The Mediating Powers of Reproductive Technologies

An ethical technology assessment of Preimplantation Genetic Diagnosis, Non-Invasive Prenatal Testing, Sperm sorting and CRISPR/Cas9

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Abstract

This thesis is an ethical technology assessment of the reproductive technologies Preimplantation Genetic Diagnosis (PGD), Non-invasive Prenatal Testing (NIPT), sperm sorting and CRISPR/Cas9. It analyzes the mediating effects of these four technologies on the experience and actions of prospective parents, and on (1) the concept of reproductive autonomy, (2) the goals of medicine and (3) the slippery slope arguments. This is done with the use of the *technology mediation* approach, which is based on a post-phenomenological perspective that understands an intertwined relation between technology and human beings and between technology and ethics. By means of this approach, it becomes possible to understand the impact of technology on our ethical reflection, and it allows for insight which is useful for the evaluation and (re)designing of technologies. This thesis extracted eight mediating effects of the four reproductive technologies on both the experience and actions of prospective parents, namely four mediations of experience: (1) *perception of the unborn, (2) reproduction as a decision-making process, (3) perception on diseases and disabilities, and (4) experiencing risks*. And four mediations of praxis: (5) *the praxis of choosing, (6) having to choose a child, (7) decisions about what lives are worth living, and (8) weighing risks*. These mediating effects have both an increasing and decreasing effect on the concept of reproductive autonomy, they put pressure on the concepts of health and disease in the goals of medicine, and they show how the decision-making mechanism contributes to the idea of a slippery slope towards 'eugenics' and 'designer babies'. These results show a shift in perceptions and actions regarding reproduction and are useful as content for the evaluation and (re)designing of the reproductive technologies.

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Chapter One – Introduction

The options for prospective parents[1] to have genetically related and healthy children with help of reproductive technologies have increased intensively over the last two decades (Deech & Smajdor, 2007; Rulli, 2016). Today, as well as in the past, there have been some mixed feelings regarding these new technologies, varying from fear of 'designer babies' to fantasies about the 'New Humans'(Bredenoord, 2018). For example: the development of *in vitro* fertilization (IVF), with the birth of the first 'test tube baby' Louise Brown (Bellver Capella, 2015; Deech & Smajdor, 2007), the creation of the birth control pill in the early nineteen sixties (Berger, 2014), and more recently the birth of the first genetically modified babies in November of 2018 (Cyranoski & Ledford, 2018), have all led to societal discussions. The role and impact of the technologies in these cases are quite substantial. In the west in 2018, one in thirty children is born with the use of IVF (de Visser, 2018), the birth control pill has led to a sexual revolution (Berger, 2014), and everybody is now talking about genetics.

Reproductive technologies seem for a large part accepted in societies, however, ethical reflection on the current use and future implementations of these technologies is never really done. In this thesis, it will be argued that an ethical technology assessment is a valuable addition to the current ethical reflection on reproductive technologies. This thesis will use the philosophy of the *technology mediation* approach, which explains how technologies have the power to mediate people's perceptions and actions, because technology, human beings and morality are intrinsically related (Verbeek, 2011, 2015). With this philosophy as an approach, this thesis will show how having an understanding of the mediating effects of reproductive technologies can contribute in understanding the ethical considerations and how these technologies can cause a shift in our ethical reflection.

Reproductive technologies

Reproductive technologies are technologies and treatment used for human (and animal) reproduction, including assisted reproductive technology (ART), prognostics, contraception, and 'other' technologies that are, for example, still under development (Haan, 2017). ART are technologies like IVF and Preimplantation Genetic Diagnosis (PGD). Prognostics are

[1] prospective parents are persons who intend to conceive in the foreseeable future (van der Hout, Dondorp, & de Wert, 2019).

primarily testing technologies that give information about, for example, the likelihood of a pregnancy based on the quality of semen or the chance of having a child with a disorder or a disease. An example of the latter would be Non-Invasive Prenatal Testing (NIPT) and the ultrasound. All 'other' technologies are mainly developing technologies that are either considered too controversial by the scientific community, like artificial wombs and Prenatal Genetic Engineering (PGE) (also known as human germline editing technologies) (Bredenoord, 2018).

Throughout this thesis I will be using four different types of reproductive technologies as examples on which the analyses will focus. These technologies represent the domain of current and future technologies, including diagnostic and testing technologies, selection and modifying technologies. These four are: PGD, NIPT, sperm sorting and CRISPR/Cas9. For the analyses it is also useful to not only look at new and emerging technologies but also at currently implemented technologies, like PGD and NIPT, because of the extensive literature on the ethical reflection of those technologies. These can be used to extract current values and considerations.

Ethical difficulties of reproductive technologies

As mentioned earlier, there are many discussions on the use and development of reproductive technologies (Bredenoord, 2018; Haan, 2017). It is wondered, whether we should allow these technologies to be more influential and universally practiced. This is very difficult to answer, since these technologies touch upon a lot of different and complicated aspects of our human lives (Deech & Smajdor, 2007). For a start, these technologies are developed for helping people to reproduce and to give birth to healthy children. However, these technologies have the potential to do much more. To use PGD here as an example, this technology is currently used to examine embryos *in vitro* in order to prevent the birth of children with 'serious', 'high risk' genetic conditions. Because the technology allows for the screening of the full genetic profile of the embryo it can also detect other, less serious conditions and characteristics concerning the embryo, including (biological) sex. (Soto-Lafontaine, Dondorp, Provoost, & de Wert, 2018). In most countries it is not allowed to use PGD for sex-selection for non-medical reasons[2]. However, it is imaginable that prospective parents would

[2] Sex-selection for non-medical reasons is for example allowed in the United States (US) under the name of 'family balancing'. Families who have had only girls or only boys, can use reproductive technologies to pre-select an embryo of the opposite sex. In some cases, it is also done for couples who desire a first born with a specific sex. An explanation for why this is possible in the US is because of the lack of a governmentally funded health care system and partly because legislation is arranged differently per state (Bayefsky, 2018).

want to be able to control this aspect of reproduction as well in the future (Haan, 2017; Kalfoglou, Kammersell, Philpott, & Dahl, 2013). On the other side of this spectrum, CRISPR/Cas9 is a genetic engineering technology that will enable us to 'rewrite' human DNA, by modifying, adding or removing specific DNA sequences that are responsible for certain traits or abnormalities (Liao, 2019). The potential use and implementation of all four technologies evoke all sorts of moral concerns and questions, like for example: what it means to be human (Verbeek, 2011).

Ethical assessment of technology

New technologies pose new types of ethical questions. Trying to answer them demands a thorough ethical analysis which identifies the most important arguments and considerations. Doing ethics during the process of technological developments is important. It is often argued that ethics is always a little too late (Jongsma, Bredenoord, & Lucivero, 2018). To overcome this, the ethical reflection needs to start in an early stage of the development, before the technology is done developing and all the important decision are made (Bredenoord, 2018). This can be called 'ethics parallel research', which strives for 'ethics by design' (Bredenoord, 2018; Jongsma et al., 2018). How is this done? It is important to identify the ethical and societal concerns before you can start evaluating and (re)designing the technologies (Bredenoord 2018). Reproductive technologies influence human reproduction, so it is valuable to understand what the most important arguments and considerations are in relation to that. However, it is very difficult to identify the ethical concerns of the future implications of technologies at an early stage of the process. This is called the *Collinridge dilemma* (also known as the *dilemma of control*) (Bredenoord, 2018; Collingridge, 1980; Kudina & Verbeek, 2019). This dilemma states that when technologies are still at an early stage of development, it is impossible to know how it will affect human beings and their societies; you simply do not have the information (Collingridge, 1980; Kudina & Verbeek, 2019). What often happens is that undesirable consequences are discovered by the time that the technology is already part of the whole economic and social sphere. At that point controlling the development of the technology is almost impossible (Collingridge, 1980).

Although we might not be able to predict how technologies will affect human beings and their worlds, ethical reflection is still very much needed. To be able to make sure these technologies do not cross any moral boundaries we highly value, we have to make sure we have an idea of what values are at stake because of these technologies. It does not mean that we have to hold on to our current values at all time. Ethics is always about provisional fixed

points, which means that ongoing ethical reflection and adjustments are needed. The term provisional fixed point was introduced by John Rawls in his book: 'A Theory of Justice', which means that our moral judgements are provisional, temporary conclusions. At all times, we have to go back and forth between our considered judgements and our principles, which can lead to the revising of our existing judgements[3] (Rawls, 1971). We can only do this, by trying to discover the relevant ethical concerns. The question remains: how to do so?

In this thesis I will do this both by (1) looking at ethical consideration presented in the current ethical debates that are affected by the technologies, (2) by exploring the mediating effects of technology (in this case reproductive technologies) and (3) trying to understand the impact of the mediating effects of technology on the ethical considerations.

To have an idea of the current ethical considerations, it is useful to zoom in on the so-called 'human enhancement debate'. In this debate, a lot of important ethical arguments are mentioned that touch upon the potential use of the four mentioned reproductive technologies. This debate is a good illustration of what people fear or are excited about and what the arguments are for allowing the technologies to develop in a certain direction or to put a hold to the development all together.

The human enhancement debate

Within the human enhancement debate there are many discussion about, for instance, what ought to be the proper goals of medicine and health care (Juengst & Moseley, 2019). This debate represents the thin and complicated boundary between medical treatment for restoring or sustaining the health of a diseased person, and medical practices that are used to go beyond what is necessary to restore or sustain a good health (Schermer, 2013). To clarify that boundary, concepts of health, disease and treatment must be interpreted and defined. Technologies that put a lot of pressure on the boundaries between treatment and enhancement, are subject of this debate. Reproductive technologies can be considered as main topics of this debate, since they touch upon all of these concepts.

In the debate, there are proponents and opponents of these reproductive technologies. Proponents of these technologies are called 'transhumanists' and 'bioliberals'. These groups of people are rather positive about the technologies and embrace the developments around

[3] In 'A Theory of Justice', Rawls refers to this state of affairs as a reflective equilibrium. It is an equilibrium because its goal is to coincide our principles and judgments; and it is reflective since we know to what principles our judgments conform (Rawls, 1971). This if often used as a method to come to moral coherence in the practical ethics and especially in bioethics (Arras, 2007)

human enhancement. More importantly, they claim that human reproductive, and human enhancement technologies in general, will offer enormous potential for deeply valuable and humanly beneficial uses (Bostrom, 2010). They hold that human nature is improvable with the use of technologies and that with those, our healthy lifespan can be promoted, our intellectual and physical capacities extended, and we can get an increased control over our own mental states and moods. All of which are considered positive developments (Bostrom, 2010).

Bioethicists Julian Savulescu and Guy Kahane argue from the principle of (procreative) beneficence for the moral significance of choosing or selecting a child who, given its genetic capacity, can be expected to enjoy the most well-being (Savulescu & Kahane, 2009). Furthermore, many transhumanists and bioliberals think that, from the principle of justice, these reproductive technologies should be available to all individuals. This is a right that prospective parents have, it is part of their reproductive autonomy to be able to decide *if* and *which* reproductive technology to use for the betterment of their child to be. Some transhumanists even think that parents have the moral obligation to use the reproductive technologies available to them to create the best possible life for their future child(ren). Savulescu, for example, argues that we improve our children already through environmental interventions that affect their biology (diets, sports, education, etc.) to increase their opportunities in life, and that this is no different from altering their biology directly through the use of enhancing technologies (Savulescu, 2016).

Opposite to the transhumanists and bioliberals are the 'bioconservatives'. According to them, human reproductive technologies might undermine our human dignity or will erode something deeply valuable about our human condition (Bostrom, 2010). Some people view the impact of reproductive technologies negatively, since they are afraid that it will have unintended consequences, such as 'designer babies' and eugenics practices (Bredenoord, 2018; Sandel, 2009).

According to Michael Sandel, advances in reproductive technologies are unjust. We should appreciate children as if they are 'gifts'. This means that we ought to appreciate children as they come and "not as objects of our design, or products of our will, or instruments of our ambition" (Sandel, 2009, p. 45). To him, this is a typical example of the unnatural and unjustified dominance of men over nature (Sandel, 2009).
The concern for eugenics, is also often posed by people who are against the implementation of enhancement technologies. Eugenics, which literally means 'good birth', is a complex

subject and is often associated with the selective breeding programs and massive killings promoted by the Nazi regime in Germany (Goering, 2014). Eugenics can be separated into two different aims: one is called 'positive' eugenics, since it encourages people of good health to reproduce with one another to create good births. The other one is called 'negative' eugenics, which aims at ending certain diseases and disabilities by discouraging or even preventing people from reproducing (Goering, 2014). It is argued that the use of reproductive technologies is eugenic, because it allows for valuing some lives over the others as if some lives are unworthy of life (Knoppers, Bordet, & Isasi, 2006).

From ethical considerations to a technology assessment

There are, of course, many more arguments to discuss. However, this thesis will focus on three ethical considerations that are influenced by a large degree by the developments of reproductive technologies. These ethical considerations are (1) the concept of reproductive autonomy, (2) the goals of medicine, and (3) the slippery slope argument. These considerations are also represented in the enhancement debate. What is missing in the current literature is an ethical technology assessment of the reproductive technologies. This type of assessment will concentrate on the impact of the technology itself regarding our ethical deliberation, on how technology relates to us and in what ways technology is putting our current values at stake. Here, I will go beyond the enhancement debate and will assess these meta questions on technology, which then can be used to start evaluating, reshaping and designing the technology accordingly.

Ethical technology assessments

The aim of a technology assessment is to reflect on the possibilities and consequences of new and/or emerging technologies (Haan, 2017; Palm & Hansson, 2006). Since the 1960s, countries have dedicated offices and institutions to research short- and long-term consequences of the implementation of new and emerging technologies (Palm & Hansson, 2006). The goal of these assessments is to come to an early awareness and understanding of what the social, economic, political and ethical consequences of the introduction of new technologies in society might be (Haan, 2017). However, Palm and Hansson argue for a separate ethical technology assessment (eTA). In their opinion, technology assessments on the ethical consequences fails quite often because of a lack of adequate training to identify and address ethical issues in technology development (Palm & Hansson, 2006). It is, nonetheless, the task of ethicists to reflect and support the ethical reflection during the design

processes of technologies. New and emerging technologies often give rise to previously unknown ethical concerns and conflicts about the desirability and permissibility (Palm & Hansson, 2006). Technology is thus intertwined with morality. With that being said, it is important that the relationship between technology, human beings and societies are taken as "an interplay between technological potential and social values" (Palm & Hansson, 2006, p. 550).

According to Peter Paul Verbeek, philosopher of technology, this is in line with a post-phenomenological approach (Verbeek, 2007, 2011). Post-phenomenology also follows the interrelation between technology and human beings and their worlds. There is no strict separation between the object (technology) and the subject (human beings). Technology can be understood as 'a mediator' of human experience and action (Verbeek, 2008a, 2011). According to Verbeek, exploring this mediating character of technology is very well suited to be used for the assessment of technologies (Haan, 2017; Verbeek, 2011). This can be called: the 'technology mediation approach'. The *technology mediation* approach shows that technology co-shapes our ethical deliberation by mediating our experience and actions. This active contribution and the intimate appearances of technologies in the lives of human beings, has a moral dimension. "Making visible this close intertwining of technologies and human beings, enables us to take responsibility for these intertwinements and give them 'desirable shapes'" (Verbeek, 2011, p. 163).

Other approaches are for example the 'techno-moral change' approach initiated by Tsjalling Swierstra (Swierstra, 2016; Swierstra, Stemerding, & Boenink, 2009) and the method of sociotechnical experiments by Ibo van de Poel (Van de Poel, 2013). The goal of the 'techno-moral change' approach is to develop scenarios to anticipate how technologies influence moral frameworks, in order to inspire technological practices and policy-making (Swierstra, Stemerding, and Boenink 2009). These scenarios are also supposed to contribute to societal learning of the introduction of new technologies. The strategy of techno-moral scenarios includes society and morality. It believes that looking at the (new) technologies from this perspective, will truly help evaluate the desirability of them (Swierstra et al., 2009).

According to Van de Poel, we cannot predict the societal impact of new technologies, and therefore, we need to deal with innovations as 'social experiments' (Kudina & Verbeek, 2019; Van de Poel, 2013). Instead of asking whether a specific technology is ethically acceptable, we should ask whether it is ethically acceptable to experiment with that new technology in society and what the conditions for those experiments should be (Van de Poel, 2013).

In order to understand the impact of the development of reproductive technologies and the ways these technologies influence our ethical reflection, it seems that the *technology mediation* approach is most valuable. Swierstra's approach does not address this dynamic of the interaction between technology and morality, and Van de Poel's approach does not include this at all and is more of a trial-and-error method (Kudina & Verbeek, 2019).

The theory of technology mediation describes the established relation between users and their environment, where technologies should not be solely understood as a function or an instrument, but as an active mediator in the relations between humans and their world (Verbeek, 2001, 2009b). Since technologies help shape the experiences and practices of human beings, they too provide answers to the central ethical questions, though in a material way (Verbeek, 2011). Ethics is about the questions of *how to act* and *how to live*, and in our technological culture these questions are not answered exclusively by human beings (Verbeek, 2011).

Exploring the mediating power of reproductive technologies is, as I believe, very important for the ethical assessment of the reproductive technologies. Exposing the mediating effects will help us understand how these technologies influence our ethical reflection. By looking how the four reproductive technologies mediate our perceptions and actions, will allow us to come with more concrete points of application for ethical reflection. This knowledge is important for the evaluation of how to design or reshape the technology in a more appropriate way.

Aim of this research and method

Therefore, the aim of this research is to analyze the mediating effects of the reproductive technologies (PGD, NIPT, sperm sorting, CRISPR/Cas9) on our experience and action, and to understand their impact on the ethical considerations regarding reproductive autonomy, the goals of medicine and the slippery slope towards eugenics and designer babies.

In order to fulfill the aim of this thesis, the *technology mediation* approach will be used to identify specific mediating effects of the reproductive technologies. However, since the *technology mediation* approach lacks a concrete method for identifying specific mediation effects, I will follow the philosophy behind it and propose a method of my own. In short, this method explores the ways in which the technologies mediate our experiences by highlighting

some parts of reality while reducing others, and the ways specific actions are invited by the technologies while others are inhibited. Together with a literature study on both the philosophy of technology and the technical information about the four reproductive technologies, this thesis will be able to delineate multiple mediating effects of the technologies and discuss their impact.

Thesis outline

Furthermore, before analyzing the mediating effects of the reproductive technologies, this thesis will start by describing the four reproductive technologies in **Chapter Two**. Here, all the technical and practical information will be discussed that are important for having an understanding of the use and intention of these technologies. The practical scope and limits will also be discussed, which will provide insight into the (factual) potential of these technologies. In **Chapter Three**, a short history of the philosophy of technology will be discussed and the *technology mediation* approach will be explained in more detail. The information in this chapter will lay the foundation for the method that will be used in Chapter Five. In **Chapter Four**, this thesis will come back to the area of reproductive technologies and will discuss the concept of reproductive autonomy, the goals of medicine and the slippery slope argument. What then follows, is the actual analysis of the mediating effect of the four reproductive technologies, which will be done in **Chapter Five**. In this chapter, concrete mediating effects of the technologies on prospective parents their experience and actions will be delineated. From this analysis follows that these mediating effects have an impact on the reproductive autonomy of prospective parents, the goals of medicine and the slippery slope argument. Finally, in **Chapter Six**, it is concluded that there will be a shift in perceptions and actions regarding reproduction and that this insight is useful for an evaluation and the (re)design of the reproductive technologies. Here, a few suggestions will be given of what questions need answering and it will be emphasized that further empirical research needs to be executed in order to include more ethical considerations and give more weight to the mediating effects.

Chapter Two – Reproductive Technologies

In order to be able to explore the mediating effects of reproductive technologies and understand their impact in the current ethical reflections, a layman's understanding of the function and purpose of reproductive technologies is required. Therefore, the aim of this chapter is to present thorough and relevant background information about the four reproductive technologies, being: PGD, NIPT, sperm sorting and CRISPR/Cas9. Each technology will be explained based on their purpose, technicalities and their potentials and limits. The goal of the latter is to separate facts from fiction. Namely, this chapter will also explain for which medical cases these technologies are an option and for which cases they are not. I am aware that some of the information presented in this chapter already have some ethical relevance. However, the ethical aspect of this thesis will be discussed in more detail from Chapter Four.

Natural fertilization

The natural reproductive system requires a functional (1) uterus, (2) egg cell and (3) sperm cell. The egg cell carries half of the DNA from the female, and the sperm cell carries half of the DNA from the male. These two cells fuse together, and the resulting cell is called a zygote. The zygote has now all the genetic information for the upcoming development: life. The genetic information is usually spread across forty-six chromosomes: twenty-three chromosomes from the female (mother) and the other twenty-three from the male (father) (Deech & Smajdor, 2007).

Natural fertilization is a delicate process. If one of the components is dysfunctional, missing, or disturbed, natural fertilization fails or comes with complications. (assisted) Reproductive technologies provide reproductive options for various people with different reproductive problems and/or challenges. Such cases are: (1) infertility, caused by (a) dysfunctional uterus, egg or sperm cells, (2) absence of a uterus, egg or sperm cells, in cases of single parenting or same sex relationships, and (3) risk of transmitting a genetic disease. So, reproductive technologies can create the possibility of having children for people who would in the past have been excluded from reproduction by age, sexual orientation or relationship status even if they were not biologically infertile, and for people who would have a risk of transmitting a genetic disease or disorder (Deech & Smajdor, 2007).

Important to understand is that there are always the possibility of *de novo* mutations in the reproduction process that could lead to offspring with a disease or disorder. *De novo* mutations are genetic alterations that are present for the first time in one family member. This is the result of a mutation in a germ cell of one of the parents, or it arises during the process after fertilization (PDQ® Cancer Genetics Editorial Board, n.d.).

Now that the basics of human reproduction and reproductive technologies have been covered, the individual reproductive technologies can be discussed.

I. PGD

PGD is part of an assisted reproductive technology, used for the genetic testing of embryos (Dondorp & de Wert, 2018; invitra.com). PGD was developed to help both prospective parents who have a known high risk of transmitting a serious monogenetic disorder and couples that carry a chromosomal abnormality that may either lead to a pregnancy loss or to the birth of a severely handicapped child (Soto-Lafontaine et al., 2018). For various genetic abnormalities that could be occurring in families, PGD can detect whether an embryo has that specific abnormality.

PGD can only be used in combination with IVF or intracytoplasmic sperm injection (ICSI) (PGD Nederland, n.d.-a). This means that before testing the embryos, women need to undergo hormonal treatment to be able to harvest multiple oocytes (immature egg cell), who then can be fertilized through either IVF (by combining the oocytes with sperm cells in a laboratory dish) or ICSI (by injecting a single sperm cell into a mature egg) (National Health Service, 2010). About three days after fertilization, the embryos will be 6 to 8 cells large. This is also the moment to retrieve one or two cells that can be analyzed through a biopsy for the presence or absence of the relevant genetic mutation or chromosomal abnormality, see Figure 1 (Dondorp et al., 2014). This procedure can take 12 up to 72 hours (Handyside, 2010). At this stage, the cells are still omnipotent (they have not specialized yet), but are capable of creating a human being, and therefore, they can safely be regarded as a representation for the offspring (Soto-Lafontaine et al., 2018; Wüstner, 2006). After the analysis of the biopsies, the unaffected embryo(s) can be selected and made ready for transfer to the uterus (Soto-Lafontaine et al., 2018). This will take place around 4 up to 6 days after fertilization (Handyside, 2018). The affected embryos will be discarded or used for scientific research.

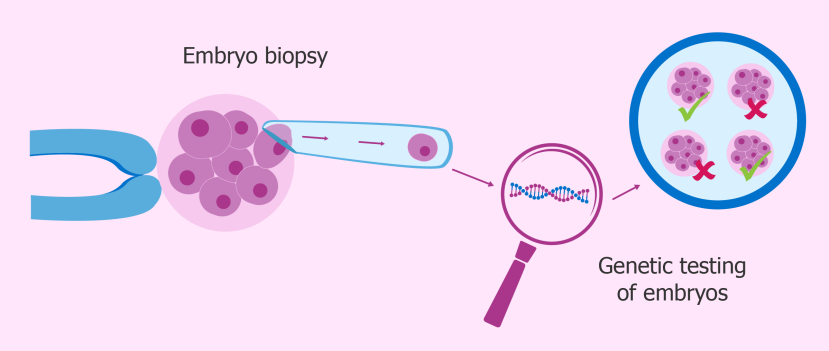

Figure 1. Simplified image of PGD. Left you see how one or two cells are retrieved from the embryo, for the biopsy. The right part of this image represents the testing of multiples embryos on the presence or absence of a genetic mutation and the results of that test.
Retrieved from: *https://www.invitra.com/preimplantation-genetic-diagnosis-pgd/* (2019)

PGD was introduced in the early 1990s, and has become an established reproductive option for people in many countries (Soto-Lafontaine et al., 2018). Furthermore, data about PGD, collected by *The European Society of Human Reproduction and Embryology* (ESHRE), show an increase in interest for PGD over the last decades in most European countries (Handyside, 2010). In fact, PGD is an official treatment in the hospitals or medical practices of most European countries. In those countries, it is often required to meet the criteria stated by the so-called 'medical model' in order to receive an indication for PGD. The medical model, in essence, allows PGD for prospective parents who are at risk of transmitting a genetic disorder or handicap to their offspring, or of having a failed pregnancy due to a chromosomal disorder (Human Fertilisation & Embryology Authority, n.d.; PGD Nederland, n.d.-b; Soto-Lafontaine et al., 2018). European countries like Denmark, France, Germany, the Netherlands, Norway, Sweden and the UK, have further qualified this model by emphasizing that the couple or individual needs to have a 'significant' or 'high risk' of bearing a child with a 'serious' genetic or chromosomal disorder (Soto-Lafontaine et al., 2018). To review the requests, most countries work with (multidisciplinary) ethics committees, that will help determine to a large extent which applicants are acceptable and which not. Criteria that are often used to determine whether a request for PGD should be accepted are based on the severity and treatability of the disease, the likely expression and progression of the disease, the penetrance[4] of the mutation, and the mental stability of the prospective parents (Dondorp,

[4] The term 'penetrance' represents the distribution of individuals with the mutation who show symptoms of the disease or disorder (Scitable, n.d.-a).

Wybo; De Wert, Guido; de Die, 2019; Soto-Lafontaine et al., 2018). Examples of types of diseases that PGD is requested for, are: Huntington Disease, Cystic Fibrosis, BRCA mutations with high penetrance (that can lead to breast and ovarian cancer for (young) women and breast and prostate cancer for males). In a lot of countries, these diseases are put on the list of diseases for which PGD is almost automatically allowed (Human Fertilisation & Embryology Authority, n.d.; PGD Nederland, n.d.-b; Soto-Lafontaine et al., 2018).

Scope and practical limits

The technological developments to better detect abnormalities in embryos makes it possible to detect more and more abnormalities in the embryos. This leads automatically to the expansion of conditions for which PGD is accepted, but this also means that there will be new types of requests coming in for the use of PGD. In some cases, this leads to the reconsideration of laws and regulations. An example is the acceptance of PGD to select an embryo based on sex, to avoid the transmission of a serious sex-linked genetic disease or disorder (Bredenoord, Dondorp, Pennings, & De Wert, 2010). Sex-linked[5] diseases or disorders are generally X-linked recessive[6], which is caused by an alteration of one gene in the X-chromosome. Because boys only have one X-chromosome, they will develop the condition when they have a gene alteration on their X-chromosome. Girls show less or no signs of this recessive X-linked condition, because they have a second unaltered copy of the gene on their other X-chromosome, which normally compensates for an altered gene. Girls with a gene alteration on one of their X-chromosomes are called a *carrier* for the X-lined recessive condition (National Health Service, 2014). Couples who want to avoid transmitting a X-linked condition to their future children are allowed to select an embryo based on sex. As mentioned before, boys have a higher chance of experiencing the symptoms of this X-linked, when carrier of the condition. For 'serious' X-linked diseases and disorders with a high penetrance mutation, the selection for a female embryo is sometimes requested. Apart from the potentials, PGD has also a limitation. PGD on its own is a very reliable technology (the

[5] Sex-linked describes the pattern of inheritance when a mutated gene is present on a sex chromosome. These sex chromosomes are different in shape and number in males and females. Males have an X- and a Y-chromosome, while females have to X-chromosomes. The sex of the offspring is determined by the class of sperm (Scitable, n.d.-b).

[6] The term recessive is used to describe the inheritance pattern of certain traits. There are recessive and dominant inheritance patterns, and they describe how likely it is for a certain trait to pass from a parent to an offspring. For a recessive allele (gene variant) to produce a recessive trait, the offspring must have two copies: one from each parent. For a dominant allele to produce a dominant trait, the offspring only needs one copy from one parent. Both terms are useful for the prediction of the probability that an individual will inherit certain traits, especially genetic diseases and disorders (Genetic Science Learning Center, n.d.).

detection of an abnormality is almost 100% accurate), but because it cannot be done without IVF, the whole procedure is considered quite demanding. IVF is invasive for women and it has a 30% of resulting into a successful pregnancy. This is something prospective parents have to take into account when going into the process of PGD.

II. NIPT

NIPT is a way of examining a small fragment of fetal DNA by taking a sample of blood from a pregnant woman. This small fragment of fetal DNA, also known as cell free DNA (cfDNA), can be found in the mother's blood (Genomics Education, 2019). From the blood, the cfDNA can be isolated and examined for a range of abnormalities. The test is primarily used for the detection of aneuploidies (which is the presence of an abnormal number of chromosomes in a cell), especially the trisomy 21, 18 and 13, that cause Down's-, Edwards'-, Patau's syndromes[7]. The fragments can also be tested for a specific gene or DNA sequence (Strachan & Read, 2011).

From 2018 onwards, NIPT is introduced in most European countries for screening the mentioned syndromes. According to medical professionals, NIPT is an accurate and quick test, and a better alternative to the other screening tests (combined test, which includes the ultrasound and a hormonal blood test, and the amniocentesis) (Nuffield Council of Bioethics, 2016). In many European countries, like the UK, Belgium and the Netherlands, NIPT is offered as part of a fetal screening program for all pregnant women, both women with a high risk of having a child with one of the syndromes and women who do not initially have such a high risk (NIPT consortium, n.d.; Nuffield Council of Bioethics, 2016; Rijksinstituut voor Volksgezondheid en Milieu, 2019; Universitair Ziekenhuis Antwerpen, n.d.). When the results of the NIPT return positive, prospective parent will be offered an amniocentesis for a definitive diagnosis.

The reason why NIPT is offered to all pregnant women in countries like the UK, Belgium and the Netherlands, has to do with creating the ability for prospective parents to make their own choices about their pregnancies. NIPT offers accurate information, that can help in making well-considered decisions. This statement has a lot of implications, which not all people agree upon. One can think about the consequences of knowing that you will give

[7] Down's syndrome is caused by an extra copy of chromosome 21 in each cell. Edwards' syndrome is caused by an extra copy of chromosome 18, or some extra chromosomal 18 material. Patau's syndrome is caused by an extra copy of chromosome 13 or some extra chromosomal 13 material. All three conditions are rarely inherited, and the vast majority occurs through a spontaneous mutation (*de novo)* (Nuffield Council of Bioethics, 2016).

birth to a child with Patau's syndrome. This type of information might lead to an abortion or to the birth of a child of which you know has a low life expectancy.

Scope and practical limits

NIPT can also be used for the diagnosis of other genetic diseases and disorders, such as Cystic Fibrosis, and it can also determine the sex of the fetus (Nuffield Council of Bioethics, 2016). As mentioned in the section about PGD, this procedure might be requested by prospective parents who are known carriers of serious sex-linked genetic diseases or disorders (i.e. Duchenne) (Genomics Education, 2019). However, this procedure of sex selection is currently only made available through private providers (Nuffield Council of Bioethics, 2016). A limit of NIPT would be that after a positive result, an amniocentesis still needs to be executed for a complete diagnosis. An amniocentesis is invasive and does not go without risks (e.g. miscarriage). It is also known, that NIPT has a lot of 'false positives' (Nuffield Council of Bioethics, 2016). This means that the test shows a positive indication for a chromosomal abnormality, which turned out to be a false alarm after the amniocentesis.

III. Sperm sorting

The technologies to sort sperm before the process of fertilization are still in development. Switzerland is currently the only European country which has been using a sperm sorting technology for a clinical study (De Geyter et al., 2013). The goal of these types technologies is to separate the sperm into X- and Y- chromosome bearing sperm cells, in order to be able to select for the sex of the offspring (De Geyter et al., 2013; Kalfoglou et al., 2013). The reason why these technologies are not made available in most countries, is because organizations like the Food and Drug Administration (FDA) in the United States (US) do not believe those technologies to be reliable enough for clinical application (Kalfoglou et al., 2013). Reliable in the sense that they are not able to guarantee for a 'high enough' percentage of success in selecting a boy or a girl. In addition, these technologies are also not widely made available because of disagreement about whether it is accepted to use these technologies for medical and non-medical reasons.

There are two different methods for sperm sorting: (1) One is the method of *MicroSort*® , and (2) the other is called: *the Ericsson method*.

MicroSort® works by exposing sperm cell to a fluorescent dye. The sperm cell are passed through a flow cytometer, which is able to sort the sperm cell on the basis of cell

fluorescence with a laser beam (Dondorp et al., 2013; Kudina, 2019). Sperm cell with an X chromosome glow more brightly and indicate a girl. This technology has proven to be approximately 92% effective for selecting and the birth of girls and approximately 83% effective for selecting and the birth of boys (Dondorp et al., 2013; Genetics and IVF Institute, 2017; Kalfoglou et al., 2013). This is the only sperm sorting technology that received FDA approval to conduct clinical trials amongst couples who have a risk of having a child with an X-linked disease (Kalfoglou et al., 2013; Karabinus, 2009; Marazzo, Karabinus, Johnson, & Schulman, n.d.).

The Ericsson method is considered especially good with helping prospective parents who desire a boy and works by placing sperm into a test tube along with a substance (albumin) in increasingly thickened layers (Grunebaum, 2017). The sperm cells have to swim all the way down through the layers. Only the fastest sperm will make it to the bottom, which in this case is believed to be the Y-chromosome bearing sperm cell. The Y-chromosome has less mass, and is therefore, probably faster. The X-chromosome has more difficulty with swimming through the layers of albumin serum The 'winning' sperm cell could then be artificially inseminated by the ovulating woman or used for IVF (Grunebaum, 2017). The success rate of this technique is around 70-75%.

Scope and practical limits

As mentioned in the paragraphs on PGD and NIPT, there are sometimes requests by prospective parents for sex-selection in order to avoid the birth of a child with a genetic disease or disorder. Here, this type of technology could be considered as an alternative for the prenatal diagnosis (PND). However, when using this technology, it is still desired to use some type of screenings test or diagnosis, to make sure the fetus or embryo is free from the genetic disease or disorder.

The technique of sperm sorting could be helpful as a preselection tool for sex selection through PGD or PND (Dondorp et al., 2013). Preselection can limit the chances that PGD will result in only embryos of the wrong sex (which is not exceptional if women have a low oocyte production). In addition, it would help in avoiding perhaps difficult decisions about whether or not to terminate a pregnancy with PND (Dondorp et al., 2013).

IV. CRISPR/Cas9

CRISPR/Cas9 is a relatively new genetic engineering technology that enables researchers to alter DNA sequences, by the modification or the removal of specific DNA sequences that are

responsible for certain traits or abnormalities (Liao, 2018, p. 98). It would thus have the potential of correcting genetic defects, treating and preventing the spreading of diseases. This is both applicable to human and animal genomes, and in the food and agricultural industries to improve and protect crops (Vidyasagar, 2018). Since this thesis is be about the mediating effects of reproductive technologies, the focus on CRISPR/Cas9 will therefore only be on its use for editing human genomes. The other purposes are simply irrelevant in this context.

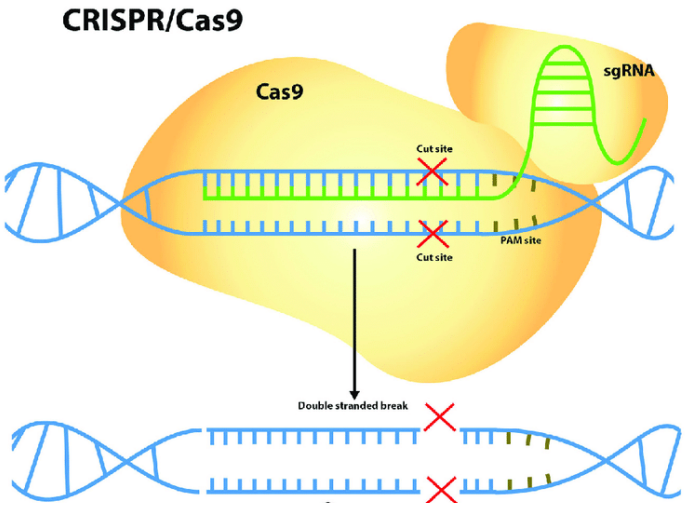

Figure 2. CRISPR/Cas9 – The Cas9 cutting enzyme is depicted in yellow, which contains the guide RNA (sgRNA, in green) to guide the complex to the genetic location of interest (DNA, in blue). (*Cribbs and Perera, 2017, p. 626)*

The CRISPR/Cas9 system consists of two components: a scissor component and a so-called guide RNA. The latter component guides the scissor to the place where it needs to make a cut (Figure 2). This guide RNA is highly modifiable and very specific. Because of these characteristics, the CRISPR/Cas9 system became widely used in biomedical laboratories since its emergence in 2012. Due to its promised efficiency compared to other genome-editing tools, and because of its possible effective correcting of genetic defects, it is hypothesized that this technology can correct pathogenic genetic mutations (Cribbs & Perera, 2017; Vidyasagar, 2018).

Scope and practical limits

Although this is a rapidly developing technology, there are some practical limitation to the use of CRISPR/Cas9. The first and major issue is the possibility of off-target effects in areas of the genome. Off-target effects could lead to significant and negative changes in unknown

long-range enhancer regions of the DNA (Cribbs & Perera, 2017). This is partly due to some challenges with the current delivery methods of the CRISPR/Cas9[8] (Cribbs & Perera, 2017).

Since in most countries PGD is considered to be the legal (and ethical) standard for preventing the birth of children with serious genetic diseases and disorders, it is important to investigate in which situations CRISPR/Cas9 (or PGE in general) would be the only or best option for parents who desire a healthy and genetic related child. From the literature, six different situations can be described where PGD would not be possible or ineffective and CRISPR/Cas9 would be considered the best possible option for prospective parents (Cribbs & Perera, 2017; The National Academies of Sciences Engineering and Medicine, 2017):

1. For couples with autosomal recessive diseases (e.g. Cystic Fibrosis), that are both homozygous;
2. For couples with at least one homozygous person with an autosomal dominant disease (e.g. Huntington's disease);
3. In a situation of co-dominance, which is the pairing of two different mutations in a given gene, and combinations of specific alleles of two or more gene (e.g. Alzheimer disease with two copies of the *AP0E e4 allele);*
4. In situations where the survival of people with severe recessive diseases like Cystic Fibrosis or sickle-cell anemia. With the improvement and advances in medical treatments, the possibility cannot be dismissed that there will be an increase in the number of situations in which both prospective parents are homozygous for a mutation;
5. In cases where mutations compromise fertility. For example, women who carry mutations, e.g. Fragile X and BRCA-1, that cause the loss of oocytes during oocyte development or postnatally;
6. Due to external factors, like cancer treatments and environmental chemicals can also reduce the ovarian reserve in women, who wish to avoid transmission of a genetic disease. In this case, women have less embryos available to screen from each cycle of

[8] Two delivery systems for modifying a cell's DNA are to be distinguished. First, there is the implementation of CRISPR/Cas9 via a transfection reagent (virus like sequence) or viral vectors, which is then to be implemented in the nucleus. This virus will be able to fuse with the nucleus and will be able to give order where to cut and where to adhere the DNA strand (Cribbs & Perera, 2017). In this way, CRISPR/Cas9 can do its assigned 'job'. The second method is *electrophoresing*, which will break the cell membrane for a millisecond with an electrical pulse. During that millisecond, a piece of DNA with the CRISPR/Cas9 can be injected.

superovulation, and consequently the chance of establishing a pregnancy with an unaffected embryo (though IVF PGD) is lower.

(Brokowski & Adli, 2019; Cribbs & Perera, 2017; The National Academies of Sciences Engineering and Medicine, 2017)

Important to note here is that in any case of using CRISPR/Cas9 or any other PGE technology, PGD would be still be required to validate whether the edit was successful or not (Cribbs & Perera, 2017; The National Academies of Sciences Engineering and Medicine, 2017). This also means that the procedure needs to take place *in vitro*. The downsides of *in vitro* procedures were discussed in the PGD section.

Summary

This chapter reviewed four reproductive technologies, that are both good representatives of the different types of reproductive technologies, and good representatives of currently used technologies and technologies that are still under development. Table 1 summarizes the important aspects of the four reproductive technologies and the overlapping characteristics. This information will be used for the completion of the analysis in Chapter Five.
After the practical information, I can now elaborate further on the philosophy of technology that will be used to analyze the four reproductive technologies.

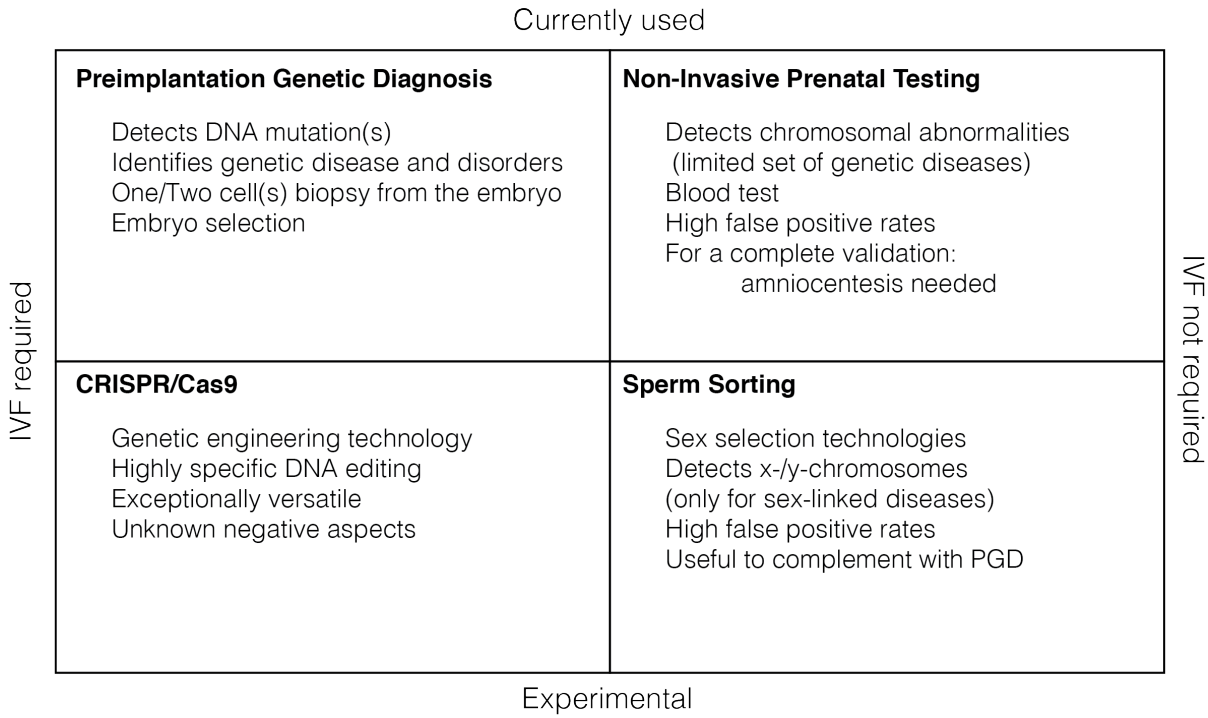

Table 1. Summary of the four reproductive technologies.

Top: currently used technologies PGD and NIPT. Bottom: experimental technologies CRISPR/Cas9 and Sperm sorting. Left: DNA specific, IVF required. Right: low genetic resolution, high false positive rates.

Chapter Three – The Technology Mediation Approach

The Ethics of Technology

"Technologies, thus, while being the fruits of human creativity, manifest not merely as neutral tools but also as productive elements in co-shaping how people perceive the world, each other and themselves". (Kudina 2019, p. 16)

In the introduction of this thesis, the phenomenon of an *ethical* technology assessment was briefly mentioned. Because of the intertwined relation between technology and morality, this assessment emphasizes the need for ethical reflection during the design processes of technologies. In this chapter, this shift in technology assessment will be put into more context and it will discuss the development of the philosophy of technology. After that, the *technology mediation* approach by Peter Paul Verbeek will be explained in more detail. I have chosen to follow this approach, since Verbeek claims it to be an improvement compared to the approaches in the past. I accept this improvement and believe it to be an important addition to the assessment of both current and new technologies. As discussed in the introduction, there are of course other approaches. However, it is not the aim of this thesis to find out which one of the approaches is the best for an overall ethical technology assessment, but it is to understand how technologies, reproductive technologies more specifically, influence our ethical reflections and in what ways these technologies contribute to our ethical considerations. Within the complex and dynamic landscape of philosophy of technology I have come to the conclusion that the *technology mediation* approach, explained by Verbeek is a valuable approach and meets the aim of this thesis. In order to use this approach, I will explain the philosophy behind it and how different aspects of the approach can be used in the analysis in Chapter Five. Since there is no clear method for the *technology mediation* approach, this chapter therefore, provides as a foundation for the approach that will be used in Chapter Five.

Short history of the philosophy of technology

It is not necessary to describe the full history of the use and the innovation of technology by human beings to explain how important technology has become in our everyday lives. It is safe to assume that neither of us can even imagine a world without the presence of

technologies (Ihde, 1990; Verbeek, 2001). The question here is, what kind of impact does technology have in our lives?

Thinking about and observing the transforming impact of technology in our lives, was already done in the beginning of the seventeenth century by Francis Bacon. Bacon argued that we should acknowledge the "force, effects and consequences of inventions", because of their changing powers that affect human beings and the world around them (Bacon in Achterhuis, 1999, p. 1). This remark of Bacon was picked up in the 20th century by thinkers like Martin Heidegger, Hans Jonas and Jacques Ellul, who are now considered to be the first-generation, classical philosophers of technology, or even the 'founding fathers' of philosophy of technology (Achterhuis, 2001). What these philosophers had in common was their transcendental- and historical-philosophical focus on understanding technology in terms of its conditions for possibility (Verbeek, 2011). This means they focused on the ways technologies had represented reality and with that the kind of reality they had created (Achterhuis, 2001; Verbeek, 2011). These philosophers occupied themselves with an approach of backwards questioning, rather than forward looking at the changes accompanying the development of a technological culture (Achterhuis, 2001; Verbeek, 2001).

One of the most important revelation of this period of time was a new technological approach to reality. According to the classical philosophers, modern technology had broken down the hierarchy in the relation between human beings and a symbolic cultural reality. This meant that technology no longer was seen as something human, but as something more than the manifestation of human culture (Achterhuis, 2001). This was a response to the Industrial Revolution, where a large impact of technologies on society became visible. Before the Industrial Revolution, it was thought that technologies expand the possibilities and capabilities of human beings in a positive way (Franssen, Lokhorst, & Van de Poel, 2018). Technology was mostly viewed as an independent, separate force existing alongside human beings and outside the control by human beings (Kudina, 2019). Technology, in this sense, was considered neutral, which meant that whether they are good or bad depends on its users. So, in one way, it was thought that technologies increased our capabilities, and in another way it was thought that we were victims of the brute forces of technology (Franssen et al., 2018; Haan, 2017).

Heidegger, for example, rejected these views and thought about technology from a phenomenological perspective [9]. To him, it was important to understand technology as something more than just a 'means to an end' or a 'human activity' (Verbeek, 2001). Heidegger's view on technology was not a very positive one, as were the views of some of his fellow classical philosophers. Heidegger warned for the negative influences of technology on the meaning of human life and culture. There was a fear amongst philosopher that human beings would become powerless slaves of technology (Achterhuis, 2001; Franssen et al., 2018). However, the phenomenological approach (the shift in understanding technology and human beings as interrelated), was an important revelation (Verbeek, 2001, 2006).

Empirical turn

Around the 1980s and 1990s, a strong dissatisfaction with the understanding of the classical philosophical approach led to a so-called 'empirical turn' (Achterhuis, 2001; Verbeek, 2011). Against the pessimistic and abstract approaches of the classical philosophers of technology, a more empirically informed approach of theorizing technology came into being (Achterhuis, 2001; Verbeek, 2011). This approach included attention to concrete developments in technology and society, and to empirical studies of such developments (Brey, 2010). Its aim was to understand technologies itself both in terms of their structure and nature, and in terms of their social, cultural and ethical implications (Verbeek, 2011). It was thought that on the one hand, social-cultural factors determine the process of technological developments, but at the other hand that technological development was accompanied by transformations of society (Achterhuis, 2001). This would provide insight into, for example, the way to develop these technologies to overcome negative impacts (Brey, 2010).

Let me zoom in on American philosopher of technology Don Ihde as an example of this empirical turn. Ihde, inspired by Heidegger, developed a rater descriptive phenomenological philosophy of technology that describes how technologies can mediate between humans and their environment (Brey, 2010; Ihde, 1990; Verbeek, 2001). Ihde believes that there is no such thing as a 'thing-in-itself'. Here, Ihde follows a Heideggerian perception of reality: we experience things as they are revealed to us, because we have no direct access to reality, since

[9] Phenomenology is a philosophical discipline that studies the structures of experience. Phenomenology holds that subject and object – in later phenomenology this becomes 'human beings' and 'the world' – cannot be understood independently of each other, but only as always related. Human beings cannot be experienced apart from their relations to the world, and the world cannot be experienced apart from people's relations to it (Verbeek, 2001).

"we never find ourselves in *the* world, but in *our* world. To relate to the world is to interpret it. Things are what they are by virtue of our relations to them, just as we are what we are in terms of our relations to things" (Heidegger in Verbeek 2001, p. 121). Instead of focusing on technology as something in itself, Ihde focused on technological artifacts. Technological artifacts are the manifestation of the process behind the technology coming together: both function and appearance (de Vries, 2016; Ihde, 1990). Instead of trying to understand the implications of technologies in historical context, like Heidegger, the question becomes "what form of world-disclosure is *made possible* by technological artifacts?" (Ihde in Verbeek, 2001, p. 123). Technological artifacts facilitate people's involvement with reality, and in doing so it co-shapes how humans can be present in their world and how they perceive the world (Verbeek, 2011). In this sense, technology can be understood as mediators of the human-world relationships (Verbeek, 2011). The relation between human beings and the world is extended or stretched out through the technological artifacts, and thereby, broaden the area of sensitivity of people's bodies in relation to the world (Ihde, 1990; Verbeek, 2001).

Ihde analyzes this human experience in terms of perception. There are two sorts of perception, namely *micro-perception*, which represents our bodily sensors, and *macro-perception*, which is an interpretive, hermeneutical dimension (Ihde, 1990; Verbeek, 2001). The one does not exist without the other: we both need a bodily-sensory perception and an interpretation of what has been sensed to be able to experience (Ihde, 1990). According to Ihde, these types of perceptions are mediated, or 'co-shaped' by the technological artifacts. To refer to the quote at the beginning of this chapter, technologies cannot be considered as neutral instruments that facilitate our human existence, but actively contribute to the ways we live our lives and the way we perceive the world around us (Kudina, 2019; Verbeek, 2011).

Other approaches also focused on developing a more contextual, less deterministic theory of technology and even borrowed some parts from Critical Theorists and science and technology studies (STS)(Brey, 2010). This led to a less dystopian and a more pragmatic and balanced attitude towards modern technologies. In addition, it places emphasize on alternative ways of developing and using technologies that is more in line with moral ideals (Achterhuis, 2001; Brey, 2010).

However, the increased focus on the technologies or technological artifacts themselves and their relation to society, let to a rather descriptive approach. It was criticized for not providing any normative analyses. The focus on the relation between technology and society, made it difficult to have a critical stance towards technology, because society was

often seen as a product of technology (Verbeek, 2011). It was clearly in need of an ethical approach.

Ethical turn

In the first decade of the 21st century, there was an explosion of ethical approaches to technology. This included the emergence of a variety of ethical subfields, like *nanoethics*, ethics of information technology, ethics of biotechnology, etc. (Verbeek, 2011). These ethical reflections started to focus on the actual technologies and the technological developments from ethical theories, frameworks, and principles. However, they did not address the complex relation between technology and society, or the intertwined relation between technology and morality (Verbeek, 2011). In this way, it was ignored how frameworks and principles are co-shaped by the way technologies put the values within those frameworks and principles at stake and that they are, thus, a product of technology.

To overcome all of the problems mentioned above, philosopher of technology Peter-Paul Verbeek argues for the *technology mediation* approach. This approach puts the intertwined relation between technology and morality at a central place in the normative, ethical reflection. It makes the close relation between human beings and technology visible, and it aims to make it possible to take responsibility for the interrelatedness and to give it desirable shapes (Verbeek, 2011). Verbeek argues that it needs the incorporation of both the empirical and ethical turn: it involves an analysis of the mediating powers of specific technologies in human existence, and it involves an ethical relation to these mediations (Verbeek, 2011).

Technology mediation approach

In order to understand the moral significance of technology, we need to understand the mediating powers of technologies that have an effect on our lives (Verbeek, 2011). Verbeek explains these mediating powers by referring to the ideas of Heidegger and Ihde. The philosophical analysis of technological mediation is thus based on phenomenology, or more specific: post-phenomenology. It is inspired by the phenomenological understanding of experience and the interrelatedness of humans and technologies, but it takes its starting point in the empirical analysis of actual technologies (Verbeek, 2001, 2011). Still central in this perspective, is the idea that technologies play an actively mediating role in the relation between humans and reality. Technological artifacts facilitate the experiencing of reality for human beings, and therefore, when they are used they co-shape how humans can be present

in the world and how the perceive the world (Verbeek, 2011). Technologies in this understanding, are not neutral: they mediate people's perceptions, actions, experience and existence.

A medical technology that shows these mediating effects and which is often used in the literature as an example for its imaginary power, is the ultrasound. The ultrasound, which was introduced in the early 2000s, is usually performed in the 20th week of the pregnancy to assess the fetus for anatomic and structural abnormalities. In this way, the ultrasound is capable of showing a part of the human body, which is most of the time subject to imagination, namely: the fetus in the womb. One of the described mediating effects of this technology is the development of an early relation between future parents and their future child (Kudina, 2018; Verbeek, 2006, 2008b, 2011). This technology helps future parents see, perceive and interpret the fetus and the women's body. Showing the fetus can potentially influence the decision-making process in terms of health and disease and the ability to prevent the birth of children with a disease or disorder (Verbeek, 2006). Although, the ultrasound is generally seen as a good way for checking the condition of the fetus and for preparing parents for what is to come, it has consequences for people's moral decision-making (Verbeek, 2007).

The relation between humans and technologies are thus much more complicated than just their functionality and use. Viewing technology as 'just a tool' leads to a separation of the human subject and the technological object. This separation cannot explain the complex interrelation between humans and technologies as mentioned before. A way of thinking about this relation is thinking about it in terms of 'hybridity'. This involves trying to make sense about how technology and human beings shape each other and how technologies are an element of our human nature. The example of the ultrasound earlier also shows this dynamic. The technological instrument of the ultrasound helps perceive the unborn child. This cannot be understood by us without acknowledging the mediating role of technologies in our perception and understanding (Verbeek, 2015).

In order to understand this mediating role of technology, Verbeek has distinguished between two perspectives of mediation: mediation of experience and mediation of praxis. Mediation of experience explains the different ways reality can be interpreted and presented to people (Verbeek, 2011, 2015). The main focus here is *perception*. Mediation of praxis explains how human beings are invited to act in their world and how they shape their existence (Verbeek,

2011, 2015). The main focus here is thus *action*. I will discuss both perspectives in more detail and I will also explain how these two perspectives are useful as approaches to analyze the mediating effects of reproductive technologies.

Mediation of experience

The aim of this section is to find out how these technologies mediate human experiences and interpretations of reality. Verbeek, based on the work of Don Ihde, identified seven types of relations between human beings and technologies that explain how technologies are present the lives of human beings and how they help humans perceive the world around them. These relations are: 1) *embodied relations,* which describe the unity between technologies and human beings, which is directed *at* the world; 2) *hermeneutic relations,* here technologies represent the world to human beings, which is in need of an interpretation; *3) alterity relations* describe the interaction of human beings with technologies with the world in the background of this interaction; *4) background relations,* here the technologies shape the context of our experience in a way that is not consciously experienced*; 5) cyborg* relations concern technologies that merge with the human body, into a new hybrid being*; 6) interactive relations* concern technologies that interact with human beings, and *7) augmentations* is a term used for the technologies that both are able to embody with human beings and are able to represent the world in a parallel screen (Ihde, 1990; Verbeek, 2001, 2015).

Because the focus of this thesis is on the reproductive technologies, not all types of relationships are of equal importance. For this thesis, I consider the hermeneutic relation to be the most important relationship.

A *hermeneutic relation* describes the unity between technologies and the world. In a hermeneutic relation, the world is transformed by the technology into something interpretable. We can read ourselves, as it were, into many possible situations without actually being there (Ihde, 1990). An example is the MRI scan, that represents brain activity, but one needs to be able to interpret the shown visualization in order to tell something about the reality (Verbeek, 2011, 2015). I believe that the four reproductive technologies share this characteristic relation to human beings. The technology itself does not immediately represent reality to human beings, but needs to be interpreted in order to arrive at that version of reality. It is also possible that these four reproductive technologies would fall under a new not jet presented description of the relationships between technologies and human beings. But for

now, the most important understanding is the fact that technologies mediate our relationship with reality, and that they transform what we perceive (Verbeek, 2011). For reproductive technologies this means that this representation of reality needs to be interpreted first, in order to fully grasp this version of reality. Then it becomes clear how these technologies highlight some aspects of reality and hide other. These capacities are called *amplification* and *reduction* and are part of the intentions of technologies. This makes technologies not neutral, both because they mediate from some sort of intention and because they play an active role in showing a version of reality (Swierstra, 2015; Verbeek, 2011). For the analysis in Chapter Five, in order to understand the mediating effects of reproductive technologies on the experience of human beings, I will look at what part of reality these technologies amplify and what parts they reduce.

Mediation of action

The next question is how technological artifacts influence people's action and the way they live their lives (Verbeek, 2011). According to French Philosopher of Technology Bruno Latour, human action is most of the time co-shaped by their material environment (the things they use). He explains how we can see this influence as a 'script'. Just as a script for a film, technological artifacts specify how their users are to act when using them (Latour in Verbeek, 2011). A much-given example is the work of a speedbump on a road, that has a script: "to slow down". The speedbump does not necessarily tell us to slow down in so many words, but it does have the power as material thing to suggest action. This is what Latour calls: "translation of action" (Latour in Verbeek, 2011, p. 10). The scripts of artifacts *suggest* or *invite* specific actions and *discourage* or *inhibit* others, or even further: they can enable or stimulate us to undertake certain actions, and forbid or discourage us to take others (Swierstra, 2015; Verbeek, 2011). In Chapter Five, these capabilities will be the main focus for understanding how reproductive technologies mediate human action.

To summarize, technological artifacts mediate our perceptions through their intentions by amplifying some aspects of reality and by reducing others. They mediate our action by means of scripts, which specify how to act when using the technology, and they can invite or inhibit certain actions.

In addition to that, technologies are context-dependent, and can have several functions. Ihde calls this the *multistability* of technologies. This means that although designed

for a specific function, a technological artifact can have multiple stabilities or interpretations per context.

Mediation and morality

Both these active contributions and intimate appearances of technologies in our daily lives have moral dimensions. Furthermore, the quality of their contribution and their close relation to our existence can be assessed in terms of morality (Swierstra, 2015; Verbeek, 2011). Some of these roles and developments can be considered 'good' or 'bad', or 'desirable' or 'undesirable'. Ethics of technology is useful for understanding technological practices and developments in terms of moral relevance. However, technologies themselves also have moral dimension. According to Verbeek, morality is no longer a solely human affair, because of the moral relevance of technological artifacts. Technologies may lack consciousness, rationality, freedom and intentionality, and therefore, lack moral agency, but as mentioned before, they can play an actively mediating role in the relationship between human beings and their world (Verbeek, 2011). Verbeek argues that moral agency should, therefore, be seen as a result of the interaction between human beings and technology, and cannot only be considered as intrinsic property of human beings like in the traditional philosophy. In the traditional philosophy, moral agency is mainly ascribed to persons who can decide right from wrong and who can be held accountable for their own actions (Beauchamp & Childress, 2012). Technology on its own cannot do so. However, moral actions and decisions are the products of the human-technology interactions (Verbeek, 2011). Therefore, moral agency should be ascribed to the ensemble of human beings and technology (Verbeek, 2009a).

This means, that when we explore the contribution of reproductive technologies to ethical reflections, we must investigate the mediating effects on human beings perceptions and actions, and interpretations on the basis of which we make moral decisions together with or because of the technologies.

Summary

In this chapter I have briefly described the history of the philosophy of technology. This contributes to the understanding of how the *technology mediation* approach came about. The *technology mediation* approach is a merge of all the important revelations from both the empirical and ethical turn. It illustrates the influential power that technologies have on our moral decision-making by mediating human beings' experiences and actions. Mediation of experience describes the way how technologies can amplify some aspects of reality while

reducing others. Mediation of action describes how actions are invited and inhibited by technologies. The active contributions and intimate appearances of technologies in people's everyday lives, have moral dimensions and influences our ethical reflection. To understand the contribution of reproductive technologies to our ethical reflection, it is useful to explore these two mediating effects more specifically.

Therefore, in the following chapter, three important ethical considerations will be discussed that are often mentioned in the debate about the development of reproductive technologies. It is likely that these considerations will be put under a lot of pressure because of the mediating character of technologies. Furthermore, including technology and its effects into the ethical assessment will provide for a more thorough understanding and a better ethics by design.

Chapter Four – Current Ethical Considerations

In the previous chapter the focus of attention was on the philosophy of technology and the *technology mediation* approach. It was explained how the *technology mediation* approach incorporated aspects of both the empirical and the ethical turn. The approach describes how there is a relation between human beings and technologies, and it explains the complex interaction between ethics and technology.

As mentioned in the introduction of this thesis, to understand the potential influences of technologies on morality, an ethical analysis parallel to the development and implementation of these technologies is necessary. Preferably at an early stage of development, before the technology is realized and done developing. By having early ethical reflections, we can strive towards an 'ethics by design' (Bredenoord 2018; Verbeek 2008a). However, an early identification of the ethical and societal issues and implications is difficult and leaves us almost powerless, because it is impossible to predict how it will affect human beings and their societies (Collingridge, 1980; Kudina & Verbeek, 2019). This hurdle, called the *Collingridge dilemma*, illustrates the lack of information we have at the beginning of technological developments and the lack of grip we have on the effects of technologies once they are done developing (Bredenoord 2018). Nonetheless, an ethical analysis might be even more important than ever in this situation. Reflecting upon the ethics of technologies will help with understanding in which ways technologies put our values at stake and it will help with guiding the process of technological developments into desirable shapes.

The aim of this chapter is to discuss a few ethical considerations regarding the four introduced reproductive technologies, that are dominant in many debates, including the enhancement debate (see introduction). These are in my opinion, considerations whose current provisional fixed point are and will come under a lot of pressure due to the mediating power of the four technologies.

I am well aware that there are many more ethical debates and consideration regarding reproductive technologies, however, I cannot discuss all of them within the scope of this thesis. Therefore, I will focus on three very different ethical considerations. It is not the aim of this thesis to argue whether these ethical considerations are valid and true, but it is to discuss the role of these technologies within these ethical reflections.

First, I will explain the concept of reproductive autonomy and how it relates to the reproductive technologies. Second, I will discuss the goals of medicine and how there is a tension between the limits and potential of the technologies. Lastly, the slippery slope argument will be discussed, concerning the fear that the development of the reproductive technologies will lead to 'designer babies' or eugenics.

The concept of reproductive autonomy

The first and commonly discussed concern is the concept of reproductive autonomy. Autonomy, in a healthcare setting means the choice and the power of individuals to make free informed decisions about, for example, treatments and care they receive (Beauchamp & Childress, 2012; Nuffield Council of Bioethics, 2016). Autonomy originates to the Greek word for 'self-rule' and is often understood as a state of being "free from both controlling interference by others and limitations that prevent meaningful choice" (Beauchamp and Childress 2012, p. 101). Most theories of autonomy hold two conditions for autonomy, one being *liberty* (independence from controlling influences), and two being *agency* (capacity to intentionally act) (Beauchamp & Childress, 2012).

Reproductive autonomy is an important principle in pluralistic, liberal societies. In a pluralistic society, where people have different opinions on what 'the good life' entails, people need as much freedom to make their own decisions based on the values and principles they uphold. This also includes people's freedom to decide to have children or not, and if so, how many. It also refers to decisions about whether or not to make use of reproductive technologies, such as ARTs, or prenatal testing (for example NIPT), and the power to make decisions about the health of their possible future offspring (Dondorp et al., 2014; Nuffield Council of Bioethics, 2016). Reproductive autonomy, in short, will be defined as the choice and power of individuals to make free informed decisions regarding reproduction.

The concept of reproductive autonomy is even legally protected within the European Convention on Human Rights, article 8: *the right to respect for private and family life* (European Court of Human Rights, 2018). The main focus of the law is based on a negative conception of reproductive freedom[10], which means that reproductive choices have to be free from control or obstacles by the government or others. However, there is also a positive

[10] The term negative reproductive freedom or autonomy is based on the two concepts of liberty introduced by Isaiah Berlin (1958). Berlin identified two concepts of liberty, namely negative and positive liberty. Negative liberty means the absence of constraints or barriers. Positive liberty is the possibility to act, to take control over one's life and realize one's purpose (Berlin, 1969).

understanding of reproductive autonomy, which is about creating opportunities for people to self-actualize and achieve their goal of starting a family or having healthy children, by giving people access to reproductive technologies (Bredenoord 2018). This type is also very important for a full understanding of the relation between the reproductive technologies and human beings. On the one hand, there is an understanding that people need to be able to make their own decisions about reproducing without interference by, for example, the government. On the other hand, there is an understanding that people should have the opportunity to achieve their goals by having the options to do so. It is therefore considered that reproductive technologies have the potential to strengthen the individuals' positive autonomy, if it means that people would have the power to make autonomous decisions about the means for founding a family and if it means that it makes people more confident in their reproductive choice (Wüstner, 2006). In the cases of couples who risk transmitting a genetic mutation onto their children, or who have fertility problems (infertility) or challenges (same-sex couples, single parents etc.), reproductive technologies enable them to a) have a child of their own, and b) have a healthy child of their own (Wüstner, 2006).

How does this relate to the four technologies? As mentioned before, prenatal testing, like NIPT would allow for the informed decision about continuing or terminating a pregnancy. For now, NIPT is only used to detect chromosomal abnormalities, but it is not unimaginable that it becomes possible to detect other abnormalities, like for example the BRCA- gene mutation, or characteristics, like for example sex. More information about the child to be, might increase the reproductive autonomy of prospective parents because they can make a more informed decision about the future of their child to be. Technologies like PGD, sperm sorting and CRISPR/Cas9 have the same kind of structure. They have the potential to allow couples to make all sorts of decisions based on their own beliefs and desires. This would be, of course, a large increase in people's reproductive freedom.

However, if these prenatal testing technologies like NIPT, become even more available for more abnormalities, or even become part of the standard or routine in prenatal care, it might become difficult for prospective parents to refuse prenatal testing. Especially, if prospective parents feel pressured by their surroundings and feel like they have to justify their decision not to use the test (Nuffield Council of Bioethics, 2016). Societal pressure on couples to use these technologies for both the birth of a healthy child and a genetically related child, might minimize their reproductive freedom. It is feared that it cannot be guaranteed that these couples have made their decisions free from controlling interference.

The goals of medicine

The second aspect that leads to many discussions, is the question of what should be considered as the goals and the boundaries of medicine and healthcare. In the literature, there are many different formulations of what the goals of medicine are. According to Daniel Callahan, for example, the goals of medicine "encompass the relief of pain and suffering, the promotion of health and the prevention of disease, the forestalling of death and the promoting of a peaceful death, and the cure of disease when possible and the care of those who cannot be cured" (Callahan, 1998, p. 385). According to Maartje Schermer, the goals of medicine include the cure of disease, the relief of pain and suffering caused by diseases, and the promotion of health (Schermer, 2013, p. 438). What exactly can be considered as part of the goals of medicine depends to a large extent on the concepts of health and disease. Some people or institutions uphold a very narrow definition of health; referring to someone's 'normal functioning' (Boorse and Daniels in Schermer, 2013), and some uphold a more broad definition. The World Health Organization, for example, defines health as "a state of complete physical, mental and social well-being and not merely the absence of disease or infirmity" (World Health Organisation, 1946). This indicates that the goals of medicine are not static or a fixed set of criteria. They are more like a 'point of departure' for a normative discussion in which notions like health, disease and well-being are central concepts. They are not written in stone, but are changeable and adaptable (Schermer, 2013). The goals of medicine can also be seen as a provisional fixed point, that is in need of a constant back and forth between our judgements and principles.

But how does this relate to reproductive technologies? According to Bioethicist and philosopher of Medicine Søren Holm, the two relate because of how reproductive technologies are understood as medical procedures. Labeling the inability to reproduce 'naturally' and the risk of having a child with a genetically transmitted disease or disorder as a medical problem, leads to the medicalization of reproducing (Holm, 2009).

Although many reproductive technologies, like PGD and NIPT are labelled as medical procedures, the question remains whether some practices can be considered as a medical treatment or whether they are more in line with the idea of enhancement or something else. Currently, for PGD much weight is given to the medical model. In most European countries, this model is a 'strict' guideline that states that couples needs to have an indication that they are at 'high' risk of transmitting a 'serious' disease or disorder (Soto-

Lafontaine et al., 2018). However, because PGD can be used for so many other cases and for other preferences (like less serious diseases or conditions, determining the sex of the embryo, athletic genotypes etc.), the medical model comes under a lot of pressure (De Wert, 2005). Furthermore, we might not consider the other types of preferences as medically relevant now, but this might as well change in the future. The distinctions between serious and non-serious, medical and non-medical is not an objective one (just like the concepts of health and disease), and will fluctuate according to social needs and expectation, but also to the progress of science and medicine (Deech & Smajdor, 2007)

For 'future' technologies like sperm sorting and CRISPR/Cas9, the medical model could in principle still be of relevance. As long as these technologies are dependent on medical assistance, it is likely that there will be some criteria couples need to fulfill in order to undergo a specific treatment. However, those criteria might change and be different than what is now considered medically relevant. Social expectation and changes in lifestyle affect what is considered to be medically relevant. Reasons for using reproductive technologies that we now might consider as enhancement, might be considered as medically relevant or even medically urgent in the future, because of technological solutions (Deech & Smajdor, 2007).

The slippery slope argument

The slippery slope argument is often mentioned in the debate about the desirability of further implementation of technologies like PGD and NIPT, but also about the use of CRISPR/Cas 9 and sperm sorting. The structure of a slippery slope argument is as follows: if you accept situation A, you will end up accepting the following steps B and C, which will lead to situation D. Situation D is something you do not want, therefore, you should not accept situation A (Potma, Veen, & Beaufort, 2016; Swierstra, 2016). The situation in a slippery slope argument is often very black and white, with little nuance. It also makes the assumption that there is no room for deliberation about the steps in between situation A and situation D, and that regulation is not powerful enough to prevent situation D form happening (if indeed considered undesirable by many).

Designer Babies and eugenics

One of the slippery slope arguments in this debate is that the development of prenatal testing, selecting technologies like PGD and sperm sorting and editing technologies like CRISPR/Cas9, lead to designer babies (Bredenoord, 2018). Designer babies are babies that

are selected, edited, or chosen based on certain characteristics, including beyond the medically relevant. This might lead to eugenic practices, which includes making judgements about what lives are worth living. It is thought that once parents are able to choose, for example, the sex of their child, it may be difficult to justify stopping at choosing other characteristics, such as eye color, intelligence, especially if it is thought that these selections give children an advantage in society or life in general (Strong in Kalfoglou et al. 2013).

It is feared that these situations are made possible by an unjust expansion of the criteria for which these technologies are allowed and will, therefore, lead to the complete feasibility of human beings. Science fiction stories like *A Brave New World* by Aldous Huxley (1932) and *Frankenstein* by Mary Shelley (1831) are often referred to as undesirable outcomes of the implementation of human selection methods. Although they are science fiction, these stories do illustrate the fear and emotions people have regarding a negative and uncontrollable outcome. Or at least these illustrations and stories fill up the gaps people have, because living in a world with designer babies is perhaps too difficult to grasp.
Although these fears are not be entirely valid (due to, for example, practical limits and the possibility for *de novo* mutations), they are useful and should be taken seriously to some extent. Martha Nussbaum calls these fears and emotions 'moral markers', because they indicate that there are some important values under scrutiny (Nussbaum in Bredenoord, 2018). These fears and emotions also call for ethical reflection. Only then, we will be able to rearrange the arguments and values in such a way that we don't hold on to our presuppositions and we can continue the debate based on well informed arguments (Bredenoord, 2018).

In addition, what now might seem as a doomsday scenario, might be completely normal in a few decades. With the first born IVF-baby, Louise Brown, people feared that this would lead to the manipulation of reproduction altogether and that it would be the end of all natural human reproduction (Potma et al., 2016). Or with the development of the birth control pill for women, it was feared that women would start working and would ignore a 'natural process of fertility' by deciding when to get pregnant (Berger, 2014; Potma et al., 2016). Nowadays, these fears of manipulation by IVF and the birth control pill are no longer seen as problematic or points for concern.

Summary

In this chapter, the concept of reproductive autonomy, the goals of medicine and two slippery slope arguments have been discussed. These ethical considerations are important in the

ethical debates about the development of reproductive technologies. Reproductive autonomy concerns the ability and the different types of choices prospective parents can make. The goals of medicine are dependent on the interpretation of concepts like health and disease. And lastly, the slippery slope arguments show a fear that the development and implementation of these technologies will unavoidably lead to designer babies and eugenic practices. The aim of this chapter is to lay the groundwork for the analysis in the next chapter. In Chapter Five, the impact of the mediating effects of PGD, NIPT, sperm sorting and CRISPR/Cas9 will be analyzed in relation to these three ethical considerations.

Chapter Five – Analysis of the Mediating Effects

of PGD, NIPT, sperm sorting and CRISPR/Cas9

"The assumption behind these technologies is that people want to have a biological related and healthy child" (Bredenoord, 2018, p. 22).

The focus of attention in the previous chapter was on three ethical considerations regarding PGD, NIPT, sperm sorting and CRISPR/Cas9. First, the concept of reproductive autonomy was discussed as a fundamental value in pluralistic, liberal societies. There are two understandings of reproductive autonomy: negative- and positive reproductive autonomy. Secondly, the goals of medicine were discussed as a concept that is often referred to in the debate about the desirability of reproductive technologies. The goals of medicine are no fixed set of criteria and are to a large extent determined by the interpretation of concepts like 'health' and 'disease' (Bredenoord, 2018; Deech & Smajdor, 2007). Lastly, the slippery slope arguments were discussed. These arguments illustrate a negative view on the development and implementation of these reproductive technologies.

The aim of this chapter is to explore the mediating effects of PGD, NIPT, sperm sorting and CRISPR/Cas9 and understand how they co-shape the meaning and importance of these ethical considerations, by putting certain values at stake. In this way, it becomes possible to identify subjects for moral reflection and to take responsibility for the interrelatedness of technology and human beings and give this a desirable shape.

Method

The way how this chapter will be organized is by following the philosophy of the *technology mediation* approach, that describes mediating powers in terms of the mediation of *experience* and the mediation of *praxis* (Verbeek, 2011). In short, with mediation of experience, the focus lies on the way the technological artifact presents reality to its user. The way technological artifacts do this, is by amplifying and reducing certain aspects of reality. Mediation of praxis will focus on what kind of prescribed action the technological artifact is inviting or inhibiting, when being used by its user.

For the analysis of this chapter, I will also use this separation of mediating powers to provide a clear description of mediating effects. The focus of attention are the prospective parents, who I consider to be the potential users of these technologies.

This analysis will present some concrete mediating effects of the four technologies. Some of them will be technology specific and some of them will concern the reproductive technologies all together. Because the aim of this thesis is to provide a first step towards a technology-inclusive ethical reflection, and because it attempts to include future implication, the analysis is mainly hypothetical. Namely, it concerns a hypothetical situation in the future where the technologies are adopted, and no ethical reflection or ethical technological assessment has taken place.

For this analysis some literature is used, this includes literature on the *technology mediation* approach, the reproductive technologies (as discussed in Chapter Two), and perceptions on embryo's, fetuses and the decision-making processes. In addition, this analysis will also make use of the assessment of the ultrasound by Verbeek (as discussed in Chapter Three) as an example of how mediating effects can be described. From this I have extracted four mediations of experience, namely, *perception of the unborn, reproduction as a decision-making process, perception on diseases and disabilities, and experiencing risks*. And four mediations of praxis, namely: *the praxis of choosing, having to choose a child, decisions about what lives are worth living, and weighing risks*. These eight mediating effects will be discussed individually, however, some of them will have overlapping features. After that, these mediating effects will be discussed in light of the ethical considerations from Chapter Four. The aim of this section is to provide a visualization of how these reproductive technologies co-shape the meaning of the ethical considerations.

I. Mediation of experience

When exploring the mediating effects of technology on our experience, we should look at how the technologies transform what we perceive (Verbeek, 2011). Technologies do this by highlighting some aspects of reality, while hiding others (Swierstra, 2015; Verbeek, 2011). In the next sections, I will discuss four mediating effects of PGD, NIPT, sperm sorting and CRISPR/Cas9 on the experience of prospective parents.

I.I Perception of the unborn

One of the mediating effects of all four technologies concern the ways they highlight the unborn. By highlighting the unborn at an early stage of development, the unborn becomes more of a separate being, then as a part of the woman's womb (Verbeek, 2011). The way these technologies do this is by amplifying the characteristics of the unborn. Sperm sorting does this by treating individual sperm cells as potential candidates for insemination, which highlights the possible sex of the future child. As a consequence, prospective parents might expect the unborn child to behave in certain sex-specific ways and possibly start expressing this by already addressing the unborn as a boy or a girl (Kalfoglou et al., 2013). The latter might also occur with the other technologies that allow for sex-selection. Furthermore, these technologies have the potential to allow prospective parents to worry for other characteristics of their unborn child as well. Some of those worries have to do with the wish for wanting a healthy child, free form a genetic disease or disorder, and other wishes might have to do with specific traits and capabilities (e.g. athletic capabilities, hair color etc.). This amplification on the characteristics allows for an early focus of the unborn as a separate being.

In addition, these technologies also have a way of treating the embryo and fetus as a patient. This is both because of the medical setting in which these technologies are used, and because of the role of these technologies have. These technologies are presented as solution to the possibility of having a child with a disease or disorder. The medical setting in which these technologies are and will be used, suggests that care is the overall value within this practice (Kudina, 2019). Knowledge about the condition of the unborn child becomes part of this idea of care, in the same way that the corresponding action after discovery can be seen as possibilities of care (Kudina & Verbeek, 2019). These technologies will translate the results of that discovery in terms of medical variables, which translates the unborn child into possible patients (Verbeek, 2007, 2011).

I.II Reproduction as a decision-making process

A second mediating effect is a result of how these technologies highlight all the choices prospective parents have to make. In this process, there are possibly three stages in which choices have to be made: before, during and after the use of the reproductive technologies.

For NIPT, this means that the first step for prospective parents is decide whether they want to receive information about the health of their fetus. The second step is to decide what to do with that information. The detection of a defect with the test will translate the situation into 'choosing a child' or choosing to terminate the pregnancy (Verbeek, 2011). After that, if the prospective parents decided to choose for the child, they have to make a choice about how

to take care of the child. If they choose to terminate the pregnancy, the choice has to be made whether to try again.

For PGD, the first step is to make a decision about whether you want to select an embryo without the genetic disease or disorder. The second step is to make a decision based on the characteristics and quality of the existing embryos. When there are no embryos without the defect or no non-carrying embryos are available, prospective parents have to make a choice about whether they want to continue anyway, to implant a second- or third best embryo (which would possibly result into the birth of a child with a disease or disorder), to go for another IVF-cycle or to stop trying all together.

For sperm sorting, the decision-process starts with the choice for a specific sex. To know whether this selection was successful or not, prospective parents have to choose from other reproductive technologies to gain certainty. Sex-selection for the purpose of preventing the birth of a child with a genetic disease or disorder would mean either the use of PGD or a prenatal test. After that, the same steps regarding PGD or NIPT apply.

Lastly, when choosing CRISPR/Cas9, couples would have to make decisions on what to edit and for which purpose. Furthermore, if it turns out the edit did not succeed (which can be tested with PGD), prospective parents have to make a decision to try again or to conceive in a different way.

What follows, is that these technologies amplify reproduction as a decision-making process and reduce the perception of how reproduction is stochastic. This will be elaborated further in the section about the mediation of praxis, to explain the influences of the 'script' of these technologies on the actual decision-making praxis.

I.III Perception of diseases and disorders

Another mediating effect of these technologies on people's experience affects the way people perceive concepts of diseases and disorders. Because PGD, NIPT, sperm sorting and CRISPR/Cas9 highlight the possibility that there might or could be something 'wrong' with your unborn child. These technologies are there to help people to have healthy and genetically related children. Labelling the inability to conceive naturally or the possibility of having a child with a genetic disease or disorder as medical problems, or as 'wrong', highlights the need for a solution. These technologies amplify the perfect and healthy life, which is free from a genetic disease or disorder, and it reduces the value of the lives of people who do have a genetic disease or disorder. In this way, the concepts of disease and disorder are associated with medical solutions that are offered at early stages of life.

I.V Experiencing risks

The last mediating effect is a result of the way these technologies present a specific version of reality prospective parents. One of the ways these technologies present reality is in terms of risks and probabilities. From the literature on reproductive technologies, three types of risks can be derived. The first type are the risks that people have before using the technology. For example: a couple has a very low chance of getting pregnant, or a couple has a 50% chance of having a child with the BRCA-mutation. The second type are the risks concerning the use of reproductive technologies, for example: with sperm sorting there is low risk that the identification of the sperm cell went wrong and will lead to the birth of a child of the opposite sex, or: risks that come with the termination of a pregnancy. Lastly, the third type of risks are presented by the technologies, for example: after a positive NIPT, prospective parents will hear that they are probably pregnant with a child with down syndrome, or: there is a high chance that the child will be resistant to HIV, because of a successful edit. These are just a few examples of the three types of risks prospective parents have to deal with. Prospective parents have to make their decisions based on these types of information. There have been studies that show how difficult it is for people to make rational decisions based on chance and probabilities (Maglio & Polman, 2016). A lot of different factors influence the way people weigh different types of risks. However, for these technologies, it is the only way to present these details, i.e. in numbers of probabilities. These technologies amplify the uncertainties that are present in the process of reproduction. It is up to prospective parents to interpret these uncertainties and weigh the presented risks and probabilities against each other in order to make a good decision. However, this is proven to be very challenging.

To summarize, these four mediations of experience show some specific ways in which the technologies highlight certain aspects of reality and reduces others for prospective parents. The technologies shape the way prospective parents perceive their unborn, it highlights prospective parents as decision makers about their unborn, the pregnancy and the risks involved. These technologies emphasize the wish for a healthy child, which influences the perception of having a child with a disease or disorder. Labelling the inability to have a genetically related and/or a healthy child as a medical problem, emphasizes the need for a medical solution.

II. Mediation of praxis

First of all, the quote by Annelien Bredenoord at the beginning of the chapter already illustrates one of the defining characteristics of the reproductive technologies. Behind these technologies lies the assumption that people desire to have genetically related and healthy children (Bredenoord, 2018). This means that these technologies are designed to fulfil this desire for prospective parents. This becomes visible in the way these technologies invite people to act in a certain way, namely in the way how prospective parents are invited to make all kinds of decisions.

II.I The praxis of choosing

The most important mediating effect that has an impact on the way prospective parents act is the amount and the different types of choices they have to make regarding the reproductive technologies. As described above, these technologies exist because of the understanding that people desire to have healthy and genetically related children. In a way, these technologies are inviting people to act upon that desire. The way prospective people can act in relation to these technologies, is by making all kinds of decisions. As mentioned in *section I.II*, there are a lot of those, and all of them are able to serve the purpose of having a healthy and genetically related child. In the following sections, these decisions will be discussed in more detail.

II.II Choosing a child

One of the choices prospective parents are invited by the technologies to make is what kind of child they want to have. The four technologies do this in their own way. PGD, allows prospective parents to select an embryo. The current criteria for PGD state that selection is allowed based on medically relevant reasons. Here, the choice for a healthy or 'the healthiest' embryo seems most obvious. PGD would invite prospective parents to select the 'best' embryo available to them, because it would serve purpose of having genetically related and healthy children. NIPT invites prospective parents to make a decision between choosing a child or choosing to terminate a pregnancy. It does this with presenting information about the condition of the fetus. Sperm sorting invites prospective parents to choose for a child with a specific sex. And lastly, CRISPR/Cas9 gives prospective parents an option to specifically modify, add, or remove DNA sequences that are responsible for certain traits or abnormalities in their future child (Liao, 2019).

II.III Decisions about what lives are worth living

Another choice prospective parents have to make when using reproductive technologies, that is related to the section above, is the one about what kind of lives are worth living (Knoppers et al., 2006). The value of a healthy child is already embedded in the script of the technologies and invites prospective parents to act upon that value. However, what is understood with healthy or with diseased is to a large extent based on the personal judgements of people and might change overtime.

The technologies facilitate these types of decisions by offering prospective parents the choice for a healthy child. With PGD, prospective parents can select one embryo over the other based on the idea that 'that life is worth living (a bit) more'. With NIPT, prospective parents are able to make a decision about the life of their fetus, whether that is worth living by offering it the alternative of terminating the pregnancy.

Sperm sorting and CRISPR/Cas9 are different in this sense. Sperm sorting involves a sex-related perception of what life is worth living more and CRISPR/Cas9 allows for the choice to edit the unborn in such a way that its life becomes worth living (more).

II.IV Weighing risks

The last mediating effect has to do with (1) how reproductive technologies present information on which prospective parents have to base their decisions, and (2) with how reproductive technologies invite prospective parents to make risky decisions. As mentioned in *section I.IV*, reproductive technologies highlight certain aspects of reality in terms of risks and probabilities. This means that the choices prospective parents have to make, are also based on these risks and probabilities. Nonetheless, the procedures of these technologies are also not without risks. So, the risks people have of having a child with a disease, disorder or other characteristics has to be weight against the risky procedures of these technologies.

For PGD, for example, this could mean weighing the risk of having a child with a genetic disease or disorder against a 30% chance of a successful pregnancy (due to IVF).

With a positive result from the NIPT prospective parents have to make a decision whether they want to undergo an amniocentesis. This invasive examination increases the risk of a miscarriage (ratio: 1 in 300 women). Here, obtaining certainty about the health of the unborn child might be considered worth the price of losing a healthy unborn child as a result of the recommended test (Verbeek, 2011).

Besides the fact that there are still a lot of uncertainties about the accuracy and side effects of CRISPR/Cas9, it is also a technology that requires assistance of other reproductive technologies. This makes the overall practice still quite invasive for women to undergo. Here,

a successful edit needs to be weight against the risks of having to undergo IVF and other diagnostic tests.

This also holds true for sperm sorting. Apart from the fact that the technology itself is not yet considered accurate enough, it cannot provide any information about the success of the procedure on its own. In order to have this information, the use of another reproductive technology is required, and therefore, the use of sperm sorting has to be weight against the risks that come with those other reproductive technologies.

To summarize, mediation of praxis has to do with the way these reproductive technologies invite prospective parents to make all different kinds of choices, namely: what kind of child they want to have, what kind of lives they think are worth living and how to weigh different types of risks. Behind these technologies lies the assumption that people desire to have genetically related and healthy children. This assumption is of great influence on the way these technologies invite prospective parents to make their decisions in that same direction.

The impact of the reproductive technologies on the ethical considerations

To consider the full impact of the current and emerging reproductive technologies, this section will incorporate the ethical considerations (Chapter Four) and the abovementioned technology mediated effects.

The concept of reproductive autonomy

The concept of reproductive autonomy was understood as the choice and power of individuals to make free informed decisions regarding reproduction. Two main distinctions of autonomy were brought up: negative reproductive autonomy (the ability to make decisions free from controlling interferences) and positive reproductive autonomy (the ability to choose, for example a reproductive technology, to help realize the goal of reproducing).
In the light of positive reproductive autonomy, the availability of reproductive technologies inherently increases the positive autonomy. Namely, the possibilities for people to achieve the goals of having genetically related and healthy children are dependent of the availability.

Apart from this, the choice of technology themselves allow for more autonomous decisions. These technologies invite people to make all kinds of decisions about their unborn child. The fact that there are all these choices to make by prospective parents, would suggest an increase in people's reproductive autonomy. However, people's effective autonomy might be at risk. The amount of choices and information on which these people have to base their

decisions, are a threat to their good and rational decision-making ability (Maglio & Polman, 2016; Scheibehenne, Greifeneder, & Todd, 2010).

Coexistent of this phenomenon, one must also consider that this technology is used in a medical setting and that this technology can discriminate between 'healthy' and 'diseased'. These words intrinsically carry the need of a medical solution, and the prospective parents are invited to choose one. But because of this, the technology will guide prospective parents in a certain direction of action, which can be seen as a decreasing effect on people's reproductive autonomy. This can be interpreted as extra problematic, because these people are already more vulnerable by their reduced effective autonomy.

The goals of medicine

The mediating effects of the reproductive technologies put a lot of pressure on the goals of medicine. Here are three reasons why: (1) because reproductive technologies invite prospective parents to make decisions that contribute to the creation of a child with the best possible health, or the 'best' possible life. This because of the underlying assumption of these technologies that people want to have genetically related and healthy children. In this way, the technologies suggest a certain direction of action to prospective parents that might be in need of a broader definition of the concepts of health and disease. This goes together with the potential of some of the technologies, i.e. PGD and CRISPR/Cas9, to select or edit embryos based on many other conditions or characteristics. (2) Because of the way these technologies let prospective parents make their decisions based on risks and probabilities. In this way, risks and probabilities become an important aspect of the concepts of health and disease. This requires an interpretation of these risks and probabilities in such a way that it becomes clear what can be understood as a threat to an unborn's life and what not. And (3), because both the experience of 'care' as the overall value regarding the four reproductive technologies and the interpretation of the unborn as a possible patient, contribute to the idea that these technologies automatically fall under the goals of medicine. In a way, it is indeed difficult to perform these practices outside the medical domain. Most technologies are dependent on the assistance of technologies that require medical care. For PGD and CRISPR/Cas9, IVF is required, which is considered to be an invasive treatment that needs medical supervision. In some cases, NIPT is dependent on the amniocentesis, which is also an invasive procedure dependent on a medical setting. Therefore, a medical and health care setting seems to be most appropriate for these technologies. However, the purposes and potential of these technologies

will not be in line with the current understanding of the concepts of health and disease right away.

The slippery slope arguments

In Chapter Four, there were two main slippery slope arguments discussed. One was the slippery slope towards eugenics, and one was the slippery slope towards designer babies. In a way, because of the mediating effects it becomes clear how the technologies contribute to these two ideas. To start with eugenics, this argument is mainly used to address the concern that the implementation of these technologies would lead to making judgements about what lives are worth living, and that allowing people to make judgements and decisions about characteristics and traits for selection or edits, will give some children an advantage in society or life in general (Kalfoglou et al., 2013). A few of the mediating effects from the analysis above do suggest that prospective parents are invited to make decisions about what lives are (a bit more) worth living and that technologies suggest a certain direction for action that contributes to the health of their unborn. In this way, the technologies contribute to something that comes close to the idea of eugenics.

Next, the fear of designer babies. Designer babies were described as babies that are selected, edited, or chosen based on certain characteristics. The mediating effects of the four technologies show how reproduction can be experienced as a decision-making process and how parents have to make all kinds of choices before, during and after the use of these technologies. This contributes to the understanding of how prospective parents can *choose* a child, which has some similarities with the public understanding and fear of the development towards designer babies. However, both fears are very extreme and suggest that there is no room for a redesign of these technologies during their development. But this is exactly the aim of a technology assessment.

Summary

In the first part of this chapter, the mediating powers of PGD, NIPT, sperm sorting and CRISPR/Cas9 were discussed. The aim of this analysis was to come to distinct mediating effects of these four reproductive technologies on the experience and actions of prospective parents. In this way, the influential role of technology in the relation between human beings and their world becomes more apparent. From this analysis, eight concrete mediating effects followed. These concern the way prospective parents will experience their unborn child and how they will interpret concepts of health and disease, life and death. The technologies also

highlight reproduction as a decision-making process, which invites people to make choices about what child you want to have, what kind of life is worth living, what is the 'best' option, and how to weigh all of the risks and probabilities that come with reproduction and reproductive technologies. In the second part of this chapter, the impact of these mediating effects has been discussed in relation the ethical considerations from Chapter Four. The aim of this section was to analyze how the technologies contribute to the understanding of these ethical considerations. The way these technologies highlight certain aspects of reality for prospective parents and invite them to act in a certain way, has an impact on the meaning of the ethical considerations. From this analysis followed that the mediating effects have both an increasing and decreasing effect on reproductive autonomy, that they put pressure on the goals of medicine and that they explain how the technologies contribute to the fears described by the slippery slope arguments. In the next chapter, an interpretation of these results will be given and a conclusion will be made.

Chapter Six – Conclusion and Discussion

The aim of this research has been to assess the mediating effects of the reproductive technologies (PGD, NIPT, sperm sorting and CRISPR/Cas9) on our experience, action and ethical considerations. In order to distinguish several mediating effects, the *technology mediation* approach is used. This approach is based on a post-phenomenological perspective, that understands an intertwined relationship between technology and human beings, as well as between technology and morality. Values and (moral) practices may transform as a result of the mediating powers of specific technologies. These mediating powers of technologies can be explained as the ways in which technologies influence our experience by highlighting some aspects of reality, while reducing others (mediation of experience), and as the ways in which some actions are invited by technologies while others are inhibited (mediation of praxis).

Based on this philosophy together with important technical information about reproductive technologies, PGD, NIPT, sperm sorting and CRISPR/Cas9, eight concrete mediating effects were delineated by this thesis. These included four mediations of actions*: perception of the unborn, reproduction as a decision-making process, perception on diseases and disabilities, and experiencing risks*. And four mediations of praxis: *the praxis of choosing, having to choose a child, decisions about what lives are worth living, and weighing risks.*

With these mediating effects, this thesis was able to provide for an analysis on the impact of these reproductive technologies on our ethical considerations. For this analysis, the concept of reproductive autonomy, the goals of medicine and the slippery slope arguments were used and were analyzed in relation to these mediating effects. These analyses show the impact and contribution of the technologies on the meaning and the importance of these considerations. For the concept reproductive autonomy this means both an increasing effect on peoples positive autonomy because of the availability of the technologies, and a decreasing effect on peoples effective autonomy due to the amount of choices and the amount of information on which they have to base their decisions, and by the way technologies guide a certain direction of action. The goals of medicine are under a lot of pressure due to the central values of ‘health’ and ‘care’ that are both represented in the underlying assumption of these technologies and the medical setting. This implies health and care-related practices, but in order to realize this, a shift in the understanding of the concepts of health and disease

needs to take place. In addition, the style of communication of these technologies are in terms of risks and probabilities. It is proven to be very difficult to make decisions based on these terms, therefore, an interpretation of these risks and probabilities in the context of health and disease is necessary. In the context of the slippery slope arguments, the mediating effects show how the technologies can contribute to these publicly feared situations of eugenics and designer babies. The decisions and choices prospective parents have to make regarding the value of the lives, characteristics of their unborn, does have some similarities with what people fear to be in line with eugenic practices and designer babies.

To be more specific, from this it needs become clear to what extent reproductive autonomy should be protected. In order for prospective parents to make good and rational decisions about their unborn, they might need help with the interpretation of results. In order to provide help with the interpretation of results, it needs to be clear how risks and probabilities are to be interpreted. It raises questions like: when is a risk or probability considered to be a threat for someone's health, and when does a probability fall under the medical domain or is in need of a medical solution? Furthermore, it raises the questions whether it is even appropriate for prospective parents to make these kinds of decisions about the lives of their unborn and whether it is appropriate at all to experience reproduction as a decision-making process. The answers to these questions are useful for the (re)designing of these technologies in a more desirable and ethical way. Finding the answers to these questions can be done in all sorts of ways. One way is to start an ethical reflection on, for example, the appropriateness of experiencing reproduction as decision-making process. Another way would be to have an ethical discussion about the interpretation of risks and probabilities in relation to concepts of health and disease. Together with the mediating effects and the impact of the technologies on the ethical considerations, it becomes clearer what aspects or impacts of the technologies call for ethical reflection and it stimulates a better and informed discussion.

To conclude these results imply several shifts in perceptions and actions regarding reproduction, based upon the assumption that the development and the implementation of these technologies continue. This conclusion can be seen as a first step in creating an understanding of the impact of the introduction of new and emerging technologies. In addition, the results are also useful as content for the evaluation and (re)designing of these technologies. The identified mediating effects are valuable starting points for moral evaluation and public discussion.

Within Chapter Six, this thesis identified eight mediating effects, which guided the work and was part of the *technology mediation* approach. However, some limitations concerning the methodology are worth noting, which did not have the chance to be discussed within the earlier chapters.

A concern of the *technology mediation* approach is the speculative nature of this approach. This could be interpreted as highly subjective and prone to bias, and therefore can feel unsatisfactory. One reason for its speculative nature is because this is a young approach and a (scientific) method is lacking.

In this thesis, I circumvented the speculative nature of the *technology mediation* approach by remaining close to the available literature of a similar technology (e.g. the ultrasound). At the places where literature was lacking, I tried to follow the philosophy behind the approach that was written in the book *Moralizing Technology* by Verbeek (2011), as much as possible. In the future, a more empirical approach can be taken along. Kudina and Verbeek have tried to illustrate mediating effects of the Google Glass, by studying people's experiences and practices through online discussions. From this study, the authors argued that it was possible to illustrate possible mediating effects.

In the broader picture, technology is not the sole factor in steering and co-shaping the moral perceptions and actions of human beings. There are other normative and psychological structures that are also of moral significance for human experience and action.

Furthermore, I acknowledge the existence of other structures shaping the world of tomorrow. However, the result of this thesis showed that the *technology mediation* approach itself is a valuable addition to technology assessments. Particularly, when other philosophical assessment methods seem to ignore this influence of technology on the experience and actions of human beings, or overlook the mediating powers of technology that have a large impact on our ethical deliberations all together. By following the *technology mediation* approach and by using both technologies that are already adopted by society and technologies that are still under development as examples, it was possible to already validate some of the mediating effects based on current practice and current shifts in values, which is not possible with other philosophical approaches.

Reproductive technologies are currently subject of many ethical discussions. The potential use and implementation of current reproductive technologies, and the new emerging technologies evoke all sorts of moral concerns and ethical questions. This thesis made the

impact of the technologies become visible, and this thesis can be used as a groundwork for moral evaluation and discussions to possibly steer the development of technologies in the desired direction, before it is too late.

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