



Recipes for 3D experience improvement

Handbook for medical and industrial
– crafts school VET practitioners





E-learning. Credits:

<https://www.cae.net/top-10-e-learning-trends-for-languages-in-2019-ii/>

3D and Virtual Reality Technologies for VET“. Project Reference: 2019-1-HR01-KA202-061006 is an Erasmus + program funded project within key action „Cooperation for innovation and the exchange of good practices“. Action type is Strategic Partnerships for vocational education and training. Total project duration is two years.

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Why are new technologies and ***3D and VR for VET project*** important for the medical and industrial-craft school?

In the 21st century, the development of new technologies has advanced so much that it offers us almost countless opportunities, from entertainment, work to help with everyday tasks. 3D, VR technology and artificial intelligence have also evolved to such an extent that somewhere they can replace the human factor, which can scare people (job loss due to replacing the human factor with a machine), but the truth is that everyone should have enough knowledge about new technologies and take advantage of them to help us, not to replace us.

The best example of how new technology can help us and how important they are is their application in medicine. Specifically, in the teaching of medicine since high school days. In addition to lectures and textbooks, practice is a key factor for the medical profession. But the period spent in exercises at school and in practice in the hospital can rarely prepare students for what awaits them when they are employed because it is simply impossible to go through all the situations that can happen.

Therefore, new technologies fit perfectly into their school curriculum to provide everyone with equal conditions of practice and equal knowledge, and to bring them significantly closer to the various situations in which they may find themselves (eg surgeries, emergency room admissions, home visits, etc.). Knowledge which they would get would increase their value, and at the same time make learning especially interesting and attractive, which I believe would contribute to the additional motivation of the students themselves. It is worth mentioning at the time of the pandemic when the practice is disabled or very limited how much this way of learning would help students.

Also, the industrial - craft school could make multiple use of new technologies by implementing them in its curriculum. Similar to medical school, they can use new technologies to help them learn and practice, but on the other hand, knowing how it works in some

professions could certainly help in terms of development and improvement of new technologies and their implementation in their school and elsewhere.

In both schools for better acquisition of new knowledge and skills in new technologies the best way is to create specialized education modules which will combine self-paced learning online with practical exercises offline. This project will develop a prototype learning system that can evolve rapidly, and the universality of application would easily ensure the exchange of expertise, experience and good practice with partner organizations in Croatia and abroad. Furthermore, another great value of this project is that it will pay special attention to designing suitable materials for blind and visually impaired people as well as people with physical disabilities.

We all shy away from the unknown and many people have an aversion to learning new technologies and new things in life in general (what we know is the safest), but those who love to learn should work hard to raise awareness of the importance of lifelong learning and the possibilities it opens up to us, and to show by example how much wealth on all levels can bring us coming out of our comfort zone.

Striving for better technology education
for VET students – the motto of 3D and VR
for VET consortium
- - - - X

“

When we listen with the ear of our heart (full
body listening), we experience our prophetic
nature and share our messages with the world.

-Vanessa F. Hurst

Research is creating new knowledge.

-Neil Armstrong

”

Scope of this handbook

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The special focus of this handbook is on the target audience of vocational educational areas.

The main objective of the project is the dissemination of knowledge to the pupils, students, professors and other enthusiasts in the field of new trending technologies of CAD modeling, 3D printing, and Virtual reality. In table 1 a short description of intellectual outputs are presented.



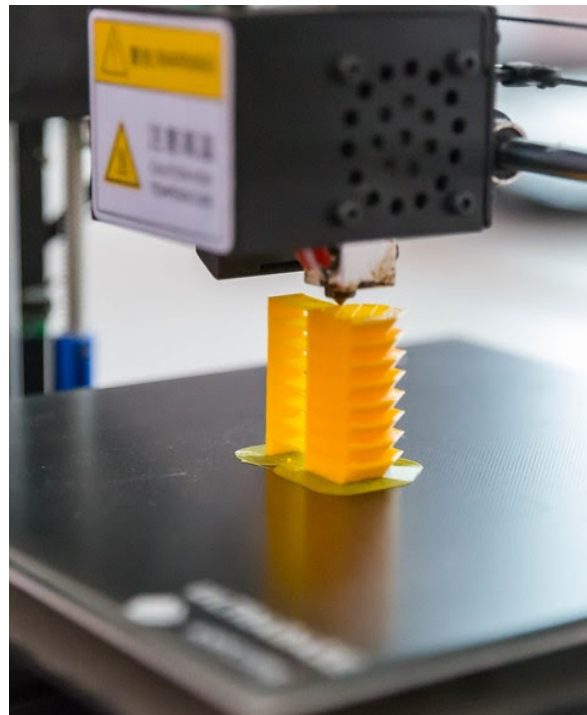
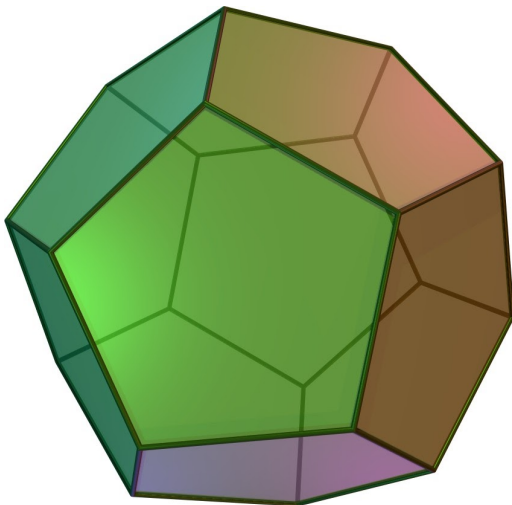
Teacher. Credits:

<https://elements.envato.com/young-happy-female-teacher-with-arms-crossed-stand>
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Table

Overview of the Intellectual outputs		
	Output title	Category of staff
01	Recipes for 3D experience improvement	Teachers/Trainers/Rese archers
02	Open, online, digital education - E-learning course/module - Guidelines for 3D and VR experience	Teachers/Trainers/Rese archers

Materials described in this handbook can provide an extensive source of structured information for Vocational education and training activities.



3D printing model. Credits:
<https://www.mime.asia/how-3d-printing-in-indonesia-will-start-working/>

CONTRIBUTION: 3D and VR for VET Erasmus+ project consortium



University Juraj Dobrila, Pula, Croatia

University of Pula started its mission in 2006, but it includes entities that exist from the 1960s. It is organized into several constituent departments based on the principle of integrated structure. It has 240 staff in total and 3,600 students enrolled. Located in a 3,000 years old town situated in the South of Istria, the most evolved region in Croatia and with a distinct cultural diversity due to its geographical position and historical heritage.

The University is made up of departments, faculties and an academy: Faculty of Economics and Tourism, Faculty of Educational Sciences, Faculty of Humanities covers the entire spectrum of history, classical and roman philology, Croatian, Italian and Asian studies, Faculty of Interdisciplinary, Italian and Cultural Studies, Academy of Music, Faculty of Informatics, Department of Natural Sciences and Health Studies and Department of Engineering. The university offers two undergraduate studies in Marine science and Nursing program and doctoral study in social sciences.

Institute for Science and Technology VISIO was founded in 2008. as a scientific part of Juraj Dobrila University of Pula. Main goals are developing of science and technology, professional work, analyses, expertise and research & development projects in the area of social, humanistic, natural, technical, biotechnical sciences, biomedicine and health, arts, the interdisciplinary field of science and the interdisciplinary field of art. Institute is aiming to raise a new generation of potential scientists and researchers. VISIO presents the technology of 3D printing and 3D printed microscopes, made in the

VISI0 laboratory. Invested efforts and pure love for science have already been rewarded with numerous national and international awards, proving the significance of this initiative. Principle is Assoc. Prof. Sven Maričić.

Industrijsko-obrtnička

škola Pula

Industrial-crafts high school, Pula, Croatia

Industrial Craft School Pula is a vocational, education and training school which educates students between the ages of 15 and 18 in the field of the electrical, civil and mechanical engineering and shipbuilding industry. School has 180 students, 30 teachers and 15 other staff. All teachers have a university education and many of them have industrial experience as engineers, project managers and supervisors from work in industry and construction.

As a lower vocational secondary school in dual system of education the school gained rich experience with organizing workplaces for its students in industry, companies, services and other organizations in a real work sector. School's main goal is to provide work-based learning based on its long-time experience.

Industrial Craft School Pula offers adult education in vocational curriculums. Adults can acquire a diploma and additional vocation when they are unemployed, to upgrade their knowledge with new skills, competences and knowledge needed in today's working environment.



Medical high school, Pula, Croatia

Medical School Pula has been operating since 1956 and has 48 employees. It educates students in three educational programs, namely nurse, physiotherapy technician and midwife. The school teaches 260 students in 11 classes.

Every year, the school participates with its projects in national meetings of health schools in the Republic of Croatia and the Istrian region under the auspices of the Agency for Vocational and Adult Education and SEMEP.

Medical School Pula is the holder of two projects in the Istrian region of health. School cooperates and implements activities with various associations such as: League Against Cancer, Istrian Dystrophic Society, Association of Blind and Visually Impaired People of Istria, Association of the Deaf and People Listening to Istria, Croatian Red Cross and Shelter for the homeless, homes for the elderly and infirm “Alfredo Stiglic” and “Sveti polikarp”, home for mentally ill adults “Vila Marija” and Children’s Home “Ruža Petrović”. Medical School Pula participates in professional conferences at the inter-county and state level where we present our results.

The school is working on several locations, and the construction of a new school building is being prepared, which would enable better working conditions, and through the mobility of students and teachers, the acquisition of new knowledge and skills to internationalize them would be ensured.

Previous experiences of the school in project activities:

The school was a partner in the project Improving school curricula with the aim of promoting a healthy lifestyle (Grant scheme: Modernization of school programs in vocational schools in accordance with the changing needs of the labor market / economy 2012-2014), and is currently a partner in the project “DROP-APP: give a voice to young people through new technologies to combat school drop-out!”, 2014-2017 within the Erasmus + program, Key Activity 2.

The school was also the holder of an international project entitled “Health Literacy for Independent Living”, 2018-2019 under the Erasmus + program, Key Activity 2. The project aims to develop health literacy as a key factor in disease prevention and health promotion in a functional, interactive and a critical level in students and target age groups.

Holder of the Erasmus + project, key activity 1 “Health care and rehabilitation in gerontology and palliative care” 2016-2017, 2016-1-HR01-KA102-021848. Project activities within this project relate to the mobility of students studying general care nurse – general care medical technician and physiotherapeutic technician-physiotherapeutic technician in Dublin, Ireland, which will be implemented in the period from 01.04.2017. to 15.04.2017. accompanied by two vocational teachers. During the mobility, students will do 80 hours of practical work in retirement homes.

The school has experience in projects as a partner and project holder. Through mobility projects KA1 wants to strengthen its ability to implement projects and raise school quality, but primarily to take the opportunity to provide its students with internships abroad to improve their secondary education and become more competitive in the post-secondary labor market.



Mediterranean institute for life sciences, Split, Croatia

The Mediterranean Institute for Life Sciences (MedILS) is a private and independently funded, international, non-profit research institute. Led by enthusiastic professionals, MedILS strives to create and sustain a top-quality research environment for international and local exceptional scientists. The research interest of MedILS primarily focuses on developing highly original, multidisciplinary approaches designed to provide novel insights into the fundamental concepts of the molecular biology of aging and age-related diseases. As a leading research institution in Croatia, MedILS employs 30 international and Croatian researchers. Research at MedILS is based on the scientific concept and project of Prof. Miroslav Radman with the focus on molecular bases of aging, mutation, cellular death and diseases caused by aging, and the role of cellular communication in health and disease. The primary scientific goal of MedILS is the

improvement of public health through the detection and development of targeted prevention of prevalent diseases, new diagnostic methods, and treatment of age-associated diseases, engaging in original biomedical research in the field of the biology of aging and age-associated diseases including carcinoma. The basic concept is that aging is not a disease but the cause of all age-associated diseases.

Apart from research activities, MedILS also organizes various scientific events with the goal of promoting science and the dissemination of new knowledge and research results of the scientists at MedILS, as well as a partner, domestic and international institutions.

MedILS has an experienced management team which currently manages 4 EU projects and 2 privately funded projects. Successful management of the CACAO project will be based on that experience, and in particular on the coordination of PROMISE (Personalized Medicine Inquiry-Based), Erasmus+ project, 2019-1-HR01-KA203-061010.



Technical University, Cluj-Napoca, Romania

The Technical University of Cluj-Napoca, which is an “Advanced Research and Education University” comprises twelve faculties in the two academic centers, Cluj-Napoca and Baia-Mare, as well as in locations, such as Alba-Iulia, Bistrita, Satu Mare and Zalau. The educational offer, aligned to the Bologna system, includes bachelor’s, master’s and doctoral programs, as well as continuous training programs. The study programs are conducted in Romanian, but also in international languages, respectively English, German and French.

The University offers over 205 bachelor and master degree programs, at the faculties from Cluj-Napoca, being concerned also with the international exchange of scientific values, and this trend is found in the over 400 inter-university collaboration agreements or in the

large number of students mobilities. Opening up towards the European and world space of education and research through a steady process of internationalization is one of the major objectives of the university.

Research is, along with education, the main priority of the Technical University of Cluj-Napoca. In all faculties of the university there are research structures, from collectives, groups and laboratories, to research centers and platforms. The performance anchored in the socio-economic environment, the international visibility and cooperation as well as the scientific novelty and interdisciplinary are some of the characteristics of the research environment of the Technical University of Cluj-Napoca. Open research directions are oriented towards global priorities and perspectives: from the Information and communications technology to Renewable Energy and Ecology; from superconductivity, spintronics and nanomaterials, to management, 3D printing and robotics; from manufacturing to electrical engineering, to the automotive and the home of the future, or to urbanism and society.



University of South-Eastern Norway, Norway

USN was established on 1 January 2016, when Buskerud and Vestfold University College merged with Telemark University College. It has approximately 18,000 students and 1,600 staff, spread over eight campuses: Drammen, Vestfold, Kongsberg, Ringerike, Bø, Notodden, Porsgrunn and Rauland. Aiming to have a regional foundation, and with eight campuses, the USN has a strong presence in one of Norway's most exciting and dynamic industrial regions.

Faculty of Technology, Natural Sciences and Maritime Sciences (TNM) is located in Kongsberg Campus, and offers bachelor's and master's degrees in a variety of disciplines, including engineering, science, and maritime studies, as well as four doctoral programs. Campus Kongsberg is located within the Krona Knowledge and Cultural Centre of Kongsberg and in close vicinity to several of Norway's leading

technology companies within the armaments industry, aviation and shipping as well as the oil and gas industry.

InSciEd *Tamara Milosevic, Paris, France*

Tamara Milosevic holds a Ph.D. in biology, and has done interdisciplinary life science research, as well as educational research, delivered as papers, conference talks and posters. She is a founder and a director of her micro-enterprise (auto-entrepreneur), registered in France as an SME since 2015. As an independent consultant in pedagogical innovation, she specializes in higher education and life-long learning. Her primary activity is helping higher education institutions transform their curricula to meet the needs of the 21st century learners, through student-focused active learning and interdisciplinary project-based learning. Her engagement with teaching teams helps them deliver the training that increases the acquisition of disciplinary and transversal skills of learners, thus helping them meet the needs of the 21st century job market. Her approach consists of advising educational leaders on the choice and variation of online, offline and blended learning modules, pedagogical support to teaching teams to implement experiential learning in their classrooms, as well as support to evaluate the impact of pedagogical innovation and disseminate the results locally and globally, via conferences and articles. In addition, she provides “train the trainers” programs on all levels, creating adapted intensive workshops to train the educators in active learning methods, use of technology in the classroom, alternative assessment methods (self- and peer-evaluations), implementing project-based learning, and designing coherent curricula.

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New technologies in vocational education

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The essential keyword

→ **VOCATIONAL EDUCATION** = [education that prepares people to work as a technician or to take up employment in a skilled craft]

Sometimes living our lives we forget about how vocational education is important and the fact that without it our world would be completely different. Often we even think that it is less worth compared to other educations and that's a shame. Nevertheless we can all do something about it and emphasise the importance of vocational education, especially through projects like **3D and Virtual Reality Technologies for VET**.

New technologies such as 3D printing, VR and artificial intelligence are developing every moment and if we make the effort to learn about them and implement them in our everyday life we will certainly have a lot of benefits. Developing special education modules which will consist of blended learning online self-paced and offline in practical training along with educating teachers is a great opportunity to include them in curriculums of Medical, Industrial - crafts schools and other institutions that teach vocal education.

Collaboration with many other schools, universities, institutions and partners will give a huge contribution to the project and through experience exchange there will always be a new look on the project goals.

Take home messages

- **Idea 1** is that vocational education is irreplaceable.
 - **Idea 2** is that new technologies give us new ways of learning.
 - **Idea 3** is that power lies in collaboration.
-

MODULE 1

UNIT 1 Basic information, introduction to new technologies in vocational education - - - - X

The essential keywords

- **CUSTOMIZE** = [to make or change something according to the buyer's or user's needs]
- **LEARNING** = [the activity of obtaining knowledge]

On the modul 1 of this handbook an overview will be made of the new and trending technologies used in today's world in the field of mechanical and computer engineering. We will look at leading companies in their fields and modern production production. Being able to identify and to implement new technologies that are changing the way products are being manufactured or presented will put students at a significant advantage in the work market.

The emerging manufacturing process of 3D printing in the field of additive manufacturing is a must know for students of technical schools and universities. 3D printers are a type of industrial robot that are changing the way products are being prototyped and customized for every single customer. Therefore 3D printers can be considered as the leaders of the mass customization era.

As the leading tool for high precision and mass production manufacturing processes, CAD and CAM softwares will be elaborated and explained.

The world of robotics and automated systems is changing mass production, by being able to perform the required tasks quicker, better and more reliably than humans.

Virtual reality (VR) and artificial reality (AR) are not changing the way companies can present their products, but are also enabling students and workers to learn new skills in a safe virtual environment without the need of expensive equipment.

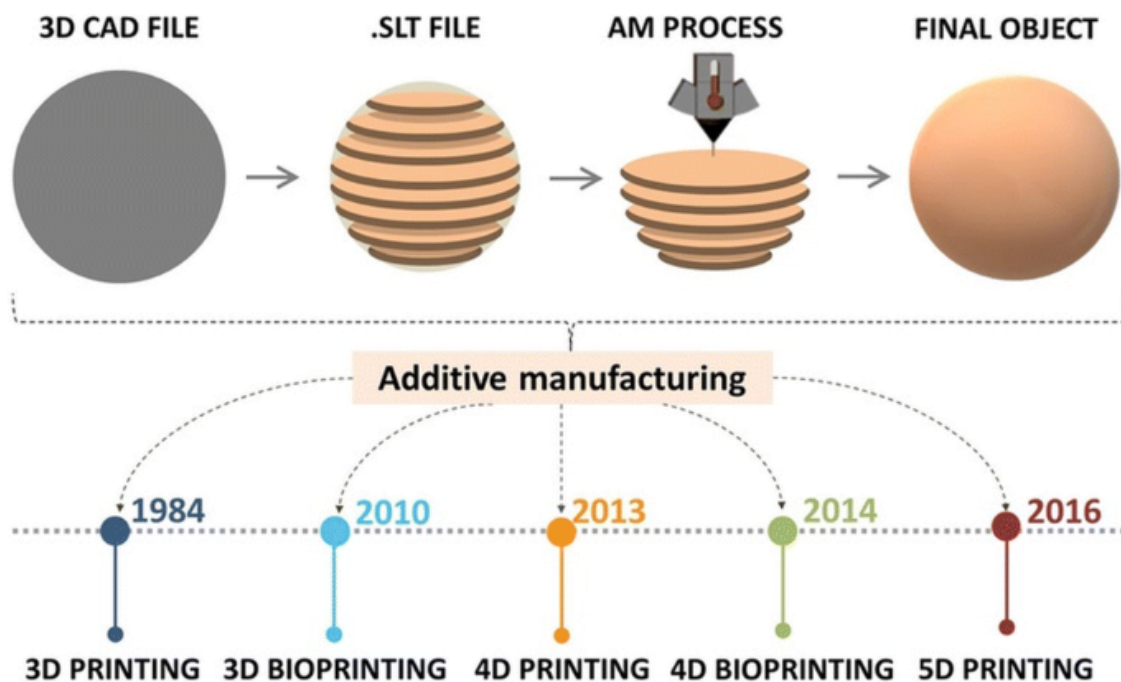
UNIT 2 Additive technologies in professional design practice

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The essential keywords

- **A.M.** = [Additive manufacturing]
- **3DP** = [3D print]
- **STL** = [file format]

3D printing or additive manufacturing (A.M.) technology is a way to create objects directly from a digital file. Unlike conventional processing methods that remove material in order to reach the desired shape, additive technologies apply the material layer by layer until the final shape of the product. The benefit of 3D printing is that it doesn't require expensive molds or long preparation in order to get started. Therefore 3D printing represents the easiest, cheapest and the fastest way to generate real life prototypes.



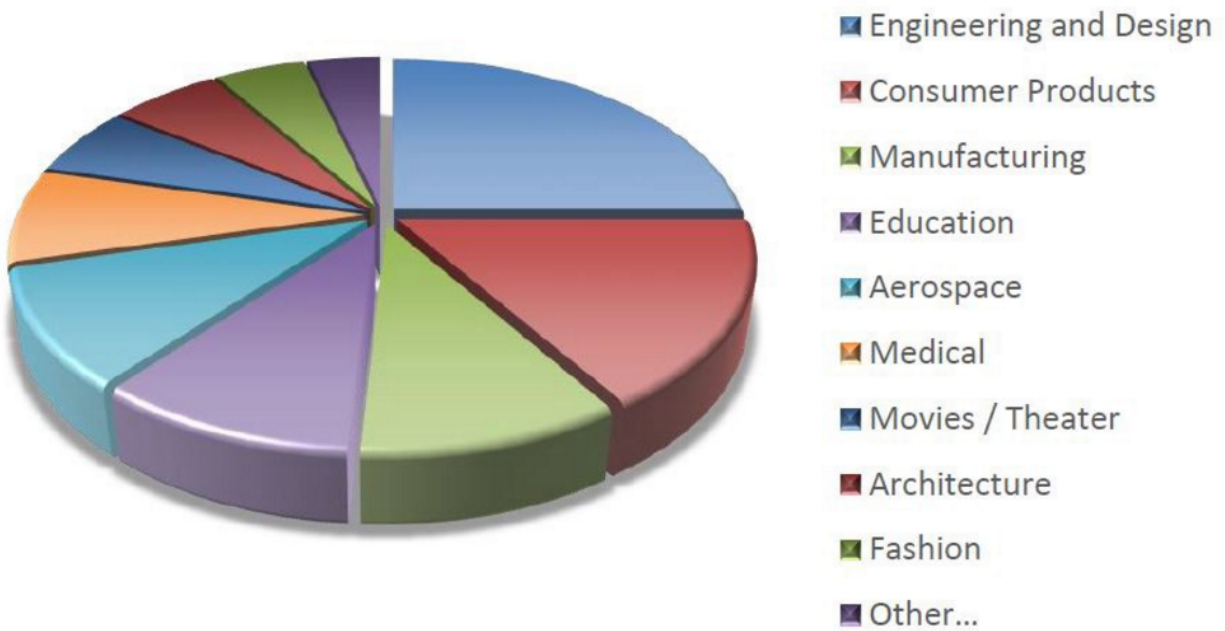
3D printing process. Credits: <https://doi.org/10.1007/s10924-020-01722-x>

An overview through the history of 3D print

- ❑ The beginning of 3d printing began in 1980 (Hideo Kodama - Nagoya Municipal Industrial Research Institute), with the first functional "Rapid-prototyping" system using photopolymers.
 - ❑ In 1984, Charles Hull invented stereolithography - which allows the computer to create 3D models, which can later be used to create a tangible object. Without stereolithography, 3D printing as we know it today wouldn't be possible.
 - ❑ 1990 Scott Crump developed Fused Deposition Modeling (FDM) technology, the most widely known form of 3D printing used mostly by hobbyists all over the world.
 - ❑ In 1999, scientists were able to develop an organ from a patient's stem cells with the support of 3D printing.
 - ❑ In 2002, the first miniature kidney was 3D printed.
 - ❑ 2005 - Reprap - 3D printers become available to the general public.
 - ❑ 2008 - Makerbot's Thingiverse - website for downloading free 3D CAD models.
 - ❑ 2011 - the first 3d printed car.
-

Application of 3D prints

- ☐ Prototyping
- ☐ Replacement parts
- ☐ Making parts of a complex geometric structure
- ☐ Industry
- ☐ Product personalization



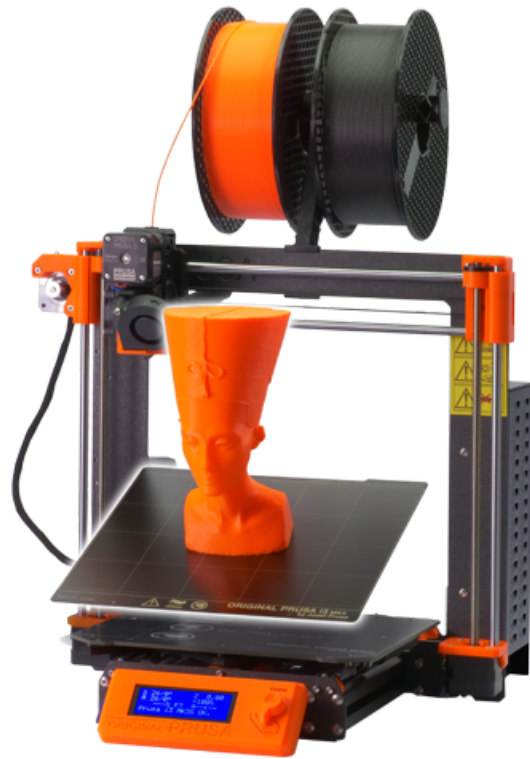
Application of 3d printing. Credits:

www.medium.com/autodesk-university/real-world-applications-of-3d-printing

Some of the 3D printing technologies

Fused Deposition Modeling (FDM)

The FDM 3D printing technology is the most widely used form of 3D printing throughout the world. The raw input material comes in the form of filament. This method of 3D printing is used mostly for creating plastic prototypes. The way it works is that the filament is extruded through the head of a 3D printer, which melts the filament at elevated temperatures. The melted filament is then pushed through the nozzle of the 3D printers head. The nozzles can vary in diameter. The most common nozzle is the one with 0,4 mm diameter. If the diameter of the nozzle is smaller, the quality and the details of the 3D printed part will be better, but the print time will be longer. Vice versa, if the nozzle is bigger the printer will be quicker, but the quality will drop. FDM represents a simple technology that can deliver high quality products.



*FDM 3D printer Prusa i3 mk3.
Credits: <https://www.prusa3d.com/>*

ADVANTAGES

- ☐ Low cost of printing
- ☐ Simple
- ☐ Accessible to the general public

DISADVANTAGES

- ☐ Limited dimensional precision
 - ☐ Visible lines of material layers
-



*SLA 3D printer Original Prusa SL1.
Credits: <https://www.prusa3d.com/>*

Stereolithography (SLA)

SLA is a form of 3D printing technology that creates a 3D object using UV rays and liquid photopolymer. The UV rays are used to cure and fix thin layers of the resin to achieve an unprecedented level of details. With this method high quality parts are produced down to the smallest detail. Layer resolution of 16 microns and precision of 0.1 mm can be reached. It also supports a wide range of materials, not just plastic. Stereolithography is ideal for making extremely precise parts, or parts where the emphasis is on details (eg making jewelry).

ADVANTAGES

- ☐ High precision
- ☐ Smooth surface
- ☐ Ability to print a large number of materials

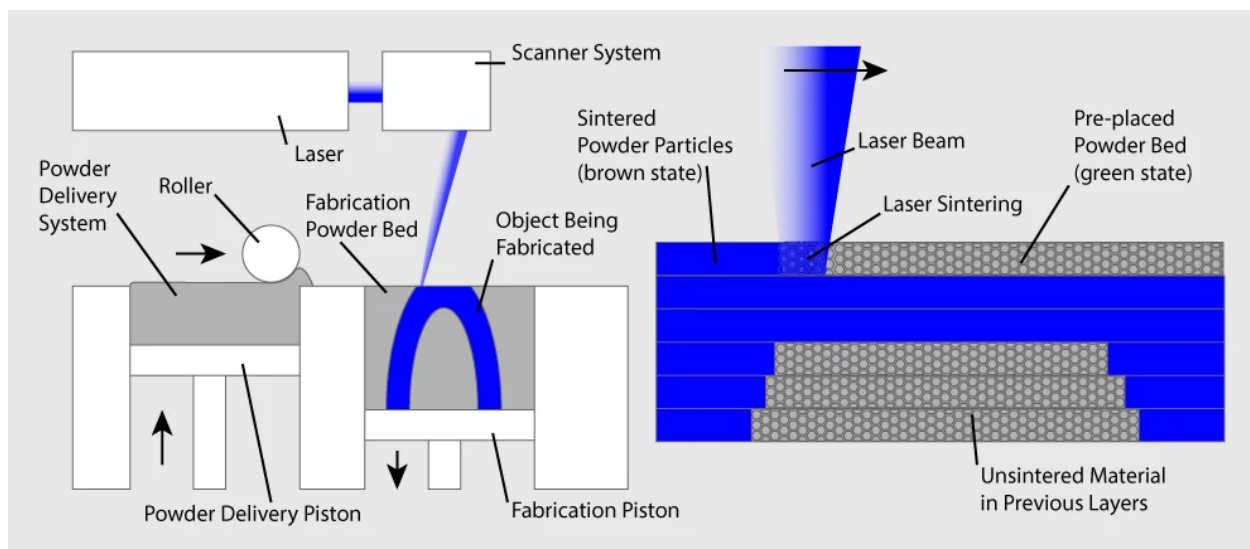
DISADVANTAGES

- ☐ Parts degrade if exposed to the sun for a long time
 - ☐ Relatively fragile parts
 - ☐ More expensive than FDM
-

Selective Laser Sintering (SLS)

The laser sintering material comes in powder form. The material is heated to a temperature slightly below the melting point. The powder is spread on the work surface (0.1 mm of powder per layer). The laser sinters the powder particles and they solidify. Some of the most popular materials used for creating 3D printed parts with this method are:

Nylon / TPU (elastomer) / Alloy of carbon fiber and nylon / PA 11



SLS 3D printing process.

Credits: <https://3dprinting.com/>

ADVANTAGES

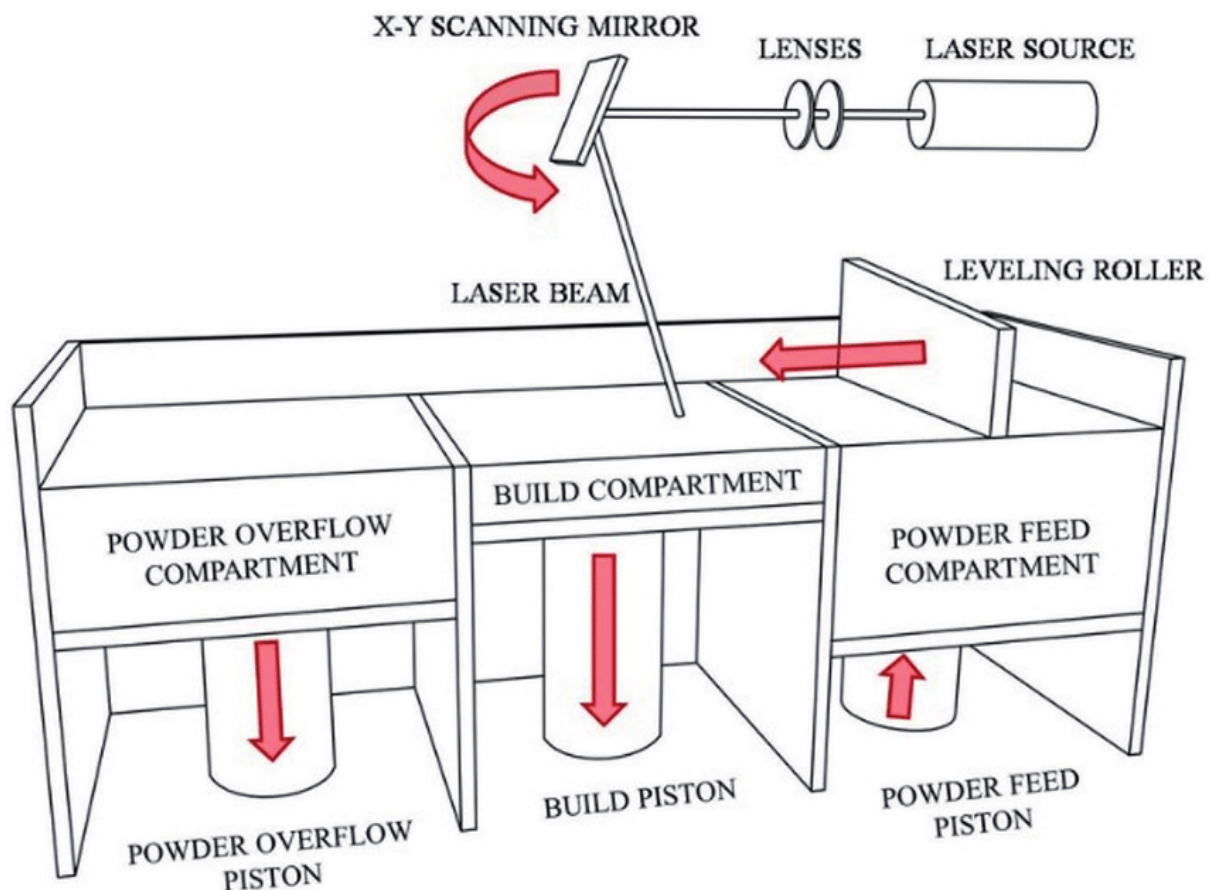
- ☐ Ideal for making functional prototypes.
- ☐ There is no need for support material in complex geometry.
- ☐ Possible production of smaller series (automation).

DISADVANTAGES

- ☐ More expensive than FDM and SLA.
- ☐ After each print, dust remains on the work surface and needs to be cleaned.

Direct Metal Laser Sintering & Selective Laser Melting (DMLS, SLM)

Both the DMLS and SLM methods produce parts similar to the SLS method. UV rays connect the particles layer by layer. The only difference is that these methods are used for the production of metal parts. SLM completely melts metal particles, while DMLS heats the metal powder to a level where the metal particles bond at the molecular level. Support is required for both DMLS and SLM, which is later removed mechanically or by a CNC machine.



DMLS & SLM 3D printing process.

Credits: DOI: 10.5772/intechopen.89804

https://www.researchgate.net/publication/337695042_Utilization_of_Additive_Manufacturing_to_Produce_Tools/stats

ADVANTAGES

- ❑ Manufacture of metal parts.
- ❑ Excellent mechanical properties of parts.

DISADVANTAGES

- ❑ Very expensive processing
- ❑ Specialized CAD software
- ❑ Limited workpiece volume

Take home messages

- **Idea 1** is that 3D printing represents the easiest, cheapest and the fastest way to generate real life prototypes
 - **Idea 2** is that you can choose between at least four different 3D printing technologies depending on your needs
 - **Idea 3** is that 3D printed models have a broad range of applications in life and work
-

UNIT 3 Examples of good practice in cross-sectoral cooperation in vocational education

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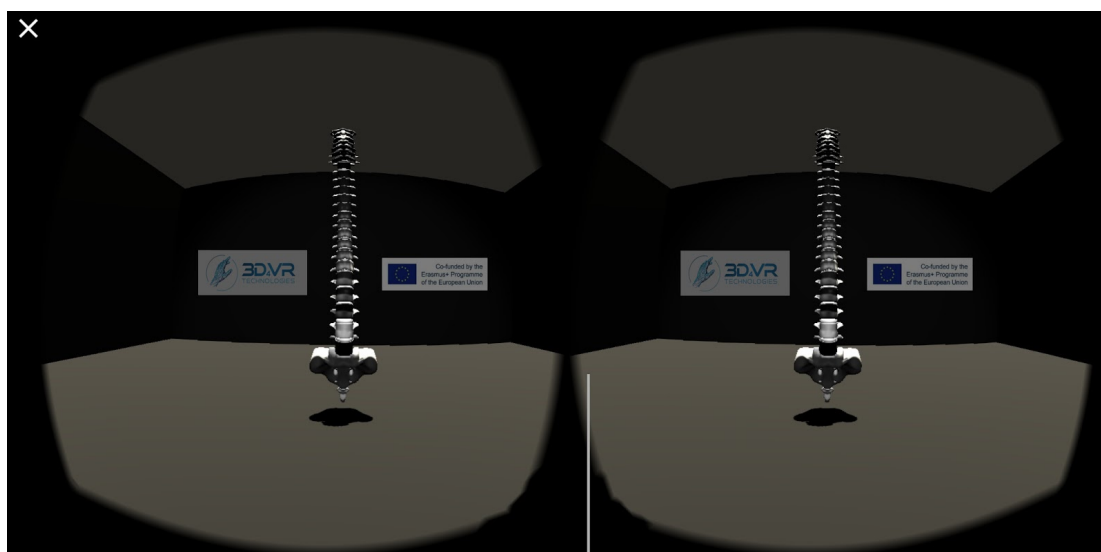
The essential keywords

→ **VR** = [Virtual reality]

→ **AI** = [Artificial intelligence]

Virtual reality (VR)

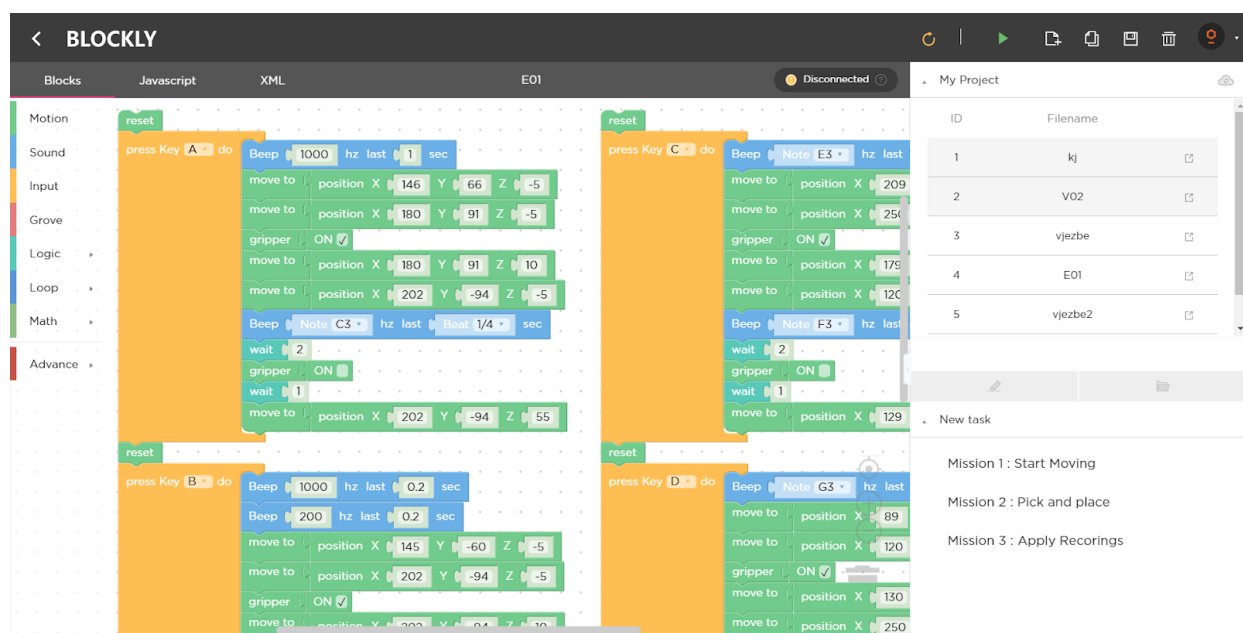
Virtual reality environment(s) could potentially help in order to gain better experience in the vocational system. For the purpose of the project, a special VR model environment has been developed. For the purpose of training, a spine model for Medical school was installed into mobile phones and laptops. By help of virtual glasses one can observe a spine model in an environment that hasn't been used in this school so far.



A VR environment for education.

Robotics and automation

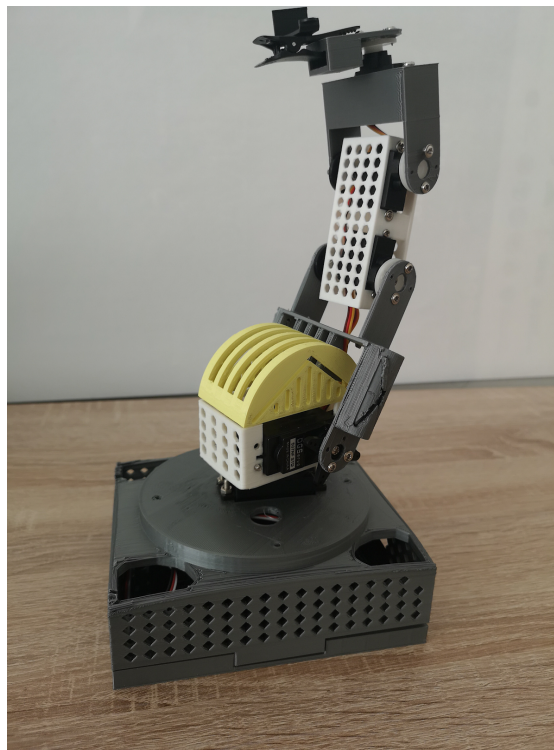
The field of robotics and automation covers a wide range of knowledge and skills, from electronics, mechatronics, CAD modeling, programming, construction, etc. There are different ways to control a robotic arm. There are some softwares that allows beginners to make their first steps in programming, automating and controlling the robotic arm. One of the softwares that is beginner friendly is called Bolcky, and it allows you to make the first steps into programming without any knowledge of the programming language. The commands are shown in a form of blocks that are attached to each other in order to interact with the robotic arm. The commands in the form of blocks are then converted in the programming language that is understandable for the robotic arm.



Programming the robot with Blockly

Additive technologies in robotics

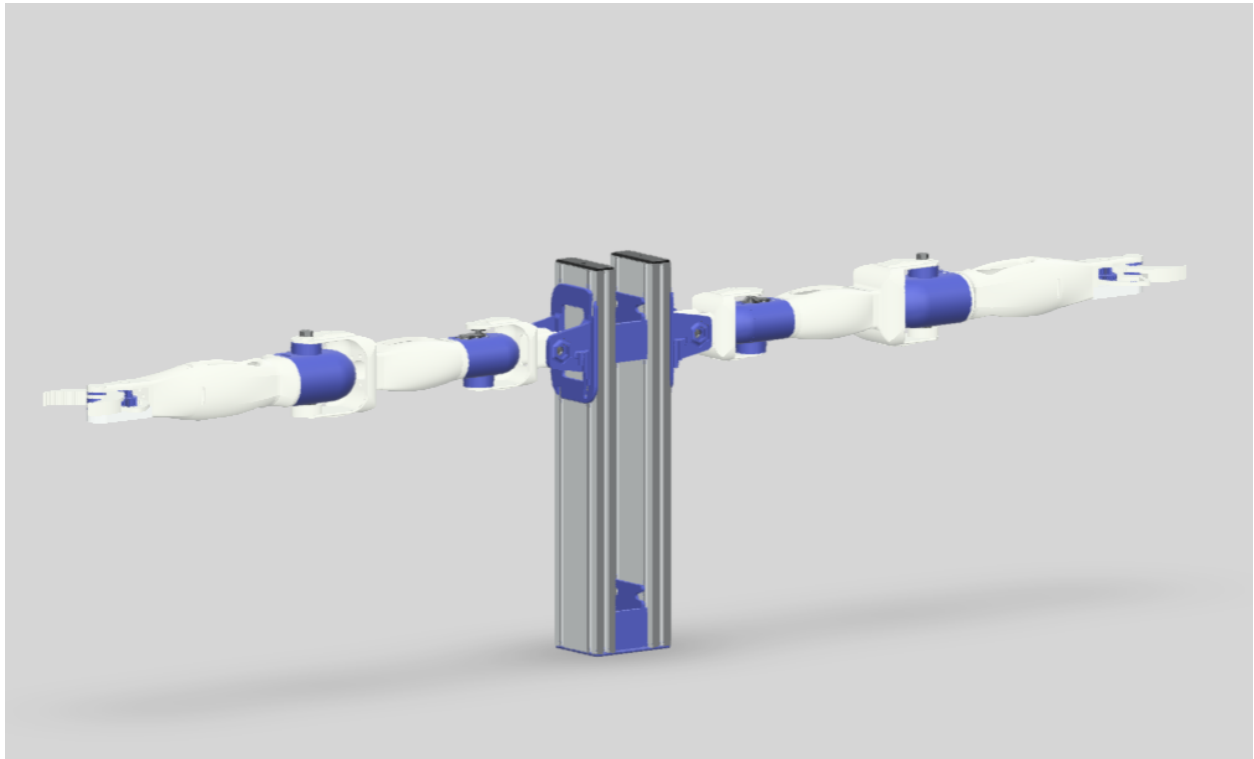
Additive technology can be used in robotics for fast creations of real life functional prototypes. Different parts and components of the robotic arm for example, can be 3D printed, directly after the generation of a 3D cad model, therefore additive technologies represent the quickest and easiest link from a virtual 3D CAD model, to a real life prototype.



3D printed prototype of a robotic arm

CAD/CAM

Students can use CAD CAM softwares in order to create new models and explore existing ones. The creation of CAD models is one crucial skill in the engineering world, and a crucial step in prototyping and production.



CAD model of the dual robotic arm prototype, 3D and VR for VET project model.

Artificial intelligence (AI)

Certainly the biggest innovation in the field of technology is artificial intelligence (AI). Artificial intelligence is a part of informatics that deals with the capabilities of computers to learn new concepts and to make tasks that require a certain form of intelligence. All machines and computer programs that are able to learn and later independently make certain decisions, conclusions, and act accordingly, have some sort of artificial intelligence. The goal of Artificial Intelligence is to create independent systems that are able to function independently.

The development of artificial intelligence can be shown in seven steps:

1. Simulation of human brain function.
 2. Program the computer to use the general language.
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3. Classify virtual neurons in a way that they can create a concept.
 4. Find a way to determine and measure the complexity of the problem.
 5. Self-improvement.
 6. Abstractness.
 7. Randomness and creativity.

The first five of the initial seven steps in the development of artificial intelligence have been largely completed. Abstractness and creativity are areas that are still being worked on intensively to complement the development of artificial intelligence.

Where is AI being used?

Artificial intelligence has only made a big leap in recent years. Today AI is used not only in education, development and laboratories, but it's also slowly being implemented in our everyday lives through social media, and search engines. Many industries and big companies are also starting to implement some sort of AI in their business. AI is directly related to the amount of data available on the internet. It sounds incredible that in just the last two years only, 90% of the world's online data has been created. Thanks to today's supercomputers, it is possible to process and use such huge amounts of data. You must have noticed something like this by now. Big companies like Facebook, Google, Amazon, Ebay, Youtube, all use AI to market the data they receive from our computers.

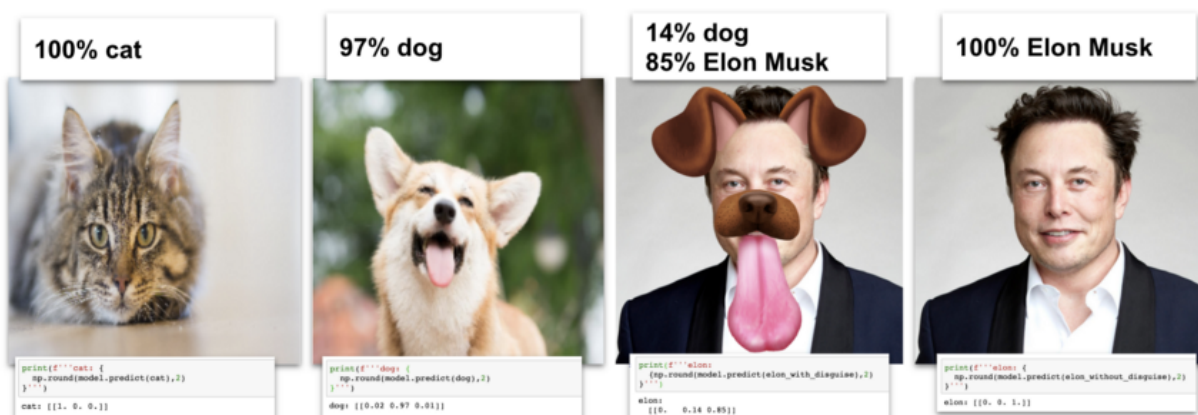
How AI works?

Like humans, the computer acquires new information over time. The more information it possesses, the more powerful the computer will be. Unlike humans, the computer does not forget information over time, and is also better and faster than a human at sorting data and finding a pattern between data.

However, the way man and computer learn differs significantly. While it is easy for a human to tell the difference between a dog and a cat, with a computer it is somewhat more complex. Learning starts from the code that the programmer writes, but it is not possible for that code to cover the whole range of data, which can often be contradictory. Take the example that a programmer entered a code in which he says that cats have pointed raised ears, while dogs have rounded lowered

ears. This would be considered as a kind of data generalization, however there are of course types of dogs that have pointed raised ears.

Therefore, the goal of machine learning is not to write the perfect code that will cover all possible scenarios, but the goal is for the computer to learn independently as a human being, based on experience, to deduce itself and find the correct algorithm. In the case of a dog and a cat, we want to give the computer as many samples (pictures) of both animals as possible, and define the type of animal. In the beginning, it is probably to be expected that the computer will often make mistakes, but the more time passes, the smarter it will become and the errors will eventually go to zero.



AI learning systems dog vs cat.

Credit: <https://towardsdatascience.com/cat-dog-or-elon-musk-145658489730>

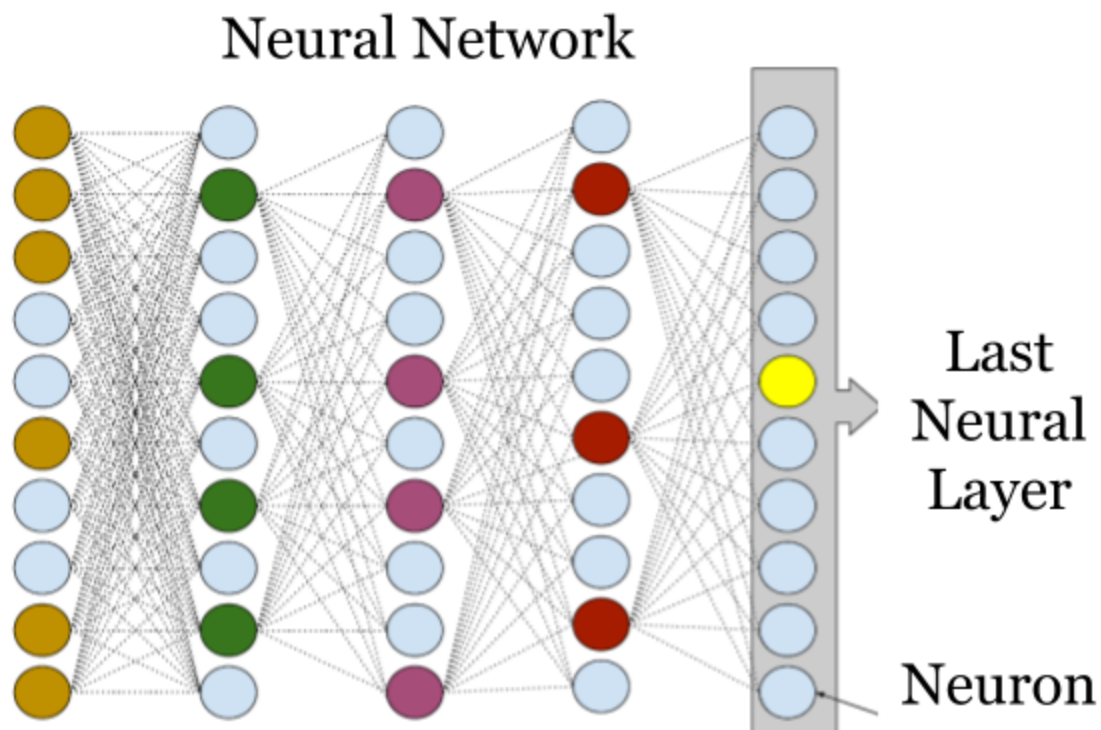
What are neural networks?

Neural networks are inspired and created on the model of the human brain. There are several types and variations of neural networks, but the most basic is the so-called Multilayer Perceptron (MLP).

In order to understand what virtual neural networks are, we must first answer 2 important questions, what are virtual neurons and how are they interconnected? A neuron can be thought of as a certain value between the number 0 and the number 1. Each neuron can therefore assume any value between these two extremes, where 0 represents the

minimum extreme (e.g., off) while 1 represents the maximum extreme (e.g., on). This number is called the activation number.

A series of neurons is called a neural layer, while further a series of neural layers is called a neural network. A neural network can be made up of thousands of neural layers, that are made up of billions of neurons. The neural layers are interconnected, meaning that the activation of neurons in layer 1 determines the activation of neurons in layer 2. Activated neurons from the 2nd layer further activate neurons in the 3rd layer, etc.



Scheme of the Neural Network process. Source: Lectures Sven Maričić, Ivan Veljović, Juraj Dobrila University of Pula 2020.

UNIT 4 Virtual reality (VR)

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The essential keywords

- VR = [Virtual reality]
- AR = [Augmented reality]
- MR = [Mixed reality]

Virtual reality, also known as VR, uses a headset with a built in screen that displays a virtual environment for the user to explore. It's a new technology that is growing at a rapid pace. Using the head tracking technology it allows the user to experience the 3D environment moving the head and walking through space.

Augmented reality or AR is a little different then VR. Augmented reality allows us to take virtual 3D models and layers them on the real world around you. It also allows us to walk around the virtual object that we can see on display, that is placed in the real world environment.

So with VR we can create an entirely fictional world, while with AR we can create a fictional element and put it in the surrounding environment.

Virtual and augmented reality are both changing the way we use screens, allowing us to have new and interactive experiences. They are both growing at high pace, and are being used in a variety of different ways, from medicine, real estates, industrial plants to education and more.

There is also a third form of similar technology called mixed reality. In the mixed reality real world objects coexist and interact with digital objects. It's a hybrid between VR and AR, and it can take place in either the real world or in the digital one.



VR and AR differences.

Credit: <https://www.robotlab.com/blog/what-is-the-difference-between-ar-and-vr>

Take home messages

- **Idea 1** is that VR and AR gives us new and interactive experience
- **Idea 2** is that both VR and AR provide us with benefits
- **Idea 3** is that MR can take place in either the real world or in the digital one

UNIT 5 The basics of robotics and automation

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The essential keywords

→ **PID controller** = [proportional-integral-derivative controller]

→ **I/O** = [Input-output (interface)]

→ **DOF** = [Degrees of freedom]

The word robot comes from the Czech word “robot” which means forced labor. Robotics is a technical science that covers the fields of mechanics, electronics, informatics and automation with the purpose of connecting a machine (robot) with a computer. The purpose of robots is to make work and life easier for humans by:

- ☐ performing tasks that are potentially dangerous to life or health
- ☐ performing difficult and/or repeatable operations
- ☐ performing tasks in difficult and dangerous conditions

The robot is controlled by a computer, and it has sensors (touch, heat, light...) that allow it to navigate in space. The information read by the sensors is sent back to the computer where it is processed and then again sent back to the robot. The computer and the robot communicate via an input-output interface.

Robots are used anywhere from industry, medicine, army, space exploration, education and more.

Basic concepts

When talking about robots, especially when talking about robotic arms, there are some basic concepts that have to be understood.

The table below shows a list of terms used when talking about robotic arm, as well as a brief explanation of these terms.

Table of basic terms used in robotics.

Term	Explanation
The kinematic pair	Consists of 2 interconnected parts of the robot.
Kinematic chain	Consists of two or more connected kinematic pairs.
Joints	Allow freedom of movement of the robotic arm.
DOF (degrees of freedom)	There are 6 degrees of freedom of movement: 3 translations (X, Y, Z axis), 3 rotations (around X, Y, Z axis).
Manipulator or "End-effector"	Similar to a human hand, it is the part of the robotic arm that accepts an object or tool. The end-effector is used to perform the tasks required of robots.
Workspace	A space in which the end-effector can perform work.

Actuators	An actuator is a component of a machine that is responsible for moving and controlling a mechanism or system. The actuator is most often an electric motor (DC, AC and stepper). Less often hydraulic and pneumatic motors.
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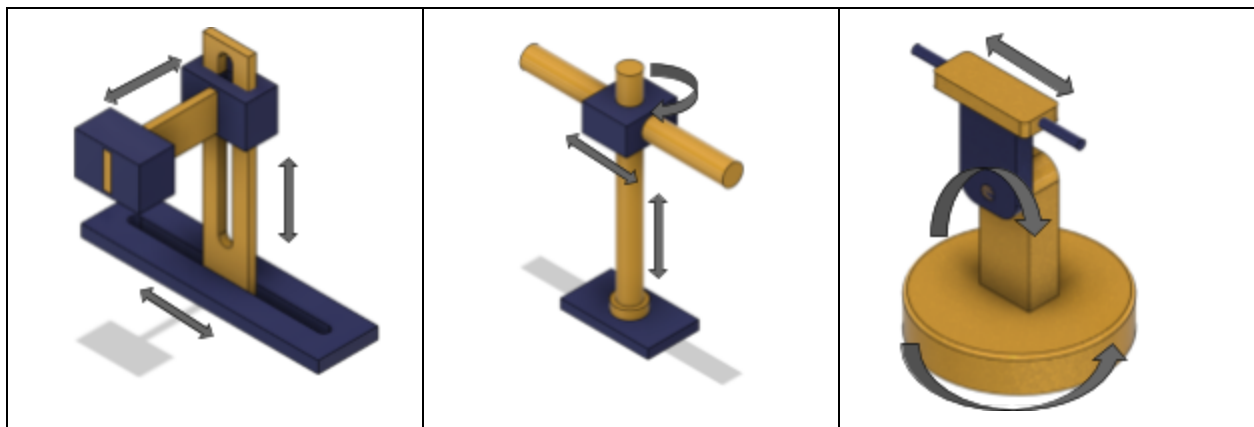
Robot arm configuration types

The shape and volume of the working space depend on the type and positioning of the robotic arm joints, as well as on the structure of the manipulator. Therefore, there are 4 basic structures, i.e. configurations of the robotic arm:

- ☐ Rectangular (TTT - 3 translation joints)
- ☐ Cylindrical (RTT - 1 rotary and 2 translational joints)
- ☐ Spherical (RRT - 2 rotary joints and 1 translational)
- ☐ Rotary (RRR - 3 rotary joints)

There is also a fifth specific configuration called SCARA which is characterized by the position of all three axes which is vertical.

Table of robotic arm configurations. Source: Lectures Sven Maričić, Ivan Veljović, Juraj Dobrila University of Pula 2020.



Rectangular Configuration TTT	Cylindrical Configuration RTT	Spherical Configuration RRT
		
Rotary Configuration RRR	SCARA Configuration	

When to use different types of electric motors in robotics?

There are 3 main types of electric motors:

- ❑ DC motors - we use them when fast and continuous shaft rotations are required (eg in electric cars).

DC motors convert direct current into mechanical energy, and they do so with the use of magnetic fields. They are generally the most expensive type of electric motor, and are able to transmit the highest torques. They always work at the strongest power with



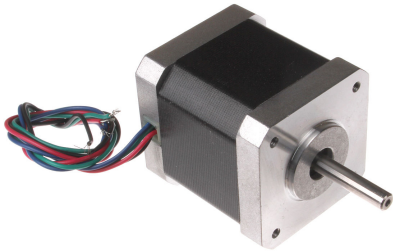
the strongest torque (which also means they consume more electricity). They have a very short response time. It is a type of motor that rotates the shaft as long as they are energized. Additional elements, like controllers, need to be connected to determine the position of the shaft.

DC motor

Credit: https://commons.wikimedia.org/wiki/File:DC_Motor.jpg

- ❑ STEPPER motors - are used in applications that do not require high rotational speed, and in which we want to have a high degree of control over the position of the shaft (eg in 3D printing where the position is extremely important).

Similar to DC motors, they always run at the highest power with the highest torque (which also means they consume more power). The main difference between DC and stepper motors is that stepper motors divide the rotation into a number of equal steps. The motor shaft can therefore be moved and stopped at any of these points without the need for different sensors to send feedback. The response time of stepper motors is slower compared to DC motors. They are easily controlled by a microcontroller.



Stepper motor

Credit: https://simple.wikipedia.org/wiki/Stepper_motor

- ❑ SERVO motors - we use them in applications that require high speeds, high torques and limited shaft speed (eg for robotic arms).

Unlike DC and Stepper motors, Servo motors have limited shaft rotation (there are versions in which the shaft can rotate 60° , 90° , 180° , 360°). So we can get at most a whole circle around the axis of the axis, and most often it is a half circle or 180° . The advantage in these engines lies in the fact that they are more precise, and that their power and torque can be controlled, but they also transmit less torque compared to the previous two. With the help of a servo motor, it is easier to determine its position. They are easily controlled by a microcontroller and are extremely fast.



Servo motor

Credit: <http://c2.com/cybords/wiki.cgi?ServoMotor>

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- ❑ PID controller - a proportional-integral-derivative controller is a control loop feedback mechanism widely used in industrial applications

Take home messages

- **Idea 1** is that the purpose of robots is to make work and life easier for humans.
 - **Idea 2** is that there are 3 main types of electric motors.
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UNIT 6 The use of additive technologies in robotics, creation, and presentation of solutions

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The essential keyword

→ A **ROBOTIC ARM** = [substitute for 3D printing machine]

3D printing technology has experienced enormous progress and growth since its beginnings, only 40 years ago (1980), and this growth continues at an exponential rate. As the additive manufacturing technologies are evolving, the fields on which they can be used are expanding as well.



Today there are different types of 3D printers which are different in size, price and the ability to print different materials, from plastic to metals. Most of the 3D printers use the common Cartesian coordinate system, but there are some companies that are experimenting with other ways to control a 3D printer. The new concepts involve using a robotic arm as a 3D printer. The very design advantages of using a robotic arm, instead of the classic Cartesian machine for 3D printing, are significant. The Cartesian 3D printing machine has 3 degrees of freedom for the movement, which involves the translation along the x, y and z axis. The robotic arm however, has 6 degrees of freedom for movement, involving 3 translations along x, y, z axis and 3 rotations around the x, y, z axis.

3D printed robotic arm example.

The advantage of a larger number of degrees of freedom lies in the fact that the 3D printing head, called the extruder, can access the model from different angles and positions. That allows the making of even more complex parts with greater details and with minimum or no support material. The great thing about additive manufacturing is that we can create components with the 3D printing technology that will be used in making a 3D printer.



3D printed robotic arm example.

In the picture above is another external example of how 3D printing can be used to create mechanical components for the robotic arm. This exhibition was done in the Ericsson Nicola Tesla Summer camp by students to test and explore different functional prototypes of the 3D printer robotic arm. The use of additive technology in robotics can help students in learning and acquiring different prototyping skills.

UNIT 7 CAD / CAM

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The essential keywords

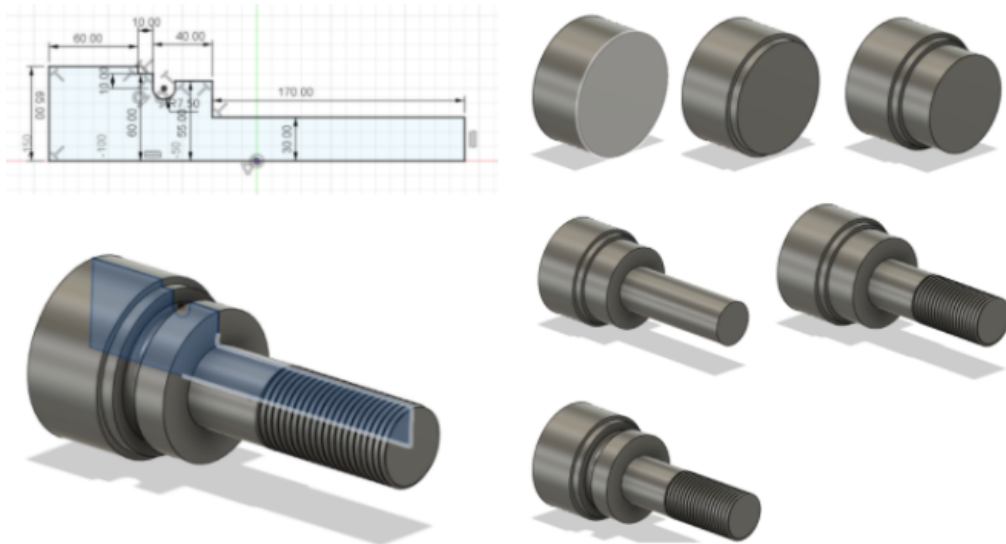
- CAD = [Computer Aided Design]
- CAM = [Computer Aided Manufacturing]

In today's World it's impossible to even imagine having a serious production and manufacturing process without the help of CAD CAM softwares. CAD CAM software is used whether it is the production of toys and furniture or more complex production in the automotive, aerospace or marine industry.

CAD

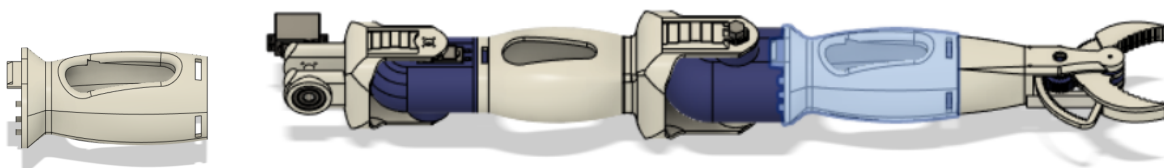
The acronym CAD stands for Computer Aided Design. This softwares allows us to create virtual 3D models of the project we are making on our computer. We can see and have a better understanding on how our product is going to look like and how it's going to work. Flaws and errors can be detected with more ease before the product has entered the manufacturing process, saving us time and money. Using the created 3D models it's easy to make manufacturing and assembly drawings of different components, to be used in the manufacturing process.

The interesting thing you learn when creating CAD models is that there is no wrong way of creating a model, there can only be an easier and most effective way to do it. Taking for example the model on the picture below. The same model can be done in two or in six different steps, generating the same end result.



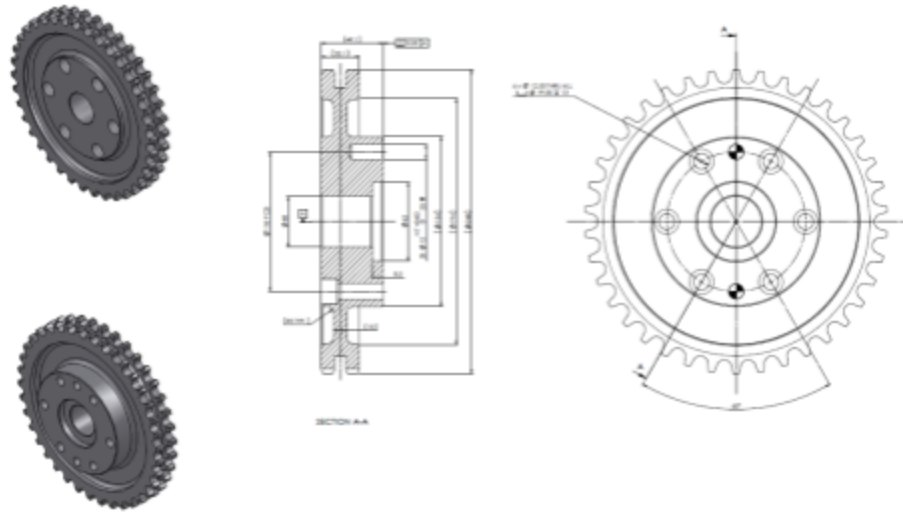
Two different approaches in creating a CAD model. Source: Lectures Sven Maričić, Ivan Veljović, Juraj Dobrila University of Pula 2020.

As it was mentioned before, CAD models can be used to generate single components, but also to put these components into assemblies. In that way we can have a better understanding on how the desired components interact with each other.



Making assemblies out of single components. Presented model was designed and developed primarily for industrial-crafts school usage. Made for 3D and VR for VET project.

After the final iteration of CAD model was generated, manufacturing and assembly drawings can be created. Presented model of robotic arm was intentionally designed and produced within the 3D and VR for VET project. Primarily focused as a novel model for educational activities in industrial-crafts school but can also be used in Medical school as well.



Creating drawings of 3D models.

Today there are many different CAD softwares to be used. Some of them are free, some have to be paid for receiving a licence, and for some an educational licence can be made in order to use the software for free. In the table below is a list of some of the most common CAD softwares, divided per level and per paid or free licence:

Free CAD softwares:

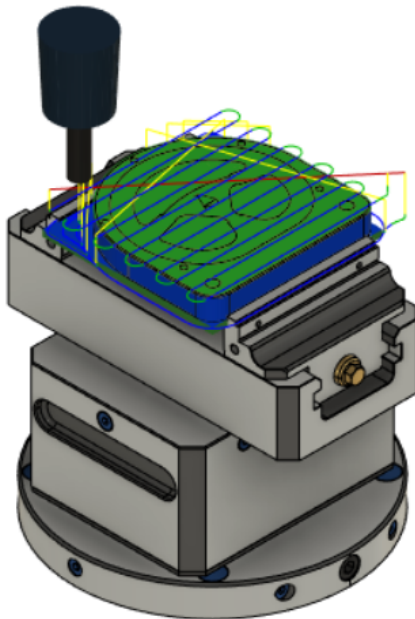
- ☐ TinkerCAD - Beginner level
- ☐ BlocksCAD - Beginner level
- ☐ Fusion 360 - Intermediate to professional Level. (Free licence for students, educators & academic institutions)
- ☐ AutoCAD - Professional level. Free and fully functional version to download for students and faculties.

Paid CAD softwares:

- ☐ Creo - Intermediate Level.
- ☐ Solidworks - Professional Level.
- ☐ Inventor - Professional Level.
- ☐ Rhino - Professional Level.
- ☐ CATIA - Professional Level.

CAM

The acronym CAM stands for Computer Aided Manufacturing, therefore it is easy to assume that this software helps us in the manufacturing process. CAM is used after the desired CAD model was created in order to perform the simulation of the manufacturing process. In that case the CAD model is an input parameter for the CAM environment, that's why it's referred to as CAD-CAM. CAM software is used to create detailed instructions, in the form of the so-called G-code, in order to drive computer numerical controlled machines (CNC). The G-code tells the machine how to actuate the motors in order to move the tool, follow a specific path and change the desired speed. Drawings, 3D CAD models and other data can be used to make detailed instructions used to drive some sort of automated tool. CAM helps manufacturers improve their time to market capabilities.



The advantages of using CAM software are many and include:

- ☐ Less chance for manufacturing error
- ☐ Provides high-speed machine tool paths
- ☐ Minimise cycle times
- ☐ Reduce tool wear
- ☐ Reduce machine wear
- ☐ Improved cutting quality
- ☐ Generates G-code, allowing for a quicker item production
- ☐ Helps in reduce of material wastage

CAM tool path simulation.

Credit: Fusion 360 CAM sample training (www.autodesk.com)

Take home messages

→ **Idea 1** is that CAD CAM softwares are essential for a serious production and manufacturing process

UNIT 8 Industrial application analysis and 3D modeling approach

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The essential keywords

- **CONCEPT1** = [modeling]
- **CONCEPT2** = [simulation]
- **CONCEPT3** = [validation]

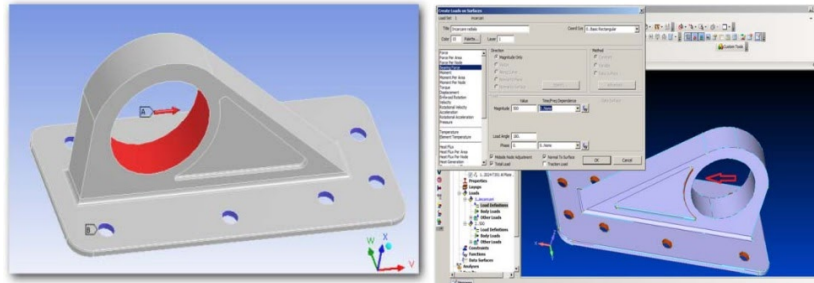
3D Topology optimization for aerospace industry

The use of 3D modeling in the context of industrial application is very large and complex, being related to the domain, but also peculiarities of the products that are being developed. For instance, one of the main aims in the aeronautic industry is to decrease the weight of the parts, in order to reduce the fuel consumption, so in this sense the main aim of the 3D modeling is to find ways in optimizing the shape of the part, by using programs that are related to topology optimization, but in close correlation with programs that are used for the finite element analysis purpose, in order to determine its mechanical behavior.

Last, but not least the manufacturing process of the part plays one important role in this case, since modeling of a part has to be correlated with technological restrictions. In order to understand the peculiarities on how the 3D modeling approach has been applied in the case of 3D printed components that was made for the aerospace industry at the Technical University of Cluj-Napoca, Romania.

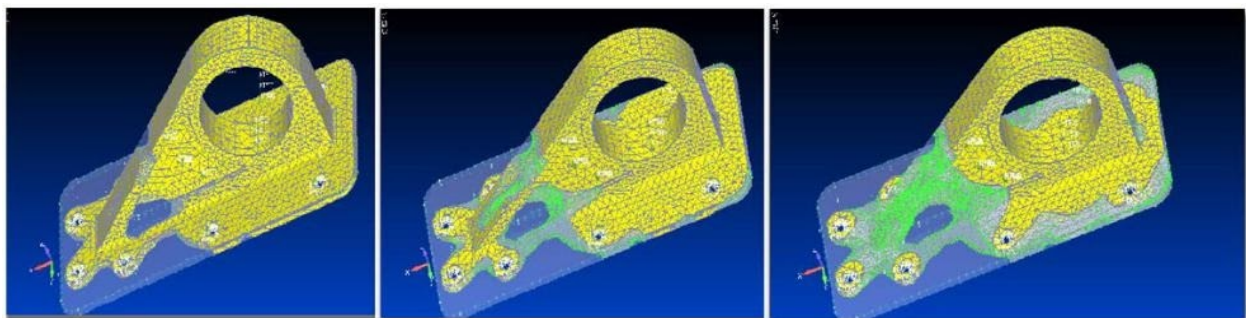
The research performed in the field of aerospace industry was focused on the redesigning and analysis of one part shown in the figure, with the aim of decreasing its weight without affecting its mechanical strength at the end. For the redesigning process of the airplane component, a dedicated topology optimization program called Femap NX

Nastran was used, knowing that in the bore area of the component ($\varnothing 50[\text{mm}]$ - size diameter), a force will be applied on the entire circumference and knowing that the base area of the component is fixed with 8 screws on the airplane fuselage. These were the main constraints that were applied in the case of the airplane component.



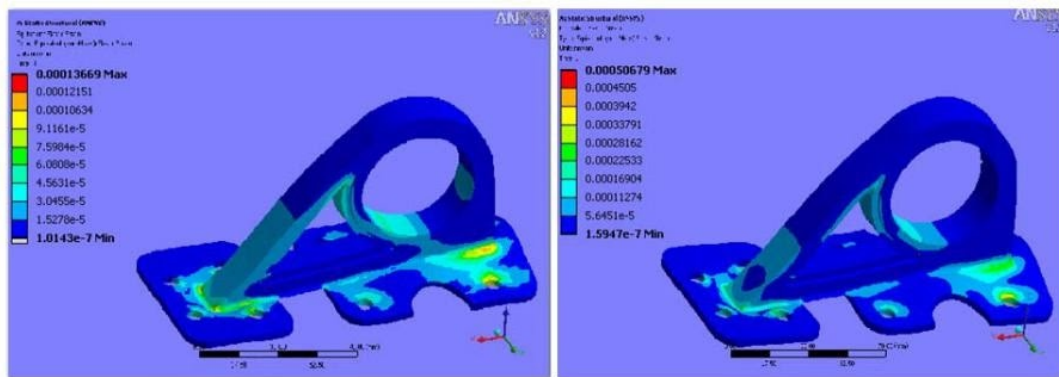
Topological optimization of airplane component

Two types of materials were considered for the made analysis - TiAl6V4 and AlSi12, as well as the mechanical characteristics, such as Tensile strength, Yield strength or Poisson ratio, undertaken from the material file datasheets of the producers. After the mesh was generated, by specifying the percent volume reduction in the FEMAP program (variable percent), it was possible to observe that a significant volume of the material can be removed in the connecting area of the base plate and supporting leg of the component. Same observation was valid in the case when the TiAl6V4 or AlSi12 material was considered for the manufacturing of the airplane component and with the increasing of loading force from 500 [N] to 3000 [N], range that was considered for the made analysis.



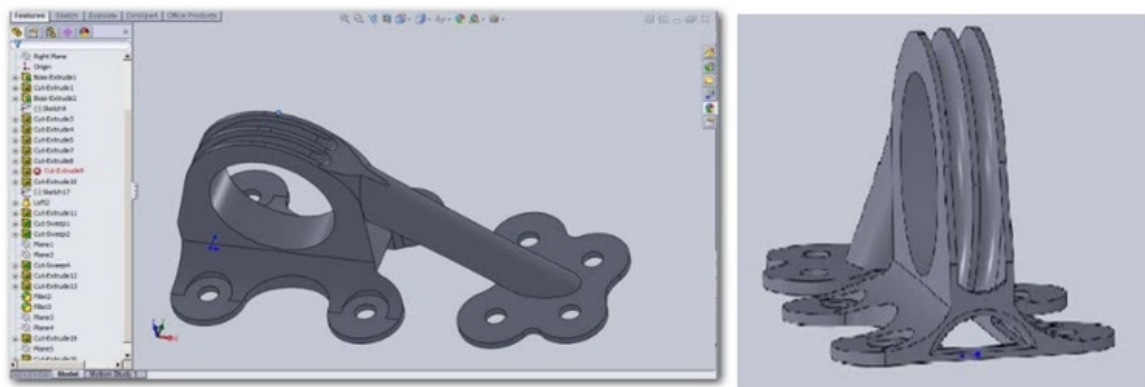
Results of optimization made with Femap Nastran program

Based on the results obtained using the Femap NX Nastran program, the optimized shape of the airplane component has been designed using SolidWorks CAD program. Further analyses regarding the mechanical behaviour of the fixing clamp were required to be made using the ANSYS FEA program. Kinematical and technological constraints were imposed according to the functional role of the part and appreciations were made regarding the stress and strain values of the component made of considered materials (TiAl6V4 or AlSi12).



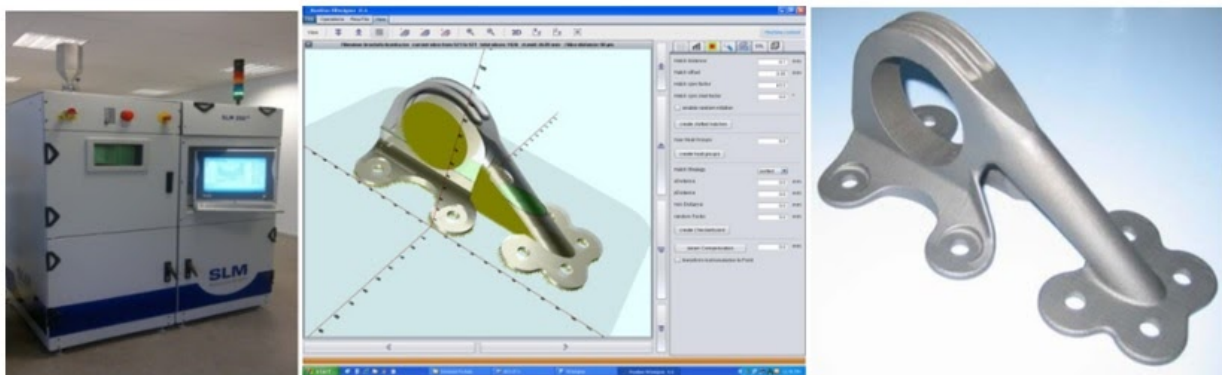
Mechanical behavior of the airplane component analyzed by FEA method

Taking into account the results that were obtained after the finite element analyses that were made by using the ANSYS FEA program it was possible to redesign the airplane component in order to reduce its weight.



CAD airplane component after FEA validation

The changes that were made at this stage of the analysis in terms of reducing the weight of the component were not as significant as were done using the Femap NX Nastran program, but were possible to be realized without affecting the mechanical behaviour of the component. The horizontal traverse has been eliminated in the new optimized version of the component that has been designed using SolidWorks CAD program. Taking into consideration the results of the FEA analysis, and, considering a safety coefficient of 4 times higher than the maximum stressing force, it was possible to determine that the aluminium component will not resist to such a value, so therefore it was decided to manufacture the component of TiAl6V4. The airplane component was manufactured from Ti6Al4V powder material, using the SLM 250 HL equipment from the SLM Solutions GmbH Company in Luebeck, Germany.

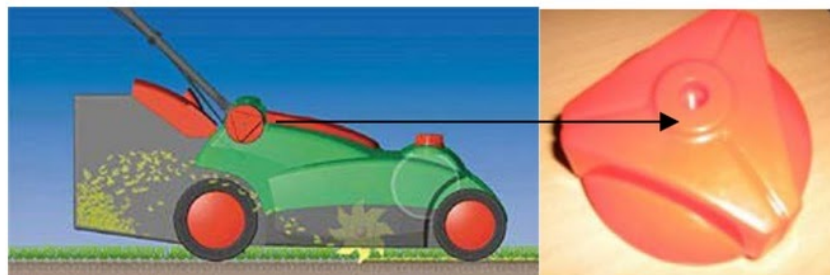


Airplane component manufactured by 3D printing

CAD modeling for new product development made by 3D printing and injection molding

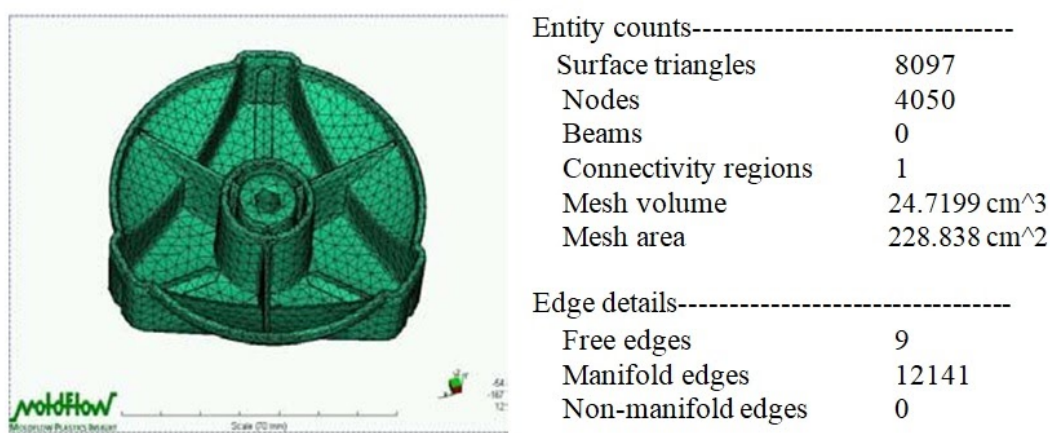
Due to technical improvements, better process control and the possibility to process all kinds of metals, a shift to Rapid Tooling (RT) and Rapid Manufacturing (RM) came up in recent years. Many applications could take advantage of this evolution by using the 3D printing technologies, not only for visual concept models and onetime functional prototypes, but also on developing new products by using

tooling molds, tooling inserts and end-use functional parts with long-term consistency. One case study (lid component of a grass cutting machine has been analyzed, manufactured by SLS and finally experimentally tested, within a project work, jointly at the Technical University of Cluj-Napoca and one injection molding company from Romania.



Lid component of a grass cutting machine

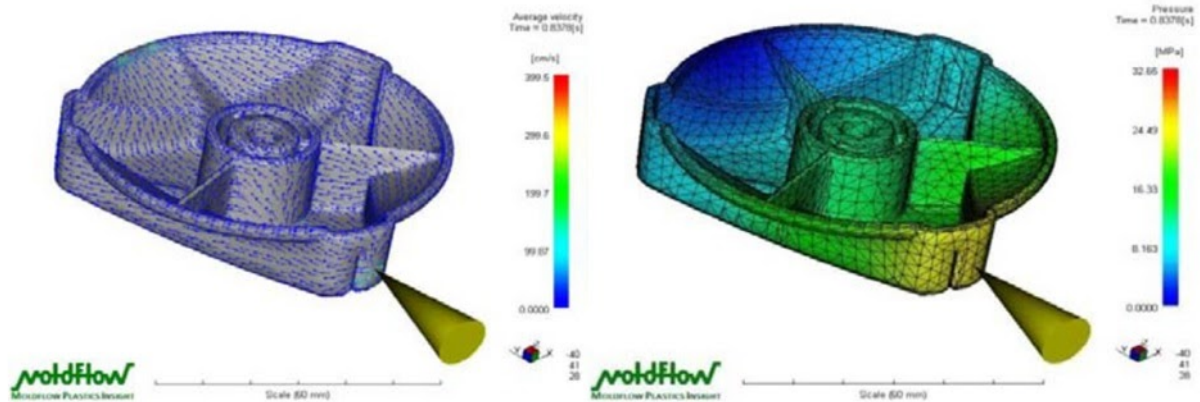
The Moldflow software was used to simulate the molten plastic flowing to fill up the cavity. The main purpose of this simulation was to find out some information regarding the technological parameters that have to be used within the injection molding process.



Moldflow Finite Element Analysis

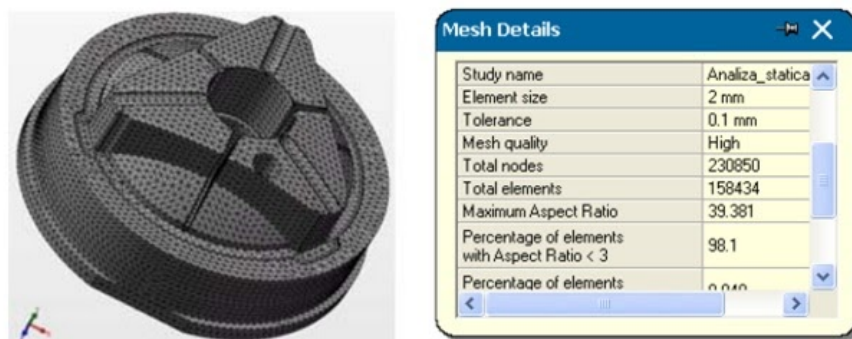
On the beneficiary company request, the selected material was Schulamid PA6 (30% Glass), having 260°C as maximum melting temperature

and 60°C, as the recommended mold's temperature. A preliminary analysis was made on this stage, related to the best gate location and the plastic fiber orientation during filling the molds and with the purpose of finding the optimal technological parameters used within the injection molding process.



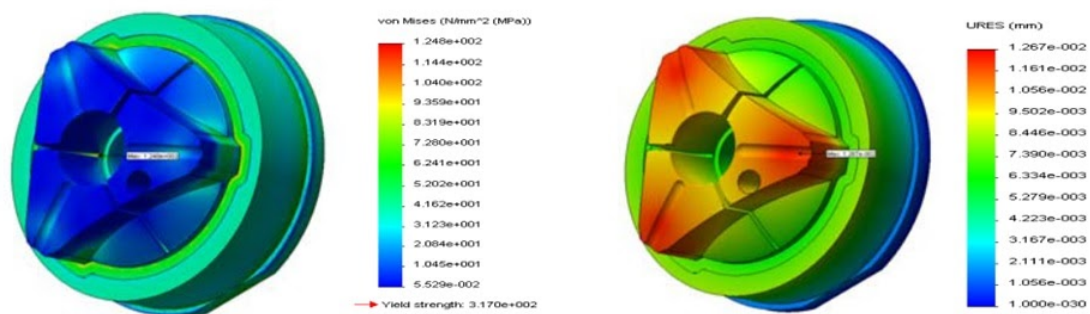
Optimal technological parameters reached for injection molding process

The technological parameters determined within Moldflow software were used accordingly on the injection molding tests that were made at the injection molding company using the tools that were manufactured by selective laser sintering (SLS) 3D printing technology at the Technical University of Cluj-Napoca, Romania. The value of injection pressure and clamping force were obtained using Moldflow software were needed for the second finite element analysis that was made to determine the durability of the injection molding tool made by SLS.



CAD model of the mold to be analyzed by SolidWorks Simulation

For performing the finite element analysis, first of all, the CAD model of the SLS tool (the punch) has been loaded into the SolidWorks simulation FEA program. The mechanical and thermal characteristics of the metallic powder (Laserform St-100 material) were introduced into the finite element analysis, kinematic and technological constraints were imposed, and results were reached for determining the mechanical (strain-strain) properties, but also the durability of the SLS tool (the life cycle of the mold).



Results of the SolidWorks simulation analysis

The virtual model of the SLS tool was transferred to the SLS machine from the Technical University of Cluj-Napoca and was manufactured from Laserform St-100 material. After manufacturing on the SLS machine, the SLS tools went into a post-process stage that is obligatory needed in the oven for getting the final metallic part.



Tools manufactured by selective laser sintering 3D printing technology

There were some dimensional contractions during the SLS process and post processing. That is why, it was necessary to carry out finishing operations to the punch and die afterwards. These finishing operations were performed at the injection molding company, using hand tools for finishing, in order to obtain a perfect close of the tools.



Injection molding machine and punch made at TUCN at work

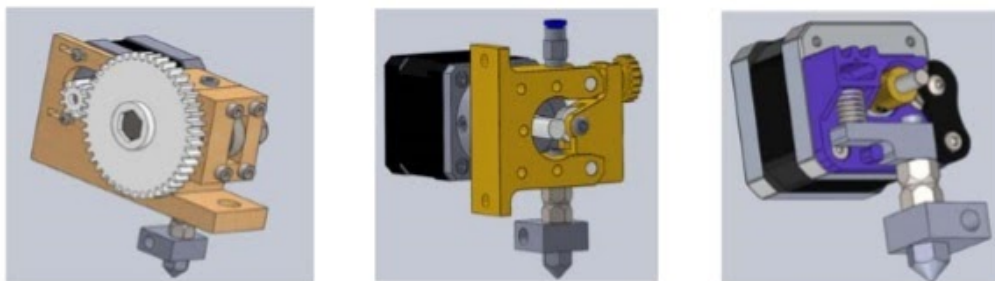
The tests of the SLS tools behavior were made at the injection molding company , using a Krauss Maffei 90/340 A injection molding machine, using the technological parameters determined within the Moldflow analysis. The punch's plate was fixed onto the mobile assembly of the injection molding machine and the die's plate onto the fixed assembly of the injection molding machine. The injection molding tests were made using polyamide PA 6 + 30 % fiber glass material. Approximately 30,000 parts were successfully injected.



Injected molded parts using the SLS tool

Designing of innovative 3D printing extrusion systems for testing new materials in accordance with industrial needs

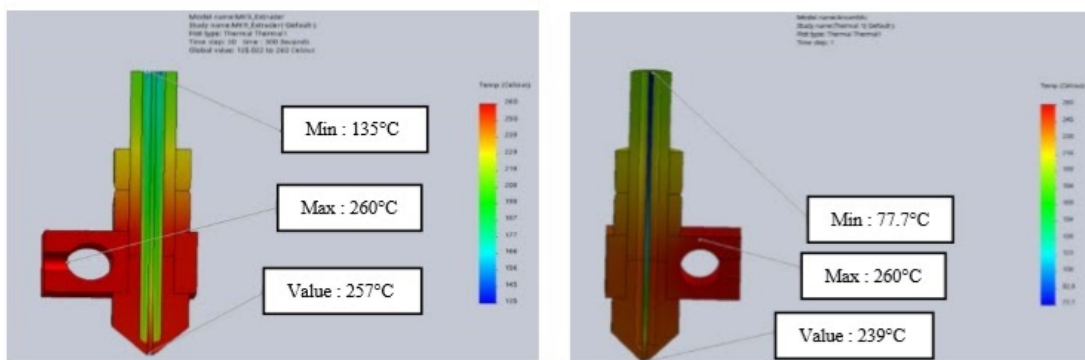
Desktop 3D Printing for metallic parts is a new direction and represents one of the latest trends within the Additive Manufacturing domain, being given and defined mainly by the requirements of the industrial companies in terms of materials and products that needs to be rapidly delivered on the market. At the Technical University of Cluj-Napoca there was research focused on the redesign of the extruded system of the 3D printer, for producing metallic parts for one company that produces electronic components. Technological parameters were optimized to manufacture samples that could be further on mechanically and electrically tested. Three constructive versions were proposed based on the principle used by the classic 3D printers, the extruded material being in the form of a filament. This type of extruder incorporates a stepper motor, which drives a filament feeding mechanism, generally consisting of a driving wheel, actuated by the stepper motor and a driven wheel, the filament being fed through the respective wheels



Innovative extruding systems designed using SolidWorks

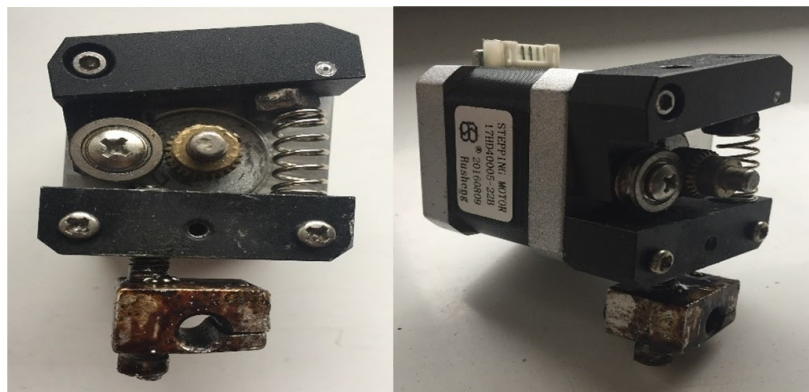
In order to choose which version is optimum from the point of view of the overall dimensions, total mass of the assembly, wire feeding accuracy, reliability and maintenance and the total manufacturing cost were analyzed and was concluded that the most reliable is the third one, due to its simple construction, the ease of manufacturing, the costs and difficulty to assemble the parts together.

For validating the design, a finite element analysis method has been considered to be realized with the SolidWorks Simulation module. A critical aspect of the analysis is the intensity of thermal demands to which the assembly is subjected, demands imposed by the thermal characteristics of the extruded material. The material considered as raw material for this research was Sn60Pb40 in the form of a filament with a diameter of 1.5 mm. The optimum extrusion temperature of this type of material varies slightly around the temperature of 188 °C.



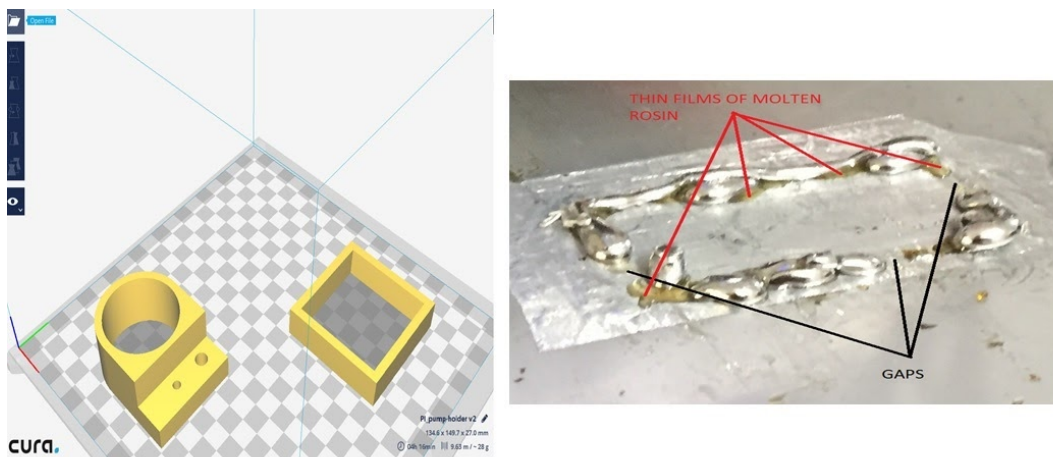
Finite Element Analysis to estimate the thermal behavior of the extruder

After performing the finite element analysis, it was decided that the best option is the combination of aluminum, brass and steel for the manufacturing of the hot-end of the sub-assembly extrusion system, rather than manufacturing it entirely from plain carbon steel.



The manufactured and assembled extrusion system

The decisive factor for this decision was the fact that the thermal conductivity of the aluminum and brass is much better and the fact that the parts are very small, the difference in terms of costs between the two analyzed alternatives, being insignificant in this case. The extrusion system was manufactured and tested on a commercial 3D desktop printer, Prusa i3 type that is available at the Technical University of Cluj-Napoca (TUCN).



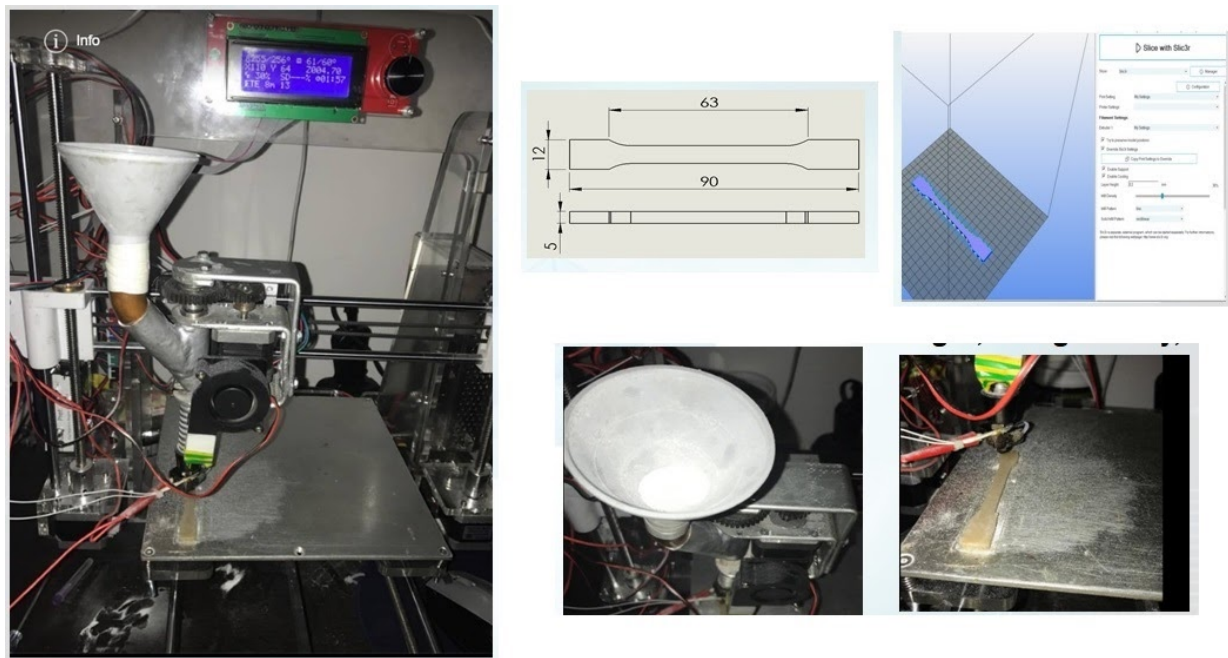
Tests made on 3D printing using the original conceived extruder

For the slicing process of the model and technological parameters settings, the printer uses a program developed by Ultimaker, called the Cura software. This software is widely used worldwide, with a number of advantages over other control and slicing programs, such as the possibility of introducing a much larger number of technological parameters than the ones which are possible to be introduced within other slicing programs on the market, with an improved visual interface and with the possibility of scaling models, much simplified.

Based on the results reached on experiments, it was decided to mount an hot air gun on the carriage that is holding the extrusion system, a holder part which was designed in SolidWorks software and was then made on a 3D printer by using PLA material. The holder was then fixed on the sub-assembly extrusion system by using a screw. 3D printing

equipment developed at TUCN was modified in accordance with industrial companies needs for testing several types of materials (plastics and composites), in the filament, powder state form or in the form of pellets.

Designing of the components was made in CAD software programs, while the analysis was made based on finite element methods, the final validation being made based on the experiments performed on real 3D printing machines and mechanical tests afterwards.

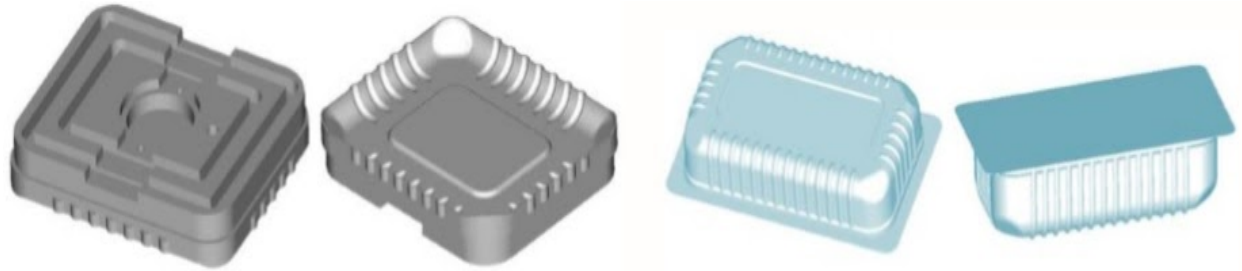


3D printing equipment adapted in order to test new materials in concordance with industrial companies needs

Decreasing of the manufacturing time for a thermoforming mold by applying DFM principles

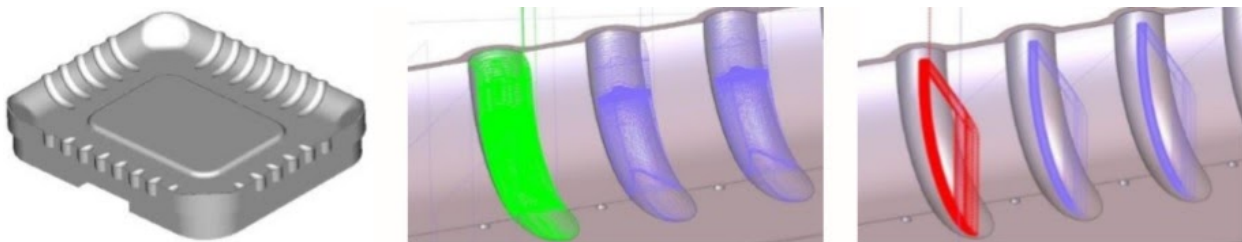
In order to succeed, the researchers must design products in the right manner from the first time for optimal manufacturing, cost, quality, time, and functionality. DFM (Design for Manufacturing) is a methodology for product development or product improvement projects in which designers and manufacturing engineers work together to design

the product's manufacturing and assembling processes at the same time they design the product itself. In the following, a design for manufacturing analysis will be presented how it was realized by using DFMXpress in order to identify and eliminate the critical design issues of the thermoforming mold, that increase the manufacturing complexity and cost.



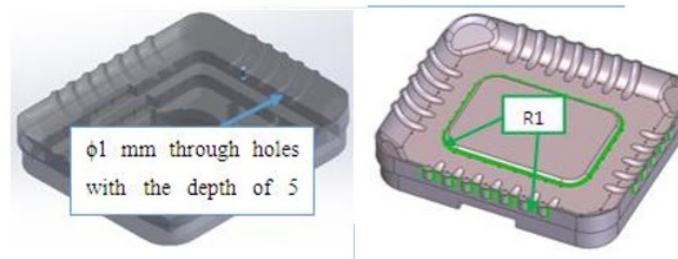
The obtained plastic food-container after thermoforming process

An important step of the designing process is the material selection. In this case, the part is made of aluminum alloy EN-AW-5083 H111 which is known for its exceptional performance in extreme environments because it is highly resistant to the chemical attack that might occur in industrial chemical environments. In order to determine the manufacturing time of the “Thermoforming mold”, it was necessary to realize the CNC program required for this issue. In this case, EdgeCam program was used to generate the necessary tool paths in order to obtain the final part.



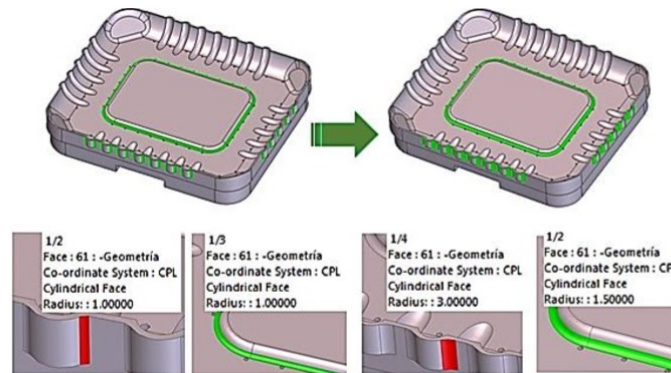
The analyzed tool path strategies in the case of the thermoforming mold

After obtaining a redesigned part based on the recommendations of the DFMXpress software, the machining method of the part was changed using less special tools and more tools with higher diameter. These modifications had a significant influence on the machining time. DFMXpress is a rules-based Solidworks add-in that allows the designer to compare its files against known, good design for manufacturing rules. Within Solidworks, the DFMXpress add-in was opened, the Rule File was selected and the desired values for DFMXpress check were set. For Manufacturing Process the “Mill/Drill only” option was chosen, taking into consideration the fact that the thermoforming mold is a CNC milled part.



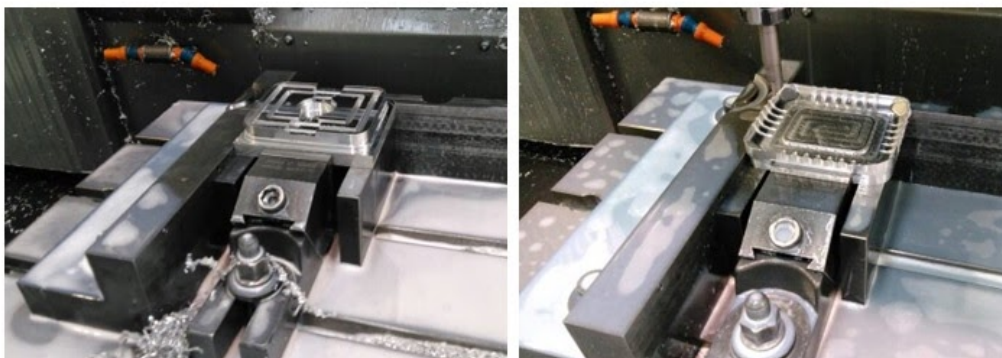
Failed Hole Depth/Diameter Ratio rule and Inaccessible Feature

The Hole Depth/Diameter Ratio rule failed due to the fact that the predefined value of 2.75 for this rule parameter was taken into consideration during the DFM analysis. The DFMXpress program considers that the marked features are either not easily accessible for machining (the tool holder assembly is not able to approach the feature and a long slender cutter is required which is not desirable) or require a special cutter for machining. Using the DFMXpress program, a redesign of the thermoforming mold was made based on the failed rules and recommendations given by the DFM program. The R1 radiuses, at the outside and at the bottom of the thermoforming mold, were changed, taking into consideration the fact that the Inaccessible Feature rule failed due to these features.



The redesign of thermoforming mold based on recommendations of DFMXpress

The computer aided manufacturing and the decreasing process of the machining time by applying optimal tool path strategies, was followed by a design for manufacturing analysis realized with the help of DFMXpress program, in order to identify and eliminate the critical design issues of the thermoforming mold that increase the manufacturing complexity and cost. Taking into consideration the fact that the required quantity of this thermoforming mold is 25 parts and the manufacturing cost for one hour is equal to 28 euros, machining time was reduced with 825 minutes (approximately 14 hours) for the whole process and the manufacturing costs were also reduced with 392 euros in this variant. Redesigned thermofolding mold was produced on Mazak VTC 200C Vertical Maching Center within one company that is activating in the food sector in Romania.



The redesigned mold used for producing the plastic food-container

MODULE 2

UNIT 1 Artificial Intelligence and Machine Learning in Oncology

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The importance of machine learning integration in cancer diagnosis

Early cancer detection and prognosis is an essential aspect of healthcare. Cancer is the second leading cause of death worldwide and has significant impacts on the economy as well as human lives. Researchers all over the world devote their whole career to help cure cancer; every year, huge advancements are made in diagnostics and drug treatment. But unfortunately, for many soon-to-be cancer patients, it's still not enough. In the hope of saving countless lives, researchers have turned to more futuristic diagnostic methods using intelligent machines. Scientists have faith that the rise of machine learning technology will help them not only find a suitable cure for cancer but stop its development altogether.

Artificial intelligence (AI) and machine learning (ML) have been slowly making their way into healthcare since the 1970s, changing the way doctors diagnose and treat various medical conditions. Modern iterations reduce the cost of medical bills and make disease identification faster, which means patients start treatment sooner and their quality of life is increased. This makes a world of difference to cancer patients, whose conditions are often life-threatening and require urgent care. Some experts say the probability of survival is 10 times higher if cancer is found early.

Overlooked cancer sites are one of the most harmful types of diagnostic errors in primary care. Cancer diagnosis is problematic even when using multiple tests, such as x-rays, MRI and biopsies. For example, white marks in breast tissue can either be normal or cancerous, and this can lead to both false positive or false negative diagnosis. Computer programs can be taught to analyze patterns clinicians may miss and interpret medical images in a new way. Between

2012 and 2019, over 20 000 papers analyzing AI performance in diagnostics were published. Only 25 of them compared the performance of AI and healthcare professionals, but the results clearly show their performance was equal. However, this is not a reason to fear machines taking over the medical field, but a chance to become better physicians by cooperating with new technology. While AI solutions can do given tasks well, physician's experience and human contact with patients cannot be replaced.

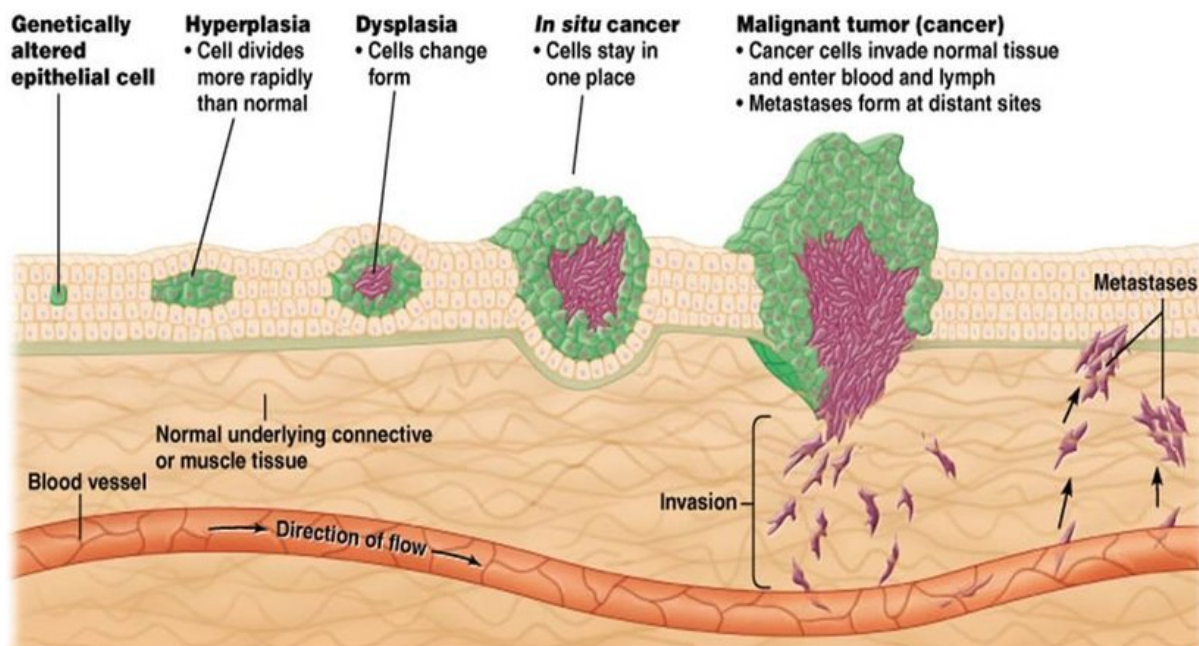
Pathophysiology - understanding cancer

The path to more advanced technology starts with understanding the basics of cancer development and what it does to the body. So, what is cancer? Cancer is a group of more than 100 diseases involving uncontrolled cell growth which can potentially spread to other parts of the body. The term cancer is different from tumor, even though they are often used interchangeably. A tumor is a mass of cells which divide abnormally and is usually categorized as benign or malignant; benign being non-invasive and staying within its tissue of origin, while malignant tumor is more likely to move into other parts of the body via blood or lymph. If a new tumor is established, the pathological sites are called metastases.

At the beginning of cancer research, scientists believed its development was caused by chemicals, radiation or viral infections. Since then, science and medicine have come a long way. Today we understand that many different molecules and gene mutations are involved in the formation of cancer. Tumors are made of cells that exist within our body and do not come from a foreign source. Modern theories suggest that all the cells within a tumor growth have the same "mother" cell, which at some point transformed and started growing uncontrollably. This cell and its "children" divide throughout the years, forming a tumor which ultimately has an ill effect on the body and causes symptoms known as cancer. Additional mutations are accumulated over some time, creating subpopulations that can divide and mutate further. Multiple independent cancer subclones can coexist

within the same tumor, and this feature is associated with poor prognosis.

Cancer cells do not cooperate with other cells in their environment and look different from their healthy neighbors. These cells have an abnormally large nucleus and are genetically unstable. Random deletions, duplications and rearrangements of their chromosomes make them display unusual traits. The loss of contact inhibition and less dependence on growth factors in the environment are the changes all cancer cells have in common. These changes allow the cells to grow without restraints.



Stages of tumor development and the mechanism of metastasis.

There are two categories of genes which control most of the cell division process, also known as the cell cycle. One category consists of proto-oncogenes; the other includes tumor suppressor genes. These genes keep cell growth in check, helping each tissue and organ maintain their size and function. The human body requires balance to function properly, and any changes in genetic material that isn't mended can cause various health problems. Cells are usually very efficient in repairing their DNA and it takes many years for enough mutations to accumulate in one cell to cause cancer. Studies suggest

5-10 genetic modifications are needed to transform healthy cells into cancerous.

Proto-oncogenes code for proteins that receive and process signals from surrounding cells in a tissue. Division is stimulated by the release of growth factor into the space between cells, which then attaches to specific receptors on the walls of neighboring cells. This signal is transferred from protein to protein until it reaches the cell's nucleus where various genes become active and start the growth cycle. Mutations make proto-oncogenes become oncogenes, which cause cells to grow and divide excessively. Oncogenes can affect different parts of the previously mentioned signaling pathway, stimulating cells to overproduce growth factor or sending growth-promoting signals to the nucleus when no growth factor is present. Tumor suppressor genes usually inhibit these rogue signals, but they are inactive if mutations occur.

Human cells have a few other backup systems in case errors occur in the cell division process. The DNA repair system is very important because environmental carcinogens and toxic products of the cell metabolism constantly damage our genetic material. Errors can also occur during DNA replication and can become a permanent feature in the cell (a mutation) if they are not repaired. If an essential component is damaged, the affected cell might receive a signal for programmed death, also called apoptosis. A product of tumor suppressor genes called p53 is heavily involved in this process. Its mutations can impact not only cell growth but the response to radiation and chemotherapy as well.

There is also an essential system that limits the number of times a cell can divide, and it involves the segments of DNA at the end of chromosomes. These segments are called telomeres, and a part of them is chipped away after every replication until they reach a minimal length. Cells then stop dividing, or further shortening causes the chromosomes to break apart. Cancer cells do not exhibit this behavior because they, unlike mature, healthy cells, have an enzyme called telomerase that replaces parts of telomeres lost during replication.

Human cells have a total of 20 000-25 000 genes. There are many different types of cells because they use those genes differently, selecting which ones to turn on and off. The future of diagnosis lies in the ability of scientists to understand and compare "signatures" of healthy and cancer cells. These "signatures" or "fingerprints" help tell groups of cells apart. For example, bone and muscle cells mostly express entirely different genes. Some genes are expressed in both cell types, but in different quantities or the final product is different. Since cells change on a molecular level during their transformation to cancer cells being able to notice these changes can help in detecting, diagnosing and treating cancer. It can also help in calculating whether the cancer will progress and how fast. The main goal in healthcare is to notice cancer in its early stages and prevent its development completely.

The problem with cancer as a group of diseases is that everyone has some risk of developing it during their lifetime. However, the risk of developing a particular type of cancer depends on exposure to cancer-causing agents and individual traits such as family history, habits, etc. Even if a population consciously avoids all environmental carcinogens and has no inherited genetic mutations, about 25% of people would still develop cancer as a random occurrence within the body. The suggested course of action is to minimize contact with known carcinogens (like the ones in cigarettes), get yearly checkups and participate in screening programs.

On a positive note, survival rates among cancer patients have been steadily increasing throughout the years. This is likely due to the advancements in detection such as new imaging techniques and different types of blood tests. Cancer is hard to diagnose by symptoms alone because they are non-specific and usually occur when the tumor has grown considerably or even metastasized.

★ [Why We Haven't Cured Cancer](#)

Video 1. A brief overview of cancer pathophysiology and how it limits the effectiveness of treatment but also drives global research.

While the risk of eventually developing cancer will always be there, it can be minimized on a personal and national level. Individuals can alter their habits to improve their health, while government agencies work on improving public exposure to carcinogens. This also includes laws like the ones that limit alcohol and tobacco sales to people under 18 years of age. But such laws don't limit individual freedom and permit adults to take personal risks if they are willing to face the consequences.

Science and modern medicine play an important role in enhancing both personal and public healthcare. The knowledge supplied by experts can be used to understand, recognize and treat various illnesses and medical conditions. But as scientific information is becoming more publicly accessible, people begin to self-diagnose and rely on their physicians less. While everyone is encouraged to choose for themselves, ignoring well-proven facts can have unwanted health consequences. We should be grateful for the wonders of modern medicine, but not dependent on it and use the accumulated knowledge to our advantage. Prevention is worth a lot more than cure, both for ourselves and others.

Cancer prediction and prognosis

Prevention and early detection of cancer can be achieved through the widespread practice of screening. Screening is a strategy used in medicine to look for unrecognized conditions in apparently healthy, asymptomatic populations. Even though numerous strategies for early detection and prevention are available, overusing them can lead to overdiagnosis and subsequent overtreatment. Clinical and experimental evidence continuously provides new methods for cancer diagnosis,

focusing on precision medicine. Recent innovations use molecular knowledge and environmental factors to calculate the risk of developing cancer.

As cancer takes a long time to develop, there are plenty of opportunities to detect precancerous sites and intervene before the tumor is fully formed. Since cancer is the second leading cause of death across the globe, both personal and community efforts must be made to reduce its incidence. Several prevention mechanisms have been identified and divided into primary, secondary and tertiary processes. Primary prevention includes lifestyle and diet changes, such as frequent exercise, quitting smoking, limiting the intake of food rich in animal fat and using sunscreen. Using protective therapeutics is also a way to prevent cancer, including systematic vaccination. Early detection, treatment or removal of precancerous sites fall under the category of secondary disease prevention. This includes routine screening which is currently available for colorectal, breast and prostate cancer. Tertiary prevention is initiated after cancer diagnosis, focusing on improving the patient's quality of life and survival. Understanding the mechanisms behind cancer development and using established prevention strategies will enable healthcare professionals to take better care of both future and current cancer patients.

Premalignant cells display several molecular and genetic changes compared to both healthy tissue and malignant lesions. Observing these changes can be crucial in understanding how certain types of cancer develop and progress. Unfortunately, finding molecular patterns in early cancer lesions is expensive and requires large tissue samples. It is also redundant in most cases since the majority of premalignant lesions don't progress to invasive cancer. Detection of these lesions is problematic even in conventional screening methods, such as mammography for breast cancer and PSA (prostate-specific antigen) for prostate cancer. False-positive results can lead to unnecessary follow-ups like biopsies and drug treatment, even though the detected premalignant lesions may never progress and endanger the patient's life. When implementing any cancer prevention strategy, it is

important to note the risk-benefit ratio. Overdiagnosis is a drawback of screening and should be avoided as it can harm patients. This is evident in the diagnosis of breast cancer. Even though the frequency of overdiagnosis is low, its health consequences are significant. Other subjects of overdiagnosis in cancer include melanoma, prostate, renal and thyroid cancer. Renal cancer is mostly found accidentally during abdominal imaging, while thyroid cancer can be found when investigating thyroid function abnormalities.

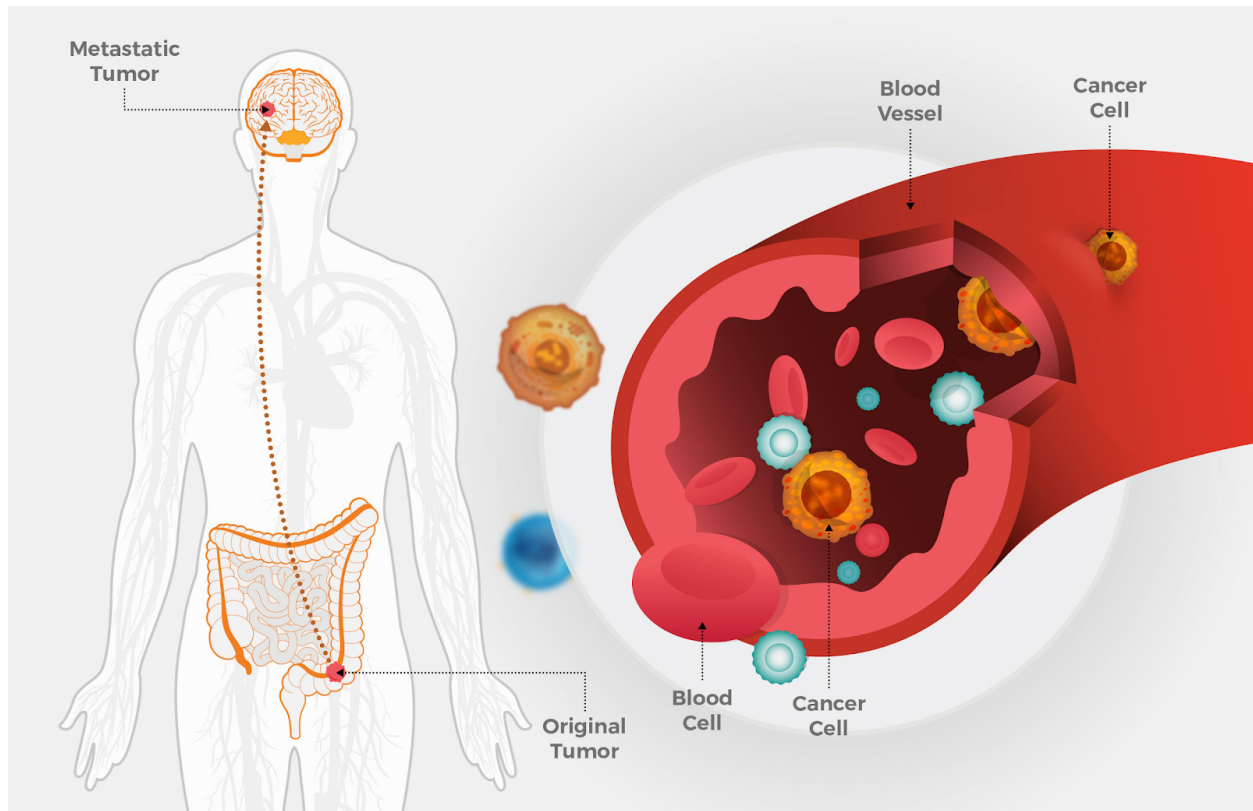
Table: Tests and screening procedures for various types of cancer.

Cancer site	Test or procedure
Breast	Mammography
Cervix	Pap test (cervical cell cytology) HPV DNA test
Colorectal	Fecal immunochemical test, fecal occult blood test, multitarget stool DNA test Colonoscopy, CT colonography, flexible sigmoidoscopy
Lung	Low-dose CT
Prostate	PSA (prostate-specific antigen) test with or without digital rectal examination

An important part of tracing cancer initiation and progression is identifying biomarkers associated with these pathways. Biomarkers (fully named biological markers) are a broad category of molecules that can be measured in the body and predict disease incidence or outcome. These molecules can be either DNA, RNA, proteins or metabolites. Ideal biomarkers should be directly associated with and involved in cancer processes, be highly sensitive and specific, have non-invasive detection and a reasonable cost-benefit ratio. In breast cancer diagnosis, molecular profiling of estrogen, progesterone and human epidermal growth factor receptors is done to identify potential

biomarkers. If well-known mutations are found, treatment is easier since highly specific drugs are available. Examples include tamoxifen for ER-positive cancers and trastuzumab for HER2-positive cancers.

Scientific innovation is leaning towards less invasive techniques for early cancer detection, such as isolating circulating cell-free DNA (cfDNA) present in blood (plasma, serum), urine and other bodily fluids. There are different types of cfDNA. Some are present in healthy individuals like cell-free fetal DNA (cffDNA) during pregnancy, while others might indicate the presence of disease like circulating tumor DNA (ctDNA). Most of the circulating DNA is released into the bloodstream when natural cell-death (apoptosis) happens, but precise mechanisms are still unknown. Both circulating tumor DNA and circulating tumor cells can be isolated from previously mentioned samples and checked for molecular alterations. The use of these markers in clinical practice is limited. Some hospitals don't have the resources to perform these tests, while others realize the biomarkers of interest might be produced by non-cancerous cells or might not be specific to certain types of cancer.



Circulating tumor cells can detach from the primary tumor as single cells or part of a cluster. These cells can then enter the bloodstream and migrate to distant organs to form metastases.

Tumor markers released into the bloodstream can be useful for multi-cancer detection from a single test. This method is sometimes called liquid biopsy. Present cancer screening methods target individual organs and population-wide screening is recommended for just 4 types of cancer – breast, cervix, colorectal and prostate. Screening for other types of cancer is done only in high-risk individuals. Examples include pancreatic cancer screening when family history is present, lung cancer screening for smokers and hepatoma screening for patients with chronic liver disease. Despite being in the high-risk group, some patients are not screened. This is where tests detecting circulating tumor DNA in blood samples would be useful. Obtaining blood samples is much easier and doesn't have long waiting lists like radiology exams do. Recently, an AI program was

designed to calculate lung cancer likelihood in plasma (Lung-CLiP) by analyzing the content and quantity of ctDNA. It was trained on early-stage lung cancer samples. Scientists hope that, in the future, this program can be applied to other types of cancer. Patients with positive tests would then be examined with appropriate imaging techniques.

Table: FDA approved cancer biomarkers currently used in clinical practice.

Marker (Full name)	Cancer type
AFP (α-Fetoprotein)	Liver
PSA (Prostate-specific antigen)	Prostate
CA125 (Cancer antigen 125)	Ovarian
HE4 (Human epididymis protein 4)	Ovarian
CA15-3	Breast
CA27-29	Breast
CA19-9	Pancreatic Ovarian
CEA (Carcinoembryonic antigen)	Colorectal Gastric Pancreatic Lung Breast
HER2/neu (Human epidermal growth factor receptor 2)	Breast
Tg (Thyroglobulin)	Thyroid
hCG (Human chorionic gonadotropin)	Testicular Ovarian

The above-listed cancer biomarkers are mostly used to monitor therapy and detect recurrent disease (relapse). Exceptions include PSA used for prostate cancer screening, as well as AFP and hCG used for diagnosis of corresponding cancer types. There are several tests in use that measure serum levels of multiple biomarkers and combine results into a cancer risk index. In ovarian cancer prediction, the OVA1 test is a valuable tool to assess the likelihood of a peritoneal mass to be malignant. The test searches for the presence of 5 biomarkers. Included biomarkers are CA125 and 4 different proteins present in the blood. Combining immunoassay results with an AI algorithm that calculates the risk of malignancy has shown promising results. Immunoassays measure the number of biomarkers present with the use of antibodies.

However, the OVA1 test should not be used for screening because of its low specificity. Abnormal results do not necessarily mean the patient has cancer, as the biomarkers picked up by the test could be elevated in benign conditions. The test is primarily used to assess the likelihood that malignant lesions are present when the results of clinical and radiological evaluation are inconclusive. This is done prior to surgery. It is important to understand which tests can or cannot be used in the screening of asymptomatic patients.

False-positive or false-negative results can leave a lasting impact on both their physical and mental health. Ovarian cancer is problematic because there are no reliable screening procedures to detect it early. Measuring levels of CA125 and transvaginal ultrasound are in use, but the results are often uncertain. Scientists hope the use of AI can point out the inter-relationships between CA125 and malignant processes in the body, as its levels can be elevated in multiple types of cancer. Transvaginal ultrasound is already being automated, and the developed algorithm has the ability to classify tumors as benign or malignant. It has shown an accuracy of over 90% on a small number of samples, but it has yet to be tested on a large number of cases.

In breast cancer, the Tyrer-Cuzick model can estimate risk based on breast density, age, family history of cancer, age of the first period and menopause. It is used for informative purposes and helping women consider genetic counseling and testing. Even though it is described as the most comprehensive cancer risk assessment model, modern technology is beginning to overshadow it. An AI model using mammograms to calculate risk put double the amount of women who eventually developed breast cancer into the high-risk group. By improving the model, it will be able to predict which women will develop breast cancer in the next 5 years with more accuracy. This also reduces healthcare cost and patient's exposure to x-radiation since mammograms will be done less often.

Medical AI systems can fail when used in a different population than the one it was trained in. So far, the model detecting biomarkers of breast cancer has been successful in black women, even though the population used in training was predominantly white. The system must be tested in different countries and even continents before it can become a standard diagnostic process.

In cervical cancer, AI technology has been utilized in several recent studies. The aim is to reduce the workload of cytopathologists by separating malignant lesions from normal cytology, reduce observer bias and provide consistent classification. A complex supervised learning algorithm was presented in 2017, focusing on separating cells by shape, texture and color features. It showed high accuracy and precision (both over 98%), proving to be effective in early detection of cancer. The algorithm used Bethesda system of classification to label Pap smear images, which requires lots of training and expertise. AI has been used to personalize cervical cancer screening based on medical history and genetic profile, using Pap reports and HPV testing results. Several algorithms providing patient-specific recommendations for future screening, risk prediction and disease management have been tested. Their performance was inadequate, but they might be useful in the future after further optimization.

A condition that involves the abnormal growth of cells on the surface of the cervix is called cervical dysplasia. It is not a type of cancer, but has the potential to become cancerous and spread to nearby healthy tissue. Almost all precancerous lesions are caused by HPV (human papillomavirus), usually found when a Pap test is done. Since HPV is the most common sexually transmitted infection globally, most sexually active people are infected by it during their lifetime. In the general population, routine HPV testing is not necessary for men but has been endorsed for women. Despite the worldwide implementation of screening and vaccinations programs, cervical cancer is still a major health issue. This is where AI technology proved useful, identifying the exact HPV genotypes connected to cervical dysplasia that persists even after treatment. With the help of AI, several HPV-induced mutations have been analyzed in head and neck cancers. Artificial neural network (ANN) analysis was used. The information it provided can be helpful during patient counseling and to implement new vaccination programs.

In colon cancer, screening is somewhat problematic because patients are reluctant to provide stool samples, and colonoscopy requires extensive preparations. There is a multi-analyte blood test in development that utilizes AI to recognize disease-associated patterns in cell-free DNA, focused exclusively on colorectal cancer biomarkers. The results are promising so far and patients are more compliant because the procedure is non-invasive. People with higher than average risk of colorectal cancer, however, require colonoscopic surveillance. Conditions that increase this risk include inflammatory bowel disease and adenomas. Adenomas are benign tumors with glandular tissue structure. They can form colonic polyps and are usually treated as precancerous, as they may transform to become malignant. A real-time AI system was developed to help doctors diagnose early-stage colorectal cancer and precursor lesions during colonoscopy.

In lung cancer, computed tomography (CT) is being used more often for screening patients at risk of developing the disease. It uses a low dose of X-rays to create its images, some of which were used to train an AI model to predict the number of patients who will develop lung cancer within a year. The model outperformed radiologists when only one scan was available for diagnosis, reducing the number of both false positive and false-negative results. With multiple scans, their performance was equal. Future efforts will focus on combining the knowledge of experts with the computer's abilities to produce even better results.

Early detection of pancreatic cancer would be beneficial because 70-80% of patients are diagnosed at an advanced stage. Only about 5% live for more than 5 years after diagnosis. Since this type of cancer is not very common, screening everyone would be inefficient, exposing patients to unnecessary tests and potential side effects. There is potential for AI technology to recognize individuals with a higher risk of developing pancreatic cancer. An AI model was created in the UK to determine who is at risk by assessing symptoms, diseases and medications of various patients in the two years prior to cancer diagnosis. By recognizing trends in these large amounts of data, the system can narrow down the number of people that need to be screened and increase the chance of surviving this cancer.

AI should be used as a tool to identify high-risk cases and help with an uncertain diagnosis. As the population is aging and precision medicine is evolving, pathologists will do their job better if they are provided with better tools. However, recent biostatistics data shows early cancer diagnosis is losing its benefits as treatment methods become more effective. While the 5-year survival rates are higher, in 10 or 25 years, the same amount of people die of cancer, with or without screening. Short term survival rates are also raised because non-progressive tumors are detected more often. Such tumors have a good prognosis even without treatment but can cause other health problems if the patient undergoes surgery and chemotherapy. Overdiagnosis is a genuine problem, and the stress it causes to the patients should not be ignored. Still, 5 years is a long time for both patients and their families, so healthcare professionals have a valid reason for trying to prolong it by any means possible.

Cancer classification

In biomedicine, the accurate classification of diseases and its subtypes poses a major challenge. To diagnose cancer means to accurately identify the pathological site of origin and the type of cells involved. Primary site is a term used to describe the original or first tumor in the body. The same cancer cells can spread to other parts of the body and form secondary tumors or metastases, but this possibility is determined by the primary site. The most common sites of cancer include breasts in women, colon, lungs, prostate, cervix and skin. Metastases have the same characteristics as primary cancer and the spread to lymph nodes, bones and lungs define the stage of cancer.

Many signs and symptoms can indicate the presence of cancer in the body. Diagnosis is problematic because those symptoms are non-specific and usually appear when the tumor has significantly grown. Nevertheless, imaging methods and lab tests may be performed when either the patient or physician has doubts. The preferred method to establish or rule out the diagnosis of cancer is a biopsy, which is a

process of removing tissue for microscopic evaluation. If the tumor mass is inaccessible, imaging techniques are used to locate and visualize it before the biopsy is performed. Examination of malignant tissue enables the classification of tumors and histologic grading while revealing the extent of its spread (pathologic staging).

It's important to identify which type of cell was transformed into cancerous because different types have different growth rates and prognosis. Cells usually differentiate into many types as they develop, so there may be multiple types within a tissue or organ. Once cancer diagnosis has been confirmed, pathologists try to determine how closely malignant cells resemble healthy, mature cells. This process is called grading. Low-grade cancers are well-differentiated, cells look relatively normal and the disease has a better outlook. High-grade cancers are poorly differentiated and tend to grow quickly.

For many types of cancer, doctors use the TNM staging system. Staging can be clinical or pathological. Clinical staging uses results of tests done before surgery, including physical examinations, imaging scans and biopsies. This is important when physicians are reviewing treatment options and trying to get an idea of the patient's prognosis. Pathological staging is based on what is learned about cancer during surgery and gives more precise information about the outcomes of treatment. Not all types of cancer use TNM staging. Exceptions include central nervous system tumors, cancers in children, cancers in the blood and female reproductive organs.

Table: TNM staging system.

Primary tumor (T)	
TX	Primary tumor cannot be evaluated
T0	No evidence of a primary tumor
Tis	Carcinoma in situ, cancer cells are present but have not spread to neighboring tissue
T1, T2, T3, T4	Tumor size and/or amount of spread into nearby structures
Regional lymph nodes (N)	
NX	Regional lymph nodes cannot be evaluated
N0	Nearby lymph nodes do not contain cancer
N1, N2, N3	Size, location and/or number of nearby lymph nodes affected by cancer
Distant metastasis (M)	
MX	Distant metastasis cannot be evaluated
M0	No distant cancer spread has been found
M1	Cancer has spread to distant organs or tissues

Staging might be done again if the cancer grows, spreads or comes back (recurs) after therapy. This process is sometimes called restaging, and it means the procedures for initial diagnosis have to be done again. This includes physical exams, appropriate imaging methods, biopsies, etc. The new classification doesn't replace the original one. The staging described at diagnosis remains the most important factor when considering treatment options and survival rates.

AI and deep learning technology have found many applications in the process of medical diagnosis. Over the years, methods ranging from neural networks to autoencoders have proved to be useful in image-recognition tasks. Today, two classes of AI methods are commonly used. The first one has features defined by mathematical equations and can be quantified using computer programs. It is useful for classifying patients to provide clinical decision support. Since it utilizes predefined features, it can't adapt well to interpatient variations seen in imaging techniques such as CT or MRI. This is why more and more research is dedicated to the second method using deep learning. Deep learning algorithms don't require prior definition by human experts and provide information automatically. This enables them to analyze all sorts of data and be applied to a variety of clinical conditions. Radiologists identify pathological processes by noticing changes in image intensity or unusual patterns, which is highly subjective. When trying to automate examining medical images, machines have yet to surpass expert radiologists. But AI technology performs undeniably better in complex tasks, such as noticing more features, saving time, predicting malignancy likelihood and tumor segmentation. Segmenting both tumor and healthy tissue is very important for radiation treatment, but human readers simply don't have the capacity to notice the subtle variations in texture or shape.

Cancer cells can be of similar size, shape and structure, making them harder to identify by imaging techniques. Advanced learning technology can help find existing patterns in cell morphology connected to specific mutations and biological processes. A convolutional neural network (CNN) named Inception V3 that processes raw images was trained to distinguish between healthy tissue, lung adenocarcinoma and lung squamous cell carcinoma. The model analyzed whole-slide images from lung biopsies, which are high-resolution files created by capturing many small images from a microscopic slide and montaging them together. This CNN was also capable of predicting whether mutations exist in 6 different genes usually responsible for lung adenocarcinoma.

Researchers stated that future improvement should be focused on detecting changes in the tumor microenvironment. This was done a year later when another CNN model was developed to classify lung cancer cells based on their appearance. The major cells types present were identified as tumor cells, stromal cells (connective tissue cells) and lymphocytes. Observing how the cells are distributed in the malignant tissue can reveal growth patterns of cancer cells, their relationship with the tumor microenvironment and the intensity of the body's immune response. This tool was named ConvPath and it's meant to help pathologists find tumor cells faster. It can also be used to predict patient prognosis and response to treatment. Future improvement should be focused on extending these methods to other histological subtypes.

Tumor type classification from genomic data such as mutations, copy number alterations, gene expression and methylation can be done but is not a part of routine clinical care. Analyzing molecular data from tissue biopsies of solid tumors has shown promising results, sometimes prompting cancer reclassification and change of therapy. Studying molecular profiles is a way to improve the link between biology and disease. Researchers used a random forest classifier to predict tumor site of origin and it displayed accuracy of 95% when analyzing cancer types with distinct genomic changes. This technology can be useful when the tumor's tissue of origin is unknown, and when deciding whether tumors in the central nervous system are primary or metastatic. A patient can also have two separate types of cancer and labeling them correctly (not as metastases) significantly changes the treatment plan. If implemented correctly, AI can have a powerful role in supporting clinical decisions. It can complement standard histopathological and imaging methods, resulting in improved diagnostic accuracy.

In cancer diagnostics, even the results of a highly invasive procedure such as biopsy can be ambiguous. Using the wrong drugs and radiation treatment plan can have ill effects on the patient's body without actually affecting the cancer. When sorting cancer into subtypes, pathologists have started to turn to artificial intelligence to classify the tumor. One of the more advanced methods in use is a methylation-based classifier for cancers of the central nervous system. Methylation is a process of attaching hydrocarbon molecules to DNA, specifically to cytosine and adenine bases. It modifies the activity of genes without causing a mutation. Since novel methylation profiles are continuously discovered, there is no way for a pathologist to be able to define them all. This is where computers excel, finding patterns the human eye might have missed and categorizing them into groups. Studies show that 12-14% of brain tumors have been misdiagnosed, which is a significant number. The implementation of AI algorithms could significantly cut those error rates. However, methylation profiling is expensive so scientists hope simpler biomarkers can be found for differential diagnosis of cancer.

Rather than only identifying potential biomarkers, machine learning algorithms can be used to understand and define underlying disease mechanisms. Disease biology is very complex, and identifying associated genes might provide more answers as to why a particular clinical phenotype is presented in a given individual. Deep learning algorithms can be trained to explore how gene, protein-protein and chemical interactions change when a disease is present compared to healthy states. This process can be developed and implemented into precision medicine to identify patients who are more severely affected by a disease or determine who should receive a certain type of treatment.

Bladder cancer is a fairly common and aggressive type of cancer. A lot of early stages and even more advanced stages of bladder cancer are discovered late because patients don't notice symptoms or think something benign is causing them. Current methods for diagnosis include cystoscopy and biopsy. Both procedures are highly invasive, expensive and might have severe side effects for the patient. Researchers have been working on a multilayer perceptron (MLP) algorithm, which can analyze metabolites present in urine samples and connect them to different stages of bladder cancer. Carbohydrates like galactose and starch are linked to early-stage, while amino acids are linked to late-stage bladder cancer. Observing changes in metabolite concentrations in urine can be an effective method for detecting and monitoring cancer. These changes mostly happen due to mutations in genes that regulate metabolic pathways. Connecting affected metabolites to corresponding genes can help determine the best treatment for each patient.

While cystoscopy is an essential procedure for diagnosing and monitoring bladder cancer, some lesions may be overlooked. Because small and flat tumors are challenging to identify, they can negatively affect treatment if they are missed during surgical resection. There is a study proposing a support system for the cystoscopic diagnosis of bladder cancer with the help of a convolutional neural network. The AI system displayed high accuracy when classifying tumor lesions, but has to be further developed to become a part of clinical practice. The algorithm still needs surveillance by physicians, especially when examining inflammation-induced changes in the mucous tissue of the bladder.

Another rapidly growing area of research is the use of AI in gastrointestinal endoscopy, a procedure used to examine a person's digestive tract. Several algorithms were developed to help detection and optical diagnosis of colon polyps, but there are other aspects of gastroenterology that need to be improved. An important issue is the management of early gastric cancers. Predicting how deep cancer has invaded through the layers of the gastric wall is crucial when considering the metastatic potential and whether surgery will be necessary. There was a promising AI model developed that used deep learning to identify highly invasive cancers. It has very high specificity and if it can be applied in clinical settings, it will help minimize overdiagnosis and unnecessary surgical procedures.

The main imaging method in breast cancer is mammography, the gold standard for detecting early-stage breast cancer before clinical diagnosis. When introducing AI into the diagnostic process, most researchers are focused on improving this method. Mammography is considered effective in reducing mortality related to breast cancer, resulting in a large number of women being screened. This creates more work for radiologists and the need for AI assistance, as the amount of data being generated is getting larger every day. Other relevant methods include histopathology and ultrasound, with much less attention given to breast MRI. The use of MRI has been increasing because of its significant contribution to lesion classification, segmentation, disease progression and response to treatment. Various machine learning algorithms were developed over the years, from support vector machine (SVM) to CNN, with encouraging results. Unfortunately, the reliability of the system is still too low for diagnostic use, but there is potential. Due to the large amount of morphologic and dynamic data that can be extracted from it, MRI remains the most appealing method for implementing AI.

MRI might not be suitable for all patients. Since it uses a magnet to obtain images, it can be unsafe for patients with implanted medical devices. Impaired kidney function limits the use of contrasting agents and psychological conditions such as claustrophobia make the procedure challenging to endure. With such patients, ultrasound might be recommended, being overall cheaper and providing images in real-time. There were attempts to implement AI technology into ultrasonic equipment, but it should be noted that most systems cannot generate images and perform AI analysis simultaneously. A simplified neural network was combined with a GPU workstation to help physicians locate tumor lesions in real-time with good accuracy. So far, it was tested for breast cancer detection, but it could be a valuable tool in daily clinical practice. Since the developed algorithm uses less computational power, it could be embedded in multiple smart devices in the future.



An external GPU workstation enables the simultaneous use of ultrasound and AI assistance in real-time.

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There is a growing number of patients visiting endocrine specialists for thyroid nodules because of increased use of screening programs and highly sensitive imaging techniques. These nodules are solid or fluid-filled lumps of thyroid cells in the thyroid gland. Deciding whether a lump is benign or malign is challenging, and diagnosis requires the use of multiple diagnostic methods. Cytology supported by ultrasound imaging is widely used today, but a quarter of results turn out unclear and malignancies are not accurately identified. Scientists propose the use of high-resolution color ultrasound and 3D scanning of the whole neck area, which can provide more precise results than conventional grayscale imaging. These techniques are ideal for training and validating AI systems. AI has shown great performance in cytological and ultrasound analysis of the thyroid gland. Its sensitivity has shown to be equal to that of experienced radiologists, but unfortunately, the specificity is still too low for clinical use. Nevertheless, AI algorithms have the potential to combine imaging results, patient history, clinical examinations and thyroid lab results to support endocrinologists when deciding whether surgery is necessary.

In prostate cancer, the results of the biopsy can be insufficient. Samples are usually taken from predetermined locations on the prostate, sometimes missing the actual cancer site. To remedy this, multiparametric magnetic resonance imaging (MRI) is being used. It is a special type of scan that creates more detailed pictures of the prostate than a standard MRI. It does this by combining four different types of images and using contrasting agents. The results are a subject of debate between radiologists and correct identification of the tumor mass requires years of training. This presents a challenge in hospitals in developing countries, which don't have such experts in their ranks. AI programs can provide rapid diagnosis, more accurate prognosis and better treatment in regions that lack radiologists.

FocalNet is an AI-based system, trained on pre-operative multiparametric MRI scans of patients waiting for prostate removal surgery. When asked to determine the rate of malignancy in a new set of scans, its performance was identical to experienced radiologists'. This can improve diagnosis when radiologists are not available or remove variability between readers. Multimodal images have improved the accuracy of tumor characterization and assessment. Other examples include PET hybrids: PET-MRI and PET-CT. These techniques can be further explored without sacrificing image details by implementing more advanced algorithms. Hybrid PET-CT has already shown good results in patients with lung cancer and lymphoma. A convolutional neural network was used to automatically detect, localize and classify potential malignant tissue on whole-body scans. Even though several algorithms exist, in practice the majority of software need manual corrections to produce accurate results. This happens because radioactive tracers used to visualize organs and tissues don't distribute evenly, due to differences in tumor and body composition. An example is poor uptake in adipose tissue. It is important to consider these aspects because a higher concentration of tracers indicates higher chemical activity in certain tissues.

Technology analyzing stained tissue samples under a microscope is not only less expensive, but accessible to more hospitals as well. Analyzing slides under a microscope is prone to errors because it depends on subjective judgement and skill level of the pathologist. Microscopy is at a disadvantage when examining subcellular structure, which needs specific reagents, specialized equipment and complicated procedures. Even then, the original condition of the sample may be disturbed if stains are used and affect diagnosis. Automated high-throughput imaging (HTI) is an advanced microscopy technique with the ability to discover how drugs change cell morphology. Some of these changes may be invisible to the naked eye, while machines can notice them and even predict the effect of drugs on unrelated molecular targets. This means that once the neural network has been trained, it can be used in other analytic procedures, not only microscopy.

Cancer therapy heavily relies on diagnosis and staging of cancer. Microscopic assessment of tissue samples is cost-effective but requires trained pathologists. To improve accuracy and efficiency of cancer diagnosis, a solution using an analog microscope with real-time AI-based overlay was proposed. A deep learning algorithm processes each image and produces a heatmap as output, outlining the suspected cancer site. Pathologists can then see the additional information over the original view through the eyepiece. This method was tested so far for detecting metastatic breast cancer and the classification of prostate cancer with Gleason grading with good results.

★ [Detecting cancer in real-time with machine learning.](#)

Video 2. Pathologists and engineers present an AI-powered microscope that points out potential cancer sites. It is essential to realize the technology offers only clinical decision support. Cooperation between pathologists and AI is required for it to be useful in routine diagnostic procedures.

There is a growing incidence of skin cancer and it presents a huge opportunity for automated detection. Diagnosing skin cancer, especially melanoma, early causes a drastic reduction in mortality. Recent work using AI has been focused on dermoscopy and clinical photographs because such data is easy to acquire. A dermatoscope is used to capture digital photographs of magnified suspicious skin lesions to find potentially malignant patterns. Clinical photography may pose a challenge in the automated analysis because the capture device is not in contact with skin and background artifacts may confuse the AI. While clinical testing of CNN in dermatology is still in progress, mobile apps to diagnose concerning spots on skin have the potential to help both patients and researchers. Apps inform patients whether they should visit a specialist while images can be sent to researchers to help develop better methods for diagnosis. This mobile technology has potential because it is available to a large number of people from the comfort of their own home.

Numerous diseases are aided by computer systems, with leukemia being the one with the highest number of fatalities among children and young adults. Leukemia is a group of blood cancers that originate in the bone marrow. It causes abnormal growth of white blood cells, which are the cells of the immune system involved in protecting the body against infections. Microscopic analysis is the most common method to diagnose leukemia, and it's prone to errors since it's done manually. An automatic method using blood smears was proposed to reduce workloads for pathologists, combining SVM and CNN algorithms. CNN was used to extract features from images while SVM was used to classify them as either pathological or not. Since the proposed method doesn't require segmentation, it can be applied to multiple databases and produce excellent results. Segmentation means separating a region of interest from the background of the image. While the segmentation process can be a great foundation for feature extraction and classification, it is prone to errors when applied to images with different characteristics than the ones used in training. This new method's accuracy was over 99%, and with some fine-tuning, it will hopefully become suitable for routine diagnostic use.

White blood cells in leukemia display subtle changes in their surface molecules which can be used to separate them from healthy cells. With the development of markers that can specifically bind to those molecules, multiparameter flow cytometry (MFC) is becoming a valuable tool in diagnosis, classification and monitoring patients with leukemia. In laboratory hematology and immunology, flow cytometry is a commonly used technique. It measures the amount of the laser beam that passes around the cells and bounces off of particles inside of the cell in a fluid mixture, usually a blood sample. The results are presented as different graphs, showing the count, size and internal complexity of cells. The more complex version of the method, MFC, can measure multiple parameters on each cell simultaneously, with cells being labeled with different fluorescent colors. The number of markers used in flow cytometry has significantly increased over the years to allow for a more precise diagnosis of leukemia and other hematological disorders. The need for faster and more accurate diagnosis is an excellent opportunity for deep learning to be introduced into this method. The collaborative use of self-organizing map (SOM) and CNN has shown promising results so far. Further improvement for rare disease subtypes can be expected when more samples are available for training the models.

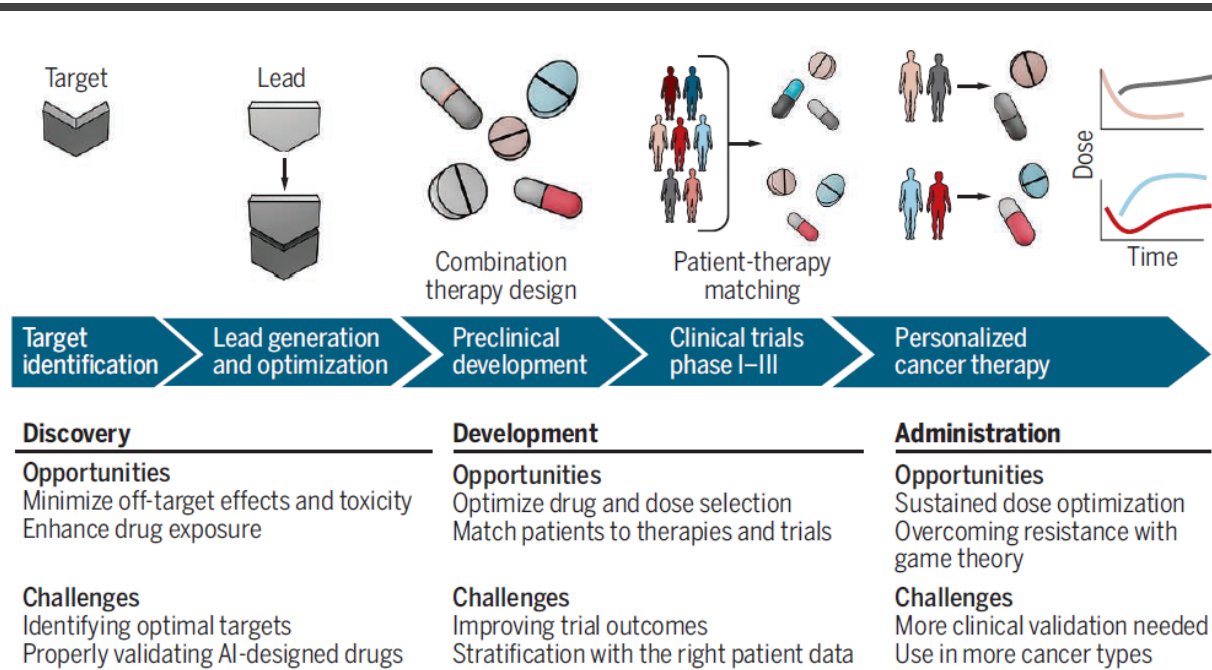
Cancer treatment

There are multiple types of cancer treatments and most patients will receive more than one. The goal of primary treatment is to remove cancer lesions from the body completely, and it's mostly done with surgery. Clinicians may also decide on radiation therapy or chemotherapy, depending on the type of cancer present. Adjuvant treatment is used to eliminate any leftover cancerous cells after primary treatment to improve prognosis. Chemotherapy, radiation and hormone therapy are commonly used for this purpose. If this kind of treatment is done to reduce the size of tumor before surgery, it's called neoadjuvant therapy. To relieve side effects of treatment and symptoms of cancer such as pain, palliative treatment might be used. Other commonly used procedures for cancer management include bone marrow transplant, immunotherapy and targeted drug therapy.

Modern cancer treatment is based on the anatomical location and tissue of origin of the primary tumor. If cancer has metastasized, it is important to identify the primary site with imaging or pathological examination. When solid tumors recur after treatment or progress, diagnostic tests including laboratory tests, imaging procedures and biopsies need to be done again. Different populations of cancer cells might exist in the same tumor or between the primary tumor and the site of metastasis. To determine a tumor's molecular profile and choose the right treatment, tissue samples are usually taken from a biopsy or diagnostic surgery. Both methods cannot accurately capture the complete genomic landscape of patients' cancer.

Since targeted therapy is based on biomarkers of the tumor microenvironment and mutational status acquired via biopsy, certain populations of cancer cells can be missed. If cells with resistance-inducing mutations are overlooked, chemotherapy might be ineffective and cause a devastating relapse. This is evident in brain tumors which are not only aggressive but show extensive cell-by-cell molecular differences. Tumor lesions are continually changing and evolving, modifying its genetic composition and even location through metastatic spread. Therapeutic intervention can further encourage this evolution, allowing cancer to explore resistance mechanisms and mutate due to the effects of cytotoxic chemotherapy. The cells that survive treatment can repopulate the tumor and appear to be more aggressive because of their resistance to initial drug therapy. There has not been much therapeutic progress to remedy this issue, and it emphasizes the need for more advanced technology to repeatedly monitor entire tumor lesions, not only at the site of the biopsy.

Imaging techniques are often used to assess response to treatment because they are non-invasive and easy to implement into clinical practice. However, successful response to therapy might not result in tumor shrinking, and the need for procedures measuring something other than size is rapidly increasing. With the rise of machine learning technology, imaging features can be combined with gene expression profiles, copy number alterations and clinical data.



Different stages of cancer therapy can benefit from the implementation of AI, but several challenges must be overcome for it to revolutionize clinical practice.

AI has the potential to improve several aspects of cancer therapy, such as drug discovery and development. This includes drug production, quality testing and admission to patients. AI platforms can analyze biomarkers to accurately match patients to clinical trials and personalized cancer therapy with individual patient's health records. Radiation therapy can also benefit from AI assistance, from choosing the right dosage depending on the size of the tumor to selecting complementary chemotherapy drugs. AI can be taught to develop 3D renderings showing the best way to distribute radiation for each patient so therapy can be started sooner. In surgical procedures, AI found its role in robotics and decision support systems.

Drug repurposing involves evaluating a library of drugs in use or in clinical trials, hoping some can be used to treat multiple diseases. However, it is difficult to repurpose compounds because they have to be compared with drugs already used for treatment and see if they interact with each other. This was made easier by adding data about structure, activity and other properties into publicly available databases. Chemists can consequently focus on evaluating the accuracy of their search algorithms, rather than how to label each new molecule so it can be compared to others.

Even though many advances have been made in technology and understanding human biology, the process of drug discovery still takes a lot of time and resources. The probability of a drug successfully completing clinical trials is 11.83%. Designing drugs can be done through retrosynthesis, where target molecules are recurrently transformed into more simple, known compounds. Chemists choose the most promising transformation pathways, but there is no guarantee that the body will process molecules the same way. Another way to design drugs is by exploring compound libraries. It involves a search done by machines to select molecules with desired properties and pharmacological effects. This is where deep learning technology can produce great results since it generates pharmacologically active compounds from a small set of starting templates. There is no need to search through existing databases, and results are visible immediately. Once the neural network is trained, it continues to learn and improve on its own by evaluating previous results. Since the neural network is still a computer, no matter how advanced, skilled user input is required to keep it from generating similar drugs.

Reinforcement learning was used to fully design a new compound in just 21 days, compared to conventional drug development that takes approximately 1 year. Another platform was able to predict compound and target cell receptor binding. This is useful for minimizing drug binding to receptors with similar structure, but not relevant to the patient's disease and therapy. During drug development, compounds are also tested with each other to address multiple drug targets and provide more efficient treatment. However, compound interaction can produce unforeseen toxicity. AI can be used to identify the best drugs for combination therapy while providing optimal doses and minimizing toxicity. There are ongoing clinical trials for an AI technology platform to establish new drug combinations and identify patients who might be more responsive to treatment. It is currently used to personalize multiple myeloma therapy. The platform uses a small amount of blood or bone marrow sample to map the drug response for cancer cells of each patient.

Biomarkers such as genomic alterations can be used to predict response to treatment and patient outcomes, which provides more accurate results than pathology. Artificial intelligence, genomic biomarkers and patient health records have been combined in SYNERGY-AI study, which helps in pairing oncology patients with promising clinical trials. Since every cancer is unique to the patient, AI will soon be needed to ensure individualized treatment. Drug-resistant tumor cells can eventually cause treatment to fail if high doses of therapeutics are used.

Differences in patients' biorhythms can also change the efficacy of drugs and their toxicity. Calculating both dosage and optimal time for drug administration for each patient manually is impossible since clinicians are already overwhelmed with large amounts of medical data. This is why scientists claim personalized medicine will be impossible without the help of AI, which can make sense of multi-factor data without slowing down the workflow. AI is beginning to redefine clinical standards of cancer therapy, improving drug accessibility and offering advanced personalized care.

It has to be noted that more work needs to be done to fully integrate genomics and electronic health records (EHR) to allow for precision diagnostics. Machine learning methods linking gene composition to medical conditions are still inconsistent as well as names on laboratory tests ordered by doctors. It is essential to work on integrating information systems because it improves the whole healthcare process, from the accuracy of tests used for diagnosis to patient satisfaction.

★ [The Future of Cancer Research](#)

Video 3. A patient's struggle with life-threatening stage 4 cancer. The video emphasizes how important innovative approaches are to combat specific cancer types and how the need for precision medicine grows with each passing year. It also shows how a patient's determination and education can open pathways to new treatment options instead of waiting for science to make the first move.

Predicting cancer recurrence and survival

Most research defines survival as any incidence of cancer in which the patient is still alive five years following diagnosis. Medical statistics are commonly used for cancer prognostics, but often fail to provide accurate results. Clinicians are also concerned about patients' risk of developing cancer, tumor recurrence and death after treatment. All these aspects are important when choosing the right therapeutic procedure for the patient. While AI is rarely used in prediction, the ability to use multi-factor data is encouraging a lot of global research in that area.

For some types of cancer, such as prostate cancer, making prognoses is difficult. Current methods either require complex algorithms for making predictions, have low accuracy or have trouble finding genes with significant mutation difference between groups with different prognosis. For ovarian cancer, the results of research are more promising. A combination of statistics and unsupervised clustering was used to predict outcomes and identify patients with poor survival rates in hopes of personalizing treatment. The images were obtained from CT, which is done routinely before the operation. Since the entire ovary mass is analyzed, extracted prognostic and biological information is more accurate than single-site biopsy.

Certain types of machine learning algorithms perform better than others when calculating cancer survival rates. Random forest learning method has shown good accuracy in cancer survivability prediction, particularly in patients with breast cancer. For cancers with high incidence and high mortality, such as advanced colorectal cancer, lung and prostate cancer, survival time is more beneficial when measured in months. This requires the use of advanced algorithms but provides valuable information to clinicians when choosing treatment. Benefits are usually weighted against risks, and highly effective treatment might be used despite the side effects if the patient has little time left.

In earlier years, cancer survivability was estimated based on clinical features of tumors and medical expertise of clinicians. Today, all kinds of medical information are collected to improve hospital efficiency, and a growing amount of cancer data is stored in databases which are available for constructing machine learning models. AI can transform data into insight and has the ability to simultaneously handle medical history, physical examinations, laboratory, imaging and genetic data.

Using gene signatures to predict metastases prognosis and adjust drug therapy has shown great potential, with only 50 genes necessary for accurate results. However, researchers concluded better results could be achieved by combining both clinical and genetic marker information. A study combined genetic variants with demographic risk factors to calculate the possibility of breast cancer development in an unknown individual. A machine learning technique called gradient boosting was used to analyze collected data. Researchers found that the genes interacting with demographic risk factors were involved in apoptosis, angiogenesis (formation of new blood vessels) and estrogen pathways, which can outline potential targets of treatment.

Analyzing clinical data alone can also provide valuable insight into critical factors for disease progression. Various research work suggests age at diagnosis, tumor size, number of lymph nodes positive for metastasis and even the month of diagnosis can influence cancer prognosis. It is interesting to note that patients diagnosed in July or August have a higher risk of death, as described with statistical methods.

A common non-pharmacological approach used to help cancer patients cope with their disease and possibly live longer is psychotherapy. There is scientific data to back up the claim that social support and encouraging emotional expression affect the rate of disease progression. During oncological treatment, there are multiple procedures that can cause distress and pain such as chemotherapy, surgeries and hospitalization. Modern technology offers promising support to cancer patients with the evolution of virtual reality (VR). VR is a computer-generated virtual environment which can support patients during their stay in the hospital or offer rehabilitation at home. The immersive real-time animation generated by the system serves as a distraction to reduce pain and allows patients to disconnect from the stress-inducing hospital environment.

The future of AI in healthcare

Many scientists believe that AI will play an important role in the near future as the main driver of precision medicine. In the last few years, a lot of research was focused on improving AI-assisted screening and diagnosis. Treatment recommendation and prediction of survival or metastasis sites is still challenging, but there's hope that AI will eventually master these domains as well. Imaging methods might be automated very soon since machines have shown great performance when analyzing radiology and pathology images. Speech and text recognition are already in use to improve patient communication and capture clinical notes. Some healthcare providers have experimented with chatbots and using mobile apps to make appointments or refill prescriptions. Another potential opportunity for automation is nursing, where machine learning can help reduce paperwork so more time can be spent with patients. Some possible applications include automatic appointment scheduling, identifying patients that might require urgent care and data integration from multiple diagnostic procedures.

Healthcare professionals have mixed feelings on the use of AI technology, looking forward to reduced workloads but not losing their jobs entirely. Saving time can help save patient lives, as machines can assist clinicians by flagging urgent cases. AI can also help reduce diagnostic errors. Research suggests the performance of deep neural networks is on par with real-life experts when it comes to diagnosis of skin and brain cancer, sometimes even outperforming them. Still, most experts believe AI won't be completely replacing either clinicians or radiologists in the next few decades.

A prominent issue in the application of AI in healthcare is the "black box problem", meaning that clinicians don't know how machines generate their predictions. Development of maps and other visualization helps remedy this problem. It can even be used to spot if models have been manipulated by feeding special cases into it. The need for transparency might cause AI algorithms to become less accurate in their predictions. In turn, they should be easier to interpret and tailor to a patient's individual needs. Even though the black box problem exists when humans work in medicine as well, unexpected and unwanted decisions made by deep learning algorithms cause greater discomfort. While misjudgment can happen in healthcare, it is uncertain who will be held responsible when an AI system was involved in the decision. Discrepancies in diagnostics can arise because of differences between patients or diagnostic error and bias. Clinicians should be able to provide feedback for the algorithm to implement, while the algorithm should actively inquire clinicians about uncertain cases. Bias should be countered by allowing experts to disagree with system behavior.

AI algorithms trained on a particular population are rarely tested on others, simply because data may be labeled differently or previously unnoticed small factors may confuse the machine. Changes in hospital IT systems and machines taking medical images also affect the algorithm's accuracy. Different populations can have distinct demographics and traits. AI usually doesn't have the ability to generalize across a population without additional training and validation data. The same system cannot be used in Europe and America without displaying different specificity and sensitivity, which can harm the diagnostic process.

AI development and implementation should be controlled every step of the way by several people, from software developers, government agencies to medical professional bodies. Each should be well informed on the use of AI and held responsible for any safety or quality issues that arise. Collaboration is essential due to the fact that physicians require more training in science and machine learning, while most data scientists don't have medical backgrounds. There are also concerns regarding privacy and competitiveness when sharing patient health information between institutions.

Most healthcare organizations don't have adequate infrastructure to collect data needed to train algorithms. Patients of different ethnicities can receive incorrect diagnosis if the system is not evaluated and recalibrated manually after implementation. Huge potential lies in the use of cloud computing and EHR. Still, the main issues are quality of entered data and patient privacy which disables data sharing between different healthcare departments or institutions. A large amount of data is still being collected and stored physically, from doctor's notes to radiographic images. There is a growing need for healthcare administration staff which can organize incoming patient data and monitor any new algorithms that may be implemented in the future.

While practitioners do benefit from clinical decision support systems, overreliance should be avoided. Some scientists are concerned that the widespread use of AI will decrease human knowledge and capacity over time. It is becoming evident that reading medical journals is no longer enough to keep up with the innovations in clinical practice. Education needs to focus on helping medical professionals understand how to extract useful information from massive amounts of data available and leave the rest to algorithms. If used responsibly AI technology will not damage patient-doctor relationships, but allow clinicians to devote more time to challenging cases. Appropriate education on the advantages and limitations of AI use is crucial for preserving trust, which is vital to effective healthcare.

It is important for physicians to understand the tools they are working with adequately. Many of them already expressed discomfort when it comes to statistics. This affects their ability to explain the meaning of predictive values and survival rate calculations to their patients. Physicians educated in mathematics and technology are more confident in the benefits of AI. Machine learning can also be a gateway to further education, helping new healthcare workers become confident in their skills by pointing out information they might've missed. Modern technology will inevitably transform the field of medicine. Both present and future medical professionals should be confident in navigating this new area to get the most out of personal and professional opportunities AI will provide.

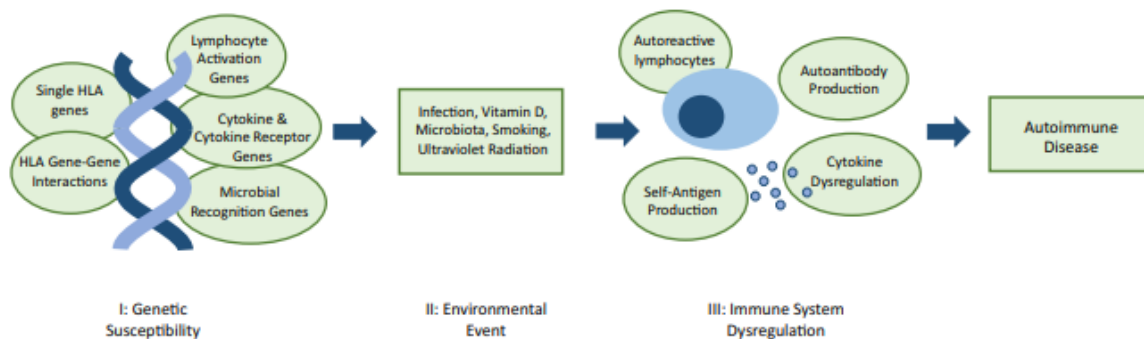
UNIT 2 Applications of artificial intelligence and machine learning in autoimmune diseases

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One of the most complex and adaptable system in human organism is the immune system, serving as a sentinel between diverse environmental stimuli and bodily responses, via numerous cellular and molecular interactions. Its main purpose is to defend and clear the organism from any cells or molecules that are not part of the body and are recognised as „not self“. Autoimmune disease arises when the immune system starts to recognise components of the body, or „the self“, as „not self“, activating different cells and pathways to attack tissues and organs of the body. There are over 80 known autoimmune diseases, the most common and research being type 1 diabetes, coeliac disease, multiple sclerosis (MS), psoriasis, and rheumatoid arthritis. This class of disease is already very prevalent in the human population and prevalence continues to grow by estimated 9% every year¹. If the prevalence of cardiac diseases and cancer continues to drop, autoimmune diseases could become the leading cause of illness and the highest burden on a country's economy in developed countries.

The reasons for extreme rise of these conditions are largely unknown, but certainly correlated to drastic environmental changes and lifestyle trends in modern times. In the words of Fred Miller, USA based environmental health and autoimmunity scientist: “Our gene sequences aren’t changing fast enough to account for the increases. Yet our environment is—we’ve got 80,000 chemicals approved for use in commerce, but we know very little about their immune effects. Our lifestyles are also different than they were a few decades ago, and we’re eating more processed food.”

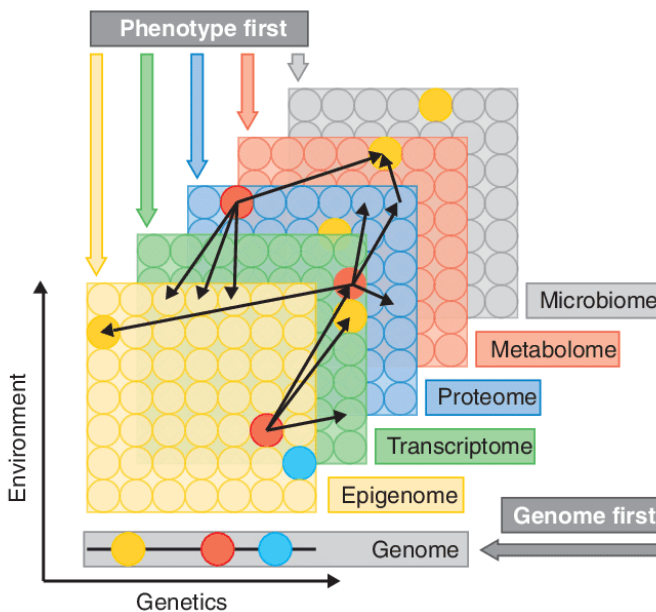
Three elements contributing to development of these conditions are genetic disposition, environmental factors and immune system dysregulation. Specific individual combinations of genes regulating immune system interactions can lead to a person being predisposed to immune dysregulation ab initio (without environmental induction) or following exposure to different microbial agents, foreign antigens etc. The final result could be formation of autoreactive lymphocytes, cytokine dysregulation and self-antigen and autoantibody production.



The three elements participating in the autoimmune disease development. I genetic disposition (a specific combination of genes like the ones encoding for human leukocyte antigen (HLA) proteins that affect the regulation of the immune system), II some of potential environmental triggers, III examples of immune system dysregulation events.

Due to extremely high individual genetic and environmental variability the manifestation of an autoimmune disease is also extremely diverse and complex, in the domain of a single disease, as well as among them. The data used to diagnose and prognose the disease encompass numerous clinical data types, such as laboratory tests and examinations, symptoms at diagnosis and images obtained via colonoscopy, CT (computed tomography) and MRI (magnetic resonance imaging). During the last few decades, other, more personalized types of data are also being produced and gathered, coming from “omics” technologies, including genomics, epigenomics, transcriptomics and proteomics. Introduction of this type of data can help create a more complete picture of autoimmune disease, leading to novel insights and

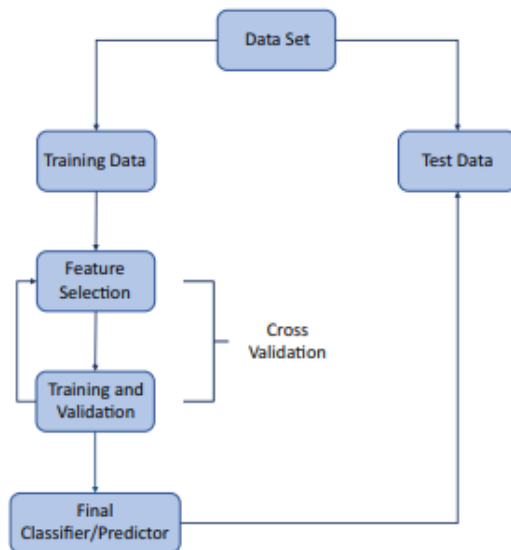
development of better treatments. “Omics” data are very abundant, complex and differential among patients, calling for highly sophisticated and advanced methods for their classification, unification and disposition to clinical use. The only way to manage this complexity and to combine and interpret together clinical with “omics” data is by using artificial intelligence algorithms, especially machine or deep learning.



Diverse types and interconnections of multiple omics data4.

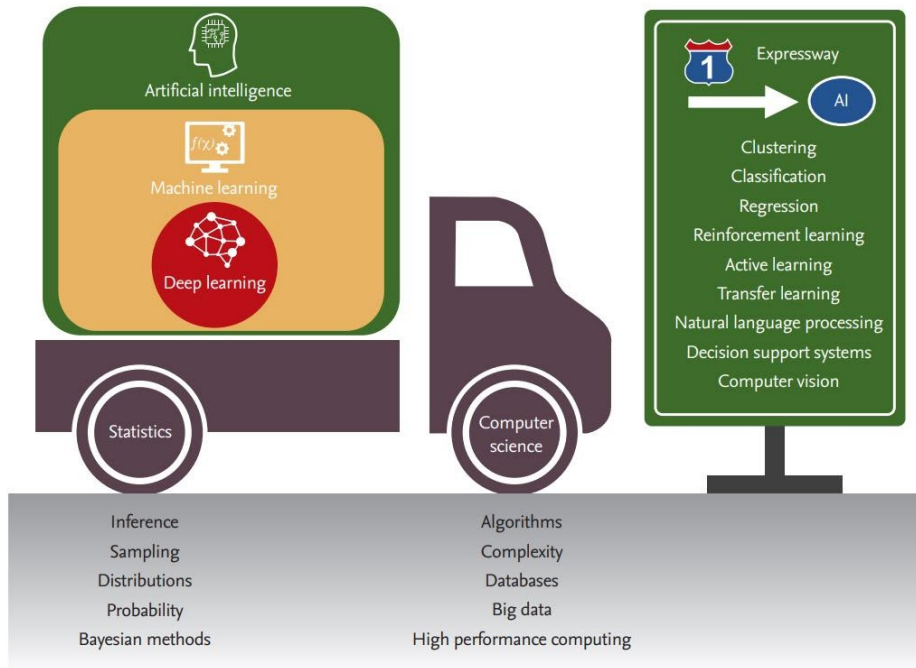
Artificial intelligence (AI) is the study of methods to imitate intelligent human cognition, like recognizing logical and semantic patterns in the large sea of data, making connections and classifications, assigning identity to novel input entities and predicting outcomes, the last two processes being the final purpose of AI use in the field of autoimmune diseases. Two ways of learning in algorithm development include supervised and unsupervised learning. During supervised learning, an algorithm is trained on a training dataset to recognize the patterns that are associated with specific labels (i.e. healthy and diseased). Following the learning stage, an

algorithm can assign labels to novel data, by generalizing patterns established in the training data to the test data.



Simplified workflow for developing a machine learning model. Presented is the cycle of feature selection, training and validation.

Commonly used methods of supervised learning include neural networks, decision trees, random forest, support vector machine and natural language processing. In the unsupervised learning training data are unlabelled and the algorithm attempts to find and represent patterns within the data, like identifying clusters based upon the similarity of the examples. Mostly used methods of unsupervised learning are hierarchical clustering and self-organizing maps. There are no general recommendations regarding the use of the most appropriate method, since their selection is always situation specific and dependent on data type, size and dimensionality.



An overview of fields related to learning from data.

The application of ML in the field of autoimmune diseases is categorized into six wide areas: patient identification, risk prediction, diagnosis, disease subtype classification, disease progression and outcome and monitoring and management and was researched on 169 studies so far, demonstrating a variety of data and methods used. For the purpose of identifying autoimmune disease patients from electronic medical records natural language processing was used. This process is expected to substitute the current diagnostics via billing codes, which has error rate between 17 and 77%, significantly improving diagnostics. Prediction of disease risk and identification of novel risk factors through feature selection was performed for inflammatory bowel disease, type 1 diabetes, rheumatoid arthritis, systemic lupus erythematosus and multiple sclerosis. Most studies employed genetic data and the most used methods included random forest, support vector machine and logistic regression.

Application of ML to diagnosis helps distinguish diseased from control cases, differentiate between diseases with overlapping symptoms and

phenotypes and examine classification of autoimmune diseases. Classification of disease subtypes was performed for RA, IBD and MS on clinical, genetic, transcriptomic and proteomic data using mostly unsupervised clustering approach. To predict disease progression and outcome, severity, treatment response and survival prediction mostly used type of data was clinical, processed by support vector machines, random forest and neural networks. ML in monitoring and management was focused mostly on type 1 diabetes and predicted blood glucose levels and hypoglycaemic events using support vector regression.

In summary, the ML models and methods used are very heterogeneous and can be difficult to decide which method to use in clinical application. Careful consideration of data type and context should be performed and possibly a combination of different models used in order to improve their performance. So far, the most used type of data represents clinical and laboratory data. In future, more omics data should be integrated and interpreted along the former ones, considering their vast abundance and informative character, especially in terms of personalized medicine. High success of AI and ML in the field of cancer research, where identification of specific molecular pathways and targets informed individualized treatment that improved cancer prognosis, both in patient outcomes and quality of life, proved this approach highly valuable and necessary for the future of successful treatment. The field of autoimmune diseases is awaiting similar improvement, being of the same degree of heterogeneity and complexity on the individual level, by using ML methods to unify the vast body of patient data and provide personalized treatment options appropriate for the medicine of the future.

UNIT 3 Artificial intelligence in radiology

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The essential keywords

- **CT** = [Computed tomography]
- **MSCT** = [Multislice computed tomography]
- **MRI** = [Magnetic resonance imaging]

Radiology is the medical discipline that uses medical imaging for diagnostic and radiation for treatment. Some of the most essential radiological methods are X-ray radiography, ultrasound, computed tomography (CT), multislice computed tomography (MSCT) and magnetic resonance imaging (MRI). All of them are used to diagnose or treat diseases of various organs and organ systems. In radiology, interdisciplinary collaboration between clinical specialists, radiologists, radiology technicians and nurses is crucial.

Specialists in all other areas often work with radiologists to make a diagnosis, monitor therapy, perform simple procedures, or even for treatment. For this reason, radiologists must have a good knowledge of the anatomy, physiology and pathophysiology of the whole human body. They must also be familiar with the advantages and disadvantages of every method, know how to apply them and interpret the images. Given the amount and kind of information, it is logical that radiology is an ideal niche for the implementation of AI technology. Medical imaging is an area that is growing fast, and there is too much workload for radiologists who, according to some research, should analyse one scan every 3-4 seconds. Of course, it is physically impossible to do that. Therefore, AI should be considered as a tool that will facilitate the

work of radiologists and reduce their workload. AI is increasingly seen as a team member, one who can't get tired and can analyse scans without a break.

★ Augmenting Radiology with AI

Video 1. What is the idea behind the implementation of AI in radiology? What do radiologists expect from AI? How can AI improve radiology?

Physician burnout is a global problem currently in healthcare, and AI may offer a solution. The introduction of AI technology will reduce burnout because AI will be able to take over a good part of routine work, and radiologists will monitor the system and intervene when needed. What AI will provide to radiologists is the ability to focus more on specific, difficult cases that require their expert assessment. It will also allow case prioritisation which is very important as it is sometimes difficult to single out the more important ones from the mass.

As with everything, there are various challenges with introducing AI into the clinical practice of radiology. First of all, it is necessary to involve radiologists in the development of algorithms because computer scientists do not have the necessary medical knowledge. Skills that only radiologists possess in image segmentation and condition description are required. Also, it is necessary to harmonise the segmentation, marking the images, the way of entering information and sharing information to develop the most precise algorithms that can be used as quickly as possible in broader clinical practice. Because AI is most present in radiology, there is a particular fear that AI will replace radiologists. Instead of looking at AI as a threat, it would be better to consider it as a tool that will make it easier for radiologists to work, while also providing more sophisticated and accurate analysis by identifying specific patterns on images that are not visible to the human eye. Radiology is so much more than only image interpretation. Radiologists also need to communicate the diagnosis to other physicians or patients, consider patients' history and preferences, perform interventional procedures and much more. These are tasks that cannot be performed by AI.

★ [Will artificial intelligence replace radiologists?](#)

Video 2. If you don't believe us, then you will indeed believe the words of one radiologist himself. In the next video, the radiologist explains why AI will not replace radiologists, but also why radiologists should not be afraid of AI.

Conventional radiography

Conventional radiography is a medical imaging method that produces two-dimensional images by x-ray radiation. The principle of the method is based on the detection of radiation that reaches the detector after passing through the irradiated area. Depending on the composition and density, tissues and organs will absorb different amounts of radiation. Bones, which are denser than soft tissue, will absorb a more significant amount of radiation than, for example, the lungs, which are of low density. By detecting the intensity of transient radiation, we get an image in which the structures can be distinguished. The most common applications of x-ray radiography are mammography (breast scan), chest, abdominal and skeletal scans. Mammography is mostly used on women to screen for breast cancer, and you can read more about it in the chapter on cancer.

In orthopaedics, conventional radiography is still the most widely used for a number of reasons, such as affordability, cost, speed, and low radiation levels. The most common reason for coming to the emergency room is the suspicion of a bone fracture, and the first step is usually taking an x-ray for diagnosis. Recently, machine learning has advanced to the level that it is possible to solve visual tasks, such as object detection, image segmentation and classification, with the help of ML. This feature is beginning to be widely used in medical imaging. Few neural networks were developed that can determine the presence of a fracture, but also laterality, exam view and the body part that is on the image with an accuracy comparable to a radiologist. If we take into account the fact that incorrect fracture identification is responsible for up to 80% of medical errors in the

emergency department, it is clear why we should strive to improve the analysis of x-rays. Misinterpretation of a fracture can have serious consequences for the patient's health, which include malunion, the development of arthritis or osteonecrosis. In order to provide the best possible health care, it is necessary to work on reducing medication errors. By introducing machine learning in practice, it is possible to help young, less experienced doctors in the emergency department, who make mistakes more often.



(A) Left is a typical radiograph, input to the model. Right is a heat map on the radiograph that represents the model's confidence that a particular location is part of the fracture. (B) Close-up views of four additional examples. Reprinted from "Deep neural network improves fracture detection by clinicians", by Lindsey R. et al., 2018, *Proceedings of the National Academy of Sciences of the United States of America*, 115, 45.

Another near-perfect domain for the development of machine learning algorithms is chest radiography. Lung diseases are one of the most common medical conditions in the world, and chest x-ray is a common examination in most of those conditions. Algorithms are currently

being developed for several different uses, some of which are an assessment of lung nodules, detection of changes in the lungs caused by tuberculosis, cystic fibrosis, or screening for pneumonia. The reason why a lot of studies are focused on the detection of pulmonary tuberculosis is that tuberculosis is the leading infectious disease in terms of mortality, and especially affects immunodeficient patients. Although it is advisable to avoid routine screening, increased scanning of risk groups is recommended. If we talk about pneumonia, the most important thing is the correct and timely detection of pneumonia in children. According to the World Health Organisation (WHO), pneumonia is the leading cause of death among children under the age of 5, killing approximately 2 million children a year. Since pneumonia can be caused by a virus or a bacterium, it is important to know the exact cause for therapy to be correct and to achieve the desired outcome.



Examples of normal chest X-ray, X-ray of chest with bacterial pneumonia and viral pneumonia. Reprinted from “Identifying Medical Diagnoses and Treatable Diseases by Image-Based Deep Learning”, by Kermany D.S. et al., 2018, Cell, 172, 5.

Chest x-ray analysis is based on finding abnormalities relative to a healthy image. When it comes to x-ray, lung abnormalities are mostly white compared to lung tissue (which is “black” due to its low density). They are different in density, shape and position. In order for the analysis to be as accurate as possible, a high level of expertise of the radiologist is required. Some studies have shown that

AI can increase accuracy and precision even for experienced radiologists. Despite the fact that AI in many cases shows better results than radiologists, the best approach is a cooperation between radiologists and AI.

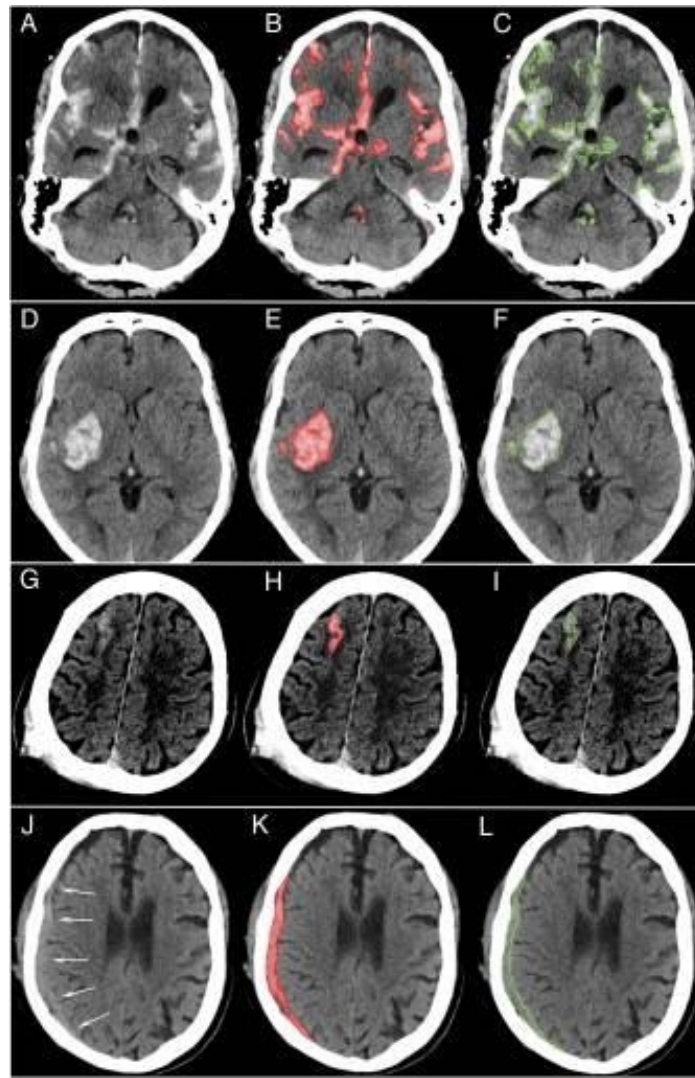
Computed tomography

Computed tomography is a medical image method that uses x-ray scans from different angles. These measurements are then computer-processed and used to produce a tomographic (cross-sectional) image of specific areas. By means of this procedure, it is possible to obtain an image of the internal organs in the desired part without invasive procedures. By combining images from different angles, we get a 3D view of a particular organ. This means that the CT scan actually contains a whole series of separate images which can make the analysis more difficult compared to simpler two-dimensional (2D) images. Today, this is one of the most common screening tests for various conditions. It is used to scan the brain, lungs, heart, thyroid, blood vessels, extremities and abdomen. The application of CT in oncology is maybe the most significant, but here we will look at some more applications. The implementation of AI for CT scan analysis has a twofold meaning – it can speed up and improve the accuracy of the analysis, but it can also be used to improve the quality of images taken at lower radiation concentrations to reduce global radiation exposure while maintaining image quality.

Osteoporosis is a disease in which there is a decrease in bone density, mostly in the elderly. The causes are various, mostly related to hormones and the ageing process in general, but other conditions, medications, or lifestyle habits can also be the cause. Due to osteoporosis, the elderly are more prone to bone fractures, including vertebrae. T-score shows how much bone density is higher or lower than the bone density of a healthy 30-year old adult. Before spinal

surgery, it is important to know the T-score or the extent to which the vertebrae are affected by osteoporosis. If osteoporosis is advanced, it can cause problems such as loosening the screws. To facilitate surgery planning, an ML algorithm has been developed that can assess the condition of osteoporosis based on CT scans. A simple model like this can help reduce the likelihood of subsequent complications following spinal surgery. The biggest problem is actually the lack of usable data. It is crucial to make physicians aware of the importance of data collection and sharing. It is desirable to collect as much quality data as possible; models will be developed that are more accurate in their assessment.

CT is also often used for detection and evaluation of neurologic emergencies, such as intracranial haemorrhage that usually requires emergent surgical intervention. In addition to determining the need and approach to surgery, evaluation of acute intracranial haemorrhage may be important for the management of thrombolytic therapy in acute stroke. A particular challenge that arises when analysing a head CT is that the abnormalities in the brain that need to be detected are quite small (around 100 pixels) relative to the size of the entire image (a 3D visual containing approximately one million pixels). Despite the challenging task, an algorithm has been developed that can identify, segment, and classify the area affected by intracranial haemorrhage at a level comparable to experts.



Patch-based fully convolutional neural network segmentation of acute intracranial haemorrhage. Reprinted from “Expert-level detection of acute intracranial haemorrhage on head computed tomography using deep learning”, by Kuo W. et al., 2019, Proceedings of the National Academy of Sciences of the United States of America, 116, 45.

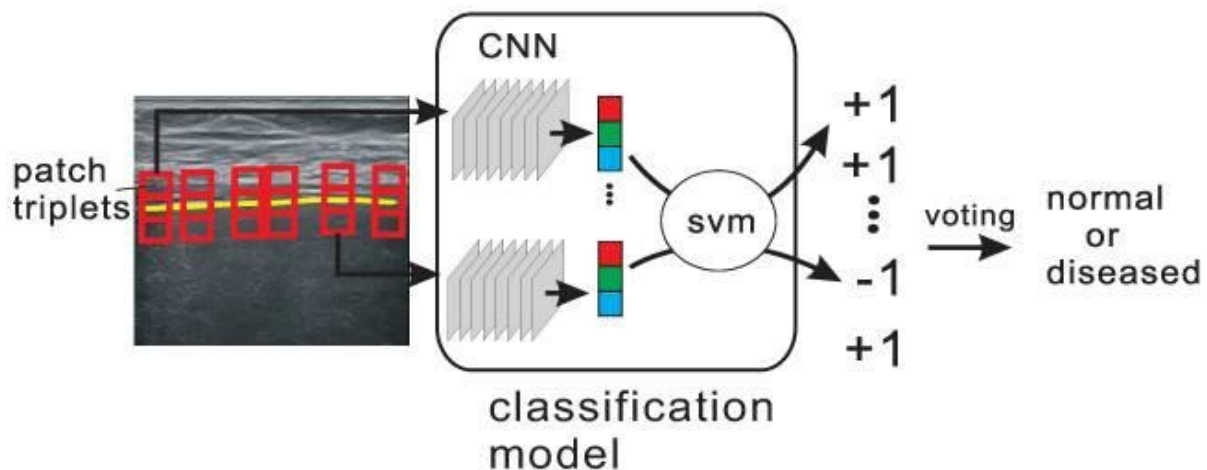
Medical ultrasound

Medical ultrasound, or diagnostic sonography, is an imaging method that uses ultrasound waves that humans cannot hear (frequency $>20\,000$ Hz) to create an image. Ultrasound waves echo off tissues with different reflection properties and therefore reveal the anatomy of the observed tissue. Ultrasound has many advantages over other imaging methods, some of them being cost, ease of application, no harmful radiation or contrast agents are used, it is possible to perform the procedure in clinics and hospital rooms. Of course, there are some drawbacks too. There are limitations in what can be recorded by the method, the analysis is quite complex and requires great expertise, the quality of the recording varies depending on the physical structure of the patient, and also bones and air can interfere with the recording. The applications of ultrasound in medicine are numerous; it is often the first examination in the process of making a diagnosis. Precisely because of its wide application, it is an ideal field for the application of AI. Here we will mention some examples, but there will be even more in specific chapters.

For most people, the first association for ultrasound is pregnancy. So it is not surprising that AI models are already being developed that will facilitate and speed up this process. Ultrasound is used in pregnancy to monitor the development of the baby, and it is important to take good pictures so that the right conclusion can be drawn from them. Therefore, an AI algorithm has been developed that can recognise a good image in real-time and capture it without the physician having to do it by himself. This video briefly shows the application of the mentioned algorithm:

Cirrhosis of the liver is a disease that is on the list of the most common causes of death according to the WHO. The most significant cause of cirrhosis is chronic liver infection such as hepatitis B, but

it can also be long-term alcoholism, some parasites, medications, and toxins. Ultrasound, CT and MRI can all be used in the diagnosis, but since ultrasound is non-invasive, non-ionising and the cheapest technique, it is the first step. Ultrasound images of the liver of healthy people and patients diagnosed with cirrhosis were used to teach the neural network to recognise subtle differences in tissue structure between healthy and cirrhotic liver. One of the important features was to learn the algorithm to detect the liver capsule, which is crucial for the diagnosis of cirrhosis. A certain amount of images is needed to train the algorithm, by which the algorithm will be able to learn to detect the capsule, as well as the clinician does. By observing the tissue above and below the capsule, but also the capsule itself, the algorithm could determine with great accuracy whether the image showed a healthy or cirrhotic liver.



Scheme of the liver capsule guided ultrasound image classification. Reprinted from “Learning to Diagnose Cirrhosis with Liver Capsule Guided Ultrasound Image Classification”, by Liu X. et al., 2017, Sensors, 17, 1.

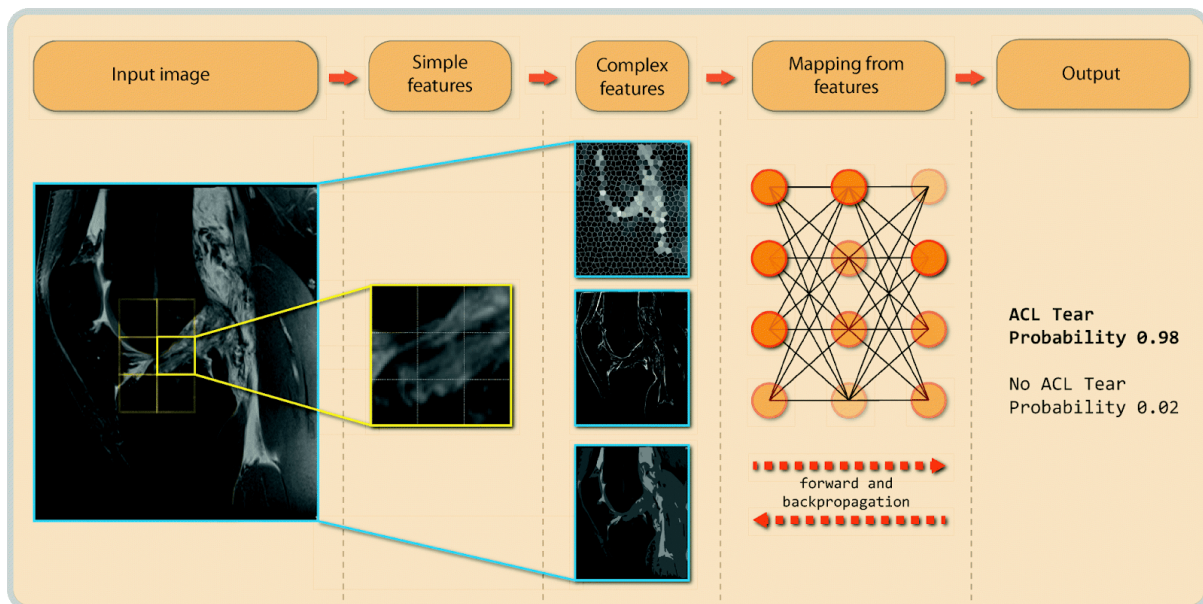
The thyroid is one of the largest endocrine glands in the human body, and it is involved in a number of processes important for maintaining homeostasis. In case of suspicion of some pathological process in the thyroid, ultrasound is usually recorded. Segmentation and classification of ultrasound images are crucial in diagnosis, prognosis, and planning further health care. Using CNN, it is possible to automate the process of image analysis, and it is most commonly used to detect and classify thyroid nodules. Nodules can be benign and malignant, and proper assessment is crucial so that malignancies can be surgically removed. However, it is important when training the algorithm to be careful to use precise and accurate data so as not to misdiagnose benign nodules as malignant and thus lead to unnecessary interventions. Like most such algorithms, this is not yet in clinical practice, and it will probably be some time before this happens. The reason why more time is needed is that it is necessary to collect a large amount of standardised data, adjust the work of physicians to the implementation of AI, but also to wait for the period when patients will be more inclined to these procedures.

Magnetic resonance imaging (MRI)

Magnetic resonance imaging is a non-invasive imaging method used in radiology to produce detailed anatomical images usually of soft tissues like brain, nerves, muscles, ligaments, heart and so on. It is used for disease detection, diagnosis, and treatment monitoring. The method is based on proton excitation and detection of the changes in the direction of the rotation of protons found in the water and fat in tissues. Since MRI does not use X-rays or ionising radiation, it is often seen as a better choice than a CT scan.

Musculoskeletal radiology is a large and important branch of radiology in which the application of deep learning is increasing. It is used for lesion detection, fracture detection (mentioned earlier when

speaking about conventional radiography), classification, segmentation and much more. One of the most common injuries to the musculoskeletal system are knee injuries; an MRI is usually a procedure of choice in such cases. The reason why is that MRI demonstrated high accuracy in diagnosing different pathological conditions in this field. Image analysis of anterior cruciate ligament (ACL) tears, meniscal tears or any other abnormality can be quite complicated and time-consuming. The development of a deep learning model that will be based on a large number of recordings learns to recognise features that distinguish a normal scan and one that contains an injury can greatly speed up this process. An analysis that can take tens of minutes for the clinician, for a deep learning model it takes only a few seconds. Deep learning models for this purpose can be used as a decision-making tool by radiologists as well as orthopaedic surgeons. Proper assessment of an MRI scan of the knee injury is important to identify patients who will benefit from surgery, but also to plan physical therapy depending on the condition.



Schematic chart of how features are extracted in a CNN, with mapping from features performed to arrive at weighted probabilities at the output

function. Reprinted from “Current applications and future directions of deep learning in musculoskeletal radiology”, by Chea P. and Mandell J.C., 2019, Skeletal Radiology, 49.

In addition to the already mentioned application in image analysis, AI can be used for other non-interpretive tasks. Deep learning tools can be used for automated protocolling, improving MRI image quality and reducing MRI acquisition times. Due to the length of the procedure, MRI scans often have motion artefacts. There is a general tendency to shorten the duration of MRI, to increase patient collaboration, to make the process more comfortable for them, but also to reduce the amount of noise on the scans. These applications would possibly enter clinical practice more easily because the algorithm is not directly involved in the decision-making process related to the medical profession but only facilitates the imaging process and ensures better image quality.

And what could the future of AI bring to MRI? It is an open question, and many hope that AI will allow the synthesis of new images based on existing ones. This would facilitate training algorithms and avoid bias. Also, recently there has been a development of deep learning algorithms that would be used to generate radiological findings from reports associated with individual scans. In any case, this is an area that offers many more opportunities for AI, and it will be interesting to see what happens in the future.

Radiology in the future

The future of AI in radiology is uncertain due to a number of open questions, but also possibilities. Because of the amount of information provided by radiology, especially because the data is mostly images, there are many ideas in which more AI can be included in the process and what it can offer to radiologists. One of the important challenges is the development of algorithms that will be

able to perform multiple tasks because the algorithms available today are developed exclusively for one task. This is also one of the reasons why AI will not replace radiologists. AI algorithms can outperform radiologists in individual tasks, but they are not yet able to combine different sources of information to create a complete picture of an individual patient. Another goal for the future is to develop DL algorithms that will reduce annotation time. Of course, it is necessary to strive to improve the accuracy of existing algorithms and try to extend their application beyond the data used for training.

This is just a brief overview of some radiological methods and examples of AI implementation in various medical imaging tasks. Through the other chapters some more applications will be mentioned. The aim was to summarise the breadth of radiology and the multitude of possibilities where AI can be used to improve the quality of health care provided by radiologists. In any case, AI will still participate in shaping radiology as a medical profession, and radiologists need to be open to the new possibilities that this new technology will offer.

As a conclusion, this is the video that briefly shows everything we presented here:

★ [Will artificial intelligence replace radiologists?](#)

Video 4. "Will Artificial Intelligence Replace Radiologists? - The Medical Futurist", YouTube, uploaded by The Medical Futurist, 4 April, 2018

UNIT 4 Challenges of artificial intelligence in medicine

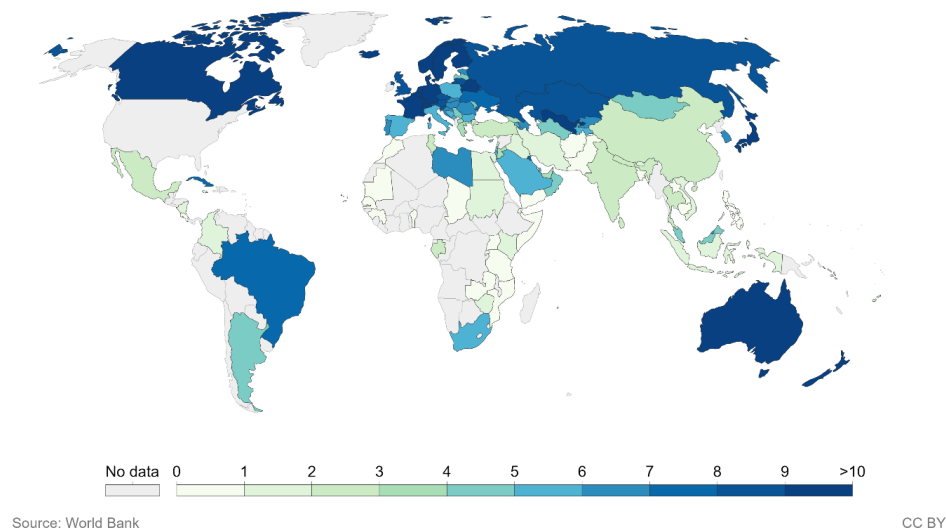
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Through this handbook, only a fraction of the possibilities of applying artificial intelligence and other advanced technologies in medicine are presented. But despite all the advantages, there are still some challenges in implementing AI into clinical practice, as shown through the examples mentioned here. In this chapter, we will give a brief overview of these challenges to raise awareness of what needs to be improved and pay attention in the future to meet the full potential of AI. The challenges are different, from economic, technical to ethical.

Nurses and midwives per 1,000 people, 1990 to 2016

Nurses and midwives include professional nurses, professional midwives, auxiliary nurses, auxiliary midwives, enrolled nurses, enrolled midwives and other associated personnel, such as dental nurses and primary care nurses.

Our World
in Data



Nurses and midwives per 1000 people, 1990 to 2016. Reprinted from Our World in Data, 2016

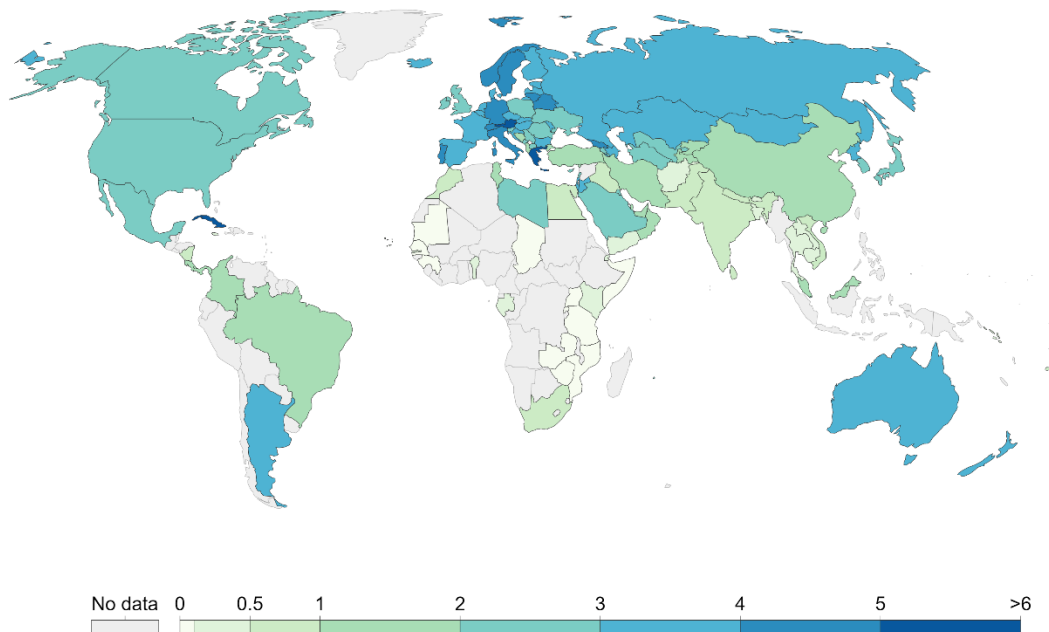
Credit: www.ourworldindata.org

A large difference in wealth and development between countries could be one of the problems. On the one hand, less developed countries can hardly finance everything needed to develop such technology, procure the necessary equipment and educate a sufficient amount of staff. Such algorithms require extremely powerful but also expensive computers. Until recently there were few such computers in the world. Today, this is changing, but mostly this technology is still available to highly developed countries.

On the other hand, less developed countries generally have a bigger problem with the lack of health professionals. Therefore, maybe such countries might be more open to accepting and implementing the AI models more quickly into clinical practice to compensate for the lack of workforce, but also the lack of expertise. Numerous studies have shown that the use of AI algorithms can greatly reduce unnecessary procedures, surgeries, and rehospitalization. This ultimately leads to lower health care costs, which may be more important for poorer countries. Even within developed countries, there are regions where there are fewer health professionals and medical equipment, and it is not always possible to offer full health care. AI can offer less developed regions the opportunity to connect more easily with other professionals and provide the population with access to the best care in order to reduce traveling and thus the personal cost of the patient. Economic inequality has always existed, but health is a field where we should all be focused on reducing the impact of economic inequality on the quality of care. Humanity should be the main guiding principle in efforts to solve this problem.

Medical doctors per 1,000 people, 2016

Medical doctors include generalist physicians and specialist medical practitioners.



Source: World Bank

CC BY

Medical doctors per 1000 people, 2016. Reprinted from Our World in Data, 2016.

Credit: www.ourworldindata.org

The animations of the attached pictures showing the inequality in the number of physicians and nurses in the world through the years are on these links:

★<https://ourworldindata.org/grapher/physicians-per-1000-people?time=2016>

★<https://ourworldindata.org/grapher/nurses-and-midwives-per-1000-people?tab=map&time=2016>

Due to the large proportion of older physicians around the world, there is a certain barrier caused by ignorance and unwillingness to change. Older generations of physicians find it harder to adapt to

innovative changes in healthcare, and more effort is needed to embrace new technology in their practice. It is now clear that technology will affect almost all spheres of our lives, including the health system. Because of this, it is crucial to change educational programs, introduce courses and programs that will provide new knowledge and skills to future health professionals. Young healthcare providers need to learn how to work with AI and how to get the best out of that collaboration. If there is a successful merger of healthcare providers and AI, the focus of healthcare may also shift from treatment to prevention. This shift would cause positive changes in society because it would reduce health care costs, but also increase people's quality of life. For this to happen, it is important to motivate health professionals that know so much about human health, but are also aware of the possibilities of AI, to cooperate with computer scientists. This collaboration is key in developing algorithms that will be accurate enough. One of the challenges is to develop algorithms that will not lead to excessive diagnosis or bias. Overdiagnosis can be a very big problem if it starts to occur exponentially in the health system as it will cause examinations, procedures and therapies that the patient does not necessarily need. This can ultimately again lead to the development of unwanted complications, and we would achieve the opposite effect and do more damage than we would help the patient. Therefore, it is important that we are confident in the accuracy and precision of the algorithm before introducing it into clinical practice.

To avoid over- and under-diagnosis, it is crucial to have a lot of quality data. This has been mentioned a lot in previous chapters, but we will mention this problem once again. It is necessary to satisfy both the requirement of quality and quantity to develop the best possible algorithms. It is impossible to develop an algorithm that can be used widely without a sufficient amount of data. But, of course,

quantity is not enough and must be accompanied by quality. Differences in the way data are recorded may make it difficult to use it. It would be ideal for achieving some minimum of features that need to be collected or in the case of scans marked in a specific way so that the data can be used as much as possible. Once the algorithm has been developed with a sufficient amount of quality data, it can serve as a tool in the process of diagnosis, determination of therapy and other tasks during treatment. What is still a problem for many is the inability to understand how the algorithm came to a conclusion. Machine learning algorithms are also called 'black boxes' because it is generally impossible to follow their analysis step by step. The reason for this is that these algorithms can find a link between input and output data in a way that the human brain cannot. Requiring full explainability of algorithms may not be the right approach, although there is still a frequent tendency to do so. Perhaps it would be better to ensure monitoring of the development of the algorithm itself, pay attention to the quality of the data, check its accuracy and precision, but also enable the provision of feedback by users.

If we are talking about the technical problems encountered by the implementation of AI in clinical practice, then we need to mention, in addition to the already mentioned problem related to hardware, the problem of developing satisfactory algorithms. This problem is a set of several smaller problems. Most often the algorithm is sufficiently precise and accurate only on a specific group of data that affects a small part of the population, a specific hospital or something similar. Such algorithms cannot be transferred to use outside these frameworks, and this is something that should be improved in the future. It is desirable to develop uniform algorithms that can be applied anywhere. It is also necessary to carefully design the development of the algorithm and the type of data used to train the algorithm. Careful selection of data should ensure avoiding the bias

of the algorithm. The algorithm can be biased due to bias in the training data or in the prior categorisation of the data. It is possible to test the algorithm for bias by offering “triggers” of discrimination in the data; these can be, for example, age, gender, race, ethnicity. By testing the algorithm, it is possible to minimise the risk of discriminatory bias. For example, it is often the case that the algorithm “learns” that a particular gender is more prone to developing certain conditions, which may not correlate with the truth, but this conclusion is derived solely because of the dominance of data obtained from one gender. Also, the algorithms developed so far are mostly examples of so-called narrow artificial intelligence; they can perform one task very well. They often surpass physicians in this specific task, but the problem is that it is only one specific task. They are still not able to perform more different tasks, much less connect knowledge from multiple tasks at the level as people do to ultimately come to a conclusion. It is assumed that narrow AI will be the only type of AI we will be able to perfect for a long time to come. One should be aware of this because it means that AI does not replace healthcare professionals but only facilitates or speeds up some of their duties.

The fact just mentioned can modulate the next problem we will talk about, and that is the fear of physicians that new technologies will “take their jobs”. Digitalisation is turning the job market upside down, so this is not something specific for health care. There are different predictions about which and how many jobs will be replaced by robots, AI algorithms and other new technologies in the future. This fear is especially present among radiologists, but it is common in other specialisations as well. According to some studies, this accelerated advancement of technology and the emergence of AI in medicine even influences the choice of specialisation. In other words, young medical students are sceptical of radiology precisely for fear

that they will eventually be replaced by AI. It is possible that this is one of the reasons why a certain percentage of physicians refuse to adapt and embrace new technologies in clinical practice. The job of a physician is not a linear process, and simple analysis of data obtained by tests or recordings is not enough. Diagnosis, prescribing therapy, and conducting health care is a complex process that requires creativity and problem-solving skills. It's something AI and other technologies can't, and probably won't be able to achieve yet. A holistic approach to the patient is the best way to provide the highest quality health care. It is also impossible to replace the empathy that doctors provide, which the patient greatly values. This human relationship between the patient and the doctor; their cooperation in the treatment process is something that is impossible to replace with AI. Only the physician can contribute to the emotional component of the experience during the treatment. When it is necessary to communicate a diagnosis or therapy that will potentially change a patient's life, hardly anyone will do it better than a physician. The more healthcare professionals start to look at AI and other new technologies as a tool, and less as a threat to working sooner their successful collaboration will happen, all to the benefit of patients and the healthcare system. Also, innovators developing new technologies for medical application should not aim to replace physicians but to achieve cooperation with them and make their work easier in such a challenging and demanding environment.

Here is an interesting video that briefly summarise reasons why AI will not replace physicians:

★ [5 reasons why AI will not replace physicians](#)

Video 1. "5 Reasons Why A.I. Will Not Replace Physicians – The Medical Futurist", YouTube, uploaded by The Medical Futurist, 20 July, 2018

On the other hand, there is a fear, stemming mainly from patients, that physicians may rely too much on AI and be less critical of the diagnosis and therapy recommended by the algorithm. It is important to remain sufficiently critical of the technology, that is, to further check the decision of the algorithm on more complex cases and tasks. Partly to monitor the effectiveness of the algorithm, and partly to allow physicians to further improve their skills. Patients are perhaps the most neglected party in this whole story. It is important to mention their rights that need to be considered when talking about AI in medicine. Something we have emphasised a lot and on which the development of AI algorithms is based is the need for a large amount of medical data. All of this information comes from actual patients who must be informed of the manner and purpose of using their personal health information but must also agree to it. The problem of data security in the age of big data is a major challenge in healthcare. A balance needs to be achieved between protecting patient privacy and the benefits of using data for society. In other words, it is important to provide patients with assurance that their data is not being misused, but it is also important to enable research and innovation that require a lot of patient health data to advance the future health care. More and more efforts are being made to create legal frameworks that will protect patients from privacy violations. In the EU it is General Data Protection Regulation (GDPR). This regulation also covers health data and provides rules for the proper collection and use of health data. If the violation of privacy happens, it is possible to look at it from two perspectives – consequentialist and deontological. The consequentialist approach considers the real consequences that have harmed the patient. These can be, for example, employment problems due to health conditions. On the other hand, the deontological approach considers violations that did not cause harm or that the patient may not be aware of. For example, it could be taking data from smartphones for the purpose of

some research without the data being used in the end. It is a question of the ethical correctness of this act, regardless of the fact that the person did not experience the harmful consequences. Due to the possibility that electronic health records will soon collect data outside the health system (social, educational, etc.), but also data from social networks there are a lot of ethical issues in this regard. Is this the data that healthcare providers need to have access to? How relevant and accurate is the data from social networks? And a lot of other issues that might arise. There are probably a lot of pros and cons for this, and time will tell what will happen. In the digital age, privacy violation is a very big challenge, and there are numerous efforts to make people aware of the importance of security and privacy.

Finally, we leave you with a short video of the benefits and potential risks of introducing artificial intelligence into healthcare:

★ [Artificial intelligence in healthcare : benefits and risks](#)

Video 2. “Artificial Intelligence in Healthcare: Benefits and Risks”, YouTube, uploaded by The Doctors Company, 16 December, 2019

UNIT 5 Cardiovascular diseases as one of the leading causes of morbidity in the world

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The essential keywords

- WHO = [World Health Organisation]
- CVD = [Cardiovascular disease]
- DALY = [Disability-adjusted life-years]
- EHR = [Electronic health record]

According to the World Health Organisation (WHO), ischaemic heart disease and stroke are the two most common causes of deaths in the world. It is estimated that 17.5 million people die from cardiovascular diseases (CVDs) every year. Approximately 80% of CVD-related deaths occur in low- and middle-income countries. But not only that CVDs can lead to a fatal outcome, but they can also reduce a patient's quality of life. We can measure this by calculating disability-adjusted life-years (DALYs) respectively summing the years of potential life lost due to premature mortality and the years of productive life lost due to disability. In 2016, the global burden of disease for CVDs for women was 20% and for men 24% of the total burden. All of this means that CVDs are a significant threat to human health.

Some people are more likely to get CVDs because of the risk factors. The main risk factors are hypertension, dyslipidemia, gender (male are more likely to develop CVDs), age (male over 55 years and female over

65 years), smoking, diabetes, obesity (BMI ≥ 30 kg/m²), family history of premature CVD, kidney disease and many more. Some of these factors are non-modifiable, like inheritable predisposition, but fortunately some we can modify. Proper diet can moderate body weight, but also blood cholesterol levels. Patients should be advised to increase their intake of fruits, vegetables, fish and whole grains and eliminate or at least reduce the consumption of processed meat, sugar-sweetened beverages and salt. Regular physical activity for at least 30 minutes a day will significantly decrease the risk of CVDs. Lifestyle can also be adjusted – reduce smoking and drinking alcohol. These are non pharmacological measures that can have a high impact on the development of CVDs. Regardless of pharmacological treatment, these lifestyle adjustment measures should always be implemented.

The condition that underlies most CVDs is dyslipidaemia. Dyslipidemia occurs when someone has abnormal levels of lipids in their blood. The most common forms of dyslipidemia involve high levels of low-density lipoproteins (LDL) or bad cholesterol, low levels of high-density lipoproteins (HDL) or good cholesterol and high levels of triglycerides. Healthy blood lipid levels vary from person to person, and there is no strict limit. But there are target values we want to achieve in primary and secondary prevention. For primary prevention target value is total cholesterol < 5.0 mmol/L and for secondary prevention it is < 4.5 mmol/L.

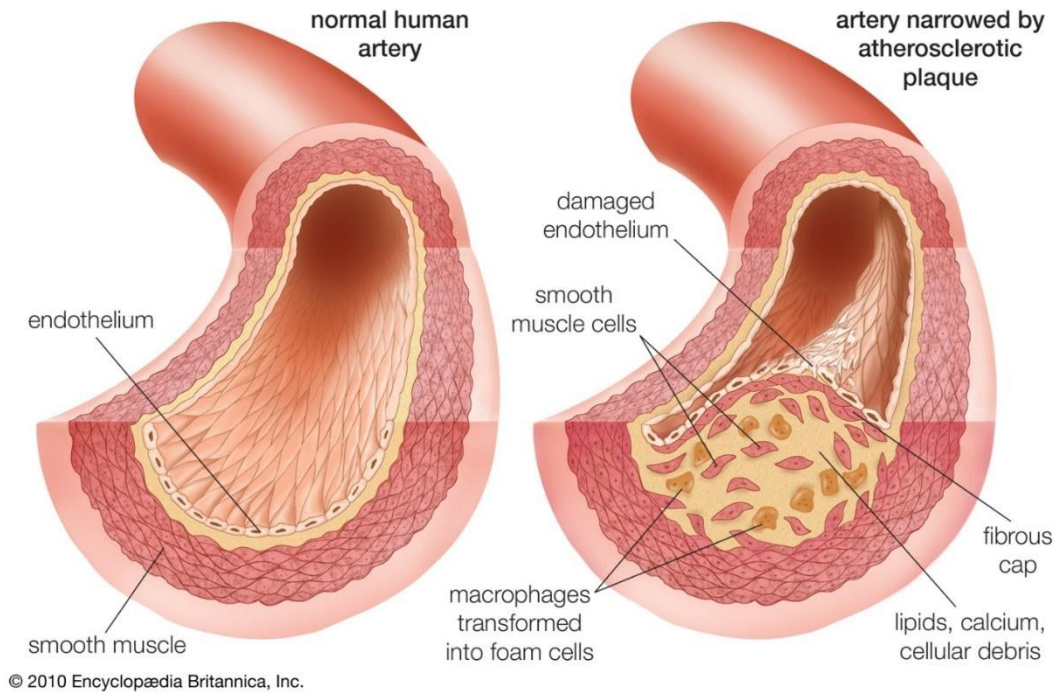
Just to get a better picture of CVDs, watch this simple video in which risk factors and prevention are explained:

★ [Understanding cardiovascular disease : Visual explanations for students](#)

Video 1. “Understanding Cardiovascular Disease: Visual Explanation for Students”, YouTube, uploaded by Zero To Finals, 9 January, 2019

In most cases, CVDs begin with atherosclerosis. Atherosclerosis is a disease that affects tunica intima of middle-sized and big arteries which results in narrow and thick vessel walls. Everything starts with a high level of low-density lipoproteins (LDL), or as it is called 'bad cholesterol'. These particles can enter tunica intima through dysfunctional endothelium of the vessel. Once it starts to deposit in tunica intima LDL is oxidized, and this oxidized LDL then activates endothelial cells. Activated endothelial cells express receptors for white blood cells, which will allow monocytes and T-cells to move into the tunica intima. After entering tunica intima monocytes become macrophages that will take up oxidized LDLs and become foam cells. These foam cells are crucial in atherosclerosis because they promote migration of smooth muscle cells from tunica media into tunica intima and proliferation of smooth muscle cells. Smooth muscle cells will then produce collagen, which will lead to hardening the plaque. Stiffening of the artery wall leads to hypertension because the heart is trying to pump blood against the artery wall that will not expand with extra pressure. During the process, foam cells die and release their lipid content. Therefore plaque grows and leads to stenosis. Stenosis is the abnormal narrowing in a blood vessel. Blood flow is reduced due to stenosis, which is crucial in conditions like angina and peripheral vascular disease. If the plaque becomes too big, it will rupture. When the plaque ruptures, the process of coagulation is initiated to stop the plaque from spilling its content. In this process, a thrombus is formed, and it can impede blood flow and cause serious problems. Thrombus can block a distal part of the vessel and cause ischaemia. Ischaemia is the leading cause of acute coronary syndrome or heart attack.

Atherosclerosis



Atherosclerosis. Reprinted from Britannica, 2010

Credit: www.britannica.com

Another critical factor in developing cardiovascular disease is hypertension. Hypertension or high blood pressure is a condition of permanently elevated blood pressure in arteries. High blood pressure usually, same as dyslipidemia, does not cause any symptoms, and that is why it is extremely dangerous. People can have high blood pressure for years, even decades, without even knowing it. It is essential to emphasize the importance of treatment for high blood pressure to increase a patient's adherence. Optimal blood pressure would be 120 mmHg systolic and 80 mmHg diastolic. Everything up to 140/90 mmHg is considered high but normal and does not require pharmacological therapy, only lifestyle changes. But everything more than 140/90 mmHg is considered hypertension and should be controlled with medications. There are three grades of hypertension, and depending on the grade and risk factors, the therapy also varies. The target value of blood

pressure for patients with hypertension in most cases, is <140/90 mmHg. This can also vary depending on other comorbidities (diabetes, chronic kidney disease).

Classification	Systolic blood pressure (mmHg)	Diastolic blood pressure (mmHg)
Optimal	<120	<80
Normal	<130	<85
High normal	130-139	85-89
Hypertension		
Grade 1 Hypertension (mild)	140-159	90-99
Grade 2 Hypertension (moderate)	160-179	100-109
Grade 3 Hypertension (severe)	≥180	≥110
Isolated systolic/diastolic hypertension		
Grade 1	140-159	≥90
Grade 2	≥160	≥100

Adopted from the British Hypertension Society guidelines.

Hypertension classification. Reprinted from “Factors affecting diagnosis and management of hypertension in Mazowe District of Mashonaland Central Province in Zimbabwe: 2012”, by Mungati M. et al., 2012, BMC Cardiovascular disorders, 14(1), 102.

There are a lot of conditions worth mentioning, but we will just say something more about the most common ones. An arrhythmia is a group of conditions which are characterized by irregular heartbeat (too fast or too slow). The heart rate that is too fast (above 100 beats per minute in adults) is called tachycardia while a heart rate that is too slow (below 60 beats per minute) is called bradycardia. Some types of arrhythmia have no symptoms, but when symptoms are present, it might include palpitations, dizziness, passing out, shortness of breath and

chest pain. Most types are not severe, but some arrhythmia predisposes a person to complications such as stroke or heart failure. This is a large group of conditions, but we will single out one that is important to us – atrial fibrillation. Atrial fibrillation (AF) is the most common severe arrhythmia characterized by the rapid and irregular beating of the atrial chambers of the heart. AF is associated with an increased risk of heart failure and stroke. A severe complication of AF is forming a blood clot (thrombus). In AF, the lack of an organized atrial contraction can result in the stagnation of the blood in the left atrium or left atrial appendage. The lack of movement of blood can lead to thrombus formation. If the thrombus gets into the blood circulation, it is called an embolus. Embolism can then cause blockage of blood flow and affect the tissue that that vessel supplies. The CHA2DS2-VASc score predicts the risk of future stroke in people with AF. The score is used to determine whether treatment with anticoagulation therapy is required. Depending on the points scored, we can predict the risk.

Table: CHA2DS2-VASc Score points rules.

	Condition	Points
C	Congestive heart failure (or left ventricular systolic dysfunction)	1
H	Hypertension	1
A ₂	Age ≥ 75 years	2
D	Diabetes Mellitus	1
S ₂	Prior stroke, TIA or thromboembolism	2
V	Vascular disease	1
A	Age 65-74 years	1
Sc	Sex category	1

The most common cardiovascular disease is ischaemic heart disease or coronary heart disease. It is the term given to heart problems caused by narrowed heart arteries. The main symptoms of coronary heart disease are chest pain (angina), heart attacks and heart failure. Heart palpitations and unusual breathlessness are also often symptoms. Angina pectoris is a condition recognizable by chest pain due to reduced blood flow to the heart muscle. Main causes of angina pectoris are atherosclerosis or spasm of the arteries that supply the heart muscle with blood (coronary arteries). Stable angina usually occurs as chest discomfort after some activity (running, walking, lifting) with minimal or none symptoms at rest. Unstable angina is recognized by sudden pain at rest, increased pain intensity and angina lasting 15 minutes or more. A heart attack is a more severe condition than angina, and it requires urgent hospital care. Some heart attacks are sudden and intense, but most of them start slowly, with mild pain or discomfort. These conditions cannot be cured, but treatment can help manage the symptoms and reduce the chances of complications.



*Heart attack warning signs. Reprinted from American Heart Association, 2016.
Credit: www.heart.org*

A stroke is a medical condition when the blood supply to part of the brain is reduced or interrupted, preventing brain tissue from getting enough oxygen and nutrients. Brain cells die very quickly in such conditions, so prompt treatment is crucial to minimize brain damage and other complications. Signs of a stroke include trouble speaking and understating others, paralysis of the face, arm or leg, problems seeing in one or both eyes, headache and difficulty walking. There are two leading causes of stroke. A blocked artery causes ischemic stroke, and hemorrhagic stroke is caused by leaking or bursting of a blood vessel. Sometimes there is only a temporary disruption of blood flow to the brain, and this condition is known as a transient ischemic

attack (TIA), and it does not cause lasting symptoms. A stroke can cause temporary or even permanent disabilities, depending on how long the brain had a lack of blood flow and which part was affected. These complications are severe, for example, paralysis or loss of muscle movement, difficulty talking or swallowing, memory loss, thinking problems and many more, that is why prevention is essential. Leading a healthy life can preserve heart and brain health.

Cardiovascular risk calculators

Giving the severity of these diseases, it is clear prevention is essential. In addition to non-pharmacological measures mentioned earlier, there are also drugs for these conditions. Prevention of CVDs can be primary or secondary. Primary prevention is trying to prevent CVDs in patients that never had it, while secondary prevention is trying to prevent further cardiovascular events in patients that already had angina, heart attack or TIA. The first step is always optimizing modifiable risk factors (diet, smoking, alcohol consumption, body weight, exercise) and treating comorbidities (reasonable control of diabetes). When deciding the drug treatment, it is crucial to categorize patients. Not everyone requires the same treatment. There are several ways of doing that, but most calculators predict cardiovascular risk as a percentage risk of having a stroke or heart attack in the next ten years. If the risk is $> 10\%$, then it is recommended to start taking statins (atorvastatin 20 mg before going to sleep, for example). All patients with chronic kidney disease or diabetes type 1 for more than ten years should also take statins as prevention because they are a high-risk group of patients. The goal is to reduce non-HDL cholesterol for about 50%. After three months lipids should be checked if the goal is achieved and if it is not then the dose of statin should be increased. In secondary prevention, a combination of drugs is generally used. The antithrombotic agent is a drug that reduces the formation of blood clots. Antithrombotics can be

used both in primary and secondary prevention. The most common antithrombotic in secondary prevention is aspirin (acetylsalicylic acid) in a low dose of 100 mg. Statins are prescribed in a higher dose (80 mg) for secondary prevention. Beta-blockers have a significant role in secondary prevention and are almost always prescribed if can. Beta-blockers should not be prescribed to patients with asthma. Since this is already a severe condition, patients should also take ACE inhibitors. ACE inhibitors are antihypertensive drugs that have a protective effect on kidneys.

Given all the above, it is evident that there is an excellent opportunity for artificial intelligence (AI) to be part of the health system in the segment of cardiovascular diseases. AI has been proven to be an essential factor that may affect the level of medical services. Until the present day, AI technologies have been applied in cardiovascular medicine, including precision medicine, clinical prediction, cardiac imaging analysis and intelligent robots. The inclusion of AI in the medical process can have a positive effect on both patients and physicians. From the patient perspective, AI can be handy for monitoring the course of therapy, medication reminders, counselling and warning of key CVD symptoms. On the other hand, from the perspective of physicians, AI can help them collect information about patients (such as medical history), connect electronic medical records systems and reduce the workload of physicians. Gathering information about each patient and processing them correctly can improve health care.

Speaking about clinical prediction, AI has also offered physicians the opportunity to give more accurate predictions for patients. Clinical guidelines are developed based on the best available evidence to aid clinical decision. Evidence-based medicine aims to implement proven and verified information into clinical practice.

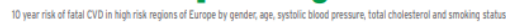
There are a lot of scoring systems that deal with predicting the risk of cardiovascular disease within a specified amount of time. These calculators should only be used for patients with no prior history of coronary heart disease because those are already high-risk patients. Some of the calculators are the Framingham Risk Score, Systemic Coronary Risk Evaluation (SCORE) and QRISK. They all use complex mathematical equations to predict the probability of a cardiovascular event in the next ten years.

Few risk factors such as age, sex, blood pressure, dyslipidaemia, smoking, body mass index (BMI) and diabetes mellitus provide sufficient information that can be mathematically modelled to provide the numerical value of the risk. Depending on the calculator, different factors are taken into account. Mathematical equations are arrived based on the processing of a large amount of data (such as blood test results, blood pressure values, comorbidity history and so on). Using these data, hazard models are being used to estimate the coefficients for each risk factor. When the coefficients are known, they can be easily related to the basic risk equation.

The Framingham Risk Score is an American gender-specific algorithm that was first developed based on data obtained from the Framingham Heart Study to estimate the 10-year risk of developing coronary heart disease. To improve the predictions, cerebrovascular events, peripheral artery disease and heart failure were later added as disease outcomes, on top of coronary heart disease. The updated version includes age, sex, total cholesterol, HDL cholesterol, blood pressure, use of antihypertensive drugs and smoking. The main criticism of the Framingham Risk Score is that it overestimates the risk to the European population because the data were collected among the American people. Also, the data are now quite old.

Because of the different risk between populations, SCORE is more often used in Europe nowadays. The SCORE database combines results from 12 European cohort studies, 250 000 patient-data sets, 3 million person-years of observation and 7 000 fatal cardiovascular events. The risk is shown in charts that are very easy to use.

Two versions are available - for countries with low risk and countries with high risk separately. The risk estimation is based on gender, age, smoking, systolic blood pressure and total cholesterol. The SCORE risk function can be calibrated to each country's national mortality statistics. Because of that, national versions already exist for some countries and can be used to give more accurate predictions. SCORE also has the electronic and interactive version - HeartScore. It is designed to facilitate the calculation of the risk, but also to provide useful advice, save patients' data and see patients' progression.



Credit: www.escardio.org

treatment, migraine, corticosteroid and atypical antipsychotics use, severe mental illness, systemic lupus erythematosus (SLE) and erectile dysfunction. Many of these factors have been added to the calculator in the latest QRISK version after noticing a connection with cardiovascular risk. A new version is released every year because of changes in population characteristics and improvements in data quality. To ensure the algorithm keeps up to date it is remodelled to the latest version of the QResearch database each year.

Artificial intelligence in cardiology

Although still widely used, these are very simple scoring systems that can be taken to a new level with the implementation of more sophisticated AI models. Over time, they will be more helpful to patients for eventual self-assessment or as initial condition assessment, while more advanced prediction methods based on machine learning will be increasingly used in clinical practice. In the future, AI techniques may be crucial in the evolution of cardiovascular (CV) medicine. CV clinical care currently faces significant practical challenges such as poor achievements in prevention, low cost-effectiveness, overutilization, inadequate patient care and high mortality rates despite all the effort and cost. It is essential to achieve good interdisciplinary cooperation to enable clinically meaningful automated and predictive data analysis. Some big data, such as genome sequences, metabolic information, proteomics, gut microbiome sequencing or cardiac imaging, are too large and heterogeneous. Also, they change too quickly and are too unique to be analyzed and used manually, or in these simple systems, we mentioned earlier. Since CVDs are complex and heterogeneous, because they are caused by multiple genetic, environmental and behavioural factors, AI has a great potential to exploit all this big data linked with CVDs and improve health care in cardiovascular patients. It is necessary to strive for more significant progress in

the use of data instead of using only simple score systems or traditional CV risk factors.

Before we get into the details of the application of artificial intelligence in cardiology, it would be great to watch a video that briefly shows the advantages of implementing AI in cardiology:

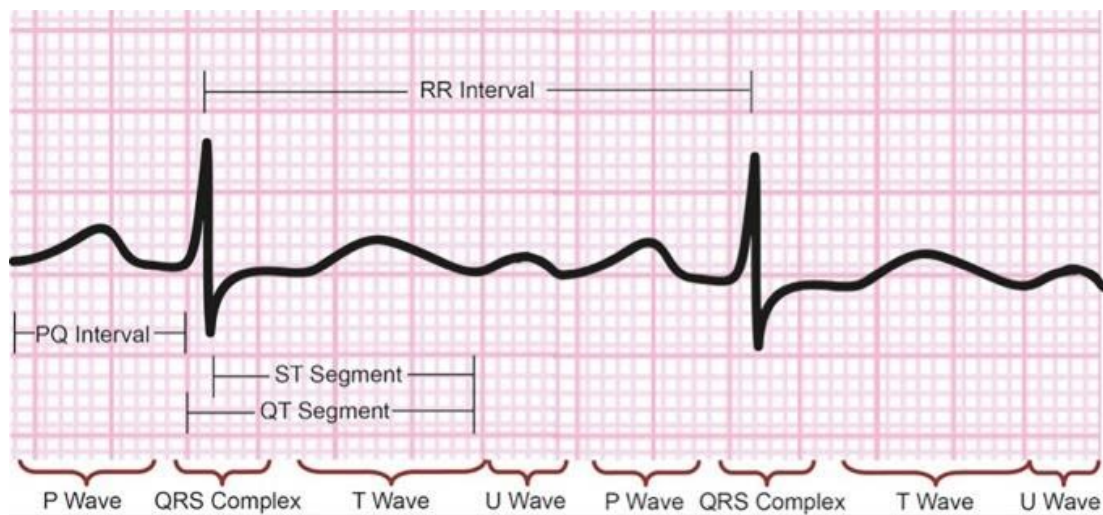
★ [Artificial intelligence in cardiology : a futuristic view of AI in cardiology](#)

Video 2. “Artificial Intelligence in Cardiology: A Futuristic View of A.I. in Cardiology”, YouTube, uploaded by Mayo Clinic, 8 August, 2019

Medical imaging has been a perfect niche for the application of AI in medical practice due to the current reliance on expert image interpretation. Cardiovascular imaging is one of the most significant standards for the diagnosis of CVDs, and through AI technology, it is optimizing the accuracy and quality of images. For example, each pixel can be considered in multiple ways. For example, edges and borders can be identified, movement can be characterized, colour can be extracted, and image density can be a factor for image classification. Images can also be enhanced (manually or automatically) by defining shapes within the image (i.e. border of the left ventricle). Even ejection fraction (a measurement of how much blood the left ventricle pumps out with each contraction) can be calculated easily with machine-learning models. Also, deep learning can be used in pattern recognition in various syndromes and image recognition in CV imaging. It holds great potential for identifying novel genotypes and phenotypes in heterogeneous CVDs. Since deep learning can perform tasks without human assistance, it may discover unique factors in score systems or add risk factors to existing models that we did not include. With deep learning, left ventricular ejection fraction may be predicted from ECG

patterns or coronary calcium score, which can be a significant improvement and can also reduce workload.

The most common method that is affordable, fast and simple is electrocardiography (ECG). Therefore it is an area of intense research in terms of machine-learning. It is not considered an imaging method, but the algorithms analyze the scan similarly as it does with the imaging scans. An electrocardiogram is a graphical representation obtained by electrocardiography showing the time-dependent voltage of the electrical activity of the heart. Using electrodes placed on the skin, it detects electrical changes during the cardiac cycle. While it may seem very simple graphically, there are several conditions that will give a significantly different ECG signal than normal. Using machine-learning algorithms, the first step in interpreting the ECG signal is to classify them as normal or abnormal heart activity.



Normal ECG signal. Reprinted from “Artificial Intelligence versus Doctors’ Intelligence: A Glance on Machine Learning Benefaction in Electrocadiography”, by Ponomariov V. et al., 2017, Discoveries, 5, 3.

Depending on the algorithm, a number of classes vary. This is the most developed application of machine-learning to the ECG. Signal analysis algorithms can identify heartbeats of different nature which is the

basis for further diagnosis, prognosis or choice of treatment. Any change in waves, intervals or segments of the ECG signal is detected, and the totality of the received signals is processed by the algorithm. If the message is normal, there is no need for further interpretation, but if it is not then algorithms can analyze specific changes in more detail. One of the problems in detection of cardiac abnormalities via ECG signals is that the ECG patterns are highly dependent on the time point of the recording and can also change over time depending on whether the patient is in symptomatic or in asymptomatic phase. That means that ECG signals will look completely different during these phases. If the patient is monitored during the asymptomatic period, it can lead to misdiagnose and thus cause later medication errors in the treatment process. What can even make it more difficult to interpret signals accurately is the fact that different diseases can show similar ECG signals. To increase the detection threshold, it is important to record ECG regularly and combine information obtained by recording with symptoms and other tests. Something from this field that is interesting and challenging is long-term monitoring in real-time used for patients in intensive care units (ICUs). Patients in ICUs are patients who need to be closely monitored. Therefore the ICUs are an ideal place to implement AI technology that will continuously analyze ECG signals and have the ability to alert health care providers in case the patient's life is endangered. Even outside the ICUs, these real-time algorithms can be used to monitor heart activity through wearable devices. These devices could then be offered for high-risk patients and would be an easy way of collecting data without time burdening the patients and physicians. Wearable devices could be a way to move the clinic to the home and could be especially useful for monitoring elderly and chronic patients. Development of these devices will reduce the cost of the health system and enable physicians to spend more time with patients.

These devices can be as simple as smartwatches that are already quite present.



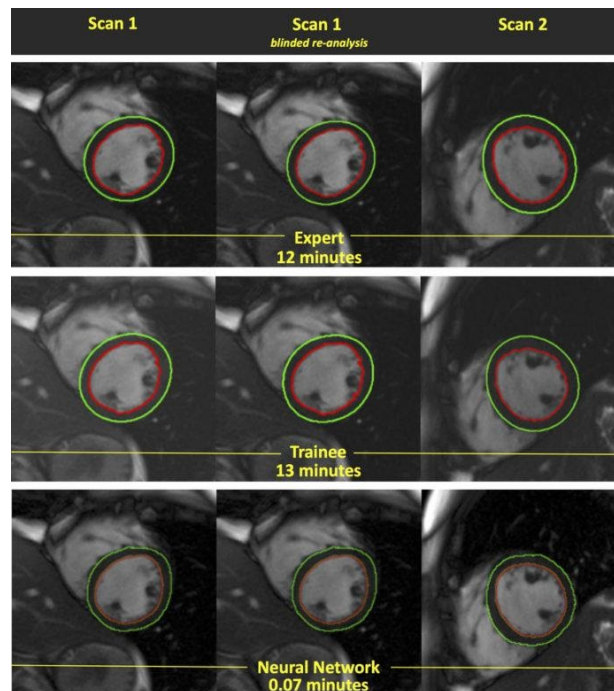
*Wearable device. Reprinted from iMedicalApps, by Giunti G., 2014.r
Credit: www.imedicalapps.com*

In most cases, supervised machine learning is used for previously defined classification, while unsupervised machine learning is mostly used for denoising signals or to cluster data into groups. For example, unsupervised machine learning model can be used to extract fetal QRS complex from the maternal ECG or for clustering of ECG signals in Holter records. Quite often, there is a combination of supervised and unsupervised learning to process complex data in the best possible way. For this reason, an interdisciplinary collaboration between clinicians, scientists and computer scientists are essential.

As said before, AI is increasingly used for image and movement recognition, and the perfect application method is magnetic resonance imaging (MRI). MRI is a non-invasive test used to diagnose medical conditions. MRI uses a powerful magnetic field, radio waves and a computer to produce detailed pictures of internal body structures.

Cardiac MRI is performed to help physicians detect or monitor cardiac disease by:

- evaluating the anatomy and function of the heart, major vessels and the surrounding structures
- diagnosing cardiovascular disorders such as cancers, infections and inflammatory conditions
- assessing the effects of coronary artery disease such as limited blood flow to the heart muscle and scarring after a heart attack
- monitoring the progression of certain disorders over time
- evaluating the effects of the surgical procedure
- evaluating the anatomy of the heart and blood vessels in patients with congenital heart disease



Time comparison between neural network and radiologist.

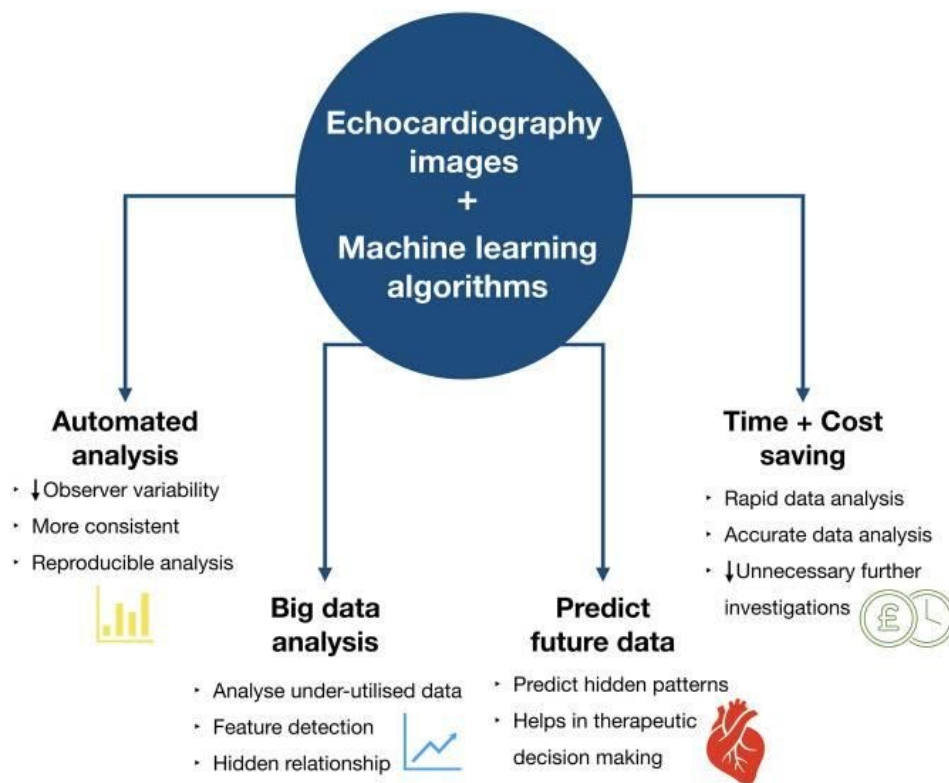
Cedit: Cardiology 2, 2019, retrieved from www.cardiology2.com

As we can see from figure 7., MRI is a common and important method used in the process of diagnosing and monitoring the progress of

cardiovascular diseases. Many critical clinical decisions (such as the timing of cardiac surgery, implantation of defibrillators and therapy treatment) rely on accurate interpretation of MRI scan. According to new research, cardiac MRI analysis can be performed 186 times faster than humans when using automated machine learning. Which means utilizing AI to analyze scans could lead to saving days per year for each physician. Physicians can use this time to talk to patients more and get to know their problems to improve health care even more with this additional information. Many ML models have already been developed to analyze the results of cardiac magnetic resonance imaging (MRI) scans to make a precise prediction for every patient. One of them was able to measure the movement of 30 000 points that are marked on the heart structures in each heartbeat. When combining these data with patients' health records, the software can predict the abnormal conditions that will lead to patient death. The accuracy of software prediction was far higher than the physicians' predictions. Another group of scientists used a deep learning algorithm for automatic segmentation of the right and left ventricular endocardium and epicardium to measure cardiac mass and function. And the list goes on - quite a few studies have already been published on that topic. Most of them are promising on the potential of AI in healthcare. However, despite significant progress and good results, there are still some limitations and problems when applying these technologies in clinical practice. Most algorithms show satisfying results, but only within the database used to create the algorithm. It practically means that algorithms are limited and cannot be applied outside specific frameworks.

Another method that plays a vital role in the diagnosis and assessment of patients with CVDs is echocardiography. It is an ultrasound of the heart. Echocardiography is standard since it is non-invasive and yet very informative. The main drawback is that the analysis highly

depends on the operator, and it also takes a lot of physicians' time. Current guidelines require precise quantification and interpretation, which can be time-consuming and even difficult for inexperienced physicians. To avoid such situations (fig. 8.) and to improve the accuracy and quality of health care, research in the field of AI models that will be able to analyze echocardiograms is increasing. Although the application of AI to echocardiography is at an early stage, several apps have already been developed. These models mostly cover image recognition, classification and quantification. In other words, all the work that takes minutes or even hours of physicians' time can be done by algorithms in just seconds.



Advantages of machine learning assisted echocardiography interpretation.
 Reprinted from “Artificial intelligence and echocardiography”, by Alsharqi M. et al., 2018, Echo Research and Practice, 5, 4.

Speaking about imaging procedures, we cannot exclude computed tomography (CT). CT is an imaging procedure that produces images of specific areas using computer-processed X-ray measurements taken from different angles. It allows us to see the anatomy of organs without surgery. In the last 50 years, this method has become one of the leading medical procedures for prevention and screening for disease. In cardiology, it is mostly used for coronary CT angiography which is a necessary examination of the condition of the coronary arteries and for coronary CT calcium scan - looking for calcium deposits in the coronary arteries that can narrow vessels and increase the risk of a heart attack. The tasks for which the largest number of algorithms have been developed and to which the most attention has been paid in the field of cardiac CT are:

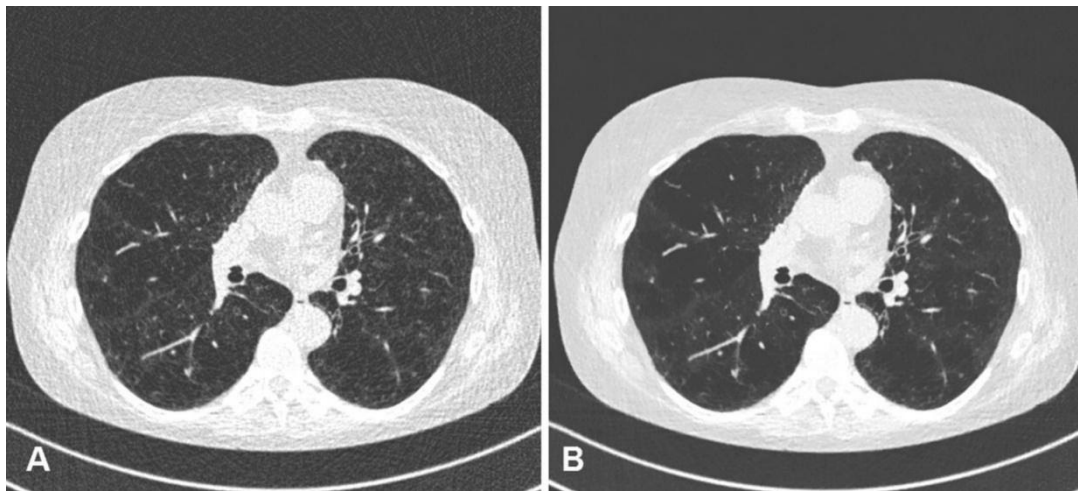
image improvement - some deep learning algorithms can improve image quality or be used to convert non-contrast CT to contrast CT scans. The main reason for developing this kind of algorithm is increased radiation exposure to society, which can be especially problematic for younger patients. The use of a lower dose of radiation gives us low-quality images. The goal is to improve models using AI algorithms so that lower radiation doses can be used while maintaining the same image quality.

Diagnostic classification - it is used to determine the presence of cardiac diseases, such as coronary artery disease which is one of the leading causes of mortality in the world. AI algorithms can observe some things that are invisible to the human eye. Algorithms analyze haemodynamic changes and evaluate coronary artery tree. Improved analysis can lead to early detection, which is the primary goal.

Object detection and segmentation - it is mostly based on labelling each pixel as either belonging to the target object or not. For

example, the most common task is the segmentation of coronary artery calcium (CAC), a strong predictor for cardiac events.

Prognosis and outcome prediction – CT scans are usually combined with some other inputs to predict mortality and the risk of CVD events, figure 9.



Example of noise reduction with DL algorithm. (A) low dose chest CT image, (B) noise reduced low dose chest CT image generated by AI algorithm.

Reprinted from “Application of artificial intelligence in cardiac CT: From basics to clinical practice”, by Van den Oever L.B. et al., 2020, European Journal of Radiology, 128.

These tasks are often combined. For example, calculating the CAC is a process of segmentation, but the score can be used for prognosis. Implementing AI in cardiac CT can solve multiple problems – it can reduce radiation exposure, save up time, give an early and more precise diagnosis.

Electronic health records (EHRs)

Analyzing all these scans can be very informative, but it is also essential to put that information into context. What does it mean for

a specific patient? What is the next step? The answer is that we want to upgrade the data obtained by analyzing images with information from health records. That will give us a better insight into possible diagnoses and ultimately be crucial in determining further treatment. To automate the process of reviewing health records, it is necessary to introduce electronic health records (EHRs) everywhere. EHRs are promising data sources and have the potential to facilitate access to medical data. Data that can be a part of EHRs are medication history, past medical history, physical assessment, nursing notes and care plan, present symptoms, lifestyle, earlier diagnoses, test results, procedures, imaging data, treatment, discharge, immunization and so on. In the future, it will be necessary to incorporate even more information in EHR systems, such as electronic interviews, self-documentation and nursing documentation. New EHR systems can minimize the need for duplicate data collection and can integrate a large amount of information accumulated during the patient's life. There are even systems that can link other data sets, such as general population health and lifestyle surveys, disease registries, educational data, social care and different, with EHRs for each patient individually. EHR systems can be incorporated into many areas of healthcare - from everyday use in clinical practice to research. Some of the research applications of EHRs could be epidemiologic and observational research, safety surveillance, regulatory purposes and clinical research. Using EHRs for assessing trial feasibility and facilitating patient recruitment is an already accepted application. Extracting data from EHRs can make patient recruitment easier and more efficient by obtaining the best possible target group of patients based on EHR data.

The use of EHRs in clinical practice can be enhanced by the use of deep learning models. By implementing the DL models, it is possible to use EHR data for detection or classification of diseases, predicting

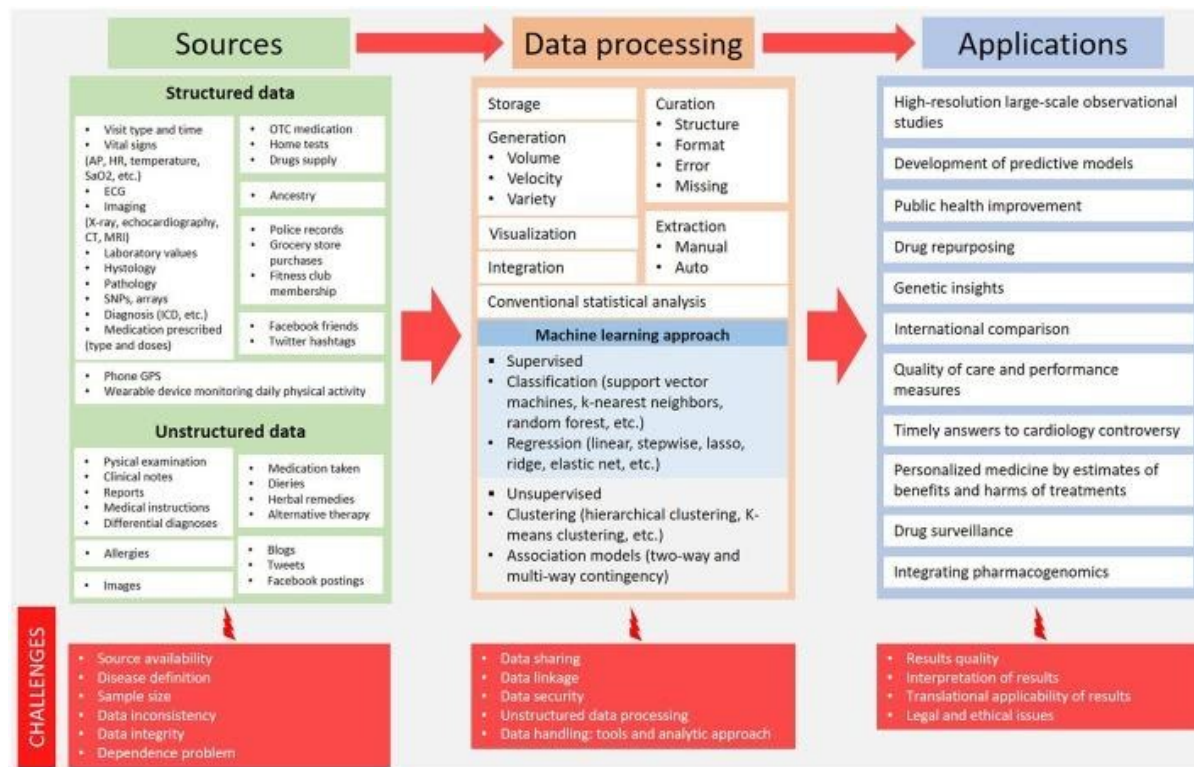
clinical events, deriving feature representation of clinical concepts and even data augmentation. Depending on the task, it is necessary to choose the most suitable model that will give the best results. Today there are already several different neural network models that can be applied to such situations.

Disease classification - the main goal is to develop models for connecting the input EHR data to the output disease target using multiple layers of neural networks. It is possible to use disease-specific datasets such as cognitive assessments, vital signs, medical images and onset of disease. Combining all these information neural networks can detect data connectivity and classify diseases based on it.

Predicting clinical events - neural networks establish relationships between patient medical history and future events. It is possible to make predictive models of future events, for example, mortality, which is especially important in cardiovascular care since CVDs are the world's first cause of mortality.

Concept embedding - neural networks can be used for mapping the EHR data to the phenotype of interest. Unsupervised models without labels are mainly used for this purpose, but it is essential to use massive EHR databases. Each EHR consists of a sequence of visits while each visit includes multiple medical concepts (diagnosis, procedure, medication codes). This hierarchy dictates the design of models that can search for information in both the sequential nature of visits and the co-occurrence of codes within a visit.

Data augmentation - it includes data synthesis and generation techniques. With the advancement of technology, it is possible to gain synthetic data comparable to real data.



Big health data overview. Reprinted from “Big Health Data and Cardiovascular Diseases: A Challenge for Research, an Opportunity for Clinical Care”, by Silverio A. et al., 2019, Frontiers in medicine, 6.

Deep learning can take raw data processing to a new level, minimizing the need for pre-processing and feature engineering. DL models are a great tool for identifying diseases or predicting clinical events and outcomes given time series data. However, although there are many advantages of implementing DL models, several challenges are present. First of all, the quality of data and labels still need improvement. Quantity means nothing if the data we have is not of good quality, in which case it will be difficult or even impossible to use them. Data quality and validation are especially crucial in implementation of EHRs in clinical trials. Errors in EHRs can occur for several reasons, including busy workloads of the staff or a non-user-friendly system. Emphasizing the importance of keeping accurate and precise EHRs is key to increasing the quality of the data we will have at our disposal

later. What is also a big problem is incomplete data capture, usually in regions where patients receive care from different health care providers using different EHR systems that are not linked or even receiving care from a provider that does not use EHRs at all. Heterogeneity between systems complicates sharing data because different systems usually have differences in quality and terminology. Sharing information through systems is a crucial step for getting the complete picture of a patient's health and embracing physicians to discuss which procedures and drugs work best. A big step forward for enabling EHRs to be used across hospitals and regions would be achieving agreement on a minimum set of common data. However, even if there is enough quality data, there is also a problem of multi-modality of the data. EHR data include numeric values (e.g. lab tests), textual clinical notes, continuous monitoring data (ECG, EEG), medical images, and codes for diagnosis, medication and procedures. Finding patterns among this multimodal data can improve health care, but at the same time, it can be challenging to develop the systems due to the heterogeneity of the data. Multitask learning is the solution for this problem, and that requires complex algorithm architecture.

Also, a hot topic is the problem of privacy of information and ethical approach to it. People preserve their privacy by having controlled access to their data. It is essential to take care of the security of patient data and to control to whom this data is available. Several projects have recently provoked popular reactions when data has been shared with large corporations that already have certain information-sharing scandals, such as Google and Amazon. However, the potential benefits of data sharing and implementing EHRs for the entire community should be considered.

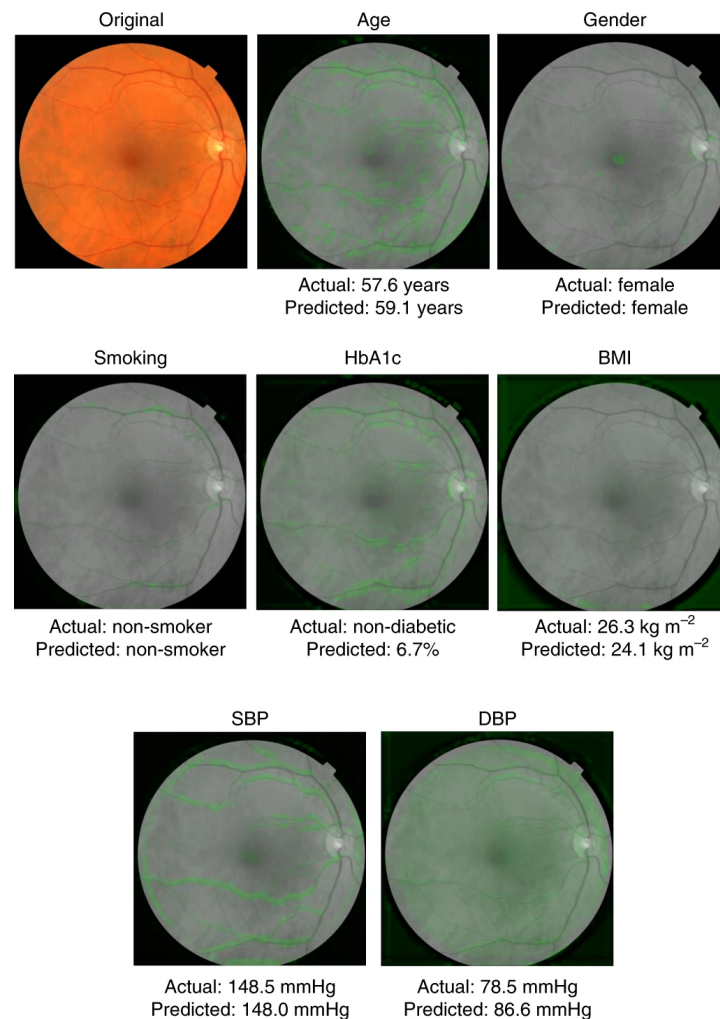
When it comes to CVDs, because of the global burden, it is crucial to invest in sustainable health and research policies. Great inequality between the need for data and actual resources highlights the

importance to develop new forms that will enable analyzing large amounts of information regarding CVDs cost-effectively. The use of advanced systems that will allow a complete analysis of available data will improve health care, but thus also reduce the cost caused by repeated procedures and tests, medical errors, misdiagnosis or wrong therapy. Each of us should be involved in collecting but also sharing data in a way that is as accurate as possible and can be easily used. So far, EHRs have not lived up to their full potential, but by identifying problems and improving systems, it may be the way to reach it.

Cardiovascular risk and retinal scan

Risk stratification is a key to identifying and managing risk patients for CVDs. Most of the CVD risk calculators mentioned earlier are widespread, but there is an aspiration for their improvement. Important phenotypic information is ones of vascular health; that information may further refine risk prediction. Due to the high interest in finding better and simpler ways to determine CVD risk, an unusual algorithm has been developed. It is a DL algorithm that analyses the retinal image. The goal was to explore if retinal images can give signals connected to cardiovascular risk. Advantages of this method are that it is quick, cheap and non-invasive, while most other calculators and algorithms require blood tests. Markers of cardiovascular disease, such as hypertension and cholesterol emboli, can often manifest in the eye. When developing the algorithm, the scientists also singled out heat maps that show exactly which anatomical features were taken into account when making the decision. In other words, on black and white retinal images, the areas that the neural-network model was using are highlighted in green. Based on the image, the algorithm was able to predict gender, age, smoking status, BMI, systolic blood pressure, diastolic blood pressure and major adverse cardiac events. What is fascinating is that this algorithm was

more precise in determining gender from the retinal image than most of the people would be by looking at a person. Of course, there is no need to implement this algorithm to determine patients' gender but the astonishing power of artificial intelligence to improve cardiology is something to think about.



Attention maps for a retinal fundus image. Top left is a sample retinal image in colour from the UK Biobank data set.

The remaining images (figure 11.) show the same retinal image in black and white, green areas of the heat map show areas that the neural network model is using to make the prediction for the image. Reprinted from “Prediction of cardiovascular risk factors from retinal fundus

photographs via deep learning”, by Poplin R. et al., 2018, Nature Biomedical Engineering, 2, 3.

Smartphones and cardiology

Smartphones and tablets have become essential devices to users in recent years, and that is the reason why everyone is trying to affect those users in the best possible way. Cardiology is no different - a lot of apps and systems have been developed for cardiovascular patients and those who want to improve their heart health. Mobile technology might increase the effectiveness of prevention of CVDs. Mostly we are facing mobile heart and vital signs monitoring systems, such as blood pressure tracking and heart rate monitoring, and medical calculators. These are tools that were created to ease keeping data for patients and to inform them if something is not right with their heart. There are also some mobile cardiac rehabilitation systems, blood pressure measurement and CPR instruction. As mentioned before, external monitoring devices development is on the rise. Electrodes that can be connected to smartphones then measure ECG and pulse. These data can then be stored on the phone and help physicians in treating patients. Now more and more smartphones are already coming with a health app in which blood pressure, pulse and other symptoms can be recorded as a type of digital diary. Since physical activity is important for heart health, some fitness apps specialized for CV patients have been developed. This is only another evidence of how critical the problem of CVD mortality is and a lot of technology and research is involved in the advancement of cardiology. Smartphones are also present in low socioeconomic societies which means that health-related mobile applications might provide an opportunity to overcome barriers to cardiac care access in these areas. But the increased number of low-cost health-related apps also raises some questions about the quality and relevancy of the same. Are apps developed according to evidence-based medicine and in cooperation with

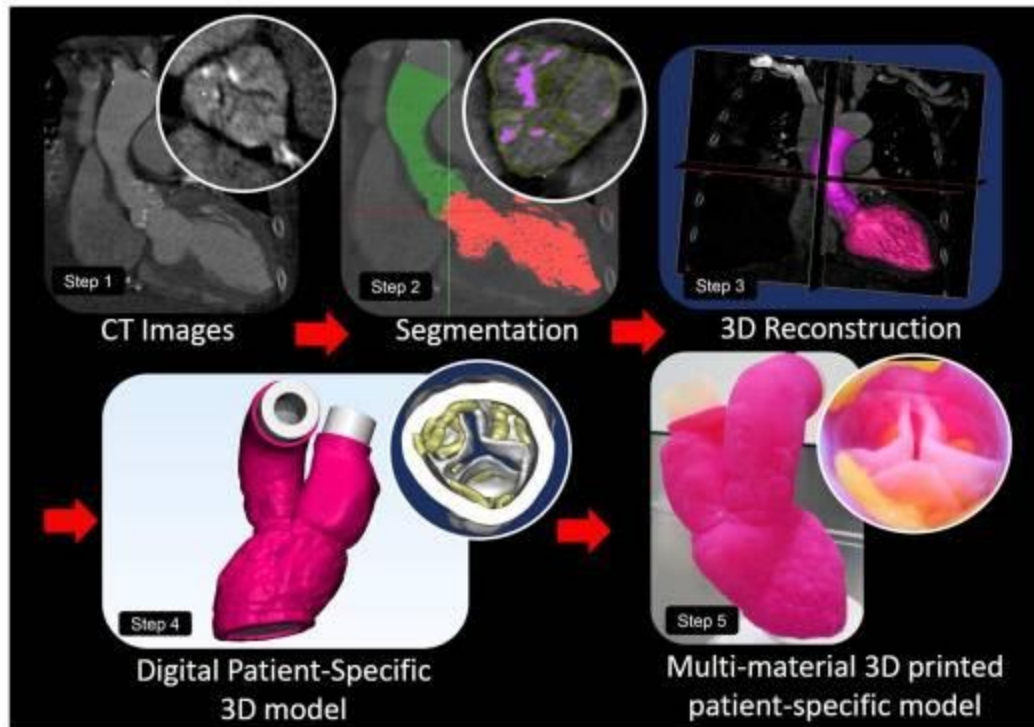
cardiologists? Are they user-friendly? Mobile technology can be a great tool, but we still need to be careful while using it.

Three-dimensional (3D) printing in cardiology

Three-dimensional printing, also known as additive manufacturing, is a technique used for producing physical models from digital ones. It is a computer-controlled construction of the 3D object by depositing material layer by layer. The possibilities of implementing 3D printing in cardiology are numerous, but everything starts with imaging. CT and MRI scans are the basis for developing digital models that will then be printed. The goal is to create a patient-specific 3D model using CT, MRI and 3D echocardiography patient datasets. Image segmentation, or determining which pixels belong to which anatomical unit, is a critical step in developing a digital model. Combining images from different angles and obtained by different methods enables creating a more precise model. CT scan has the advantage because it can image patients with pacemakers and other metal implants, while MRI is not compatible with it.

On the other hand, MRI is widely used for modelling congenital heart and vessels and intra-cardiac tumours. This 3D digital model can later be modified within computer-aided design (CAD) software in such a way that by changing colours and materials the desired differences between regions are highlighted, depending on what we will use the model for. For example, it is possible to print every heart region in a different colour or even to print it in transparent materials, so it is easier to see inside of the heart model. There are several different technologies of 3D printing that can be used for medical purposes and which one to choose depends on what the model will be used for. Also, material exploration for 3D printing is rapidly progressing so that materials that can mimic the mechanical properties of some cardiac tissues are already available. The big issue is that it is still not

possible to achieve the full functionality of the model, but we are approaching this with bioprinting. Problem with classic materials is they lack a lot of features of the real tissue (such as contractility and conductivity), so they can be used just for developing educational and helping tools. New techniques offer a possibility of bioprinting, which means that instead of rigid materials, it uses cells and other bioactive factors to create functional living constructs. These complex architectures can be used for pharmaceutical study and tissue regeneration. Cardiovascular bioprinting is still in its infancy, but it has a bright future.



Steps in 3D printed modelling of a patient-specific anatomy. Reprinted from “Cardiac 3D Printing and Its Future Directions”, by Vukičević M. et al., 2017, JACC: Cardiovascular Imaging, 10, 2.

Once developed and printed, these 3D printed patient-specific models can be used for multiple purposes, such as:

Anatomic teaching tools – creating models for anatomic teaching and demonstrating can be useful for teaching medical professionals about some specific heart abnormalities. Still, it can also be used by health providers to educate patients about their conditions. A physical model that can be used to explain anatomical deformities more efficiently is a great way to improve communication between physician and patient.

If you want to hear how useful it is to the patients, you can watch this video:

★ [How cardiologists use 3D printing to save tiny lives](#)

Video 3. “How Cardiologists Use 3D Printing To Save Tiny Lives”, YouTube, uploaded by Gizmodo Australia, 16 July, 2018

Functional flow models – some conditions disrupt the ideal blood flow through the heart, and that can cause problems if not treated in time. Sometimes it is challenging to visualize blood flow using 2D and 3D scans, so printing functional models give a better insight into the blood flow. These models are often printed from transparent materials, so it is easier to visualize complex flow dynamics.

Procedural planning – application of 3D printing that is mostly used for patients with congenital cardiovascular diseases, since their heart usually has a complex and unique anatomic structure. 3D printed models can provide more precise and straightforward insight into the condition of an individual patient, which can be crucial in planning a procedure. It is also used for the preoperative and intraoperative surgical management of implant placement and cardiac tumour. Using different colours and materials, it is possible to accurately separate tumour tissue from surrounding tissue, which is hard to achieve with 2D and 3D scans.

Here is a video showing a real case of applying 3D heart model in surgery planning:

★ [How 3D printing is revolutionizing heart surgery](#)

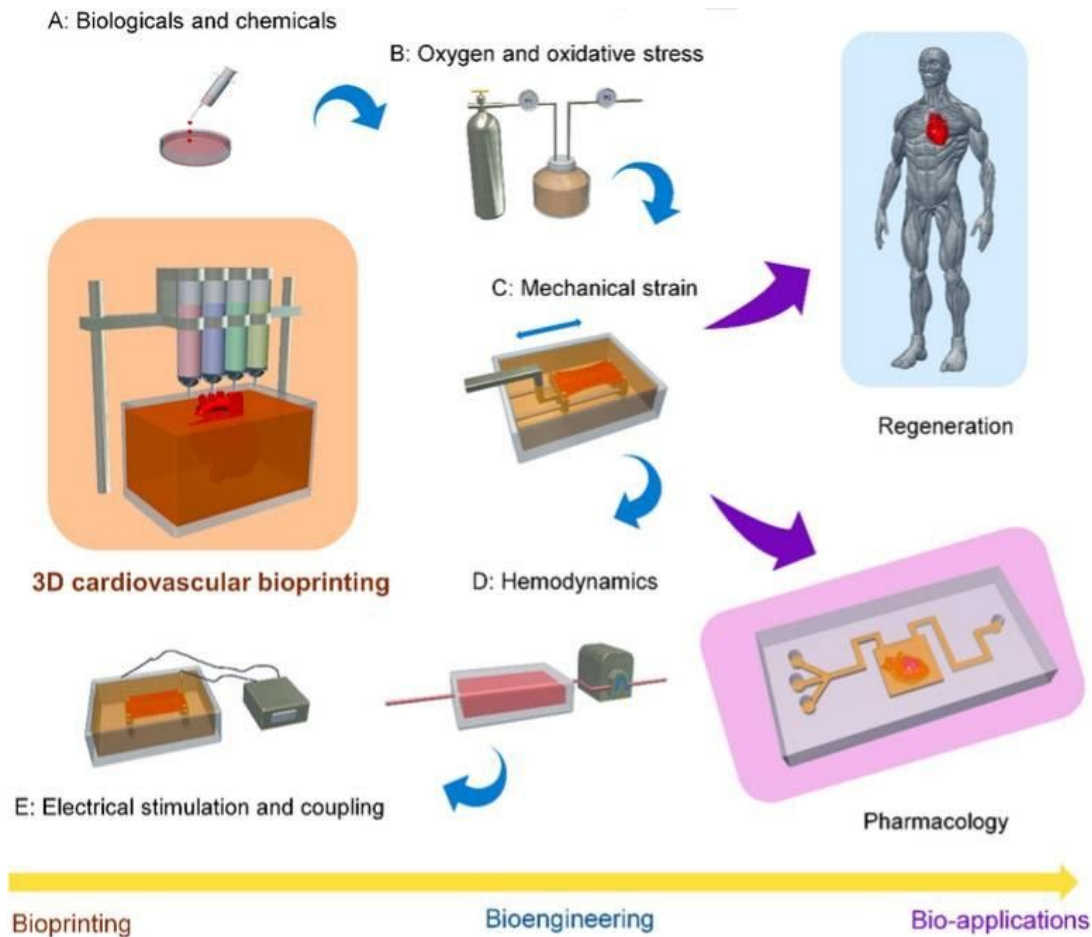
Video 4. "How 3D-Printing is Revolutionizing Heart Surgery", YouTube, uploaded by Freethink, 3 January, 2019

Device innovation – especially significant for the development of transcatheter mitral valve replacement devices. For this procedure, it is important to know the specific anatomical features of each patient in order for the procedure to be as successful as possible. The creation of an anatomically accurate and deformable 3D model enables the assessment of the influence of anatomical structures on the implantation of the device, but also the influence of the device on native structures.

Pharmacological study – the idea is to use bioprinting to develop a model of the cardiovascular system that will be used for in vitro research. In vitro studies are necessary for the initial preclinical phase of new drug development when determining its toxicity and interactions with targets. Classic 2D and 3D cell cultures are usually used. Still, by bioprinting, it is possible to develop models that will better reflect in vivo conditions and thus improve the accuracy of the study. 3D bioprinting enables the creation of systems that also have some of the functional features of the cardiovascular system, such as contractility, which can be very important in pharmacological studies.

Regeneration – research on possible applications of bioprinting in the field of tissue regeneration is focused on the myocardium, heart valves and vasculature. Cardiovascular implants can be fabricated from either synthetic or biological materials. Either way, implants must meet the anatomical and physiological characteristic of the patient's

tissue. This is a very challenging area that is yet to reach its peak, but with the development of materials and technology, progress can be expected.



Schematic diagram of the techniques, bioengineering methods and applications of 3D cardiovascular bioprinting in regeneration and pharmacology. Reprinted from “3D bioprinting for cardiovascular regeneration and pharmacology”, by Cui H. et al., 2018, Advanced Drug Delivery Reviews, 132.

As we can see, 3D printing can improve cardiovascular care, but there are still no studies that systematically and quantitatively monitor the impact of 3D printing on the quality of care. Nevertheless, most cardiologists respond positively to the use of 3D models, as do most patients who have had the opportunity to encounter this technology.

Regardless of the studies, the positive feedback from physicians and patients already speaks enough about the benefits of this technology. The future of cardiac 3D printing will definitely be interesting to follow. Implementing 3D printing in congenital heart disease treatment, surgical planning, developing patient-specific prosthesis and devices and many more areas can change the way of cardiovascular interventions.

Virtual reality for stroke rehabilitation

After having a stroke, many patients have difficulties in moving, speaking, thinking and other motor and cognitive abilities. All these disturbances can create problems in leading a regular daily life. Virtual reality (VR) and interactive video games are increasingly being used as post-stroke therapy to improve the locomotor system and cognitive thinking. Virtual reality uses interactive, computer-based simulations for users who can engage in virtual environments and events. Therapy is designed to simulate real-life situations using a virtual environment and thus creates exercises that are not feasible in a hospital environment, such as crossing the street. VR and video gaming can provide added value to therapy that traditional therapy does not offer and can enable longer duration of therapy because it does not require as much time for healthcare professionals as regular therapy.

There are many examples of already developed devices and programs used worldwide for stroke rehabilitation. This is just one such example:

★ [Reality \(VR\) and rewellio's innovative stroke therapy software](#)

Video 5. "Virtual Reality (VR) and rewellio's innovative stroke therapy software", YouTube, uploaded by Rewellio GmbH, 13 December, 2018

Most of them are focused on the return of upper limb function because it is a very common consequence of stroke which is a big problem in everyday life. But there are also many other programs, not only for upper limb function.

VR has the potential to provide patients with virtual tasks to improve problem solving and other skills after a stroke. Tasks often involve interacting with a virtual environment using a joystick, console, camera, motion sensor or some other device that allows the patient to engage. Today, gaming consoles that are primarily developed for recreational use, such as the Nintendo Wii, PlayStation and others, are also increasingly used for therapy. These consoles offer a platform for implementing programs for stroke rehabilitation. The goal is to engage the patient and to enable as many different tasks as possible to improve various functions - balance, posture, gait, walking speed, thinking, problem solving and many others. Although this type of therapy is not yet in routine use, its enormous potential to improve health care for stroke patients is not negligible. Studies still do not show the superiority of VR over traditional therapy, but specific areas are identified in which VR nevertheless offers better outcomes than traditional therapy. This is an area that will evolve further over time and be increasingly present in clinical practice.

UNIT 6 Introduction to machine learning

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The essential keywords

- **ML** = [Machine learning]
- **SVC** = [Support vector classification]
- **SVR** = [Support vector regression]
- **DNN** = [Deep neural network]

Machine learning (ML) is a subfield of artificial intelligence that gives computers the ability to learn without being explicitly programmed. This process involves the development of algorithms that adapt their models to improve their ability to make predictions. We say that a program uses machine learning if it improves at problem-solving with experience.

There are two types of Machine learning: unsupervised and supervised. Supervised machine learning is mostly used. The main difference between supervised and unsupervised ML is that in supervised ML, we need to label data. In supervised ML we gave the specific algorithm a data set in which the „right answers“ were given, and based on this we can see if the algorithm correctly classified the samples on the data set. Example of a supervised ML algorithm is when looking at medical records, and we try to predict cancer as malignant or benign. Unsupervised machine learning algorithms are mostly clustering algorithms that are used to organise large data sets or to find outliers. In an unsupervised ML algorithm, we provide the unlabeled data to the algorithm and the computer tries to connect the data by extracting features and patterns on its own. Example of an unsupervised ML algorithm is when we take a collection of different

genes, and we try to find a way to automatically group these genes into groups that are somewhat similar or related by different variables, such as lifespan for example.

Supervised machine learning

Supervised machine learning can be used for regression or classification. It requires to divide the input dataset into the training and test dataset. Usually, the training dataset is about 70-80 % of the whole input dataset, and the rest is the test dataset. On the training dataset, a certain algorithm is learning how to label the data if the classification algorithm is used, or a regression algorithm - learning the relationship between the variables. In this part we will say more about most used supervised machine learning algorithms: linear regression, logistic regression, support vector machine and neural networks.

Linear regression

Linear regression is a model that is in wide usage for analysing multi factor data. It assumes the linear relationship between the input variables and the single output variable. Therefore, using linear regression, the output variable can be calculated by a linear combination of the input variables. The output variable is sometimes called dependent since it can be predicted by analysing input variables, and the input variables are often called independent variables. If there is one input or independent variable, the method is called simple linear regression, and if there are multiple input variables, the method is called multiple linear regression. Linear regression is appropriate when the dependent variable has a linear relationship to the independent variable. All regression methods use the independent variables to predict the outcome of dependent variables.

Simple linear regression finds a correlation between independent and dependent variables and therefore, can predict the outcome of a new dependent variable. Linear regression cannot find a distinction between the dependent and independent variable, and therefore can not be used for solving classification problems. Simple linear regression finds the straight line, called the least-squares regression line that can best describe observations in the dataset. The formula for simple linear regression is $y = x\beta + \epsilon$, where y is the dependent variable that can be either continuous or categorical value, x is an independent variable that always has a continuous value, β is regression coefficient, and ϵ is constant.

A proportion of variance in the dependent variable that is predicted from the independent variable is called the coefficient of determination R^2 . The values of the coefficient of determination are in a range from 0 to 1. An R^2 of 0 means that the dependent variable cannot be calculated from the independent variable and an R^2 of 1 means that the dependent variable can be computed from the independent variable without the error. An R^2 that ranges between 0 and 1 represent the extent of which dependent variable is predicted from the independent variable. For example, if R^2 is 0.5, that means that 50% of the variance of the dependent variable y is predicted from the independent variable x . Linear regression can be used for predicting values like prices of houses, grades of students based on datasets that contain variables based on which we can predict these values (area of the house, grades of students from previous year).

Standard error represents the average distance that observed values fall from the regression line. Thus, a standard error is the measure of the average amount that the regression line overpredicts or underpredicts. A coefficient of determination and standard error are inversely proportional. As the coefficient of determination is

increasing, the standard error is decreasing, and therefore we get more accurate predictions.

Logistic regression

Logistic regression is the method for classifying data into discrete outcomes and is in wide usage today as one of the most popular learning algorithms. Linear regression is not a good idea to use for classification problems, since the dependent variable y that is being predicted can be larger than one or less than zero if we are using linear regression. One of the properties of the logistic regression is that the output of logistic regression is always between zero and one. Thus, the predictions in logistic regression are never bigger than one or less than zero. The logistic model is used for classification problems, like finding the probability of a particular class or event existing such as pass/fail, win/lose, alive/dead or healthy/sick. If we are trying to build a logistic regression classifier to predict benign or malignant skin tumour, then based on some features of the tumour like size, colour or the shape of the skin tumour, the predicted value y may be one if it is a malignant tumour, and one otherwise. When hypothesis outputs some number, we are going to treat that number as the estimated probability that y is equal to one on new input x . For example, in our example with a benign and malignant tumour, if hypothesis outputs the number 0.8 then there is 80% chance of tumour being malignant, and 20% chance that it is non-malignant. The decision boundary is a separating line between the part where the hypothesis predicts the dependent variable as one from the part where the hypothesis predicts that the dependent variable is equal to zero. The decision boundary is property of the hypothesis and the parameters of the hypothesis and is not a property of the dataset. A cost function takes two parameters in input: hypothesis function and output. Cost is the penalty that the algorithm pays if the result of a hypothesis function is incorrect. If predicted value y is equal to

one, and the result of the hypothesis function is equal to one means that the hypothesis exactly predicted the dependent variable, so then the cost is zero. Thus, if we correctly predict output, then the cost is zero.

When we apply linear and logistic regression to a specific dataset, they can have an overfitting problem that can cause them to perform very poorly. Overfitting can be caused if we have too many features. Thus, the learned hypothesis fits the training set very well but fails to generalise on new examples. This problem is the opposite of the underfitting, where the learned hypothesis fits poorly to the training set.

If we have a lot of features, and very little training data, then, overfitting can become a problem. We can reduce overfitting by reducing the number of features or by regularisation. With regularisation, we can keep all the features, but reduce magnitude/values of parameters that are used in linear or logistic regression. This approach of regularisation works well when we have a lot of features, each of which contributes a bit to predicting dependent variable value.

If we run the learning algorithm and it doesn't do as well as we are hoping, it will be because we have either a high bias problem or a high variance problem. Knowing which problem of these it is, is critical to figuring out how to improve the performance of the learning algorithm. Bias or underfit problems are usually when cross-validation error is similar values like the training error since in the underfitting we already have a high training error. Variance or overfit problem is when training error is very low because the training set is very well described by the hypothesis function, so cross-validation error is much bigger than training error.

Deep learning (Deep neural network)

Deep learning is the field of machine learning that consists of a neural network with many hidden layers. Neural networks models are inspired by the way the human brain works. Neural networks were widely used in the 80s and early 90s of the last century, and their popularity decreased in the late 90s. They are in wide usage today in many applications since recently computers have become fast enough to run large scale neural networks. Neural networks with one hidden layer are an example of a classical machine learning algorithm. Deep learning is an artificial neural network with multiple nonlinear hidden layers, and it can be considered as a subcategory of machine learning. It consists of an input layer, multiple hidden layers, and an output layer. During the process of training, deep learning architectures weight parameters are optimised in each layer. This process results in learning the most relevant pieces of information from the data. There are many repeats of the optimisation process on the training set. These repeats of optimisation are necessary to find a right fit of algorithm parameters and that the network can learn from the training set so that it can later as correctly as possible classify the data on test set or any other new data.

A single cycle of optimisation process consists of output calculation in each of the layers and propagating this output in the next layer so that in the final output layer the error between the outputs and given labels is measured. The error signals in each optimization step backpropagate, and gradients are calculated based on all weights. The next step in optimisation is the update of the weight parameters using an optimisation algorithm based on stochastic gradient descent. Stochastic gradient descent performs updates for each small set of data examples. Layer output values are calculated by multiplication of the input vector that consists of output values of each node in the layer by weight vector of each of the nodes (units) in the layer. As

a result of multiplication, we get a weighted sum. The final output values of layers are calculated by applying nonlinear functions (like a sigmoid function) to the weighted sum.

Deep neural networks or DNN are most suitable for analysing high dimensional data. One of the wide usages of DNN is image recognition. Using DNN, we can find unknown and abstract patterns and correlations on datasets, and therefore we can learn more about data. One of the key differences between classical machine learning and deep learning is that classical ML doesn't handle well with raw data and needs human help in setting the parameters. In contrast, deep learning when set to motion can be unsupervised, and we cannot know what is happening in hidden layers or how the algorithm is finding connections between the data.

Support vector machine algorithm

SVM is a machine learning algorithm for classification. It is a supervised ML algorithm that can find patterns in large and complex datasets. This algorithm is most widely used for solving classification problems, for example classifying tumours as benign or malign. Neural networks, an algorithm that is also used for extraction of complex and non-linear relationships between features, can give a reliable result only when a massive number of data are available. Due to a large number of data that was used to train NN, overfitting was often observed in applications that used NN. Overfitting means that the algorithm performs excellently on the training dataset, but poor results or estimates are observed in the test dataset. Due to shortcomings of NN in the early 1990s, an SVM algorithm was developed as another option for non-linear tasks. It is considered that success behind providing reliable results based on SVM lies in the ability to learn with the small number of features and high computational efficacy. SVM algorithms can be divided into two subcategories:

Support Vector Classification (SVC) and Support Vector Regression (SVR).

A line that is dividing a group of samples of the dataset (several classes) based on some features is called separating hyperplane. This separating hyperplane is not only the feature of SVM but also from other algorithms. The SVM algorithm differs from other algorithms based on the way this separating hyperplane is selected. A hyperplane in SVM is chosen because a maximum difference between the hyperplane and features of the class exists. The hyperplane in SVM is called maximum margin separating hyperplane. A hyperplane is one of the reasons why SVM performs excellently in correctly predicting the class of the new samples (those samples on which the training set was not performed). Since many datasets cannot be separated clearly because there always can be some outliers, the soft margin can be defined. A soft margin tells us how many samples can be misclassified when determining separating hyperplane. Determination of this parameter can be challenging since we want to keep the large margin between correctly classified samples. In that way, a soft margin represents the trade-off between hyperplane violations and the size of the margin. One more important parameter for the SVM algorithm is the kernel. A kernel is a mathematical trick that projects the data from a low-dimensional space to a space of higher dimensions. It can be said that for any dataset with consistent labels there exist linear functions that enable linear separation of labels. Though, it must be careful with increasing dimensionality of data based on kernels. There is a term in a machine learning field called the curse of dimensionality, while variables are rising, the number of possible solutions is also increasing but exponentially. It, therefore, becomes more problematic for the algorithm to select the correct answer. The result of this can lead to overfitting, where the algorithm performs

very well on the training set or fits too well with the training set and therefore performs poorly on the test set.

Unsupervised machine learning

Unsupervised machine learning, as opposed to supervised learning, does not require human supervision. Using unsupervised machine learning methods, we can find previously unknown and undetected patterns in the data where there is no need to label the data. Some of the most popular methods for unsupervised machine learning are Principal component analysis or PCA and hierarchical clustering.

Hierarchical clustering and principal component analysis

Principal component analysis is a method that uses a classic dimension reduction approach. It is used to reduce the complexity of large datasets and increase their interpretability with minimum information loss. Principal component analysis can be done on a covariance or correlation matrix. The covariance matrix is used when variable scales are similar, and the correlation matrix when variables have different scales. Using the correlation matrix is a process of standardizing each of the variables to the mean 0 and standard deviation 1. PCA with and without the standardization will give different results.

Hierarchical clustering is a method of the grouping of similar objects into groups called clusters, where each object in the cluster is like other objects in the same cluster, but dissimilar with an object from other clusters. There are two types of hierarchical clustering: agglomerative and divisive. In agglomerative hierarchical clustering each observation or object has its own cluster in the beginning but later are joined as we move up the hierarchy. In divisive hierarchical clustering, all instances start as one cluster and later are separated based on similarity. In order to decide how to group objects or

observations, it is necessary to have a measure of dissimilarity between the set of observations.

Both, PCA and hierarchical clustering can be used to see how a dataset looks and to find outliers or groups with similar features that cluster together.

UNIT 7 Virtual reality in surgical training

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As both the medicine and development of novel medical technologies rapidly advanced in recent decades, the way of teaching and training medical professionals had to be adapted to those changes and advance too. This progress and the need to improve medical training is especially prominent in diverse surgical fields. One single technique that pulled both the medical performance and training to the next level of complexity and interactivity was laparoscopic surgery in the 1990s. Laparoscopy and other types of minimally invasive procedures imposed the necessity to create more advanced techniques to learn surgical skills. The absence of tactile feedback, the need for precise hand-eye coordination and a change from 3D to 2D perspective were characteristics that fitted very well with virtual reality (VR) and simulation, which therefore became introduced in the field.

One of the first studies demonstrating the correlation between the early training phase (less than 10 performed surgeries) and surgical errors was also conducted in the field of laparoscopic cholecystectomy. The findings showed that 90% of common bile duct injuries occurred within the first 30 operations of a trainee surgeon and that, from the first to 50th operation, the rate of error reduced 10 times. By replacing the real with the virtual patient, the initial phases of the learning curve, with slow progress and numerous errors, can be performed in a dynamic, reality-mimicking environment which provides for quality surgical training, but without surgeon errors inflicting damage to the patient¹.

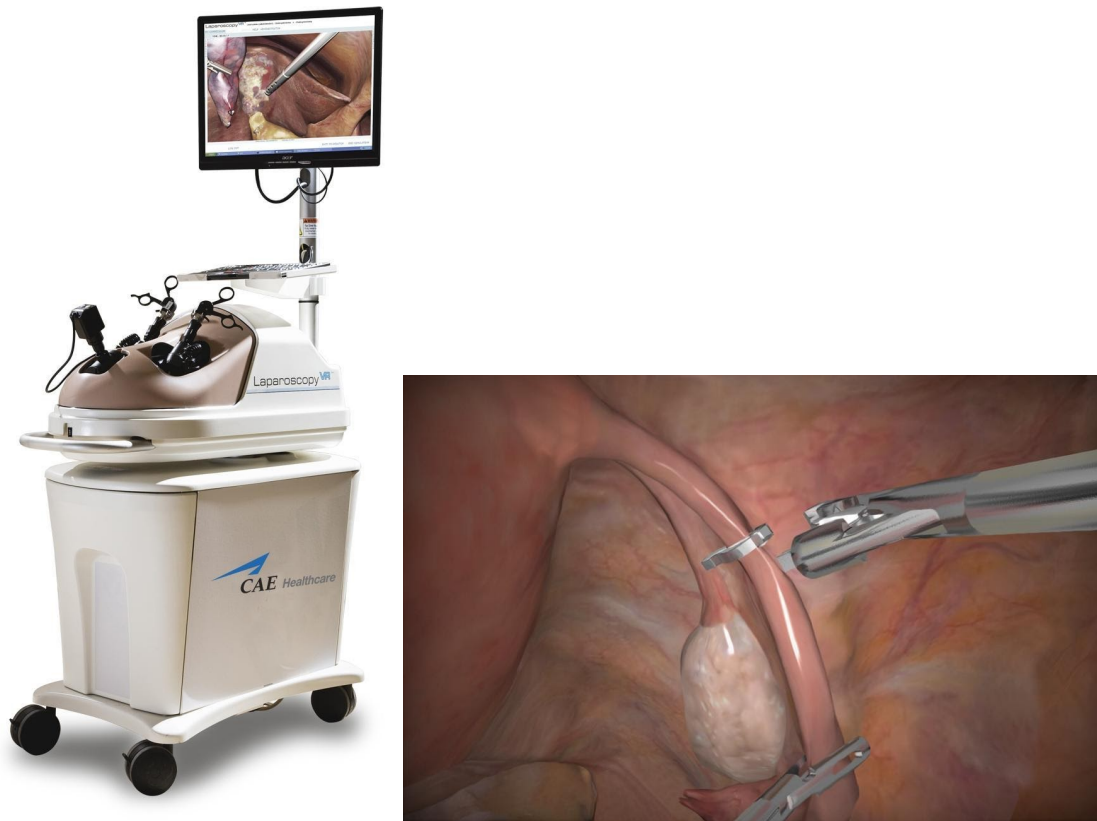
Taking into consideration economic factors that negatively impact the quality of surgical training, such as the length of performing procedures, time demands in the operating theatre, fatigue of senior

surgeons which lead to limiting working and teaching hours etc, the use of VR in the training becomes a fortunate solution to stated limitations.

Introduction of simulation laboratory, as a protected, safe learning environment, allowed for trainees to practice various skills and procedures on a wide variety of surgical simulators, as a part of dedicated learning. Apart from learning the flow of specific procedures, the trainees are developing spatial, perceptual and psychomotor skills, especially hand-eye coordination and subtle movement refinement. Along these skills, the ones of crucial importance for a successful surgeon, such as critical thinking and decision making in clinical setting and automatism of certain performance, are being taught superiorly to the classic training. The possibility of on-sight, direct automated feedback and opportunity to correct virtual mistakes on a spot, make for further important improvements in surgical training.

The first surgical simulator to use VR was created at NASA and constituted an artificial lower limb model to simulate tendon transfer. The novel possibility introduced was the opportunity of planning and stepwise optimization of the operation. At the present time, VR technology has evolved to the point where personalized, actual patient data can be used in a simulation to complete virtual run-through the operation steps before actually performing it. Based on images from CT (computed tomography), MRI (magnetic resonance imaging), angiographic and other scans, a 3D model of an anatomic detail to be operated on can be constructed, placed in an interactive 3D virtual environment, allowing for the operation to be simulated on2. The 3D aspect of the simulated imagery eases surgical planning and improves the accuracy, producing safer procedures. An example of improved image representation acquired through 3D modeling is the case of one aneurysm surgery planning, where the detail of artery attached

to the top of the aneurysm became visible only after comprehensive modeling, which lead to probably saving a patient's life by instructing a different, safer surgical approach.



On the left, laparoscopic surgery simulator. On the right, a closer view into the simulation of the laparoscopic cholecystectomy.

Assessment of the improvement of surgical skills, both technical and nontechnical, is of vital importance in the development of next generation simulators, trainers and programmes. Technical surgical skills encompass spatial skills, eye-hand coordination, knowledge of anatomy and complication management. Nontechnical skills include decision making, communication and team interaction³. Recently, other types of non formal skills that can be simulated are being introduced into VR training, such as developing empathy and learning bedside manners.

Metrics for objective assessment of technical surgical skills mostly encompass error score, time needed to perform certain procedures, instrument length path and economy of movements. The user's score is then compared to the expert's score, providing a relative measure of acquired proficiency¹. VR-to-OR (virtual reality to operating room) transfer is another indicator of the successfulness of VR approach, representing the ability of simulation-based training to improve clinical performance. One of the first studies to explore VR-to-OR transfer was performed in 2001. at the University of Yale, comparing VR-trained and untrained groups in their performance of the gallbladder dissection from the liver edge. The trained group performed 29% faster, with 5 times less organ injuries and 9 times higher likelihood of finishing the surgery [5].

VR imposed a novel surgical learning strategy in a more complete sense. Previous “see one, do one, teach one” model of learning operations, based on observational learning, was substituted by a model of deliberate practice. Honoring three stages of skill acquisition, cognitive, associative and autonomous, VR simulated training allowed for their significant improvement. Simulation provides autonomous, self-directed, structured, replicable learning experience of different complexity adapted to specific trainees needs, and as such, is fitting very naturally into the specific nature of surgical training [3].

★ [Fundamental VR - FeelRealVR in action](#)

Video 1. An example of VR simulated surgery with all of its graphic and didactic components.

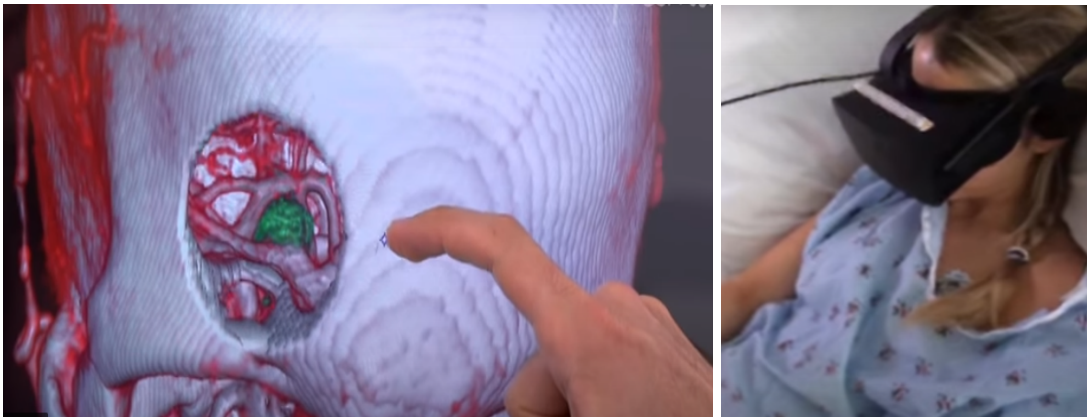
The need for feedback and mentoring is also being fulfilled in VR simulated learning. The most important characteristic of productive feedback is its timely and regular delivery, qualities that are much easier obtained in a VR setting, without lack of instructor's presence, objectivity and in situ provision. The feedback is immediate, objective and automatic, which also allows for mistakes to be corrected during the practice and procedures repeated until learned, regardless of the presence of the instructor¹. Furthermore, by means of using augmented reality, in its form of telemonitoring, surgeons can seek expert advice in a face of a complex and unfamiliar case. Senior surgeons can follow the surgery in real time and provide guidance at critical steps, while also predicting possible difficulties. Other types of augmented reality include navigation solutions, where by using special headsets providing so-called "X-ray vision", surgeons can see through patients and achieve more precision. The headsets can also collect video data from the surgery, and with assistance of machine learning make automated recommendations, such as highlighting critical structures not to be damaged or coordinate the whole surgical team [6].



Augmented reality surgery. Specific anatomical structure of individual patient are being displayed in front of the surgeon while performing surgery

Limitations of the VR use in surgical training include the impossibility of graphics to fully substitute for reality, very low level of haptic feedback, generic models and reduced accessibility, among others. All of these aspects are being addressed and expected to be more and more improved with time¹.

The most complete implementation of VR techniques is found in surgical settings where everything is adapted to individual patients, practicing in this sense a truly personalized medicine. 3D models are made, presented and researched by means of VR, surgeons perform virtual surgery using the same specific model, while virtual presentations are offered to patients themselves, which often reduces pre-surgery anxiety and includes them in the course of their treatment in a very educated and personalized way.



Bringing virtual reality to brain surgery.

*On the left, a 3D model of the part of the brain planned for reconstruction.
On the right, a patient being presented with medical problematics and
surgical approach by using VR.*

Credit:

<https://www.freethink.com/videos/bringing-virtual-reality-to-brain-surgery>

UNIT 8 Virtual Reality in Therapy

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The essential keywords

→ **FPS** = [Frames per second]

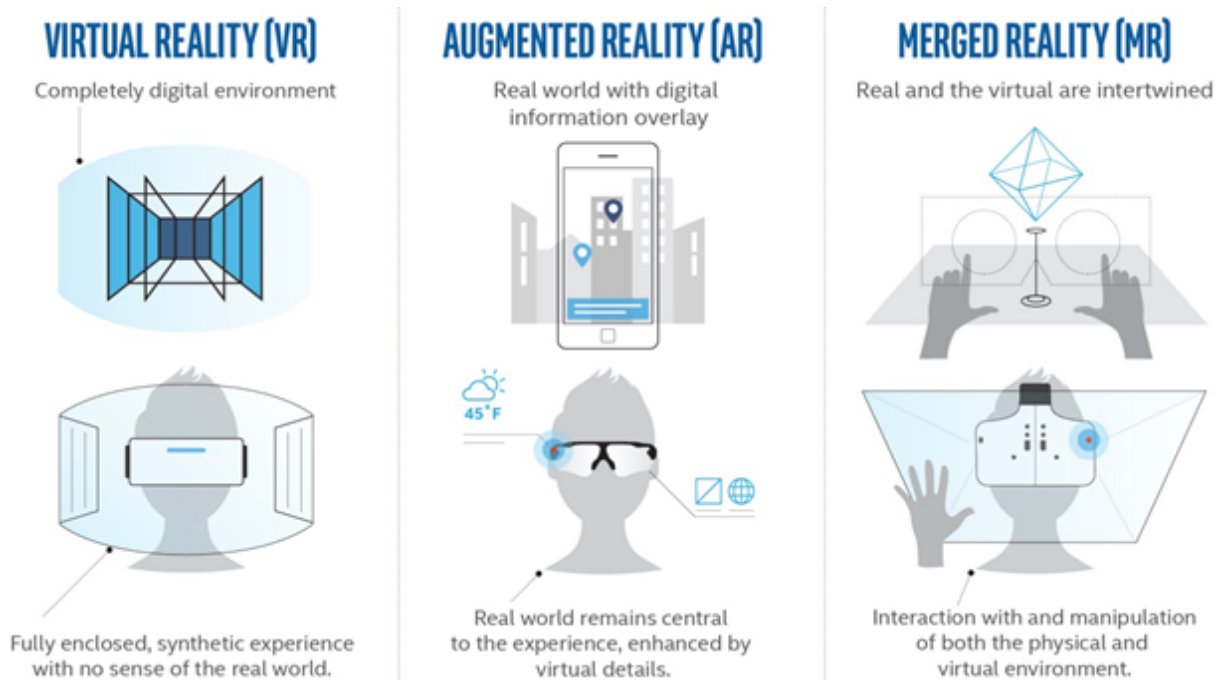
→ **fMRI** = functional MRI

Virtual reality (VR) is a simulated experience consisting of three-dimensional, computer-generated environments. This technology is no longer unaffordable to individuals and can be used through mobile phones or head-mounted devices at work, home or on the move. Potential applications are found in the areas of entertainment, science, industry, art, education and medicine. VR technology seeks to create immersive virtual worlds that people can interact with.

Hardware and software technology are essential elements in creating a VR experience, but the key components are human participants. The developers must understand the capabilities of human perception and create systems that can properly interact with the user's senses. Human's physical and mental limitations must be taken into account since it's easier to change the computer interface to match the human one than the other way around. An example includes reducing the rendered field-of-view and changing the number of details present depending on how close to the object the viewer gets to avoid overloading the user with sensory information. Image resolution also has a significant impact on how realistic the virtual world is, and developers should aim for over 90 frames per second (FPS) to avoid nausea or disorientation. Higher refresh rates mean realistic movements and less delay between the user's input and image output.

Extended reality platforms can be grouped into three categories: head based, stationary and hand-based. The head-mounted display is the one

most people associate with VR. Graphic images are displayed in the helmet or glasses, and this enables the participant to look around the computer-generated world in a natural way. The participant can also interact through voice commands, gloves or hand-held game controllers. The stationary system is not worn or carried by the participant and can be created through distinctly designed rooms with multiple large display screens. Hand-based technology requires the participant to hold a smartphone in their hands which displays the information. This can be achieved through smart binoculars or smart glasses as well.



Different types of “realities”.

The first appearance of VR in healthcare was in the 1990s for colonoscopy and upper gastrointestinal tract endoscopy simulations. VR has proved useful in the medical education of physicians and surgeons. It can also be applied in other aspects of medicine such as physical and psychological therapy. Some more well-known applications include phobia and PTSD treatments. Over time, using VR as treatment has extended to other conditions such as schizophrenia, anxiety disorders,

ADHD, pain management and post-stroke rehabilitation. The treatment was also successful for some patients with Parkinson's disease, spina bifida and spinal cord injuries.

Research data suggests VR is more effective than standard cognitive behavioral therapy that includes talking to a psychotherapist. It has shown good results in reducing anxiety in patients with phobias, but direct exposure is still more effective in some cases. VR can also be used to assess PTSD severity and even diagnose patients with the condition. When it comes to pain management, VR has been used as a distraction for phantom limb pain and patients with burn wounds during dressing changes. It has proved helpful in soothing patients during uncomfortable medical procedures such as dental surgery or cystoscopy. Distractions included walks in virtual environments, target-aiming tasks and even video games. However, playing video games doesn't require the use of VR to relieve stress in patients.

VR technology could potentially be offered in dental clinics to reduce anxiety in patients, especially during lengthy procedures. A study on a small number of patients showed the younger male population benefited from the use of VR the most and had a good experience with it. However, one-third of the participants expressed their dissatisfaction with the use of VR. Some older patients, women and individuals with severe anxiety claimed the experience made them uncomfortable and not being aware of what the dentist was doing induced more stress. The younger generation might prefer this technology more because they were exposed to it for almost their whole lives. Still, if VR provides them with a sense of comfort, healthcare facilities should at least consider offering it. It can take years of practice for an individual to be able to clear their mind in a stressful situation, so distractions such as VR should be welcome and serve as an alternative to anxiolytic drugs.

Decreasing stress levels in general could potentially be done through the use of VR. Patients who learned relaxation techniques can practice them in a VR setting, and the system can simulate stress-inducing everyday situations to see how well they cope. VR-based mindfulness apps can offer help on the move. Other isolated but promising studies include the treatment of depression and eating disorders to induce self-compassion in patients. VR can also be used to minimize addictive behaviors, such as tobacco consumption and gambling. Gamblers can participate in a simulation to experience how their thrill-seeking urges can result in significant financial losses.

VR allows detecting brain activity during natural social interactions and everyday tasks. In neuroscience, this is done through functional MRI (fMRI), a technique that measures neuronal activation by detecting blood flow changes in the brain. It's based on the assumption that blood flow increases when a region of the brain is being used. Comparing brain activity in multiple patients doing interactive tasks is challenging because of environmental distractions and different thought patterns between individuals. VR offers a controlled environment and enables neuroscientists to associate activation of specific brain regions to actions or thoughts which were previously missed or didn't seem connected.

Simulations can be applied in neurorehabilitation, mostly focusing on balance disorders and recovery after suffering a stroke. Virtual environments can be highly engaging and offer variety to patients whose conditions require practicing repetitive tasks. Studies on children with cerebral palsy and patients with walking difficulties due to multiple sclerosis have proved vivid visual and audio cues can improve gait. Seeing a virtual tile floor and hearing steady footsteps have helped both groups of patients walk faster and take bigger steps. It is presumed this happens because the realistic environment helps the brain bypass damaged areas and encourages reflexive responses.

The potential use of VR for personalized assessment and rehabilitation both at home or in a clinical setting remains mostly unexplored. VR technology has precise tracking sensors that can be used to recognize improvements in muscle control that would otherwise go unnoticed. It can also simulate situations that would be dangerous for some patients to perform in a clinical setting. An example is walking and balancing tasks on raised platforms for patients with balance disorders. VR can also be used to manipulate sensory inputs like touch and hearing with special gloves or audio cues. A sense of balance and position of body parts can be altered through simulations; the patient's avatar in the virtual environment doesn't have to mimic real-life movements. Presenting the patient's actions to be of a smaller range of motion than they really are can be beneficial when trying to train their motor system to produce larger movements. VR can provide exposure to diverse settings, which is known to induce neurons to form new connections and enhance motor learning. This is especially valuable in the treatment of elderly patients.

For patients looking to gain strength and balance to return to their everyday life, VR can be a valuable tool in physical therapy. Simulating familiar activities like grocery store shopping make the patients more willing to perform exercises like reaching for objects at different heights than standard therapy gyms. Activities can range from playing sports like soccer and making their own food to video game-like environments where they dodge cannonballs. Having a goal that's clearly visible to the patient has made a difference in their motivation and progress. VR has helped patients endure longer therapy sessions; some even refused to give up before they beat their high score. The technology makes conscious movement seem more natural, either through displaying an altered view of a patient's real actions during exercises or providing objects that can be interacted with. Being in a virtual environment has improved balance in patients with

walking difficulties and enabled patients who experienced physical trauma to achieve a wider range of motion. Since the patients are fully immersed in the simulated world, their movements aren't held back by anxiety and pain. In the therapy gym, the patient is focused solely on what their body is feeling and fear can slow down progress. VR also gives a sense of purpose to a patient's movement since physical therapy often requires repetitive exercises.

★ [Virtual Reality in Physical Therapy](#)

Video 1. A look at VR therapy from the perspective of both physical therapists and patients.

VR doesn't offer benefits only to patients but to doctors as well. For decades young surgeons required training in the operating room to hone their skills. The training hours have been reduced in the 2000s by government agencies because the increased number of surgeons in training also increased costs, raised ethical concerns and reduced work hours for senior surgeons. The education system had to start using animal models, videos and e-learning to compensate for this change. One of the recent approaches employs VR technology. The simulations can help both students and their supervisors. The models are very realistic and can react to student's actions if any mistakes are made. The training session can be recorded to compare and analyze the student's performance so senior surgeons can freely leave if there is an emergency in the hospital. VR has the most benefit when it's used to simulate time-consuming and risky procedures, such as laparoscopy. While in training, the students hold the instrument in their hand while looking at a virtual patient and various images that provide more patient-specific information (vital signs, MRI, CT). Similar VR systems have been developed to simulate orthopedic, ophthalmological and resection surgery. However, the accuracy of this kind of training must be improved. There is more work to be done to

make 3D models as realistic as possible and additional data should be provided so the students can be introduced to patients with rare conditions or uncertain diagnosis.

★ [Using Virtual Reality to Train Physicians for Pediatric Emergencies](#)

Video 2. Doctors in training participate in a VR exercise to help them navigate high-risk situations. Students can be exposed to multiple different scenarios with the use of VR, and this enables them to avoid future medical errors due to stress or unusual symptom manifestations.

Nurses in training are also being exposed to the VR technology. Some universities offer immersive exercises in which students can go to a patient's house to tend to their wounds, as well as get to know the patient and their habits. Students can also participate in a virtual hospital setting where they communicate with the patients, administer medicine and check vital signs. Patients can range from pediatric to elderly, and the realistic scenarios help students retain what they've learned.

The VR technology has proved to be a highly effective method in therapy or at least equally as effective as standard treatment procedures. The high cost of equipment with optimal performance is delaying the global usage of this technology. Fortunately, the financial burden is becoming lighter every year due to the rapid advancements in the electronics industry. VR has the potential to fundamentally change the way physical and mental conditions are approached in healthcare facilities. This emerging technology can be set-up almost anywhere since it requires only the specialized headset and controllers. Newer iterations don't require connection to a PC because all the necessary hardware is built into the headset. Once the VR experience or game is developed, it doesn't have to be tailored to every population separately, and this is a significant advantage compared to some other therapeutic programs. The risk for side-effects

is minimal even if the treatment doesn't provide satisfying results. Recent trends seem to favor VR-friendly computer-generated media and consumer devices. As the implementation of VR technology into everyday life increases, it may soon become a regular part of both research and therapy.

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