Biology Term Paper 5A

Passive Medical Implants

From Marvin Aelen and Diana Mock

Table of content

1. Preface

What is especially interesting when talking about bone replacements and just biotechnology in general is part of the future. Bone replacements have changed at the same time that technology has evolved. The facts that there are many current researchers trying to improve 3D printed bone replacements, says a lot about the technical development in the last years. It is also clear that humanity has evolved in the technical aspects and it's mind blowing how much we can do now that was not even thought of a couple of years ago. In this paper we want to answer how fast this technology is evolving and what future progress we can expect. Another question we find fascinating is the question of ethics in context to surgical interventions in our bodies.

2. Introduction

Futuristic seen, you could say "it's a solution for everything". When something in our body doesn't function anymore, you replace it by an artificial human made object.
This is the basic idea. But from there we are still far away.

Thus back to the beginning. Already in the antique shells were used as dental implants. Similarly the ancient Chinese used carved bamboo pegs as artificial teeth (MCNULTY 2015). But until the 20th century there was no technology involved. 1958 the first pacemaker was implanted (YOUNG, 2013). Among medical implants we differentiate between active and passive implants. Active implants (electronical) are powered implants. They mostly use electric power and tiny motors. On the opposite passive implants are passively (mechanical) replacing or supporting structures in an organism.

In the past decade numerous discoveries were made. 3D-print has much improved. A new branch of science has been built. Regarding our research the most significant achievement has been made in the science of materialography. By modifying the surface or so called topography of the implants on the nanometer precisely it's possible to regulate the adaption of the body cells to the metal. But more on this later (4.0 Visit of Institute). (DE WILD, 2018)

However an exoprosthesis (or just prosthesis) could maybe be an alternative treatment in future. Now a days they are mostly used to replace a whole missing body part. Similarly in this area of medicine is also much research going on. Nevertheless a big con is that it's a machine which first has to be learned how to use

and therefore is (at the moment) a team of therapists and scientists needed. I think that no one wants to wear a machine instead of a body part when not necessary.
Unless a huge step in prosthesis technology takes place, it's not really an alternative treatment but for cases where an implant is not possible.

3. Description of the technique

Bone grafting and bone replacement surgeries are similar but still very different. In many cases bone grafting has to be done before bone replacements. However many times bone grafts can be an alternative option for bone replacements and vice versa. As bone grafts have such a close connection to bone replacements, we are going to first explain what bone grafting is and how they work, and then what bone replacements and bone supporting implants are and how they work.

3.1 Bone grafting

Bone grafting or regeneration is a surgical procedure that uses bone to fix damaged bone and also to grow bone around an implanted device. Bones are able to regenerate completely when space to grow into is provided. When bone grafts are used native bone will grow and replace the graft material completely, resulting in an area of new bone. The fundamental properties bone grafts have are osteogenesis[1], osteoinduction[2], osteoconduction[3] and structural support. Not all the bone grafts have the same properties. Depending on the patient's medical situation, the physician decides which graft is best. There are different types of bone grafts: autograft, allograft, synthetic allograft.

Autografts are made of bone from the patient's own body. If for example the graft is taken from the hipbone, the patient would undergo surgery and a piece of the hipbone would be removed. In this case the patient undergoes two surgeries. But there is less risk of infection and rejection.

Allografts use bone from a cadaver from a tissue bank, where the cadaver has been frozen and stored. But they can also be from a living donor. Allografts are used mostly in reconstructive hip, knee or long bones surgery and patients who have lost bone due to trauma or tumors. The most noticeable advantage of allograft tissue is

---

[1] Osteogenesis: when osteoblasts from the graft material contribute to the growth of new bone
[2] Osteoinduction: stimulation of osteoprogenitor cells to differentiate into osteoblasts to begin the formation of new bone.
[3] Osteoconduction: when bone graft material serves as scaffold for new bone growth.

that the patient only undergoes one operation, as no graft has to be taken from its own body.

Synthetic allografts are made of ceramic-based materials. One example is hydroxyapatite, which is the main mineral component of bone. It has osteoconduction, osteoinduction and osteogenesis but it lacks the structural strength required.

3.2 Bone replacements and bone supporting implants

As said before bone replacements are similar to bone grafts. Bone grafts fill the bone defect and resorbs completely, stimulating the formation of new bone. On the other hand bone replacements fill bone defects and do not resorb. They fill the space without encouraging new bone growth.

Bone replacements are usually made out of titanium. Titanium is a metal used for medical procedures because it is strong, lightweight, corrosion resistant, non-toxic, biocompatible, long-lasting, flexible and elastic. The alloys titanium 6Al4V and 6Al4V ELI are the most common types of titanium used in medicine. Medical grade titanium is used to produce pins, bone plates, screws, bars, rods, wires, expandable rib cages, and finger and toe replacements. It is used in hip and knee replacement surgeries. But also for shoulder and elbow joints and as protection for the vertebrae after back surgery. (CRAIG SCHANK)

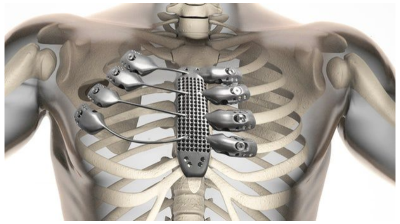


Fig. 1: 3D printed rib cage made out of titanium.

Medical titanium has a greater fracture-resistance when used in dental implants. In these implants the titanium screw acts as the root of the tooth. (AZOM, 2003) The bone forming cells attach to the titanium screw and form a bridge between the tooth implant and the body's bone. (CRAIG SCHANK) In dentistry it is very common that a bone graft has to be done before the tooth implant can be placed. (See Fig. 2)

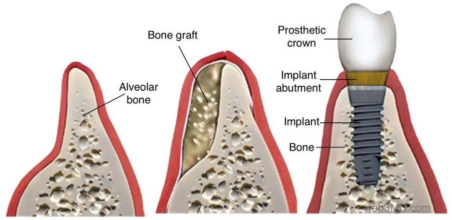


Fig. 2: The figure shows the 3 phases: pre-bone graft, after bone graft and after implant.

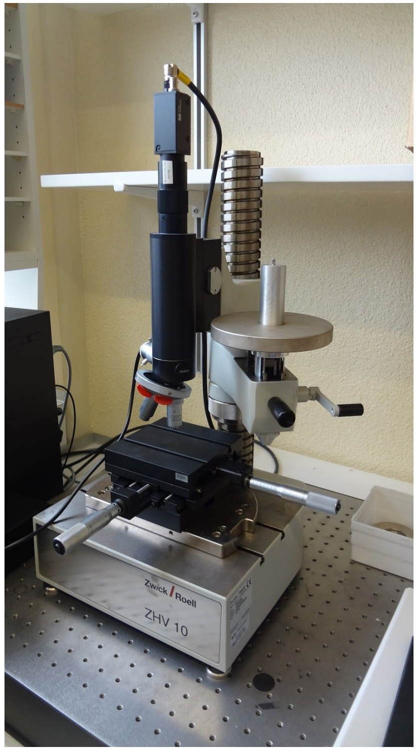
Bone replacements and bone supporting implants have improved. There have been various researches going on, to 3D print the implants and make them more compatible with the body. This makes the implant easily and rapidly customizable. Bone supporting implants are not replacing any bone but helping it have more support and have more strength.

But there are also other types of bone replacements being researched and 3D printed: artificial bones. The goal here is to print replacements that mimic real bone. Different materials have been tested, but the right mix has not yet be found. This is particularly difficult as the materials the replacements are made out of have to be porous and strong enough. (MARY BATES, 2017) (SCIENCE DAILY, 2017)

4. Visit of the Institute for Medical and Analysis Technology, FHNW

The labs, where they research and produce medical implants are, belong to a specialised part of the FHNW. The course of study is called Life Science. This apartes are all very expensive and rare as well. Especially of the titanium 3d-printers are only a few in whole europe. In any case, we were not allowed to take many pictures because there are many parts of confidential and sensitive research projects clamped in the machines and around us.

The main lab is composed out of many different hand operated machines. They are used to process the surface of implants and their models, to cut, drill and as well to measure the temper of the materials. This is done by diamond cutters and a diamond tip which is slipped over the surface and so measures the roughness on nanometers precisely.



Another measuring apparatus is the one in figure 3. It’s a diamond tip which is pressed into the material to then visually observe repression with the light microscope which is on the second arm of it.

In a second room all 3D printers and 3D scanners were located. From known hobby printers to Laser Engraving Machines everything is present. In a next room they had many different machines called tribometer (fig. 4) to measure the durability and lifespan of any kind of implant. To measure this, they make a model of the bones and the implants on it. The machine then is moving these bones over a million times. Sensors on the model which are captured by cameras then provide data to study wear on the medical implant.

Further there is an operation room located in the lab facilities as well as ovens and sterile packaging machines to deliver the products to hospitals.

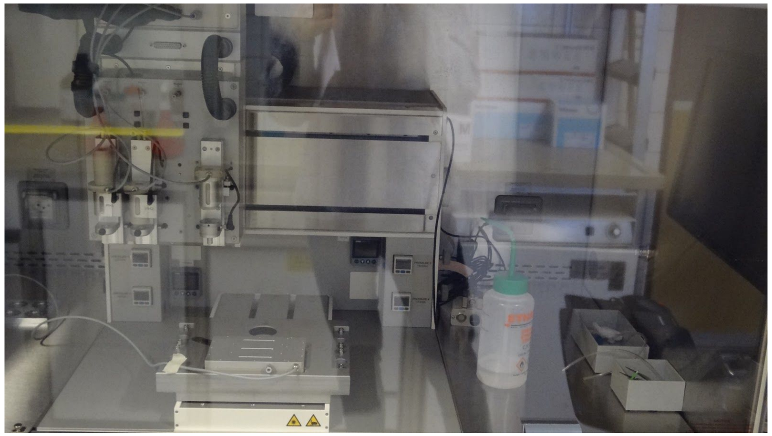
Fig.3: Light microscope with camera on the left arm and Diamond Tip with crank on the right arm. (AELEN, 2018)

In the last visited Laboratory room they had a special 3D printer (fig. 5) which is able to print small organic structures with body cells. These cells then are used to look how the body would react on the implant concerning cytotoxicity.

Unhappily it was not possible to make an interview with any scientist from this research institution. Nevertheless we thank Prof. Dr. Michael de Wild for showing the lab facilities of the FHNW regarding to our topic.

Fig. 4: Picture of an opened and inaktive tribometer. (AELEN, 2018)

Fig. 5: Inside of a cell 3D printer (AELEN 2018)



5. Discussion

5.1 The future of bone replacements

There are various researches about 3D printed bone replacements going on all over the world. But the goal is very similar in all the researches. It is to make bone replacements more efficient and customizable to the patient's needs. This is sometimes not that easy especially if there is time pressure. Customizing a bone replacement could take too much time and by then it will be to late. Also 3D printed bone replacements are more precise.

As said before, current researches are also trying to find the perfect materials for these implants. "When designing artificial bone scaffolds it's a fine balance between something that is porous enough to mix with natural bone and connective tissue, but at the same time strong enough for patients to lead a normal life.", according to Hossein Montazerian, research assistant with UBC Okanagan's School of Engineering. This is important because the materials could change the patient's life after the bone replacement. (SCIENCE DAILY, 2017)

5.2 Ethical aspects

Many physicians prefer to use newer techniques as they are innovative and sometimes more efficient. That is why new technologies are beneficial and are always encouraged. Also patients want newer drugs and medical technologies because they want the best they can get. But new technologies always bring some ethical issues.

Any new medical technology or drug has gone through phases of testing and also limited clinical trials before being handed to physicians for use. The problem with this is that these new technologies and drugs are not tested in large groups of people because the exact side effects are usually unknown. What was tested in animals and worked for animals could have different effects in humans. (JAMES D. CAPOZZI AND ROSAMOND RODHES, 2015)

According to Nienke Jones, "[...] any medical device which is allowed on the market, i.e. has a "CE" mark, qualifies as a "low risk" study. The ethics committee reviews the low risk studies with fewer members as a "high risk" study. Testing of medical implants has just been made stricter in the EU [...]; Switzerland will adapt its legislation to match the EU Regulations, to keep the Mutual Recognition Agreement

in place. [...]". This means that newly, stricter guidelines are also followed by them even though Switzerland is not in the EU.

For example the FHNW had to compose a 50-60 page dossier about 3D-printing of titan implants. Only after three years of ethical study of the EKNZ they were allowed to test them on animals and after again ten years of study it was finally possible to test implants out of titan on humans. (MICHAEL DE WILD, 2018)

But even then when the new technologies are used in hospitals it is partly unknown if they are going to work in such big groups. In the article Ethical Challenges in Orthopedic Surgery James D. Capozzi and Rosamond Rhodes say, " When new technology is released for general use, that release is often based upon the experience of a few investigating specialists. Often, those initial investigators have dedicated enormous amounts of time and efforts to developing expertise with the new technology. Once the technology is released for general use, however, the clinical outcomes may be vastly different from those reported by the investigative group." This is mainly because surgeons have sometimes different techniques and ways of doing the same operation. When using a completely new technology for them they have to figure out what works best while doing it correctly. And also most of the time they have to be self taught as the physician who developed the technology may not be able to show it in detail. (JAMES D. CAPOZZI AND ROSAMOND RODHES, 2015)

6. Summary

Passive medical implants have been used for decades to solve problems in our bodies weather it is because of traumas or diseases. Bone replacement surgeries are often done to replace a bone completely or to support it. Bone replacements are used mostly in dentistry in tooth replacements, in hip replacements and rib replacements.

In the past decade technology has advanced tremendously causing implants to have significant improvements especially with the 3D-printers. Numerous researches are trying to print artificial bones that are porous, strong and more efficient mimicking real bone to fit the patient's body like a glove. The key to achieve the goal lies in the materials and the printer. This is a technology that is still being researched and tested. That is why it is hard for us to estimate when approximately the goal will be reached.

The exact future of implants is really unclear because at the speed we are going almost everything can be possible. But it is clear that the development of implants relies on how advanced the technology actually is.

7. References

Internet

AZOM (2003). „Titanium Alloys in Medical Applications"
URL: https://www.azom.com/article.aspx?ArticleID=1794
(Last retrieved: 25 January 2018)

CRAIG SCHANK. „Titanium: The Medical Metal of Choice"
URL: http://www.supraalloys.com/medical-titanium.php
(Last retrieved: 1 April 2018)

JAMES D. CAPOZZI AND ROSAMOND RODHES (2015). „Ethical Challenges in Orthopedic Surgery".
URL: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4596168/
(Last retrieved: 7 April 2018)

JOHN HOPKINS MEDICINE (2016). „The Search for Better Bone Replacement: 3-D Printed Bone with Just the Right Mix of Ingredients"
URL:
https://www.hopkinsmedicine.org/news/media/releases/the_search_for_better_bone_replacement_3_d_printed_bone_with_just_the_right_mix_of_ingredients_
(Last retrieved: 25 March 2018)

MARY BATES (2017). „Making Bone Replacements With A 3-D Printer".
URL:https://bioengineeringtoday.org/emerging-tech/making-bone-replacements-3-d-printer
(Last retrieved: 25 March 2018)

MCNULTY DERMOT (2015). „The History of Dental Implants"
URL: https://www.thedentalgeek.com/2015/03/the-history-of-dental-implants/
(Last retrieved: 05 April 2018)

PRASANNA KUMAR, BELLIAPPA VINITHA AND GHOUSIA FATHIMA (2013). „Bone Grafts in Dentistry".
URL: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3722694/
(Last retrieved: 15 March 2018)

SCIENCE DAILY (2017). „Looking To The Future Of Bone Replacement".
URL: https://www.sciencedaily.com/releases/2017/08/170817092724.htm
(Last retrieved: 31 March 2018)

UNIVERSITY OF THE WEST OF ENGLAND (2016). „New discovery strengthens how bones bond to titanium orthopaedic implants".
URL: https://medicalxpress.com/news/2016-01-discovery-bones-bond-titanium-orthopaedic.html
(Last retrieved: 06 April 2018)

YEUN-HO JOUNG (2013). „Development of Implantable Medical Devices: From an Engineering Perspective"
URL: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3797898/
(Last retrieved: 05 April 2018)

Interviews/Oral transmission

JONES NIENKE, (23.03.2018). „Written Interview about Ethics regarding medical implants".
Contact: https://www.eknz.ch/kontakt/
Frau Nienke Jones
Manageress
E-mail: nienke.jones@bs.ch
Tel. 061 268 13 54

DE WILD MICHAEL, (22.03.2018). „Guided tour in the Labs at "Hochschule für Life Science FHNW" and explanation (oral)".
Contact: https://www.fhnw.ch/de/personen/michael-de-wild
Prof. Dr. Michael de Wild
Lecturer
E-mail: michael.dewild@fhnw.ch
Tel. +41 61 228 56 49

Figures

Fig. 1:
URL:https://gizmodo.com/the-worlds-first-3d-printed-titanium-rib-cage-is-a-medi-1730034483
Fig. 2:
URL: http://neodentistrykyle.com/blog/bone-grafting-and-augmentation-implants/
Fig. 3, 4, 5: Marvin Aelen (2018)
Picture on Cover sheet by FHNW, 2009, page 2 URL:
https://www.swissphotonics.net/libraries.files/de_wild.pdf

8. Appendix

8.1 Written Interview with NIENKE JONES (23.03.2018), Managing director of the scientific secretariat, Ethics Committee northwest/central Switzerland EKNZ

1. What ethical aspects have to be considered in projects around medical implants?

The current Human Research Act is based on a risk adapted approach, which means that any medical device which is allowed on the market, i.e. has a "CE" mark, qualifies as a "low risk" study. The ethics committee reviews the low risk studies with fewer members as a "high risk" study. Testing of medical implants has just been made stricter in the EU (see Medical Device Regulation); Switzerland will adapt its legislation to match the EU Regulations, to keep the Mutual Recognition Agreement in place. The Medical Implants will therefore have to follow even stricter guidelines and "high risk" clinical trials will have to be done, in order to get a market approval.

2. What would be the biggest problems in using Neurotic implants in our society? What are possible solutions to reduce the gap between poor and rich?

As with any new drug/device, the side effects are often unknown. The ethics committee is supposed to balance the risks versus the potential benefits, however, with new implants (and first-in-man drugs), neither is known fully in advance. It is therefore important, that the unknown risk is reduced to the littlest risk possible (adequate pre-clinical testing), both doctor and patient are aware of these unknowns (adequate information to the doctor and patient), and adequate information is given during the trial of new side effects, should they appear.

In research projects, there are no gaps between poor and rich. Anybody who qualifies for the study can participate at no costs to themselves or their insurance. Once a device is on the market, the price is decided by other bodies. The ethics committees have no say in this.

3. What is your attitude to micro technology in the human body?

The EKNZ supports clinical research and the advancement of human science. If the technology is duly tested in the preclinical phase, it should be able to proceed to clinical testing in man. Every research project will be evaluated according the ethical principles of

Emmanuel and if the technology is completely new, an external expert will be taken on board to assess the project.

4. How do you judge artificial intelligence as a danger in connection with active implants?

The EC would have to assess the chance that the artificial intelligence device takes any wrong decisions and what the consequences of those malfunctions would be.

5. How do you think the population will react to noticeable changes in the capacity of human beings?

This really depends on the way the neural implants are being used. If it is to treat a disease like Alzheimer's, Paraplegia or Stroke, the general public will likely be positive about the changes. Any enhancement of the human capacity of an otherwise healthy person would probably cause a public debate.

6. What are the most discussed aspects regarding implant in your institution?

The EKNZ currently reviews projects with implants, however none with artificial intelligence yet. An aspect that is often discussed is the lack of knowledge about the long-term side effects of the implants.

8.2 Notes from the Lab

med. technology-->medical implants (mostly fixed by screws)

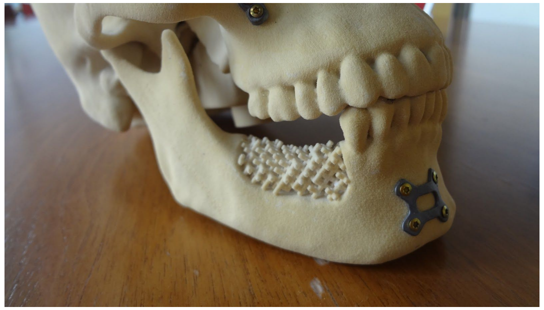
4 sheets about the research
-Antibacterial Implant Surface by Electrochemical Copper deposition
-Cytocompatibility
-Fabrication of NiTi samples by selective laser melting
-Open-porous shape memory implants for temporary or permanent bone replacement

Important in this research:
Topography to achieve the wished function of the implant (on the nanometer exactly)
The Biology and Chemistry of the surface…
-->**materials science/materialography** (Danger when not correct: **Cytotoxicity**)
-metallography
-Most implants are made out of titanium (powder)

-->In an apparatus he called “titan builder” which is a very rare and big 3D-printer that prints with titanium

Ethical inspection until you are allowed to test your technology:
-On animals; 2-3 years around 50-60 pages documentation
(risk-benefit assessment/analysis)
-On humans; again around 10 years of inspection
-Institution: ethics commission-->Swissmedic

Active and passive implants:
active (technological): 3D-printed heart, pacemaker (Herzschrittmacher), hearing implant, neuroprosthesis
passive (technical): bone replacements (permanent or temporary), screws/joint replacement, tubes, (braces, breast implants(Si))



(Picture made in the Lab)