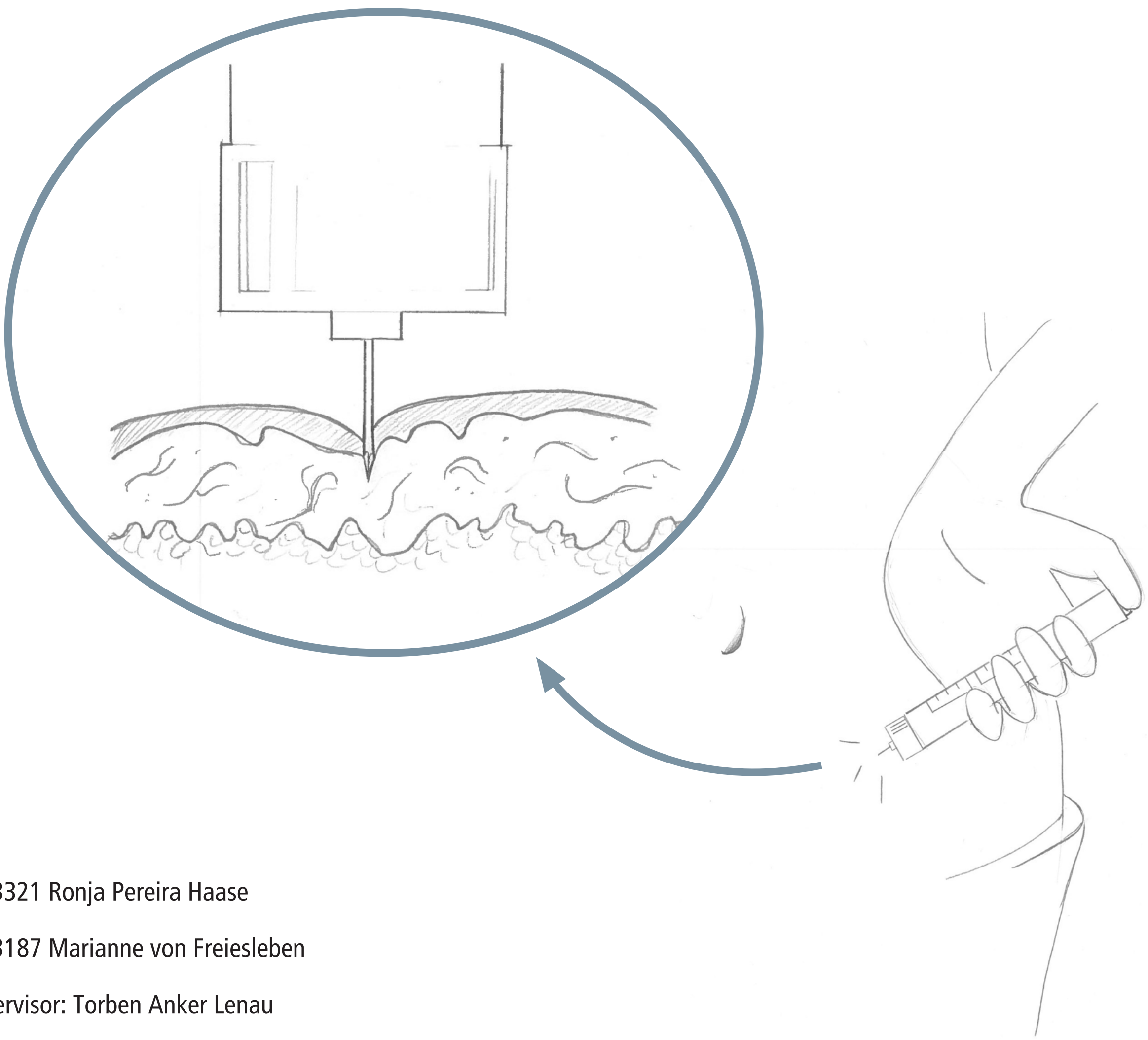
POLYMER-BASED INSULIN NEEDLES

– IMPROVED HYPODERMIC DRUG DELIVERY



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Abstract

Abstract

This project aims to develop a plausible polymer-based insulin needle concept, with focus on the needle and the mechanical challenges the replacement of stainless steel with polymer brings. The project covers an investigation of the context and function of an existing insulin needle product (NovoFine 32G, 6mm). Possible improvements in the three dimensions of sustainability are found. Relevant knowledge concerning biological and mechanical phenomena is obtained through an academic literature study. Mechanical challenges such as buckling and deformation of the needle tip are addressed. Design methods are used to conceptualize eight suggestions for a polymer-based insulin needle. One concept is selected. The geometry of the selected concept is experientially tested in relation to buckling, deformation and friction. It is also sought to experimentally determine mechanical properties of skin, in order to detail the requirements of the insulin needle. The knowledge and experiences obtained through the project are used to finalize a concept.

The developed insulin needle concept in this project fulfils the same functions as the existing insulin needle. The needle concept is 6 mm long and has a solid 3-sided pyramid shaped tip geometry with a slope of 80°. The tip area of the needle is 46 μm2. The outlets of the needle tube are placed at the sides of the slope side of the pyramid tip. The needle is made of the stiff polymer material Liquid Crystal Polymer (LCP) that has a Young's modulus of 10.6 MPa. The needle and the needle hub are microinjection molded in one piece. The concept has great potential for being superior on economical sustainability compared to the NovoFine needle. A rough estimation says that the polymer-based insulin needle concept developed in this project can decrease the unit price of the insulin needle product by 33 %. The values of the mechanical properties of skin are not clear in the literature. The puncture force of the outermost layer of human skin in vivo is experimentally tested. It is determined that the NovoFine needle punctures the skin with a force lower than 0.07 N. The polymer-based insulin needle concept column is found to have a factor of safety on 20 against buckling. This value is based on experimental tests of the existing insulin needle and theoretical calculations of the polymer-based insulin needle concept.

Table of Content

Preface

This is the bachelor thesis *Polymer Insulin Needles – improved hypodermic drug delivery* by Ronja Pereira Haase (RH) and Marianne von Freiesleben (MvF). The period of the project stretched from the 2nd of February to the 9th of June 2015. Both authors of the project are students in Design and Innovation at Denmark Technical University.

ACKNOWLEDGEMENT

During this project we have received supervision and guidance from a number of people whom we would like to acknowledge:

Our supervisor Torben Anker Lenau, Associate Professor at the DTU Department of Mechanical Engineering, for constructive feedback and for challenging our understanding and findings.

- Our co-supervisor Professor Rajan Ambat, Professor at the DTU Department of Mechanical Engineering, for letting us use the equipment of the Depatment.
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- Design and Innovation master student Thomas Dam Poulsen at DTU for knowledge sharing and discussions concerning microinjection molding.
- Klara Sofie Bengtsson for giving us a deeper understanding of the life with diabetes and providing us with products related to medical treatment of diabetes.
- The Department of Pulmonary Medicine at Herlev Hospital for letting us observe and interview nurses during their work.

READING INSTRUCTIONS

The report can be read as a separate document. The yield of the reading will increase if accompanied by a study of the appendix. The project was divided into six phases. The chapters of the report follow the division of the six phases:

Chapter A: Context & Function – *Introduction to the context and function of the existing product*
Chapter B: Sustainability Analysis – *Possibilities of sustainable improvements*
Chapter C: Academic Literature Study – *What does the literature say?*
Chapter D: Conceptualization – *Idea generation, concept generation and concept selection*

Chapter E: Concept Testing – *Test of aspects of the concept(s)*
Chapter F: Final Concept– *Calculations and presentation of the final concept*

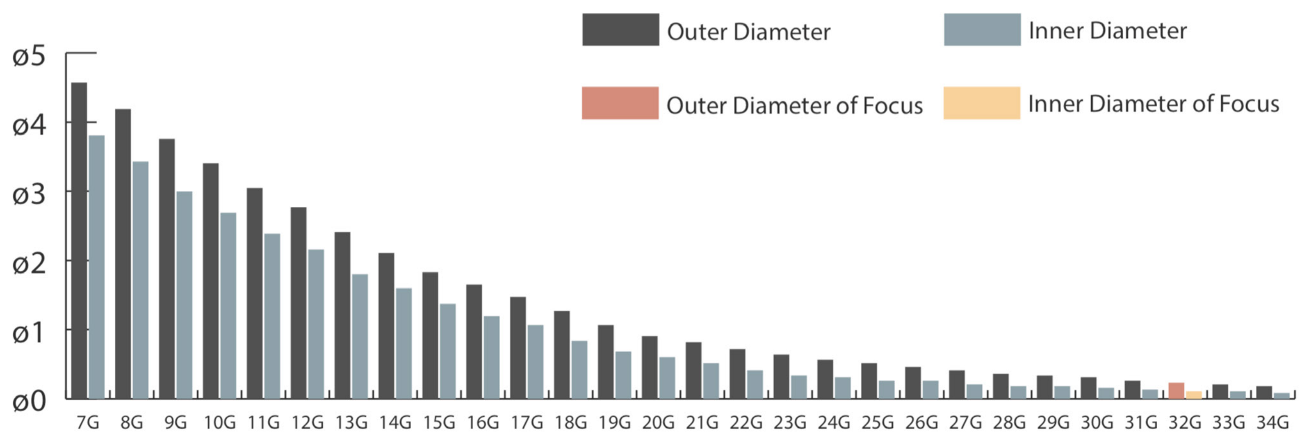
Each chapter begins with an introduction to the chapter content and ends with a conclusion on the findings of the chapter. The prefix of the appendix labels indicates to which project phase the particular appendix belongs. The following number in the appendix label represents the order in which the appendix occurs in the report.

Some of the calculations and graphs in the report were made in mathematical programs with Danish settings. These calculations follow the Danish notation standard. Whole numbers are divided from decimals with"," instead of ".". In the written part of report the American notation will be used.

Prologue

This project is based on a project proposal presented by our supervisor Torben Anker Lenau. The project proposal concerned the development of hypodermic needles in polymers. Hypodermic needles are a common term for hollow needles used to inject or subtract fluids from beneath the skin (Science Museum UK, no date). Hypodermic needles are used in many different contexts. *Gauge numbers* (G) systematize the hypodermic needle sizes. The gauge number refers to the number of dies the needle tube was drawn through using 19th century production methods to accomplish the needle's final diameter (Kucklick, 2012). The preferred length and diameter of hypodermic needles vary depending on the type of injection. It was chosen to narrow the focus of the project down to insulin needles in a Danish context. Novo Nordisk's *NovoFine insulin needle size 6mm, 32 G (ø0.23/ø0.15)* was chosen to represent the stainless steel needles in the project. As seen in Fig. 1 NovoFine is a small hypodermic needle.

Fig. 1. Needle Gauge Comparison. The bars of the graph represent the outer and inner diameter of the different gauge sizes. The focus in this project is a 32G hypodermic insulin needle.



Project Description

PROJECT MOTIVATION

Diabetes is a disease which requires the patient to take insulin injections frequently. This results in a high consumption of stainless steel insulin needles. The introduction of polymer needles provides an opportunity to address some of the problems, associated with the traditional stainless steel needles used for insulin injections. There appears to be five main issues with the traditional needle, which can be improved by the repl of the polymer needle. The five main issues concern the three dimensions of sustainability:

- Social sustainability. *Reuse of needles* & *lack of disposability in parts of the world*
- Environmental sustainability. *Use of limited resources* & *energy*
- Economical sustainability. *Use of economic resources*

The assumptions that the polymer needle will improve these issues were not verified before the project. It will to some extent be investigated during this project.

PROJECT OBJECTIVE

Diabetes is a disease, which requires the patient to take insulin injections frequently. This results in a high consumption of stainless steel insulin needles. The aim of this project is to investigate the possibility of replacing the stainless steel insulin needle with a polymer based solution. The investigation should include a study of the existing insulin needle and its context. It should be considered if the development of the polymer-based solution can be justified from a sustainable perspective. The knowledge required to conceptualize a polymer-based insulin needle should be obtained through a study of relevant literature. A conceptualization process should explore the solution space through relevant design methods. To get closer to a plausible solutionn, qualified ideas should be tested experimentally. The project should result in a suggestion for a plausible polymer-based insulin needle concept.

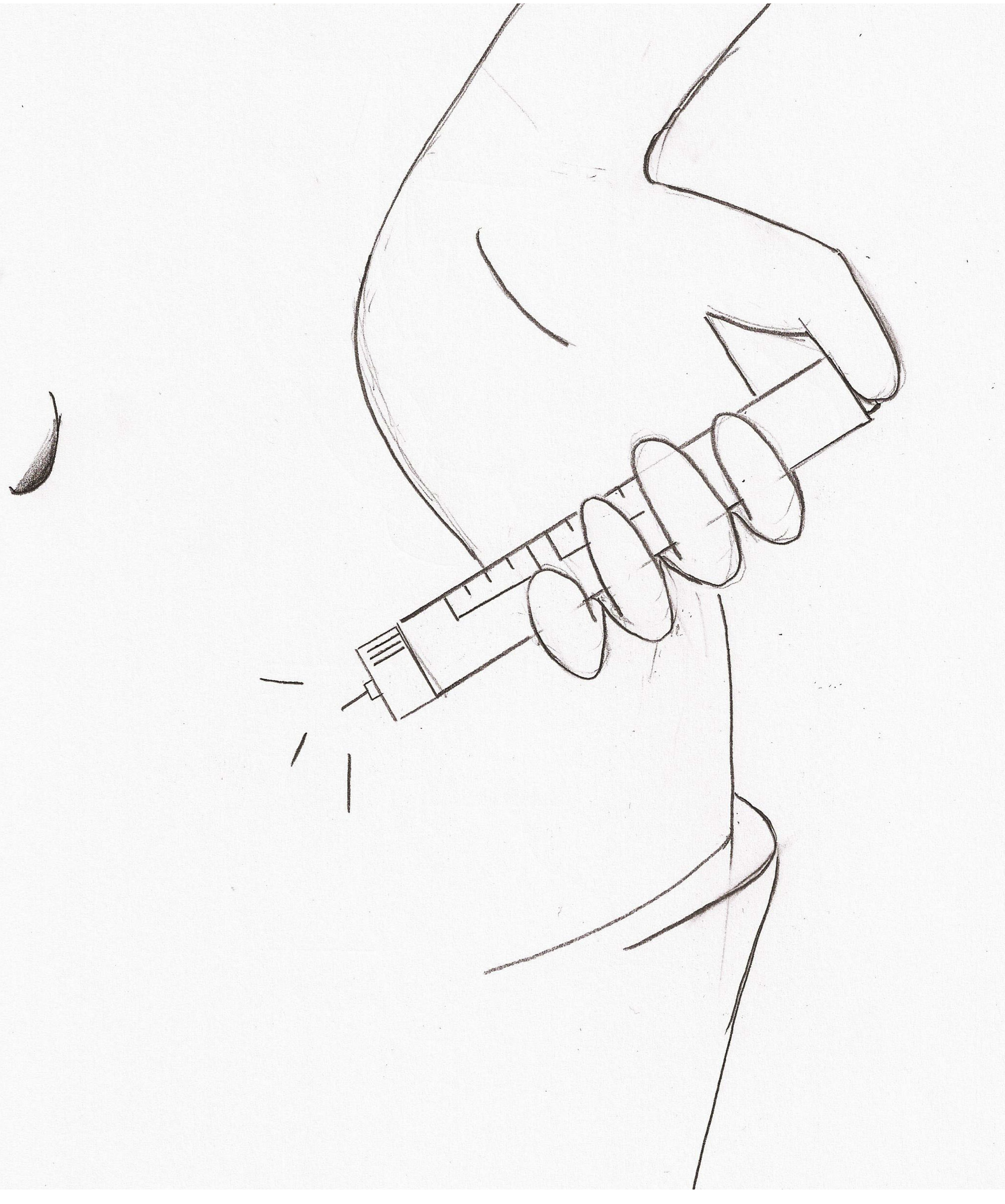
LEARNING OBJECTIVES

After the project we will be able to:

- Stage and plan a product design project
- Select and use relevant design methods
- Frame the context in which a product is operating
- Analyze the function, context of use and sustainability of an existing product
- Gain deeper knowledge of materials and mechanics for the purpose of the design
- Find and understand novel and relevant scientific papers
- Implement a conceptualization process (creative and systematic idea generation, concept generation and concept selection)
- Use a biomimetic approach to gain inspiration in the design process
- Establish a product specification and use it for concept evaluation
- Experimentally investigate mechanical requirements and principles of chosen concept(s)
- Compare the existing product with the final concept
- Document and communicate findings in scientific English

Chapter A

CONTEXT & FUNCTION



Introduction

This chapter begins with a short introduction to diabetes as a biological phenomenon. This projects aims to replace the stainless steel insulin needle with a polymer-based insulin needle.

This project aims to develop a polymer insulin needle with the same functions and context of use as the existing product. A presentation of the user context of the existing insulin needle product *NovoFine* is given. At the end of the chapter the main functions of the stainless steel needle are determined. Other ways to fulfil the functions are discussed.

METHOD

- *Diabetes as a Biological Phenomenon. Information on diabetes as a biological phenomenon was obtained through study of literature.*
- *Context of Use.* The human actors and flow related to the patient with diabetes was mapped. Field study of a patient with type 1 diabetes (user 1) was made. User 1 was observed for one hour during dinnertime. Her use *of the disposable insulin pen 'FlexPen' and insulin needle 'NovoFine 6 mm 32G' was observed*. The manuals of the insulin pen and insulin needle were studied (appendix A1, *User Manual of Novo Nordisk's FlexPen*; appendix A2, *User Manual of Novo Nordisk's NovoFine Needle*).
- *The Function of the Insulin Needle. The primary functions of the insulin needle were determined after* Tjalve (1979, p. 9). *It was examined if other products could fulfil the main function of the insulin needle by studying research papers.*

Diabetes as a Biological Phenomenon

RESULTS

Diabetes is a common name of diseases where the patient has a high glucose level in the bloodstream, caused by a malfunction in the insulin system. The role of insulin is to regulate the blood glucose level (appendix A3, *The Physiological Effects of Insulin*). 1 out of 18 Danes has diabetes (Diabetesforeningen, 2014). The prevalence of diabetes is increasing. During the last ten years the number of patients with diabetes has doubled in Denmark (Diabetesforeningen, 2014).

Diabetes is traditionally differentiated in the two categories *type 1* and *2 diabetes*:

- Patients with type 1 do not produce insulin at all (appendix A3, *The Physiological Effects of Insulin*). Type 1 diabetes constitute of around 10% of the diabetes patient in Denmark (Diabetesforeningen, 2014). Type 1 diabetes is typically developed in the childhood or adolescence. The exact cause of type 1 diabetes has not yet been found. Type 1 is a more critical from of diabetes than type 2 diabetes. Patients with type 1 diabetes are totally dependent on insulin medication. Patients with untreated type 1 diabetes will die.

Patients with treated type 1 diabetes take insulin injections several times a day (appendix A4, *Life with Type Diabetes 1 and FlexPen*).

– Patients with type 2 diabetes either have an inadequate production of insulin or low insulin sensitivity. These patients constitute around 90% of the diabetics. The majority of the patients get the disease in their adulthood (Diabetesforeningen, 2014). Less than half of the patients with type 2 diabetes need to get daily insulin injections.

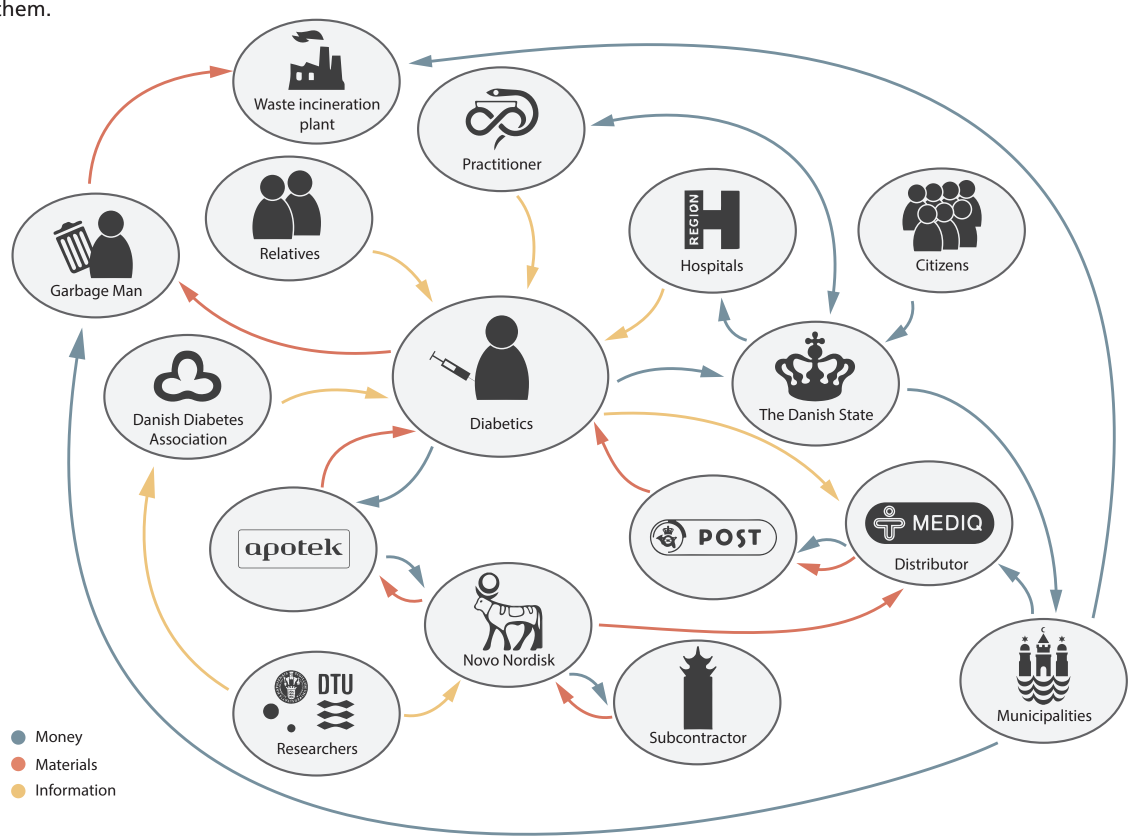
Context of Use

RESULTS

MAPPING OF KEY HUMAN ACTORS

Fig. A1 gives an overview on the key human actors and flows related to the use of the insulin needle. The *patient with diabetes* is the main user of the insulin needle. The *practitioner* advises the diabetic on what kind of medication to take and the standard dose (appendix A4, *Life with Type Diabetes 1 and FlexPen*). *Novo Nordisk* is the manufacturer of insulin and NovoFine insulin needles (Reuters, 2014). The diabetic orders her/his insulin needles through *Mediq Danmark A/S*. The *municipality* pays for insulin needles for diabetics. The user throws the insulin needle out together with the domestic waste after use. The *garbage man* transports the waste to the *waste incineration plant*. Here the insulin needles get melted at a high temperature together with other metals from the domestic waste. The end product is a low value product of mixed elements (Amager Recourse Center, 2014).

Fig. A1. Map of the human actors related to the insulin needle and the flow between them.



USE OF INSULIN PEN AND NEEDLE

User 1 has type 1 diabetes. She is a woman in her early twenties. Appendix A5, *Flow Model of User 1 - Type 1 Diabetes* illustrates the flow user 1 have in connection with her insulin medication. <indsæt lille billed fra *Flow Model of User 1 - Type 1 Diabetes* > User 1 takes two different kinds of insulin: She takes a long acting insulin dose twice a day. A short acting insulin dose is in average taken five times a day. The dose of the short acting insulin varies from day to day. It highly depends on her diet and activities on the specific day. In average she injects an insulin needle into her thigh seven times a day. A full description of the sequence of taking the insulin medication can be found in appendix A4, *Interview: Life with Type Diabetes 1 and FlexPen*. A detailed description of the use of the insulin needle is found in appendix A6, *Use of NovoFine Insulin Needle 0.23/0.25x6mm.*

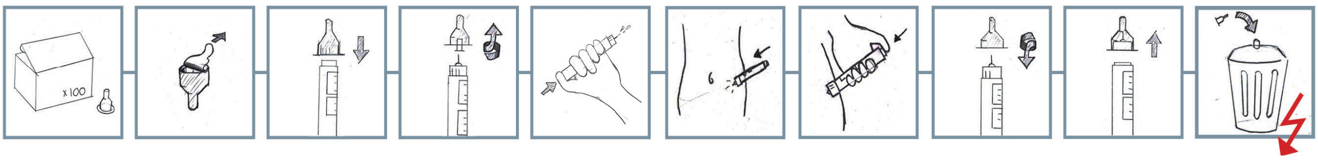


Fig. A2. Sequence of taking the insulin medication. Breakdown: The user does not always discard her needle after it has been used the first time. Some times she saves it for reuse.

According to the user manual the insulin needles should only be used once. The insulin user often reuses the insulin needle one or two times. The reuse of the insulin needle will be discussed in the next chapter in the section on the social sustainability.

Function of the Insulin Needle

RESULTS

FUNCTIONS OF THE NOVOFINE INSULIN NEEDLE

The main function of the stainless steel insulin needle and the insulin pen is:

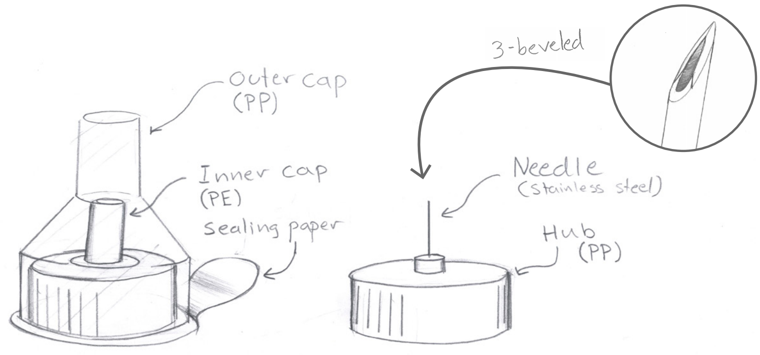
– *To provide the diabetics with a substitute for the insulin they can not produce themself*

The two primary functions of the insulin needle itself are listed in the table:

Function	Mean
Penetration of the diabetic's skin	Sharp 3-beveled tip and a needle column in a stiff material (stainless steel)
Transportation of insulin from an external device into the body of the diabetic	Hollow needle allows a flow of insulin

An insulin needle product does not only consist of a needle. The NovoFine insulin needle consists of five components, as illustrated in Fig. A3.

Fig. A3. Illustration of five components of the NovoFine insulin needle.



The functions of the four other components of the insulin needle product are:

Mean	Function
The outer cap	Keeps the insulin needle sterile until use Prevention against needle-stick injuries
The inner cap	Protection of the needle and user
The needle hub	Gathers the components Attachment to the insulin pen
The sealing paper	Keeps the insulin needle sterile until use

OTHER DIABETES CARE PRODUCTS

The most popular insulin device today is the insulin pen. The insulin needle fulfils its main function in combination with an insulin pen. Other products such as the insulin pump also exist (For & Pharmacist, 2013). Since the first insulin injection was given in 1922, the medication form of diabetics has undergone incremental innovation. All the incremental innovations are based on some kind of insulin injection devices. Research is done on developing a non-needle based diabetes treatment. A description of the exciting alternative and future potential diabetes medication products are presented in appendix A7, *Competitive Products on the Diabetes Care Market*.

DISCUSSION

The functions of a polymer-based insulin needle must fulfil the same two primary functions as the stainless steel needle. Other kinds of diabetes treatments can be developed fulfiling the main function. A new radical diabetes treatment could threaten the relevance of a polymer-based insulin needle. Radical innovation of diabetes treatment seems to have longer development and implementing prospect than the development of a polymer-based insulin needle. But how does the polymer-based insulin needle provide an incremental improvement of the stainless steel insulin needle? An answer to this question is saought in the following.

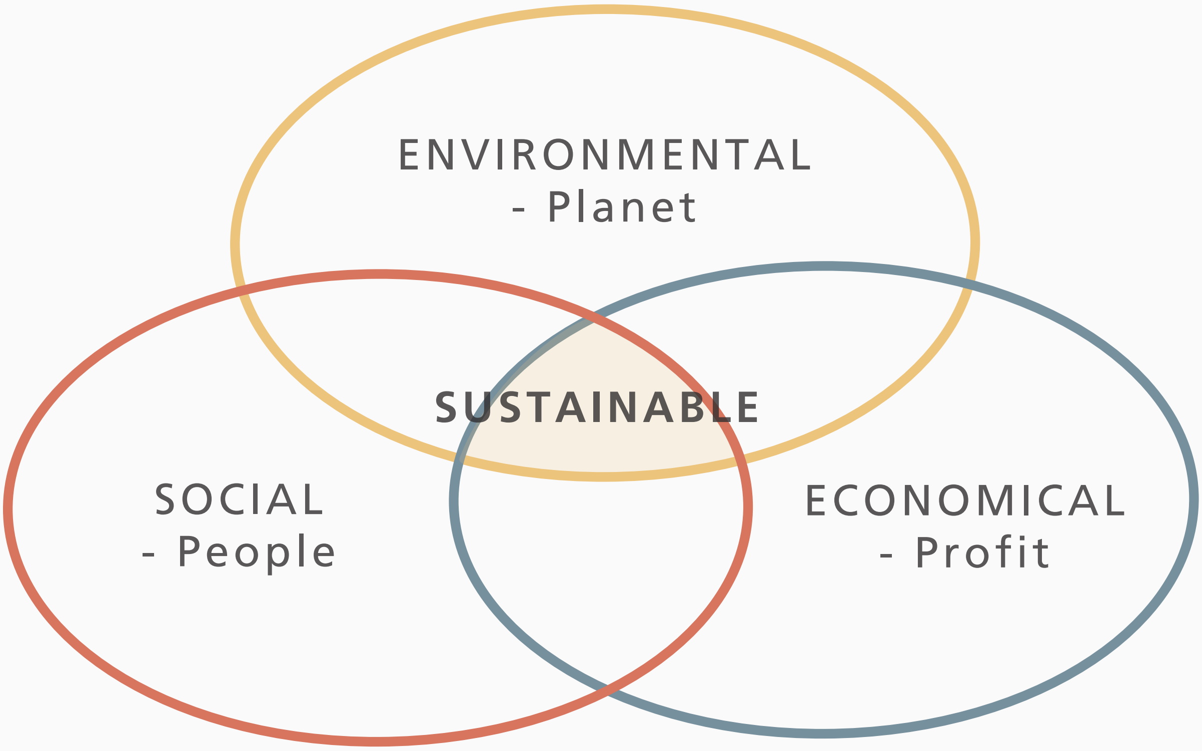
Conclusion

Diabetes is a disease where the patient has problems with the regulation of his/hers blood glucose level. Type 1 diabetics do not produce insulin at all. To survive the patients with type 1 diabetes need to get a supply of external insulin. The most common way to achieve this is by taking multiple insulin injections daily using an insulin pen and needle. The insulin needle is a device that transfers the insulin from the insulin pen into the skin of the diabetic. The two primary functions of the stainless steel insulin needle were found to be:

Function	Mean
Penetration of the diabetic's skin	Sharp 3-beveled tip and a needle column in a stiff material (stainless steel)
Transportation of insulin from an external device into the body of the diabetic	Hollow needle allows a flow of insulin

The polymer-based insulin needle must perform the same functions as the stainless steel insulin needle. An insulin needle product does not only consist of a needle. It also consists of other components. Their functions are to provide protection and keep the needle sterile. The needle hub provides an interface between the insulin needle and the pen.

Chapter B
SUSTAINABILITY CHECK



Introduction

It may be wise to investigate possible benefits of a potential product before investing in the development of the product. In the last chapter the following question was asked: “Does the polymer-based insulin needle provide an incremental improvement of the stainless steel insulin needle?” An investigation of possible benefits of the development of a polymer-based insulin needle is presented in this chapter. The investigation is based on the three dimensions of sustainability: *Social, environmental* and *economical.* In order for a solution to be sustainable it needs to create value in all three dimensions. The investigation of possible benefits of the social dimension includes a discussion on whether the polymer-based insulin needle has potential to create more value for the user. In the environmental dimension the material use of insulin needles is investigated to see what the potentials of a material replacement are. It is investigated if a annually use of polymer-based insulin needles can potentially result in lower energy consumption than a annually use of a steel insulin needle in the light of the entire product life cycle. In the economical dimension it is investigated if the introduction of the polymer-based insulin needles has the potential for reducing the overall expenses used on the consumption of the existing stainless steel insulin needles.

METHOD

The calculation in this chapter is based on Novo Nordisk’s *FlexPen* and the matching stainless insulin needle *NovoFine* size 32G (ø0.25/ø0.23), 6mm. These were chosen as representatives of the existing insulin products because FlexPen is the most sold prefilled insulin pen worldwide (NovoNordisk, 2009). Estimates of insulin dosage, number of injections per day and reuse are based on data of user 1 (female, type 1 diabetes, weight: 60 kg., reuses needles once).

– *Social sustainability.* To investigate the possiblity of polymer-bades insulin needles creating more value for the human actors the model of *Value Framework concept* was used (den Ouden, 2012, chapter 3). Literature and articles were studied to obtain more information *about reuse and waste disposal in foreign countries.*
– *Environmental sustainability.* It was calculated how much stainless steel is used annually on insulin needles. The calculation was based on the assumption that the insulin-using diabetics need seven injections daily and an estimated number of insulin-using diabetics worldwide. The estimatied number of regular insulin-using diabetics worldwide was based on a found number of diagnosed diabetics worldwide and the ratio of type 1 and 2 diabetics in Denmark (Diabetesforeningen, 2014). Furthermore it was estimated that 1/5 of the type 2 diabetics can be considered as type 1 diabetics. (For further details of the estimate of insulin-using diabetic patients worldwide, see appendix B1 *Estimate of Material Use for Insulin Needles.*) The volume of stainless steel used per insulin needle was based on the measurements of the NovoFine insulin needle and an assumption of 2 % material waste during

production (appendix B1, *Estimate of Material Use for Insulin Needles*). The five phases of the life cycle (*raw materials, production, distribution, use,* and *disposal) for* NovoFine 32G, 6 mm were investigated. In order to compare the energy consumption during the life cycles of polymer-based and stainless steel insulin needles a functional unit was defined. The functional unit includes the three dimensions: *quality, quantity* and *time in use* (Borkenfelt et al., 2000, p. 13-14). Two functional units for two different analyses were defined: One functional unit pertained to the needle itself, the other one to the whole needle product. Polycarbonate (PC) was chosen as the polymer material in the analyses because of its hard– and stiffness and because it is a commercial material. Cambridge Engineering Selector's Eco Audit tool (CES, 2015) was used to calculate the annually energy consumption for one diabetic's use of insulin needles. The estimated material volume of the polymer components and the paper seal can be found in appendix B2, *Estimate of Polymer Volume of Needle Components*. The volume of the needle is found in appendix B1 *Estimate of Material Use for Insulin Needles*. A screenshot of the CES Eco Audit Tool and the settings for the analysis can be found in appendix B3, *CES Eco Audit Tool.*

- *Economical sustainability.* The data on the stainless steel used in NovoFine needles where found in CES. The estimation on how high a percentage the stainless steel needle itself represents of the total annually insulin medication were made on basis of the data from user 1. The use of the glucometer, medical consultations etc. were not included in the calculations. The unit prices of a NovoPen and NovoFine needle were based on the market prices at pharmacies in Denmark. An estimate of the price of the other components of the insulin needle product was based on prices found of corresponding polymer parts online (Appendix B4, *Price Estimate of Polymer Components of NovoFine*). The price of the stainless steel component of the insulin needle was estimated by subtracting the estimation of the polymer parts from the unite price of the NovoFine insulin needle. A sensitivity analysis was made by increasing and decreasing the parameters of the calculation.

Social Sustainability

RESULTS

MODEL OF VALUE FRAMEWORK

A description of the Model of Value Framework applied on the polymer-based insulin needle can be found in appendix 5, *Value Creation.* An important conclusion from the value analysis was that the value for the user must not be decreased. The new needle should preferably increase the user's quality of life: The needle should not be harder to insert in the skin or create more pain etc.

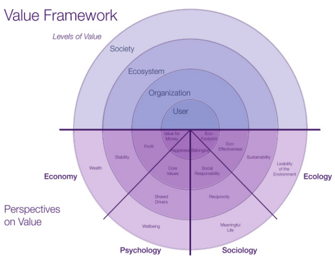


Fig. B1. Model of value framework (den Ouden, 2012, chapter 3).

SOCIAL SUSTAINABILITY ASPECTS OUTSIDE DENMARK

In many countries a sustainable system for garbage disposal is not established. To melt steel requires very high temperatures (above 1500 °C) (CES, 2014). Without a developed system for garbage disposal it is difficult to dispose of the insulin needles in an appropriate manner. Instead the insulin needles are dropped near the place of use or at landfills. This form of garbage disposal creates a risk of needlestick injuries (Kim & Colton, 2005). It is important to take the financial capacity of the diabetic individuals into account in an evaluation of an insulin needle's social sustainability in a global perspective. In many countries the diabetics need to pay for the insulin needles themselves. The expenses to purchase of insulin needle can have a huge impact on the individual diabetic and his/her close relatives. In developing countries the expenses to insulin for one diabetic can reach half of a family's income (Independent Diabetes Trust, no date).

DISCUSSION

REUSE

In the section *Context of Use* in the last chapter it was found that the diabetics reuse the insulin needles. The needle is sterile when the user acquires it. After the plastic caps and the bottom seal have been removed, the needle is no longer sterile (appendix A6, *Use of NovoFine Insulin Needle 0.23/0.25x6mm*). According to Torrance (2008) the reuse of insulin needles leads to deformations of the needle and can result in bending and breaking of needle tips. Some studies question that reuse of insulin needles is problematic (US National Library of Medicine National, Institutes of Health, 1992). The majority of the reviewed studies problematize the reuse of insulin needles. The reuse is linked with the development of lumps in the adipose tissue (Misnikova, Dreval, Gubkina & Rusanova, 2011). Though the development of lumps in the adipose tissue can lead to complications with the insulin medication (Gyldendals den store Danske, on date). A polymer-based insulin needle can potentially be more difficult to reuse than a stainless steel insulin needle due to the different properties of the material. Diabetics in Denmark have no obvious economical incitement to reuse the insulin needle. User 1 reuses the insulin needle, beacuse she is too "lazy" to replace the insulin needle. If the polymer-based insulin needle does not allow this "laziness" the diabetics might consider the polymer-based insulin needle as less social sustainable.

Environment Sustainability

RESULTS

STAINLESS STEEL USE

Fig. B2. A standard Copenhagen garbage container is of 660 liters

It is estimated that there are 59.7 million type 1 diabetics and 537 million type 2 diabetics worldwide (appendix B1, *Estimate of Material Use for Insulin Needles*). If reuse of insulin needles is not considered, a total amount of 170 m^3 stainless steel is used globally in the annually production of insulin needles. This corresponds to the volume of 256 standard Copenhagen garbage containers.

THE LIFE CYCLE & FUNCTIONAL UNIT

Two different functional units were defined as follows:

– *A type 1 diabetic's annually consumption of insulin needles (the insulin needle itself only)*
– *A type 1 diabetic's annually consumption of insulin needle products (all components of product included)*

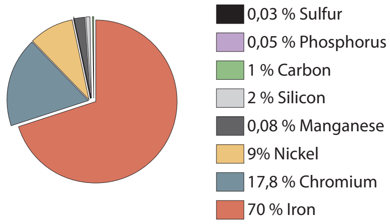


Fig. B3. Chart of the weight ratio of the material components of stainless steel AISI 304/JISG 4305 (source CES, 2015).

NovoFine insulin needles are made of *stainless steel AISI 304/JISG 4305* (McElligott, 2010). As seen in Fig. B3 the main material of stainless steel is iron. Stainless steel 304 also consists of big amounts of chromium and nickel. These are all limited resources.

The analysis of the overall product life of the stainless steel needle is visualized in Fig. B4. A detailed description of the input and output of the five life cycle phases can be found in appendix B7, *Raw Materials*; appendix B7, *Production*; appendix B8 *Distribution and Use*; appendix B9 *Disposal.*

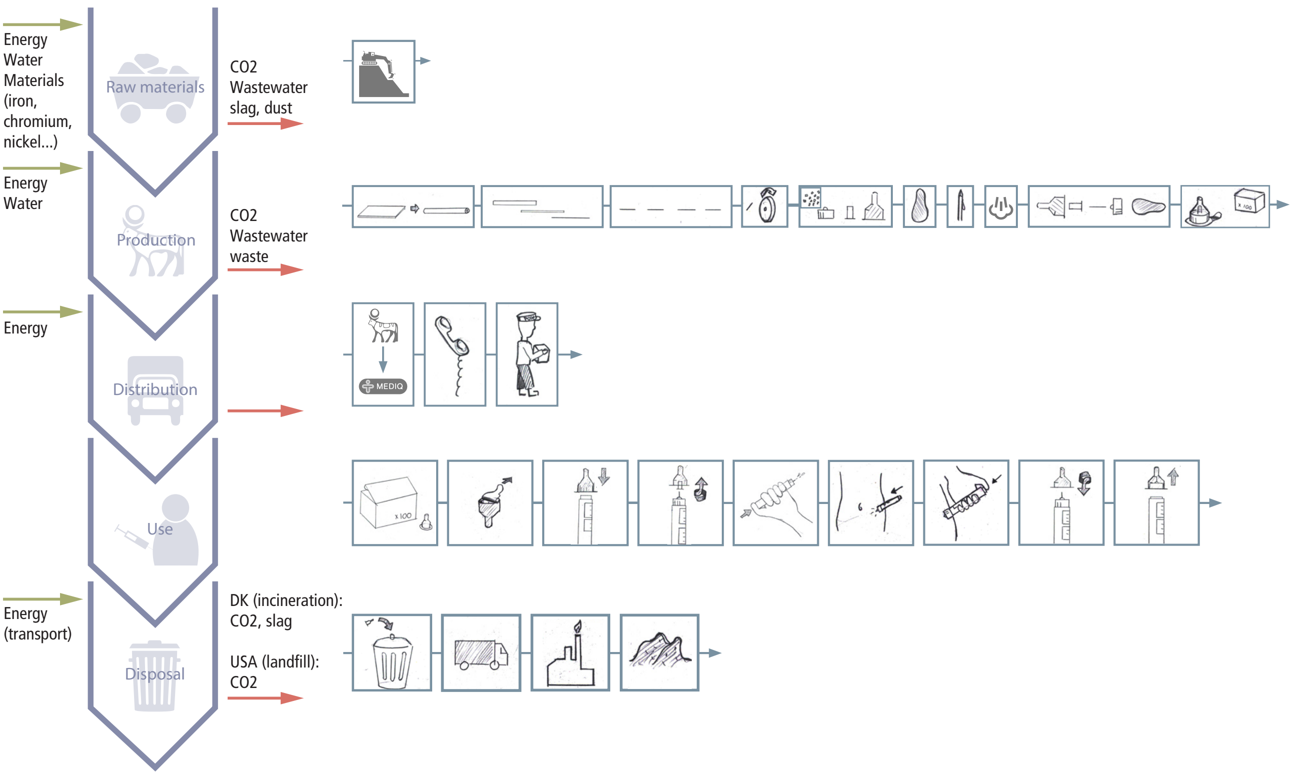


Fig. B4. Life cycle of the stainless steel insulin needle with phases and activities

The phases and energy consuming activities in the life cycle of the stainless steel insulin needle are listed in the table below.

Phase	Energy Consuming Activity
Raw materials	Extraction
Production	Tube drawing, cutting, grinding, adding lubrication, assembled with the other components
Distribution	Transportation
Use	
Disposal	Transportation, waste incineration

ENERGY CONSUMPTION — THE NEEDLE ITSELF

The annually energy consumption of the PC and stainless steel insulin needles were estimated.

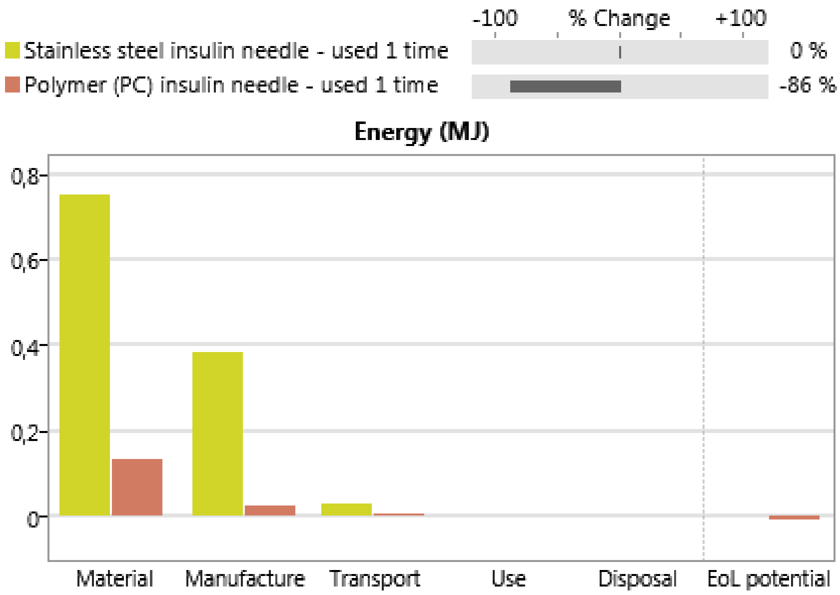


Fig. B5. Energy consumption of PC and stainless steel needles during their life cycles.

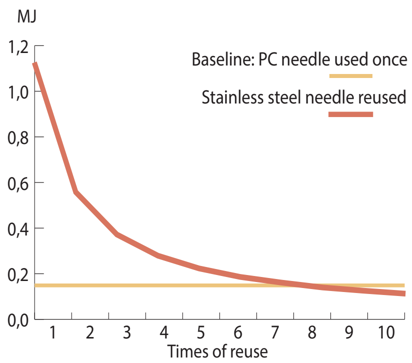


Fig. B6. The brown line shows the reduced energy consumption of the stainless steel needle due to the number of times it is reused. The yellow line is a baseline representing the energy consumption of an non-reused PC needle with the same material volume as the stainless steel needle.

As seen in Fig. B5 the life cycle of a needle in PC has a 86 % lower energy consumption than the life cycle of a stainless steel needle. The main energy consumption of the life cycle occurs in the *material phase*. The *manufacture phase* also constitute a big part of the energy consumption. The stainless steel insulin needle can be reused 8 times before a PC needle of the same material volume will cause higher net energy consumption, if it is assumed that the PC needle is not reused, whereas the stainless steel needle is (see Fig. B6).

ENERGY CONSUMPTION – ALL THE NEEDLE COMPONENTS

As mentioned in chapter A, an insulin needle does not only consist of a needle.

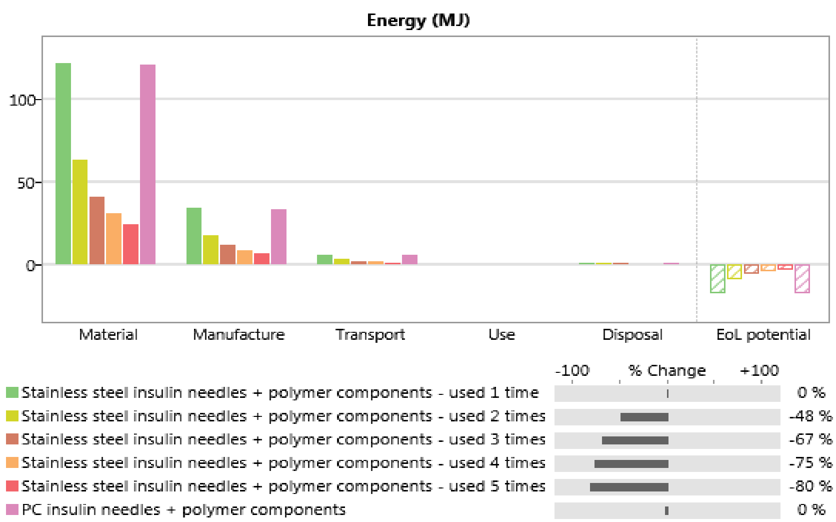


Fig. B7. Energy consumption of PC and stainless steel needles during their life cycles. Polymer components included.

Fig. B7 shows the energy consumption of a stainless steel and PC insulin needle product according to the functional unit. All the components of the insulin needle product are included. The product with a stainless steel needle is calculated as reused up to 5 times. This is compared with an insulin needle with a PC needle of the same material volume. Now when all the components of the insulin needle are included in the estimate, the reduction of the energy consumption through the product life cycle is minimal (less than 1 %). If it is calculated that the stainless steel insulin needle product is reused once and the PC insulin needle product is not, the stainless steel needle has approximately half the energy consumption of the PC insulin needle.

DISCUSSION

There is a limited amount of the elements of stainless steel in the world. After the diabetic has used the insulin needle the stainless steel of the needle is down cycled. It is mixed with other kinds of metal. The garbage disposal system of insulin needles in Denmark was explained in Chapter A. If the 170 m^3 stainless steel could be replaced by a more sustainable material, it will be environmentally beneficial. The amount of stainless steel used annually worldwide on insulin needles is calculated with the assumption that none of the diabetics reuse their needles. If it is assumed that all diabetics reuse insulin needles once, the annually consumption of stainless steel is halved to 85 m^3. The estimated amount of stainless steel used annually on insulin needles seems insignificantly small in comparison to many other product areas where much bigger amount of the stainless steel is used. Though in this case the stainless steel is not recycled.

The assumptions of the estimation are open to discussion. All the diagnosed diabetics worldwide might not be medicated with insulin. A large percentage of the world's diabetics live in third world countries, where money and distribution of medicine might be a problem. On the other hand it is reasonable to assume that the diagnosed diabetics have some sort of access to medical care, since they have been diagnosed. The exact global distribution of type 1 and 2 diabetics is also unknown. Furthermore it is not taken into account that a part of the insulin-using diabetics use insulin devices that do not include insulin needles.

There are no energy reductions to gain from changing to a polymer solution when all the components of the insulin needle product are included in the analysis assuming that the polymer needle will not be reused to the same extent. The volume of the stainless steel is minimal in comparison to the rest of the components of the insulin needle product. If an energy reduction is the goal of development of a new insulin needle, a reduction of volume of the insulin needles' polymer components should be considered rater than a polymer needle.

The analyses were based on many assumptions. The use of CES Eco Audit Tool provides a quick overview. The method also provides some uncertainties:

– The materials and production methods selected in CES give "standard" values. It is hard to say if the actual materials and production methods will in reality have a higher or lower energy consumption than this analysis shows.

- It was not yet known which material(s) and production method(s) would be used for the new insulin needle. PC and injection molding is selected to represent the material and production method of the polymer-based insulin needle. The final selected material(s) and production method(s) might have higher or lower energy consumption.
- Some of the material is wasted during the manufacturing of the stainless steel needles. It was assumed that 2 % of the stainless steel is wasted during the process. No waste of PC during the manufacturing process was assumed.

Overall it is a very rough estimate, but it is used as a guideline for further work.

Economical Sustainability

RESULTS

PRICE OF STAINLESS STEEL NEEDLE

A NovoFine insulin needle product costs 2.30 kr. per piece. The plastic part of the needle costs 0.45 kr. according to the estimate in appendix B4, *Price Estimate of Polymer Components of NovoFine*. If it is assumed that the rest of the insulin needle price is the price of the stainless steel needle, the stainless steel needle costs 1.85 kr. It was estimated how much of the 1.85 kr. is the price of the raw material:

$$Price\ of\ material = Density \cdot Volume\ of\ needle \cdot Price\ per\ kg$$
$$= 8030\frac{\mathrm{kg}}{\mathrm{m}^3} \cdot 0{,}4 \cdot 10^{-9}\mathrm{m}^3 \cdot 34\frac{\mathrm{kr}}{\mathrm{kg}} = 0{,}0001\mathrm{kr}$$

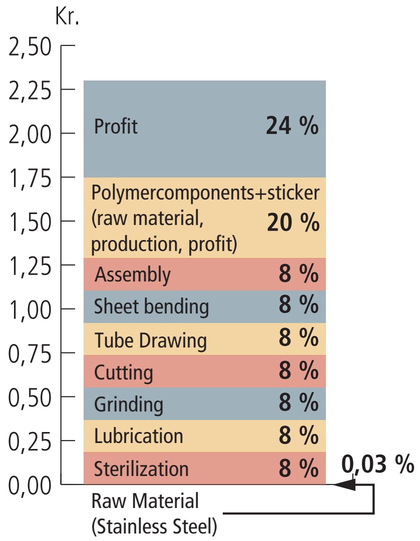


Fig. B8. Estimated shares of the NovoFine product price

According to this price estimation, the raw material of the insulin needle costs less than 0.01 kr. (0.005 % of the insulin needle product price). A rough estimation of what generates the 1.85 kr. was made. It was assumed that the profit of the stainless steel part represents 24 % of the total insulin needle product price. The rest of the 56 % of the insulin needle price was assigned to the production of the needle. The stainless steel needle undergoes 7 production processes (sheet bending, tube drawing, cutting, grinding, lubrication, sterilization and assembling with the other components) according to the illustration of the life cycle of the stainless steel insulin needle in Fig. B4. The rough assumption was made that each of these 7 processes has the same share in the cost of the production of the stainless steel needle. The result is that each of the prduction processes individually counts for 8 % of the price of the NovoFine insulin needle product price (0.18 kr.).

STAINLESS STEEL PRICE SHARE OF INSULIN MEDICATION

Based on the data from user and the cost of the polymer parts at 0.45 kr., the stainless steel part of the NovoFine insulin needle costs 25 % of the annually medication of insulin (Appendix B10, *Stainless Steel Percentage of Medication Price*). If the same calculation were made without any reuse of the stainless steel needles, the stainless steel needles would count for 43 % of the annually insulin medication.

A sensitivity analysis was made of the calculations (appendix B10, *Stainless Steel Percentage of Medication Price*). The variable parameters of the sensitivity analysis are listed in the following table:

Variable Parameters	Variation of value
Dose of the insulin medication per injection	27/37 unit rapid acting insulin & 0/30/40 unit long acting insulin
Number of daily injections	2/ 7 injections per day
Reuse of needles	0/ 1/ 2 times
The price of the plastic parts of the needle	0.2 kr./ 0.45 kr. / 1.15 kr.

In the sensitivity analysis the stainless steel insulin needle itself constitutes between 5-43% of the annually insulin medication.

DISCUSSION

The price of the raw material of the stainless steel seems to have a minimal influence on the price of the stainless steel insulin needle. What causes the high price of the stainless steel needle? In the last section, *Environmental Sustainability,* it was seen that the production phase had many processes. It seems reasonable to say, that a big part of the 1.85 kr. is caused by expenses of the manufacturing process. A part of the price could also be constituted of profit and assembly of the components. Another factor could be that the actual price of the raw material is more expensive than CES suggests, though the raw materials of the needle would still cost less than 0.01 kr., if the price of the material was 10 times higher. There does not seem to be a big economical potential in changing the raw materials of the needle only. There seems to be potential in improvement of the economical sustainability of the product, however, if a change in the raw materials provides an opportunity for cheaper manufacturing methods. Polymer is frequently associated with cheap manufacturing methods.

Reuse of the insulin needle seems to have a positive effect on the economical sustainability of insulin needles, althoughnot in a direct manner, because reuse of insulin needles can results in physical consequences and increased medical bills. The insulin dose and the reuse of needles are very individual. Especially the insulin injections for type 2 diabetics vary. It is difficult to estimate how many times a needle is reused. Some patients reuse the needle more than once, others never reuse it. The variables of the insulin dose and reuse are judged to be the most uncertain variables of the estimation. The estmation of the diabetics' annually insulin dose and use of insulin needles is based on user 1 (woman, weight 60 kg.). The average weight of adults in Denmark is 75 kg. (Statens Institut for Folkesundhed, 2007). One of the factors influencing the amount of the insulin dose per person is weight. A 60 kg. woman may not be representative as basis fo calculating the proper dose for the average diabetic. On the other hand a significant part of the type 1 diabetic users are children. Weight is not the only important factor influencing the amount of the insulin dose. Diet, physical exercise etc. also have a huge influence.

Conclusion

The polymer-based insulin needle seems to have potential to improve some of the sustainability aspects of the stainless steel insulin needle. If the polymer needle could prevent reuse of the insulin needles, it is indicated that polymer needles be more *socially sustainable*. Though at this point it is not completely clear how. An insulin needle that can be burned at a bonfire seems to improve the social sustainability of the needle in poor countries. Seen from an *environmental* perspective there is no big reduction of the energy consumption to gain by replacing the stainless steel insulin needle with a polymer-based one. It was assumed that 170 m^2 stainless steel is anually used on insulin needles. A polymer-based needle could be made of a renewable or in other ways a more sustainable material. According to a rough estimate the stainless steel needle accounts for 25 % of a diabetic's annualy insulin medication. It looks like expenses of the production methods of the needle could cause the majority of the price (56 %). An improvement of the insulin needle's *economical sustainability* seems possible if a polymer needle could provide a cheaper production method.

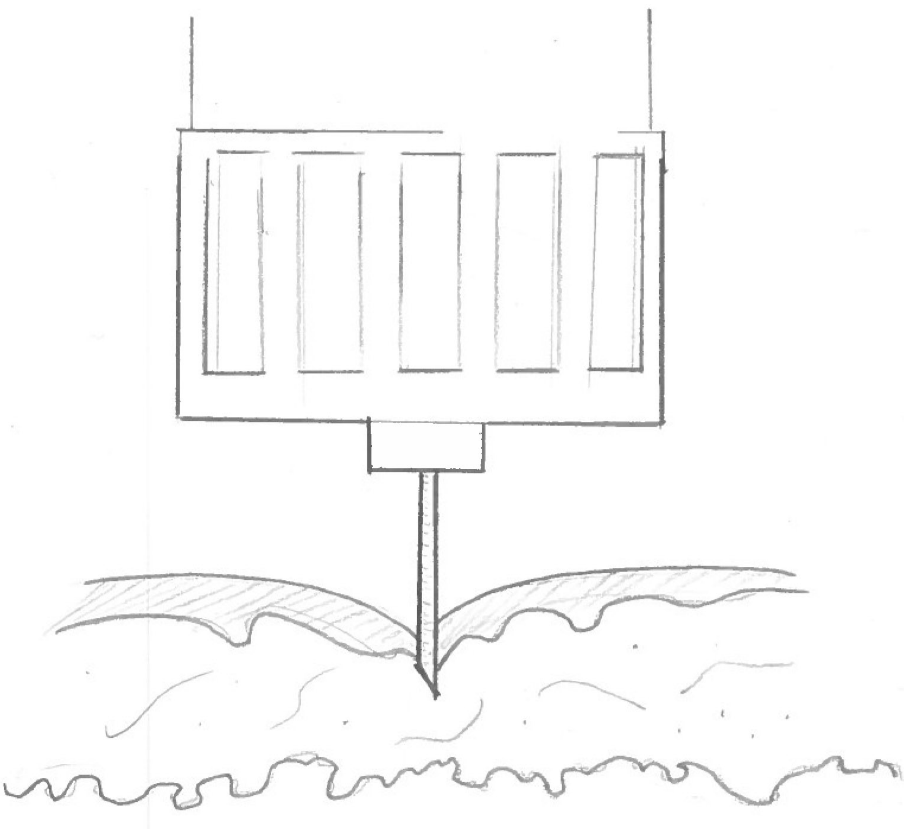
Some of the possible improvements in the three dimensions of sustainability contradict improvements in another of the dimensions. Most research seem to suggest that reuse of insulin needle should be avoided from a social sustainability point of view. Reuse of insulin needles is recommendable from an environmental or economical perspective of sustainability. Once a stainless steel insulin needle is reused, the potential benefits of the environmental and economical dimensions of sustainability are minimized. The table below summarises the pros and cons in the three dimensions of sustainability:

Dimension of sustainability	**Subject**	**Pros – polymer insulin needle**	**Cons – polymer insulin needle**
Social	Reuse	Physical complications (?)	Cost, energy consumption
	Disposability in poor countries	Burnable at low temperatures	Toxins from burning polymer
Environmental	Energy consumption	Lower energy consumption during the production phase per needle	A higher net price of insulin needle consumption is reached if the stainless steel insulin needles were reused and the polymer insulin needle cannot
	Use of limited resources	Material of the needle is not based on stainless steel	Material of the needle might be based on petroleum
Economical		Lower price per insulin needle	Higher net price of the insulin needle-consumption if the stainless steel insulin needles were reused before and the polymer-based insulin needle cannot

These observations will be taken into consideration during the following design work. It is estimated that the biggest potential of sustainable improvement lies in the economical sustainability dimension.

Chapter C

ACADEMIC LITERATURE STUDY



Introduction

An academic literature study was made in order to gain background knowledge on the technical challenges of the polymer-based insulin needle. To guide the academic literature study following 7 hypotheses were made:

- An insulin needle of a polymer material has bigger mechanical challenges than a stainless steel needle of the same geometry
- Deformation of the needle tip depends on the needle tip geometry
- The insulin needle needs to be sharpest when it punctures the skin
- The penetration force will rise as the needle penetrates further into the skin
- The mechanical properties of skin varies
- The needle will cause less damage to the skin, if the needle moves down in the skin layers by *cutting its way through* instead of *pressing its way through*
- A bigger needle diameter causes more pain

The 7 hypotheses are investigated in the five sections of the chapter:

- *Review of related DTU projects* – Earlier findings and results of two related bachelor projects
- *Polymers* – General polymer properties and challenges
- *Mechanical theories* –Mechanical theories related to the challenges of the insulin needle
- *Needle tip geometries* – What is the optimal needle tip geometry?
- *Skin* – penetration of skin as a biological and mechanical phenomenon

METHOD

Ten hypotheses were formulated to guide the academic literature study.
In the academic literature study scientific papers and academic books were reviewed. DTU FindIt and REX were the primary search engines used. Google was used for information searches and as inspiration for search words. Reference lists from relevant articles and former DTU projects were reviewed in the search for relevant literature.

Reviews of Related DTU Projects

RESULTS

BENJAMIN JOHANSEN AND SØREN BOESEN

The two Design and Innovation students Benjamin Johansen and Søren Boesen wrote the bachelor thesis *Medicinsk injektion inspireret af naturen* in spring 2013. The project concerned the development of an alternative polymer-based solution for the hypodermic needle. They used a biomimetic approach. They sought inspiration from the mosquito. The final concept addressed the buckling issue related to hypodermic needles made of polymer. An image of the final concept is seen in Fig. C1. The protection cap of the hypodermic needle serves as a protection cap against needlestick injuries and as a support structure against buckling. The protection cap has pre-cut slits. When the needle penetrates the skin, the protection cap stays on top of the skin and deforms because of compression as shown in Fig. C1. The slits make the protection cap deform in such a way that the polymer needle column is supported in the theoretical critical locations during penetration of the skin. The full review of the bachelor thesis can be read in appendix C1, *Review of* Medicinsk injektion inspireret af naturen.

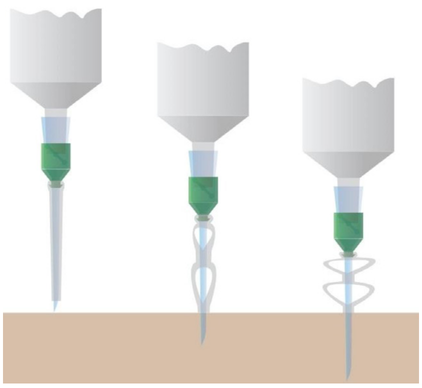


Fig. C1. Johansen & Boesen's needle-concept — inspired by the mosquito (Johansen & Boesen, 2013)

JACOB MORTENSEN AND RASMUS LUNDGAARD

The bachelor thesis "Polymer Needles for Medical Injections - Identifying the Potential through an Experimental Approach" from fall 2014 was also based on a study of the mosquito. The two authors, Jacob Mortensen and Rasmus Lundgaard, are mechanical engineer students. Their thesis was more technical than the one presented by Johansen and Boesen. They were inspired by Sophie Gacs' bachelor thesis on mosquito-inspired polymer needles. Mortensen and Lundgaard claimed that the challenges concerning hypodermic needles in polymer could be divided into two challenges:

- Buckling of the needle column
- Deformation of the needle tip

Using theoretical calculations and experiments Mortensen and Lundgaard claimed they had solved the buckling problem. Their solution was based on a sleeve shortening the effective length of the needle, similar to the concept of Johansen and Boesen. They addressed the problem with deformation of the needle tips but did not have a final conclusion on this. From a variety of tip geometries they conclude from their Finite Element Method (FEM) analysis that the tip geometry of a symmetric cone will deform least. A full review can be read in appendix C2, *Review of* Polymer Needles for Medical Injections.

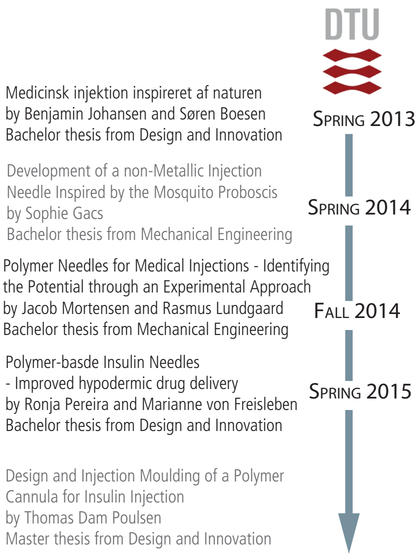


Fig. C2. Shows the time line of former and ongoing DTU projects concerning hypodermic polymer needles

DISCUSSION

Johansen and Boesen's concept was still on an early conceptual level. They made a few simplified calculations on their concept. There was still a lot of work to be done in order to verify the concept. For instance they had not addressed the material issue of their concept. They had yet to find a very elastic material for the sleeve. After an injection the sleeve needs to get back in the starting position in order to protect the users from needle stick injuries as intended. Furthermore Johansen and Boesen did not address the problem with needle tip deformation.

Mortensen and Lundgaard's solution was not ready to be applied to an existing syringe system. According to their findings the sleeve could support the needle during puncture of the skin. They did not clarified if the sleeve could be pressed sufficiently together to let the needle penetrate into the desired depth of the skin. Furthermore there did not exist a polymer needle the sleeve concept could be applied to. Mortensen and Lundgaard made a FEM model of the skin to simulated deformation of different shapes. Their FEM model was not completely successful. It stopped before the needle could puncture the skin.

Polymers

RESULT

PROPERTIES AND CHARACTERISTICS

A study on the mechanical properties of materials in general was made (appendix C, *Material Properties*). Polymers will be more sensitive to deformation than the stainless steel needle when a polymer needle tip hits the skin. Some of the big differences are the stiffness and strength of the two materials. A high Young's modulus indicates high stiffness of the material. A material with a high compressive strength means that a high load can be applied to the material before it starts to collapse. Polymers and stainless steel have different material properties. Polymers typically have a Young's modulus that is around 100 times lower than metals and more than 10 times lower compressive strength (see Fig. C3). Polymers are more sensitive to thermal or chemical changes in the environment. For most polymers an increase in temperature decreases the modulus of elasticity and reduces the tensile strength.

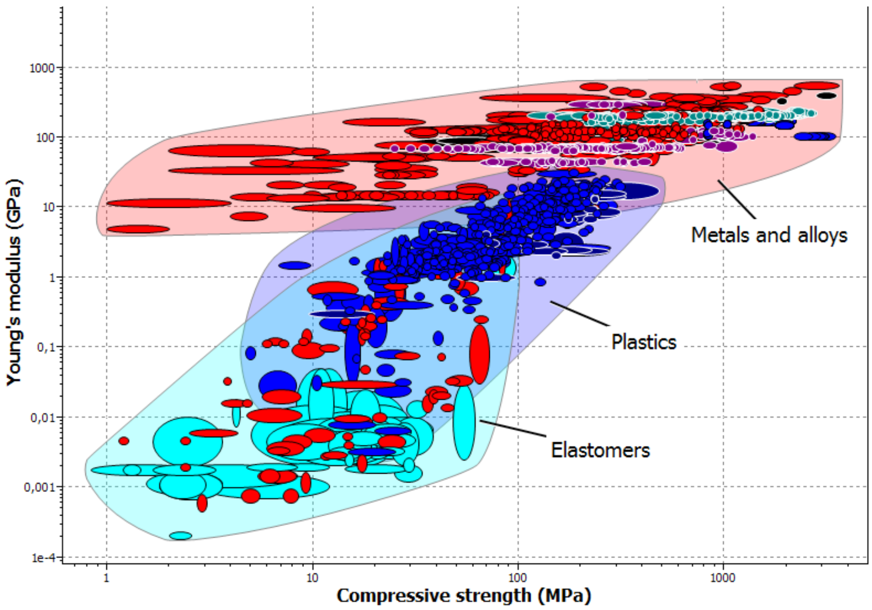


Fig. C3. Material properies (CES, 2015).

Polymers are divided in wo main groups: thermosets and thermoplastics.

- *Thermosets* are crosslinked network polymers with chemical bonds between the molecules, which are created as the material is heated because of chemical reactions. These chemical bonds are not broken when the material is reheated and the polymer therefore stays hard.
- *Thermoplastics* soften when heated because the heat breaks the mechanical likes between the molecules and become solid when they are cooled down. The hardening is reversible and repeatable. Thermoplastics are relatively soft and the mechanical properties depend a lot on whether the material is amorphous or crystalline. *Amorphous polymers* have randomly ordered chains, which allow the material to stretch in many directions. This often makes the material very elastic. In *crystalline polymers* the molecule chains are ordered and folded. This creates less elasticity but makes them more brittle. Thermoplastics are the most commonly used polymers and they are available in many different qualities depending on the purpose of the product (Callister, 2010).

INCREASING STRENGTH AND STIFFNESS OF POLYMERS

There are different ways of increasing the stiffness and strength of polymers. The stiffness of a polymer can be increased by adding a filler fiber such as glass or carbon fibers. Even in the micro scale of insulin needles it will be possible to increase stiffness by adding fibers. Another way of increasing mechanical properties of polymers is by designing high performance polymers, which are extra crystalline (Callister, 2010).

USE OF POLYMER IN THE MEDICAL INDUSTRY

There are many regulations regarding the use of materials in medical devices. They depend on what the use of the product is. It should be considered if the material follows international classifications for medical application such as the European ISO standards. Insulin needles go under the ISO 7886-3:2005(en) (ISO, 1984). The important issues are that the materials should not chemically react with the skin, and it should be possible to sterilize. In appendix C4, *Sterilization Matrix of Plastics*, is shown a table from the book *Handbook of Polymer Applications in Medicine and Medical Devices* (Nawrat, 2009) where polymers and their sterilization abilities are presented. Examples of sterilization methods for polymers are steam, dry heat, ethylene oxide, and gamma radiation (Nawrat, 2009).

DISCUSSION

Choosing the right polymer for the insulin needle is very important. For this project it is important that the polymer is stiff and strong. It was concluded in the fist phase of the project that the needle needs to be cheap. Therefore the polymer should be suitable for mass production of insulin needles. Mass production by injection molding is often cheap because parts can be made in one piece without secondary operations. Thermoplastic injection molding is generally cheaper than thermoset injection molding because thermoplastics wear the mold less. More material is wasted in thermoset injection molding because hardened thermoset cannot be remolded (Rebling Plastics, no date). If a reinforced polymer is chosen, it is important to make sure that the filler does not affect the skin in any negative way. It is also important that the increments of material properties are effective even in the small scale of insulin needles.

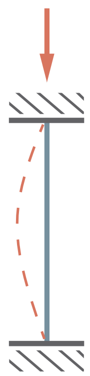
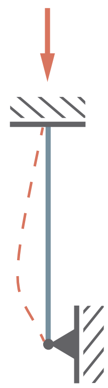
Mechanical Theories

RESULTS

When the polymer insulin needle penetrates the skin in a perpendicular angle, the two main mechanical challenges are: Buckling of the needle column and deformation of the needle tip. The deformation of the tip will be axial compression or vertical bending (deflection) depending on how the needle hits the skin surface.

COLUMN BUCKLING

Buckling describes the phenomenon, when a column has a sideway failure because it is exposed to an axial load. The critical load is the load that needs to be applied before the column starts to buckle. It depends on how the two ends of the column are fixed, the effective length, second moment of area and Young's modulus of the tube material. Until the insulin needle punctures the surface of skin, the tube of the needle can be simplified as a column, with a clamp/ simple supported boundary condition. The needle is clamped in the needle hub and simple supported on the skin surface. As the needle moves into the skin the simple supported condition gradually becomes a clamped condition. As the needle moves into the skin, the effective length of column varies. The formulas of the four relevant cases to describe the needle tube during penetration are listed in the table bellow:

Boundary conditions	Clamped/Clamped	Clamped/Simple supported
Deflected shape		
Critical Load	$\frac{4\pi^2 E I}{L^2}$	$\frac{2.046\pi^2 E I}{L^2}$
Critical Load at Variable Length	$\frac{4\pi^2 E I}{(L-x)^2}$	$\frac{2.046\pi^2 E I}{(L-x)^2}$

L: Effective Length
E: Young's modulus
I: Second Moment of Area
P_{cr}: Critical Load
x: Displacement in skin

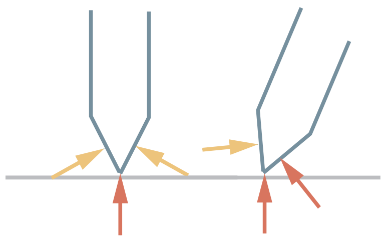


Fig. C4. perpendicularly or skewed hitting needle tip.

TIP DEFORMATION

If the needle tip is perfectly symmetric and hits the skin perpendicularly, the reaction force will be symmetrically distributed on both sides of the tip. This will lead to an upward-pointing resulting force. Only axial compression will happen which eventually results in a rounded tip depending on the compressive strength of the material. The needle will seldom hit the skin in a perfectly perpendicular angle and not all needles have symmetric tips as shown in Fig. C4. The resulting force will be on the side of the needle and will lead to bending (deflection) of the needle tip.

- *Axial Compression:* When a needle tip is pressed perpendicularly against the skin, it will be subject to axial deformation. The cross section area of the tip varies along the length of the tip. The deformation of a needle tip is categorized as non-uniform. The contraction can be described as follows:

$$d\delta = \frac{F}{EA_x}dx \Leftrightarrow \delta = \int_0^L \frac{F}{EA_x}dx$$

  where δ is the contraction length, F is the applied force E is Young's modulus and A_x is the cross section area according to x (Riley et al. 2002, p. 128).
- *Beam Deflection:* A tip that is affected by a force big enough from the side will bend. The phenomenon can be approached with the theory of beam deflection, if the tip is seen as a fixed beam affected by a load at the tip (Fig. C5).The deflection of the tip can be calculated by integrating the *differential equation of the elastic curve* (Riley et al., 2002, p. 489-498).

$$E\frac{d^2y}{dx^2} = \frac{Fx}{I_x} \Leftrightarrow y = \iint \frac{Fx}{EI_x}$$

  Where F_x is the applied force, x is the distance from the tip, E is Young's modulus and I_x is the second moment of area depending on x (Riley et al., 2002, p. 497). The second moment of area influences a beam's resistance against deflection.

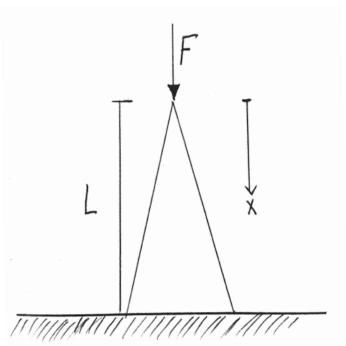


Fig. C5. Axial deformation.

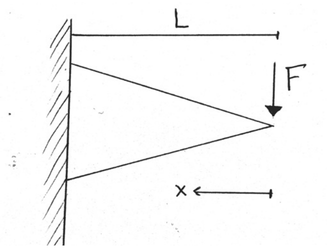


Fig. C6. Beam deflection.

DISCUSSION

From the formula of Euler Buckling Theory it was seen that when Young's modulus decreases the critical load will decrease. Increasing the second moment of area and/or decreasing the effective length can compensate for a decrease of Young's modulus. In the case of hypodermic needles it should be noted that the effective length varies depending on how far the needle is inserted into the skin. Mortensen and Lundgaard (2015) showed that by adding a supporting sleeve it would be possible to avoid buckling and still have a thin and long hypodermic needle. Their analysis was based on hypodermic needle size 21G, and with our focus on insulin needles (32G, 6mm) it is worth considering if the short length of an insulin needle will be enough to avoid buckling during penetration of skin and still with a reasnable safety factor.

The theory of axial compression and beam deflection suggests that the faster the cross-section area grows and the bigger second moment of area the tip has, the less the deformation. It should be noted that this equation only takes the stiffness of the material into account. It does not tell when or how the material will yield. After the yield point the material will be subject to plastic deformation which is not linear and very unpredictable. Therefore this point should be avoided by choosing a material with sufficiently strong to penetrate the skin without yielding.

Needle Tip Geometries

RESULTS

THEORETICAL COMPARISON OF TIPS GEOMETRIES

The different tip geometries need to be compared somehow. What is the "optimal" needle tip geometry? In order to get closer to an answer this question a basis for comparison need to be established. It was chosen to compare geometries with the same grinding angle. This means that the tip will have the same vertical height from the bottom of the grind to the tip. A cone, a 3-sided and a 4-sided pyramid will be compared for their theoretical resistance to deformation.

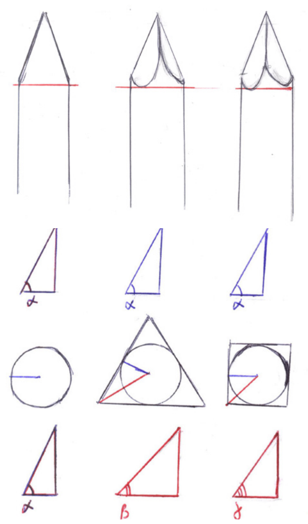


Fig. C7. Tip geometries with the same grinding angles.

- In *axial compression* of the three geometries with the same grinding angle the 3-sided pyramid should withstand this the best. Theoretically the 3-sided pyramid should have the biggest cross section area at a given distance from the tip as seen in Fig. C7. The cone will be the one with smallest cross-section area and the one that deform the most during axial compression.
- *Beam defection* of the tip the one that has the biggest second moment of area is most resistant. (appendix C5, *Second Moment of Area - Inscribed Circle*). Theoretically the 3-sided pyramid will also have the biggest tip area.
- When the same geometry with different *steepness* is compeared, a less steep geometry will theoretically be more resistant to both axial compression and bending, Also a solid tip is more resistant than a hollow tip in both cases.

TIP DEFORMATION IN LITERATURE

O'Leary and Simone et al. (2003) compared beveled tips, cones and 3-sided pyramids in different sizes. They showed that smaller needle tips require less resistance force against the skin, but were also more likely to bend. A coned or a 3-sided pyramid tip bends the least because the symmetry creates an even distribution of the force. Furthermore it was shown that a 3-sided pyramid tip creates the smallest resistance force. The beveled tip and the cone create the highest resistance force (O'Leary, Simone et al., 2003).

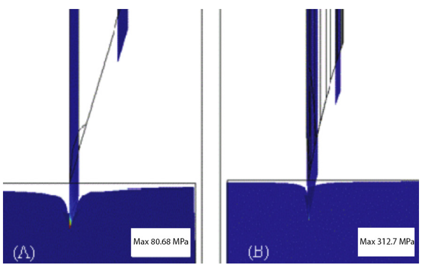


Fig. C8. *shows how skin deforms under needles with different curves. Numerical analysis by* Ensaldo-Renteria et al (2014)

Ensaldo-Renteria et al. (2014) analyze needles with different curvature. Their analysis showed that by using a needle with a steeper curvature the skin will reach its yield point earlier because the stress consecration on the skin is higher. They argued that this will create less pain because a smaller area of the skin is affected (Ensaldo-Renteria et al., 2014).

In the bachelor thesis by Mortensen and Lundgaard (2015) experiments showed that there is a correlation between the needle size and the penetration force. By numerical analysis they showed that stress on the skin was lower for a polymer needle than for a steel needle of same geometry. They argued that this is because the polymer tip deforms and the contact area gets bigger.

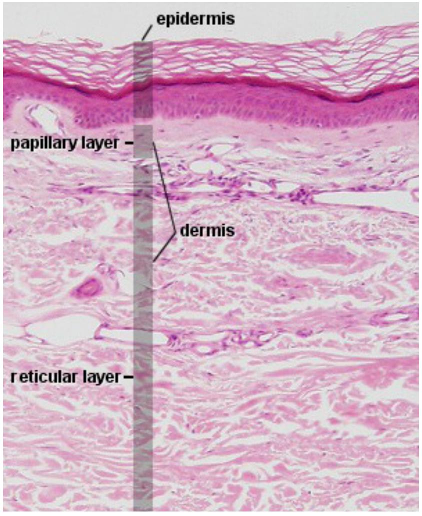
In Mortensen and Lundgaard's comparison of different tip designs it was concluded that a solid and symmetric tip will be less likely to deform because of a symmetric distribution of force on the tip and therefore apply the highest stress on the skin (Mortensen & Lundgaard, 2015).

DISCUSSION

When a needle with a lower Youngs's modulus hits the skin, the tip will deform. As the tip deforms the contact area with the skin is increased which means that the stress on the skin becomes lower. Because of this it will take more force to penetrate the skin (appendix C6, *What is sharpness?*). A steeper tip will create more stress on the skin surface, but a steeper tip will also be less resistant to both axial compression and bending. The optimal steepness needs to be found.

Theoretically and in literature the 3-sided pyramid is most resistant to both axial compression and bending when it is compared with a cone and a 4-sided pyramid with the same grinding angle. It is important to consider which geometry has the least resistance force on the skin surface and creates the lowest friction in the skin.

Skin



THE LAYERS OF THE SKIN

The skin constitutes the boundary between the body and the surrounding world. One of the main functions of the skin is to prevent foreign bodies from enering the body. The skin is divided into two main layers, epidermis and dermis. The underlying tissue is called the hypodermis.

- The *epidermis* is the outermost layer of the skin which a high density cells. Around 95 % of the cells in the epidermis are keratin-producing cells. Keratin is the material of horns and hooves. The top layer of the epidermis is called *Stratum corneum*. It is around 10-20 µm thick. It is packed with flattened dead keratin-packed cells (Henry et al., 1998). There are no blood vessels in the epidermis layer, so the dermis provides the epidermis with nutrients.
- The *dermis* is divided into two sublayers: *Stratum papillare* and *Stratum reticulare*. These two layers consist of the same extracellular components such as collagen fibres, elastic fibres and ground substance. The collagen fibres are thinner in the papillary dermis than in the reticular dermis. The collagen gives tensile strength to the dermis. The elasticity of the skin is provided by the elastic fibres (Xu & Lu, 2011).
- *Hypodermis* primarily consists of fat. The thickness of this layer is very indi-

Fig. D9. Cross-sectional view of the skin (Lecannabiculteur, no date)

vidual. It highly depends on gender, lifestyle, BMI and locationon the body. The larger blood vessels are found in the hypodermis (Appendix C7, *The Layers of the Skin*).

VISCOELASTIC PROPERTIES OF SKIN

The layers of the skin create very complex mechanical properties. Skin is a heterogeneous and anisotropic material. It has a non-linear stress-strain relationship. Skin can be characterized as a viscoelastic material due to the combination of both viscous and elastic behavior. The mechanical behavior of viscoelastic materials is explained in appendix C8, *Viscoelastic properties*. The viscoelastic properties of the skin are mainly due to the epidermis and dermis. Figure Fig. C10 explains what happens when skin deforms.

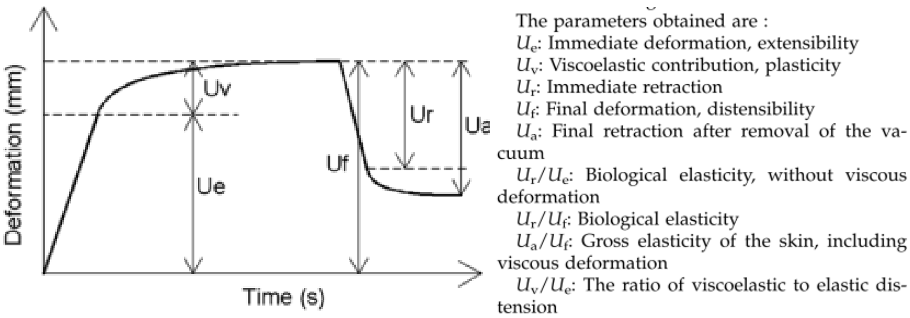


Fig. C10. (Boyer, Gaetan, Laquièze, L.,& Le Bot, 2009)

The springback of the skin after deformation is referred to as damping. It is shown that skin becomes more viscous and less elastic with age. Stiffness and damping depend on hydration and the hydration level decreases with age. The investigation of BMI shows that the hypodermis has a small influence on the damping, as damping increases with BMI (Boyer et al., 2009). The viscoelastic properties of skin are discussed in appendix C9, *Viscoelasticity of Skin*.

MECHANICAL VALUES OF THE SKIN

The suggested mechanical values of skin in the literature vary a lot. A suggestion from Kim & Colton (2005) of the Young's modulus of the skin layers is listed in Fig. C11

Layer	Thickness (mm)	Young's modulus (MPa)
Stratum corneum	0.02	12 000
Living epidermis	0.1 – 1.5	16
Dermis	1.5 – 4	12
Subcutaneous fat	1.25	20

Fig. C11. (Kim & Colton, 2005)

It was sought to find a value of the ultimate tensile strength (UTS) of the skin in order to know what pressure the needle tip will be exposed to. Four suggestions of UTS were found in the literature. All four suggestions were based on tensile test experiments on skin from human corpses. The results are listed in the table below.

Where	UTS [MPa]	Age [years]	Area
Jansen & Rottier (1958)	3-14	0-90	Abdomen
Dunn & Silver (1983)	2-15	47-86	Abdomen & thorax
Jacquemoud et al. (2007)	6-13	0-90	Various
Annaidh (2013)	13-30	81-97	Back

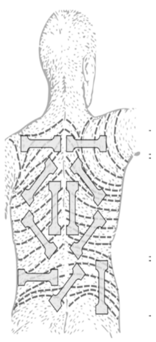


Fig. C12. Areas of the skin used by Annaidh, 2013.

MECHANICAL PHASES OF INJECTION IN SKIN

It was not possible to find concrete data on needle injections in vivo skin. In literature several experiments have been conducted on pig organs and skin.

Fig. C13. A graph of the injection in a pig lever (after Maurin et al., 2004), achieved by the combination of tactile sensing and medical imaging. In this paper, we study the forces involved during in vivo percutaneous procedures for the development of a force feedback needle insertion robotic system as well as the development of a realistic simulation device. The paper presents different conditions (manual and robotic insertions.

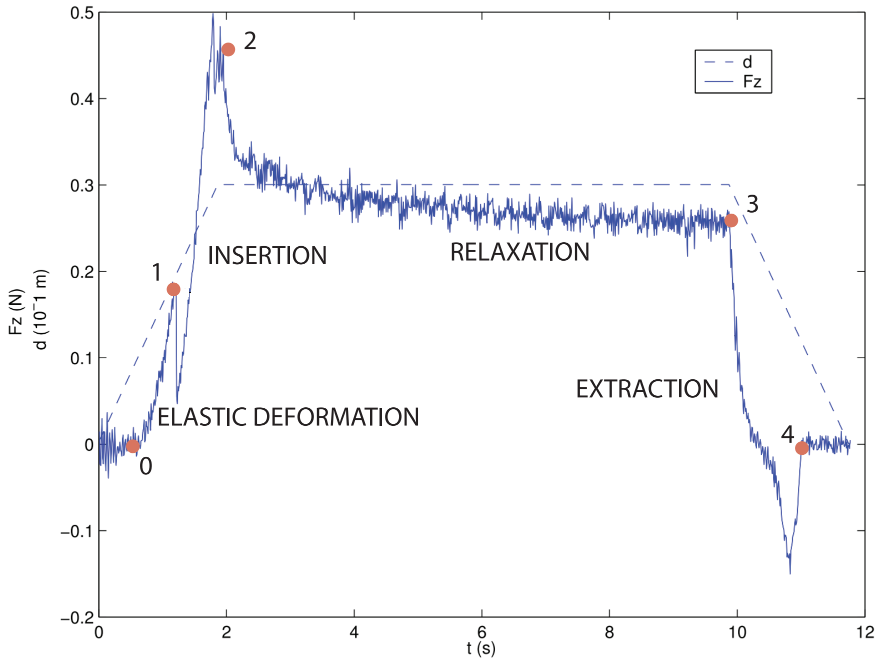


Fig. C13 shows a graph of the injection in a pig lever. The injection can be divided into four phases:

- Phase 1: Elastic deformation (point 0-1)
- Phase 2: Insertion (point 1-2)
- Phase 3: Relaxation (point 2-3)
- Phase 4: Extraction (point 3-4)

The penetration of the skin consists of the two phases: *plastic deformation* and *insertion*. The plastic deformation phase ends, when the needle has punctured the surface of the skin. When the surface of the skin is punctured the skin deforms plastically. Elastic energy is released and the penetration force drops momentaneously. During the *insertion phase* the penetration force increases to a higher value than the puncture force. This is caused by an increasing friction on the needle, as the needle gets further into the skin. In the *relaxation phase* no more penetration force is applied to the needle. During this phase the drug is delivered. The needle is pushed slowly upwards during this phase due to the elastic energy that is stored in the tissue and the flow of medicine into the skin. In the *extraction phase* the needle is extracted from the skin. Due to the friction a negative force is needed to extract the needle from the skin.

CRACK DEFORMATIONS OF THE SKIN

It was not possible to find literature on how exactly the cells in the skin are affected by insulin injections. Shergold and Fleck (2005) suggest that penetration of skin can create two kinds of crack deformations of the skin. The two different types of crack deformations are a planar crack and a ring crack.

– Planar crack is created when a sharp punch penetrates the skin
– Ring crack is formed when a flat-bottomed punch penetrates the skin

The planar crack "closes" again after penetration. The ring crack does not. This could indicate that a planar crack heals easier. A planar crack is therefore the preferred crack mode (Shergold & Fleck, 2005) (appendix C10, *Crack Deformation of the Skin*).

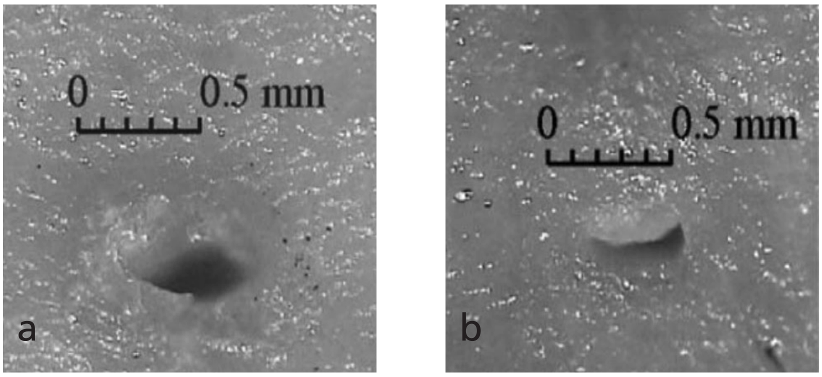


Fig. C14. Penetration of pig skin in vitro. (a) flat-ended punch and (b) hypodermic needle, 0.5 mm (Shergold & Fleck, 2005).

PAIN

Pain in relation to hypodermic drug delivery is caused by stimulation of pain nociceptors in the epidermis and dermis. When the cells of the epidermis are damaged, signal molecules are released and stimulate the nociceptors to send pain signal to the brain (appendix C11, *Pain Response Related to Needle Injections*).

DISCUSSION

From experiments it is known that penetration with a flat-bottomed punch will "hurt" more than penetration with a sharp punch of the same diameter (Shergold and Fleck, 2005). Since a flat-bottomed punch "hurts" more than a sharp needle, it is assumed that a flat-bottomed punch will cause bigger damage to the skin than a sharp needle.

The insulin needle should not only be able to penetrate the "average" human skin. It should be able to penetrate all human skins. The highest possible UTS value of skin should therefore be used in calculations of deformation of the needle tip. Four different suggestions on the UTS were found. The suggested UTS values varied from 2 to 30 MPa. The location and age of the specimens varied. The variation of the UTS values in the literature were expected since:

– skin is anisotropic
– the mechanical properties of skin vary depending on age, location of the body, etc.
– the sensitivity of biological tissues vary due to test conditions

The UTS values were based on skin from corpses. After death the skin gets dehydrated and stiffer (Memorialpages, 2005). The mechanical properties of skin in vitro must be different from mechanical properties of skin in vivo. UTS values are determined on data from tensile tests. In a tensile test the skin is pulled in a direction parallel to the skin layers. During penetration of skin, the skin is exposed to a stress perpendicular to the skin layers. Since the skin is anisotropic the value of UTS will most likely vary depending on in which direction the skin is exposed to a stress. It was not possible to find UTS values of the skin measured in the direction perpendicular to the skin layers.

Neither was it possible to find literature on when during penetration the needle needs to be "sharpest". The insulin needle has to penetrate the two layers of the skin and the top of hypodermis. Young's modulus of the outermost epidemic layer, *Stratum corneum,* seems to be significantly higher than any of the other layers of the skin. Kim and Colton (2005) suggest that the Young's modulus of *Stratum corneum* is 600 times higher than in any of the other layers. The needle will be exposed to the highest stress during penetration of the skin layer with the highest effective UTS. It has not been possible to find values on which layer has the highest effective UTS. *Stratum corneum* forms the barrier to the surrounding world, and it has been claimed that it is the toughest layer of the skin to penetrate (Xu & Lu, 2011). It seems reasonable to deduce that the tip of the needle will be exposed to the highest stress during the penetration of *Stratum corneum.*

Conclusion

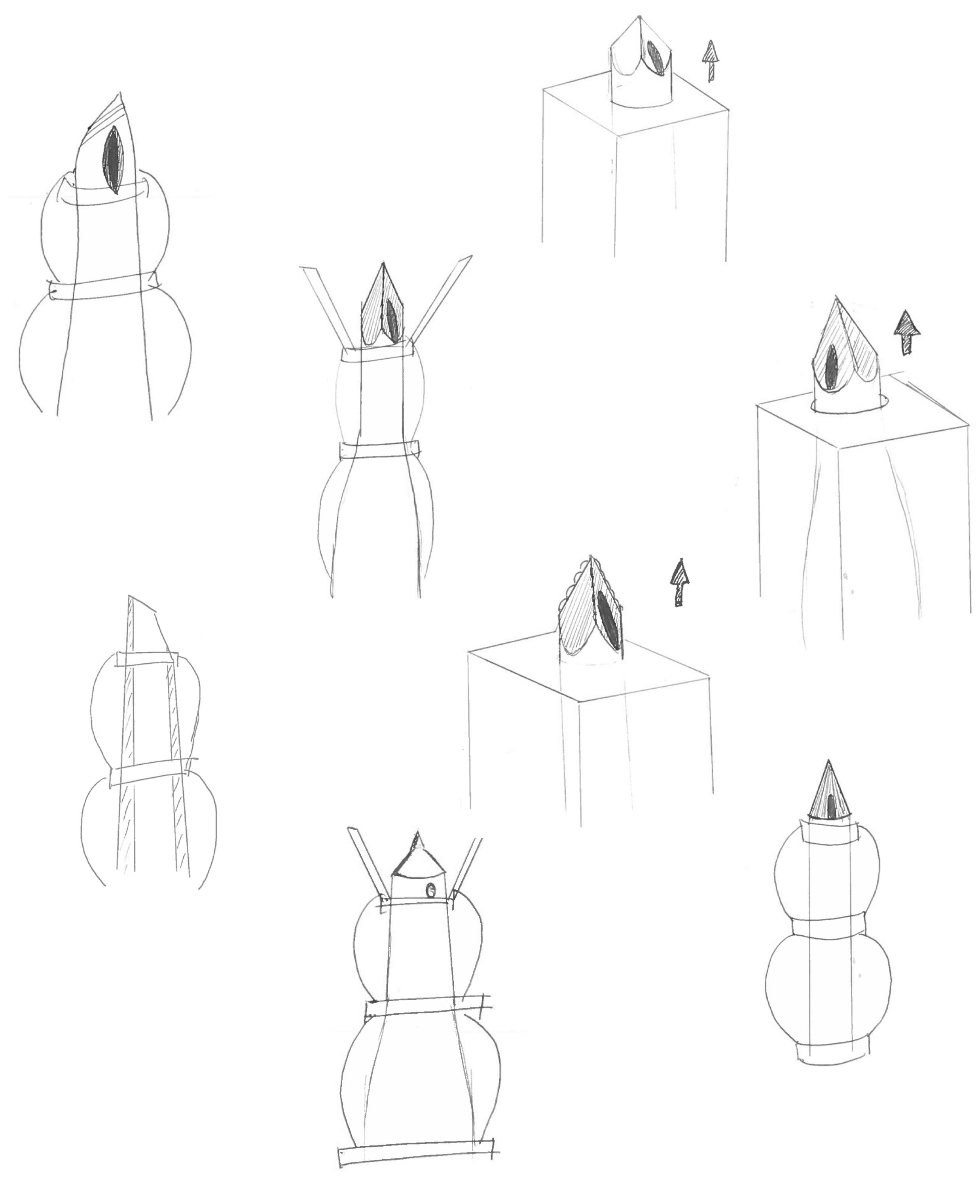
The literature study has to some extent enabled us to answer the 7 hypotheses. In some cases it has not been possible to find all the relevant literature need. The findings of the hypotheses are listed in the table bellow

Hypotheses	Conclusion	Comment
An insulin needle of a polymer material has bigger mechanical challenges than a stainless steel needle of the same geometry	Confirmed	The polymer insulin needle faces mechanical challenges due to the lower stiffness and strength of polymers: Buckling of the needle column, axial deformation of the tips, and bending of the tips. This can somewhat be compensated with fiber or filler reinforcement of the material
Deformation of the needles tip depends on the needle tip geometry	Confirmed	The deformation of the needle tips highly depends on the geometry and steepness. A symmetrical geometric will be less likely to bend during perpendicular penetration of the skin. A thin walled hollow needle tip is less resistant to deformation than a solid, because of it bigger cross-section area. A steep tip geometry will deform more because it has a lower cross-section area and second moment of area. On the other hand a steeper tip geometry creates more stress on the skin at a given force. From the theory and scientific papers the 3-sided pyramid tip geometry seems to be most deformation resistant.
The insulin needle needs to be most sharp when it punctures the skin	Partly confirmed	It was concludeds that the needle needs to be most sharp when it punctures the outermost sub layer of the skin (Stratum coreneum) because it is the toughest and stiffest skin layer. Values of ultimate tensile strength (UTS) of Stratum coreneum was not found. UTS values of skin was found. The values ranged from 2-30 MPa. For further calculation the highest value of 30 MPa will be used.
The penetration force will rise as the needle is penetrated further into the skin	Confirmed	The penetration force rises, as the needle gets deeper into the skin, because of friction between the needle and the tissue.
The mechanical properties of skin vary	Partially confirmed	Skin is an anisotropic material. It has a non-linear stress-strain relationship. The elasticity of the skin decreases as the skin ages. The damping of the skin increases with BMI. The thickness of the different layers of the skin varies depending on the location of the body, and therefore the mechanical properties also vary.
The needle will cause less damage to the skin, if the needle moves down in the skin layers by cutting its way through instead of pressing its way through	Partially confirmed	It has not been possible to find literature to verify this hypothesis on a micro scale. Observations on macro scale were found. A flat-bottomed punch will form a ring crack. A hypodermic needle will form planar crack. The planar crack in the skin heals better than the ring crack. It can be argued that the flat-bottomed punch will be pressed more through the skin than a hypodermic needle.
A bigger needle diameter causes more pain	Confirmed	A bigger diameter causes more tissue damage. More tissue damage leads to more stimulation of the nociceptors in the epidermis and dermis, and a stronger feeling of "pain" will be registered by the brain.

The findings of this chapter leads to requirements and criteria the good polymer-based insulin needle should fulfill. In the next chapter the product specification is defined.

Chapter D

CONCEPTUALIZATION



Introduction

This chapter deal with the conceptualization of the polymer-based insulin needle. The previous three chapters have accumulated knowledge and information. In the beginning of this chapter the knowledge and information from the previous chapters are used to create a *Product Specification*. This is followed by a description of the outcome of the *Idea Generation*. In the next section, *Synthesizing Concepts,* it is described how the ideas from the idea generation were systematizied and how concepts were generated from the systematizied ideas. Then follows a section concerning *Idea Validation* of the means used in the concepts. The chapter ends with a *Concept Screening*.

METHOD

The following design methods were used to generate and select polymer insulin needle concept(s):

- *Product specification.* The findings from the previous chapter were used to set up a product specification. (Ulrich & Eppinger, 2011, p. 94).
- *Negative brainstorming.* Negative brainstorming on the tip geometry was made. Each of the group members sat down with pen and paper for 15 minutes, and the group members drew the worst possible needle tip geometry they could think of to solve the functions of the insulin needle. After the 15 minutes had passed an attempt was made to reverse the negative ideas to positive solutions.
- *Biocards.* Biocards were made after the method of Lenau et al. (2010). The biocards were used as an inspiration source in the idea generation.
- *Forced visual association brainstorming.* 40 random image cards were found in a Google search on *image cards* (appendix D1, *Forced Visual Association Cards*). The pile of image cards was placed in the middle of the table with face downwards. 8 minutes were used to brainstorm on each of the six categories: Deformation, tip geometry, beam geometry, friction, preparation of skin and buckling. During the 8 minutes each group member drew image cards in turn. Each group member drew her associations on the specific category associated to the random image.
- *Function-mean tree.* Findings from the brainstorming sessions and biocards were systematized by means of a function-mean tree (Tjalve, 1979, p. 9). Each of the means was evaluated based on the product specification.
- *Morphology table.* The promising means from the function-mean tree were placed in a morphology table after Ulrich & Eppinger (2011, p. 153). 8 concept paths were drawn with the themes: *The Cheapest*, *The Intuitive, The Environmentally Friendly, The Reliable, The Safest, The Painless, Nature's Best Call* and *Author's Favorite*.
- *Idea validation.* The principles of the 8 concepts were discussed with different experts. Their points of view were discussed and considered in the validation of the used means.
- *Pugh matrix.* The 8 concepts were screened in a Pugh matrix (Ulrich &

Eppinger, 2011, p. 153). Criteria from the product specification were used as selecting criteria. The criteria were: *pain, price, penetration force, production, environment, recyclablility, durability, reliability* and *usability*.

Product Specification

RESULTS

The product specification of the polymer insulin needle concept:

Category	Requirements	Criteria	Comments
Use			
Pain		The diameter of the needle should not be bigger than the NovoFine insulin needle (32G)	Bigger diameter results in more pain during penetration
Reuse		Should disable repeatable injections with the same needle	Most literature states that reuse is not good for the patients
Maintenance		Maintenance of the needle should not be a concern for the user	
Domestication	Must be suitable for home use		The use of the needle should be intuitive. The diabetic should be able to do the injection by him/herself, after reading the manual of the needle
Function			
Penetration		Should be able the penetrate skin with the same force as the NovoFine insulin needle without buckling. (Should apply 30Mpa to the skin at the desired penetration load)	The exact number needs further investigation — a factor of safety also need to be considered
Flow		The insulin should be delivered into the human body with the same or bigger flow	A new concept should aim to avoid a decrement of flow compared to the existing product because it will decrease the value of the user
Manufacturing			
Montage	The insulin needle design must have less components than the NovoFine insulin needle [less than 5 parts]	Assembly time should be shorter than for the NovoFine insulin needle	Less components take less time to assemble
Production	Must be suitable for mass production		Low production time [further investigation needed]
Materials		Should use fewer limited resources than existing needle (resources used/ available resources) [further investigation needed]	The needle should use as much renewable-sourced polymers as possible
Temperatures	Must function in the temperature range from -40 °C to 60 °C	Should melt at temperature of 300 °C or less	Should be able to burn on a bonfire
Sustainability			

Environment	The energy consumption per needle must not be larger than the energy consumption per NovoFine insulin needle	The annual energy consumption for one diabetic's use of insulin needles should be lower than the NovoFine insulin needle	Possibility of recycling material of the insulin needle could be investigated
Cost	The unit price of a needle must be cheaper than the price of the NovoFine insulin needle (2,29 kr)	The annual price for one diabetic's consumption of insulin needles should be cheaper	
Durability/ Lifetime		"Unopened" an insulin needle product should last 2 years	
Safety			
Sterilization	The needle must be sterile before use		ISO 7886-3:2005(en). Sterile hypodermic syringes for single use (1984).
Needlestick injury		Should prevent needlestick injuries during use and the disposal phase (less annual needlestick injuries than the NovoFine insulin needle) [further investigation needed]	

Idea Generation

RESULTS

Fig. D1. Needle tip deforms it self sharp.

NEGATIVE BRAINSTORMING

The results of the negative brainstorming on tip geometries can be found in appendix D2, *Negative brainstorming on tip geometry*. One of the results from the brainstorming was the idea about a tip that deformed when pressed against the skin. An attempt was made to reverse this negative idea into a positive one. The result was the *Self-Sharpening Needle Tip*. The *Self-Sharpening Needle Tip* deforms in a way that keeps it sharp. An actual idea on how to solve the *Self-Sharpening Needle Tip* was not found at this point.

BIOCARDS

Seven biocards were made: *Mosquito Reinforced Food Channel, Mosquito's Sharp Tip, Self-Sharpening Sea Urchin Tooth, Crystal Strength of the Sea Urchin Tooth, Nepenthes Pitchers' Slippery Death Trap, Stinging Nettle Hair – Sharp by a Touch* and *The Self Penetrating Porcupine Quill* (appendix D3, *Biocards*).

- The biocard *Self-Sharpening Sea Urchin Tooth* provides a solution on how to solve the idea of a *self-sharpening needle tip*. The sea urchin teeth stay sharp even when the sea urchin bites into stones. This phenomenon is explained by predetermined areas where the tooth cracks. When a tooth starts to become dull, the outer layer of the brittle tooth will crack and a new sharp layer of the tooth is revealed.
- The biocard *Crystal Strength of the Sea Urchin Tooth* concerns the structure of the penetrating material. The teeth of the sea urchin are made of the same material as the stones it bites in. The mesocrystal structure is different in the

tooth of the sea urchin, which makes it harder than the stone (Killian et al., 2011).

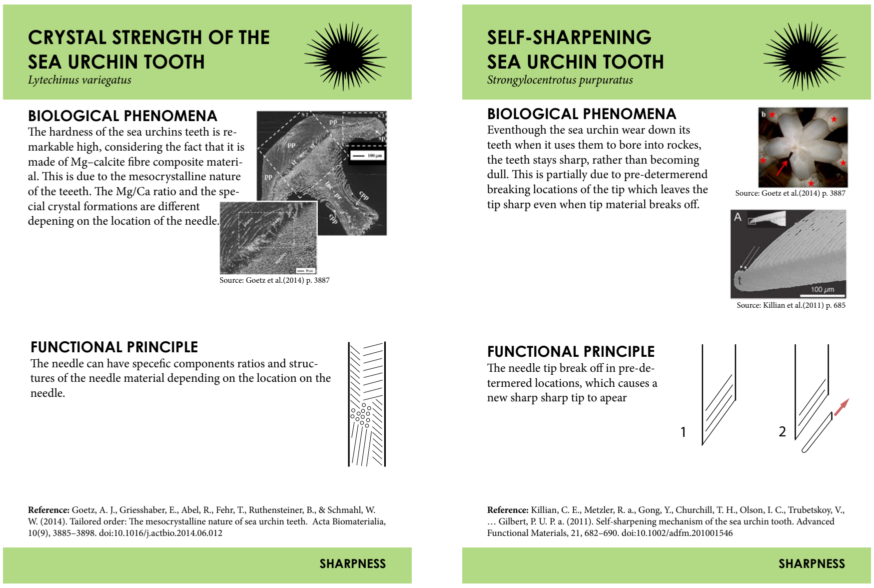


Fig. D2. The two biocards: *Self-Sharpening Sea Urchin Tooth & Crystal Strength of the Sea Urchin Tooth.*

– If the force needed to penetrate the skin with the needle is reduced, it will allow the needle column to have a lower Young's modulus. The biocard *The Self Penetrating Porcupine Quill* addresses this issue. The North American porcupine has small barbs at the tip of its quill. These barbs "cut" their way through the human skin and reduce the penetration force of a hypodermic needle of the same size by half (Cho et al., 2012).

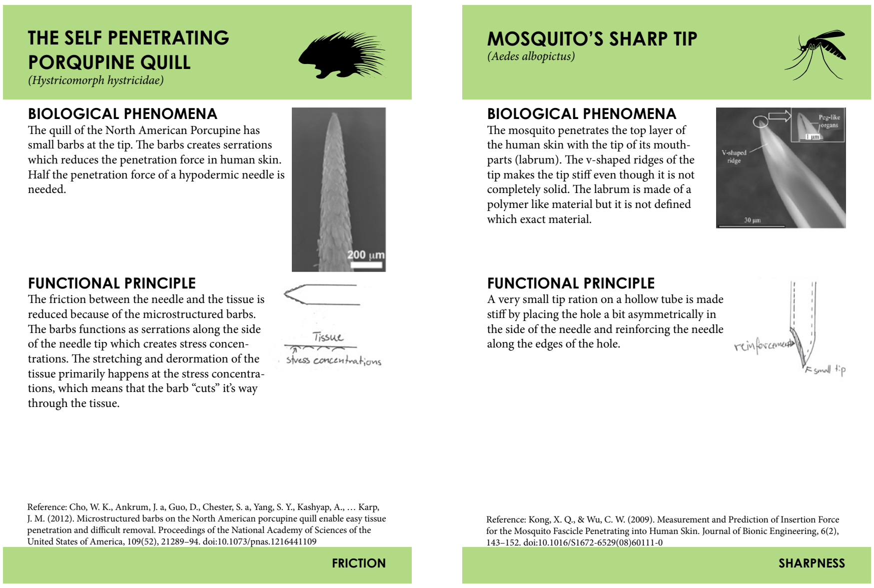


Fig. D3. The two biocards *Self Penetrating Porcupine Quill & Mosquito's Sharp Tip*

– The biocard *Mosquito's Sharp Tip* describes the mosquito's labrum (mouthpiece). The labrum has a very small tip diameter (18 µm), which easily punctures the skin due to the very high stress that the small tip applies to the skin. The hole in the labrum is placed in the side, which allows a solid tip (Kong & Wu, 2009).

Fig. D4. *Sacrifice Tip* the image card led to the idea.

FORCED VISUAL ASSOCIATION BRAINSTORMING

The drawn ideas of the forced visual association brainstorming can be found in Appendix D4, *Brainstorming on Deformation*; appendix D5, *Needle Geometry*; appendix D6, *Brainstorming on Friction*; appendix D7, *Brainstorming Preparation of Skin;* appendix D8, *Brainstorming Prevention of Buckling;* appendix D9, *Brainstorming Diverse.*

- One of the ideas from the forced visual association brainstorm was the *Sacrifice Tip*. The principle of this idea was to keep the tip sharp by having a stiff material in the center of the needle. A very elastic and ductile material surrounds the stiff material. The surrounding material will deform before the stiff material of the tip when a load is applied (Fig. D4).
- *Coating the Tip* with a stiff material was another idea to prevent the tip from deforming. The tip will be coated with a stiff material that will increase the stiffness and strength of the tip (Fig. D5).
- One of the other ideas concerned buckling prevention: The needle is shot out of the insulin pen similar to a mechanical pencil. This will shorten the effective length of the needle during puncture of the skin (Fig. D6). The idea was further investigated in appendix D10, *Pencil solution*.

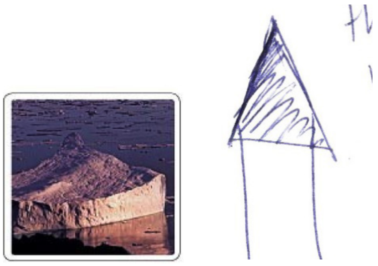


Fig. D5. The idea of coating the needle tip with a hard material was associated from an image of an iceberg.

DISCUSSION

The *negative brainstorming* gave an insight into the solutions that should be avoided. The method that accumulated the most idea was the *forced visual association brainstorming*. The images not connected to polymer insulin needles where very useful to get inspiration. The *biocards* provided fewer solutions, but the solutions had a high quality. Biomimetics is a good tool to get inspiration to concrete solutions. Through evolution nature has developed smart solutions for a lot of functional problems. Studying the nature provided concrete solutions to functional problems.

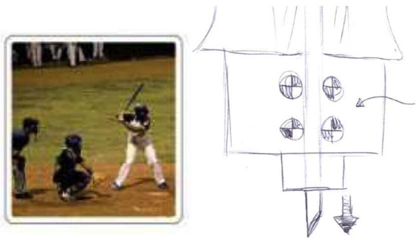


Fig. D6. Shooting a ball leds to the idea of shooting the needle out of the insulin pen.

Synthesizing Concepts

RESULTS

FUNCTION-MEAN TREE

The idea generations provided means to the needle's functions. The idea from the idea generation was systematized in a function-mean tree (appendix D11, *Function-mean Tree*). A rough evaluation was made of the quality of means of the function-mean tree.

One of the solutions which did not pass the quality check was the *Sacrifice Tip*. After further consideration it was concluded that this solution would only delay the deformation of the needle tip (Fig. D7). At first the stress will be concentrated in the elastic material. During deformation of the elastic material the stress on the skin will be too low to puncture it, as the work of the applied force will be stored as elastic energy in the elastic material. When the elastic material has reached its limit of deformation, the stiff material of the needle tip will start deforming (appendix D12, *Elastic and Stiff Needle*).

Fig. D7. *1) the elastic material bents 2) The needle tip is compressed.*

Fig. D8. Function-mean tree from appendix D11, *Function-mean Tree*. The means which were found somewhat realistic, are highlighted with orange in the function-mean tree.

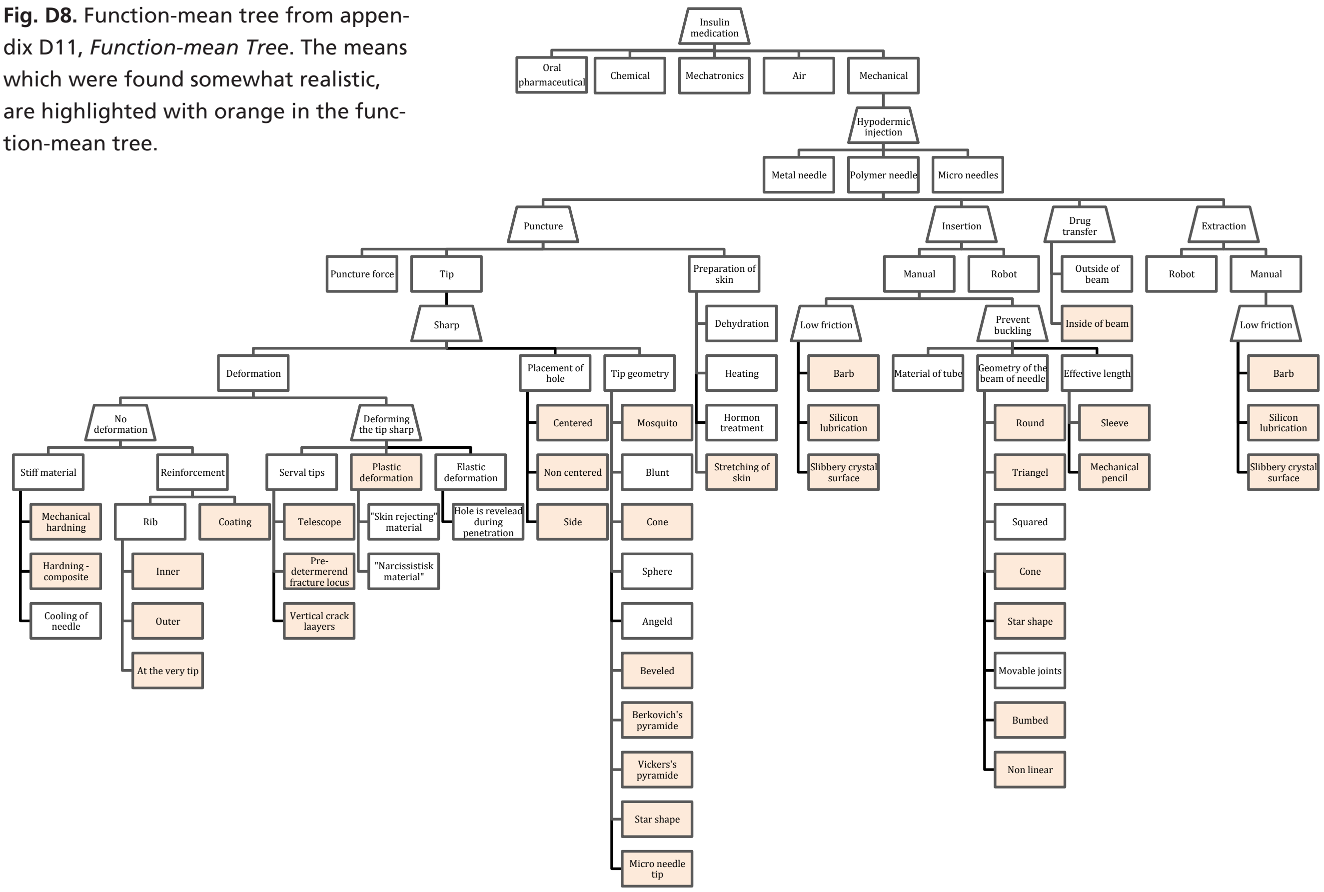
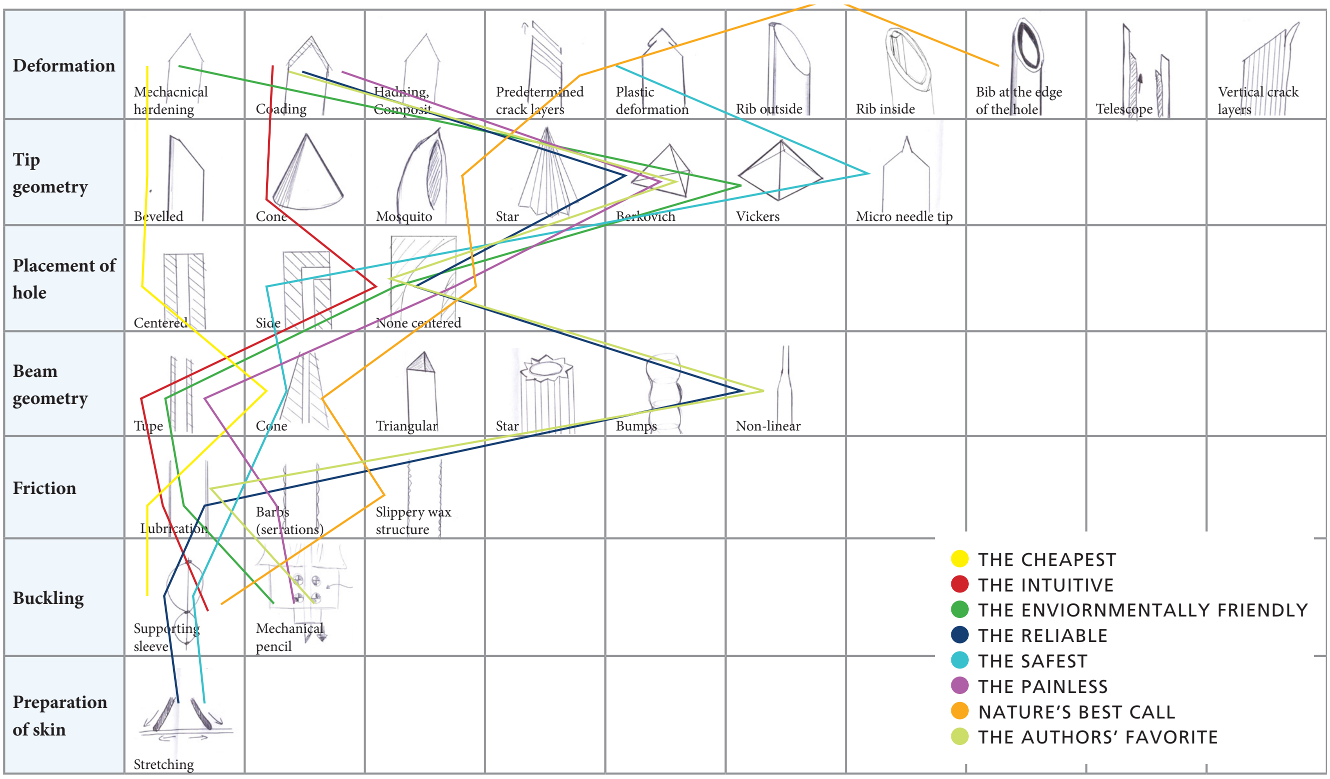


Fig. D9. Mophology Table. The colors marks the different concept paths

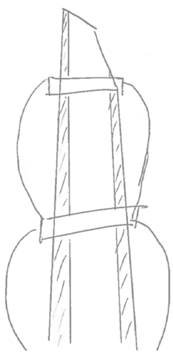
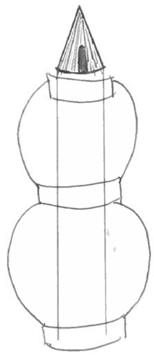
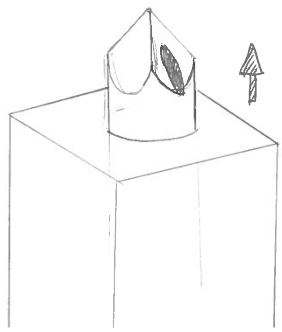
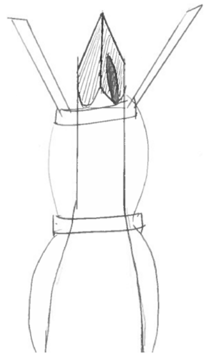
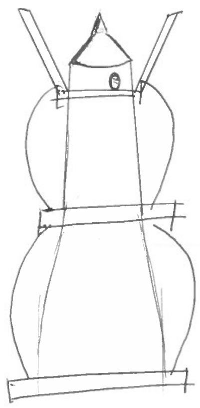
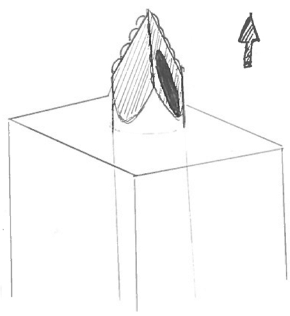
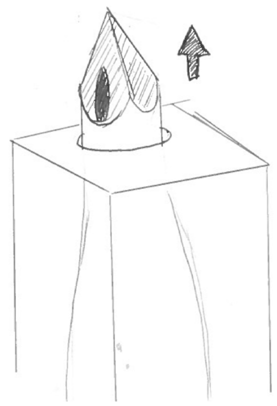
MORPHOLOGY TABLE

The morphology table and the 8 concept paths can be seen in appendix D13, *Morphology table.*



THE 8 CONCEPTS

All the concepts were made on the assumption that some kind of support to prevent buckling and a means against deformation of the tip were needed.

The Cheapest	**The Intuitive**	**The Environmentally Friendly**	**The Reliable**
			
Suitable for injection molding because the needle column is slightly angled. The placement of the hole makes it very easy to manufacture. It has a sleeve, which is estimated to be the cheapest support.	The symmetry of the needle makes it intuitive. The user does not need to consider which way it shall be turned during penetration.	The design of the insulin pen is modified. Only the needle itself is changed between use. This reduces the material use per insulin needle. The needle tip does not have reinforcement with other materials and can be recycled.	Buckling of the needle is prevented by a gradual increase of the cross-section area and the sleeve. The sleeve stretches the skin to prepare it for the injection.
The Safest	**The Painless**	**Nature's Best Call**	**Authors' Favorite**
			
The micro-needle tip punctures the skin and lets the rest of the needle through. The sleeve protects the users from needlestick injuries until use.	Serration barbs at the tip of the needle allow it to penetrate skin with minimal force. The needle has the smallest possible diameter.	This concept aims to combine nature's best solutions. The tip keeps sharp by breaking off. The hole is placed in the side to allow a solid tip. The channel hole is reinforced.	The tip is shaped as a 3-sided pyramid. Coating is added to increase the stiffness of the tip. The diameter of the needle column is slightly increased to make it suitable for injection molding. The needle column is supported during penetration by being shot out of the insulin pen.

DISCUSSION

Even if some of the means are good individually, they might not be good when they are combined with other means. Therefore 8 concepts were synthesized. The morphology table provided a lot of means. Eight concepts were made to narrow the field down. Not all of the means were used in the concepts. There is risk that some of "the good ideas" are lost, because they are not included in the 8 concepts. It is possible to pursue all possible means. The most promising means were validated with experts.

Idea Validation

RESULTS

The principles of the 8 concepts were discussed with experts. A summary of the discussion can be found in appendix D14, *Consulting with Experts*. The following ideas were disused:

- Coating of the needle tip
- Choice of tip geometry
- Polymers for medical use
- Possibility of fibre reinforced material
- Injection molding and precision of the insulin needle

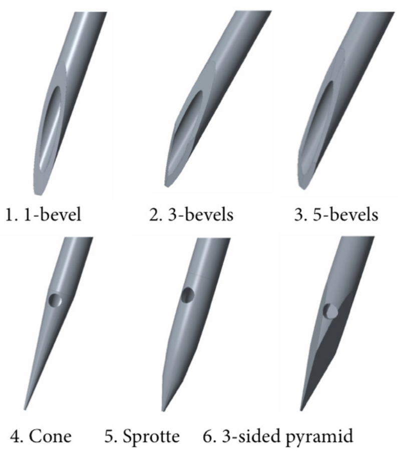
COATING

The idea of increasing the stiffness by *Coating the Tip* was discussed with professor Andy Horsewell and Guido Tosello. Andy Horsewell recommended coating with DLC (Diamond Like Carbon). He has experience with use of DLC coating on metals. DLC is very stiff (Young's modulus as high as steel) (CES, 2014), but also very brittle. Horsewell was asked if he thought there was a risk that some of the coating layer would break off inside the body. He did not think that there would be a high risk. Even if some of the ceramic material would break off inside the skin, Horsewell argued that it would not be a big issue because the material would not react with the body. Guido Tosello is an expert in the field of polymer injection molding. He has experience with DLC on polymers. According to him it will not be possible to make the coating layer sufficiently thick to increase the stiffness and strength of the needle tip. If it is possible to add a thicker layer of coating layer it will contribute to a rounder tip.

TIP GEOMETRY

Steffen Munch argued that amongst the selected tip designs the 3-sided pyramid is the easiest tip geometry to make sharp (appendix D11, *Morphology*). Tosello argued that if injection molding was used as the production method of the needle tip, a selection criterion for the tip geometry should not be easy manufacturing of mold. The price of the mold is irrelevant compared to the amount of needles that need to be produced. In connection with his master project Thomas Dam Paulsen had analyzed different needle tip designs as to distribution of stress during compression. The most promising geometry was the 3-sided pyramid. Furthermore his analysis shows that stress will mainly be concentrated in the very tip of the needle.

Fig. D10. Numerical analysis of needle tip geometries (Poulsen, 07.05.2015).



FIBRE REINFORCED

Senior metallographer Steffen Munch did not believe in a polymer-based insulin needle without use of fibre reinforcement. He believed that adding glass fibres could be a solution. Thomas Dam Poulsen suggested the glass-reinforced Liquid Cristal Polymer (LCP) A130 as a possible material of the insulin needles. LCP A130 is USP Class VI compliant for use in medical devices (Ticona, 2002). USP Class VI is a standard of biocompatibility (Medical Design Briefs, 2014). LCP is a very crystalline polymer with high stiffness. It is generally very suitable for injection molding. Tosello believes that the fibres are too big to make an impact on the stiffness of the tip. The needle would only be stiffer along the length of the beam.

INJECTION MOLDING AND PRECISION

Injection molding is an obvious choice of production method for the polymer insulin needle. Munch argued that the producing of stainless steel insulin needles is very space consuming and this will be a big improvement with injection molding. Tosello argues that one of the advantages of injection molding is that the needles can be made in one process with very fine tolerances. The tip area can be reduced to 15-30 µm. It should be investigated further if this will allow a polymer needle to have a smaller tip area than the NovoFine insulin needle.

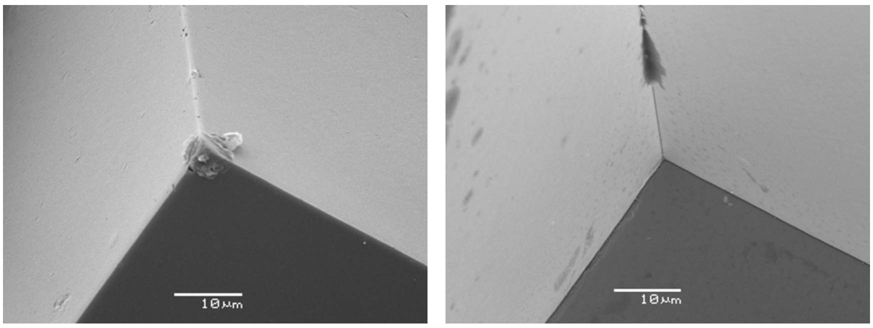


Fig. D11. Micro injection molded polymer part (Tosello et al., 2014).

DISCUSSION

For this project it was chosen to rule out the possibility of obtaining a stiffer needle tip by reinforcement with coating because of Tosello's arguments. The idea should be test in order to confirm his statement, but the right equipment was not available.

The 3-sided pyramid might be the easiest to sharpen, but maybe it was not a relevant selection factor. The 3-sided pyramid needle tip geometry has shown promise from the outcome of both the study of the literature and the consolidation with the experts.

It might be a possibility to choose a fibre-reinforced polymer. A fibre-reinforced polymer could decrease the risk of buckling because the stiffness along the beam could be increased. It should be investigated further, if the fibres will interact with the body in any negative way. Because this project did not have sufficient resources to investigate this further, it was chosen to aim for an unfilled polymer for the needle tip material. Tosello states that it is shown in the literature that a polymer-based micro needle can penetrate the skin without unfilled polymer. Therefore it should also be possible to produce a needle tip in an unfilled polymer that is stiff and hard enough to penetrate the skin. If it can be shown that a polymer-based insulin needle is mechanically plausible with an unfilled polymer, it will also be plausible with a stiffer reinforced polymer. If a further work shows that reinforced polymers are suitable, they can replace the unfilled material.

Concept Screening

PUGH MATRIX

RESULTS

In the Pugh matrix below the 8 concepts are ranked.

	0	1	2	3	4	5	6	7	8
Pain	DATUM	–	+	+	+	+	+	+	+
Price		+	+	+	0	–	–	–	+
Penetriation force		0	+	+	+	+	+	+	+
Production		+	+	+	+	–	–	–	+
Environment		+	+	+	+	+	+	+	+
Recycabliliy		+	+	+	+	+	+	+	+
Durability		–	–	–	–	–	–	–	–
Reliability		–	0	–	+	–	–	–	0
Usability		–	0	+	–	–	+	–	+
Score		0	5	5	4	-1	1	-1	6
Rank		6	2	2	4	7	5	7	1

Fig. D12. Pugh matrix and numbering of the concepts.

No.	Concept name	Rank
0	Stainless steel needle	—
1	The Cheapest	6
2	The Intuitive	2
3	The Environmentally Friendly	2
4	The Reliable	4
5	The Safest	7
6	The Painless	6
7	Nature's Best Call	7
8	Authors' Favorite	1

DISCUSSION

During the screening process it became clear that there was still many uncertainties concerning the properties of the different principles of the concepts. Tests of the principles needed to be made for further validation. The concept *Authors' Favorite* got the highest ranking and was chosen as basis for further work. Some of the promising principles of the other concepts were still kept in mind during the further investigation.

The stainless steel insulin needle was the datum in the Pugh ranking matrix. The resultwas that the stainless steel needle was better than any of the synthesized concepts in the criterion *durability*. The variety between the concepts regarding this criterion was therefore not visible.

Conclusion

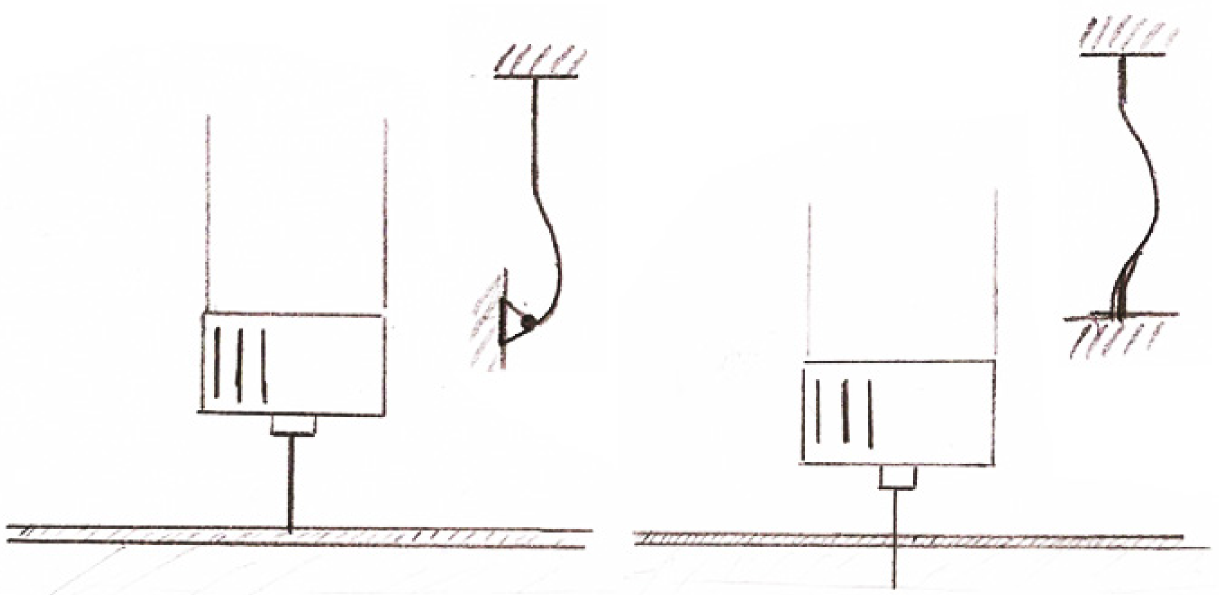
In this chapter it was presented how the chosen concept *Authors' Favorite* was crystalized and how it was selected between other crystalized concepts. The idea generation sessions provided means, which were listed in a function-mean tree. The qualified means from the function-mean tree were listed in a morphology table. The morphology table made the visualization of 8 concepts possible. Aspects of the different concepts were validated with experts. This made a concept screening of the 8 concepts possible. The concept screening was done through a Pugh matrix. The selection criteria were based on criteria from the product specification. *Authors' favorite* got the highest score. In chapter A the main functions of the insulin needle was identified. How the chosen concept fulfils the identified functions is listed in the following table:

Function	**Mean**
Penetration of the diabetic's skin	Very sharp and solid 3-sided pyramid tip ~~Coating~~ The needle column is supported by the insulin pen, which shoots the needle out
Transportation of insulin from an external device into the body of the diabetic	Hollow needle with an asymmetrically placed hole allows a flow of insulin

The concept *Authors' Favorite* originally included a coating of the needle tip with a stiff material. After consultation with the experts this solution was no longer considered attractive. The 8 concepts were synthesized on the assumption that they needed means against buckling and deformation of the tip. Actual calculation and experiments have not yet been made to support this claim. This will be investigated in the following chapter.

Chapter E

CONCEPT TESTING



Introduction

Some of the questions and hypotheses that the former chapters have led to are addressed in this chapter with five experiments. The chapter will start with a section where a polymer material is selected for the polymer based insulin needle concept. The selection of a polymer material provides values for mechanical properties that are used in some of the experiment calculations. The five experiments try to answer following questions:

- Which effects different tip geometries and grinding angles have on the friction force when the needle moves in the skin
- How small the needle tip area of the polymer based insulin needle should be
- What the actual value of the puncture force of the skin is
- If it is necessary to have a support structure on the polymer based insulin needle to prevent buckling
- What angle is the most optimal for a 3-sided pyramid taking tip area and deformation into account.

To help guide the experiments following hypotheses were made:

- *Sharp edges will create lower resistance and lower friction in the skin*
- *A steeper tip geometry will create lower resistance and lower friction in the skin*
- *The tip area of Novo Fine needles is 15 μm²*
- *The needle tip area will deform and thereby increase during penetration*
- *The stress needed to puncture vivo human skin has the same value as the UTS of 30 MPa*
- *The penetration force of a NovoFine needle 32G, 6mm will not exceed the theoretical critical buckling load of a polymer needle with the same column dimensions*
- *An 80° is suitable for the polymer insulin needle tip*

Two of the experiments are conducted in vivo human skin (in one of the authors arm). These experiments were not consulted beforehand with any of the supervisors of the project or any other DTU staff membet. Other experiments were also conducted. The deformations of different needle tip geometries were experimentally investigated, but did not provide clear results. The description of the experiment can be found in Appendix E1, *Deformation Experiment*.

Material selection

METHOD

After studying former research projects and consult with polymer expert Guido Toselleo different PEEK and PEI were investigated. This was done by a Google search on datasheets and with use of CES. Master student Thomas Dam Poulsen encouraged an investigation of LCP datasheets. The mechanical properties of the promising polymers were listed in a table and compared.

RESULTS

	Young's moduls [GPa]	Tensile strength [MPa]	Compressive strength [MPa]	Service temperature [°C]	Suitable for medical use	Thermo plastic
Datum **AISI 304/JISG 4305 Stainless steel**	193-204	520-720	210	-273–870	yes	yes
Duratron U1000 PEI	3,5	129	–	-50 – 170	–	yes
Ketron CLASSIX™ LSG PEEK	4,6	115	–	-50 – 250	yes	yes
VICTREX® PEEK 450G	4,0	98	125	–	–	yes
Ketron 1000 PEEK	4,3	115	–	-50 – 250	–	yes
Ticona VECTRA A950 LCP Unfilled	10,6	182	70	-40 – 180	yes	yes
Ticona VECTRA A130n LCP Glass Reinforced	15,0	190	100	–	–	yes

DISCUSSION

One of the big challenges of using polymer instead of stainless steel is the stiffness, which in average is 100 times lower. PEEK and PEI are known for relatively high strength, stiffness and certification for medical use. The best candidate of the studied PEEK and PEI was *Ketron CLASSIX™ LSG PEEK* with a Young's modulus of 4,6 GPa (see table above).

Thomas Dam Poulsen pointed out that the group of Liquid Crystal Polymers (LCP) had an incredible stiffness in one direction. Several of the LCPs are approved according to USP Class VI (Medical Design Briefs, 2014). The high stiffness is achieved because the polymer chains are ordered in the same direction. The producer of LCP Tirona claims that LCP are very suitable for injection molding (Tirona 2002). LCP A130 glass reinforced has a Young's modulus of 15.0 GPa. As argued in chapter D a fiber-reinforced polymer will not be chosen as basis for the calculations of this project. If it can be shown that it is mechanical plausible to make a polymer based insulin needle without fiber-reinforcement, a fiber-reinforced polymer can always be chosen later on. An unfilled LCP A950 was found with a Young's modulus of 10,6 GPa (appendix E2, *Datasheet of LCP A950*). The tensile strength of the LCP was also better than the studied PEEK and PEI. LCP can withstand very high temperatures, which is good in considering the service temperature. It melts at 280 °C which is quite high for a polymer. Whether it can meet the criteria *Should be able to burn on a bonfire* from the product specification this should be investigated further. The compressive strength of the unfilled LCP A950 is relatively smaller than the compressive strength of the other found materials. This should be investigated further on if the found value is correct and if this will be a problem for the polymer insulin needles. The other properties of the found polymers were quite similar.Young's modulus of LCP A950 will be used in the calculations of this chapter.

Needle Tip Geometries' Impact on Friction

BACKGROUND

Fig. E1. (Cho et al., 2012) Comparison of a porqupine quill and a 18G hypodermic needle

According to O'Leary and Simone, et al. (2003) a 3-sided pyramid has the least resistance against the skin. Furthermore it was found that the porcupine quills require half of the penetration force of a hypodermic of the same size to penetrate human skin (Cho et al, 2012). The phenomenon was assigned to barbs on the quill tip creating stress concentrations, which lowers the friction through skin. Besides from barbs the geometry of the tip of the porcupine quill is steeper compared to a hypodermic needle of the same diameter. It could be assumed that sharp corner edges can resemble the stress concentration of the barbs.

HYPOTHESE

In order to test the effect *the corner angles* and the *steepness* of the tip have on the friction two hypotheses were made.

- *Sharp edges will create low resistance and low friction in the skin.*
- *Steep tip geometry will create low resistance and low friction in the skin.*

Fig. E2. POM needle with different tip geometries

Two sets of five needles with different needle tip geometries were produced and numbered. One set was used in this tip deformation experiment – the other set was used in another experiment presented in appendix E1, *Deformation Experiment*. Insulin needles are very small and not easily manufactured by hand. In order to be able to manufacture the desired geometries by hand, the test subjects were scaled up 32 times. All the needles were made from an 8 mm POM rod, cut into pieces of 90 mm (Fig. E2).

Needle 1: Steep cone
Needle 4: Lowered cone
Needle 5: 4-sided pyramid
Needle 7: 3-sided pyramid
Needle 9: 1-bevelle

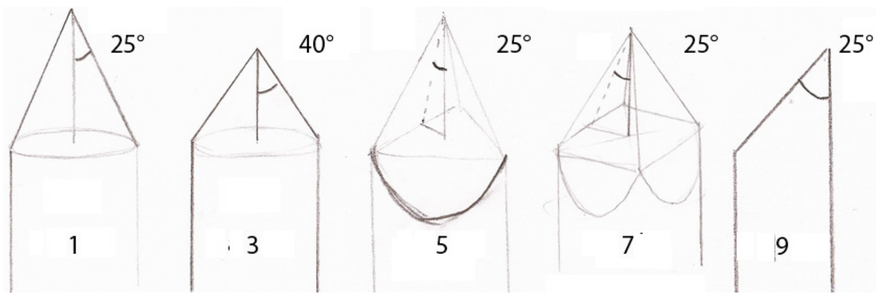


Fig. E3. The pursued angles for the POM needle tips

Fig. E4. Skin model: gelatin powder, polyurethane membrane, and skin model mount.

To achieve very sharp results the tips were grinded with a DP-U2 grinding machine from Struers, with gradually finer sand paper (500 –, 1000 – and 4000 grit). A grinding angle of 25° was pursued on eight of the needles. A grinding angle of 40° angle was pursued at needle 4. The needles were visually inspected using a Light Optical Microscopy (LOM), Leica DM1000. The achieved grinding angles of the needle tips were measured from the LOM pictures. The pictures and the measured angles can be found in appendixE3, *Before and After Pictures of POM needles*.

In the hypodermic needle industry a skin model is used to simulate the mechanical behavior of human skin in experiments. The skin model consists of a thin tough polymer membrane (polyurethane), which is stretched over a gelatin substance. The polymer membrane is supposed to simulate the puncture of epidermis.

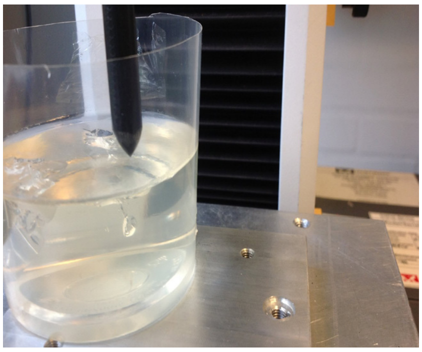


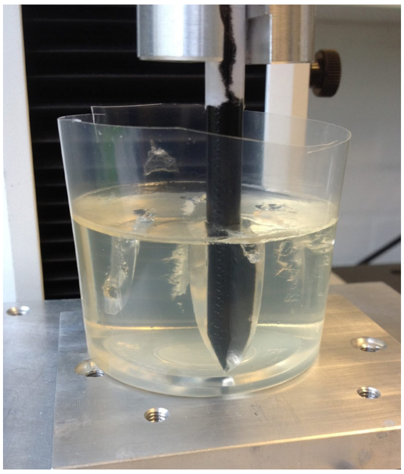
Fig. E5. Experiment setup

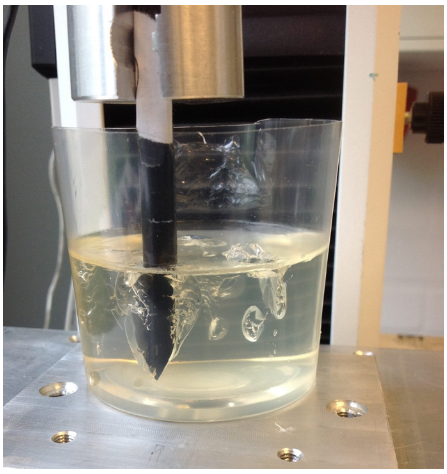
The objects of investigation in these experiments were different needle geometries' effect on the friction in the skin. Therefore the polymer membrane was not used in this experiment. Five samples of the gelatin substance were prepared in transparent plastic cups (appendixE4, *Preparation of gelatin blocks*). A block of gelatin was placed in the bottom of a compression/tensile test machine, 5940 Single Column from Instron. A needle was mounted in the machine and the gelatin block was penetrated. The applied force during penetration of the gelatin block was measured against the distance the needle pressed into the gelatin. The machine pressed down 60 mm/s was stopped after 30 mm. The procedure was repeated five times with the five needles and five samples of gelatin blocks.

RESULTS

The results of the five friction tests are compared to evaluate which tip geometry has the lowest friction force in the gelatin block. Pictures of the needles in the gelatin can be found in appendixE5, *Friction experiment photos*. Fig. E6 show the steep cone and the 3-sided pyramid and their different tracks as they cuts through the gelatin blocks.

Fig. E6. Cutting tracks. Left: cone. Right: 3-sided pyramid





Pictures of all the cutting tracks can be found in appendixE5, *Friction experiment photos*. Fig. E7 shows the test data of the five different needles.

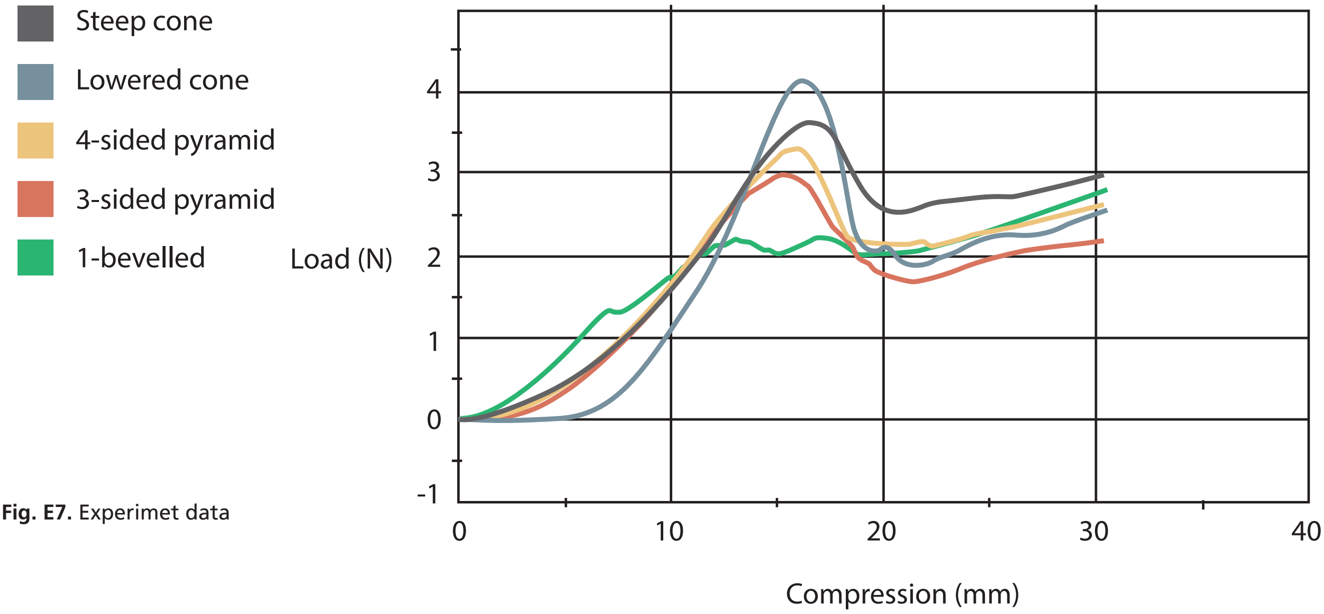


Fig. E7. Experimet data

Each of the curves atFig. E7 have a steep almost linear increment in force until around 15 mm into the skin. At 15 mm most of the graphs have their peak. The peaks represent the point where the needles break through the surface of the gelatin block. Until then the gelatin has been compressed under work of the applied load and elastic energy is stored. After the peak the forces quickly decrease as the needles moves in to the gelatin block and the elastic energy is restored. As the curves flatten they slowly start to increase again. This is because the friction increases the longer the needles have moved in to the gelatin.

The expected ranking of the lowest friction according to the hypothesis and the actual ranking of the friction at two given distances in the gelatin are listed in the table bellow.

Fig. E8. The expected ranking of the lowest friction according to the hypothesis and the actual ranking of the friction in the gelatin at 15 mm (just before the needles punctured the gelatin) and at 25 mm (after the needles have punctured the gelatin). 1 is given to the geometry with lowest (expected) friction. 5 is given to the geometry with highest (expected) friction.

Needle	**Geometry**	**Expected Ranking**	**Actual ranking** At 15 mm (pressure)	**Actual ranking** At 25 mm (friction)
1:	Steep cone	4	4	5
4:	Lowered cone	5	5	2
5:	4-sided pyramid	2	3	3
7:	3-sided pyramid	1	2	1
9:	1-bevelled	3	1	4

Before the peaks the slope of the five curves are similar. Among the symmetric tips (needle 1, 5 & 7) the 3-sided pyramid break through the gelatin with the lowest force. When the symmetric tips move inside the gelatin, the 3-sided pyramid has the lowest friction force and the steep cone has the highest. Comparing the two cones (needle 1 & 4) the steep cone broke through the sur-

face of the gelatin at the lowest force. The lowered cone had the lowest friction when moving inside the gelatin.
The beveled tip (needle 9) generally has a more flat curve than the others. It breaks through the gelatin surface at a lower force. When the experiment was stopped it had a higher friction force than both of the pyramid shaped tips and the lowered cone.

DISCUSSION

EFFECT OF GEOMETRY

Visual comparisons of the needle tips with LOM showed that the tips were not equally sharp before the experiment. This could have influenced which geometries cut through the gelatin surface at the lowest force. A very small tip diameter and sharp edges on the sides seem to help puncture and cut through the gelatin(AppendixE3*Before and after magnifications of polymer needles*). The pyramid geometries seem to have sharpest tips. The easier it is to manufacture the sharper it gets. The two cone geometries seem to have higher friction than the pyramids when moving inside the gelatin. The lower friction of the pyramids could be because of the sharp edges on the pyramid sides. At Fig. E6 the cutting tracks of the 3-sided pyramid and the steep cone can be observed. A reason why the 3-sided pyramid has lower friction than the 4-sided could be that the edges on the 3-sided pyramid are sharper because of the smaller corner angle in the triangular cross section area.

EFFECT OF ANGLE

The lowered cone breaks through the surface at a higher force than the steeper cone but the steeper cone creates a higher friction force in the gelatin. The behavior of the two cone geometries could maybe be explained by the theory that the lowered cone has a larger contact area with the gelatin. Therefore it had a lower stress concentration at a given force than the steep cone on the surface. The higher puncture force of the lowered cone might have left a wider gab for the needle to penetrate. This could be why the friction was lower for the lowered cone. This phenomenon is similar to an observed phenomenon described in Chapter C, where a flat punch created a ring crack in the skin, and the a sharp needle a planar crack (Shergold and Fleck, 2005). The ring crack caused more damage to the skin.

Tip Area of NovoFine Insulin Needle

BACKGROUND

In chapter D a picture of an injection molded polymer part was shown with a tip area of 15-30 $\mu m^{2.}$ Will this precision be enough? To get an idea on how small the tip area of a polymer insulin needle needs to be, it is relevant to investigate the tip area of the existing insulin needle. This can be used, as reference on which dimensions the polymer based insulin needle should have. It is also interesting to examine if the existing insulin needles deforms during penetration, and if it does how much?

HYPOTHESES

– *The tip area of Novo Fine needles is 15 µm2.*

– *The needle tip area will deform and thereby increase during penetration*

METHOD

Two NovoFine 32G 6mm needles were investigated. The outer and inner caps of the needles were carefully removed prior to the microscopy. Photos of the tips of the insulin needles were taken at different angles by a scanning electron microscope (SEM), Phenom ProX. In order to take a SEM picture the surface of specimens must be electrically conductive. The insulin stainless steel needles are coated with silicone. Gold coating was needed to make the surface electrically conductive. The two needles were coated with gold one at the time, at 15 mA in 150s. According to the coating machine's datasheet, coating with 15 mA in 150 s will result in a coating layer of 8 nm gold. After the pictures were taken the needles were by hand pressed perpendicularly into the surface of the skin model. The needle was not sterile after the gold coating process. The skin model was used as the penetration medium, because it was not found responsible to penetrate vivo skin with a coated needle. After the penetration of the skin model, the needles were recoated with gold at 15 mA in 90 s in the same coating machine. SEM pictures were taken again, and the tip areas of the NovoFine needles after the penetration were estimated.

RESULTS

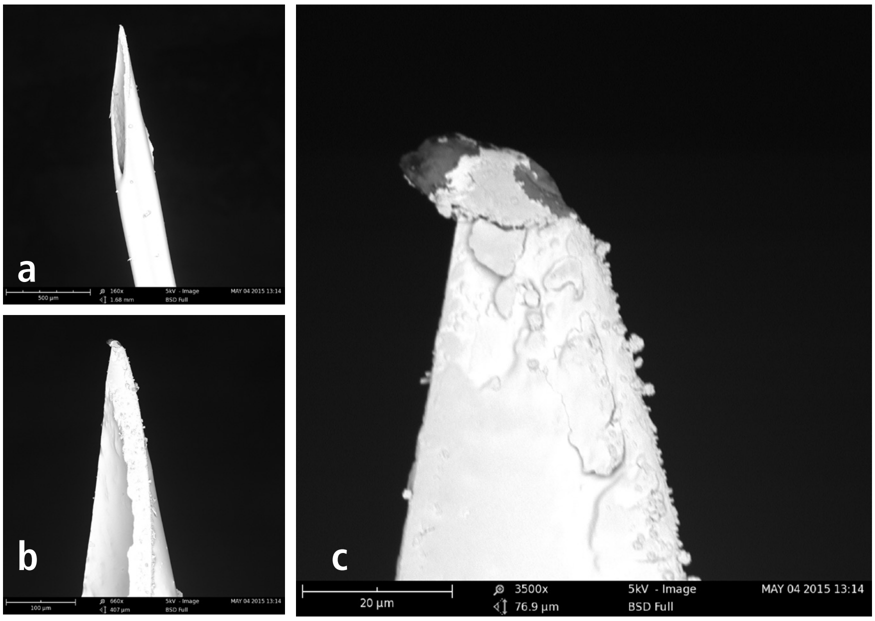


Fig. E9. SEM. Insulin needle 1 before penetration of skin model – **view 1** note scale bars. a: 500 µm. b: 100 µm. c: 20 µm

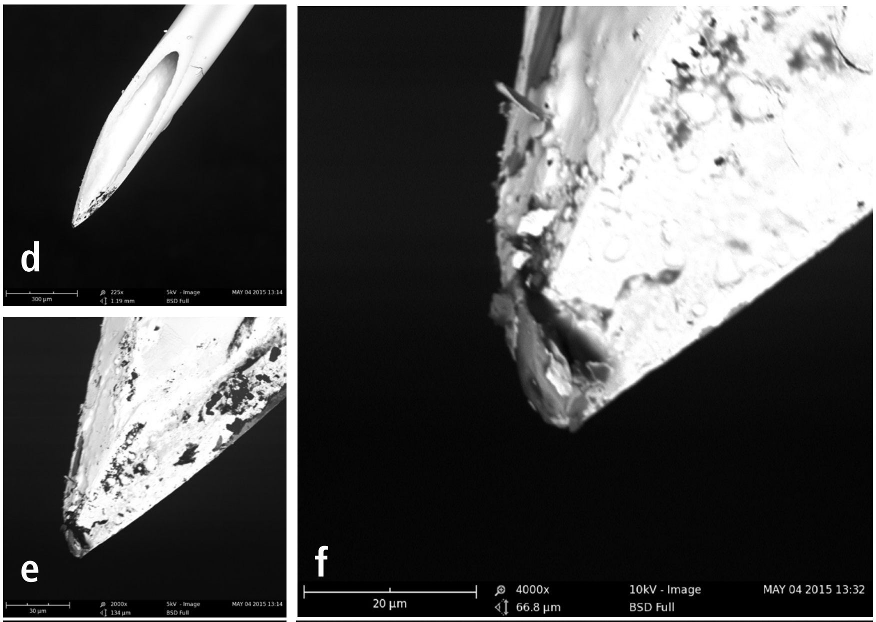


Fig. E10. Insulin needle 1 before penetration of skin model – **view 2**. Numbers on scale bars. d : 300 µm. e: 30 µm f: 20 µm

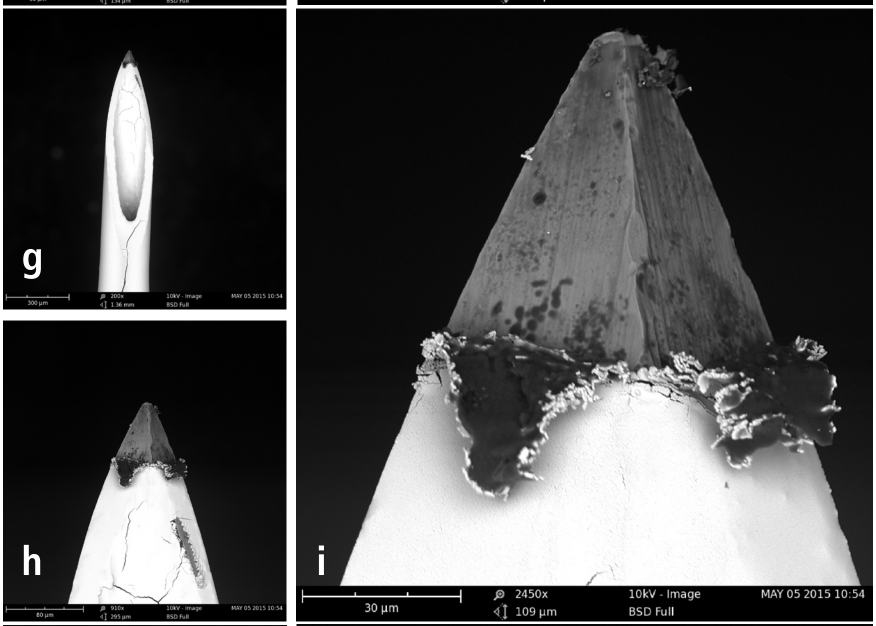


Fig. E11. SEM. Insulin needle 2 before penetration of skin model- **view 3**. Numbers on scale bars. g : 300 µm. h: 80 µm i: 30 µm

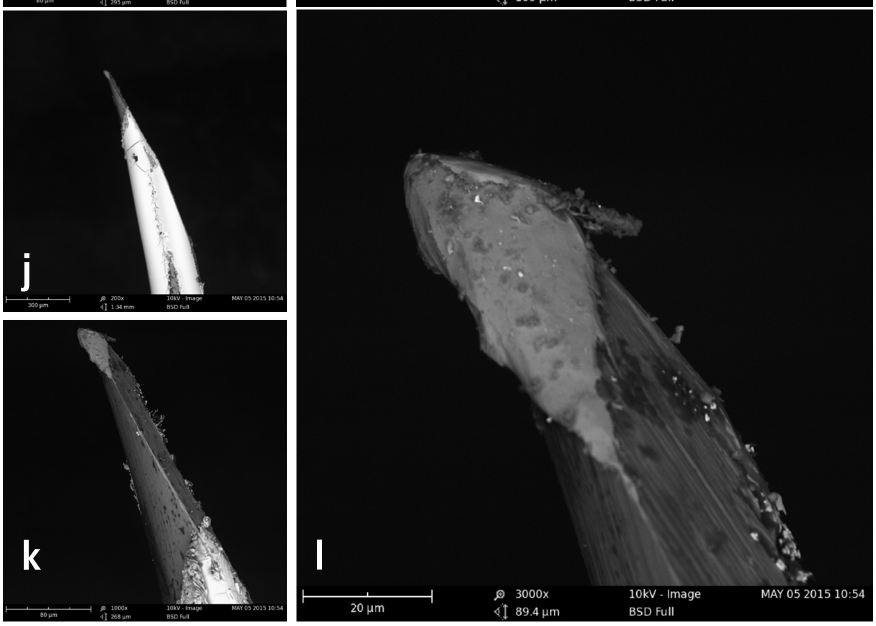


Fig. E12. Insulin needle 2 before penetration of skin model- - **view 6**. Numbers on scale bars. j: 300 µm. k: 80 µm l: 30 µm

All of the before and after SEM pictures of the NovoFine needles can be found in appendix E, *SEM of NovoFine needle before and after penetration*. The grinding edges of the needles are frayed. The needles are covered in a layer reflecting white on the pictures. The white layer has “cracks” at the sides. A difference between the two needles was noticeable at a magnification of 100 times. The tip was measured from two different angles.

Insulin needle	**Tip area before penetration**	Tip area after penetration
No. 1	15 x 20 µm	25 x 40 µm
No. 2	10 x 5 µm.	30 x 25 µm

Needle no. 1 has a bended round tip. The tip area is from the pictures of view 1 and view 3 measured to be around 15x20 µm. Some of the white layer is missing at the tip. The first 65 µm of insulin needle no. 2’s tip has a dark color. The white layer looks like it is “pealed” off from the top of the tip. The pealed material is measured to have a thickness of around 0,5 µm from view 3. Furthermore the tip of the insulin needle appears bended. The needle tip is estimated to have a tip area of 10 x 5 µm from view 3 and view 6.

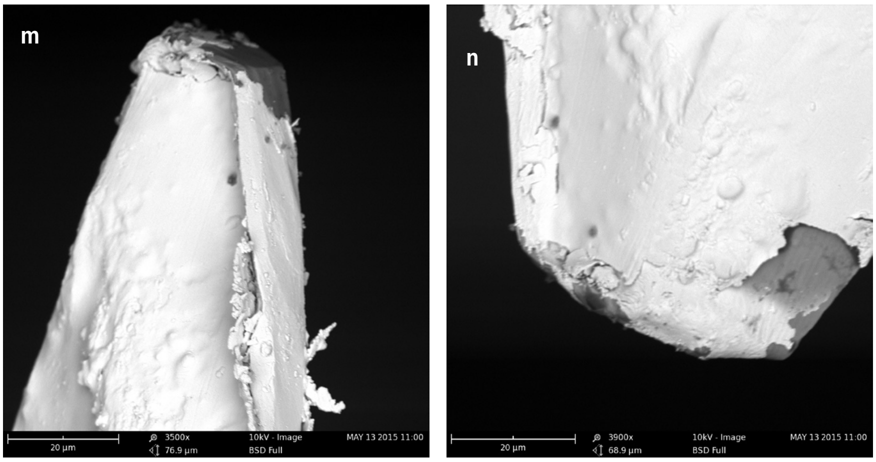


Fig. E13. m = veiw 1, n = **view 2**, number on scales: 20µm

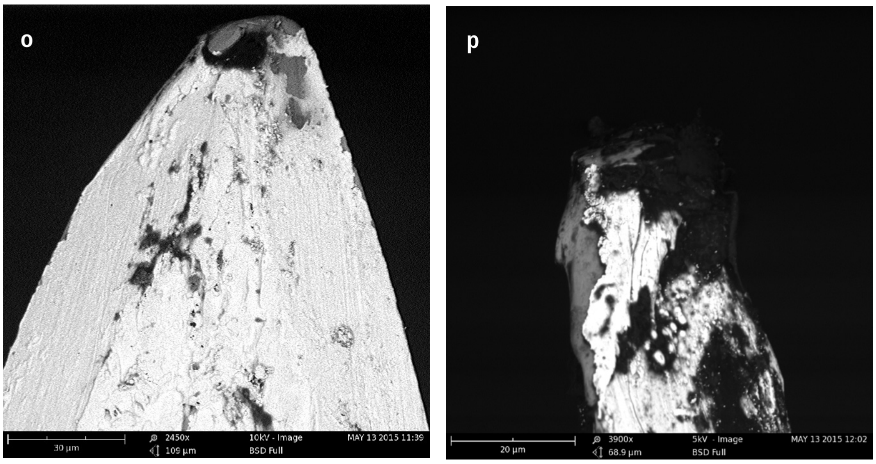


Fig. E14. o = veiw 3, p = **view 6**, number on scales: o: 30µm, p: 20µm

After the penetration of the skin model needle no. 1 seemed to have a tip area of 25 x 40 µm and needle no. 2 seemed to have a tip area of around 30 x 25 µm.

DISCUSSION

The "white" layer on the SEM photos is most likely the outer silicon layer of the needles. The pealed layer seen on needle no. 2 is not likely to be only the gold coating layer. It has a thickness of around 500 nm (see view 3) and the gold coating layer should according to the datasheet have a thickness of only 8 nm. The frayed needle edges are most likely marks after the grinding process of the needle. At view 1 the round tip of insulin needle no. 1 looks like a "chip" from the grinding process. On view 2 the tip looks like it is bended. The bending of the needle tip could be caused by something that bumped into the needle tip either before packing or during removal of the inner insulin needle cap. Even if the needle tip after the grinding process has a smaller diameter than 10 µm, the tip area that counts in relation to the penetration force is the one the insulin needle has after the user has removed the inner cap just before he/she uses the needle.

The approximation of the NovoFine needle tip area is only based on 2D photos from different angles taken with two different needles. There is a high risk that the two NovoFine insulin needles from the experiment are not statistically representative of the needle tip area. An improvement of the experiment would be to take 3D photos of the tips, and to do it on a statistically significant amount of needles.

The representative value of the tip area of the insulin needle after deformation can also be questioned. The needles were in-between the photos penetrated into a skin model. The skin model might have s higher tensile strength than the average skin, and therefore cause more deformation of the needles' tip areas.

Puncture stress of human skin

THEORY

The puncture force for a needle in the skin depends on the tip area of the needle. The puncture force can be estimated by Hook's law (Riley et al. 2002, p. 117-118):

$$p = \frac{F}{A}$$

Theoretically the pressure (p) that is needed to puncture epidermis should not vary even though the tip area (A) does. The insertion force (F) will on the other hand depend on the tip area. A smaller tip area will result in a smaller force required to penetrate the skin. In the academic literature study in chapter C the value of the pressure to puncture the skin was estimated by the ultimate tensile strength (UTS) of the skin. As previously mentioned in Chapter C the theoretical curve for penetration of the skin will look like Fig. E15.

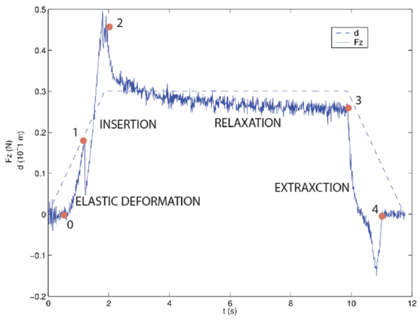


Fig. E15. Phases of skin penetration

The penetration force will rise until the needle applies a stress equivalent to the UTS of the skin is reached (according to the assumption) and the skin will puncture. After puncture the penetration force will drop instantaneously and again rise to a penetration force higher than the puncture force, due to the friction in the skin. The values of UTS found in the literature varied from 2-30 MPa. The highest UTS value of 30 MPa was chosen as value that should be used for calculations of what the needle should be able to withstand. Even though the highest value of UTS is chosen, it is not sure that it will be high enough to represent the stress needed to puncture the skin. The UTS values from the literature were based on tensile tests and preformed in vitro specimens.

HYPOTHESIS

– *The stress needed to puncture vivo human skin (UTS) is 30 MPa*

METHOD AND MATERIALS

Six NovoFine 32G, 6mm were used to puncture the skin of a living human upper arm on a woman of age 24 years. The needles were on turn mounted in a compression/tensile test machine, 5940 Single Column from Instron. The same program as in the experiment *"Needle Tip Geometries' Impact On friction"*.
The two first data sets were made in the inner side of the upper overarm, and the four others in the outer side of the upper arm. The needle was stopped after it was clear that the needle has punctured the skin (around 2 mm into the skin).

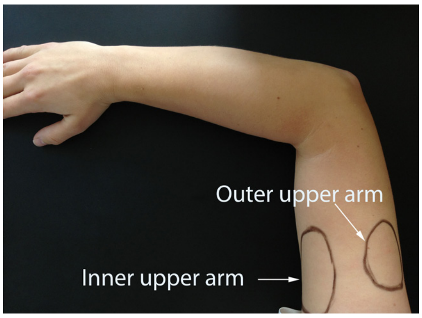


Fig. E16. Upper arm of the test person

The data from the six experiments was plotted in a graph, and interpretations of the value of the puncture force were made. These were together with the NovoFine needle's tip area estimates from the experiment *Tip Area of NovoFine Insulin Needle* used to estimate the stress needed to puncture the human skin according to Hook's law. The estimate included a maximum and minimum value of the stress.

RESULTS

PUNCTURE FORCE

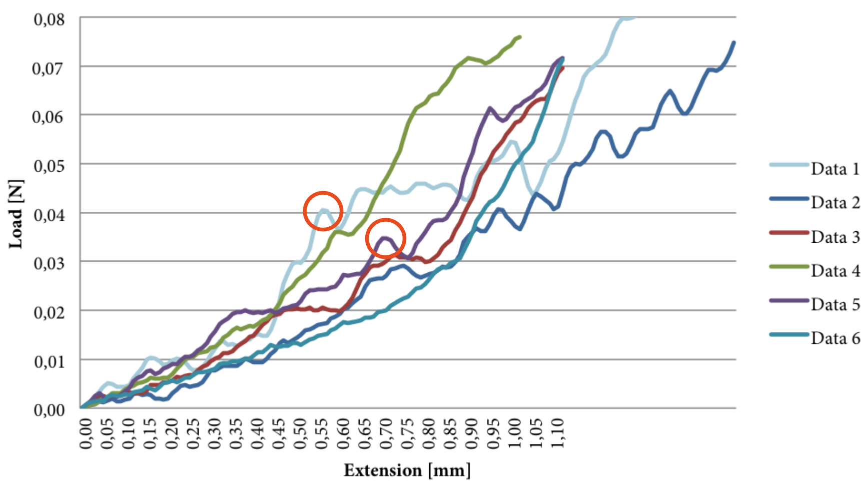


Fig. E17. Penetration of upper arm with NovoFine needle

The data of the six experiments repetition are plotted in Fig. E17. From the look of the curves it seems as if there are a lot of "noise". The functions of the data do not have any clear peaks, and it is therefore difficult to estimate when exactly the needle punctured the skin. The data sampling was stopped after the needle had punctured the skin. From Fig. E17 it can therefore be conducted that the puncture force must have been less than 0.07 N. In dataset 1 and dataset 5 it seems as if the first significant peaks are at 0.04 N and 0.035 N. The other dataset also seem to have peaks in between the interval 0.03-0.04 N.

The tip areas of the two NovoFine needles from the experiment *Tip area of NovoFine insulin needle* was estimated as followed:

Insulin needle	**Tip area dimension**	**Tip area**
No. 1	15x20 µm	300 µm2
No. 2	10 x 5 µm.	50 µm2

These were together with the estimate of the smallest peak (0.03 N) and the highest possible puncture force value (0.07 N) used to calculate a minimum and maximum scenario value of the stress needed to puncture the skin:

Minimum scenario:

$$UTS_{min} = \frac{F_{min}}{A_{max}} \frac{0.03\ N}{300 * 10^{-12}\mathrm{m}^2} = 100\ \mathrm{MPa}$$

Maximum scenario:

$$UTS_{max} = \frac{F_{max}}{A_{min}} = \frac{0.07\ N}{50 * 10^{-12}\mathrm{m}^2} = 1400\ \mathrm{MPa}$$

DISCUSSION

The calculated puncture stress values of the skin range in an interval of 100-1400 MPa. The values are 3-45 times bigger than the maximal UTS value suggested in the literature. There are three possible reasons to explain this:

- The stress required to puncture the skin will not have the same value as the UTS of the skin
- The UTS value of in vitro human skin in the literature cannot be used to estimate the UTS value of in vivo human skin.
- The values of the stress needed to puncture the skin estimated in this experiments are incorrect.

All the three reasons could be valid. Possible source of errors in the experiment could be:

- Hook's law does not take into account the fact that the penetrating media can be elastic and fold around the sides of the tips or that the force will not be distributed equally around the tip. In reality there will be a larger contact area between the needle and the skin. Because of this the actual stress to puncture the skin must be lower than the estimation shows.
- It is difficult to make a conclusion on the exact value of the puncture force of the skin from Fig. E17. From the graph it can was concluded that the puncture force of the test person's upper arm is less than 0.07 N when a NovoFine

needle is used. The puncture force is most likely less than this, because the whole needle head had penetrated the skin, when the machine was stopped. It cannot be concluded with certainty how much smaller the puncture force will be from the data. Because of the reaction time to stop the machine after the puncture of the skin, it seems likely that the puncture of the skin appears before the peaks in the interval 0.03-0.045 N.

- Another source of error could be movement of the test person or the mounting of the needle. The compression/tensile test machine is extremely sensitive. If the test person or the needle moved during penetration this could cause noise.
- Insulin injections are typically given in the stomach or in the thighs. It was not possible to place the stomach or thighs of test person in the test machine in an appropriate manner.

In order to get more clear results, the experiment should be repeated multiple times. In a repetition of the experiment it could be aimed to do the tests in body parts normally used for insulin injections. The data are all made from penetrating the skin of the same person. In order to get general values of the penetration force with NovoFine needles, the experiment should be conducted on different humans of different age, weight, sex, race, lifestyle etc.

Buckling of the needle beam

BACKGROUND

In the academic literature study of chapter C it was found the critical buckling load depends on the stiffness of the material, the second moment of area, the effective length of the column and how the ends of the column are fixed. During penetration in the boundary condition of the fixation of the insulin needle column will change form clamped/simple supported to calmped/calmped (Fig. E18). The length of the beam will also vary. Four theoretical expressions to describe the critical buckling load were presented. A sleeve solution to prevent buckling developed in two former bachelor thesis was introduced (Johansen and Borensen, 2013 & Mortensen and Rasmussen, 2015). But is buckling an issue for a polymer based insulin needle?

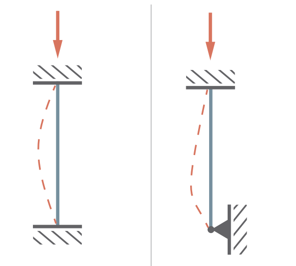
Deflected shape		
Critical Load	$\frac{4\pi^2 E I}{L^2}$	$\frac{2.046\pi^2 E I}{L^2}$
Critical Load at Variable Length	$\frac{4\pi^2 E I}{(L-x)^2}$	$\frac{2.046\pi^2 E I}{(L-x)^2}$

Fig. E18. The four theoretical expressions to describe the critical buckling load with presented in Chapter C.

HYPOTHESIS

- *The penetration force of a NovoFine needle 32G, 6mm will not exceed the theoretical critical buckling load of a polymer needle with the same column dimensions.*

METHOD

Using the formulas presented in chapter C four theoretical expressions for the critical load were calculated and plotted in a graph. One with the boundary condition clamped/clamped and one with boundary conditions clamped/simple supported. Both expressions were calculated with a constant and a varying length. The Young's modulus in the calculations is based on a Young's modulus of LCP A930. The dimensions of the needle are based on the existing stainless steel needle simplified to a column.

A NovoFine 32G, 6mm needle were mounted in the compression/tensile machine, 5940 Single Column from Instron. The needle was penetrated 5,5 mm into the outer upper arm of the test person. This was done by to the same procedure as the experiment in *Insertion pressure to pierce vivo human skin*. The procedure was repeated six times. The experimental data and the four calculated theoretical expression were then plotted together in a graph and compared.

RESULTS

The data used to calculate the four theoretical expressions for the critical load:

L	=	$6{,}0 \cdot 10^{-3}$	m
E	=	10,6	GPa
I	=	$112{,}5 \cdot 10^{-14}$	m^2
I	=	$(0{,}23\ mm/2)^2\pi - (0{,}15\ mm/2)^2\pi$	

The four functions are plotted as force against displacement of the needle into the skin in Fig. E19. Fig. E19 show the first 30 N.

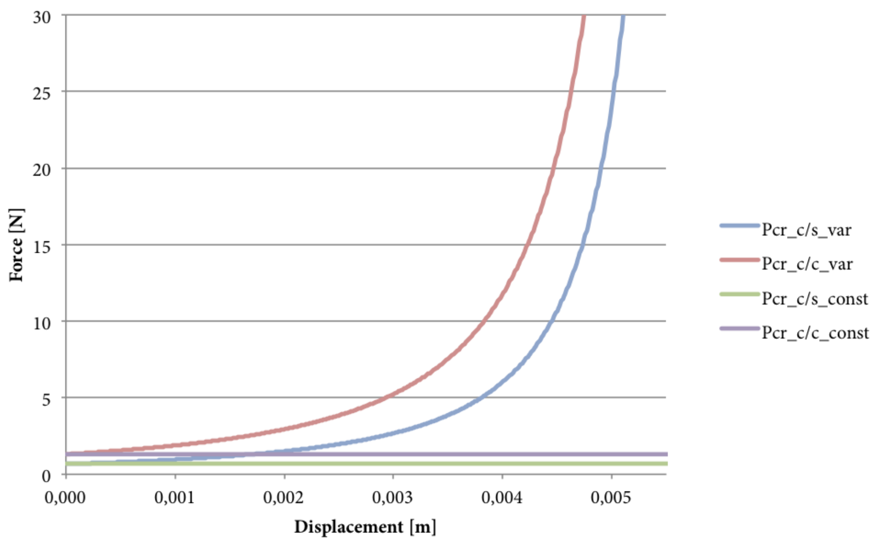


Fig. E19. Theoretical critical buckling load for polymer needle

The clamped/simple supported boundary conditions with a constant effective length (Pcr_c/s_const) and varying effective length (Pcr_c/s_var) give a critical buckling value at puncture of 0.67 N. The clamped/clamped boundary conditions with a constant effective length (Pcr_c/c_const) and varying effective length (Pcr_c/c_var) give a critical buckling value at puncture of 1.31 N. The critical load for the two curves with a decreasing effective length increases exponentially. When the needle is between 3 - 4 mm into the skin the critical load of the two curves with a decreasing effective length passes 5 N.

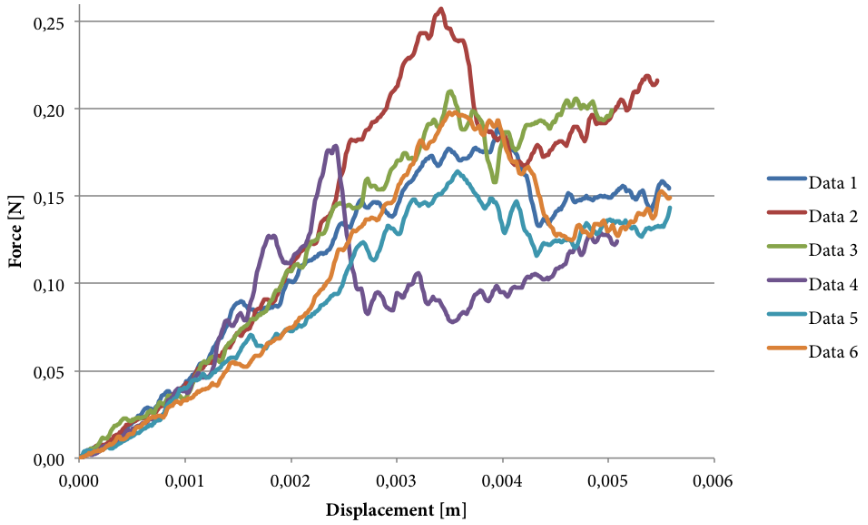


Fig. E20. Sequence of force during penetration of upper arm.

The data from penetrating the upper arm in vivo is plotted in the graph at Fig. E20. The six curves are not identical, but they have some common features. At a distance approximately 1.3 mm into the skin the six curves have roughly the same slope. After this point the penetration force rises until the needle is around 2.5 mm – 4 mm into the skin. Then the penetration force starts to decrease. The maximal penetration force of the six curves is between 0.17 and 0.26 N.

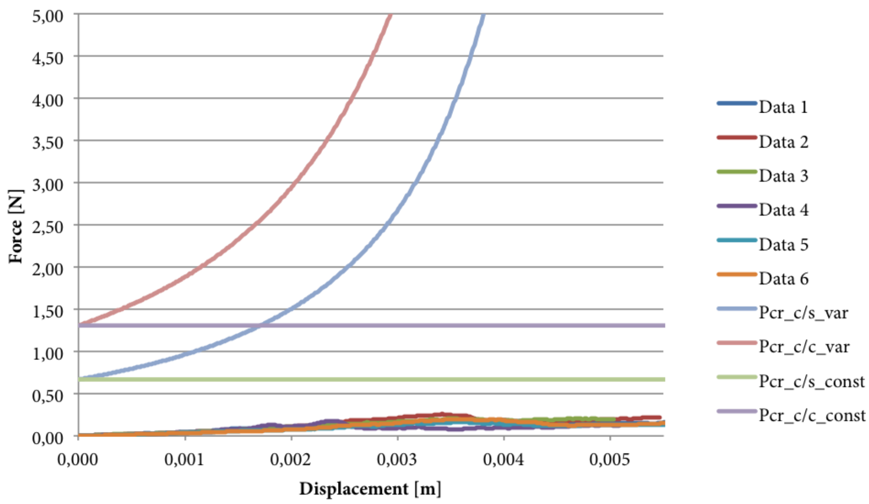


Fig. E21. Critical Buckling load with two different boundary conditions. The length varies as the needle penetrates the skin.

At Fig. E21 the two main graphs from the experiment are plotted in the same view. None of the curves of the penetration force exceed any of the four expressions of the critical buckling load.

DISCUSSION

The expression with the clamped/simple boundary condition and decreasing effective length does not make sense. As soon as the needle goes down in the skin, the skin will provide more support to the needle than a "pinned join" would. On the other hand the skin has some form of elasticity so the boundary condition clamped/clamped will neither resemble the reality. It is therefore suggested that the function for the critical buckling load is something in between the functions of the boundary condition clamped/simple supported and clamped/clamped with a varying effective length. A suggestion for the function of the critical load for the insulin needle made in A950 LCP is sketched inFig. E22.

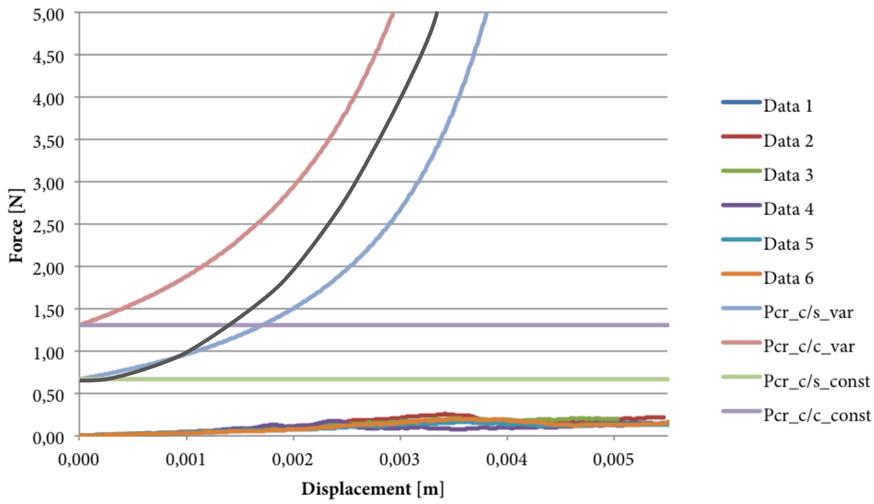


Fig. E22. The real creatical buckling load with combined boundary condition

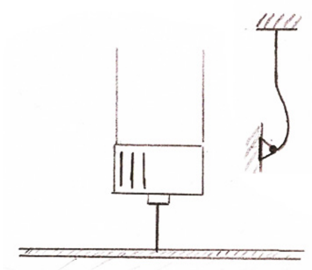


Fig. E23. Insulin needle on skin surface. clamped/simple boundary condition.

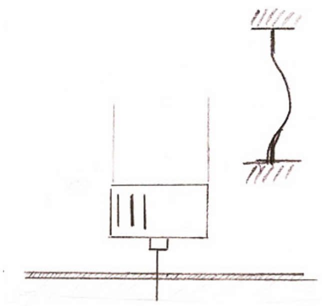


Fig. E24. Insulin needle on skin surface. clamped/clamped boundary condition

The critical part in relation to risk of needle column buckling seems to be within the first 1.5 mm of penetration. It is here where the penetration force is closest to the critical buckling load. From Fig. E22 there seems to be a theoretical safety factor of 20 during the most critical part of the penetration. These calculations suggests that a support structure against buckling such as a sleeve might not be necessary to add to the 6 mm insulin needle made of LCP A950.

This claim has to be investigated further on. The area that needs to be investigated includes:

- Which effect the tolerance of the column cross-section area has on the critical buckling load
- If the puncture force of a polymer based insulin needle will be equivalent to the puncture force of the stainless steel needle.
- What effect it has that the needle in fact is not a complete column but has a different geometry at the needle head

To increase the critical buckling load following adjustments could be made:

- The cross sectional area could be increased to fit the dimensions of the insulin needle model 30G
- The length of the column could be shortened to have the length of the insulin needle model of 4 mm.

Angle Optimization

BACKGROUND

This theoretical experiment aims to determine which slope angle is suitable for the 3-sided LCP pyramid shaped tip. Axial deformation and beam deflection will be taken into account.

In the experiment *Needle Tip Geometries Impact on Friction* it was concluded that a steep tip creates a high stress concentration on the skin. In chapter C it was argued that a steep tip has higher risk of deforming. In chapter C it was concluded that the biggest stress the needle tip is exposed to during the penetration process, is when the needle is puncturing the outermost layer of the skin. This leads to that the needle tip will be exposed to most deformation during puncture of the outermost layer of the skin. In the experiment *Puncture Stress of Human Skin* the puncture stress of the outermost layer of vivo human skin could not be determined. Neither could the exact puncture force the NovoFine needle needs to apply to the skin in order to puncture it be determined. According to the experiment the puncture force of the skin using a NovoFine needle was less than 0.07 N. How much smaller was not known. Because it was not possible to determine a qualified value of the puncture stress of human skin the puncture force of 0.07 N will be used in these calculations.

HYPOTHESIS

- *A slope angle (θ) of 80° is suitable for the 3-sided pyramid insulin needle in relation to the tradeoff between deformation resistance and sharpness*

METHOD

To examine the hypothesis the maximum accepted slope (θ) of the 3-sided pyramid tip was investigated in relation to deformation of the tip. Two different methods were used. First axial compression and then beam deflection was examined of the first 100 μm of the needle tips.

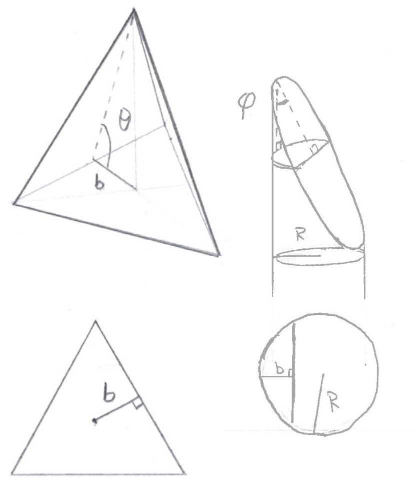
- The increment of tip area of a beveled stainless steel needle exposed to a load of 0.07 N (A_{bevel_end}) was calculated by combining the theory of *Non-Uniform Axial Compression* (Riley, 2002, p.128-129) with theory of *Poisson's Ratio* (Riley, 2002, p. 120). The tip area of the polymer-based insulin needle after it has been exposed to load of 0.07 N should not exceed A_{3pyr_end}. The smallest tip area possible to produce with today's microinjection molding methods, was chosen as the tip area of the polymer-based insulin needle before deformation (A_{3pyr_start}). It was then examined what would happened if the A_{3pyr_start} was exposed to the load of 0.07N. The cross-section area after deformation (A_{3pyr_end}) was found as a function of the angle θ*. The function of* the angle θ *was plotted in a graph against* A_{3pyr_end}. From the graph it could be seen which maximal slope angle θ would give $A_{3pyr\_end} \leq A_{bevel\_end}$. The maximal slope angle θ that resulted in $A_{3pyr\_end} \leq A_{bevel\_end}$ was desired, because this would make the tip of the polymer-based needle as steep as possible without causing A_{3pyr_end} to be bigger than the area of A_{3pyr_end}
- The theory of *Beam Deflection by Integration* (Riley, 2002, p. 494-495) was explained in chapter C. With the use of this theory it was calculated how much the 3-sided pyramid would deflect depending on the angle θ

ASSUMPTIONS

The following material values was used in the calculation:

- E_{steel} = 200 GPa (CES, 2015)
- v_{Steel} = 0.3 (CES, 2015)
- E_{LCP} = 10600 MPa (appendix E$,…)

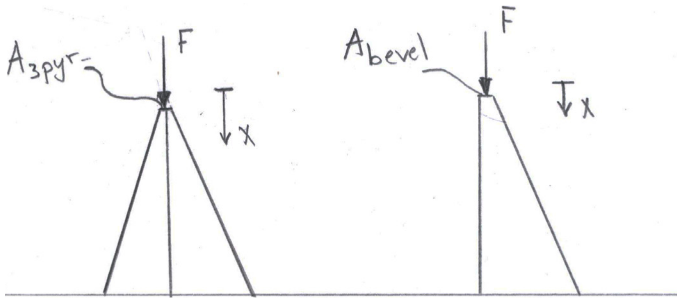
Fig. E25. Angles (θ/φ) and cross-section area of beveled and 3-sided pyramid tip.



– v_{LCP} = 0.4 (Sumitomo Chemical, no date)
Note: Poisson's ratio of the exact LCP was not possible to find

– *Axial deformation*. The 3-sided pyramid tip has a triangular cross-section area. The beveled tip has a cross-section area, is described as a circular segment (Fig. E26). Both tips are assumed to be solid. The smallest found NovoFine tip area in the experiment Tip area of the NovoFine insulin needle was 50 μm2. This value of this tip area is used as the tip area of the beveled stainless steel needle (A_{bevel_start}). The grinding angle (φ) is 14°. To make sure that the puncture force of the polymer-based insulin needle do not exceed the puncture force of the NovoFine needle it was determined that the two needles must have the same resulting tip area when they are compressed by a load of 0.07 N. The two tips are affected by the load F in the points x_{3pyr_start} and x_{bevel_start} where they each have the tip areas A_{3pyr_start} and Abevel_start (Fig. 26). x = θ is where the cross-section areas are equal to θ.

Fig. E26. 3- sided pyramid tip and beveled tip affected by the load F.



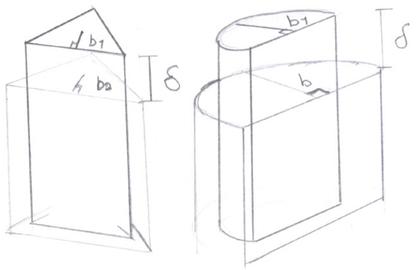


Fig. E27. Poisson's ratio. The expantion of b is calculated

The theory of *Poisson's Ratio* says that a rod, which is vertically compressed, will expand equally in all horizontal directions. The material resistance to compression depends on Poisson's ratio of the material. A high Poisson's ratio gives a large expansion (Riley, 2002, p. 120). The beveled stainless steel tip and the 3-sided pyramid tip are assumed to be straight rods. The cross-section areas of these rods are equal to the tip areas of the needles before compression. The expansion of the lengths *b* on the rods are calculated (see Fig. E27).

– *Beam deflection.* The 3-sided pyramid needle tip is simplified to be a 3-sided pyramid shaped beam fixed in one end. The other end is affected by a load of 0.07 N (Fig. E28).

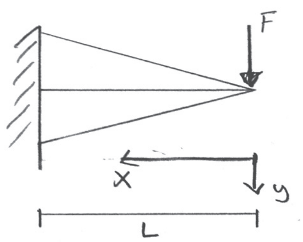


Fig. E28. Beam deflection of a 3-sided pyramid needle tip

RESULT

– The calculations of Axial Compression can be found in appendix E7 *Angle Optimization Axial*. The correlation between x and the cross-section areas of a 3-sided pyramid and a beveled tip are derived in appendixE8, *Cross-Section Areas*. By microinjection molding it is possible to achieve a tip area of 46 µm2 (4.6 * 10-11 m2) (Tosello, 2014). The tip area of the beveled stainless steel needle after elastic deformation by a load of 0.07 N (Abevel_end) was calculated to be 50.0089 µm2. This gives that the tip area of the 3-sided pyramid shaped LCP tip after deformation should be A3pyr_end ≤ 50 µm2 (5 * 10-11 m2).

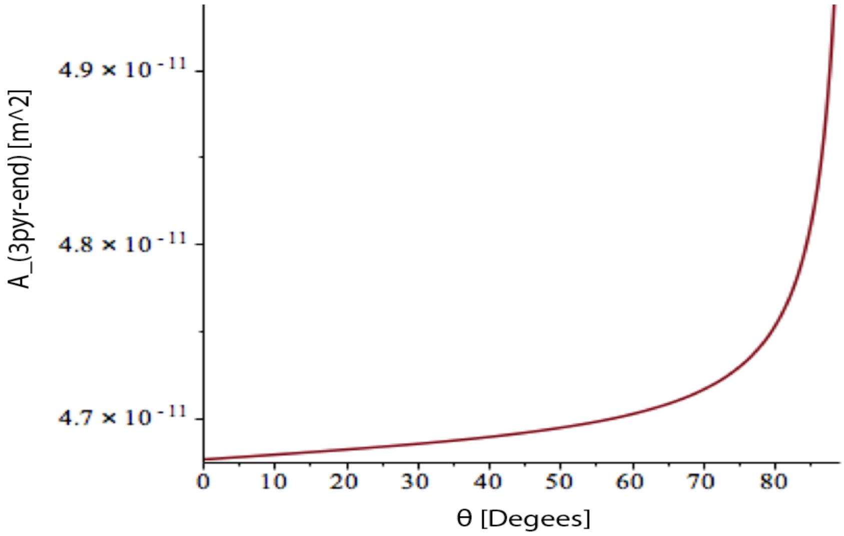


Fig. E29. Correlation between the slope angle (θ) and the resulting tip area of a 3-sided pyramid LCP tip ($A_{3pyr\text{-}end}$) with $A_{3pyr\text{-}start} = 4.6 * 10^{-11}$ m^2.

Fig. E29 shows the $A_{3pyr\text{-}end}$ as a function of the slope angle (θ). The break of the curve is at around θ = 80°. After this point the resulting cross-section area starts to grow rapidly. An angle of θ = 80° gives $A_{3pyr\text{-}end}$ = 47.5 µm^2 (4.75 * 10^{-11} m^2). This is smaller than A_{bevel_end}.

– The defection of the 3-sided pyramid needle tip is calculated as a function of the slope angle (θ). The correlation is derived in appendix E9, *Deflection of Pyramid Tip*.

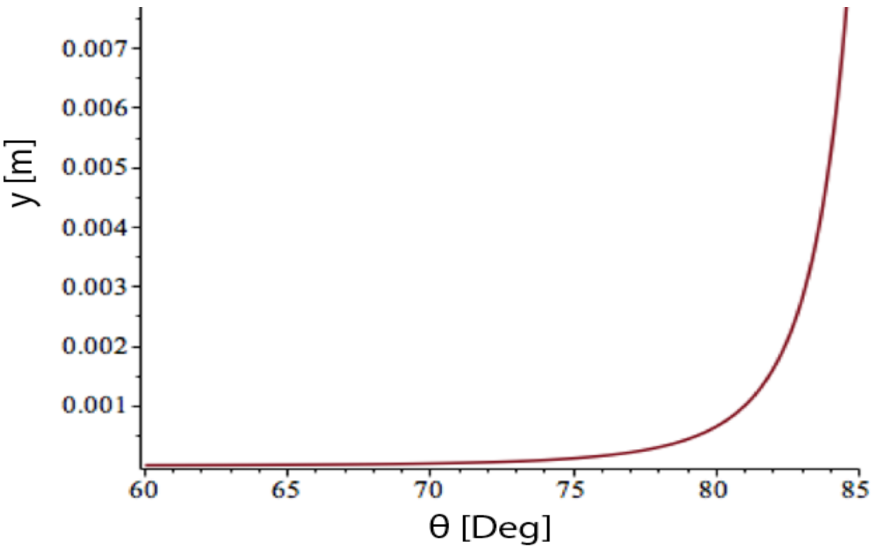


Fig. E30. Correlation between the tip angle (θ) and the deflection (y) of a 3-sided pyramid LCP tip.

Fig. E30 gives that the theoretical deflection is 6 * 10^{-20} m of a 3-sided pyramid LCP needle tip with a slope angle (θ) of 80°.

DISCUSSION

According to the calculations a slope angle of the 3-sided pyramid shaped tip (θ) of 80° gave very little axial compression and beam deflection. In these calculations the elastic deformation for the first 100 μm of the tip was investigated. Because of the growing cross-section areas of the needle tip most deformation of the tip will happen in this area.

The elastic deformation of the tip of the stainless steel needle is almost non-existing under the chosen assumptions. In the experiment *Tip Area of the NovoFine Insulin Needle* findings showed that the tip area of the needle had plastically deformed after penetration of the skin model. It could be that some of the chosen assumptions of the calculations are incorrect. Maybe the highest load of the needle tip is not at the outer most layer of the skin. Because skin is unpredictable it is hard to determine if the force on the needle inside the skin is due to friction of force on the tip. The insulin needle from the experiment had penetrated a skin model with is harder to penetrate that skin. This could also be why it deformed so much plastically.

The simplification of the calculation of Poisson's ratio can be questioned. In reality the geometries of investigation expand differently because they are not straight rods. The calculations does not takes in to account what the strength of the material is.

When a 3-sided pyramid shaped tip with a slope angle of θ = 80° and $A_{3pyr\text{-}start}$ = 46 μm^2 is *axially compressed* by a load of 0.07 N, the tip area will still be small enough to provide the required pressure to puncture the skin. If an angle of θ = 80° is chosen in *beam deflection* choosing an angle will lead to a defection of 6 * 10^{-20} m. This deflection is very small and should not influence the penetration force. Under the assumptions of these calculations the 3- sided pyramid LCP tip seams resistant enough even though LCP is more elastic than stainless steel.

When a 3-sided pyramid shaped tip with a slope angle of θ = 80° and $A_{3pyr\text{-}start}$ = 46 μm^2 is *axially compressed* by a load of 0.07 N, the tip area will still be small enough to provide the required pressure to puncture the skin. If an angle of θ = 80° is chosen in *beam deflection* choosing an angle will lead to a defection of 6 * 10^{-20} m

Conclusion

The experiments provided new insight on needle geometries and the mechanical properties of skin. The outcome of the experiments in relation to the hypotheses is listed in the table below.

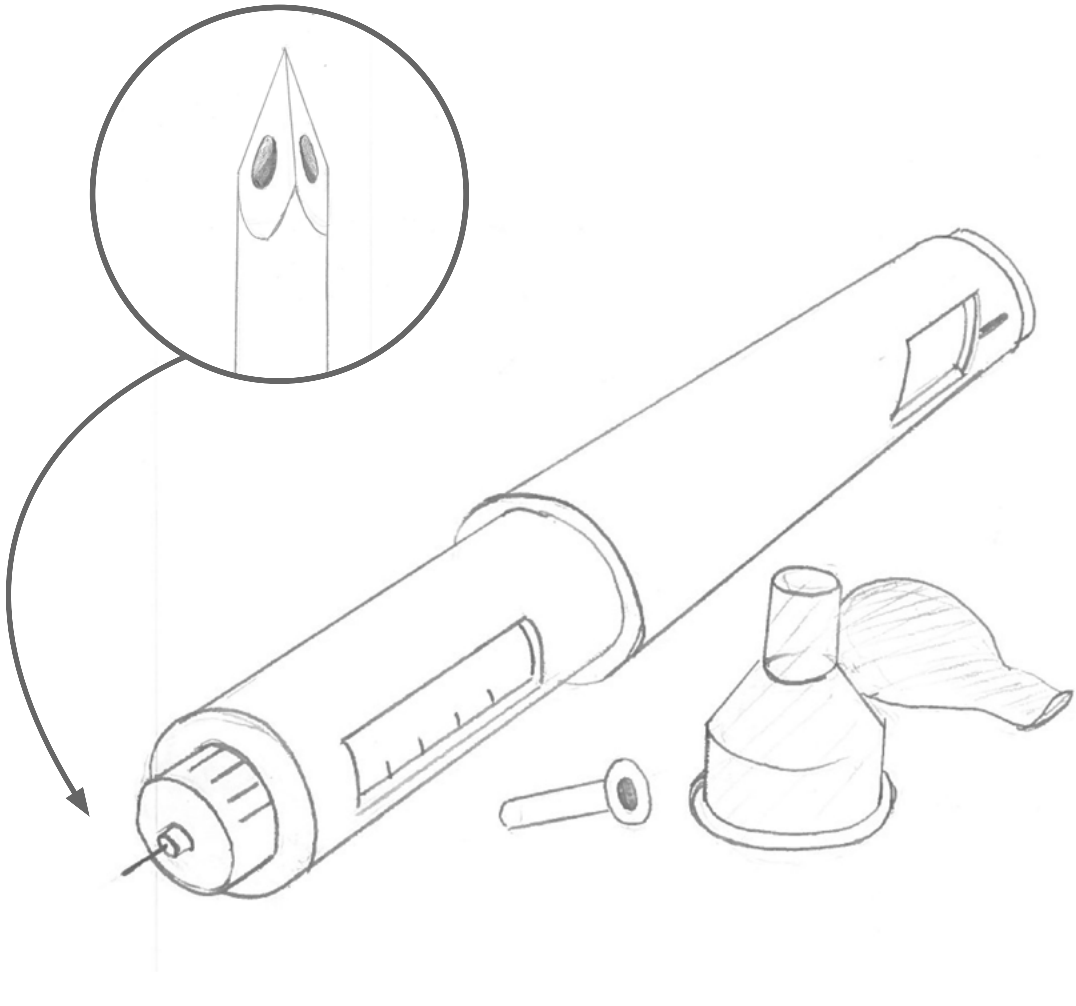
Hypotheses	Conclusion	Comment
Needle Tip Geometry Impact In Friction		
Sharp edges will create lower resistance and lower friction in the skin	Partly confirmed	The penetration forces of gelatin with 5 different needle tip geometries were compared. The 3-sided pyramid shaped tip geometry had the lowest friction force. It was concluded that sharp edges seem to decrease the friction by cutting through the elastic gelatin instead of stretching it.
A steeper tip geometry will create lower resistance and lower friction in the skin	Not confirmed	The friction forces of gelatin with a steep and lowered cone were compared. It seems as if the friction force depends highly on how the gelation is torn or stretched. A steeper tip does not necessarily have a lower friction, but it seems as if it makes less damage of the gelatin.
Tip Area of the NovoFine Insulin Needle		
The tip area of Novo Fine needles is 15 μm^2.	Not confirmed	Two NovoFine needles were visually inspected with SEM. The needle tip areas of the two insulin needles were 15x20 μm and 5x10 μm before penetration. It is not know if this difference of a factor 6 is representative for the NovoFine needle tip area. The difference could be due to tolerances the production method provides or it could be due to damage of the needle tips before the SEM photos were taken. More pictures need to be taken in order to evaluate if the two needles are representative.
The needle tip area will deform and thereby increase during penetration	Partly Confirmed	Pictures were taken of two NovoFine needles before and after they had punctured a skin model (not real skin). These showed an increment of the needle tip areas from 5x10 μm to 30 x 25 μm and from 15x20 μm to 25 x 40 μm.
Pressure to pierce human skin		
The stress needed to puncture vivo human skin (UTS) is 30 MPa	Unproven	In order to determine the pressure an estimation of a tip area and puncture force related to the tip area is needed.Determining the puncture force of the skin experimentally was not a success. It was only possible to conclude that the puncture force of the test person's upper arm was less than 0.07 N. The required pressured to puncture the outermost layer of the skin was estimated with Hook's law to be in the range of 100-1400 MPa. Using Hook's law to determine the tensile strength of skin did not seem suitable. It does not take the elasticity of the penetrated (or penetrating) media into account.
Buckling of the polymer needle column		
The penetration force of a NovoFine needle 32G, 6mm will not exceed the theoretical critical buckling load of a polymer needle with the same column dimensions	Proven	Curves of the experimental determined force required to penetrate a NovoFine needle 5 mm into a vivo human upper arm were compared with the curve of the theoretical buckling load of the polymer-based insulin needle. A safety factor of 20 against buckling was found.

Angle Optimization		
A slope angle (θ) of 80° is suitable for the 3-sided pyramid insulin needle in relation to the tradeoff between deformation resistance and sharpness	Proven	Through theoretical calculations it was found that 3-sided pyramid shaped tip with a slope angle of 80° and a tip area of 46 µm2 had minimal axial compression and beam deflection. The tip area of the polymer-based insulin needle will increase more than the tip area of a stainless steel needle assumed they are affected by the same load. Though the tip area of the polymer-based insulin needle can theoretically be smaller than the one of the stainless steel needle, because it is possible to produce a smaller tip area with the production methods the polymer-based insulin needle provides.

These findings were used to detail the final concept.

Chapter F

FINAL CONCEPT



Introduction

The findings of the last five chapters were gather to create the final concept *PolyFine* which is introduced in this chapter. The *function*, *form*, *process*, *material* and *context of use* of the PolyFine needle concept are presented. Through comparison with the findings from chapter B it is investigated if the PolyFine needle improves the *three dimensions of sustainability*. The chapter is finished with a final conclusion on the outcome of the project and suggestions for further work.

METHOD

- The *functions* of the NovoFine needle determined in Chapter A were used to list the *means* of the PolyFine needle.
- The chosen parameters of the *form* of the PolyFine needle were gathered and sketched in CreoParametric 3.0.
- The possible obtained tolerance with microinjection molding was based on studies of existing microinjection molded polymer part (Tosello et al., 2014).
- Knowledge of the material was obtained by studying datasheets of LCP A950 (appendix E2, *Datasheet of LCP A950*) and scientific papers (Kaslusky, 1993).
- The expected *context of use* for PolyFine was determined and compared with the existing context discussed in chapter B.
- The PolyFine insulin needle product was compared with the NoveFine needle on the possible *social sustainability* improvement factors found in chapter B.
- The same methods as in chapter B was used to investigate the *environmental* changes from the NovoFine needle product to the PolyFine product. The calculations were based on the functional unit from chapter B. It was assumed that the volume of the PolyFine and NovoFine product are identical.
- To investigate the *economical sustainability* of the PolyFine needle the unite price of the product was estimated. The same assumptions concerning cost of production, polymer part and the profit percentage were used as in chapter B. The price and density of LCP were based on data from found datasheets (henkelna, 2011) (appendix E2, *Datasheet of LCP A950*). The cost of changing the production facilities was not taken into account.

Describtion of the concept PolyFine

RESULTS

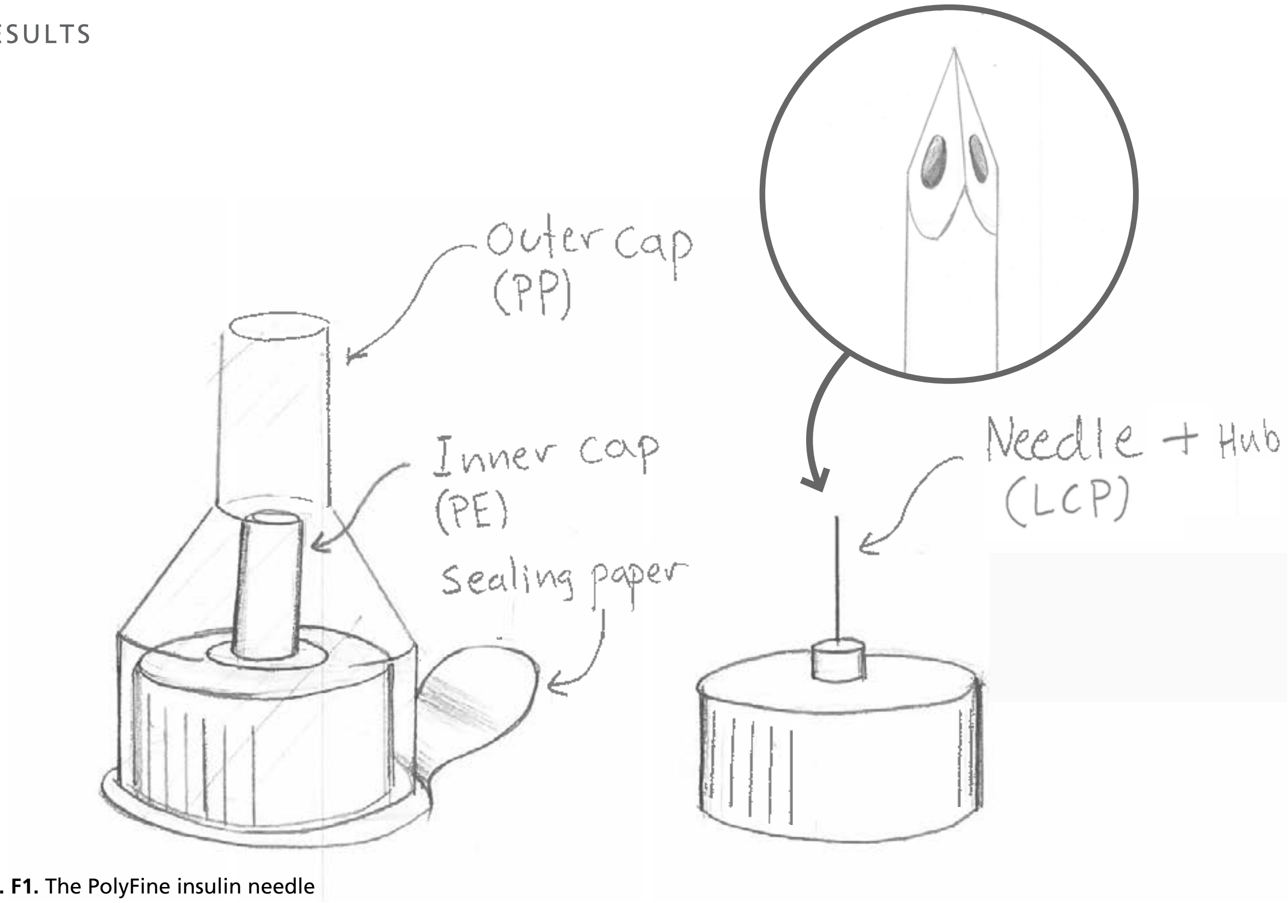


Fig. F1. The PolyFine insulin needle concept

FUNCTION

The PolyFine insulin needle fulfils the same main functions as the NovoFine insulin needle. The means of PolyFine is listed in the table bellow.

Function	Mean
Penetration of the patient with diabetes' skin	– A solid 3-sided pyramid tip – Very sharp tip (tip area 46 μm2) – Sharp edges that cut through the skin – Stiff and strong crystalline thermoplastic polymer (LCP) – The high stiffness of the LCP material prevents the needle column from buckling
Transportation of insulin from an external device into the body of the diabetic patient	– Hollow needle with three asymmetrically placed outlets allows flow of insulin

FORM

The tip geometry of the PolyFine needle is a solid 3-sided pyramid shape. The solid tip allows a bigger cross-section area. Compared to other studied tip geometries the 3-sided pyramid was found to be the most resistant geometry against deformation. This finding was partly explained by the big cross section area of the 3-sided pyramid tip shape. The PolyFine insulin needle has a small tip area of 46 μm^2. According to the calculations in chapter E the tip area of 46 μm^2 allows puncture of the human skin with a penetration force lower than 0.07 N. Compared to the other studied tip geometries the sharp corners on the 3-sided pyramid decrease the friction as the needle moves inside the skin. As the needle moves inside the skin the stress is concentrated on the sharp corners. It was found that a slope angle of 80° is an optimal angle, taking deformation and sharpness into account.

Fig. F2. Decentered outlet of insulin tube

Making a solid tip means that the outlets of the insulin tube needs to be placed decentered on the needle tip. It is chosen to make holes in all three surfaces of the 3-sided needle tip.

The needle is 6 mm long from the hub to the very tip. The needle has a wall thickness of 40 μm. This provides according to the experiment a factor of safety against buckling of 20. The needle and the hub of the PolyFine needle will be produced as one component. The needle/hub component is slightly angled so it is suitable for microinjection molding. Otherwise the geometry of the hub is identical to the geometry of the NovoFine needle hub. Besides this component the PolyFine needle contains the same components as the NovoFine needle (inner and outer cap, and the sealing paper). The Working drawing can be found in full size in appendix F1, *Working Drawing - PolyFine.*

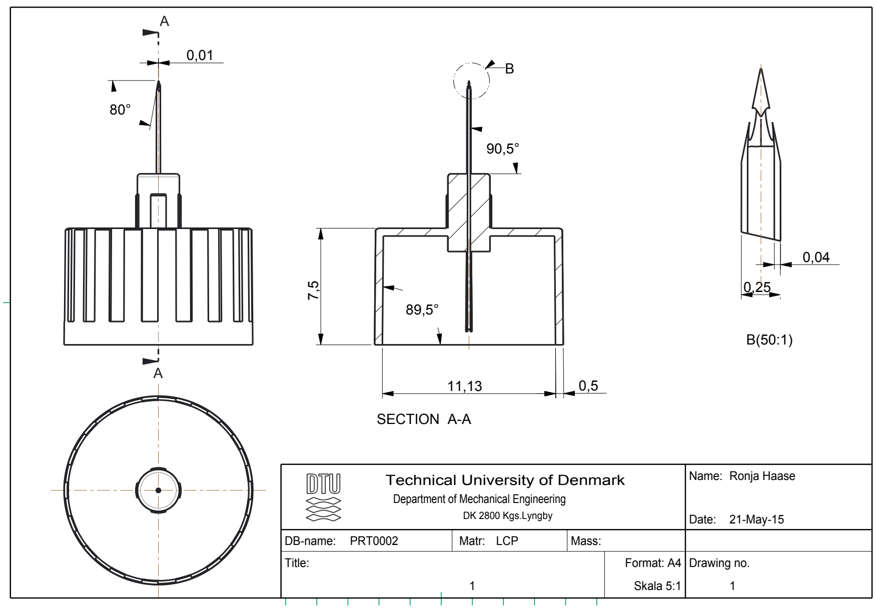


Fig. F3. The needle and the hub are made as one component.

PROCESS

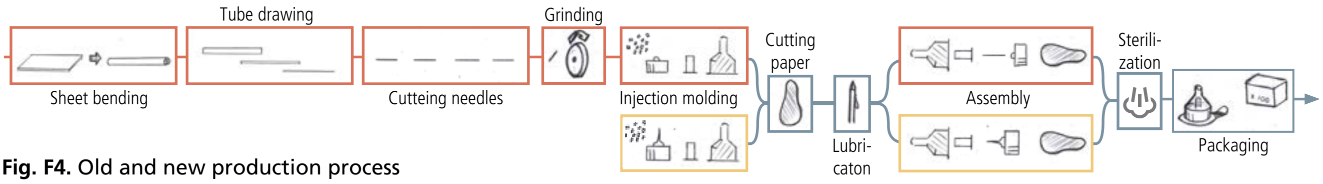


Fig. F4. Old and new production process

As seen in Fig. F4 the number of production processes of the PolyFine needle are significantly reduced. Sheet bending, tube drawing, cutting, grinding, injection molding of the hub as well as assembly of hub and needle are replaced by one single process: Microinjection molding. The lubrication and sterilization processes as well as the assembling process with the other components of the PolyFine insulin needle will be identical to the existing insulin needle. The rest of the insulin needle parts will be produced the same way as those for the NovoFine needle described in chapter B. The dimensions of the inner and outer cap, and the sealing paper can be found in appendix B2, *Estimate of Polymer Volume of Needle Components*

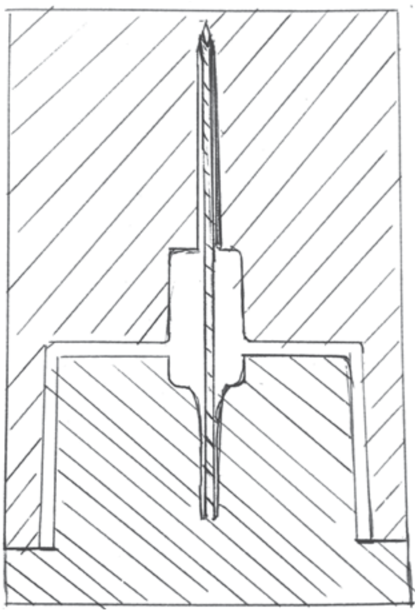


Fig. F5. PolyFine mold parts.

Material flow of micro scaled components can be problematic. To ease the material flow in the mold the microinjection molding can be done in vacuum (Tosello et al., 2014). The form of the PolyFine needle/hub component is designed so it can be microinjection molded with a single-axis system. The injection mold consists of two parts as sketched in figure Fig. F5. A mold surface roughness of 2-5 nm and 1-2 µm edge curvature on the polymer part can be achieved by using diamond mashing to produce the molds (Tosello et al., 2014). The needle will be the most critical part of the component to produce. A needle wall thickness of 40 µm will be aimed for. The microinjection molding process will enable a tolerance of ± 10 µm or less (Tosello et al., 2014).

MATERIAL

The unfilled LCP A950 is the chosen material for the PolyFine needle/hub component. LCP A950 is a thermoplastic polymer. It has a Young's modulus of 10,6 GPa, a tensile strength of 182 MPa and a compressive strength of 70 MPa. The crystalline structure of the LCP allows for minimal shrinkage in the direction of the aligned polymer chains (Kaslusky, 1993). This provides very fine tolerances. LCP A950 melts at 280 °C and can be sterilized with steam like the existing stainless steel needle (appendix C10, *Sterilization matrix of plastics*). LCP is used as a coating material in the commercial industry (Ticona, 2002), but the exact relationship between the binding ability of silicon lubrication and LCP A950 was not found. It is possible to add color pigments to the LCP material to obtain a needle/hub component in a desired color (Ticona, 2002).

CONTEXT OF USE

The context of use of the PolyFine needle resembles the context of use of the NovoFine needle described in Chapter A. The PolyFine fits the existing insulin pens. No redesign of the surface of insulin pens is necessary.

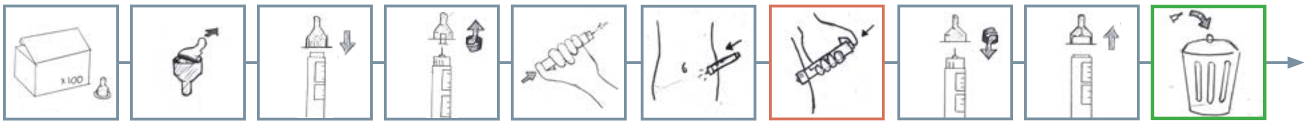


Fig. F6. green marks a possible positive change and red marks a possible negative change in the process of use.

There is a risk that the PolyFine needle will provide a lower flow of insulin because the inner tube divides into three holes. Furthermore there is a possibility that the polymer needle cannot be reused due to deformation during the first injection. It is also possible that it will not be reused because the user perceives the polymer-based needle as less robust than the stainless steel NovoFine needle.

DISCUSSION

The Young's modulus of the LCP is almost 20 times smaller than the Young's modulus of the material of the NovoFine needle. Penetrating the upper arm of the test person in Chapter E, a safety factor of 20 against buckling was estimated for the PolyFine needle. It may be discussed wheter or not the mechanical properties of the skin of test person's upper arm are repetitive. Both skin types and users can be hard to predict. Furthermore it might be discussed if a factor of safety of 20 is enough against buckling, because it is hard to predict all the possible scenarios of use. An insulin needle length of 4 mm may be considered because it will give a higher factor of safety against buckling.

A bended tube will have a lower flow than a straight tube, because the bend makes the fluid change direction. This creates friction between the wall and the fluid, which makes the fluid lose some of its velocity. Therefore the flow of insulin in the PolyFine needle will be lower than in the NovoFine needle (McDonald & Pritchard. 2011). If the flow is sufficiently low it will take longer time to inject insulin through the PolyFine needle. This may cause the user more discomfort. The flow should be optimized to create higher value for the user. This might for instance be done by increasing the inner diameter of the insulin needle

Microinjection molding provides a better tolerance, precision and bigger freedom of design of the insulin needle form than the existing production methods. The NovoFine needle has a wall thickness of 41,5 µm ± 11,5 µm. By using of microinjection molding it will be possible to achieve a finer tolerance of the needle. LCP is a thermoplastic material. Waste material from the microinjection molding process can be re-melted and reused in the next batch. Because the polymer is not linear it is not known what will happen when the material exceeds its compressive strength. If the maximal puncture force of the skin is 30 MPa, the factor of safety before the material starts to collapse is 2. It ought to be investigated if a safety factor of 2 for the compressive strength is enough. What happens when the compressive strength is exceeded? Will it break? This needs further investigation.

Sustainability Comparison

RESULT

SOCIAL SUSTAINABILITY CHANGES

In chapter B it was found that today's disposal of insulin needles causes a risk of needlestick injuries in countries with poor disposal facilities. This led to the criterion that the melting point og the needle should be less than 300 °C. With a melting point at 280 °C LCP A950 fulfils this.

The theoretical calculations of the PolyFine needle shows that the needle would possibly be able to puncture the human skin with a lower force than the NovoFine needle without risk of buckling. According to the theoretical calculations reuse of the needle will be possible to reuse, because no plastic deformation occurs.

The design of PolyFine needle aims to have the same penetration force and diameter as the NovoFine needle. Therefore the user will not experience any increment in pain. If the flow of the PolyFine needle is significantly lower user value will be decreased because the injection will take longer.

ENVIRONMENTAL SUSTAINABILITY CHANGES

In chapter B two possible areas of improvement were identified in the environmental dimension of sustainability:

- To reduce the use of limited resources
- To reduce the energy consumption during the lifecycle of the Novo Fine needles

Replacing the stainless steel with LCP means exchanging from one limited resource with another, because LCP is petroleum-based polymer. Lifecycle calculations of the PolyFine needle are made to compare it with the NovoFine needle.

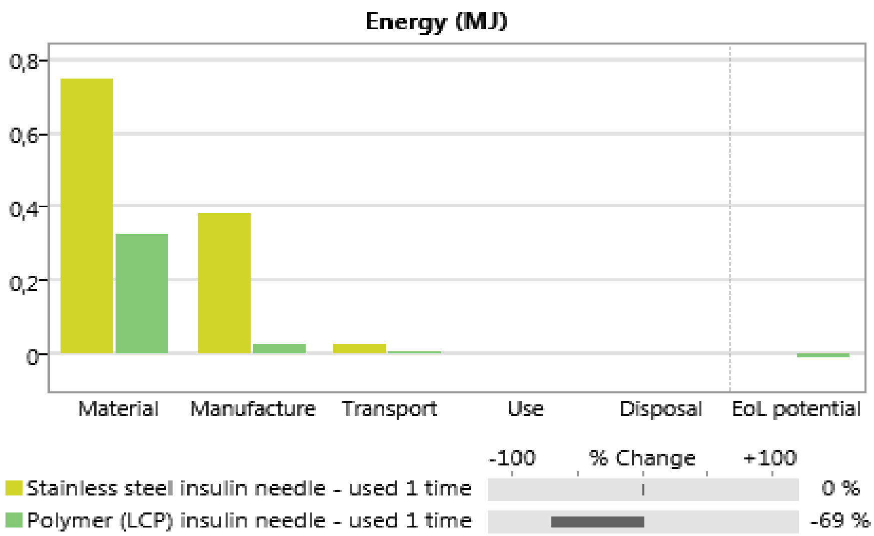


Fig. F7. Energy consumption of one diabetic's annual use of insulin needles. Stainless steel needle vs. LCP needle.

Solely comparing the material used on the needle itself in the two insulin needle products, the calculation shows that the LCP needle has a 69 % lower energy consumption than the existing stainless insulin needle.

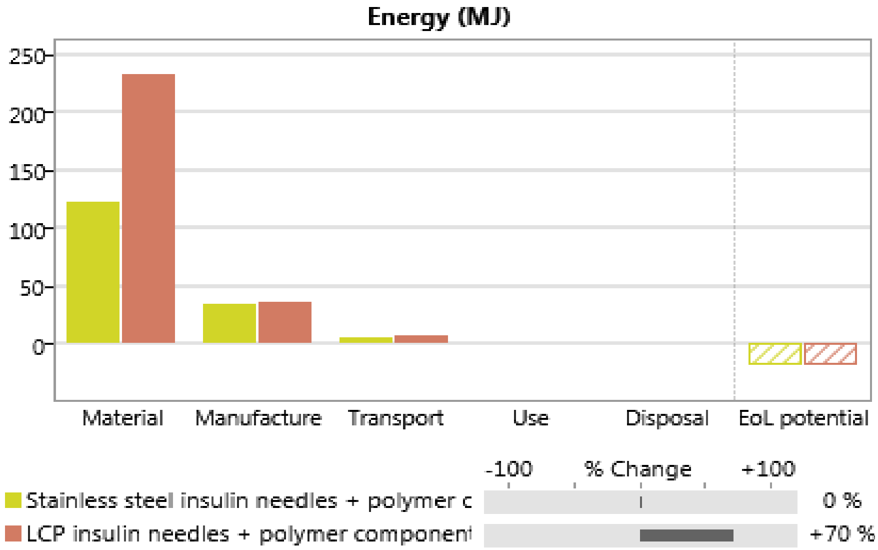


Fig. F8. Energy consumption of one diabetics annual use of insulin needles. Stainless steel needle vs. LCP needle including all product components

The energy consumption of the entire NovoFine and PolyFine insulin needle product is seen in Fig. F8. This life cycle calculation shows that the PolyFine needle product consumes 70 % more energy than the NovoFine.

ECONOMICAL SUSTAINABILITY CHANGES

The price per kilo of LCP is more than 4 times lower than stainless steel 304, but the density of the LCP is much lower than the density of stainless steel. This makes the price *per volume* of LCP slightly cheaper than the one of steel. If the price of the PolyFin's material is calculated as the price of the needle material of the NovoFine inuslin needle, the material price of the PolyFine needle material is 20 % cheaper than the price of the stainless steel needle.

$$\text{Price of needle material} = \text{Density} \cdot \text{Volume of PolyFine needle} \cdot \text{Price per kg}$$
$$= 1400\,\frac{\text{kg}}{\text{m}^3} \cdot 0{,}4 \cdot 10^{-9}\text{m}^3 \cdot 145\,\frac{\text{kr.}}{\text{kg}} = 0{,}00008\text{kr}$$

The volume price of LCP on the other hand a lot higher than the price of PP. The price of the hub material will therefore increase. The price of the raw material of the whole needle/hub component is 0.03 kr.

$$\text{Price of material} = \text{Density} \cdot \text{Volume of needle/hub} \cdot \text{Price per kg}$$
$$= 1400\,\frac{\text{kg}}{\text{m}^3} \cdot 17 \cdot 10^{-6}\text{m}^3 \cdot 145\,\frac{\text{kr.}}{\text{kg}} = 0{,}03\text{kr}$$

4 of the 7 production processes described in chapter B will be replaced by one production process: microinjection molding. In Chapter B it was assumed that one production process costs 0.18 kr. It is assumed that the microinjection modeling process will be twice as expensive as the average price of one produc-

tion proces estimated in Chapter B. The price of the microinjection molding is thereby 0.34 kr. Because the hub and needle are produced in one piece, they will not need to be assembled. The cost of the assembly process is therefore assumed to be ¼ cheaper (0.14 kr.) than in chapter B (0.18 kr.). The cost of the unaltered processes are estimated to be the same. The costs of the polymer parts are decreased with 1/3 because the cost of the hub is already accounted for. Based on these rough estimates the cost of the PolyFine insulin needle will be 1.57 kr., instead of 2.3 kr. for the NovoFine needle. This is a price reduction of 32 %.

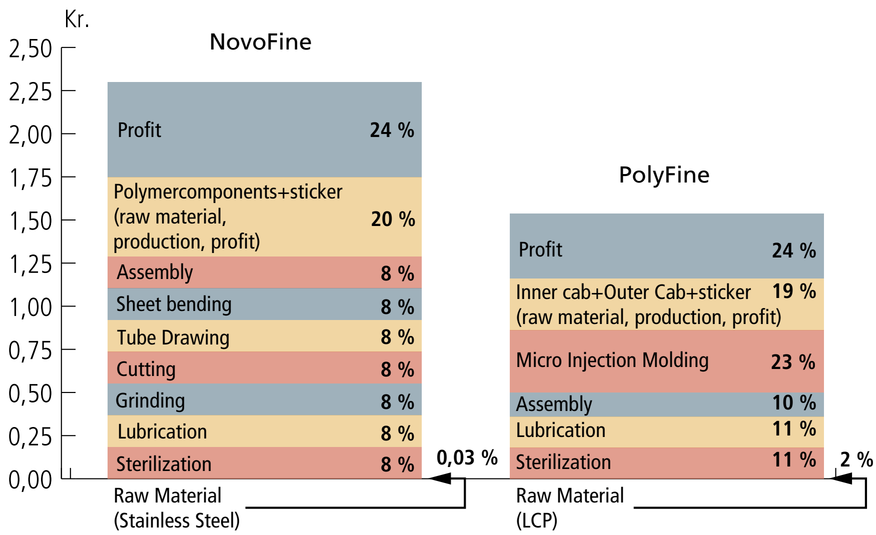


Fig. F9. Price estiamte of PolyFine compared to NovoFine

DISCUSSION

The theoretical claim that no plastic deformations of the polymer needle will occurs can be discussed. LCP's compressive strength of 70 MPa is more than twice of the strength of the maximum found UTS value of skin of 30 MPa. Though in the experiment Tip Area of NovoFIne Insuilin Needle in chapter E, it was seen that the stainless steel needle with a compressive strength of 210 MPa deformed plastically during penetration of the skin model. It was argued that this occurred because the skin model has higher a UTS than skin. PolyFine can melt on a bonfire. It can be argued that this makes it more socially sustainable considering countries with poor disposal facilities, because needlestick injuries after use can be prevented by making the PolyFine needle "unsharp" through heating at a bonfire. It has to be further examined if the LCP eventually burns if it is placed on a bonfire and if it releases toxic gasses. In a Danish context the material can be burned at the incineration plant where no people will be in direct contact with the waste gasses from the burning process.

It can be discussed whether or not a petroleum-based polymer or stainless steel is to prefer when it comes to use of limited resources. To avoid the use of limited recourses a bio-based polymer could be considered. Though in this project it has not ben possible to find a bio-based polymer that is strong and stiff enough for the application to an insulin needles. The estimation in *Envoirnmental Sustainablity* shows that a PloyFine insulin needle product will consume more energy in the life cycle than the NovoFine insulin needle product. Because the needle and hub will be produced in one piece, the whole needle/hub component will be made of LCP. The LCP raw material is a more energy consuming to produce than the PP material of the hub (CES, 2015) If energy reduction is the goal of improvement, the PolyFine needle and the hub need to be molded in two separate parts. Another argument for producing the hub and needle as two separate components is that the LCP needle must be molded in vacuum which is not necessary for the hub.

The estimation of the price of a PolyFine needle is very rough. The price of the injection molding was calculated as the price of two production processes but it could be more expensive. This could cause that estimation of a price reduction of the PolyFine product compared to the NovoFine product is less than 32 %, though overall it seems the price of PolyFine needle will be cheaper. The profit of the hub/needle was calculated to be of the same percentage as that of the NovoFine needle. If the price of the PolyFine needle declines the profit the producer of the PolyFine earns on one sold PolyFine needle will be lower than the one of the NovoFine needle. If on the other hand the PolyFine needle will not be reused in the same degree as the NovoFine needle, or will have gain a bigger marked share, because it is cheaper, the producer might gain a bigger net profit with the PolyFine needle than with to the NovoFine Needle.

Final Conclusion

The project phases lead to the following findings:

- The analysis of the *Context & Function* of the existing insulin needle provided an insight in the context of use, and the main functions that an insulin needle should fulfil were identified. The PolyFine insulin needle acts in the same user context as the studied existing insulin needle: The PolyFine insulin needle can be to the same insulin pen, and the user process will resemble the existing insulin needle. The functions and means of the PolyFine insulin needle is summarized in the following table:

Function	Mean
Penetration of the patient with diabetic's skin	A solid 3-sided pyramid tip Very sharp tip (tip area 46 μm2) Sharp edges that cut through the skin Stiff and strong crystalline thermoplastic polymer (LCP) The high stiffness of the LCP material prevents the needle column from buckling
Transportation of insulin from an external device into the body of the diabetic	Hollow needle with three asymmetrically placed holes allows flow of insulin

- The *Sustainability Check* identified possible areas of improvement of the existing insulin needle within the three dimensions of sustainability. Some of the possible improvements within one dimension contradicted possible improvements in one of the other dimensions: The reuse of an insulin needle seems to provide a risk of physical complication for the diabetic. Elimination of reuse might therefore improve the social sustainability of an insulin needle. On the other hand elimination of reuse seems to decrease the environmental and economical sustainability of an insulin needle product: The net cost and energy consumption caused by insulin needles will increase. The main improvement possiblity of the PolyFine insulin needle is to improve the economical sustainability. The change of the needle material from stainless steel to LCP provides much cheaper production possibilities. A rough estimate predicts that the unit price of the PolyFine needle will be 32 % cheaper than the one of the NovoFine needle. The project has not clarified the possibilities of reuse of the PolyFine needle. A cheaper unit price of the insulin needle may potentially minimize the incitement to reuse. Isolated the needle of the PolyFine needle consumes 69 % less energy than the isolated needle of the NovoFine during their life cycles. Including all the components of the PolyFine insulin needle the energy consumption during the life cycle increases by 70 % compared to the NovoFine needle. This is caused by the material change of the hub from PP to LCP.

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- In the *Academic Literature Study* knowledge concerning former related projects, general material science and mechanical theory, needle geometries and skin as a biological and mechanical phenomenon were gained. The main challenges of the polymer-based insulin needle were identified as buckling of the needle column and tip deformation. Former DTU projects have addressed the buckling issue with a sleeve solution. Stiff and strong polymer suitable for medical use and mass production. Of the studied tip geometries in the literature the 3-sided pyramid-shaped tip seemed most promising. The complexity of skin made it impossible to determine universal values of its mechanical properties. The most critical part of penetration of the skin with respect to deformation of the needle tip and column buckling was found to be during puncture of the outermost layer of the skin. No exact values for the stress needed to puncture the outermost layer of the skin was found. UTS values for skin were found in a range from 2 to 30 MPa. The compressive strength of the needle material of the PolyFine needle is more than twice of the highest suggested UTS value of skin, which means that the needle tip theoretically will not be exposed to plastic deformation.
- The obtained knowledge from the previous phases were used to set up a product specification for *Conceptualization*. Different design methods were used to generate ideas. The idea generation included a production of biocards, which gave concrete solutions to functional problems. It was found that the quill of the porcupine need half the force of a hypodermic needle to penetration the human skin. This was assigned to sharp barbs at the tip of the quill that "cut" their way through skin. All the ideas from the idea generation were sorted and systemized. This enabled the synthesizing of eight concepts. Aspects of the eight concepts were discussed with experts. A concept screening of the eight concepts was conducted. The concept *The Authors' Favorite* got the best score. During the screening process it became clear that different aspects of the concept needed to be tested to get a deeper insight.
- The *Concept Testing* included five experiments. Prior to the experiments the material of the insulin needle was chosen through comparison of different polymer materials. LCP A950 was chosen primarily because of its high Young's modulus. An experiment testing the impact of different geometries on friction indicated that the 3-sided pyramid shaped tip creates the lowest friction due to sharp edges. Visual inspections of the tip area of the NovoFine needle showed that the tip area was bigger than 50 μm^2. It was not possible to determine with which force the NovoFine needle punctures human skin, but it could

be concluded that the force was lower than 0.07 N. This was used to calculate the optimal slope angle of the 3-sided pyramid-shaped tip. It was assumed that a polymer needle at puncture has the same tip area (or smaller) than the stainless steel needle; it will be possible to puncture the skin with the same force. Even though the value of 0.07 N is higher than the actual puncture force, this value was used to represent the puncture force in order to make sure that the polymer needle does not get a bigger tip area than the stainless steel needle during penetration of the outermost layer of the skin. Using Theory of Axial Compression and Poisson's Ratio it was determined that 80° on the 3-sided pyramid was most optimal in the trade-off between sharpness and tip deformation. The PolyFine needle column was estimated to provide a safety factor of 20 against buckling through experimental measurements of the penetration force of the NovoFine needle in vivo human skin

- In the *Final Concept* the plausible polymer-based insulin needle concept *PolyFine* was presented. The form, material and process of the concept were described. The change of needle material from stainless steel to LCP provides an opportunity to use another production method, which is assumed to be cheaper and allows finer tolerances. The PolyFine needle's resistance to tip deformation and buckling is primarily based on theoretical calculations. The calculations show that it is plausible that the polymer-based insulin needle can obtain the same functions as the stainless steel needle without compromising the use value. Further work needs to be done, because mathematical models cannot always predict the reality.

Further Work

On a theoretically level this project shows that the polymer-based insulin needle seems plausible. Though there are still many things that should be clarified before the polymer-based insulin needle could be ready for production. The further work should include:

- Details of product finish (color of the needle/hub, curvature etc.).
- Optimizing the shape of the tube and outlet of the needle with respect to insulin flow.
- Investigation of the effect the changed tube outlet geometry has on column buckling, axial deformation and deflection of the needle.
- Optimizing the placement of the outlet of the needle tube in relation to flow of material in the injection molding process, and the obtained strength of the material on the other side of the outlet of the hole.
- If there is a more appropriate method to lubricate and sterilize the polymer-based insulin needle than using the same processes as the NovoFine needle.
- The possibility of injection molding the needle and hub as one "component" using two different materials. An idea could be first to injection mold with LCP to form the needle and then change to a cheaper an less energy consuming polymer material like PP to injection mold the hub inside the same mold.
- Estimate if it is preferable to produce the hub and needle in two parts from an economical perspective (like the existing NovoFine needle).
- Improve the environmental profile of the polymer-based insulin needle by reducing the material of the insulin needle product components. The necessity of the inner protection cap could for instance be challenged.
- Investigate if a reinforced polymer could be suitable as material of needle (if it is medically responsible, if it on the small scale will increase the mechanical strength and stiffness and can be produced).
- Investigate the possibility of making the needle in a biobased polymer.
- Make a thoroughly performed estimation of the unite price of the polymer-based insulin needle.
- Study how the user will receive a polymer-based insulin needle. Will they prefer it over the stainless steel needle?
- Investigate if the PolyFine insulin needle potentially could be reused (and if it will be).

Reflection

Both authors of this project have a background as design engineer students. During our university program the primary focus has been on design methods in the early phases of product development. This project intrigued us because we saw a possibility to gain more knowledge within the area of material technology. We also saw a possibility to get a bit further in the design phases than we are used to. Besides getting further in the design process, we also wanted to make use of the methods we have learned during our education. We wanted to investigate if the development of a polymer-based insulin needle could be justified and also develop a plausible polymer-based concept. This made the project extensive. If we should have re-planed the project, we would properly aim to focus more on a specific area, for instance the development of the needle, and leave other aspects of the project for others to consider.

The mechanical theories we have been taught during our education concerns isolated mechanical situations. It has been a challenge to make mechanical estimations of a context with living organisms because it is very complex and not easily to estimate with simple models.

Some of the information we wanted to collect has not been possible to find (for instance production methods and certain mechanical properties of skin). Sometimes this was due to the fact that it was confidential. If the project was made in corporation with an insulin needle manufacture, some of this information would might have been available. Cooperating with a company could on the other hand also have complicated aspects of the project such as confidential issues.

We chose to write our report in English, so non-Danish speakers could read it, and because we wanted to improve our written English. It has been challenging to write in English. We have not had a lot of experience with it before. Most of the used technical terms we have been taught during our education have been in Danish. Though we have not regretted our decision concerning writing in English because we have learned a lot from it.

Internal cooperation in the project group has been good. Before the project started we clarified the project expectations between us. Expectations and agreements on the frame of the project were written down in a group contract. A Gantt chart was made to guide the design process. We had 6 project phases. Each was ended with a milestone report, which was handed in to our supervisor. We divided a lot of the project work between us. The knowledge we each obtained was shared between us using appendix pages.

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