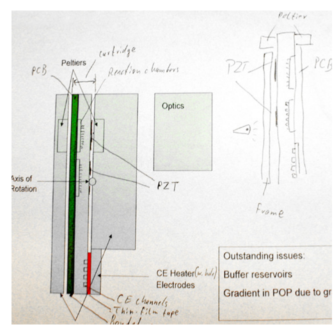




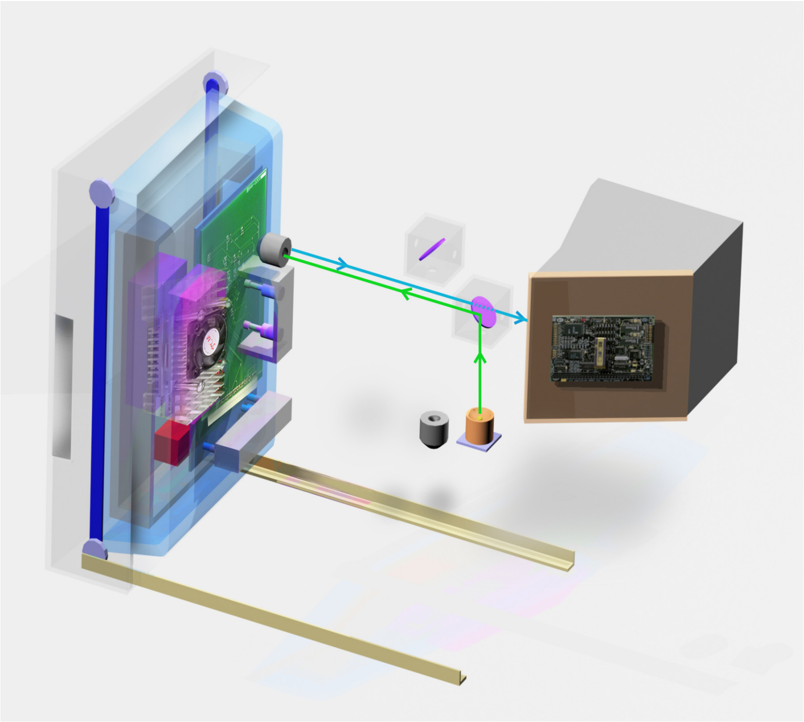
Study models for cartridge orientation.



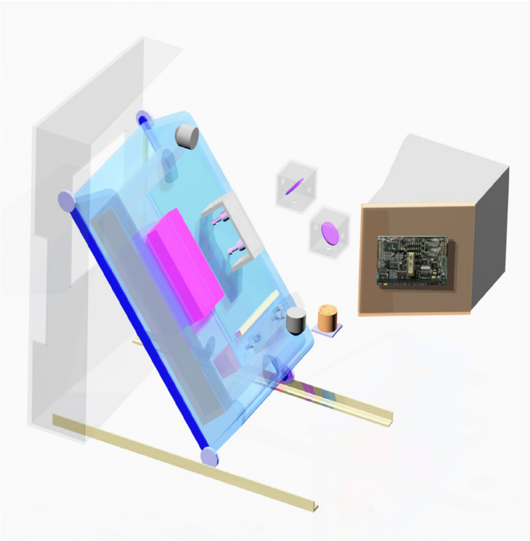




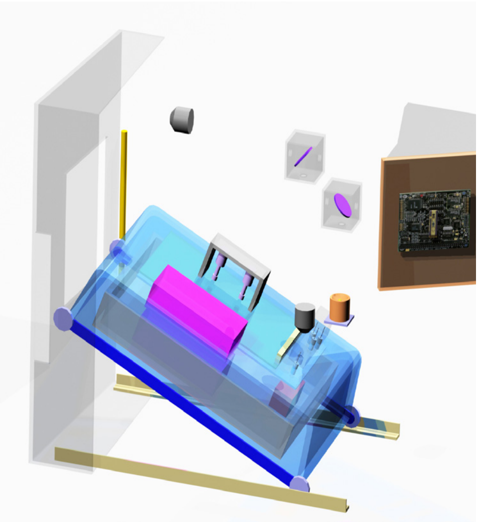
Sliding cartridge design



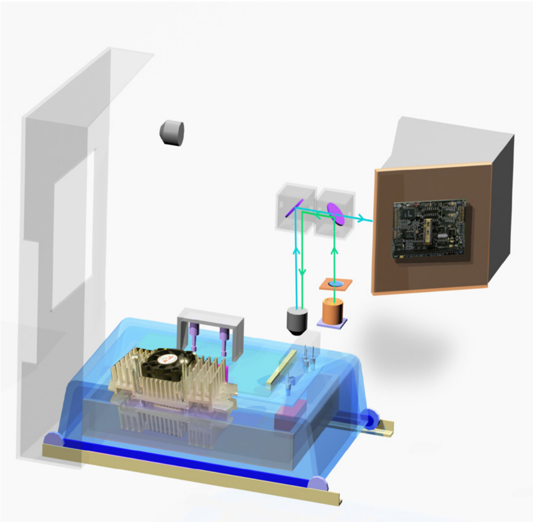
Internal architecture



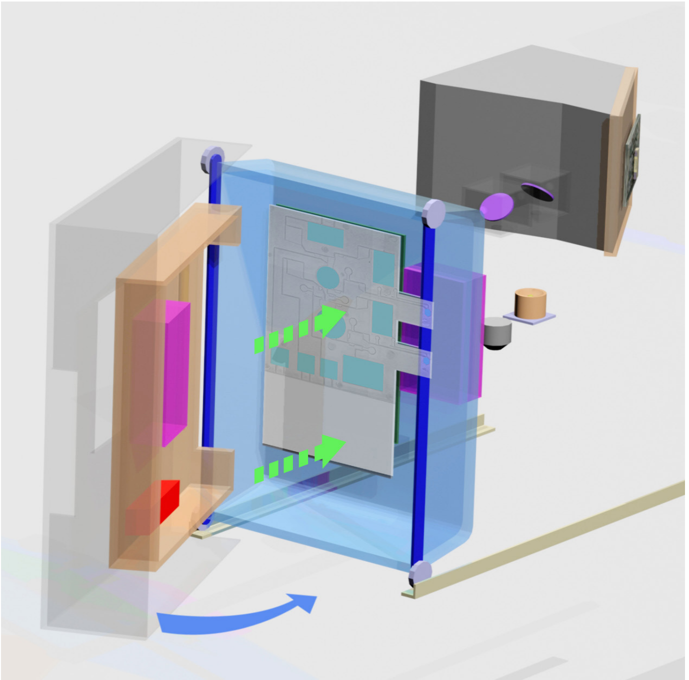
Step 1



Step 2



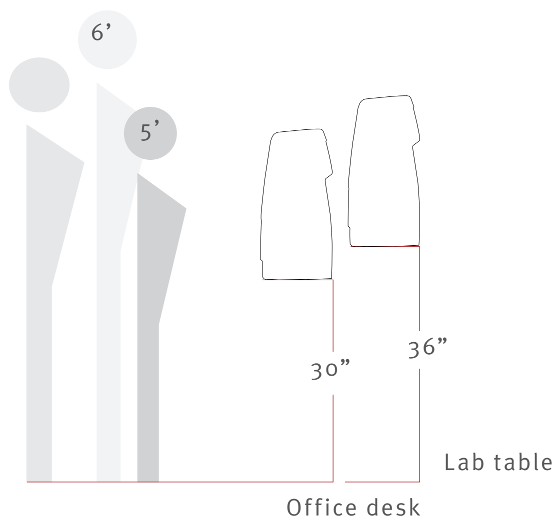
Step 3: Note the change in the reflective mirrors to direct the laser into the spectrometer.

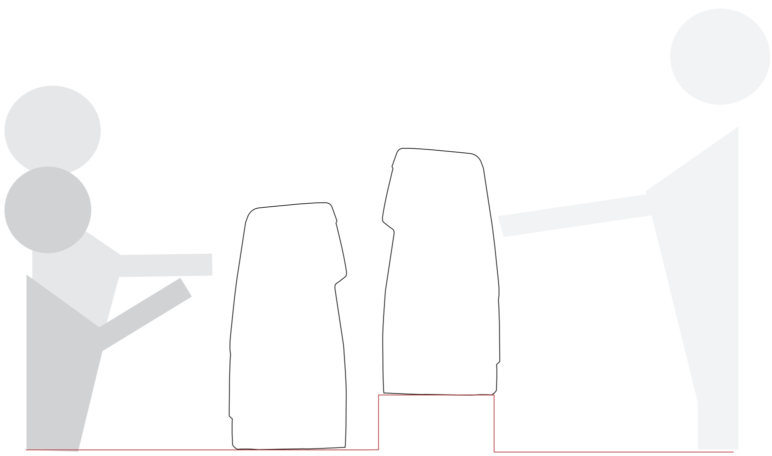


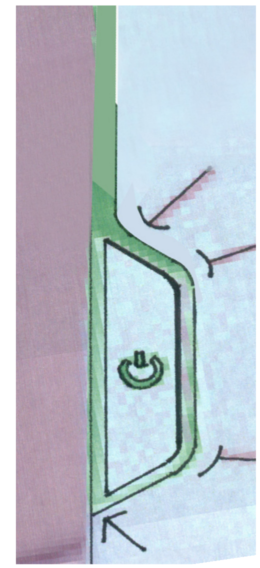
Front view

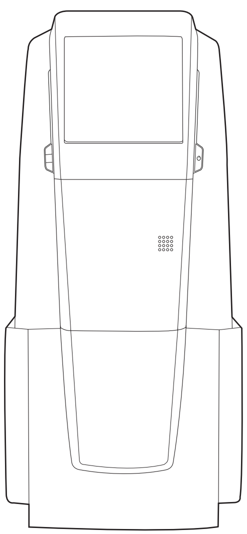
Final Design

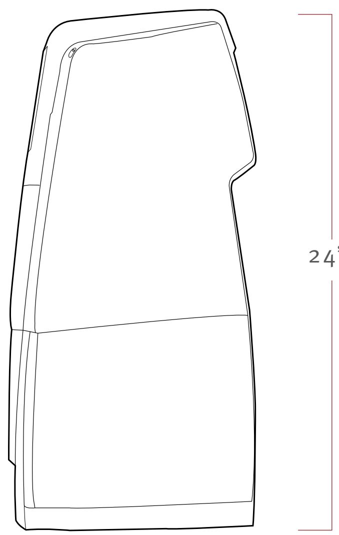
Device being used on a lab (HT36”) bench and an office desk (HT30”)

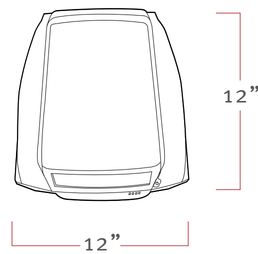


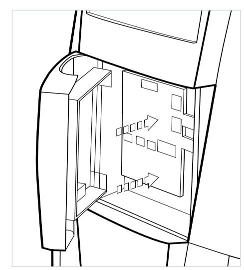


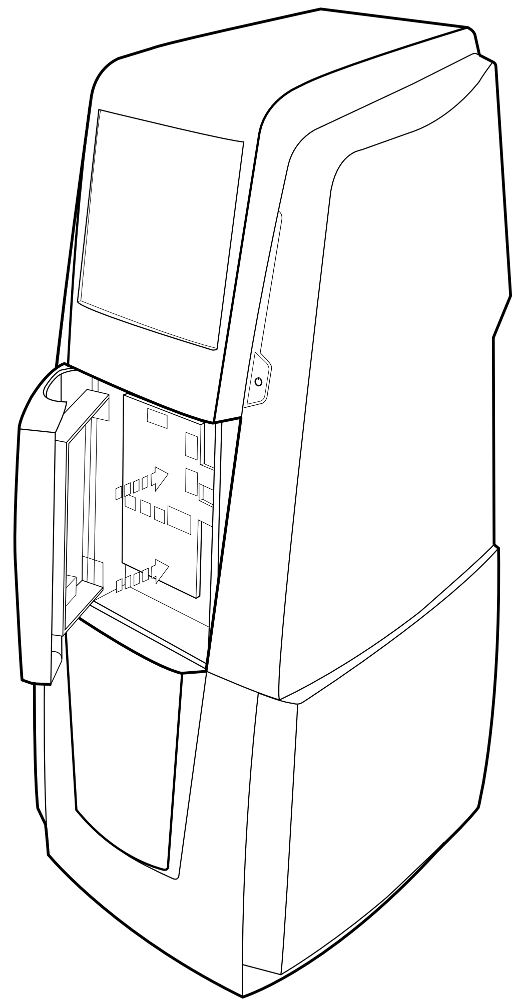






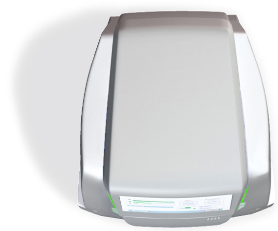


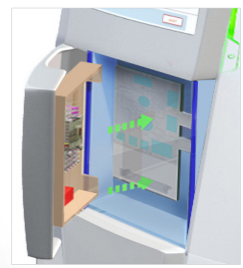




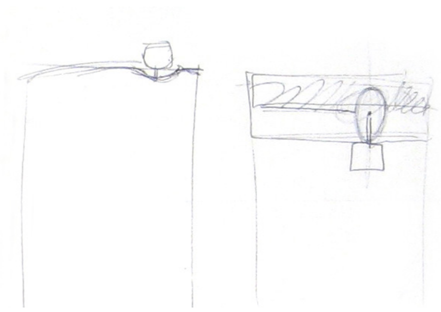
1 | 2 | 3/4 | 5

1. Front view
2. Side Profile
3. Top view
4. View showing the placement of integrated cartridge
5. A view showing the loading of integrated cartridge into the device





Sketches

1


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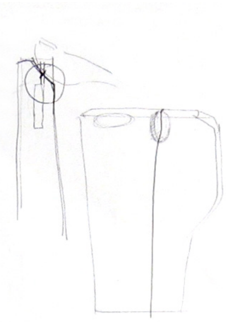

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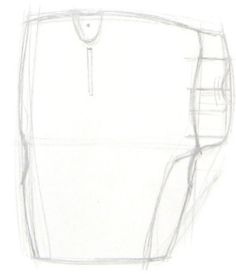

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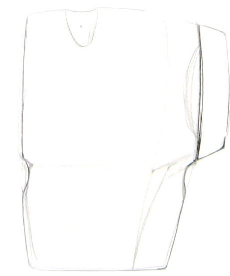

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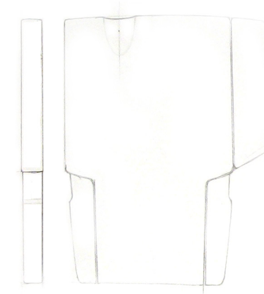

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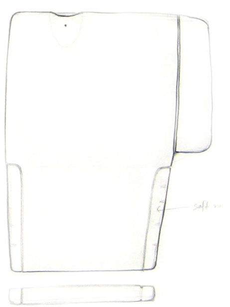

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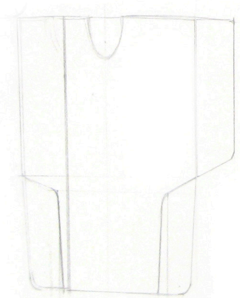

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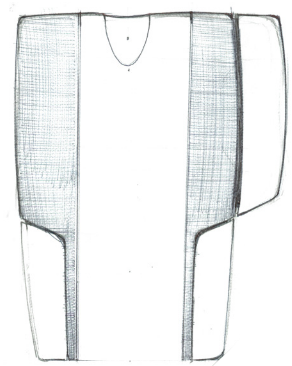
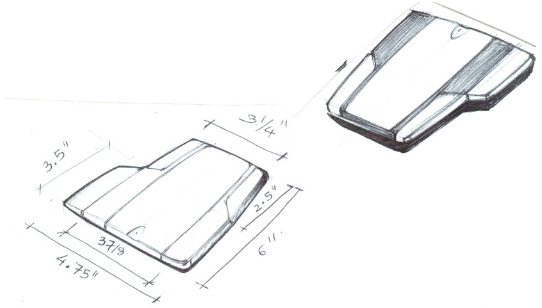
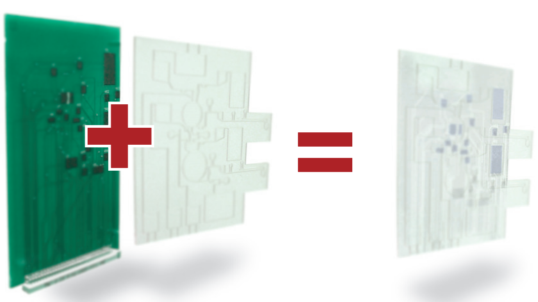




Mock-ups

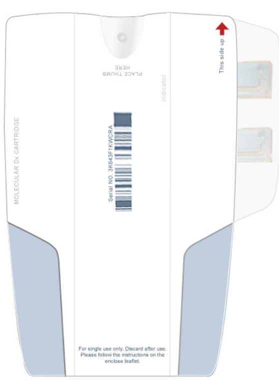
Rear view showing CE connectors



In the future, the circuit board would be printed directly on the plastic cartridge, further reducing the thickness of the overall media

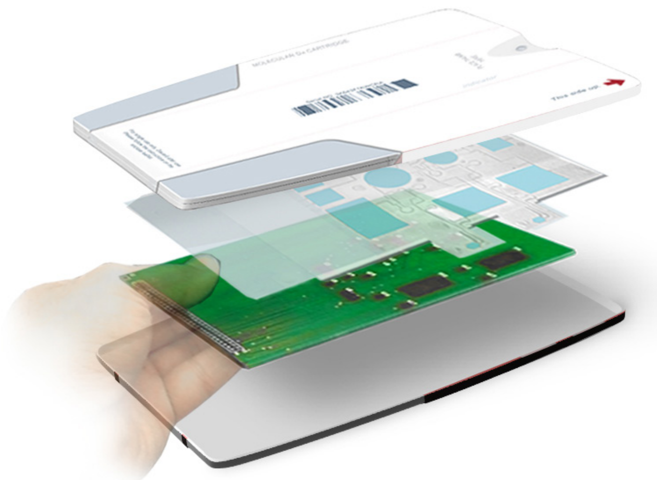
Integrated cartridge
Molecular Profiling Media

Top view

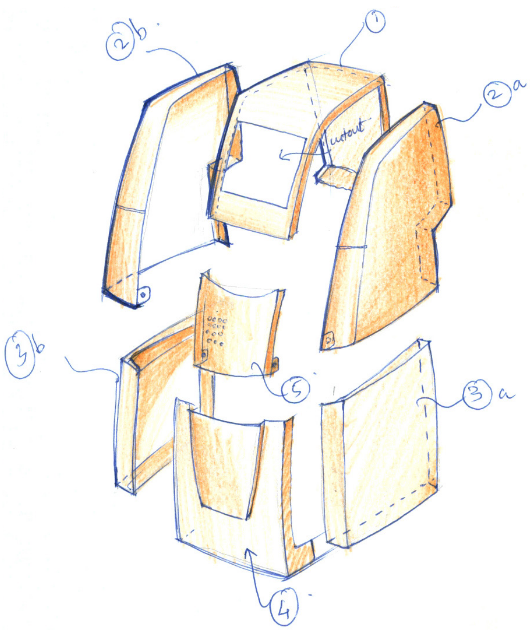


Front view

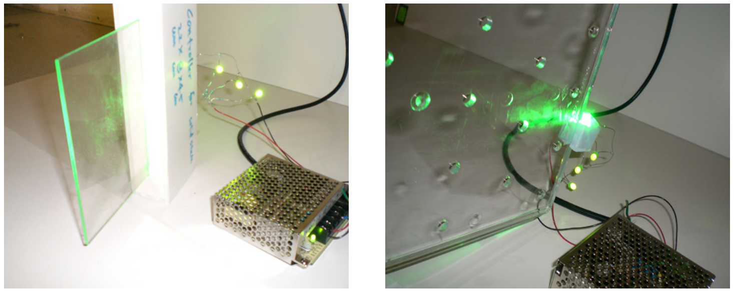
Rear view



Exploded view : Micro-machined cartridge for differential extraction/PCR and printed circuit board for actuation of integrated device

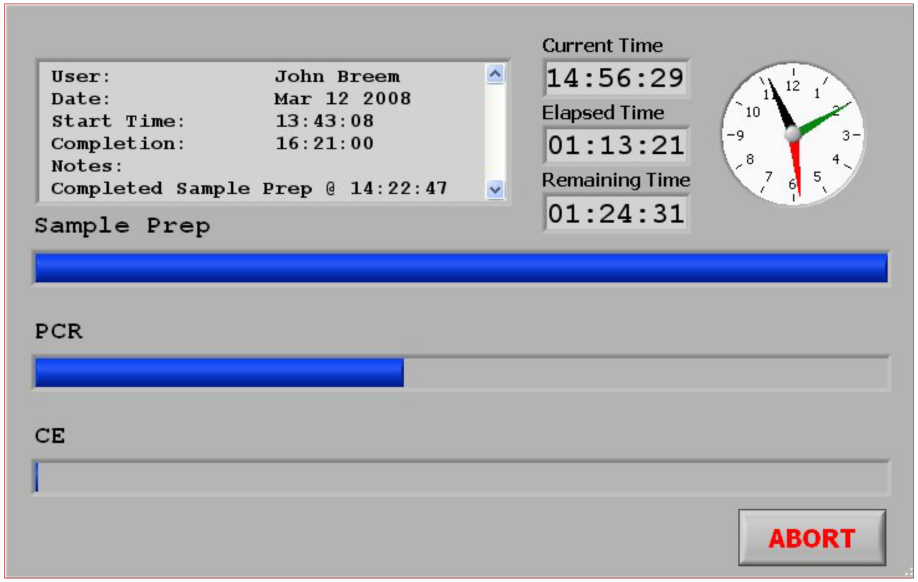


Building the model using SLA rapid prototyping

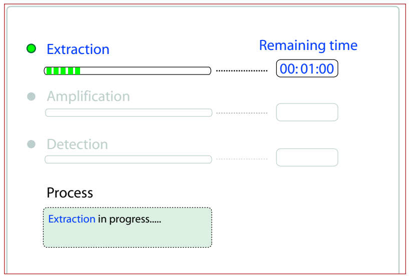


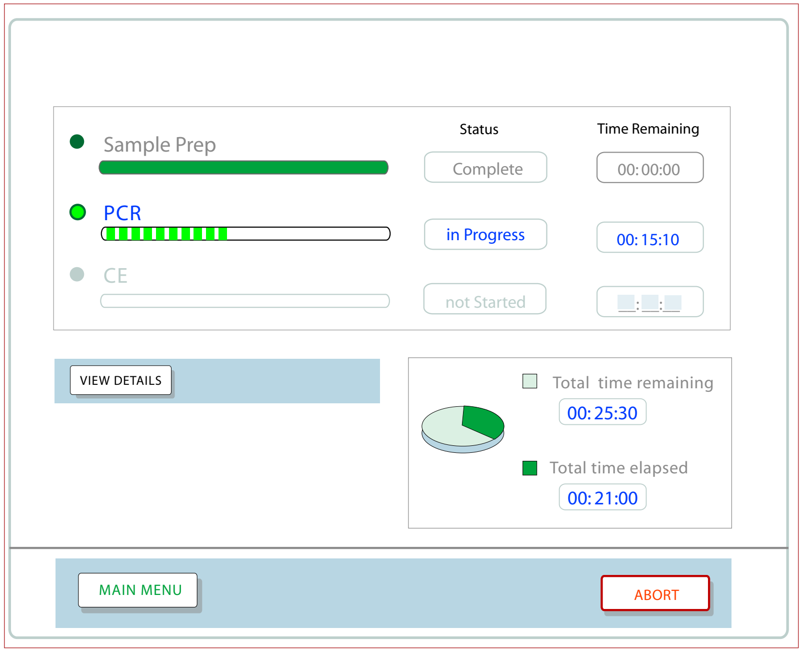
Lighting study

Final Prototype



Initial interface using Lab View software.

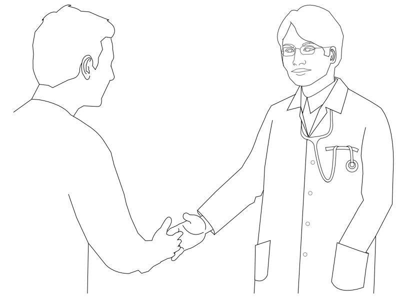




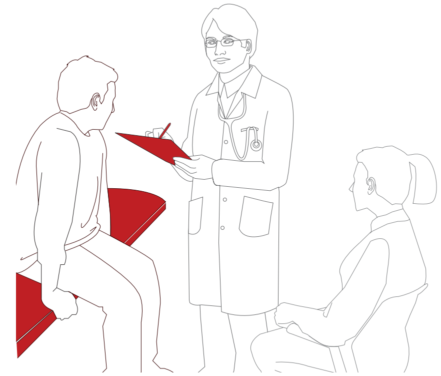
Proposed Touch Screen Interface

Future Scenario I

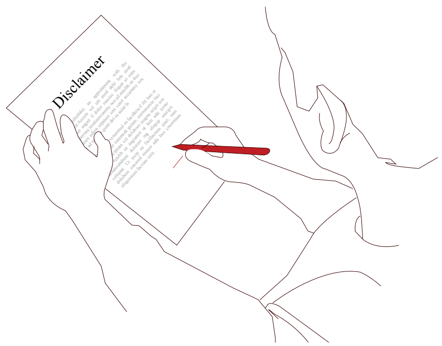
Patient schedules an appointment with the oncologist.



Patient at the oncologist's clinic.

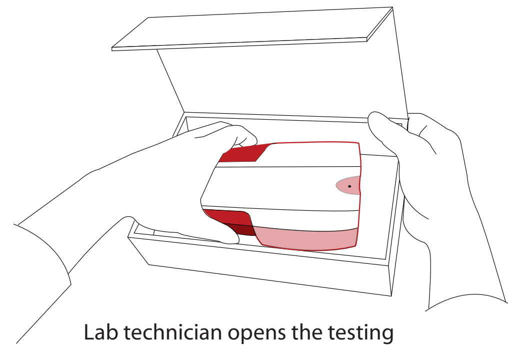


Doctor recommends Profiling.

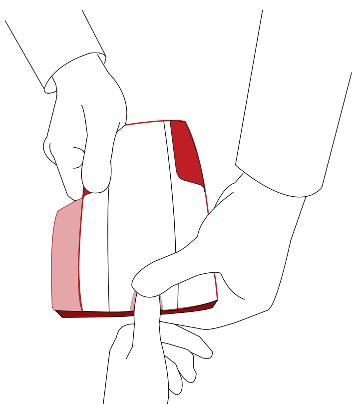


Patient signs Disclaimer.

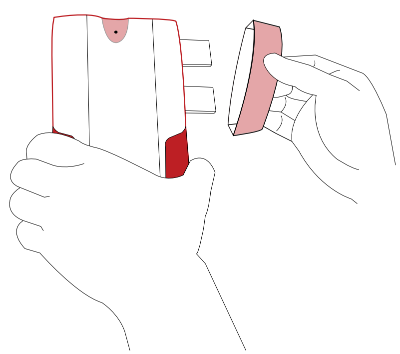
Doctor directs patient to the lab next door.



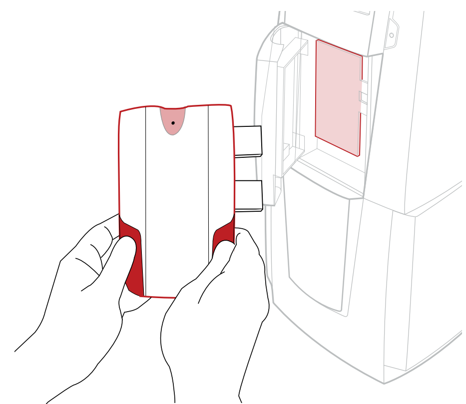
Lab technician opens the testing cartridge package.



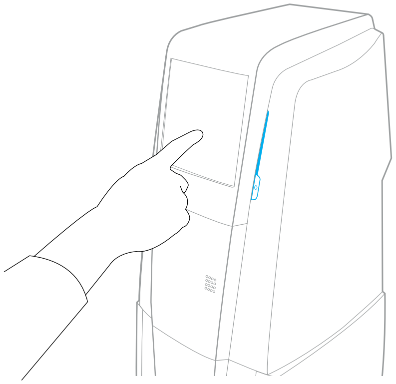
Draw blood.



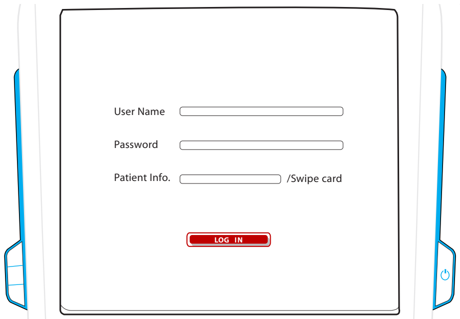
Remove the cap.



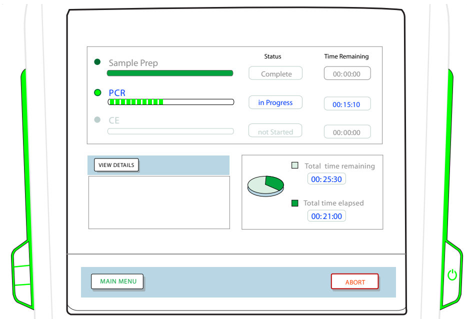
Place cartridge in the device..



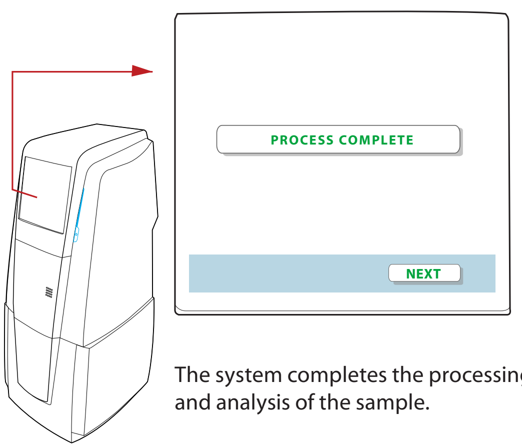
Close shutter.



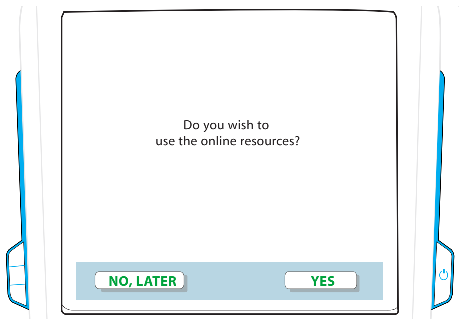
Follow instructions on the touch screen.

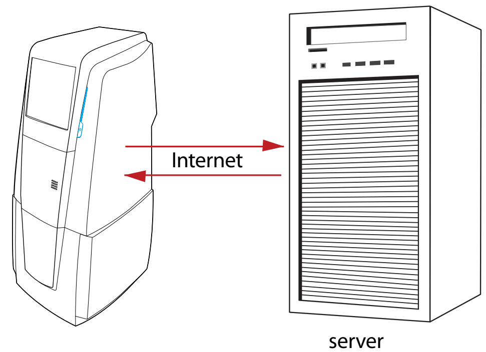


Status displayed on the touch screen.

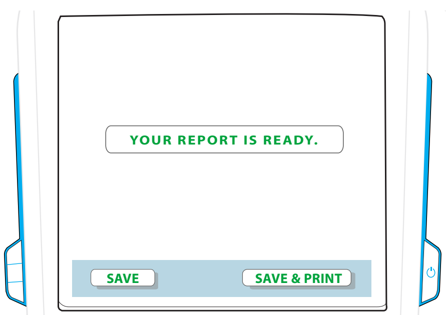


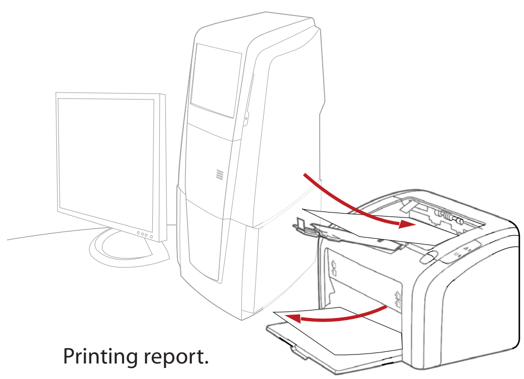
The system completes the processing and analysis of the sample.





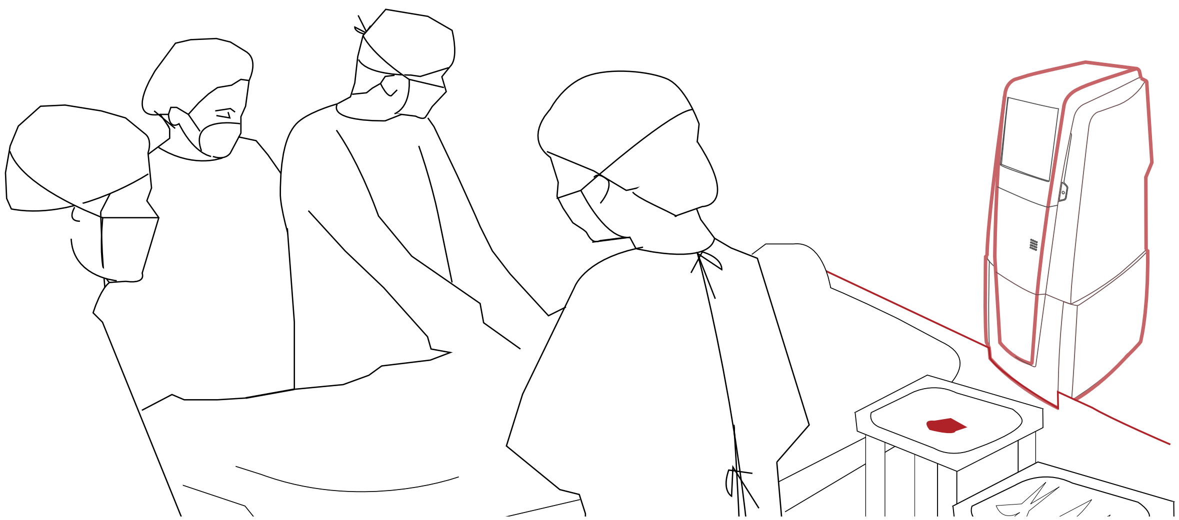
Device accesses a remote database via internet.



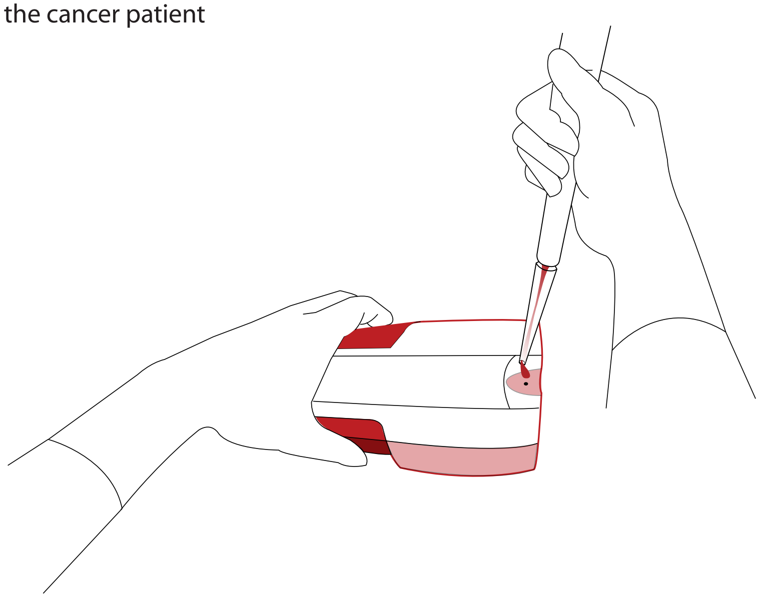


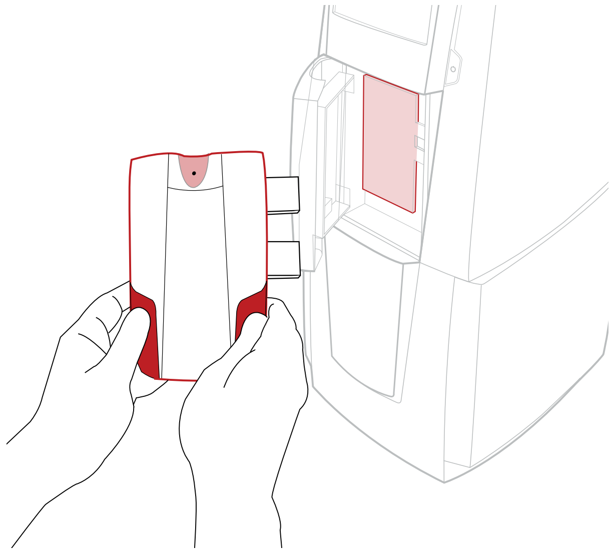
Printing report.

Future Scenario II



Oncologist obtains a tumor specimen from the cancer patient





It can revolutionized cancer diagnostics at the clinical level by providing a very powerful table top device that not only analyses a sample from a cancer patient but also has the capability to compare the results via internet with a central database.
It would enable the provision of the latest and the best testing for cancer patients to a wider patient base.

The device would not only be a tool to analyze the blood sample for cancer tests but also access the central database that would contain billions of data points generated by genetic research.

The income from the sale of the devices and sponsorship would be utilized into future research for better and cost effective platforms for Molecular cancer diagnosis.

This system would facilitate spread of molecular diagnostics in the emerging markets.

This system would be a gateway for emerging markets to participate in the Cancer Molecular Diagnostics. Enabling platform for “GLOBAL HEALTH APPLICATIONS”.

It would foster research collaborations, such as computational analyses of how genes are expressed during various stages of cancer.