

3D PRINTING IN SKIN CANCER PREVENTION FOR VISUALLY IMPAIRED CHILDREN AND ADOLESCENTS

IMPRESIÓN 3D EN LA PREVENCIÓN DEL CÁNCER DE PIEL PARA NIÑOS Y ADOLESCENTES CON DISCAPACIDADES VISUALES

IMPRESSÃO 3D NA PREVENÇÃO DO CÂNCER DE PELE PARA CRIANÇAS E ADOLESCENTES COM DEFICIÊNCIA VISUAL

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Abstract: This work aims to assist in the teaching of human morphology and in the prevention of skin cancers. It was dedicated to the design, prototyping and production, via 3D printing, of a solid model of human epidermal layers enlarged at the macroscopic level, which simulates the process of developing skin neoplasm by sun exposure. The pieces were designed to assist in the teaching of children who have some type of visual impairment. Such solids will provide the best understanding of the desired content, allowing a better understanding of the damage that exposure to the sun, carelessly, can cause.

Keywords: Inclusive Education. Epithelial Neoplasms. Primary Prevention. Three-dimensional Printing. Anatomical Models.

Resumen: Este trabajo tiene como objetivo ayudar en la enseñanza de la morfología humana y la prevención del cáncer de piel. Se dedicó al diseño, prototipado y producción, mediante impresión 3D, de un modelo sólido de capas epidérmicas humanas agrandadas a nivel macroscópico, que simula el proceso de desarrollo de neoplasias cutáneas por exposición solar. Las piezas fueron diseñadas para ayudar a enseñar a niños con algún tipo de discapacidad visual. Dichos sólidos proporcionarán una mejor comprensión del contenido deseado, lo que permitirá una mejor comprensión del daño que puede causar la exposición al sol por descuido.

Palabras clave: Educación inclusiva. Neoplasias epiteliales. Prevención primaria. Impresión tridimensional. Modelos anatómicos.

Resumo: Este trabalho tem como objetivo auxiliar no ensino da morfologia humana e na prevenção do câncer de pele. Foi dedicado ao desenho, prototipagem e produção, via impressão 3D, de um modelo sólido de camadas epidérmicas humanas ampliadas a nível macroscópico que simula o processo de desenvolvimento de neoplasias cutâneas por exposição solar. As peças foram elaboradas para auxiliar no ensino de crianças com algum tipo de deficiência visual. Tais sólidos proporcionarão o melhor entendimento do conteúdo desejado, permitindo um melhor entendimento dos danos que a exposição ao sol, de forma descuidada, pode causar.

Palavras-chave: Educação Inclusiva. Neoplasias epiteliais. Prevenção primária. Impressão tridimensional. Modelos anatómicos.

Submetido 07/07/2021 Aceito 15/10/2021 Publicado 18/10/2021

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Introduction

The word cancer comes from the Greek (*Καρκίνος*) and means crab. It was first applied by Hippocrates, the father of medicine, who lived between 460 and 377 BC. The fact that it was detected in Egyptian mummies proves that it has already compromised man more than 3,000 years before Christ. Currently, cancer is the general name given to a group of more than 100 diseases, which have in common the disordered growth of cells, which tend to invade neighboring tissues and organs. The normal cells that make up the tissues of the human body are capable of multiplying through a natural and continuous process. Most normal cells grow, multiply and die in an orderly fashion, but not all normal cells are the same (THULER et al., 2011).

This set of pathologies boils down to a genetic disorder caused by DNA mutations that, in most cases, are acquired spontaneously or induced by aggressions in the environment where the individual is. In addition, cancers often show epigenetic alterations, such as focal increases in DNA methylation and alterations in histone modifications, which originate from acquired mutations in genes that regulate these modifications. These genetic and epigenetic alterations alter the expression or function of key genes that regulate fundamental cellular processes such as growth, survival and senescence (ABBAS et. al, 2008).

The process of cancer formation is called carcinogenesis or oncogenesis and, in general, it happens slowly, and it can take several years for a cancer cell to proliferate and give rise to a visible tumor. The cumulative effects of different carcinogens are responsible for tumor initiation, promotion, progression, and inhibition. Carcinogenesis is determined by exposure to these agents, in a given frequency and period of time, and by the interaction between them. However, the individual characteristics that facilitate or hinder the installation of cell damage must be considered (THULER et al., 2011).

The skin, the largest organ in the human body, has three layers: the epidermis, the dermis and the hypodermis (subcutaneous tissue). The epidermis has other sublayers, formed by keratinocytes, basal cells and melanocytes. Melanocytes produce melanin, a brown pigment that gives color to the skin and whose function is to protect the deeper dermal layers against the harmful effects of solar radiation (A.C.CAMARGO CANCER CENTER, 2015).

According to the Brazilian Society of Dermatology (SBD, 2018), 33% of all diagnoses of malignant tumors in Brazil are skin cancer, and the National Cancer Institute (INCA) annually accounts for approximately 180 thousand new cases. It is scientific consensus that

most of these cancers are the result of the oncogenic effect (ability to cause tumors by damaging cellular DNA) of UV (ultraviolet) rays. DNA is repaired via the nucleotide excision repair pathway, which can also be damaged by extensive exposure to UV light, resulting in skin cancer (ABBAS et. al, 2008).

The main skin neoplasms are divided into melanoma and non-melanoma types. According to Abbas (2008), non-melanoma skin cancers are associated with total cumulative exposure to UV radiation, while melanomas are associated with intense intermittent exposure, as in sunbathing.

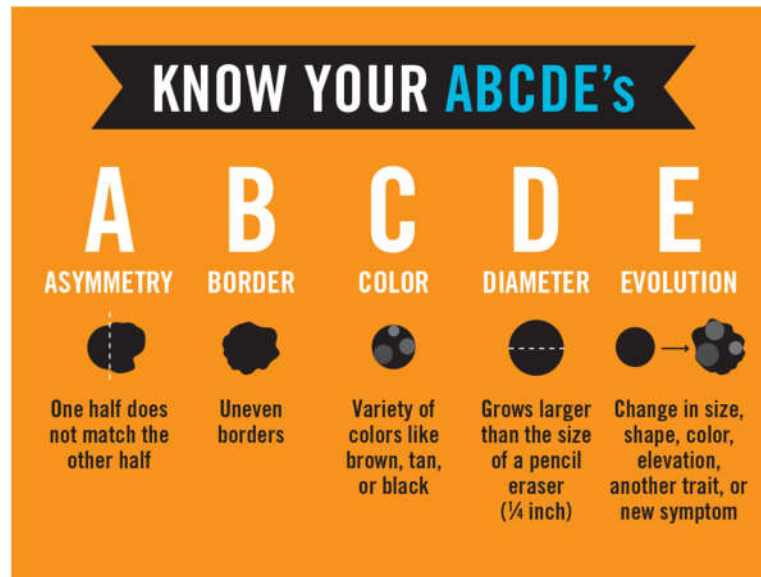
Non-melanoma skin cancer has low lethality, however, the number of individuals with the pathology is quite expressive. It is the most frequent cancer in Brazil, and corresponds to about 25% of all registered malignant tumors (THULER, 2011).

Melanoma skin cancer, on the other hand, constitutes a small portion of skin cancer cases, however, it is responsible for approximately 95% of skin cancer deaths, and its incidence has been growing worldwide in recent decades (ERLAY et al., 2012). According to SBD (2018), melanoma has the worst prognosis and the highest mortality rate, although the chances of cure are more than 90% when the disease is detected and treated early.

According to INCA (2019), estimates for the year 2020 of crude rates, adjusted rates and new cases of cancer per 100 thousand inhabitants, according to sex and primary location indicate that, in Rio Grande do Sul, there will be 570 cases of melanoma skin cancer (290 men and 280 women) and 15,800 non-melanoma skin cancer cases (8,850 men and 6,950 women), in a total of 46,060 cancer cases (24,900 men and 21,160 women). Adapting the numbers to the city of Santa Maria, whose estimated population is 282,123 people (IBGE, 2020), there would be approximately 14 cases of melanoma skin cancer and 391 cases of non-melanoma skin cancer.

To facilitate the early diagnosis of skin cancer, dermatologists indicate a simple methodology, easy to understand, which became known as the “ABCDE Method” (Figure 1). Although no home examination can replace medical consultation and evaluation, this approach helps to identify signs that could be valid indicative of epithelial neoplasms.

Figure 1 - ABCDE Method.



Reference: Adapted from (Hope Health Family Practice, 2017).

Like other types of skin cancers, the risk of melanoma also depends on individual characteristics. According to (Dimatos, 2009), in addition to environmental factors, the skin with lighter phototypes, the quantitative and qualitative presence of nevi (dark spots) and family history of melanoma are the main constitutional factors for its appearance.

According to Pró-Onco (1991), the southern region of Brazil shows the highest estimated incidence of melanoma, where the white population is greater. Porto Alegre, capital of Rio Grande do Sul, seems to show the highest estimated incidence of melanoma among the main cities in Brazil. This incidence can be even greater if underreporting is also considered (BAKOS et al., 2002).

Preventive measures are of great value in reducing the risks of developing skin neoplasms. Avoid prolonged exposure to the sun between 10 am and 4 pm, always use adequate protection, such as wide-brimmed caps or hats, sunglasses, tent and sunscreen with a minimum protection factor 15 are the precautions recommended by Inca (THULER, 2011).

Committed to the dissemination of knowledge for the prevention of skin diseases, MorfoEduca (Scientific Literacy Group in Morphological Sciences for Health Promotion) works by presenting the microscopic and macroscopic structures of the human body, correlating

them with daily life through projects that contemplate subjects relevant to the nearby population. The group provides formal scientific knowledge in a playful, interactive and contextualized way, dealing with topics such as cancer, smoking, food, obesity, inflammatory process and cardiovascular diseases. The target audience of the group are students in kindergarten, elementary and high school, who act as multipliers of knowledge in their communities. It is necessary to point out that, in this target audience, there are those who are visually impaired and that, due to their difficulty or inability to see, are also impaired in most traditional teaching formats, which is a critical social exclusion problem. It is important to mention that such exclusion often leads to dropping out of school.

According to (Salla, 2015), one of the main causes of the incidence of preventable and controllable pathologies is precisely the lack of scientific knowledge about their pathogenic factors. Most of the students who graduated from the school have great learning deficiencies about scientific concepts related to the biological structures of the human body, as well as their reactions to pathogens. This fact is due, in large part, to the poor approach by schools of themes related to prevalent pathologies and their etiological agents. Thus, Scientific Literacy (AC) would be the best empowering tool for the individual to act in the prevention and control of these morbidities, which validates the importance of the interventions carried out by MorfoEduca.

The International Classification of Diseases 11th Revision (ICD 11), which will come into force in January 2022, establishes five levels of visual function: no visual impairment, mild visual impairment, moderate visual impairment, severe visual impairment and blindness (WHO, 2021).

According to MEC (2020), considering data from the 2010 demographic census of the Brazilian Institute of Geography and Statistics (IBGE), 18.6% of the Brazilian population (36.4 million inhabitants) had some type of visual impairment. Of this total, 6.5 million had severe visual impairment, with 506 thousand with total loss of vision (0.3% of the population) and 6 million with great difficulty in seeing (3.2% of the population).

In more current data, SIDRA (2020) reports that, in the same year, there were approximately 1,698,000 people with severe visual impairment in the southern region of the country. In the 0-9 age group, in the same region, there were 22,000 people. In the 10 to 17 age group, there were 60,000 people.

So, in order to better include visually impaired students, MorfoEduca started using 3D printing technology. Considered as one of the disruptive technologies of the 4th industrial revolution, also known as Industry 4.0, 3D printing is one of the technological innovations that are radically changing the world as we know it (SCHWAB, 2017).

According to (Choonara et al., 2016), 3D printing allows to create three-dimensional products, extracting the design from a digitized file. The objects are printed by combining different materials (ceramics, liquids, powders, metal, plastic and, more recently, living cells) in layers deposited on top of each other. Using a computer-aided design (CAD) file, a 3D object can be constructed in almost any form imaginable (MERTZ, 2018).

After the design is created on a computer, it must be "sliced" in layers. Then, this modified file must be sent to the 3D printer. The basic software required for this can be offered by the printer manufacturer or downloaded for free from the internet (SAVINI; SAVINI, 2015).

The technology is being used in a wide range of applications, from large (wind turbines) to small (medical implants). Unlike mass-produced manufactured products, 3D printed products can be easily customized. As today's limitations of size, cost and speed are progressively overcome, 3D printing will become more widespread to include integrated electronic components such as circuit boards and even human cells and organs (SCHWAB, 2017).

The educational impact of this technology is already a consensus even in Brazil. In April 2019, the city of São Paulo announced the purchase of 583 3D printers for municipal schools, an investment of R\$ 3.8 million (Revista Época, 2019). The acquisition of 3D printers is part of the Restructuring project of the Educational Informatics Laboratories (LIE), of the Municipal Education Network (RME). Such investments prove the admirable potential of this technology when it comes to education.

Thus, taking advantage of the great potential of 3D printing, the group opted to use this to disseminate knowledge about epithelial neoplasms. Producing three-dimensional pieces that illustrate concepts of morphology, in theory, would facilitate understanding by students, especially by those who have some degree of visual impairment. Those, who are at a sensory disadvantage, will be able to internalize the contents more effectively by being able to touch the built structures and, consequently, will be in better conditions to prevent themselves against skin cancer.

Methodology

As this work does not use patients or their data, the approval of the Research Ethics Committee is not necessary.

In order to achieve similarity between the piece created and the aforementioned pathology, the histopathological study of the disease was necessary. For this, the authors resorted to the scientific literature pertinent to epithelial neoplasms, such as [1,22,23], focusing on microscopic slides and didactic figures that explained the typical onset and disordered cell replication of cancers.

Figure 2 – Cornified stratified squamous epithelium. Coloration: hematoxylin-eosin.
Medium amplification.



Reference: Adapted from (MOL, 2017).

In the present work, the Fused Deposition Modeling (FDM) printing process was used, and the models were designed using the TinkerCad® software (online freeware), computationally sliced using the Slic3r® software (version 1.2.9) and, finally, solidified by the Voolt3D® 3D printer, model Gi3.

The authors had some difficulty in reaching a design that was satisfactory, taking into account the similarity with the real epithelial geometries and the usability of the final product. However, collaboration with other areas of knowledge, such as engineering and digital arts,

was crucial to the progress of the work. The thermoplastic synthetic polymer used in printing was PLA (polylactic acid), chosen for its particular characteristics of greater stability and less deformity at the time of use. In addition, the material is biodegradable, recyclable, biocompatible, compostable and bioabsorbable, with corn starch as its raw material (ECYCLE, 2018).

Before reaching the final model, other designs were tried, as can be seen in (Figure 3). At first, smaller and simpler parts were built as pilots, allowing a better understanding of the printing variables and the tactile peculiarities of the solids.

Figure 3 – Pilot parts.



Reference: from the author.

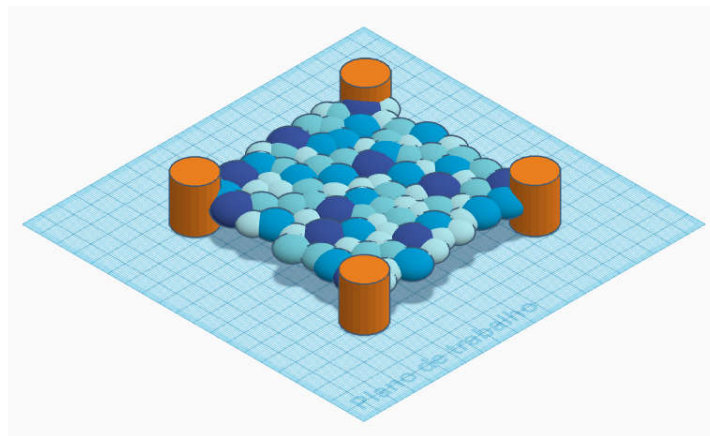
Throughout the printing process, however, about 20 previous attempts were required. Different print configurations were tried out. The many variables common to the practice of 3D printing had to be explored in order to arrive at the appropriate standard of dimension and quality of the pieces. It is important to note that the printing processes on thermoplastic materials even require the proper temperature control of the environment. Therefore, especially on the coldest days, keeping the printing room at a stable temperature was crucial for the success of the prints. Finally, the main parameters used were:

- Extrusion nozzle temperature: 220 °C (493.15 K)
- Table temperature: 60 °C (333.15 K)
- Print speeds: 80 mm/s

- Layer thickness: 240 μm

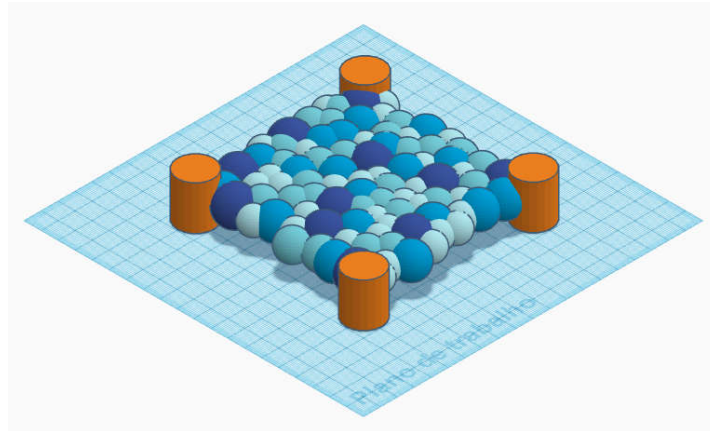
After experimentation and discussion, the authors arrived at the final model. Thus, as planned, 3 pairs of pieces were printed. The first layer (Figure 4), which simulates the outermost epidermal layer, has a flatter shape, similar to the pavement epithelium, and without the presence of neoplastic cells. The second layer (Figure 5) has more spherical cells, as in the more middle layers, and also without irregularities in terms of cell shape and arrangement. In the third and last layer (Figure 6), there is a notable structural dysmorphism, illustrating the cellular changes characteristic of those with growth irregularities typical of cancer. Further on, Figure 7 shows, in detail, the surface of the third printed layer.

Figure 4 – First layer design.



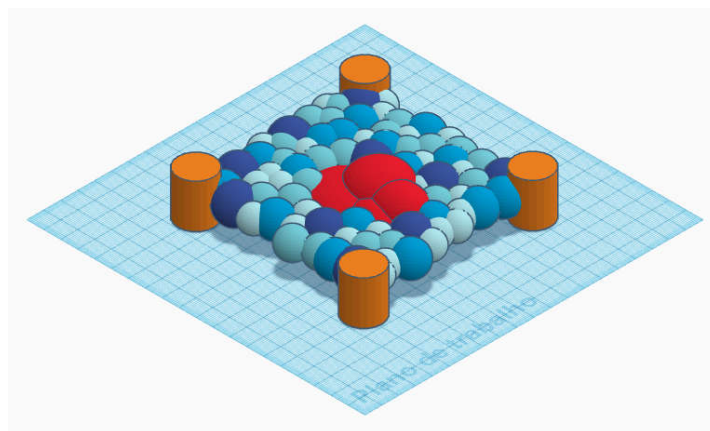
Reference: from the author.

Figure 5 – Second layer design.



Reference: from the author.

Figure 6 – Third layer design.



Reference: from the author.

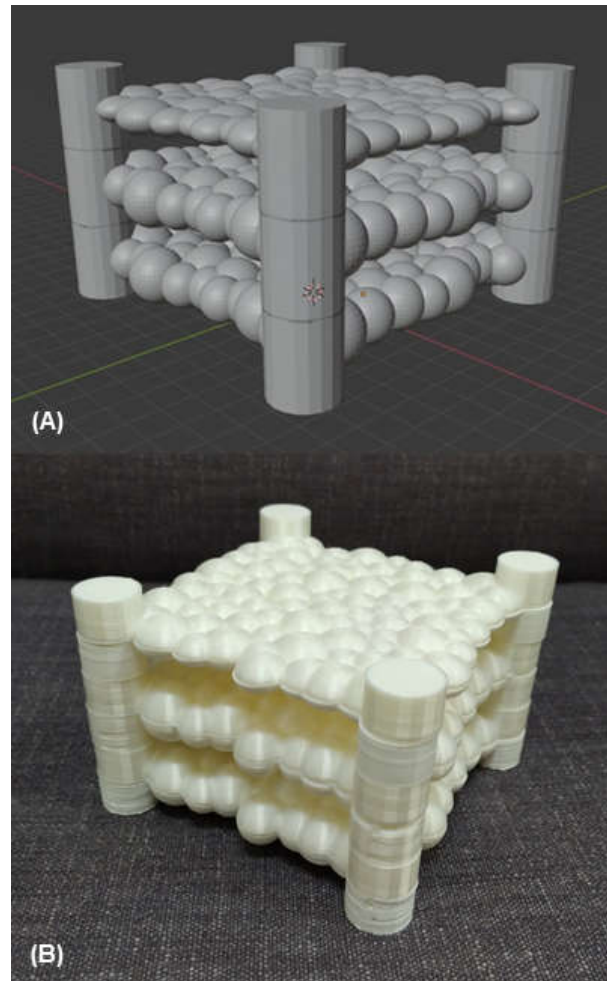
Figure 7 – Top view of the third printed layer.



Reference: from the author.

To facilitate printing, the layers were virtually sectioned horizontally, so that the base of each solid was flat. In this way, there is better adherence of the pieces to the table. Therefore, in order to obtain each of the three strata, there was a need to glue the related halves. For that, cyanoacrylate-based adhesive was used, which is the most suitable type of glue for objects produced in PLA. Next, Figure 8 presents a comparison between what was designed and what was obtained at the end of this project.

Figure 8 – Comparison between (A) the virtual assembly of the three epithelial layers and (B) the assembly of the printed set.



Reference: from the author.

Results and Discussion

Thus, as planned, three pairs of pieces were printed, thus composing the planned column of epithelial layers. In addition to the development of technical skills and competences, the authors were able to go through all the steps necessary for the realization of an idea, consequently getting involved in a university extension action with significant social impact. Nevertheless, the group's personal satisfaction was of great value.

Problems related to the proper handling of printing parameters were certainly the biggest limitations of the entire project. Understanding the many variables intrinsic to 3D printing was

crucial to achieving the desired success. The other steps took place more fluidly due to the previous knowledge of one of the authors about virtual modeling of three-dimensional images using CAD software.

In addition, due to the quarantine period under which the entire Brazilian population was subjected, the authors found themselves limited in their ability to apply the construct. Thus, it is necessary to return to face-to-face education in nearby schools to test the efficiency of what was produced.

Conclusion

In the present work, the authors were able to take the first steps towards the consolidation of a more innovative form of teaching, using printed three-dimensional pieces to exemplify concepts and systems in a more consistent way, especially for those with some form of visual impairment. Thus, we assume that this didactic will prove to be more inclusive and, consequently, more democratic.

As future steps, an opinion poll will be carried out to obtain from students and teachers the practical parameters of efficiency and the feasibility of this work. Thus, with this data in hand, we will be able to optimize what has already been done and envision new projects. There is also an intention to expand the use of the experienced methodology, applying it to health courses at the University of Santa Maria, contributing to the advancement of Brazilian education in related areas by offering better quality of learning for undergraduates, graduate students, residents and doctors.

Adhering to the open source ideology, the authors make the files created available to anyone who is interested, so that they can be used, freely, in other places and contexts. If you are interested, contact us.

Acknowledgments

The authors would like to thank the Federal University of Santa Maria and the Department of Histology for all the support offered.

Disclosure of interest

No potential conflict of interest was reported by the authors.

Data deposition information

The datasets generated during the current study are available in the figshare repository, request.10.6084/m9.figshare.14308505

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Figure Caption

Figure 1. ABCDE Method

Figure 2. Cornified stratified squamous epithelium.

Figure 3. Pilot parts.

Figure 4. First layer design.

Figure 5. Second layer design.

Figure 6. Third layer design.

Figure 7. Top view of the third printed layer.

Figure 8. Comparison between (A) the virtual assembly of the three epithelial layers and (B) the assembly of the printed set.