The custom-made body – Legal aspects of bioprinted tissue and organs

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Abstract: Progress in bioprinting, combining 3D printing technology and the science to grow human tissue in the laboratory, elicits legal analysis as to if and how the law protects a patient’s life, health and confidentiality. We argue that the Federal Data Protection Act and the Medicinal Products Act provide ample protection to the recipient of printed tissue and organs. This paper focuses on the legal situation in Germany.

Keywords: bioprinting, tissue engineering, data protection, liability for medicinal products

1 Introduction

While additive manufacturing is widely used for producing implantable medical devices, the thought of 3D printed tissue and organs is still unsettling.

Tailor-made tissue, such as skin, kidney or liver tissue, is critical not only because in Germany alone more than 10,000 people are waiting for a donor organ [Eu16], but also because of the risk of the immune system rejecting a donor organ. A risk which can only be mitigated by heavy medication. In the future, patients providing their own cells for organ growth could potentially minimize or eliminate those risks altogether. In addition, further benefits of printed tissue may include facial reconstruction, reconstruction of limbs as well as the reduction of reliance on animal testing.

Research on tissue engineering and bioprinting is on a fast track. In 2010 researchers at the Wake Forest Institute for Regenerative Medicine (WFIRM) bioprinted skin on burn injuries, which led to the closure of the wound with the printed skin being incorporated with regular skin in the healing process. [Ba16, S.4, Bi10] Although it wasn’t fully functional, a kidney was printed in 2011. [Kl15] In general, the main challenge in developing living tissue with more than 100-200 µm thickness is the lack of nutrition diffusion to the cells. [Kl15] One solution may be provided by a 3D printing technology, developed by the EU funded research project „ArtiVasc 3D“, which is able to print dendritic and porous blood vessels. [Kl15] WFIRM also developed an integrated tissue organ printer (ITOP) able not only to print tissue but also micro tunnels, which assures the proper flow of nutrition within the printed tissue. [Wa16a] A human-sized ear printed

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with the ITOP was successfully implanted on mice. Examination of the mice showed that blood vessels had formed between adjacent tissues. [Wa16a]

With scientific progress come new legal challenges. This paper seeks to identify and assess legal problems of bioprinting. To this end, basic terms (see sect. 1.1) will be explained before describing the process of printing tissue (see sect. 1.2) in order to isolate the relevant facts and legal questions for further investigation (see sect. 1.3.).

1.1 Basic Terms

*Tissue Engineering* is the growing of tissue and organs for the purpose of replacing damaged or diseased tissue. [Ba16 p.1,4; Fa14 p.97] *Bioprinting* is a manufacturing technique combining 3D printing technology with tissue engineering to bring together biological material, e.g. cells or biomolecules, into a 3D structure aimed at fulfilling biological functions. [Ba16 p.4f.; IG16]

The bioprinting process starts like traditional 3D printing by using a *computer-aided design (CAD)-file*. CAD-files are created either with a 3D scan or a specific CAD software program.

*Bioinks*, or the printing agents used to print tissue, come in two varieties: hydrogels containing cells or a biodegradable, plastic-like gel used for tissue structure. [Wa16a; Fa14 p.98; Ba16 p.5,7]

1.2 The Process of Printing Tissue

CAD-Software uses patient data from computer tomography (CT) or magnetic resonance imaging (MRI) scans to create a model of the desired tissue or organ to be printed. [Wa16a; Ba16 p.6]

For maximum acceptance of the printed tissue, cells must be isolated from the patient’s tissue samples. If a patient’s tissue is damaged, stem cells can be substituted because they can be grown into any kind of cell. [Fa14 p.97f.] Bioink, containing the patient’s cells, is loaded into toner cartridges. The printer, guided by the computer model, utilizes traditional inkjet technology to print a 3D organ prototype layer by layer. [Wa16b]

After printing, the tissue or organ is surgically implanted by a medical team.

1.3 Legal Challenges

Although experts argue that bioprinting is not yet ready for medical approval, it is only a matter of time until the first organ is used in a medical procedure. The use of patient’s data to engineer tailor made CAD-templates for printing tissue and organs requires that data protection laws are in place to maintain the patient’s confidentiality (see chap.2).
Bioprinting technology also raises product liability questions, especially because health and life of the organ recipient are at stake (see chap.3).

As bioprinting pertains to individual patient’s data used for custom 3D printed tissue and organs, the subject of intellectual property rights will not be examined in this paper.

2 Data Protection Law

The Federal Data Protection Act (Bundesdatenschutzgesetz) and the Data Protection Acts of the sixteen German states are laws based on the right to data protection (Recht auf informationelle Selbstbestimmung) which is part of the general right of privacy (Allgemeines Persönlichkeitsrecht) following article 1 (1), article 2 (1) Basic Law of the Federal Republic of Germany (Grundgesetz der Bundesrepublik Deutschland). [Go15 section 1, recital 6] Consequently, the German data protection laws do not protect all kinds of data but only data with reference to a specific person affecting his or her right of privacy. [Ze15 p.1154] Following section 1 (2) Federal Data Protection Act\(^3\), only the collection, processing and use of personal data falls within the material scope of the Federal Data Protection Act.\(^4\) According to the legal definition provided by section 3 (1) Federal Data Protection Act, personal data means any “Einzellangabe” (engl.: information)\(^5\) concerning the personal or material circumstances of an identified or identifiable individual.

In order to determine if 3D printed tissue and organs are protected under the Federal Data Protection Act (see sect. 2.2), it is necessary to examine to what degree components used for tissue printing are protected (see sect. 2.1).

2.1 The components: data from MRI or CT scans and the patient’s cells

The components used for engineering bioprinted organs fall within the material scope of the Federal Data Protection Act if they qualify as “Einzellangabe” concerning the personal or material circumstances of an identified or identifiable individual. The term “Einzellangabe” includes any kind of information. [Dammann, in: Si14, section 3 recital 5] Data generated by MRI or CT scans contain information about surface structure, shape and volume of the patient’s tissue which is about to be replicated. These individual properties, used for constructing a computer model, are information and consequently “Einzellangaben” in the sense of the Federal Data Protection Act.

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\(^3\) Henceforth only the Federal Data Protection Act is referenced since the term personal data is used in both federal and state data protection laws.

\(^4\) Bioprinting technology does not raise specific issues relative to the personal or territorial scope of the Federal Data Protection Act.

While the classification of data generated by MRI or CT scans as „Einzela ngaben“ doesn’t raise any problems, cells of human origin could be classified either as information or as information storage device. Classification of information as “Einzela ngabe” is independent of its representation or form. [Dammann, in: Si14, section 3 recital 4] Nevertheless, according to Dammann procedures and processes of the real world, for example traces as bloodstains, skid marks, fingerprints or hair can’t be considered information per se. [Dammann, in: Si14 section 3 recital 5] Information is by nature intellectual rather than material. [Dammann, in: Si14 section 3 recital 5] Therefore procedures and processes of the real world only become information either by symbolic representation or by intentional use as means of communication. [Dammann, in: Si14 section 3 recital 5] According to this view cells are an information storage medium. But by being used with the intention to replicate genetic information and specific properties of the patient’s tissue, cell samples become information as well as “Einzela ngaben” according to section 3 (1) Federal Data Protection Act. Haase argues that the human body and physical substances as original data storage devices should fall as such within the material scope of the Federal Data Protection Act. [Ha15 p.119f, 351] Collecting data storage devices or collecting personal data pose the same threat to confidentiality and personal freedom. [Ha15 p.120] Plus, information usually depends on data storage devices. [Ha15 p.120] Following Haase, tissue samples fall as such within the scope of section 1 (2), section 3 (1) Federal Data Protection Act. Since both legal opinions come to the same conclusion that tissue samples fall within the purview of the Federal Data Protection Act, it’s immaterial which view is preferable.

A more in depth study needs to be conducted whether MRI or CT scans and tissue samples could also be considered a special category of personal data according to the legal definition in section 3 (9) Federal Data Protection Act. Considerations may include that tissue samples containing diseased cell material most likely won’t be used as basis for bioprinting or that for now genetic information is not per se included in the term personal data on health but will be in the General Data Protection Regulation.

### 2.2 Printed Tissue and Organs

Having determined that the Federal Data Protection Act applies to MRI and CT data as well as the patient’s tissue samples, the assessment whether a bioprinted organ also falls within the Act’s material scope can start from two different vantage points. On the one hand, the printed organ could be considered personal data since it is the result from processing personal data. On the other hand, the printed organ could qualify as personal data irrespectively of materials used to manufacture it.

The printed organ could represent “new” personal data according to section 3 (1) Federal Data Protection Act because it represents the outcome of processing personal data. If personal data is processed and altered while reference to a specific person is maintained, new categories of personal data are created. [KW05 p.67] In this line, the probability value determined by a scoring system is considered to be personal data. [Go15 section 3
recital 3a] The printed organ combines the genetic and cellular properties with the exact shape and structure provided by the patient’s CT or MRI scans. Thus, it is a new set of personal data which also falls within the legal definition provided in section 3 (1) Federal Data Protection Act.

Regardless of its constitutive parts, printed tissue or organs may meet the requirement “Einzelangabe”, section 3 (1) Federal Data Protection Act. As mentioned above, the printed organ does not only contain information about the patient’s genetic and cellular properties but also about the shape and structure of the patient’s organ. The question, whether the printed organ as data storage unit falls within the scope of the Federal Data Protection Act or an act of intentional use is necessary, does not need to be addressed because both views come to the same conclusion. Either the printed organ itself falls within the scope of the Federal Data Protection Act, or the printed organ becomes information by means of being maintained, stored or any other intentional use of it.

Although two different vantage points exist for assessing if printed organs fall within the material scope of the Federal Data Protection Act, both come to the same affirmative conclusion. Hence, bioprinted tissue and organs fall within the purview of German data protection laws.

3 Liability Law

The ensuing analysis of product liability focuses on specific problems raised by bioprinting technology. Product liability laws allocate responsibility to compensate damages caused by defective devices that were put on the market. In Germany, legal basis for a claim are in general either section 823 German Civil Code or section 1 Product Liability Act. The first determines fault-based liability, whereas the second is an example of absolute liability. With regard to health care, specific legislation exists for different sets of products: the Medical Devices Act (Medizinproduktegesetz) and the Medicinal Products Act (Arzneimittelgesetz).

Liability claims based on the violation of the Medical Devices Act (see sect. 3.1.) revert to general product liability laws, whereas the Medicinal Products Act (see sect. 3.2.) provides its own legal basis for a claim relative to a defective medicinal product. Consequently, the critical question is whether a printed organ qualifies as medical device or as medicinal product (see sect. 3.3.) and which legal consequences the proper qualification entails (see sect. 3.4.).

3.1 Medical Devices Act

The Medical Devices Act was shaped by European legislation especially Council
Directive 90/385/EEC\(^6\) relating to active implantable medical devices and Council Directive 93/42/EEC\(^7\) concerning medical devices. The Medical Devices Act pursues the two-fold goal of consumer protection and high technical standards for medical devices. [De12 Introduction, p. 46] The Medical Devices Act’s Leitmotiv is patient’s safety. [Deutsch, in: De12, section 1 recital 4] The Act’s purpose according to section 1 Medical Devices Act is to ensure safety, suitability and performance of medical devices. The Medical Devices Act further stipulates requirements for putting medical devices on the market. Within the scope of the Medical Devices Act fall medical devices that were put as such on the market, section 2 (1), as well as devices which are considered by law as medical devices, section 2 (2). The Medical Devices Act does not provide its own legal basis for claims. Liability for defective medical devices is generally determined according to contract law, section 823 (1), section 823 (2) and section 831 German Civil Code or section 1 (1) Product Liability Act.\(^8\) [Pannenbecker, in: Te13, section 14 recital 337]

### 3.2 Medicinal Products Act

On August 1\(^{st}\), 1961 Germany’s first Medicinal Product Act came into force. Subjected to significant alterations by European legislation most importantly by Council Directive 65/65/EEC\(^9\), today’s Medicinal Product Act differs considerably from its predecessor. According to section 1 the Medicinal Products Act’s purpose is to ensure in particular the quality, efficacy and safety of medicinal products. Accordingly, the Medicinal Products Act is a classic example of consumer protection and general risk prevention legislation. [Kügel in: KMH16 Introduction recital 1] It is also a law on animal protection since it guarantees both human beings and animals a proper supply of safe medicinal products. [Kügel in: KMH16 Introduction recital 1] The term medicinal product laid down in section 2 simultaneously defines the notion itself and the material scope of the law. [Kügel in: KMH16 Introduction recital 64] Absolute liability for

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8 Accordingly, also OLG Saarbrücken, Urt. v. 3.8.2011 – 1 U 316/10, MPR 2011, 156.

defective medicinal products follows the provisions in section 84 Medicinal Products Act. Legal basis for fault-based liability is section 823 (1), section 823 (2) and section 831 German Civil Code.

3.3 Are printed organs medicinal products or medical devices?

Following section 2 (3) number 7 Medicinal Products Act the term medicinal product shall not apply to medical devices within the meaning of section 3 of the Medical Devices Act. Pursuant section 3, a medical device is any article intended by the manufacturer to be used for human beings for the purpose of treatment or alleviation of disease and which does not achieve its principal intended action in or on the human body by pharmacological, immunological or metabolic means. Section 3 number 15 Medical Devices Act does not postulate production criteria. That means medical devices are not determined according to a specific production process. Rather the notion of medical device is tied to the producer. Thus, power of definition for what is considered to be a medical device lies with the producer. [Ratzel, in: De12, section 3 recital 21] A producer in the legal sense is also a person distributing devices manufactured by third parties. However, to reiterate a sentence coined by Ratzel: the power of definition (Definitionsmacht) lies with the producer but not sovereignty of definition (Definitionshoheit). [Ratzel, in: De12, section 3 recital 2]. One could argue that bioprinted tissue could be defined as articles used with the objective purpose of treating bodily injuries or organ failure as well as replacing diseased tissue, thus, as being medical devices. But bioprinted tissue is constructed out of patient’s cells. Section 2 (5) number 4 states clearly that the Medical Devices Act shall not apply to transplants or tissues or cells of human origin nor to products, incorporating or derived from tissues or cells of human origin. Hence, printed organs do not fall within the purview of the Medical Devices Act.

Since bioprinted organs are built from of human cells, one could argue that the applicable legislation is not the Medicinal Products Act but rather the Transplantation Act. In this line, section 2 (3) number 8 Medicinal Products Act states that the term medicinal product (and thus the material scope of the Medicinal Products Act) shall not apply to organs within the meaning of Section 1a number 1 of the Transplantation Act if they are intended for transplantation to human beings. The Transplantation Act codifies the legal aspects of transplantation medicine, e.g. time of death, agreement to sample the organ etc. Its main purpose is to increase the willingness as well as the transparency of organ donations, section 1 Transplantation Act. According to the legal definition provided by section 1a Transplantation Act, organs, except the skin, are various tissues of the human body which are a functional unit with regard to structure, vascularization and capability to fulfill physiological functions with exception of advanced therapy medicinal products according to section 4 (9) Medicinal Products Act. On the one hand, the argument could be made that only tissue originally grown in a living organism falls within the definition of section 1a. On the other hand, bioprinted organs are built out of the same biomaterial, have the exact same form and (ideally) fulfill the same
physiological functions as human organs. But if bioprinted tissue fits the criteria of an advanced therapy medicinal product, arguments for or against either view can be suspended.

Pursuing the legal definition in section 4 (9) Medicinal Products Act, advanced therapy medicinal products are (among others) tissue engineered products pursuant to Article 2, paragraph 1, letter a and b of Regulation (EC) No. 1394/2007\(^\text{10}\). The aforementioned European regulation defines tissue engineered products as products that contain or consist of engineered cells or tissues and which are presented as having properties for, or are used in or administered to human beings with a view to regenerating, repairing or replacing human tissue. A bioprinted organ consists of engineered cells that have been subjected to substantial manipulation so that biological characteristics of the specific organ and its physiological functions are achieved. Plus, they aim to be a viable alternative to organ donations hence to be administered to humans. The wording “tissue engineered product” provided by Article 2 (1) lit. a and b of Regulation (EC) No. 1394/2007 applies also to bioprinted tissue because bioprinting is tissue engineering by means of a 3D printer. Thus, bioprinted organs fall not within the purview of the Transplantation Act. Instead they fall within the material scope of the Medicinal Products Act because bioprinted tissue qualifies as advanced therapy medicinal products in the sense of section 4 (9).

### 3.4 Legal Consequences

The pharmaceutical entrepreneur who placed a medicinal product on the market which killed a person, or substantially damaged a person’s body or health faces a two-fold liability: either a fault-based liability or an absolute liability. The fault-based liability following section 823 German Civil Code is generally deemed insufficient with regard to medicinal products [Brock/Stoll in: KMH16, section 84 recital 2]. As for absolute liability, regulations of the Medicinal Products Act, especially section 84, take precedence over the Product Liability Act’s regulations, section 15 (1) Product Liability Act. Although legal scholars criticized section 15 (1) Product Liability Act, its compatibility with Regulation 85/374/EEC\(^\text{11}\) was confirmed by the European Court of Justice in 2014\(^\text{12}\).

Section 84 Medicinal Products Act does mention the term *defect* as does the Product Liability Act. Nevertheless, the categories to determine if a product is defective, namely a defect of design, production or instruction, are also used by the courts to determine if a medicinal product is faulty. [Brock/Stoll in: KMH16 section 84 recital 64] The defect of

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design within the purview of the Medicinal Products Act also comprises development risks. [Brock/Stoll in: KMH16 section 84 recital 64] The burden of proof rests with the pharmaceutical entrepreneur, section 84 (3) Medicinal Products Act.

As the pharmaceutical entrepreneur is liable for design defects, it should be noted that CAD-files for bioprinting need to maintain general safety standards with respect to design just as CAD-files do in product design. CAD-files should respect the necessary safety standards and should not pose safety-related threats. [Foerste, in: FW12, section 24 recital 71] Nevertheless, more stringent requirements apply for products that pose a potential risk for a person’s life. In order to define these safety requirements, the product’s intended use and specificities of the intended user group have to be taken into account. IT security of CAD-files will gain increased importance with regard to safety requirements. In principle, the producer or the pharmaceutical entrepreneur isn’t liable for third parties intentionally tampering with his or her products. [BK15b p. 87.] Nevertheless, with regard to digital interconnectedness of the production and increased risk of safety breaches, the producer will have to ensure that no digital tampering occurs. Accordingly, the current changes in production processes call for a concept of combined protection for mechanical and digital product safety [BK15a p.1140.]

4 Conclusion

Medical approval to use bioprinted tissue on humans may well be decades away. Despite new challenges existing laws, such as the Federal Data Protection Law and the Medicinal Products Act, provide ample protection. Bioprinted tissue can be considered (containing) personal data and thus falling within the material scope of the Federal Data Protection Act. As bioprinted tissue is an advanced therapy medicinal product, absolute liability of the pharmaceutical entrepreneur is rooted in section 84 Medicinal Products Act. However, the science of Tissue Engineering and Bioprinting will also call on to national and European legislators to keep pace with technological advancement with regard to quality control and safety standards. As of the time of this writing, the German Bundesrat approved the Government’s draft bill 18/8580 implementing Commission Directive (EU) 2015/565 and 2015/566 of 8 April 2015 which regard certain technical requirements for the coding of human tissues and cells as well as procedures for verifying the equivalent standards of quality and safety of imported tissues and cells.

References


13 Confirming EuGH, Urt. v. 5.3.2015 – C- 503/13.